Statistical Analysis Plan for "Maze Out": A study protocol for a randomised controlled trial using a mix methods approach exploring the potential and examining the effectiveness of a serious game in the treatment of eating disorders.

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Introduction

This document specifies the planned statistical analysis for the study "Maze Out": A study protocol for a randomised controlled trial using a mix methods approach exploring the potential and examining the effectiveness of a serious game in the treatment of eating disorders, as carried out following the protocol published in Journal of Eating Disorders (1)

Abstract

Background: Eating Disorders (ED) are severe and costly mental health disorders. The effects of existing treatment approaches are limited and there is a need to develop novel interventions, including digital strategies that can increase engagement and effectiveness. Maze Out is a new serious game coproduced by patients and ED therapists, which allows patients to "play" with the reality of an ED and reflect on associated challenges.

Objectives: The present study has two main objectives: 1) to evaluate the effectiveness of adding Maze Out to treatment as usual (TAU) in a randomised controlled trial (RCT); and 2) to examine in depth the potential of Maze Out by examining how it is perceived and used in the context of an RCT.

Methods: Participants will be recruited from mental health care services, endocrinology departments or Community Centres offering treatment for ED. Patients suffering from ED (N=94) will be randomised to either TAU or TAU plus Maze Out. Primary outcome will be measured in terms of changes in self-efficacy, measured by a 5-item self-efficacy questionnaire (5-item SE_ED). Secondary outcome measures will include feelings of ineffectiveness and self-image, as measured by Eating Disorder Inventory, version 3 (EDI-3), Brief INSPIRE-O and Structural Analysis of Social Behaviour Intrex Questionnaire (SAS-B). Data will be collected at baseline (enrolment in the study), and subsequently 8 and 15 weeks after inclusion. Experiences of playing Maze Out will be examined in a sub-sample of participants, utilising both quantitative user analytics and qualitative interview data of patients, interview data of significant others, and healthcare professionals to explore the possible impact of Maze Out on disorder insight, communication patterns between patients and therapists and understanding of their disorder.

Discussion: To our knowledge Maze Out is the first serious game coproduced by patients and therapists. It is a novel and theoretically grounded intervention that may significantly contribute to the healing process of ED. If found effective, the potential for wide-spread impact and scalability is considerable.

Trial registration: ClinicalTrials.gov NCT05621018

Keywords: eating disorders, serious games, self-efficacy, co-production, randomised controlled trial.

Purpose and hypotheses

We hypothesize that that the addition of Maze Out to TAU for EDs will enhance the self-efficacy of participants as well as reduce feelings of ineffectiveness and insecurity, as well as increase patients' confidence in their ability to deal with physical and emotional limitations. We also hypothesize that Maze Out will reduce patients' interpersonal problems, expressed in terms of general inadequacy, insecurity, worthlessness and negative self-evaluation (i.e. self-concept)

On average, the minimum length of ED treatment (i.e. TAU) in Denmark is 15 weeks, therefore we assume that Maze Out will need to be play at least for 15 weeks for showing any impact on patients.

Therefore, the primary and secondary research questions of this study are as follows:

- Primary: Does Maze Out improve patients' sense of self-efficacy after playing for a 15-week period compared to TAU alone?
- Secondary: Does Maze Out have an impact on patients' feelings of ineffectiveness and personal recovery process compared to TAU alone

Sample size considerations

According to the protocol (1): "Since Maze Out is a novel intervention, hardly any data are available that are useful for power-calculations. Our pilot study (29) showed a pre-post mean change score of 4 based on the same self-efficacy scale as used in the current study (SD=1.5) at 8 weeks. We hypothesize that playing the game for 15 weeks will increase mean-score self-efficacy by 25%, compared to the TAU control group. Thus, with a power of 80% and alpha=5%, and an assumed dropout rate of 20%, we need to include a total N= 94 (i.e., N=47 per group) to be able to find medium effect size."

Randomization and blinding

Randomisation will be conducted using the built-in randomisation module in REDCap (Research Electronic Data Capture) from the Odense Patient Data Explorative Network (OPEN). To ensure adequate allocation concealment, the random allocation sequence will be generated before patient enrolment begins, by a member in the research group (RB) who is independent and not otherwise involved in the study. The researcher in charge of obtaining written informed consent will initiate the randomisation procedure when the patient has agreed to participation and completed the baseline measures. Patients will be informed of the results of randomization immediately after the procedure has been conducted. No stratification will take place. Preliminary comparisons based on stratification will be explored in order to inform future research using Maze Out.

Statistical analysis

Socio-demographic data gathered at baseline will be summarized through descriptive statistics. Categorical variables will be expressed as frequencies and percentages, while continuous variables will be presented with mean, range, and standard deviation.

Changes in the primary outcome self-efficacy levels over time (baseline, after 8 and 15 weeks) will be modeled using linear mixed models. Participant-specific random intercepts will be included, as well as random slopes if these improve the model fit significantly. The fixed part of the model will consist of the intervention, time, and the treatment-time interaction. To assess the normality assumptions of residuals for both fixed and random effects, normal quantile-quantile plots will be employed. If deviations from normality are observed, sensitivity analyses will be conducted using non-parametric bootstrapping with 1,000 bootstrapping samples. A significance threshold of 0.05 will be applied. Assuming the dropout mechanism is missing at random (MAR), linear mixed models deal efficiently with missing values due to dropout using the maximum likelihood estimator. Therefore, all available data will used in an intention-to-treat approach (ITT).

The secondary outcomes INSPIRE-O and SAS-B will be analyzed in the same way as the primary outcome, while the model will be adjusted to include only the two measured time-points (baseline and 15 weeks) for the EDI-3, with focus on two composite scales: Ineffectiveness Composite (IC) and Interpersonal Problems Composite (IPC) from the EDI3.

To investigate missing data patterns and mechanisms, techniques such as descriptive statistics on missingness and analysis of missing data mechanisms (e.g., Little's test) will be employed. Sensitivity analyses will be also conducted, investigating the complete case scenario and worst-case imputation to evaluate the robustness our imputed results.

Planned tables and figures and corresponding analyses.

Table 1. Characteristics of patients at baseline

Characteristics (as listed in Table 1 below, numerical characteristics marked with [numerical]) of patients at baseline will be reported as mean and standard deviation.

Characteristic	Intervention group: Maze Out (n=)	Control group (n=)	p-value
Age (numerical)			
Gender • male • female • other			
Diagnosis no (%) • F.50.0, 50.1 • F.50.2, 50.3 • F 50.4-8 • F.50.9			
Comorbidity no (%)			

• F.0 • F.1 • F.2 • F.3 • F.4 • F.6 • F.7 • F.8 • F.9			
BMI (numerical)			
Social network no (%) • parents • partner • children • friends • contact person			
Occupation no (%) • student • employed • unemployed • on sick leave			
Duration of ED no (%) • 0-6 month • 7-11 month • 12-24 month • 25-36 month • more than 3 years.			
Type of current treatment no (%) • Outpatient Group therapy • Outpatient Individual therapy • Inpatient • Other			
Duration of current ED treatment no (%) • 0-2 month • 3-5 month • 6-11 month • 1-2 years • over 2 years			
Place of treatment no (%)			
Prior treatment no (%)			

Figure 1. Enrollment and Randomization of Patients

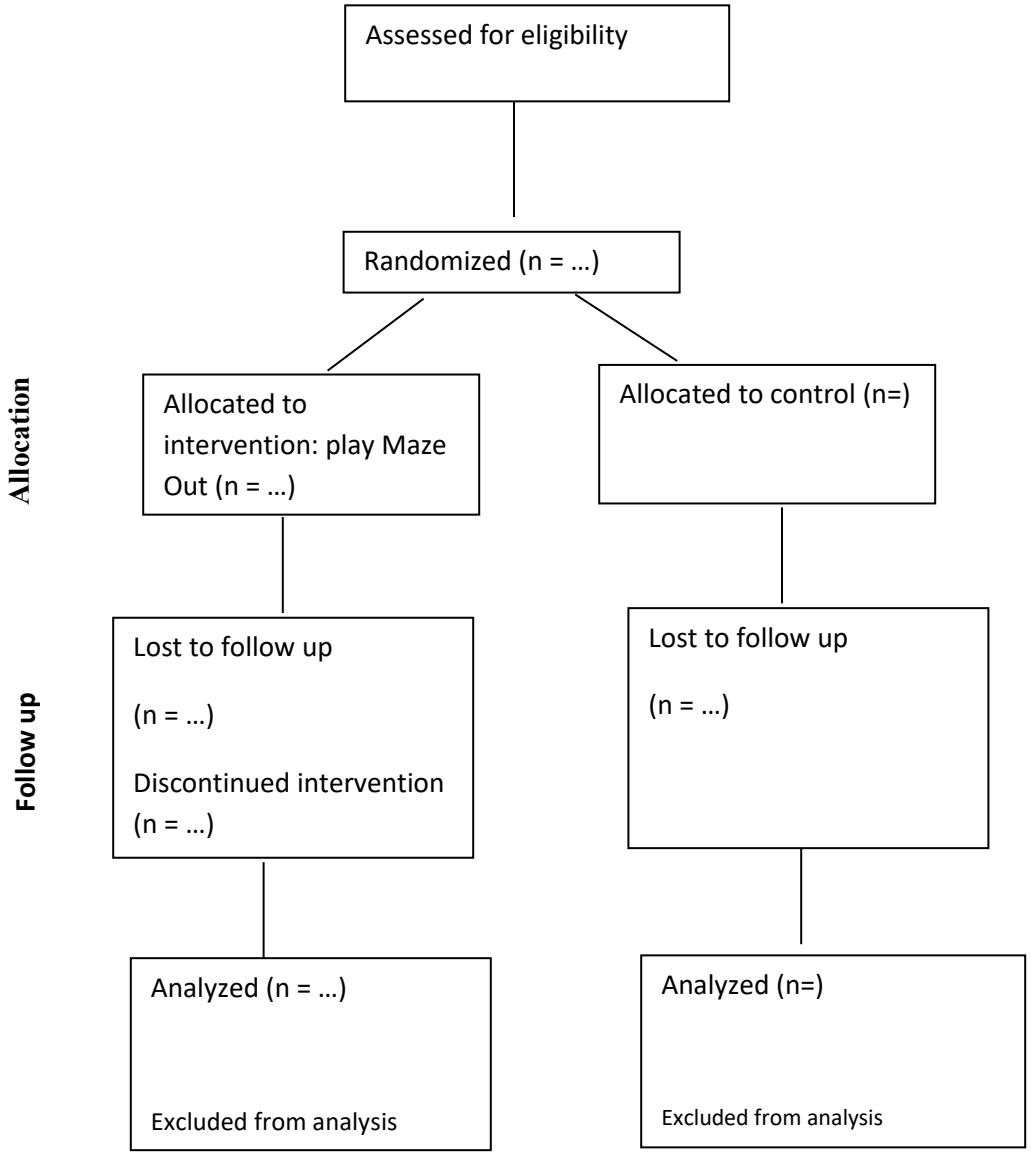


Table 2. Primary outcome and secondary outcomes

Primary outcome and numerical secondary outcomes will be analyzed by mixed effects linear regression. The mixed effects linear regression models will include a fixed effect for treatment, a fixed effect for time point (baseline, 8 and 15 uger) and a fixed effects interaction between treatment and time point.

Table 2

	Mean change from 0 to 15 weeks (95%CI)			**Mean change from 0 to 8 weeks (95%CI)**			**Mean change from 8 to 15 months (95%CI)**			
	Placebo (N=)	**Maze out (N=)**	**p-value**	**Placebo**	**Maze Out**	**p-value**	**Placebo**	**Maze Out**	**p-value**	**p-value***
Primary Self-efficacy (5-item SE_ED)										
Secondary 1 Ineffectiveness (IC-EDI-3)										
Secondary 2 Interpersonal problems (IPC-EDI-3)										
Secondary 3 Recovery (INSPIRE-O)				N/A	N/A		N/A	N/A		
Secondary 4 Self-Image (SAS-B)				N/A	N/A		N/A	N/A		

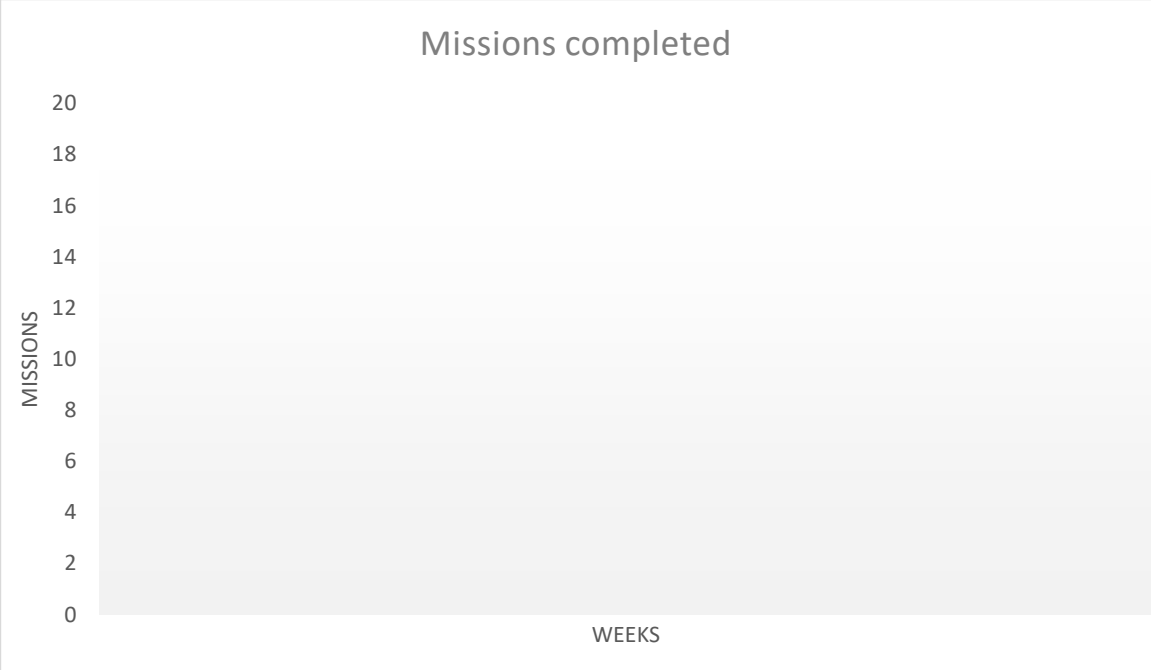
Table 3. Use of Maze Out

Data on the use of Maze Out will be collected from the back-end of Maze Out, which consists of: a) information on which portals the patient has been through; b) duration and frequency the patient has played the game; and c) answers to questions within different missions of Maze Out. These data will be collected throughout the 15-week period patients play Maze Out. Table 3 will show a) and b). The answers to questions within different missions will be analysed by qualitative methods.

Table 3

	median	mean	IQR
Missions solved			
Time spent playing			
Days between first and last log in			

Figure 2: Completed missions per week.



Appendix: Table 4

Primary outcome and secondary outcomes only for participants that answered questionnaires in both T1 and T2.