Pilot study: Brief psychoeducation for comorbid substance use disorders and internalizing symptoms

Scientific summary

Many emerging adults (18-30 years) with alcohol and other drug use disorders (AOD) suffer from concurrent symptoms of anxiety or depression, often referred to as internalizing disorders. The simultaneous struggle with AOD and other symptoms complicates access to treatment and may lead to weaker treatment results, which in turn may result in sub-adequate care. Thus, to alleviate this burden and improve the life trajectories of a large number of young people with AOD and internalizing disorders, we must intervene early before patterns of substance use, depression, and anxiety are established and cause disability and harm. However, the provision of good care is challenged because of the limited availability of relevant treatment options that can easily be implemented and managed in clinical practice. Considering the high risk of severe consequences across life areas for these emerging adults, it is of great importance to develop innovative brief evidence-based interventions that engage them at an early stage when they enrol in AOD treatment.

Against this background, the aim of the study is to develop and test the feasibility and acceptability of a short psychoeducational add-on intervention for emerging adults enrolled in community-based outpatient treatment for AOD in Denmark, who present with concurrent symptoms of depression and anxiety. The psychoeducational intervention aims to increase the clients' understanding of their difficulties and increase their confidence in the treatment plan and its positive outcome. To support acceptability and feasibility in clinical practice, clinicians and

clients at the participating site will be involved in both the development and testing of the intervention. An additional aim is to strengthen the clinical skills of practitioners who meet the client group for the treatment of AOD, but often lack the knowledge and resources to offer these clients the relevant treatment.

Contributions and novelty of the study

The study generates much needed knowledge and has promising potential for clinical treatment at a national and international level, and has great potential to benefit clients seeking treatment for AOD who also present with symptoms of anxiety or depression. The project will be the first to develop and test a simple, easy-to-use psychoeducation strategy for internalizing disorders, which is also easy to implement and manage in clinical practice. The involvement of clinicians and clients on-site is a considerable strength of the study, and ensures acceptability and feasibility, as well as implementation in clinical practice.

Background

Co-morbid alcohol and other drug use disorders and internalizing disorders is common

Anxiety and depression are the most frequent mental health problems across the globe (1), and co-occur with AOD at high rates. A large survey study found that people with AOD in the general population is approximately 20 times more likely to suffer from a co-morbid mood disorder than a person without an AOD, and 15 times more likely to suffer from an anxiety disorder (2). In the latest data from the Danish national monitoring system, the MAP-plan,

updated April 2021, 57% of the emerging adults aged 18-30 seeking treatment for an AOD reported a high number of internalizing symptoms.

Current psychopathology models identify depression and anxiety related disorders as "internalizing disorders", as they are characterised by painful internal experiences and negative affect (3-5). These types of disorders stand in contrast with "externalizing disorders", which are characterized by overt behavioural problems (3-5). Studies show that internalizing symptoms in adolescence are positively associated with the development of heavy alcohol use and drug use (6-8) into adulthood (9). In addition to constituting a risk factor for AOD, internalizing disorders present a significant burden on youth and adult people in their own right (1), and are associated with a substantial loss of quality-adjusted life years (10).

Among people with AOD, symptoms of anxiety or depression challenge the treatment process and result in lacking response to treatment, and low rates of remission (11, 12). Further, the presence of such symptoms at enrolment in AOD treatment are associated with a high need for psychiatric care. However accessing separate psychiatric care is often substantially delayed (13) and may even result in suicide (13). Therefore, it is highly important to address internalizing problems early in treatment for AODs, in order to improve treatment outcomes and quality of life for a large group of people.

Lack of relevant treatment options

At present, there are several options for treating anxiety and depression in people with AOD, such as pharmacotherapy (e.g., antidepressants) (14) and psychotherapy (15). However, treatment recruitment and retention still present major challenges in clinical practice, as clients

with internalizing disorders often have complex difficulties that can interfere with accessing treatment (15).

A promising approach for addressing symptoms related to internalizing disorders in clients enrolled in AOD treatment is psychoeducation. Psychoeducation refers to an intervention with systematic, structured, and didactic knowledge transfer for an illness and its treatment. Psychoeducation integrates emotional and motivational aspects in order to enable clients to cope with the illness and improve treatment adherence and efficacy, as well as quality of life (16). The approach involves a flexible strategy for adjusting the treatment to broaden the goal and perspective of treatment (17), and has shown positive response in preventing anxiety and depression amongst students (18). More importantly, psychoeducation appears to improve retention in treatment for clients with depression and anxiety (19), possibly because the approach entails role induction, where the client prepares for the type of interactions that she or he will experience during treatment (19).

Although psychoeducation is often a part of evidence-based treatment for anxiety and depression (20), it has not been examined systematically in the context of AOD. Emerging evidence shows that psychoeducation improves treatment retention among clients with AOD and co-morbid men health disorders (21). A small pre-post study with 80 clients with this co-morbidity found that most of the clients were able to complete treatment and reduce symptoms of mental illness (17). In this study, psychoeducation involved the relationship between substance use, mood, and behaviour, as well as coping skills, relapse prevention, and social support. However, the lack of random assignment in the study reduced the applicability of the results in terms of informing practice about the efficacy of psychoeducation. Further, the study did not involve focus on how collaborative partnerships between clinicians and researchers have

the potential to improve the utility, feasibility, and effect of psychoeducational interventions targeting co-morbid mental health problems in clients with AOD.

Aims

The objective of the present study is to develop and pilot test a brief, focused, psychoeducational add-on intervention for emerging adults (18-30 years) with AOD who present elevated symptoms of internalizing symptoms (depression and anxiety) who are otherwise unlikely to receive specialized psychiatric care for their mental health problems. The intervention will be developed and tested in a Danish community treatment setting for AOD. Prospective participants will be identified using eligibility assessment at the time of intake to treatment, utilising a widely used tool for assessing problem severity related to AOD in Denmark, the MAP-assessments (youth and adult versions). To support acceptability and feasibility in clinical practice, clinicians and clients at the participating site will be involved in both the development and testing of the intervention (22).

The study involves two work packages (WPs).

WP1: Development and revision of an add-on psychoeducation intervention targeting internalizing disorders (anxiety and depression) in community treatment. In order to ensure strong relevance and feasibility to clinical practice, the intervention will be developed and revised in collaboration with clinicians and clients from the participating site. Based on previous experience from the Impulsive Lifestyle Counselling project (23, 24), this intervention will take the form of a *guidebook* for clinicians to present to clients.

WP2: A randomized pilot trial testing the intervention with 40 clients in a two-arm randomized pilot study (n= 20/ per arm). The aim is to test the feasibility and acceptability of the intervention

and the procedures concerning follow-up. One arm will consist of the psychoeducation intervention developed in WP1, whereas the second arm involves a cognitive-behavioural intervention. Both arms will be matched on duration and intensity, and both client groups will be offered treatment after the two interventions at the participating site based on treatment needs.

Methodological basis: Theory of change

The study will employ methods deriving from the theory of change for services, which is based on the notion that by involving stakeholders, including consumers, clinical management, and service providers into the development of an intervention, the intervention will have the highest chance of success (25). Kotter's theory of change (26) is widely utilised in the context of healthcare, and demonstrates a high level of efficacy at multiple levels of management. It was, therefore, the model of choice for this project. Kotter organizes the change theory into three distinct phases; 1) “creating a climate for change”, 2) “engaging and enabling the whole organization” , and 3) “implementing and sustaining the change” (25). The three phases and the eight main principles that they involve are used as a guideline for the change theory in the current study, with the caveat that Kotter’s model has been designed to understand and facilitate global changes to an organization rather than incremental performance improvements (27). See the adapted model in Table 1 below.

Table 1. Theory of change

Kotter's principle		How will it be addressed in the present study?
Phase 1: Creating a climate for change	**1. Create a sense of urgency**	Highlight challenge of systems of mental health care and SUD being split between psychiatric and AOD services Highlight unwillingness/lack of resources and realistic options to work with clients with internalizing disorders
	2. Form a guiding coalition	Involve clinical manager, clinicians, and clients in development and testing of short add-on psychoeducation of internalizing disorders co-morbid with SUD
	3. Create a vision	Aim of developing an acceptable and feasible intervention for this client group that can improve treatment options, treatment engagement during the early phases of AOD treatment that may affect outcomes
Phase 2: Engaging and enabling the whole organization	**4. Communicate the vision**	Presentation of the project the entire staff at Gladsaxe Municipality at project start
	5. Empower others	Clinical manager, clinicians and clients are involved and supported at meetings and provide feedback during the entire study
	6. Create quick wins	Successful development, implementation, and testing of the trial interventions will be shared with at the participating site during the project and after the project.
Phase 3: Implementing and sustaining the change	**7. Build on the change** **8. institutionalise the change**	If the pilot testing shows that the intervention is feasible and acceptable, the Center for Alcohol and Drug Research, Aarhus University, will support the participating site and future implementation of the intervention, disseminate the results from the study, and plan a large-scale randomized trial involving multiple sites. (section Dissemination and scale-up).

In relation to phase 1 in the model, 'creating a climate for change', we are aware that organizational resistance to the project may arise. For instance, staff who are not directly involved in the study could experience an increase in workload as an indirect result of their colleagues' involvement in the project. However, the clinic will be compensated financially for the additional work related to the study with funding from the project, which might reduce this risk. Organizational resistance may also arise, because some clinicians, regardless of their role in the project, could be critical of the ideas behind the study, for example e that there are more effective ways to address mental health problems. In order to address this challenge, the study involves the active participation of both the clinical manager as well as clinicians and clients from the early phase of the study (WP1), which can increase the likelihood that we will successfully be able to navigate resistance while benefiting from important inputs from the management, clinicians, and clients. Further, the two principal investigators (PIs) of the study have already worked with the clinical manager, clinicians, and clients at the participating treatment site over a recent two-year period (2018-2020). During this period, the two PIs have developed treatment offers as well as participated in regular clinical practice at the site.

Finally, to reduce uncertainty related to study involvement, all staff members at the clinic, including administrative staff and other staff not involved in counselling or assessment (such as secretaries, nurses and healthcare assistants), will be informed of all aspects of the study, including the content and timeline of the study, as well as expected outcomes.

Methods

Setting

The project will be a collaboration between the Center for Alcohol and Drug Research (CADR), Aarhus University and the community treatment centre for AOD in Gladsaxe Municipality. Clinicians will be employed as treatment counsellors by the participating site from the existing staff at the clinic.

Karina L. Santos, the clinical manager at the treatment centre for AOD in Gladsaxe Municipality will oversee the implementation of the study and collaborate closely with the research team.

WP 1: Development of the psychoeducational intervention

In WP1, the researchers will collaborate with key clinicians to develop and revise a manual for psychoeducation drawing on the existing literature as well as experiences from the CADR from similar collaborations, including the Impulsive Lifestyle Counselling program (21, 23, 28) and the Danish method, MOVE (29). Two psychologists at the clinical site as well as two caseworkers will be involved in the development project. The senior physician of the clinic will oversee the project.

Participants

WP1: Counsellors (n=2), psychologists (n=2), researchers (n=2), and clients currently in treatment and participating in an already existing treatment group at the site for clients with serious psychiatric symptoms or a severe traumatic history, the “Individual Coping and Recovery Group” (n=6).

Procedure

The researchers will meet with the clinicians at half-day workshops to discuss and draft the guidebook.

The sessions in the psychoeducational intervention will include topics regarding the nature of internalizing symptoms and how they affect or could be affected by AOD. The starting/reference list of topics is provided in Table 2.

Table 2. Draft sessions for the psycho-educational intervention

	Internalizing disorders and substance use
Session 1	Difficult emotions – what are they, how do they affect a person, what do you recognize
Session 2	What strategies are related to trying to deal with the distress or to increasing energy, what strategies do you use, do they work
Session 3	The link between alcohol, illegal drugs, and excess medication and distress/low energy Withdrawal symptoms and internalizing symptoms as a result of substance use and excess medication.
Session 4	What strategies that you use to improve well-being will be good to keep – which should go – and which should be new
Session 5	Treatment options: what is pharmacotherapy and psychotherapy – what steps do you need to take, what can you expect from them
Session 6	Close and future steps What do you take with you from this intervention What do you think you need to keep moving forward (treatment, mindfulness, medication, trauma treatment, psychiatry etc.)

In the next step, the researchers will meet with the client group and together with the clinicians in order to present the guidebook and the ideas, and facilitate a discussion on the guidebook based on the extensive consumer experience of the group participants, most of whom have been in contact with both psychiatric care and AOD services at multiple occasions. The clients who will be involved in this process will be undergoing treatment for AOD in the Individual Coping and Recovery Group, which is currently run by one of the psychologists who is going to participate in the project. These feedback meetings will take place at the clinic with the presence of researchers and clinicians.

WP 2: Pilot trial

In the pilot trial, the clinicians involved in the study will offer one of two six-session interventions (each session lasting 1 hour) to clients at the site who fulfil the intake criteria for the study. The interventions conditions consist of:

1. Experimental condition: The psychoeducation intervention on internalizing disorders.
2. Comparison condition: Cognitive behavioural treatment (CBT) approach based on MOVE.

Participants

Newly admitted clients who fulfil the intake criteria (n=40), and counsellors (n=2).

Inclusion criteria: 1) seeking treatment for AOD; 2) between 18-30 years of age; 3) no plans to leave the area or serve a lengthy prison sentence over the next 3 months 4) score of two or above on the Map12 Internalizing difficulties subscale (30, 31) at a screening stage.

Exclusion criteria: 1) severe mental disorder (e.g. active psychosis); 2 cognitive difficulties; severe neuro-psychological state; 3) not willing/able to give informed consent to study participation; 4) does not understand/speak Danish in a way that makes treatment possible.

Procedures

During the first in-person contact, social workers and/or nurses at the participating treatment site will assess whether an individual is eligible for study participation according to the eligibility criteria. If the individual is deemed eligible, the same employee will verbally inform the individual about the trial and provide a participant information sheet. If the individual accepts the invitation and gives informed consent for study participation, the employee will collect the necessary information for randomization in an online questionnaire, which is forwarded to the CADR via an anonymous and secure email. The research team will ensure the confidentiality of this data by keeping the online questionnaire data and consent forms on secure servers.

Treatment providers

Treatment providers will be appointed by the clinic management. The caseworkers involved in the development of the workbook will also be delivering the psychoeducational intervention. The caseworkers who are to deliver MOVE will likewise be appointed by clinic management, and will be selected to have a high degree of experience and training. This is likely to introduce a bias, but is acceptable for a pilot and feasibility study.

Interventions

MOVE: A CBT/MI intervention for AOD

MOVE is a modular intervention that integrates elements of motivational interviewing with cognitive behavioral therapy for AOD (29). The intervention involves setting mutually agreed-

upon goals at the initiation of treatment followed by setting an agenda at each session, and working through topics using techniques such as cognitive re-structuring, coping skills training and role-playing, and problem solving. In accordance with the modular approach, therapists are trained and encouraged to switch to motivational approaches when a client present resistance to discussing a specific topic or expresses reservation about change.

The talk therapy aspects of the MOVE approach is closely aligned with the services already being offered at the clinic.

In the context of the current study, the clients randomized to the control condition are offered six sessions of MOVE. The approach is structured and involves clear goal definition, skills training, and a focus on understanding high-risk situations for AOD. However, the voucher reinforcement involved in MOVE is not part of the treatment in the context of the present study.

Ongoing evaluation and revision of the guidebook

During WP2, the clinicians who conduct the two interventions will meet to discuss the implementation of the two conditions with the research team and will be supervised by a psychologist at the site. This involves identifying gaps in the guidebook, adjusting wordings, and considering content that should be included or removed in the final version of the guidebook.

All assessments, as well as treatment planning and treatment sessions in the two conditions will be audio recorded. Randomly selected recordings that involve all counsellors who conducted each of the tested interventions in the two arms are coded to ensure intervention fidelity and integrity.

Randomization and blinding

Using information from the assessment interview clients are then randomized using the minimization method (32). The following four variables are used: 1) gender, 2) age, 3) type of substance use (alcohol misuse, The Low of Health Services § 141, use of opioids or sedatives, the Law of Social Services § 101 and other drugs such as cannabis or central stimulants, the Law of Social Services § 101), and 4) history of psychiatric mental health diagnosis (self-reported).

After randomization, the study participant are assigned to one of the two treatment conditions tested in the study.

Participants and clinicians cannot be blinded to the conditions that the participants will be randomized to, but the employees from CADR who will conduct the assessments at the follow-ups, and the one who analyses the data will be blinded.

Follow-up

A highly experienced research assistant from CADR will contact all participants at one month and three months after random assignment. Participants are going to be reimbursed for their participation in the interview with a 200 DKK gift certificate.

Instruments

Participants age ≥ 25 will be assessed using the AdultMap and participants age < 25 the YouthMap (33).

YouthMap/AdultMap include short validated tests that include measures of alcohol use disorders (34), drug use disorders, impulsivity and concentration, internalizing and externalizing problems, and a validated single item that identify psychiatric diagnosis and illegal activities. The YouthMap/AdultMap have been used in randomized clinical trials in

Denmark (33, 34) and will be used to screen for eligibility in the study. In the data collected during 2020-2021, 57% of clients aged 18-30 had elevated internalizing symptoms (unpublished data).

Wellbeing and Outcome Monitoring (WOM) will be used to monitor well-being and outcome. WOM will be used to monitor alcohol,drug use and wellbeing in the last seven days before each counselling session, and makes it possible to follow the individual client's well-being and use of substances across the trial period. WOM is used in several RCTs at CADR, and has been used in published research (35).

The Outcome Expectancies Questionnaire. This widely used 4-item measure assesses whether treatment seems logical and the degree of confidence that the participant has in the intervention, using a 0 (none) to 9 (very strong) scale (36-38). The total score is calculated by summing the responses on the four items. In line with previous studies, the condition will be phrased to refer to the condition under study here (i.e., "How confident would you be that this treatment would help you handling both emotional distress and substance use"). In terms of treatment, the respondents will be asked to respond based on "…the treatment plan as laid out at this point."

Mental health knowledge will be assessed with an adjusted scale developed for the study. This scale will assess participants' knowledge on internalizing psychopathology and other themes that is covered in both arms. At baseline and follow-up, all participants including possibly dropouts will answer a brief multiple-choice scale, which will be developed for the study and targets key elements regarding internalizing symptoms and AOD. A similar approach has been used as a measure of a primary outcome in a study on a prevention program that addressed both substance use, depression, and anxiety in adolescents (39). For the purpose of the present study, the scale will be developed in collaboration with the service users.

Symptoms of anxiety and depression. The Depression, Anxiety and Stress Scale - 21 Items (DASS-21) (40) a validated measure that is widely used in clinical trials, and including it in the pilot trial will allow us to test its feasibility and acceptability for scale-up studies.

Level of functioning (WHODAS-5) (41). The WHODAS-5 comprises five items taken from the WHODAS-2.0, a widely used measure of current day-to-day functioning that is highly sensitive to psychological interventions.

An Electronic logbook will be used to register the number of attended counselling sessions (including online contact in case of increased rates of covid-19), cancellations, no-shows, reminders, and cause of discharge from treatment etc.

Outcomes for pilot trial

Primary outcome. The Outcome Expectancy Rating Questionnaire (OERQ) will be administered at one-month follow-up after the first treatment session (36-38). The OERQ measures client confidence in treatment which is the key outcome of the pilot trial.

Secondary outcomes (collected at baseline, one, and three months follow-up)

- DASS-21 (symptoms of anxiety and depression).
- WHO-5 (current level of functioning).
- Knowledge about internalizing symptoms.
- Retention in treatment for AOD according to the E-Logbook.
- Days abstinent from alcohol/drugs/excess medication past month as assessed in the Adult/YouthMap.

- Acute mental health care (including acute and emergency care and unplanned hospitalizations). This information will be gathered from the clinic, patient interviews, and interviews with significant others of clients who are willing and able to identify such significant others.

Additional data

Clients from the Individual Coping and Recovery Group will contribute with their perspectives at group meetings with the researchers during the early phases of the development of the intervention, and during revision of the guidebook in parallel with the follow-up of WP2. The group meetings will focus on ways in which the psychoeducational approach can be improved concerning acceptability and feasibility.

Data collection plan

All outcome data are collected at baseline (i.e., prior to randomization, but after consent is given and eligibility is confirmed), at one month, and at three months post-randomization. The primary outcome measure will be adjusted at baseline to refer to the amount of information that participants have at this point.

Analyses

Descriptive statistics will be used to characterize the experimental and control groups in WP2. Quantitative outcomes will be compared using non-parametric Kruskall-Wallis tests. Data from group discussions will be analysed using a phenomenological framework consistent with the participatory research framework of the study (42). A CADR employee will analyse all data blinded to randomization status.

Ethical considerations

All study participants will complete an informed consent before participating in the study. All study participants will receive the same services than they would receive under normal (non-study) circumstances. This includes pharmacotherapy, as needed under the Danish legislation and public guidelines when deemed necessary by the physician at the site, in addition to access to non-pharmacological treatment services, all according to the Danish law of Social Services, § 101 or the Danish law of Health Services, § 107.

Clients who are not participating in the trial will not be negatively affected by the trial indirectly, since clinicians and management will be remunerated by funding from the project for the extra work needed to develop and test the treatment.

An adverse event reporting procedure will be put in place such that clients who reported any intention to harm themselves or others at study intake, follow-up assessments or during the trial interventions are promptly referred for appropriate support via the AOD treatment service. Ethical approval and approval of data management procedures will also be sought from the relevant authorities.

Dissemination and scale-up

Project results will be published in a peer-reviewed journal with Open-Access, a Danish report, and presented at national scientific conferences. Further, resulting knowledge will be published in national practice-oriented journals with Open-Access such as STOF (articles plus podcasts), on CADR's website, Facebook, and Twitter, and presented at practice-oriented conferences and networking activities. We will provide an easily accessible Open-Access Danish report at the

CADR webpage, as well as an Open-Access treatment manual in Danish and English of the tested treatments if they are effective.

Finally, a conference for approximately 120 participants will be held at Aarhus University for practitioners and relevant stakeholders in the mental health and AOD fields at the end of the project to present the study findings.

If the pilot testing shows that the intervention is feasible and acceptable, the CADR will plan a large-scale randomized trial involving multiple sites. The large-scale study will address many of the known limitations of the pilot trial, including non-random assignment of clinicians, statistical power, single site limitations, and longer follow-up using multiple sources, such as national registers.

If the pilot testing shows substantial problems with the acceptability or feasibility of the intervention, the CADR will collaborate with JD to develop alternative approaches for addressing internalizing difficulties in the early phases of treatment (see organisation below).

Organization

The research team consists of researchers with unique expertise that is required to conduct the study; associate professors Morten Hesse (MH), Birgitte Thylstrup (BT), Adriana del Palacio-Gonzalez (APG), all affiliated with Centre for Alcohol and Drug Research (CADR), and Jaime Delgadillio (JD), professor at Sheffield University, England.

MH and BT will be the principal investigators (PI). MH will administer the grant. MH and BT are responsible for the collaboration with the site during both WPs and for supervising the project and the dissemination of results. MH and BT have a long record on treatment research,

including method development and RCTs. Much of their research is conducted in close collaboration with clinical practice.

APG and JD have participated in the development of the study and will participate in the adjustment of the guidebook (WP1), data analyses (WP2), and scientific writings. APG has led several projects on young adults' well-being (emotion regulation, difficult life events, psychopathology), and has collaborated on CADR projects involving AOD among Danish youth. JD has conducted several clinical trials on treatment of AOD and co-morbid mental health disorders and has published on psychoeducation for anxiety and depression. JD will function as a research advisor based on his considerable experience with clinical trials conducted in real-world settings and extensive knowledge about both mental health disorders and AOD. JD will also ensure that the development and pilot will be relevant on a national and international level.

References

1. G. B. D. DIIPC. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789-858.
2. Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders - Results from the national epidemiologic survey on alcohol and related conditions. Arch Gen Psychiat. 2004;61(8):807-16.
3. Caspi A, Houts RM, Belsky DW, Goldman-Mellor SJ, Harrington H, Israel S, et al. The p Factor: One General Psychopathology Factor in the Structure of Psychiatric Disorders? Clin Psychol Sci. 2014;2(2):119-37.
4. Waszczuk MA, Eaton NR, Krueger RF, Shackman AJ, Waldman ID, Zald DH, et al. Redefining Phenotypes to Advance Psychiatric Genetics: Implications From Hierarchical Taxonomy of Psychopathology. J Abnorm Psychol. 2020;129(2):143-61.
5. Kotov R, Krueger RF, Watson D, Achenbach TM, Althoff RR, Bagby RM, et al. The Hierarchical Taxonomy of Psychopathology (HiTOP): A Dimensional Alternative to Traditional Nosologies. Journal of abnormal psychology. 2017;126(4):454-77.
6. Buckner JD, Schmidt NB, Lang AR, Small JW, Schlauch RC, Lewinsohn PM. Specificity of social anxiety disorder as a risk factor for alcohol and cannabis dependence. J Psychiatr Res. 2008;42(3):230-9.

7. Cho JH, Bello MS, Christie NC, Monterosso JR, Leventhal AM. Adolescent emotional disorder symptoms and transdiagnostic vulnerabilities as predictors of young adult substance use during the COVID-19 pandemic: mediation by substance-related coping behaviors. Cogn Behav Therapy. 2021;50(4):276-94.
8. Yan F, Costello M, Allen J. Self-Perception and Relative Increases in Substance Use Problems in Early Adulthood. J Drug Issues. 2020;50(4):538-49.
9. Jones TM, Epstein M, Hill KG, Bailey JA, Hawkins JD. General and Specific Predictors of Comorbid Substance Use and Internalizing Problems from Adolescence to Age 33. Prev Sci. 2019;20(5):705-14.
10. Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2197-223.
11. Brenner P, Brandt L, Li G, DiBernardo A, Boden R, Reutfors J. Treatment-resistant depression as risk factor for substance use disorders-a nation-wide register-based cohort study. Addiction. 2019;114(7):1274-82.
12. Ipser JC, Wilson D, Akindipe TO, Sager C, Stein DJ. Pharmacotherapy for anxiety and comorbid alcohol use disorders. Cochrane Database of Systematic Reviews 2015(1).
13. Thylstrup B, Bloomfield K, Hesse M. Incremental predictive validity of the Addiction Severity Index psychiatric composite score in a consecutive cohort of patients in residential treatment for drug use disorders. Addict Behav. 2018;76:201-7.
14. Danovitch I, Steiner AJ, Kazdan A, Goldenberg M, Haglund M, Mirocha J, et al. Analysis of Patient-reported Outcomes of Quality of Life and Functioning Before and After Treatment of Major Depressive Disorder Comorbid With Alcohol Use Disorders. J Addict Med. 2017;11(1):47-54.
15. Delgadillo J, Gore S, Ali S, Ekers D, Gilbody S, Gilchrist G, et al. Feasibility Randomized Controlled Trial of Cognitive and Behavioral Interventions for Depression Symptoms in Patients Accessing Drug and Alcohol Treatment. J Subst Abuse Treat. 2015;55:6-14.
16. Ekhtiari H, Rezapour T, Aupperle RL, Paulus MP. Neuroscience-informed psychoeducation for addiction medicine: A neurocognitive perspective. Prog Brain Res. 2017;235:239-64.
17. Chilton J, Crone D, Tyson PJ. Clinical Outcomes From a 10-Week Follow-Up Psychoeducational Program for Dual Diagnosis. J Dual Diagn. 2018;14(2):102-10.
18. Rith-Najarian LR, Boustani MM, Chorpita BF. A systematic review of prevention programs targeting depression, anxiety, and stress in university students. J Affect Disorders. 2019;257:568-84.
19. Delgadillo J, Groom M. Using Psychoeducation and Role Induction to Improve Completion Rates in Cognitive Behavioural Therapy. Behav Cogn Psychoth. 2017;45(2):170-84.
20. Buckner JD, Zvolensky MJ, Ecker AH, Schmidt NB, Lewis EM, Paulus DJ, et al. Integrated cognitive behavioral therapy for comorbid cannabis use and anxiety disorders: A pilot randomized controlled trial. Behav Res Ther. 2019;115:38-45.
21. Thylstrup B, Hesse M. Impulsive lifestyle counseling to prevent dropout from treatment for substance use disorders in people with antisocial personality disorder: A randomized study. Addict Behav. 2016;57:48-54.
22. Zwarenstein M, Treweek S, Gagnier JJ, Altman DG, Tunis S, Haynes B, et al. Improving the reporting of pragmatic trials: an extension of the CONSORT statement. Brit Med J. 2008;337.
23. Thylstrup B, Hesse M. The Impulsive Lifestyle Counseling Program for Antisocial Behavior in Outpatient Substance Abuse Treatment. Int J Offender Ther. 2016;60(8):919-35.
24. Hesse M, Thylstrup B. Manual for Impulsive Lifestyle Counselling. 2017.
25. Campbell RJ. Change Management in Health Care. Health Care Manag. 2020;39(2):50-65.
26. Kotter J. Leading change: why transformation efforts fail. Harvard Business Review. 1995;73(2):55-67.

27. Appelbaum S, Habashy S, Malo J, Shafiq H. "Back to the future: revisiting Kotter's 1996 change model". Journal of Management Development. 2012;31(8):764 - 82.
28. Thylstrup B, Schroder S, Hesse M. Psycho-education for substance use and antisocial personality disorder: a randomized trial. Bmc Psychiatry. 2015;15.
29. Pedersen MU, Hesse M, Thylstrup B, Jones S, Pedersen MM, Frederiksen KS. Vouchers versus reminders to prevent dropout: Findings from the randomized youth drug abuse treatment project (youthDAT project). Drug Alcohol Depen. 2021;218.
30. Pedersen MU, Thomsen KR, Heradstveit O, Skogen JC, Hesse M, Jones S. Externalizing behavior problems are related to substance use in adolescents across six samples from Nordic countries. Eur Child Adoles Psy. 2018;27(12):1551-61.
31. Pedersen MU, Thomsen KR, Pedersen MM, Hesse M. Mapping risk factors for substance use: Introducing the YouthMap12. Addict Behav. 2017;65:40-50.
32. Bally L, Thabit H, Hovorka R. Closed-Loop Insulin for Glycemic Control in Noncritical Care. N Engl J Med. 2018;379(20):1970-1.
33. Pedersen MU, Ellegaard KB, Frederiksen K, Pedersen MM, Karsberg S. MapPlan manual - afdækning og behandlingsplanlægning i rusmiddelbehandlingen. Aarhus: Center for Rusmiddelforskning, Psykologisk Institut, Aarhus Universitet; 2020.
34. Skogen JC, Thorrisen MM, Olsen E, Hesse M, Aas RW. Evidence for essential unidimensionality of AUDIT and measurement invariance across gender, age and education. Results from the WIRUS study. Drug Alcohol Depen. 2019;202:87-92.
35. Karsberg S, Hesse M, Pedersen MM, Charak R, Pedersen MU. The impact of poly-traumatization on treatment outcomes in young people with substance use disorders. Bmc Psychiatry. 2021;21(1):140.
36. Borkovec TD, Nau SD. Credibility of Analogue Therapy Rationales. J Behav Ther Exp Psy. 1972;3(4):257-60.
37. Beck JG, Clapp JD, Unger W, Wattenberg M, Sloan DM. Moderators of PTSD symptom change in group cognitive behavioral therapy and group present centered therapy. J Anxiety Disord. 2021;80.
38. Lindfors P, Axelsson E, Engstrand K, Storsrud S, Jerlstad P, Tornblom H, et al. Online Education Is Non-Inferior to Group Education for Irritable Bowel Syndrome: A Randomized Trial and Patient Preference Trial. Clin Gastroenterol H. 2021;19(4):743-+.
39. Teesson M, Newton N, Slade T, Chapman C, Birrell L, Mewton L, et al. Combined Prevention for Substance Use, Depression and Anxiety in Adolescence: A Cluster Randomised Controlled Trial of an Online Universal Intervention. Alcohol Clin Exp Res. 2021;45:75a-a.
40. Ali AM, Green J. Factor structure of the depression anxiety stress Scale-21 (DASS-21): Unidimensionality of the Arabic version among Egyptian drug users. Subst Abuse Treat Pr. 2019;14(1).
41. Sjonnesen K, Bulloch AGM, Williams J, Lavorato D, Patten SB. Characterization of Disability in Canadians with Mental Disorders Using an Abbreviated Version of a DSM-5 Emerging Measure: The 12-Item WHO Disability Assessment Schedule (WHODAS) 2.0. Can J Psychiat. 2016;61(4):227-35.
42. Massey OT. A proposed model for the analysis and interpretation of focus groups in evaluation research. Eval Program Plann. 2011;34(1):21-8.

Appendix 1. Time plan

Year	2022				2023
Period	January-February	March-April	May-June	July-December	January-June
Preparation					
Research visit					
Launch meeting with participating site					
Consumer group meeting					
Advisory board meeting					
Application for ethics approval and trial registration					
Development					
Development and revision of draft of treatment manual					
Production					
Production of preliminary manual					
Production of final manual					
Writing of article and report					
Follow-up interviews					

Pilot testing					
Evaluation and revision of manual					