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Document:
Project description

Official Study Title:
Physical Activity as Adjunct Treatment for Opioid Substitution Therapy

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Project description

1. Project title

Physical activity as adjunct treatment for opioid substitution therapy

2. Introduction

Hospital treatment of substance use disorder (SUD) patients is costly. In 2016, the combined costs of special treatment of SUD patients in Norway were NOK 3.8 billion (Helsedirektoratet, 2017). A shortening of the treatment time and an improved abstinence period/fewer relapses may reduce both this cost and the personal suffering of the persons involved.

Physical activity[1] is not a new intervention in SUD treatment. The Salem Program for the treatment of alcoholism was described by Murphy as early as 1970 (J. B. Murphy, 1970). The rationale of the program was that alcoholics seek relief from reality through self-imposed escapes and that they are physically unfit. The participants experienced clinically relevant gains in fitness during the three-month-long project, and the author expressed hope that this would enable them to "return to family, society and job under less stress than originally encountered, and (this) should contribute measurably to their rehabilitation". Gary and Guthrie (1972) found a positive effect in physical fitness, sleep pattern and self-esteem after 20 days of jogging, no intensity given, on a group of alcohol-dependent males. Sinyor et al. (Sinyor, Brown, Rostant, & Seraganian, 1982) found a long period of abstinence after a six-week physical training program. Murphy, Pagano and Marlatt (1986) observed a reduced alcohol intake in the exercise group relative to the no-treatment group in a group of 60 male-heavy social drinkers after an eight-week physical training intervention. Donaghy (1997) observed that three weeks of training increased physical fitness, but was unable to find any effect on maintaining abstinence levels. Donaghy is the only researcher who has verified abstinence by chemical control (Carbohydrate Deficient Transferrin, CDT) whereas the others have relied on self-report. Donaghy and Mutrie (1999) found that the use of physical training in SUD treatment could give positive results if the adherence to the program was high and the program itself was of sufficient quality and duration. Roessler (2010) found that a group of drug addicts of both sexes that performed physical training three times a week for a minimum of two months showed improvements in physical fitness, self-reported quality of life and energy level. One year after the intervention, 20 % were still abstinent and 50 % had downgraded their intake. In 2011 Mamen, Pallesen and Martinsen found improved mental health in a group of SUD out-patients after nine months of physical training together with a dedicated training contact. This training contact functioned as a motivator and guide for the participant during the project. The training contact should over time become superfluous, enabling the participant to do the training alone. The outcome in mental health mimicked the outcome in physical fitness; those whose fitness improved the most also showed the greatest gains in mental health.

This study will focus on physical activity among patients receiving opioid substitution therapy (OST). Norway still has a growing OST-population: 7 554 patients were enrolled in the therapy program by the end of 2016, an increase of 109 patients to the previous year (Waal et al., 2017). The clinical and psychological aspects of opioid dependence mean patients are not only at high risk of premature death due to overdose, but also frequently experience physical and mental health problems. Two different approaches dominate the current field of treatment; detoxification and rehabilitation on one hand and OST on the other. Drop-out and relapse are common in the former alternative, while OST usually has a lifelong treatment perspective with modest average treatment gains.

[1] Physical activity, physical training and exercise are used synonymously in this text. For a discussion of definitions, see Caspersen, Powell, and Christenson (1985).

It is therefore of interest to investigate how the use of physical training and training contacts may influence the effect of traditional treatment, physical fitness and mental health in a group of patients receiving OST. This should be done as early as possible in the therapy, but not before a patient has found the right level of medication and is on a fixed steady dose; however, the physical training program must be individualized with regard to content and point of commencement.

2.1 Impact on patient care

The research questions of this project are important in a public health perspective, as fewer relapses and longer abstinence time will benefit not only the individual but also the Norwegian health care system, as this will reduce the cost of SUD patient treatment.

SUD treatment is a prioritized area in Norway, but there is a notable lack of research to find new ways to keep people sober and at work. The research questions in this project are important in a public health perspective. The generated knowledge can be quickly applied to local treatment institutions across Norway, as the intervention is cost-effective and training contacts are already available in most areas.

The study is expected to have an impact by informing policy and clinical practice on the treatment of opioid dependence. In 2014, Helse Bergen HF took over responsibility for OST-patients from Bergen municipality. It is therefore of special interest to get an insight into possible rehabilitation measures in order to implement these in patient care. It is desired to give the best treatment based on research.

3. Objectives and goals

According to Donaghy and Mutrie (1999), there is a lack of research on the use of physical training for treating substance abuse. Most studies conducted have methodological flaws, such as lack of a control group, small sample sizes or no randomization. The control of the training has also varied; in some programs, sessions were guided by a coach/instructor and participation was registered, whereas in others the participants were free to do what they wanted. No study except Mamen, Pallesen and Martinsen (2011) reports the systematic use of heart rate recordings to quantify training amount and intensity. The type of physical training has also varied a great deal, so it is difficult to draw conclusions on the efficacy of physical training as an adjunct treatment of SUD. Read and Brown (2003) claim that exercise-based interventions have rarely been applied to the population of SUD patients, despite promising results. Even though opioid dependence is associated with many health problems and physical activity is known to provide physical and mental health benefits, “it remains to be rigorously tested in an opiate agonist population” (Weinstock, Wadeson, & VanHeest, 2012, p. 357).

This randomized controlled trial (RCT) is based on the hypothesis that physical activity improves cognitive functioning. The aim is to test the efficacy of physical activities for OST-patients, measured in terms of improvement of physical fitness, cognitive functioning, drug dependence and experience of improved quality of life.

The objectives of this study are to investigate (1) how physical activity affects the patient's physical fitness, and (2) how physical activity influences psychosocial and cognitive functioning.

Physical activity has a good cost-benefit ratio, is relatively easy to implement, and can help patients on several levels: They can improve their physical and mental health, as well as increase their quality of life. Many OST-patients have reduced physical health. Exercise can support them in terms of comorbidity, and to get in better physical shape. Decent physical health can prevent and improve diseases and disorders, and better shape can strengthen self-esteem and a sense of achievement. This, in turn, can increase the likelihood of successful treatment. Additionally, exercise can contribute to a change of settings, i.e. OST-patients change from a substance use/treatment environment to a sports milieu. They can become part of a community that is interested in a healthy lifestyle. Their attention can change from illness to health, both in terms of body and mind.

Another goal is for physical activity to be established as a permanent offer for all OST-patients, and that the research can strengthen and defend the existence of already established initiatives such as *Arna Aktiv* (Arna active) and *Fritid med bistand* (leisure assistance program). The use of training contacts can contribute to a lower threshold for participation in sports and aftercare services. This contact will also provide a sense of security to a vulnerable and exposed group.

The PhD candidate is responsible for the execution of the RCT. They will recruit patients, carry out the data collection and analyze the results.

4. Feasibility

4.1 Study design, choice of methodology and analysis

The number of participants is estimated at 60, recruited from OST-facilities within the Helse Bergen area. To be eligible for admission to the study, participants must (a) sign a written informed consent to participate in the project, (b) be participating in the LAR[2]-program, (c) be on a steady fixed dose of medication and (d) be at least 18 years of age. Exclusion criteria are pregnancy in women and having joined the LAR-program for less than three months ago. Enrolment in the project will be a consecutive process until the required number of participants is recruited. Participants will be randomly selected for the intervention group or the control group. The intervention group will be given their training contacts (Skrede, Munkvold, Watne, & Martinsen, 2006). Together they will decide on a training schedule that suits the individual with regard to frequency, amount and type of training. Central aspects are user involvement and individual adaptation. All training programs have in common that they include endurance and strength exercises and that the intensity will increase during the intervention period. A representative group, who will not be given an intervention, serves as the control group. The project organizer/PhD candidate will be in touch frequently with members of the control group in order to keep them motivated to stay on the waiting list and to offer social contact. The participants will also answer a Likert scale question that documents the amount of physical activity and drug use the past fortnight.

In this study, participants with particular characteristics that predispose them to have certain outcomes will be selected. This does not apply to the eventual participants since they will be randomly selected into the experimental and the control group. However, it does apply to the general selection of participants, the recruitment. Population choice is restricted since only patients interested in physical activity will participate (recruitment bias). Participation is voluntary to ensure that patients complete the trial period and thus minimize the dropout rate. OST-patients not interested in physical activity are not excluded from the project, but will most likely lack the motivation for activity/training over a longer period of time, and will therefore not wish to participate. Hence, it is difficult to obtain a representative sample of the OST-population, which will result in poor generalizability of the results. The degree to which the results can be generalized is limited; the study's results are not applicable to other groups. The selection criteria allow only a generalization to groups with similar presuppositions. Motivation is perhaps the main factor in this respect. It supposedly confines the treatment to groups that are motivated. Forcing SUD-patients to be physically active will most likely result in a different outcome. That means that the findings might only apply to patients who want to be physically active. The sample is, in this regard, not representative of the whole population. This is something one has to keep in mind when implementing training into addiction treatment. It might only be useful for patients with certain presuppositions, not for the whole population of OST-patients.

Nevertheless, the reason for only working with patients who communicate an interest in study participation is that people not interested in exercise probably will show low adherence, and adherence is a prerequisite for treatment success. Physical training is not a "quick fix" for everybody; motivation to complete the training is decisive (Donaghy, 1997).

[2] LAR = *Legemiddelassistert rehabilitering* (Opioid substitution therapy)

The number of patients interested in exercise might not be so low after all: SUD patients usually express an interest in physical activity (Powers, Woody, & Sachs, 1999), so the offer of such treatment might be welcomed.

Drop-outs, either from the intervention or the control group, may cause problems for the study. If too many participants drop out and new participants cannot be recruited, the number might get too small for the results to be statistically relevant. The number of 60 participants makes this a particularly relevant issue here. Selection and mortality are chief concerns for any clinical trial, and a particular concern in samples of patients with mental illness and/or addiction. Thus, this study utilizes a prolonged recruitment period, also beyond the desired number of participants, and will offer minor incentives to participants (t-shirts, sports water bottles etc.). On the other hand, the study has to be feasible, and it would not be a realistic assessment of feasibility to presume that many more than 60-80 participants of the target group will complete the trial.

Mortality leads to the fact that the outcomes of the experiment are unknown for the participants who drop out. Reasons for drop-outs and proportions for each group will be reported. The drop-out event itself can give important information, especially in the event of many drop-outs. It might also possible to compare those who drop out with those who continue, in terms of the outcome.

Group sessions give higher compliance, which in turn is important for the outcome for the participant, either improvement in physical fitness or substance use control (Richard A Brown et al., 2009; R. A. Brown et al., 2010; Donaghy & Mutrie, 1999; Read & Brown, 2003). The use of training contacts is therefore of interest as it increases the social element of the training.

In order to limit the number of drop-outs from the control group, the participants of this group will be given the opportunity to receive the intervention after three months. Thereby they will also get the chance to benefit from physical activity and to do what motivated them to participate in the project in the first place. Otherwise a resentful demoralization, they might develop once they realize that they are in the control group, could influence the psychosocial functioning and self-efficacy.

Another threat to internal validity is that it will not be entirely clear which part of the treatment might give positive, or negative, results. It will not necessarily be the controlled parameters that contribute to the highest degree to the outcome of the trial. We might not be able to conclude that changes in the independent variable (training) caused the observed changes in the dependent variables (physical fitness and cognitive functioning). In fact, it is likely that confounding variables (side effects of the intervention) influence the results in certain ways and degrees. The treatment is very complex, and it will not be possible to draw simple conclusions or to identify the exact cause. Extraneous variables, rather than the independent variable, may explain the outcome of the study. I.e. physical activity alone might not be responsible for positive treatment results. They might be attributed to the social element of the study. Positive feedback from others or from training contacts can strengthen the self-confidence. This, in turn, can lead to improved physical performances. Due to formerly experienced stigmatization OST-patients often avoid social arenas like sports clubs, training centers etc. Working with a training contact can make them feel less vulnerable and help them overcome this threshold. Another contributory fact is the help, or support, of a contact person.

Although the study might not be able to conclude what exact variable leads to positive effects in regard to physical activity as an adjunct treatment, it is nevertheless important to examine whether it has positive effects at all. Physical activity has been shown to be a useful companion to other types of treatment, is cost-effective compared to other treatments, and has few side-effects (Richard A Brown et al., 2009). Furthermore, it improves mental health by reducing depression, trait and state anxiety and other psychiatric problems (Richard A Brown et al., 2009; Mamen et al., 2011; Palmer, Vacc, & Epstein, 1988; Read & Brown, 2003). These are reasons why many institutions already offer physical activity as part of their treatment (Kremer, Malkin, & Benshoff, 1995; Malkin, Voss, Teaff, & Benshoff, 1993). All in all, it is perhaps more important to deepen the understanding of how physical activity can work best in the cases where it does work, instead of establishing "proof" of statistically significant and generalized causation.

Testing consists of two parts: A battery of cognitive and psychosocial assessments and an assessment of physical variables. The following paragraphs demonstrate the different methods and measures that will be used in the project.

An endurance test (ventilatory threshold/VO_{2max}) will be given. There will be strength and agility exercises as used by the KAN study (The Norwegian Directorate of Health/Norwegian School of Sport Science)[3]: Push-ups and the Stork Balance Test. The push-up test is a maximal test where the participants perform a maximum number of correct push-ups. The balance test is a timed test where the goal is to keep one's balance as long as possible.

Ventilatory threshold test: This test is performed on a treadmill. The participant starts without warming up on the starting load after being explained the test procedure and how to record the rating of perceived exertion (RPE) (Borg, 1970): stage duration 1 min, start load 6 km/h, gradient angle 5 %. Increase in load: 1 km/h. Oxygen uptake and heart rate are continuously measured during the test at 10 s intervals with the help of a metabolic cart, MetaMax II (Cortex Biophysik GmbH, Germany) and a Polar heart rate monitor (Polar OY, Kempele, Finland).

Strength and agility tests: Push-ups with a straight body, from chest touching the floor to fully extended arms. The Stork Balance Test involves keeping one's balance on one leg for as long as possible; once with open and once with closed eyes. These tests are chosen because of ease of administration and the availability of such data for comparison.

Test equipment: Treadmill: Sole Incline TT8
Metabolic analyzer: Cortex MetaMax II
Software: Cortex MetaSoft 1.11.05
RPE: Borg RPE scale (1970)

The change in endurance fitness will be evaluated on the basis of the VO_{2max}, where workload at threshold point will quantify the endurance capacity. The change in the number of push-ups and the balancing time will be used for the strength/agility measures.

The study will investigate changes in satisfaction with life, executive functions and psychological distress over a period of 12 months. A battery of cognitive and psychosocial assessments will be used (a modified version of the one used in the "Executive functions in patients with substance use disorders: effects on the course of treatment" project (Stayer study)[4]):

- National Quality Register[5]
- AUDIT-E - Alcohol Use Disorders Identification Test (Extended)
- DUDIT-E - Drug Use Disorders Identification Test (Extended)
- Symptom Checklist-90-R (SCL-90–R)
- Satisfaction With Life Scale (SWLS)
- Pittsburgh Sleep Quality Index (PSQI)
- Connors Continuous Performance Test (CPT 3)
- Behavior Rating Inventory of Executive Function - Adult Version (BRIEF-A)
- Iowa Gambling Task (IGT)
- Biweekly status update on outcome goals

Executive functions will be assessed by the Behaviour Rating Inventory of Executive Function-Adult self-report version (BRIEF-A), psychological distress by the Symptom Checklist-90-R (SCL-90-R), and satisfaction with life by the Satisfaction With Life Scale (SWLS). Substance use will be assessed

[3] *Kartlegging av fysisk aktivitetsnivå, helserelatert fysisk form og determinanter for fysisk aktivitet hos voksne og eldre i Norge* (Survey of physical activity, health-related physical form and determinants of physical activity among adults and elderly in Norway).
[4] The Stayer study is a prospective longitudinal cohort study of a group of SUD patients who started a new in-patient or out-patient treatment sequence for SUD, within the area of the local health authority Stavanger University Hospital.
[5] National Quality Register for the treatment of harmful use of/addiction to drugs

by self-reports on the Alcohol Use Disorders Identification Test (AUDIT-E) and the Drug Use Disorders Identification Test (DUDIT-E). Changes in test scores will be used to quantify the development of the mental aspects of health.

The first meeting will be between a potential participant and the project organizer. In this meeting, the project organizer will inform about the study and go thoroughly through the consent form. The participant will then sign a written consent about voluntary participation in the study.

Next, a baseline assessment will take place. The participant and the project organizer will meet at the organizer's office to complete the battery of cognitive and psychosocial assessments. Afterwards, they will meet at the test lab at Solli Hospital in order to execute the physical tests.

After testing is completed, the participant will be informed whether they are part of the intervention or the control group. The organizer will call a colleague who keeps a list generated by the approved randomization program "Random Allocation Software 2.0" (Saghaei, 2004) securely locked away. The project organizer does not have any knowledge about the order and can thus not influence the randomization process.

Participants in the intervention group will start with the introductory meeting. The introductory meeting will enable the participants and training contact to get to know each other. Good personal chemistry is important, as they will spend much time together in the coming months. It is useful to note down interests, training ambitions and self-evaluated physical fitness level at this meeting, as this will help in the planning of the training. Training with a training contact is the primary intervention. Concerning the practical procedure, training contact and participant will meet for three hours a week[6] (in either two or three sessions) for 12 weeks. The training contact will motivate and guide the participants. One goal is to enable the participants to conduct training alone by the end of the project. Training content can be chosen by the participant (to increase the likelihood of study completion) but should be feasible and consist of a combination of aerobic and muscle-strengthening activity. Training intensity should be increased gradually, to avoid injuries and create motivation. All training sessions will be recorded in a diary, where the type of exercise, time, intensity and other remarks are noted. Both the participant and training contact should make such recordings to make the documentation as complete as possible.

After the 12 weeks intervention period another testing will be conducted. This post-measurement will include the same tests as those performed at the baseline measurement.

Participants who were selected into the control group are on a waiting list for 12 weeks and receive treatment as usual. After three months they will go through the assessment procedure again. Subsequently, they will receive the same intervention as the original intervention group. They, too, will get a training contact for 12 weeks and will be tested afterwards.

As a follow-up, all participants will be assessed 12 months after baseline measurement. It is important that the post-measurement tests are carried out identically to those at pre-measurement, in order to obtain a valid result.

All sensitive data (digital and non-digital) generated is confidential and will be treated according to the standards set by the Norwegian Data Inspectorate (*Datatilsynet*) and in compliance with the Health Research Act and the Personal Data Act.

Data generated in this project will mostly be on interval or ratio level (whether the rating of perceived exertion is ordinal or interval data will not be discussed here). To express group results, the mean will serve as a measure of the central tendency, with the standard deviation expressing the spread of results within the group. If useful, the standard error of the mean (SEM) will be used to express

[6] Based on the WHO's recommended levels of physical activity for adults aged 18 - 64 years (http://www.who.int/dietphysicalactivity/factsheet_adults/en/)

the accuracy of the mean value. If results are highly skewed (skewness > 1.5), a log transformation and geometric mean will be used together with a 95% confidence interval to express central and spread tendencies. To compare results over time, an ANOVA/t-test of repeated measures will be performed with a Sidak/Holmes post hoc test. Group comparisons will be made with an ANOVA/t-test for independent groups. If the test of normality should fail (Kolmogorov-Smirnov with Lillienfors correction), the corresponding non-parametric tests will be used, i.e. the Wilcoxon-Mann-Whitney Rank Sum Test for independent t-tests and ANOVA on rank for repeated measures (Tukey post hoc). Level for statistical significance will be set at the traditional $p \leq 0.05$. Effect sizes will be calculated according to Cohen (1988) with the help of an online effect size calculator (the CEM effect size calculator, Centre for Evaluation and Monitoring, Durham University, Durham, United Kingdom: http://www.cemcentre.org/ evidence-based-education/effect-size-calculator). An effect size of ≥ 0.5 will be considered clinically relevant (two-sided). If there is a need for building indexes of different types of scores, Z-scores will be used. The statistical power of 0.8 can be reached with at least 10 subjects in two groups, based on previously published data on fitness development and depression score. Target recruitment is nonetheless set higher than this with n = 30 in each group.

4.2 Organization and collaboration

The project is affiliated with the Regional Centre for Alcohol & Drug Research (KORFOR) at Stavanger University Hospital. KORFOR is a research and competence centre, and the hub in a regional network organization of clinical and research centres in Western Norway, established in 2007 and financed by the Western Norway Regional Health Authority. The objectives of the centre and the network organization are to promote and implement alcohol and drug research projects (currently organized as nine PhD projects and nine other projects), education and other dissemination of research-based knowledge, and to contribute in the development of methods and organization of alcohol and drug treatment.

The project manager is Sverre Nesvåg, PhD, Research Director, Centre for Alcohol and Drug Research, Stavanger University Hospital (KORFOR). The main supervisor is Asgeir Mamen, PhD, Sogn og Fjordane University College/University College of Health Sciences, Campus Kristiania. Ståle Pallesen, Professor, PhD, Department of Psychosocial Science, University of Bergen and Linn-Heidi Lunde, psychologist, PhD, Haukeland University Hospital, University of Bergen will act as co-supervisors. The University of Bergen will administer tasks related to PhD courses and thesis defense according to a separate agreement. The physical tests will be conducted at Solli District Psychiatric Centre, Solli Hospital.

Collaborating partners:

- Centre for Alcohol and Drug Research (KORFOR), Stavanger
- Section LAR (OST), Department of addiction medicine, Haukeland University Hospital (Christian Ohldieck, Head of section)
- Arna Aktiv, Bergen commune (Arna active offers sports activities for OST-patients)
- Psykiatrialliansen (low threshold offer for people affected by mental disorders that provides a large range of physical activities)
- Solli Hospital
- Sogn og Fjordane University College, Faculty of Teacher Education and Sport, Sogndal
- University College of Health Sciences, Campus Kristiania, Oslo
- Queen Margaret University, School of Health Sciences, Edinburgh, UK
- Institute of Biomedical and Life Sciences, Faculty of Medicine, Glasgow University (prof. emeritus Marie Elizabeth Donaghy)
- Hordaland Idrettskrets (regional sports confederation)

4.3 Budget

The main expenditure of the project will be:

- Expenses for the training contacts:
  NOK 6 300 per 36 training sessions/participant

40*6 300 = NOK 252 000
Expenses incl. drop-out and other expenses for training contacts ca. NOK 500 000
Received fund from the Norwegian Directorate of Health: NOK 100 000
→ NOK 400 000

- Expenses for software and licenses: NOK 30 000
- Expenses for advertising/recruitment and incentives: NOK 15 000
- Expenses for equipment (medical and technical): NOK 30 000

This gives a total budget of NOK 475 000.

4.4 Plan for milestones and dissemination

2018: Clinical trial fieldwork
2018-2019: Clinical trial data analysis, article writing & submission, PhD program courses, conference attendance
2020: Remaining PhD program course points, PhD thesis submission and -defense

	2015-17				2018				2019				2020			
Apply for PhD admission	✓															
REK application	✓															
Preparation, updating (theory and research)	x	x	x	x	x	x										
Develop project protocol	x	x	x													
Establish a contract for supervision	✓	✓														
Doctoral courses in theory of science and ethics		✓														
Doctoral courses in quantitative methods							x	x								
Analyses	x	x					x	x	x	x						
Prepare and write first article					x	x	x	x								
Data collection second and third article						x	x	x	x	x	x	x				
Prepare and write second article								x	x	x	x					
Prepare and write third article										x	x	x	x			
Write report and prepare disputes														x	x	x

Table 1: Work schedule

Results from the project will be written in the form of manuscripts for publication in international peer-reviewed journals and presented at international scientific congresses such as those arranged by the European College of Sport Science and the American College of Sports Medicine. The interest group *"Nasjonalt nettverk for fysisk aktivitet innen psykisk helse & rus"* (National network for physical activity in mental health & substance use) organizes annual meetings where experiences from this project may be presented. This group is especially important to reach as they are motivated to use physical activity and have considerable clinical experience of using physical activity with SUD patients.

The project will generate important data and in such enable a number of publications for the PhD degree. The following articles have been planned:

1. Systematic literature review: Physical activity in opioid substitution therapy.
2. Physiological effects of physical training for patients in opioid substitution therapy.
3. The effect of physical training on trajectories and treatment outcome for patients in opioid substitution therapy.

4.5 Plans for implementation

The distribution of acquired knowledge will be implemented in the following settings: Presentation of preliminary findings during the project period in national and international meetings and conferences, submission of articles in peer-reviewed international journals and communication of results through Helse Bergen HF contacts in media and management.

For the nationwide implementation of the results of Stayer II, KORFOR will cooperate with the national expertise service *"Nasjonal kompetansetjeneste TSB"* (National competence service of interdisciplinary specialized addiction treatment). A national professional network for the dissemination and implementation of knowledge to the relevant clinical environment has been established and a corresponding implementation strategy will be adopted in this case.

5. User involvement

The Department of Addiction Medicine at Haukeland University Hospital has established its own panel to ensure that knowledge from users and their relatives is heard. The so-called "ruspanel" cooperates with the *RIO Rusmisbrukers interesseorganisasjon* and *proLAR Nett* (interest groups), among others. User experience is necessary to develop good services. Therefore, AFR receives support from people with experience in the form of various working groups and permanent committees, as well as in research and competence building. Within the field of mental health and substance use, two user panels have been established: the SUD-panel and the working group for mental health and substance use. These panels are invited to collaborate on the project.

Committed individual users and user organizations in the drugs field were among the initiators of Stayer study. Users experience great benefit and relevance of the results is now emerging in Stayer I. Individual users and user organizations have come with ongoing input concerning the measures and methods that should be tested in Stayer II to strengthen the cognitive, motivational and social improvement processes by change or stop in the use of drugs. Patient organizations will also be actively involved in the various sub-projects, and user organizations want to contribute to the dissemination of research results. To get a more predictable and systematic involvement of users in the project, the already involved users and user organizations, and possibly some new, will be invited to participate in a separate user advisory board for Stayer I and II, led by a key representative of *Rusmisbrukernes interesseorganisasjon* (Substance users interest organization).

This study will work together with *Arna Aktiv*, a municipal program that offers physical activity to OST-patients, and *Psykiatrialliansen*, an organization that engages in physical activity for people affected by mental disorders. OST-patients that have been part of the program will contribute to the study with their own user experience and knowledge of the patient group.

6. Ethical considerations

Approval from the Regional Ethical Committee is obtained for the study. Participation will be voluntary. SUD patients are a vulnerable group, so special care will be taken to make sure that the information and project ideas are clearly presented and understood. The Helsinki Declaration for medical research will be the foundation for research ethics. Signed informed consent will be presented, stating that the participants may withdraw at any time without giving any explanation or having to face restrictions in their present or future treatment. All participants will have anonymity as the results are to be stored with only a code number, and the code key will be kept safe by the research director. The fact that some SUD patients may have commutable diseases, such as hepatitis or AIDS/HIV, will be an important factor in the planning of the protocol, with an emphasis on the cleaning of equipment and discarding of waste.

The recruitment of the subjects will be in accordance with the gender balance in the main population. If feasible and desired, the participant will have a training contact with the same sex. Provided a

sufficient number of female participants are recruited, gender-focused research questions will be investigated and disseminated if findings are robust and of scientific value.

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