Bilag 2: Protokol

Content

1. Pilot Testing of an Aftercare Mobile Application for Relapse Prevention to Alcohol and Cannabis Use among Young Adults

[Forebyggelse af tilbagefald – Pilot-undersøgelse af en mobil applikation (app) til unge voksne med problematisk brug af alkohol og cannabis]

2. Objectives & Background

The aim of the present project is to implement a feasibility and pilot effectiveness trial to test a mobile application (app) that can be used as an aftercare intervention for young adults (ages 18-30), who have received treatment for problematic alcohol and cannabis use. These young adults are at high-risk for relapsing to their former problematic use of substances after discharge from structured treatment services, and thus a mobile app can become a useful tool for sustaining treatment goals and progress.

Under the scope of an interdisciplinary research team involving psychologists, software engineers, and computer scientists, we have developed a mobile app to support these young adults. Two prototype versions of the app were tested among young patients, from whom we received feedback to improve the app. To our knowledge, this is the first aftercare app that have been developed in Denmark, therefore, an important objective of this pilot project is to test the feasibility of its use and evaluate its usability with young adults in treatment for problematic alcohol and cannabis use. Further, the second objective of the pilot project is to obtain preliminary data on clinical effectiveness of the app as indicated by reduced substance use or abstinence.

Importance

This project will advance the design of novel, research-based clinical aftercare interventions for young adults with alcohol and drug problems (particularly cannabis). Novel interventions for this age group are important, because they can have a positive short and long-term impact, not only with regards to substance use disorders (SUDs), but also with regards to the young adults' health, education and work activities, and social and psychological well-being.

Unlike traditional face-to-face interventions, the use of digital tools for SUD interventions have the potential to intervene just-in-time (when it matters the most), and in the patients' natural environment. These advantages are crucial for interventions targeting young adults. This age group is typically difficult to engage in SUD treatment, and therefore it is very important to invest resources to develop interventions that will be relevant and of interest to them. At the same time, young adults are an optimal target group for implementing digital interventions, as they are more proficient in the use of new technologies. Lastly, because digital interventions are highly scalable, an effective mobile aftercare intervention has the potential to reduce readmission rates to SUD treatment, a common and costly pattern of service use among young adults receiving treatment for SUDs.

Youth's Problematic Alcohol and Cannabis Use

SUDs are a leading cause of disability worldwide[1, 2], and rank among the top three leading causes of disability among adolescents and young adults in high-income countries[3]. Addressing substance use among young Danes is crucial. In Denmark, substance use peaks before the age of 24[4, 5]. The prevalence of alcohol use is particularly high compared to other European countries[4,6], and to other age groups in Denmark[7]. The World Health Organization estimates that 7.7% of young people in Denmark has a clinically diagnosed alcohol use disorder (AUD)[8].

However, despite the high prevalence of problematic alcohol use among young adults in Denmark, the majority do not seek treatment for their alcohol problems[9]. Instead, young adults in Denmark are more likely to seek treatment for drug use, particularly cannabis[4,5]. In the last decade, patients are entering drug use treatment at a younger age. In 2017, 71% of the patients receiving treatment for problematic drug use reported cannabis as the primary drug, with an average age of 24 years at admission, compared to 2011, where 63% received drug treatment with an average age of 27 years upon treatment admission[4, 5]. Importantly, because cannabis problems often coexist with problematic alcohol use[10-12], it is important to develop interventions for both substances in this age group.

Relapse and Readmission in the Treatment of Substance Use

An important aim of SUD treatment involves maintaining treatment gains after treatment discharge. However, this aim is often challenged by a return to previous levels of substance use or slips[13]. A slip refers to an initial setback that may not necessarily last, whereas a relapse refers to a more severe and long-term return to previous substance use[14, 15]. Between 37% to 75% of patients who have received SUD treatment slip or relapse to alcohol or drug use within 12 months after treatment discharge[16,17]. Further, full remission from substance use is often difficult to achieve, with remission rates ranging between 38% and 51% in treated samples, depending on type of substance[18]. Therefore, developing a cost-effective aftercare intervention may not only have a positive impact on the patients' substance use and well-being after treatment, but also for public services that offer SUD treatment, by potentially reducing costs related to treatment readmission.

State of the Art: Mobile apps for substance use intervention

Mobile apps are one type of digital tool increasingly being used for (mental) health treatment services. Many of these tools can be downloaded from commercial outlets, such as Google Play and iPhone stores. An important benefit of using these apps is that by being installed in a personal mobile, they can be at hand during a person's daily life. However, the theoretical or empirical background of the commercial apps is either not known or non-existent, thus posing major concerns regarding their efficacy and safety.

Unlike mobile apps for non-clinical populations, the mobile apps developed for clinical populations typically target more than one substance (i.e., alcohol and cannabis). This may be due to the common polysubstance use in these populations[10-12]. Importantly, a study found that individuals with coexisting alcohol and drug problems were more likely to use an aftercare app compared to individuals with AUD alone[19]. This suggests that an aftercare app targeting more than one substance may have greater benefits among clinical groups, than targeting only on substance.

A couple of apps have been designed as adjuncts to regular treatment in order to improve engagement with treatment, typically with positive results[20,21]. However, only a handful of mobile apps have been developed and tested as aftercare treatment for SUDs (for a review, see[22]). One of these apps aimed at increasing awareness about cravings and triggers related to substance use among patients enrolled in methadone treatment[23]. This was achieved by identifying relevant emotional factors (e.g., anger, sadness) and external triggers (i.e., cues by places or people) leading to substance use. After a one-month pilot study, patients rated the usability of the app as high, and compared to a control group, participants who used the app reported fewer days of use of their main substance. However, the effect was not statistically significant.
Recently, an aftercare app for alcohol use disorders (AUD) was tested in Denmark[24,25]. The patients using the app did not have better outcomes in the follow-up assessments compared to aftercare as usual, neither in terms of alcohol use or coping with craving. Many factors could have contributed to these negative results, such as focusing on improving one specific cognitive skill (responding to alcohol cues) as well as the time-restricted access to the training app. To date, an American mobile app called A-CHESS is the most successful aftercare app as supported by findings from randomized clinical trials (RCTs)[26-28]. A main menu in A-CHESS gives access to a variety of support tools for users, such as psychoeducation, a weekly tracking tool for the use of substances, access to podcasts on addiction, breathing and relaxation exercises, etc. Patients may access the app when needed. The use of ACHESS over four months resulted in a decreased number of problematic drinking days and increased engagement with other after-care interventions[28].

In sum, the development of research-based smartphone apps for reducing substance use is at a preliminary stage, and the available evidence for aftercare mobile apps is both limited and mixed. However, there are positive indicators encouraging the development of new solutions within this area. Both the A-CHESS and Liang's app[24] obtained positive results (although one was only a trend). Two common factors that seem important for these positive results are that the patients can access the app when necessary, and that the app targets more than one substance. Together, these features increase the coverage of individual patient needs.

Early Group Advances: AfterCare Development App and Tests

The research team has designed and programmed an initial app prototype (see *Figure 1*), which integrates state of the art on mobile apps for aftercare, a main theoretical model on the relapse prevention model for substance use[29], and principles of human-computer-interaction.

The current AftercareApp prototype has the following main functions:

1) Help now (*Hjælp nu*). Access coping strategies that can help end users (the young adults using the app) to prevent slips to alcohol, cannabis and other substances in the short term.
2) Help later (*Hjælp senere*). The app will help end-users to identify high-risk situations for using substances. Following this, the app will give them the opportunity to choose coping strategies that could be relevant to prevent a lapse in those situations. Through a brief assessment, the app will help the patient to determine what internal (e.g., emotional experience) or external factors (e.g., places or people) can influence their use of substances in these high-risk situations.
3) Planned help (*Planlagt hjælp*). After using the "Help later" function, a brief plan for up to three high risk situations may be saved. These plans include strategies chosen by the end-users to cope with the

high-risk situation they planned for under “Help later”. The plans can be accessed by clicking on “Planned help.”

4) Calendar for goals (*Kalender*). The end users will be able to track whether they achieved their goals in relation to the chosen substances for each day. These goals are personal and may refer to reduction or abstinence of cannabis, alcohol, or other substances. The app will show different visual signs each day depending whether they met their goal or not.

As for the coping strategies that the end users can use for preventing a slip or relapse, we have selected strategies that are often used to cope with risk of relapse to substance use (e.g., contacting support people, distraction, remembering motivations and goals for reducing/stopping substance use, navigating cravings) (See *Figure 1)*. Many of these coping strategies will be known to the end users from the treatment that they received at the SUD treatment center. In addition, the end users will be able to add strategies not covered in our initial selection that they have personally used with success.

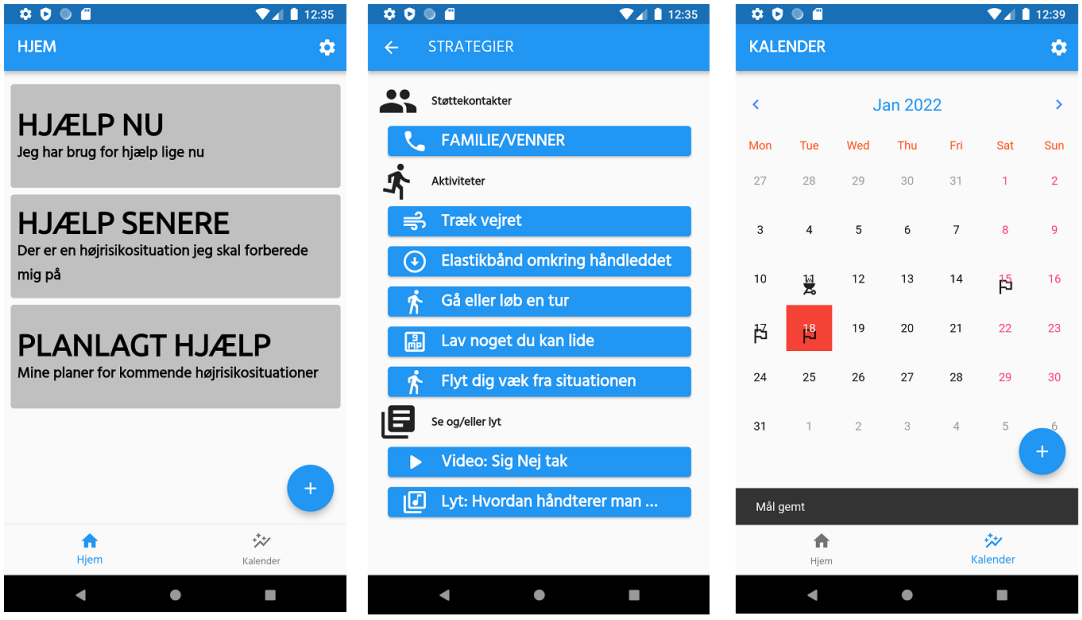

***Figure 1*. Prototype 1. Screen shots of some of the app functions.**

Tests

The initial prototype has been field tested over one week by 9 young adults that were representative of the target group (18-30 year olds), receiving treatment for SUDs). We collected their feedback through online surveys rating the usefulness of the app as well as through in-depth interviews. Key areas to be improved according to participants’ feedback were: include notifications and reminders to use the app, increase personalization of the app (user profile, add personal strategies), improve usefulness during parties (e.g., tips for drinking less), improve the visualization and calendar / goal tracking part. An improved app will be completed in July 2022, and be employed for the pilot trial. However, the key features outlined above will remain.

Project Goals

The final goal of the current project is to assess the feasibility of using the final version of the AftercareApp in clinical contexts, and to obtain preliminary data on clinical effectiveness for preventing relapse to substance use. To achieve these goals, we will employ a mixed-methods approach with quantitative and qualitative data.

Specific sub-goals in the project are:

1. Measure the frequency of the research participants' use the Aftercare App, including frequency of use of the main functions in the app.
2. Determine the effectiveness of the Aftercare App in regards with alcohol and cannabis use 6 and 12 weeks after the app is introduced to participants, by examining whether having access to the app at different time periods has an effect on substance use (See the two intervention arms in Section 3. Method).
3. Explore whether the app's effectiveness is related to the frequency with which the app is used, and/or the young adults' characteristics (e.g., age, sex), and type and severity of substance use.
4. Obtain young adults' ratings on the usability of the Aftercare App.

3. Method

Overall Design

The project will be conducted from start in August, 2022 to end of August, 2023. The study consists of a two-arm randomized pilot trial. The research participants (N = 90), will be young adults who enter SUD treatment (see Section 5. Research Participants). If the young adults meet the criteria and accept to participate, they will be assigned to either the "Immediate App Access" (IA, n = 45) or the "Delayed App Access" (DA, n = 45) condition.

As shown in Figure 2, research participants in both conditions will go through the same recruitment and induction procedures at the treatment centers where they will receive treatment. These procedures include an intake assessment and screening, recruitment and randomization to one of the two conditions. Further, participants in both conditions will be introduced to the Aftercare App in their third treatment session, and complete a short assessment (A1). Following this, participants randomized to the IA condition will be granted immediate access to the Aftercare App, whereas participants assigned to the DA will be granted access 6 weeks after the third treatment session. After the third treatment session, when the app is introduced, both conditions will be assessed in short-term follow-ups of 6 and 12 weeks (A2 and A3, respectively).

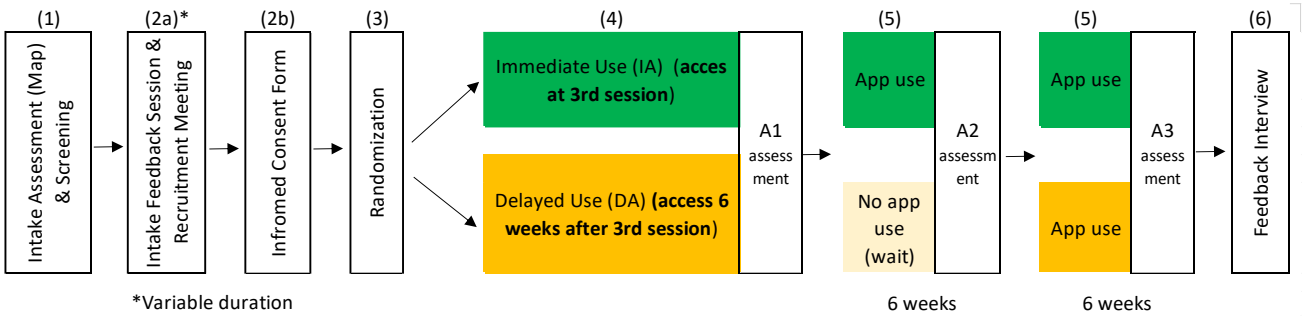

Figure 2. Process of the pilot RCT.

Hypotheses and Endpoint

We hypothesize that research participants randomized to IA, compared to the research participants randomized to DA a later access to the Aftercare App, will:
1. Report fewer days of alcohol and/or cannabis use in the A2 and A3 assessments after controlling for their substance use at baseline.
2. Use the Aftercare App more frequently after gaining access (average per week, which can only be compared at A3).

Further, we expect to find variations among participants in both conditions in regards with the frequency and preference for the different functions in the app (e.g., Help now, Help later, Planned help, Goal calendar). That is, some participants may use some of the functions more often than others. Therefore, we will attempt to identify profiles of the end users based on exploratory analyses with demographic characteristics (e.g., age, sex) and substance use history (e.g., treatment experience, main target substance).

The endpoint of this project is to evaluate the feasibility of implementing the use of the Aftercare app in clinical contexts (i.e., patients receiving or ending SUD treatment), as well as to obtain initial data on the clinical effectiveness of the Aftercare App.

Pilot Procedure

As shown in Figure 2, the study involves several steps: (1) Intake assessment (MapPlan) and eligibility screening, (2) Recruitment and informed consent (variable duration; multiple appointments), (3) Randomization, (4) Project-initiation meeting and Assessment 1, (5) Follow-up Assessments 2 and 3 (6 and 12 weeks after the initiation meeting, respectively), and (6) Final feedback interview (optional for selected participants). The overall study will take place in coordination with the four SUD treatment centers. Staff affiliated at the participating centers will assist with Steps 1 to 3, whereas the research team will be fully responsible for Steps 4 to 6.

The main assessment tool for Intake Assessmand and Screening is the MapPlan. See Sections 5 and 8, as well as Appendix 6a for more details.

(1) Recruitment and informed consent

See Section 12.

(2) Randomization

After providing with an informed consent, the participants will be randomized to either the IA or DA condition. This will be done following block randomization procedures as in previous RCTs conducted by members in the research team and in clinical research in general[31].

(3) Third treatment session: App Introduction and Assessment 1

The initiation project meeting corresponds to the third treatment session of each participant. The participant, his/her counsellor and a research assistant (RA). The RA will be present (either online or in person, depending on what is possible). At the beginning of the treatment session, the counsellor will be notified electronically by the research team to which condition the patient is assigned. Due to the nature of the two conditions, the participant cannot be blinded to the condition that he or she has been randomized to, as they will know whether they have access to the app immediately (the IA group) or 6 weeks later (the DA group).

Several key elements of the third treatment session will be the same for patients in both intervention conditions:

1. The counsellor will explain key conceptual aspects of SUD treatment that are also relevant for the app, including the concept of high-risk situations and strategies that may be useful for coping with such situations. These elements are often covered in treatment for SUD and will thus not interfere with the regular treatment that the patients receive.
2. The app will be installed and will be briefly introduced to the participants. The RA will help installing the app and provide log-in credentials for the app. The log-in credentials are personalized and will only be known to the RA and research team and the specific participant, and not the counsellor or other participants. The credentials will be saved on a secure server at Aarhus University, and only specific research members will have access to them to match data (See Section 9).
3. The RA will ask the participant to complete a brief online assessment consisting of:
    - Alcohol, cannabis, and other drug use in the last 30 days via the Time Line Follow back (TLFB)[32, 33] (Appendix 6b).
    - Anxiety and depression symptoms via the GAD-2[34] and PHQ-2[35](Appendix 6b).

The two main differences between conditions are (1) when the participants are given access to the Aftercare App, and (2) how long they can use the app for. Participants randomized to DA will be given remote access by the research team via an activating link 6 weeks after session 3 and will be able to use the app for 6 weeks, whereas participants in IA may use the app freely from session 3 and up to 12 weeks later (See Figure 2).

(4) Assessments 2 and 3

These assessments will be conducted remotely either by phone or online (TEAMS) by an RA blind to the condition. The TLFB, GAD-2, and PHQ-2 will be repeated. In addition, the research participants will complete

an online questionnaire on acceptability and usability of the app (Appendix 6c). This evaluation will happen 6-weeks after participants in each group gain access to the app. Since access to the app differs between the two conditions, the evaluation of the app will be completed at Assessment 2 for IA and at Assessment 3 for DA.

(5) Feedback Interview (Selected participants)

A subsample of 16 participants, 8 per condition, will be selected randomly and invited to participate in a feedback interview after the 12 weeks of the pilot period. By this time participants in both conditions would have had access to the app. This interview will be held online either individually or in small groups with a RA with the goal to collect qualitative and more in-depth evaluations on end users' experience of using the app. If the online is not possible for practical reasons or due to participant´s preference, the RA will meet them in person in treatment center where they were recruited. Appendix 6d contains the interview guide.

4. Qualitative and Quantitative Analyses

Summary of data to be collected

- Intake assessment and patient journal information
    - Identity and demographic variables (CPR, age, sex, education, occupation)
    - MapPlan: The MapPlan is a comprehensive assessment battery widely used in Denmark's outpatient SUD treatment centers and consists of a youth (15-25) (UngMap) and adult version (18+) (VoksenMap). MapPlan covers a number of key areas assessing the frequency and severity of various substances, including alcohol and illicit drugs. MapPlan also assesses internalizing (e.g., anxiety, depression) and externalizing symptoms (e.g., behavioral problems) (See Appendix 6a with the battery).
    - Number of treatment sessions completed by the time of the follow-up assessments A2 and A3.
    - Duration of active enrollment in SUD treatment by the time of the follow-up assessments A2 and A3.
- Assessments 1 - 3: Alcohol and cannabis use in the last month (TLFB), brief history of treatment for substance use, anxiety and depressive symptoms (PHQ-2 and GAD-2), and ratings on usability and acceptability of the aftercare app (after 6 weeks of using the app) (see Appendix 6b and 6c for content of the A1-A3 questionnaires, which will be administered by a RA).
- App use behavioral data: number of days the app was used (number of days app was opened), specific tools/sections of the app used (number of clicks), frequency with which app was used (any interaction/click on the app).
- Semi-structured interviews: qualitative data from feedback interviews focusing on the evaluation of a sub-group (n=16) of the research participants' experience of using the app in terms of acceptability, usability, personalization, usefulness, etc. Further, we will ask about potential deterrents or obstacles experienced using the app, as well as general liked and/or useful features of the app (see Appendix 6d). The interviews will tale between 60-120 minutes, depending on number of participants. The interviews will be audio recorded.

Quantitative analyses

Power analyses. We conducted a power analysis in which we used Cohen's d = .36 as effect size based on a previous study[28] p = .05, and power of β = .80. With these parameters, the required N is 63. We

will oversample by 35% (n =26) due to potential loss between the 3rd treatment session/A1 and the two follow-up assessments (A2 and A3). Therefore, our target is to introduce the app to 90 research participants in the 3rd treatment session.

Feasibility analyses.

- Based on behavioral use of the Aftercare App, we will determine how frequently the participants used the app during the trial period in general, as well as specific functions (e.g., Help now, calendar)
- We will determine whether there are differences in app usage between the two conditions, that is, based on when in the treatment the research participants had access to the app.
- If possible, we will examine what other factors may be related to a higher frequency of app use. Examining correlations of app use with other factors will help us determine if the app may be better suited for specific sub-groups within the target group. Such factors to be explored include:
    - Sex
    - Primary target substance (alcohol vs. cannabis)
    - Overall severity of substance use at intake
    - Psychological symptoms (e.g., anxiety and depression)

Intervention effects.

We will examine differences in the two intervention conditions using a repeated measures ANOVA. The primary outcome will be number of days in which alcohol and cannabis were used in each condition according to the TLFB in the A2 and A3 follow-ups). Generally, we expect that participants who had an earlier access to the app will report fewer days of substance use. The secondary outcomes will be changes in anxiety and depression symptoms (GAD-2 and PHQ-9 collected in A1-A3). Potential confounders, such as length in treatment and frequency of app use will be considered in the analyses.

Qualitative analyses

For qualitative methods, a power analyses to determine sample size is not required. However, a target sample size of 16 is in line with similar interview-based studies examining the experiences of patients who interact with a mobile app to support recovery from substance use[36]. After transcribing the interviews, we will code and analyze the content thematically. To the extent possible, the information will be arranged around the following areas (also, see Appendix 6d):

- Easiness to access the main functions and their purpose (*Help now, Help later, Planned help, Calendar goals*).
- Features most helpful to prevent slips or relapses.
- Most engaging features, even if not directly supporting relapse prevention.
- General aesthetic evaluation of the app: colors, location of buttons and menus.

5. Research participants

Research participants will be 90 young adults, ages 18-30, receiving outpatient public SUD treatment for problematic cannabis or alcohol use. The sample consists of a convenience sample facilitated by the participating treatment centers.

Recruitment. Research participants will be recruited in collaboration with three to four treatment centers. At the moment we have confirmed participation from Brydehuset, KABS City, CAS Roskilde, Horsens. See details in Section 16.

a) Inclusion criteria:

Initial screening upon intake (Step 1 in Figure 2):

1) Be aged 18 – 30 years old.
2) Own a mobile with data plan.
3) Being enrolled in outpatient treatment for alcohol or cannabis use at one of the participating treatment centers

Additional inclusion criteria after initial screening (Step 2b in Figure 2):

4) Providing informed consent to study participation.
5) Attend their third treatment session.

b) Exclusion criteria (Steps 1 and 2b in Figure 2):

1) Severe mental illness (e.g., psychosis) or dangerous behavior (e.g., aggression).
2) Severe neuropsychological disorder.
3) Not willing or able to give informed consent to participate in the study.
4) Does not speak or understand Danish in a way that makes it possible to participate in the project.
5) Took part in a prior stage of the project that focused on the app development (see p. 7 Early Advances).

6. Risk and Disadvantages

Participation in the pilot study does not have imminent or direct negative side effects. However, there might be some disadvantages experiences by research participants at individual levels, such as:

- Using additional time to complete different steps in the project, such as introducing and installing the app, assessments A1-A3 with the research team, using additional time during their daily lives while trying out the app, and taking part in the feedback interview.
- The fact of interacting with the app may confront the participants with their personal journey of recovering from substance use, which may trigger negative emotions, such as feeling upset or disappointed.
- Access to the app will be limited (6 to 12 weeks depending on the condition). If the research participants find the app useful, they might feel frustrated when they cannot continue using it (see also the Study Information Sheet (*Deltagerinformation*; Appendix 4).
- Some participants may feel pressured or worried that the research team knows whether they are using the app or not, as well as the content of their entries. While this is true, we will emphasize that we are interested in their natural use of the app (as it seems to fit to them), and that even lack of use is informative to the researchers.

- Some participants may feel overwhelmed with the various steps in the process in the study and when using the app. They will be told their participation is voluntary, and can stop any time (e.g., decline to complete the assessment, stop using the app).
- Participants may be concerned about the data that is collected through the app. The Study Information Sheet (*Deltagerinformation*; Appendix 4) will specify which data we collect and how they are stored, as well as that participants can request their data to be deleted from the project (See Section 9).

7. Biological material

Neither existing or newly collected biological material.

8. Information from patient records

The participating treatment clinics will collect and share some data stemming from the patients' regular intake assessment (MapPlan), as well as number and dates of treatment sessions in the project period and how much they talked about the app in the treatment sessions. Patients are informed about this shared information in the Study Information (*Deltagerinformation; Appendix 4*). The research team at Aarhus University will not have access to the patients' clinical journals (*patientjournaler* at the treatment clinics). Given that we, as research team, request data on number and dates of treatment sessions in the project period from counsellors in a separate survey and not from the patients' journals, these data are not completed under the regulations of the *journalføringsbekendtgørelsen*. Further, the MapPlan is a psychosocial assessment rather than a medical record (https://psy.au.dk/forskning/forskningscentre-og-klinikker/center-for-rusmiddelforskning/behandlingsportalen/mapplan). We provide details on the data and collection process under Section 9 (Processing of personal data).

9. Processing of personal data in the project

There will be two main sources of personal data in the current project:

1) Intake assesment and treatment exposure (data collected by counsellors and shared with CADR) (See Section 8).

2) Data collected directly from the AU research team:

2.1 Assessments A1, A2, and A3

2.2 Data collected via the Aftercare App.

2.3 Audio-recorded qualitative interviews.

Each source of data will be handled *ad hoc* following regulations from Aarhus University and the European Union. The data for each participant from each source will be linked together via a unique participant ID generated by the research team; see *Figure 3*. The overall data will be managed by CADR, AU. However, data on use of the app will primarily be managed by ORBIT Lab, AU. Given that both research units, CADR and ORBIT Lab, are part of AU, all data will be managed within the infrastructure (i.e., secure servers and clouds) approved by Aarhus University.

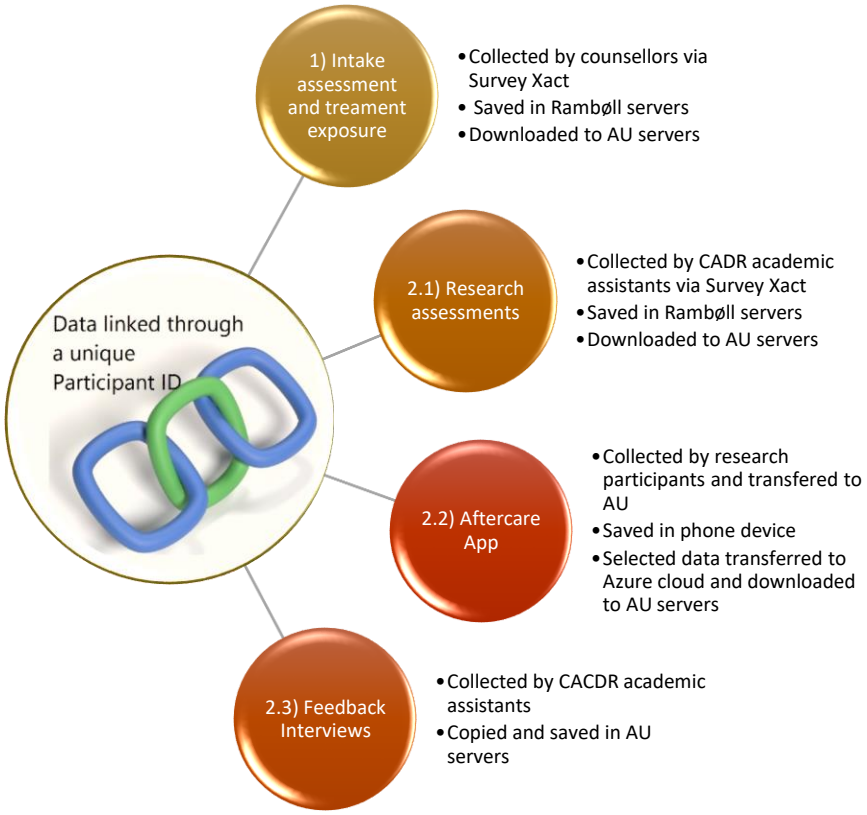

Figure 3. Different data sources.

1) Data collected by counsellors

Intake assessment (MapPlan) and treatment exposure. Assigned counsellors by the managers of the collaborating treatment centers participating in the study will enter and submit data concerning the intake assessment of patients contained in an assessment battery called Ung- and VoksenMap (or MapPlan). Further, we will collect information on indices of treatment exposure, which refers to both the number of treatment session that research participants have received and duration in treatment (e.g., start date of treatment), collected via survey.
From the MapPlan, we will obtain data on (see Section 4 and Appendices 6a and 6b for all the questions):

- Name and/or patient registration number at the clinic, and personal identification number (CPR).
- Demographic information: age, sex, education, living arrangements.
- Baseline substance use (e.g., number and amount of days using alcohol, tobacco, and illicit drugs), as well as psychological well-being.

We will also collect dates and number of sessions attended from the intake assessment and up to the time of the Assessment 3 (12-week follow-up).

Bacgkround for MapPlan. For several years, CADR and treatment centers in the Danish municipalities have collaborated to use the Ung-/VoksenMap assessments to uncover the patients' needs with the aim of formulating a treatment plan (see Section 101 subsection 2 and subsection 8 of the Service Act. Link: https://www.elov.dk/serviceloven/101/). The Ung- and VoksenMap have been developed and validated by CADR through the past 10 years of research projects and national sample surveys. Data deriving from the MapPlan (Appendices 6a an 6b) are part of the regular intake procedures in all of the collaborating treatment clinics for this project (sites have been selected for study participation based on this). Given the long-standing collaboration between municipalities and CADR, we already have access to the MapPlan data under various municipal agreements. As part of these agreements, the MapPlan data is entered by counsellors in SurveyXact (but not the patients' journals).

For all clinics, data concerning the number and date of the sessions with patients will be collected every month via secure Survey Xact questionnaires sent by the research team. The research team will not have direct access to these data in patients' journals.

Reasons for collecting the data: The above data are needed to have a baseline measurement on the severity of substance use and mental well-being upon entering treatment. These data will be used as cofounder variables in the analyses examining the potential clinical effect of using the mobile app. For example, we can examine whether longer time in treatment, or a higher substance use severity at treatment intake have an impact on either how much the app is used, or how much it helped in preventing relapse to substance use in the study period. We will not request any other information about the sessions, such as topics discussed or material covered. Further, we will not have full direct access to all electronic patient records.

The intake assessment MapPlan and treatment exposure data will not be anonymous as they will contain identifiable information (name, contact information, CPR), but data will be confidential and will be saved securely in Aarhus University servers. (See Section 4 and 8 for details on what data will be collected). Only CADR employees who handle Survey Xact, will have access to identifiable data (name, CPR), including Michael Mulbjerg Pedersen, who is employed as an AC-employee at the CADR to manage MapPlan data. Survey Xact data is saved in servers by Rambøll, a GDPR compliant Danish enterprise.

2) Data collected directly by the research team

2.1 Research follow-up assessments (A1, A2, A3) (entered in Survey Xact). Assessments 1-3 will be pseudo-anonymous (saved under a unique Participant ID generated by the research team). Assessments 1-3 will be conducted by research assistants (RAs) who will enter the data in Survey Xact (Appendices 6b and 6c). See Sections 3 and 4 for details of what data is collected in A1-A3.

2.2 Aftercare app data. We have taken several security steps to protect the data collected through the app, including: Minimizing the amount of data to be transferred out of the phone devices to the research team, encrypting data at rest (when stored), using secure data storage. Importantly, the app does not require linking the account to the participants' name, contact information, or CPR number. Further, we do not collect geolocation data. Instead, data collected through the app will be pseudo-anonymous (saved under a unique Participant ID generated by the research team). Access to the app will require

personalized log-in credentials: a confidential password and the unique User ID provided by the researchers. Therefore, the data from the app does not have direct linkage to the research participant's identity.

The data collected via the app will be handled with two different storage systems, one that is the phone itself and does not leave the device, and another that is transferred to the Microsoft Azure App Service, a special cloud storage service for mobile apps approved by Aarhus University (AU). Servers of the Azure service are stored in the North Europe region (Ireland) and meet requirements of laws and regulations in regard to data protection. Only ORBIT lab is authorized to access to the Azure cloud.

However, a large majority of the data entered in the app by the participants is planned to stay on the phone as this is for participants' use only. A smaller portion of the data will be transferred to the Azure cloud (see Table 1). The research team will only transfer data from user phones to a server that has specific research purposes, such as measuring research frequency of app use, as well as to identify in relation to which substance the app is being used more often. At a later stage, these data will be exported in CSV-format from the Azure cloud to a AU server for data analysis. ORBIT lab will be the main data manager for this data source.

Table 1. Type of app data and storage.

		Feasibility and app usage data	**Substance-use related data**
	- Free-text entered by the end users in the app, such as: strategies that are useful to control substance use, names of high-risk situations, motivations, specific goals, advantages and disadvantages. - Phone numbers for support people - Pictures used for motivation	-Number of times the research participants click anywhere in the main screen, and different app elements (Help now, Help Later, Planned Help, Calendar) -Timestamp of the clicks - Days in the calendar with any entry on goals	-Clicks on any strategies either - Answers to the questions on Help now and Help Later regarding which substance the app is used for (alcohol, cannabis, both, other).
	Locally (personal device) and thus protected by the phone's operating system (Touch ID, Face ID, Screen Lock, PINs, etc.)	1) Microsoft Azure, Microsoft's cloud computing platform for iOS and Android based mobile apps. 2) Aarhus University servers (two-step data protection). The data transferred from the app to the Azure cloud will be encrypted at rest, and will further be handled by ORBIT to prepare a *.csv file for research purposes.	

Contingency plan. In the unlikely event of data breach, the following steps will be taken:
1. All Resources on Azure will be shut down.
2. Service users with access to Azure Resources will be contacted by phone and asked to change their password for their account. People with access: Brian Vestergaard Danielsen (brian@ece.au.dk, +45 9352 1964), Henrik Bitsh Kirk (henrik@ece.au.dk, +45 9350 8832)
3. The breach will be reported to the Information Security Team on Aarhus University through https://medarbejdere.au.dk/informationssikkerhed/anmeld-sikkerhedsbrud
4. The resource owners will be informed: Jacob Styrup Bang (au181366@uni.au.dk), Anders Ebert (au27359@uni.au.dk), and Nikolaj Petersen (au561718@uni.au.dk)
5. Other members of the research team will be contacted: Birgitte Thylstrup (bt.crf@psy.au.dk, +45 2158 7881), Adriana del Palacio Gonzalez (apg.crf@psy.au.dk, +45 8716 5765).
6. Await instructions from AU IT.

More detailed information regarding app data handling and storage may be provided.

2.3 Audio recordings from interviews. The interviews, whether conducted online via Zoom (using Aarhus University accounts) or in person, will be audio-recorded, as indicated in the Study Information (*Deltagerinformation*) and consent form (*Samtykke*). The interviews will be recorded with a dictaphone and the audio files will be saved in secure AU servers (O Drive).

GDPR

Data handled by Aarhus University (either ORBIT Lab or CRF) will comply with the GDPR regulations, which includes the possibility for research participants to delete their data from both the app and the project online assessments at any time during the study period. Aarhus University will not have full control on how journal/patients' records data are handled at the participating treatment centers (storing session number and dates). However, the research participants can request that the treatment center does not transfer these data to the research team, or that the research team deletes the data that have been transferred from the centers.

Linkage and general data storage

Adriana del Palacio will be the main data manager. She will merge or link together the data from the different sources, depending on the specific analyses to be conducted. One or more merged dataset files will be linked under the unique participant ID. Identity data, such as name or CPR, will only be stored in a Survey Xact server to which even the research team will have restricted access. A separate master file linking identities (e.g., names) and unique ID numbers will only be accessed by Adriana del Palacio, Birgitte Thylstrup, and the RAs. The working datasets from the different sources, as well as the master linking file, will be saved in a project-specific O Drive, which in turn is stored in a local secure server at Aarhus University (O Drive). Access to the O Drives is only possible via a two-step password process.

All data in the different storage systems will be kept for 5 years after the publication of key articles in compliance with the Danish Code of Conduct of Research Integrity[37]. After this period *all* research data will be completely anonymized or deleted and archived in the Danish Data Archive.

The study has been registered with the office of Danish Data Protection Agency at Aarhus University (internal university record of research projects) in September 2020 and updated September 2022. Accordingly, we will follow the regulations stated in the relevant act (*Databeskyttelsesforordningen og Databeskyttelsesloven*).

Informing participants
A simplified version of the data system will be explained to the research participants in three pieces of materials. First, the Study Information sheet (*Deltagerinformation*) indicates what type of data we collect, where it is saved, and the possibility of removing it. Second, specific check-list items in the Informed Consent Form (*Samtykke*) require the approval for these different type of data to be collected (clinical records, app data, research assessment, and interviews). Lastly, the Aftercare App has a section under 'About this App' *(Om appen*) that clarifies how the data is used, as well as the option to request the data to be deleted under Settings (*Indstillinger*).

10. Financing

The project was initiated by Adriana el Palacio Gonzalez, Kasper L. Jensen, Birgitte Thylstrup and Mads U. Pedersen. The overall study are funded by Trygfonden (DKK 1,779,446) and Helsefonden (300,000 DKK), and co-financed by the Center for Alcohol and Drug Research (CADR), Department of Psychology, Aarhus University (DKK 438.676). The funds are used to pay for part-time salaries (both CADR and AU Engineering team members), compensation of participants (gift cards), transportation to/from treatment centers when meeting with the sites, conference participation, and miscellaneous running costs.

None of the research team members (see Section 16 for names and affiliations), including Birgitte Thylstrup, PI, have any financial connections with the funding agencies (Trygfonden and Helsefonden), or other potential stakeholders (e.g., treatment clinics, commercial enterprises).

2. Compensation to research participants

All participants will be compensated for their participation in the study. Participants will receive a gift card for DKK 150 (ca. 20 euro) for every assessment completed, (A1, A2 and A3). The assessments involve A1 (filling out additional data and downloading the app at the 3rd treatment session, in order to compensate for the time spent carrying out these activities. We believe that the compensation has potential to be perceived as a winning in relation to carrying out the activities in session 3. As for A2 and A3, compensation is given as part of follow-up interviews. Further, for the research participants accepting to take part in the final feedback interview will receive an additional gift card for DKK 200 (ca. 27 euro). The gift cards will be provided electronically to each participant via email.

We have submitted an additional letter to explain the rational for using giftcards for this patient population.

3. Recruitment and informed consent form

Collaboration with treatment centers. Mads U. Pedersen, Birgitte Thylstrup, and Adriana del Palacio Gonzalez have been in contact with the managers of two treatment centers (Brydehuset, KABS) since the preparation of the funding applications. As part of this process, the respective managers were made aware of the purpose and framework of the project. After obtaining financial support for the project, Birgitte Thylstrup and Adriana del Palacio Gonzalez have held various meetings with management and selected counsellors between August 2021 and May 2022. Through these meetings, we have agreed on the steps for study recruitment and contact with potential research participants described below (a-c). We are currently planning similar procedures with two additional participating sites (Roskilde and Horsens), which we expect to finalize July 2022.

Prior to study recruitment, we will hold a training session with all the counsellors that the managers at each of the four sites have assigned to the study, in order to go through the app itself and the study procedures described in this document. Managers will select and oversee which counsellors take part in the different stages of the study.

a. *Recruitment.* Recruitment will happen after participants have been screened in their treatment clinic *(*Step 1 Figure 2). The recruitment will be done by the counsellors assigned by the managers at each of the participating treatment centers using the recruitment flyer (Appendix 7) and Study Information Sheet (Appendix 4) in the sequence described below.

b. *First contact*. The first contact for recruitment takes place between counsellors and potential research participant in a private room at the treatment center where the patient is enrolled for treatment. The research team will provide with a screening checklist that the counsellors will use so that if the potential participants is eligible, the counsellor can give the recruitment flyer (Appendix 7) and mention the study briefly after completing the Intake Assessment (Step 1 Figure 2). As a standard procedure, the treatment centers the Intake assessment is followed by 1-2 "assessment feedback meetings." It will be in such feedback meetings when the counsellor will follow up the brief introduction of the project (recruitment flyer) and ask the participants if they can provide more information about the study. If the participant shows some interest and the circumstances allow, the counselor will explain the Information Sheet (*Deltagerinformation*; Appendix 4). The appendix 4 will be explained verbally and in written form. At this point counsellors can ask whether the participants are interested and ready to sign the informed consent form (*Samtykke;* Appendix 5), whether they would like to hear more in the presence of an accompanying person (e.g., in an another appointment), have more time to consider the project, or decide they are not interested in the project. A printed copy of both documents (Appendix 4 and 5) will be given to the patient.

Therefore, following Figure 2, the official recruitment meeting (Step 2a) will take place after the Intake Assessment is completed (Step 1), but before the third treatment session. The time for recruitment may be variable in each treatment center, depending on their internal intake procedures. There might also be some variation from patient to patient, depending on for example, readiness to participate, and/or need for more time to consider their participation.

c. *Informed consent form (Appendix 5)*. After the participant and counsellor have met and discussed the Study Information (*Deltagerinformation*; Appendix 4), the consent form will be explained verbally and in written form in a private room in the treatment center (Step 2b, Figure 2). To offset some of the potential negative experiences mentioned in Section 6 (Risk and Disadvantages), the research participants will be informed that they:

- Can withdraw completely at any time, even after consenting to participate.
- Can talk to the counsellor or a member of the research team if they have concerns about their process in treatment (See also Section 14, Ethics).

For participants who might be interested, but unsure about participation, the consent form may be signed at the following meeting and collected by the counsellor. Normally there is at least 1 week (7 days) between meetings, which can be used to consider their participation in the project. That is, all participants will have minimum 7 days from the day when they receive the consent form to accept or decline their participation. However, only patients who accept to participant in the study before the third treatment session will be randomized (Step 3, Figure 2), and will be able to participate in the study.

Note that given that young adults can decline to participate in the study or may drop-out from treatment before the third treatment session, we anticipate to screen and invite to the study, at least double the number of the target sample size (e.g., more than 150 young adults may be initially invited).

4. Publication of findings

Publication of results from the project is coordinated by Birgitte Thylstrup and Adriana del Palacio Gonzalez in accordance with guidelines set out in 'Guidelines for Good Scientific Practice', Committee on Scientific Dishonesty, 1998, and the Danish Code of Conduct for Research Integrity. Positive, negative, and inconclusive results of the studies will be published in international scientific journals. The findings, irrespective of their conclusions, will be disseminated through other outlets both scientific, clinical, and with the lay-person, such as open-access local reports, conferences, and meetings with local research networks and clinical centers. We expect minimum 2 scientific articles deriving for this project.

5. Ethics

The project will be conducted in accordance with the Helsinki Declaration II.
The project follows guidelines from the World Medical Association, where the researcher is obliged to protect the study participants' lives, health, dignity, integrity, right to freedom of choice, as well as confidentiality.

The study has been registered with the office of Danish Data Protection Agency at Aarhus University (internal university record of research projects) in September 2020 and updated September 2022. Accordingly, we will follow the regulations stated in the relevant act (*Databeskyttelsesforordningen og Databeskyttelsesloven*).

The project is being submitted to the Regional Committee for Medical and Health Research Ethics for the Central Denmark Region before commencement. The project will include only competent research participants who participate voluntarily after adequate oral and written information. This also includes written consent that can be considered for up to 7 days after formal invitation or recruitment.

Despite the *disadvantages* mentioned in Section 6, there are several actions that can minimize the impact of participant in the project. First, the project is planned to minimize disruptions of the regular intake and treatment process. Further, the participants in each phase of the project can withdraw from the project at any time without having to justify it. Participants may at any time request that their data not be used. Research participants will not be subjected to any kind of mental or physical pressure. Research participants will also have opportunity to obtain further information about the study by contacting the research team, which depending on the nature of the issue may include Sidsel Schrøder,
Venus V. Fabricius, Birgitte Thylstrup, or Adriana del Palacio Gonzalez. The last two are trained psychologists and have experience with treatment of young adults, assessment, and research projects where young adults are involved. They therefore have the relevant prerequisites to meet questions from both the young adults in the project as well as counsellors and managers at the participating sites. Furthermore, the research participants will continue to have contact with their treatment center during study participation in case that they experience negative effects as a result of the app use.

At the same time, there are *advantages* of participating in the study. The app can support the participants in relation to preventing slips or relapse. As shown in research, relapse is frequent after treatment for substance use. Aftercare interventions, such as this one, can help in reducing relapse risk. Further, our experience is that many participants are positive about contributing to research projects focused on improving interventions for SUD. Overall, the benefits of the study outweigh the risks.

On September 3rd 2021, the principal investigator, Birgitte Thylstrup, submitted an inquiry to Central Region's Ethics committee about the present project and was on September 20th 2021 hereby instructed to make an inquiry with The Danish medicines Agency about whether the project should be considered as a test of a medical device. On December 8th 2021, the principal investigator informed the committee that The Danish medicines Agency had assessed that the project does not qualify as a test of medical device.

None of the research team members (see Section 16 for names and affiliations) have an association with private companies, organisations, or funding bodies that have interests in the project. There are no other interested parties and there are no plans of sponsoring the project for commercial interests.

15. Compensation scheme and insurance (*Erstatningsordning*)

Does not apply.

16. Team and Collaborators

The research project is situated at Center for Rusmiddelforskning, Psykologisk Institut, School of Business and Social Sciences, Aarhus Universitet. Bartholins Allé 10, Bygning 1322, 2. Etage, 8000 Aarhus C. Region: Midt-Jylland.

Research team

Center for Rusmiddelforskning (CRF), Aarhus University

Birgitte Thylstrup, PhD., associate professor. Role: PI.; Adriana del Palacio Gonzalez, PhD., associate professor. Role: Co-PI.; Mads Uffe Pedersen, PhD., professor Center for Rusmiddelforskning, Aarhus Universitet. Role: Supervisor; Sidsel Schrøder, cand.pæd., academic assistant. Role: Academic assistant; Else-Marie Elmholdt, PhD., Academic assistant.

Institut for Elektro- og Computerteknologi (ORBIT lab), Aarhus University
Henrik Kirk, associate professor Institut for Elektro- og Computerteknologi, Aarhus Universitet. Role: App design and research; Brian Danielsen, assistant professor, Institut for Elektro- og Computerteknologi, Aarhus Universitet. Role: App design and research.

Collaborating treatment centers:

1) Brydehuset Rusmiddelbehandling. Brydehusvej 12, 2750 Ballerup. (se www.brydehuset.dk). Contact person: Jesper Tofte Graabæk, Unit manager, Mail: jfj@balk.dk, Phone: +4544773737 or +4525352910. Region: Hovedstaden.

2) KABS City, outpatient treatment with focus on drugse. Walthers Vej 2, 2. sal, 2500 Valby. (see https://stof.kabs.dk/afdelinger-i-kabs/kabs-city/). Contact person: Heidi Gøtze, unit manager, Mail: Heidi.Gotze@glostrup.dk, Telefon: 29337020. Region: Hovedstaden.

3) Center for Alkohol- og Stofbehandling (CAS). Ringstedgade 14, 16 og 22, 4000 Roskilde. (https://cas.roskilde.dk/da-dk/center-for-alkohol-og-stofbehandling/). Contact person: Winnie Jørgensen, Mail: Winniej@roskilde.dk, Telefon: Tlf. 46 31 71 35.

4) Velfærd og Sundhed, Rusmiddelrådgivning Horsens Kommune. Vesterled 1, 8700 Horsens. (https://horsens.dk/Sundhed/Sundhedsfremme/Alkoholbehandling og https://horsens.dk/Sundhed/Sundhedsfremme/Stofbehandling. Contact person: Charlotte Jensen, Unit manager, Mail: chaje@horsens.dk, Telefon: 51440599.

External collaborator

Kasper Løvborg Jensen, PhD., Senior UX researcher at Google. Role: Funding co-applicant and initial research member while affiliated at Aarhus University. Kasper changed positions during an initial stage of the project focused on app development and moved to Google. In his new external position, he will not have access to data, but will be invited to participate in publications. Further, he has confirmed that he is not interested in the commercialization of the Aftercare App.

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