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The RESCueH Programme: Testing New Non-Pharmacologic Interventions for Alcohol Use Disorders: Rationale and Methods

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Key Words
Alcohol use disorders · Practice-near research · Non-pharmacologic treatment

Abstract
Excessive alcohol consumption is one of the most important lifestyle factors affecting the disease burden in the Western world. The results of treatment in daily practice are modest at best. The aim of the RESCueH programme is to develop and evaluate methods, which are as practice-near as possible, and therefore can be implemented quickly and easily in everyday clinical practice. It is the first clinical alcohol programme to be transatlantic in scope, with implementation in treatment centers located in Denmark, Germany and the US. The RESCueH programme comprises 5 randomized controlled trials, and the studies can be expected to result in (1) more patients starting treatment in specialized outpatient clinics, (2) a greater number of elderly patients being treated, (3) increased patient motivation for treatment and thus improved adherence, (4) more patients with stable positive outcomes after treatment and (5) fewer patients relapsing into harmful drinking. The aim of this paper is to discuss the rationale for the RESCueH programme, to present the studies and expected results.

Introduction

Alcohol problems are often progressive and debilitating, and have recently been identified to be the overall most harmful drug, with heroin and cocaine in second and third place [1]. The World Health Organization has reported excessive alcohol consumption to be the second most important lifestyle factor (after tobacco use) affecting the overall disease burden in high-income countries [2]. Alcohol is a significant cause of non-communicable diseases [3].

Given the associated increased morbidity, alcohol problems represent a major economic burden for society.

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The Alcohol in Europe Report estimated that the direct costs associated with alcohol accounted for 1.3% of the European gross domestic product, while the indirect costs, such as loss of working-life years, are twice that [4]. Costs related to alcohol dependence add up to EUR 1,591–7,702 per patient in hospital costs alone [5].

Despite the magnitude of the problems caused by alcohol use disorders (AUDs), current management and therapeutic strategies for patients with chronic or severe alcohol dependency either suffer from low effectiveness or are not implemented [6, 7].

Among people with mental disorders, the disparity in numbers between those who suffer and those who actually receive treatment is vast, with the largest treatment gap existing among people with alcohol dependence. In Europe, 92% of these potentially treatment-requiring patients are not offered treatment [8].

In February 2011, the Lundbeck Foundation contacted leading researchers at the Unit of Clinical Alcohol Research (UCAR) at the University of Southern Denmark with a view to support clinical alcohol research in Denmark. After a meeting with the Foundation's officials, a research group consisting of Danish, German and US alcohol researchers was established (RESCueH research team; online suppl. appendix I, see www.karger.com/doi/10.1159/000447398).

Over the next 2 years, the group met regularly; 5 studies were planned and protocols were prepared. The 5 studies, described in a comprehensive research programme operating under the acronym RESCueH, have the following objectives:

The Relay Study: better recruitment of patients to treatment, as only a minority of alcohol-dependent drinkers currently receive treatment.

The Elderly Study: individual treatments geared to individual needs, reflecting the heterogeneity of alcohol-dependent patients.

The Self-match Study: greater patient involvement in treatment, since active involvement in treatment decision processes is essential for compliance.

The Cue Exposure Study: preventing relapse, as a return to harmful drinking is a common problem.

The Healthy Lifestyle Study: encouraging a healthy lifestyle, which may improve compliance in treatment and prevent relapse.

The research programme represents a collaboration involving psychiatry, psychology, biostatistics and health economics. In addition, it is the first transatlantic clinical alcohol programme to be implemented, spanning treatment centers located in Denmark, Germany and the US. The programme encompasses outpatient treatment facilities and somatic hospitals and will include 3,000 patients with AUDs. Online supplementary appendix I details the principal investigators, other research staff and the participating centers.

Rationale

Is There a Need for Trials of New Non-Pharmacological Interventions?

There have been many well-conducted randomized controlled trials (RCTs) concerning treatment of AUDs. Several comprehensive reviews have shown that there are specific effects of several types of well-described behavioral therapeutic interventions [9–11]. Thus, there is a good basis for providing evidence-based treatments in daily practice. However, there is a significant gap between what research shows and the treatment given in daily practice [7]. Moreover, the therapeutic strategies commonly used in specialized treatment institutions are often unsystematic, ineffective and insufficiently targeted to the specific needs of the broad and heterogenic group of alcohol-dependent patients [12, 13].

But why is the same effect not achieved in everyday practice as in research programmes? A major reason is that RCTs do not include the same patient groups as those encountered in everyday practice [14]. In RCTs, patients with medical conditions, mental disorders and a lack of compliance/motivation are often excluded from participation [15]. This lack of inclusiveness means that only 20% of patients in the RCTs represent the patients typically encountered in daily practice [14]. The therapists in routine treatment facilities meet precisely those patients who lack motivation and have medical and comorbid mental disorders or drug problems – factors that could have a negative impact on the effectiveness of treatment. In consequence, therapists find that their results fail to match the research results, and this may inhibit the adoption of evidence-based treatments [16]. It may also mean that politicians and administrative decision-makers will be less likely to recommend and pay for evidence-based treatments when they fail to produce substantial improvements in treatment results in everyday practice.

Another significant problem is that of achieving standardization of treatment and ensuring that therapists master it. For RCTs, manual-guided treatment is the norm. It is performed by highly trained therapists who receive regular supervision. The individual therapy ses-

sions are videotaped and coded in order to ensure fidelity. However, it is not known whether the therapists' expertise is retained when these activities cease [13]. The type of training received by the therapists in RCTs is often time-consuming and expensive, and it would be difficult to provide all therapists with this training in everyday life. Thus, it is unclear how the therapists' competence can be ensured, given their varying degrees of educational background, and it is doubtful whether all of them can acquire and retain the expertise shared by therapists participating in RCTs [6].

One last problem with the RCTs is the comprehensive analytical procedures at treatment initiation and at subsequent follow-ups. In some studies, the analytical procedure and the many follow-up interviews are virtually interventions in themselves and may contribute to the blurring of the active ingredients of the intervention under investigation.

The RCT is the gold standard for the evaluation of new therapeutic interventions since, given its enrolment of well-defined patient groups, the high assurance that the treatment being investigated is actually delivered, the fact that analysis is based on detailed evaluation instruments and that any differences between the groups are believed to be causal, its design ensures a high degree of internal validity. RCTs are also known as efficacy trials and are, accordingly, implemented under optimal conditions with the aim of maximizing internal validity. This is in contrast to effectiveness trials, with their focus on everyday clinical situations [17].

Methods

General Features of the RESCueH Design

The aim of the RESCueH programme is to develop and evaluate new non-pharmaceutical treatment methods that are as practice-near as possible and, hence, can rapidly and easily be implemented in everyday clinical practice. We have, therefore, chosen to conduct the studies as pragmatic RCTs, deploying methods from both RCT and naturalistic studies [18].

In all the studies, the exclusion criteria are few, and comorbidity or co-medication is allowed. This means that the enrolled patients are representative of those treated in daily practice.

The enrollees are randomized to the individual studies' interventions and control groups. We have opted for randomization since conventional statistical methods generally fail to overcome confounding by indication [19]. Such analyses are unable to control for confounders (e.g., the staff's opinion as to which treatment should be offered to the individual patient), which may be critical to the outcome of a given intervention. RCTs take account of the unknown confounders since randomization is expected to distribute potential confounders equally between intervention and control groups.

The therapists participating in the studies are recruited from the outpatient clinics' regular staff. There will be staff training as well as supervision of the individual interventions.

In most of the RESCueH studies (except the Elderly Study), the initial assessment is conducted by regular staff who are trained in the assessment instruments, and co-ratings are carried out. Few follow-up interviews are carried out.

The interventions are simple and often the need for training is fairly limited. In several studies, we compare the new intervention with treatment as usual (TAU), which also has a treatment effect. This leads to a low effect size in the relevant studies, thereby increasing the need for the enrolment of many patients in order to establish an effect of the intervention. In light of this, we have chosen to conduct several of the studies as multicenter studies, including 2 or more centers.

In the Self-match Study, the Cue Exposure Study and the Healthy Lifestyle Study, the primary outcome is to reduce alcohol consumption, which as a minimum, meets the recommendations of the Danish National Board of Health (maximum 14/21 drinks/week for women/men, with one drink containing 12 grams of pure alcohol). In the Relay Study, the primary outcome is the reduction of healthcare costs as an indirect indication that patients have reduced their alcohol consumption. In the Elderly Study, the primary outcome is abstinence or blood alcohol content ≤0.5 at any given time.

In all the studies, we have selected a significance level of $\alpha = 0.05$, but we are clear to point out the differences between the interventions, and the control groups are large enough to affect whether alcohol therapists develop an interest in teaching and applying the new methods in daily practice. In a study, Miller and Manuel [20] have demonstrated that healthcare providers are motivated to do this if there is a 10% increase in the proportion of patients who are abstinent or who reduce their alcohol consumption to the above-mentioned recommendations. By continuous measures, the study showed that therapists would require a halving or doubling of outcome variables. We have chosen to adopt the results of the study and

made power calculations based on these, disseminating the results with an indication of those differences.

For several of the studies, we have included cost-effectiveness evaluations of the interventions, which may influence decision-makers in determining whether to implement the developed interventions in practice.

Treatment Processes (Training, Supervision, Manuals and Quality Control)

The experimental interventions in the studies are made as simple as possible. Staffs are trained in the intervention method, typically by participating in a 2–5 days course, followed by supervision by an experienced project coordinator and expert in the experimental intervention. The core interventions in the studies are manualized in a very simple way as far as possible. In situations where it might be helpful, visual reminders such as brief scripts are developed for the staff, and written on 'pocket cards' that are easily accessible during the daily routine. That is the case in the Relay Study. When the interventions in the studies are particularly demanding and the need for uniformity in delivery crucial, the interventions are systematically recorded and regularly monitored by research staff. This is the case in the Self-match Study and the Elderly Study. Monitoring the interventions by means of new technology is used when at all possible. This is the case in the Healthy Lifestyle Study by means of heart rate monitors, and in the Cue Exposure Study by means of a mobile application.

Financial and Economics Evaluation

The financial costs associated with the implementation of the interventions in Danish health and social care are estimated in every case. Costs are estimated for a 1-year period of the intervention, with cost models designed to extrapolate to 5-year periods for financial planning, budgeting and priority setting. Almost all cost data are extracted from the Danish population registries at Statistics Denmark and health data. The health cost database, in particular, providing unit, procedure and intervention costs data at civil registration number levels, will be useful, enabling efficient and valid data collection both retrospectively for baseline cost data in all intervention groups and prospectively for pre- and post-intervention cost data collection in the various groups. Some specific programme cost data has to be collected ad hoc and some health and social care data has to be retrieved from local municipality registries. Cost differences between interventions are tested (bootstrapping tests with difference-of-differences). For some interventions, for example, the Cue Exposure project, cost models are both more detailed and supplemented by cost-effectiveness analysis, relating cost differences to net changes in outcome parameters.

Sample Size and Power Analysis

The size of each study has been determined based on the number of patients needed to ensure at least 80% power, in order to detect the relevant changes in the primary outcomes of each study when testing with a significance level of 5%. For both the quantitative outcomes (Relay, Self-match and Healthy Lifestyle Studies) and the categorical outcomes (Elderly and Cue Exposure Studies), we used classical power calculation formulas to compute the sample size, based on the desired value of power and detection of minimum relevant difference.

Randomization and Statistical Analysis

For the Elderly, Self-match, Cue Exposure and Healthy Lifestyle Studies, we employ an urn design when randomizing patients to treatment groups [21]. The urn design forces small-sized trials to be balanced but approaches complete randomization as the trial's enrolment progresses. This will not only allow us to obtain realistic results from small samples but ensures that the randomization is less vulnerable to experimental bias compared to more classical randomization procedures. Studies across multiple centers are randomized within each center such that treatments appear as homogeneous as possible across centers and/or countries. For the Relay Study, a conventional complete randomization procedure was used.

The statistical analyses of the data will vary greatly from study to study since there are substantial differences in the experimental designs, available data and hypotheses across the studies. Generally, however, regression modeling (including multiple linear modeling, logistic regression modeling and random effect/generalized linear mixed modeling) will be used to analyze the data and to correct for potential confounding. In all tests, $\alpha = 0.05$ will be chosen as the level of significance.

Summary of the RESCueH Studies

The RESCueH studies are set to run over a 6-year period and will be coordinated by UCAR. Set out below are brief summaries of the individual studies, which will be or have been submitted to the ClinicalTrials.gov Protocol Registration System, where more detailed descriptions are available. Table 1 summarizes each study's evaluation instruments.

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Table 1. The evaluation instruments in the RESCueH program

Domain	Reference	Purpose/content	Study	BL	Follow-up
Alcohol consumption					
Form 90-A	[30]	Primary outcome: daily alcohol use	Elderly	X	Wk 4, 12, 26, 52
Timeline follow back procedure	[31]	Primary outcome: daily alcohol use	Self-match Cue Exposure Healthy Lifestyle	X X X	Wk 26 Wk 26 Wk 26, 52
Alcohol Dependence Scale	[32]	Alcohol dependence	Elderly	X	Wk 26, 52
Drinker inventory of consequences	[33]	Adverse consequences of drinking	Elderly	X	Wk 4, 12, 26, 52
General					
Addiction severity index	[34]	Progress of change: medical, employment, alcohol use, drug use, legal, family, social and psychiatric condition	Self-match Cue Exposure Healthy Lifestyle	X X X	Wk 26 Wk 26 Wk 26, 52
AUDIT	[35]	Identification of AUDs	Relay	X	
The Danish national patient registers	[36]	Primary outcome: health care expenditure Attendance in outpatient alcohol treatment clinic	Relay Cue Exposure Relay		Wk 52, 260 Wk 26
Psychological/psychiatric assessment					
Mini-international neuro-psychiatric interview	[37]	Assess in- and exclusion criteria (DSM IV psychotic disorders)	Elderly	X	
Screening questionnaire of common mental disorders	[38]	Assess anxiety, depression, use of alcohol and somatisation	Healthy Lifestyle	X	Wk 26, 52
Inventory of interpersonal problems	[39]	Change in interpersonal problems	Healthy Lifestyle	X	Wk 26, 52
Brief symptom inventory 18	[40]	Changes in anxiety, depression etc.	Elderly	X	Wk 4, 12, 26, 52
Motivation					
Importance, confidence, readiness rulers	[41]	Changes in motivation	Elderly	X	Wk 4, 12, 26, 52
Craving					
Obsessive-Compulsive Drinking Scale	[42]	Changes in craving	Cue Exposure	X	Wk 8, 26
Penn Alcohol Craving Scale	[43]	Changes in craving	Elderly	X	Wk 4, 12, 26, 52
Desires for alcohol questionnaire	[44]	Changes in craving	Cue Exposure	X	Wk 8, 26
The Visual Analogue Scale for craving	[45]	Changes in craving	Cue Exposure	X	Wk 8, 26
Quality of life					
WHOQOL-BREF	[46]	Measures changes in quality of life	Elderly Self-match	X X	Wk 4, 12, 26, 52 WK 26
Personal happiness form	[47]	Measures satisfaction with interpersonal relations, life circumstances, physical and psychological health	Elderly	X	Wk 4, 12, 26, 52

Table 1. (continued)

Domain	Reference	Purpose/content	Study	BL	Follow-up
Physical activity					
Bruce treadmill test	[48]	Measures changes in cardio-respiratory fitness: oxygen consumption	Healthy Lifestyle	X	Wk 26, 52
International Physical Activity Questionnaire	[49]	Level of physical activity	Healthy Lifestyle	X	WK 26, 52
Coping skills and self-efficacy					
Alcohol Abstinence Self-Efficacy Scale	[50]	Assess changes in self-efficacy	Elderly	X	Wk 4, 12, 26, 52
			Cue Exposure	X	Wk 8, 26
The urge-specific strategies questionnaire	[51]	Assess the patient's use of coping skills	Cue Exposure	X	Wk 8, 26

BL = Baseline; Wk = week.

The Relay Study – Recruiting Patients to Treatment

We need better strategies to ensure that patients with AUD receive the necessary treatment for their condition. Greater use of specialized treatment for alcohol dependence needs to be a key element in society's response to alcohol problems and its consequences.

General hospitals are an obvious place to identify individuals for treatment of AUD since the condition is highly prevalent among inpatients [22]. Departments of gastroenterology, neurology and orthopedic surgery have the highest prevalence [23].

Patient contracts and reinforcement strategies are some of the more promising low-cost interventions for increasing participation in outpatient treatment. Only few studies have assessed these strategies, however. The Relay Study will test a new model for patient referral [24]. It is a multicenter study involving hospitals in both urban and rural areas and will be conducted in hospital departments that have a high number of patients with AUD.

In the experimental intervention (the Relay Model), a therapist from the alcohol treatment clinic meets the patient before discharge, and either gives advice about lowering alcohol intake or explains the importance of continuing outpatient aftercare and presents an 'attendance contract', depending on whether the patient scores ≥8 or ≥16 on the Audit Alcohol Use Identification Test (AUDIT) [23]. This contract includes information about the prognosis for alcohol disorders and options for attending outpatient care. The patient is given an appointment at the alcohol treatment clinic.

Referral As Usual – in the standard intervention – the patient is encouraged to lower drinking and/or seek treatment for AUD after discharge.

In a randomized controlled design, the Relay Model will be compared with Referral as Usual over a follow-up period of 1 year. A total of 1,000 consecutive patients admitted to the departments of gastroenterology, neurology and orthopedic surgery at Odense University Hospital (urban area) and Aabenraa Hospital, Sønderjylland (rural area), who screen positive for AUDs using the AUDIT [23] will be enrolled in the study. The primary outcome comprises the healthcare costs and social welfare costs in the year following the intervention. The secondary outcome is the number of patients beginning specialized treatment for AUD after discharge from the general hospital. Data will be collected from registers and databases and merged using the Danish Civil Registration System [25].

Enrolment of patients in the study started October 2013, and most patients have been willing to participate.

We will, however, not reach 1,000 patients due to mainly re-organization at the hospitals. We expect to reach 700 patients in June 2016, when enrolment will be concluded. Preliminary results suggest that approximately 12% of the patients on the participating departments have risky alcohol use (AUDIT score 8–15) in addition to 6% of the patients who screen positive for alcohol dependence (AUDIT score at ≥16).

The Elderly Study – Individualized Treatment

We need to provide a better service to specific patient groups. Elderly patients constitute a new and rapidly growing group that has quite different needs to other groups. No specific treatment targeted toward elderly patients is currently available. Consequently, these patients either receive no treatment or are given only brief advice from a general practitioner or are referred to treatment at specialized treatment institutions that lack specific experience with this patient group.

Elderly patients are often lonely or have feelings of loss, are afraid of being a burden on their children and on society, and often feel powerless. On the surface, their alcohol-related problems may appear less severe than those of younger patients, but comorbidity and social issues complicate their alcohol dependency. The Elderly Study [26] aims to improve the prognosis for this patient group by tailoring treatment to match individual needs.

This multicenter study is designed as a randomized controlled trial with 2 arms and will be conducted in 3 different drinking cultures. We aimed for enrolling a total of 1,000 consecutive patients, aged ≥60 years, seeking treatment for AUDs at 3 facilities in Denmark (Odense, Aarhus and Copenhagen – 400 patients), 2 facilities in Germany (Dresden and Munich – 400 patients) and a single treatment facility in US (Albuquerque – 200 patients) in the study. The patients were randomized to either of the following:

Brief Intervention, which comprises 4 sessions of Motivational Enhancement Therapy over 4 weeks. This intervention is likely to be similar to that typically offered in general practice, or possibly to the intervention offered at specialized treatment centers, which lack experience with this patient group. The intervention in this arm is considered to be basic care.

Brief Intervention plus adjusted Community Reinforcement Approach (CRA-Senior), which is the experimental intervention and comprises the same 4 sessions of Motivational Enhancement Therapy over 4 weeks, followed by 8 sessions of CRA-Senior. The CRA-Senior encourages sobriety by helping the patient create routines and activities that are meaningful to the patient and reward staying sober. Particular focus is given to establishing sober social networks.

All patients will be interviewed at treatment start (baseline), after 4 weeks, 12 weeks, 6 months and 12 months using structured interview instruments (table 1).

Enrolment of patients in the study started from January 2014. We reached >700 patients in May 2016, where enrollment was concluded. The initial power calculation was based on a power of 0.9, and with the actual number reached the power is 0.8, which is acceptable. It has been rather easy to recruit patients from Denmark and US, but more difficult in Germany. Baseline data from the first year of enrolment indicate that the elderly seeking treatment for AUD are relatively well-educated and have a stable economy.

The Self-Match Study – Involving Patients in Treatment Decisions

The choice of treatment for alcohol dependence is traditionally based on expert opinion. The few studies assessing these expert-led management decisions suggest that they are little better than chance in ensuring that a patient receives the most appropriate treatment. How then, can we better determine the most relevant treatment for an individual patient?

One option is to allow patients to make an informed choice from a menu of evidence-based treatment options, and thus 'match' themselves with the treatment. Two arguments support this. First, patients will choose options that are most likely to be acceptable or attractive to them, which is important for a process that aims to change people's behavior. Second, the ability to choose one's own course of action is likely to increase motivation. The Self-match Study will be the first of its kind to investigate the effects of 'self-matching' treatment for alcohol disorders versus assignment by a clinical expert.

The study is a randomized controlled study with 2 arms: (A) an experimental arm, involving patient self-matching to treatment, and (B) TAU, involving expert assignment to treatment. A total of 400 consecutive patients aged 18–60 years, who either at presentation or after detoxification wish to start treatment at the Alcohol Treatment Clinic in Odense, will be enrolled. The patients will be interviewed at baseline and 6 months after treatment start.

The study will start enrolment of patients in 2017. As part of the preparation of the information material to be used in study, a survey has been carried out among treatment seekers in Danish alcohol treatment institutions

and published. The survey investigated what information about treatment the patients regarded to be important to have before starting the treatment [27].

The Cue Exposure Study – Preventing Relapse after Treatment

Alcohol-dependent patients typically avoid alcohol while they are in treatment, but a significant number of patients relapse to drinking after discharge. One reason for relapse is that society constantly exposes the patient to alcohol, which induces craving symptoms.

During treatment, patients learn methods to identify high-risk situations for relapse to drinking, just as they learn strategies to avoid or tackle those situations. However, they learn by talking about what to do or not by actually trying the strategy out in real life which is likely to be more challenging. All too often, patients relapse when they face a high-risk situation in daily life, and it is only afterward that they can analyze and describe what went wrong. The question is whether we can improve the alcohol avoidance strategies that patients use in daily life situations.

The Cue Exposure Study will compare aftercare based on cue exposure delivered either by a therapist or through a smartphone application with standard aftercare, with the aim of preventing relapse to harmful drinking [28]. The rationale of cue exposure treatment is that real-life training in safe settings will give the patient greater confidence when exposed to alcohol outside the treatment institution, and may in the long-term even diminish reactions to alcohol exposure.

The study is a randomized controlled trial with 3 arms, of which 2 are experimental: (A) an experimental aftercare comprising 4 group sessions of cue exposure treatment (1 session every 2 weeks), (B) an experimental aftercare comprising 1 individual session with instruction for a smartphone application + 1 individual follow-up session 8 weeks after discharge and (C) aftercare as usual comprising 1 individual follow-up session 8 weeks after discharge, that is, no cue exposure treatment. A total of 300 consecutive patients aged 18–60 years, who finish standard treatment at the Alcohol Treatment Center in Odense, will be enrolled in the study. The patients will be interviewed at baseline just before aftercare treatment and at 8 and 26 weeks after initiation of aftercare. Data collection will include relevant questionnaires and interview instruments.

Enrolment of patients in the study started from May 2016, and currently 66 patients have been enrolled. Interest in participating in the study is high. We expect to continue enrolling patients until early 2017.

The Healthy Lifestyle Study – It Is Not Enough to Just Remove Alcohol

We need to widen the focus in treatment for AUD. Physical exercise is known to produce health-related benefits for different patient groups and has a positive effect on physical, psychological and social aspects of alcohol abuse. Physical exercise can be used both as early prevention and as part of a continuous treatment process.

Exercise can help in problem drinking via several mechanisms. Moderate exercise can decrease the urge to drink. Exercise can offer positive alternatives to alcohol by providing pleasurable states through dopaminergic reinforcement. Exercise also improves psychosocial outcomes in the form of mood management and reduces depression and anxiety. Resilience factors, such as individual and social resources (e.g., self-confidence), are strengthened by regular physical activity, especially as a group activity.

Physical exercise is a relatively new but promising treatment option in substance abuse. The Healthy Lifestyle Study [29] will test whether the addition of moderate physical training to standard treatment for alcohol dependency will increase compliance with alcohol treatment. Despite the potential benefit of exercise interventions, only few studies have tested the impact of exercise as an adjunct to alcohol treatment. The findings from these studies suggest a positive relationship between exercise and drinking outcome, but the studies have methodological limitations such as small samples, high dropout rate or lack of randomization.

The study is a randomized controlled trial with 3 arms: (A) standard treatment + physical exercise on an individual basis, (B) standard treatment + physical exercise in groups or (C) standard treatment alone. The exercise programme will be conducted 2 days a week for a total of 24 weeks. The programme consists of brisk walking or running, where the duration and intensity of the exercise increases each week as the patients' fitness level improves.

We aimed for a total of 300 consecutive patients, aged 18–60 years, presenting to the Alcohol Treatment Center in Odense to be enrolled in the study. The patients are interviewed and tested at baseline, and after 6 and 12 months.

All patients receive standard outpatient treatment at the Alcohol Treatment Center. This treatment comprises individual sessions with motivational interviewing (at the start of treatment), followed by cognitive behavioral therapy and family therapy if appropriate.

Enrolment of patients in the study began in May 2013, and was concluded in April 2015. One hundred seventy-

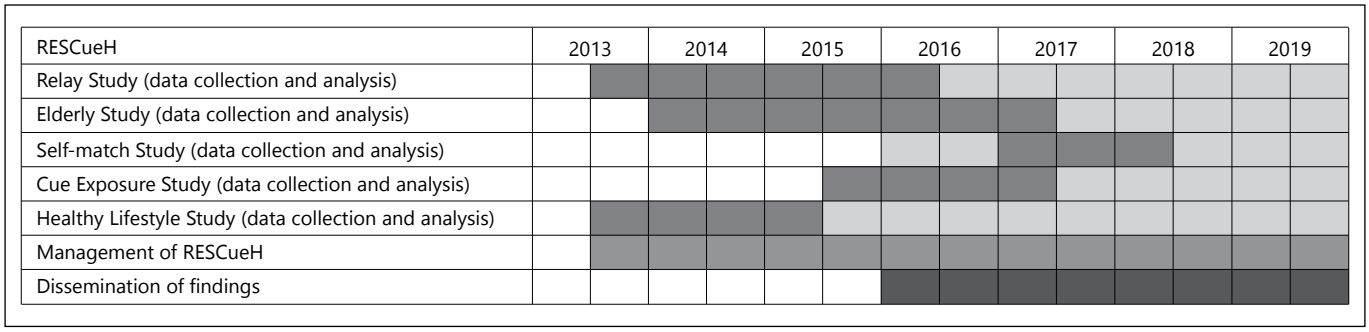

Fig. 1. The timetable for implementing the RESCueH programme.

five patients were enrolled in the study. All data, including follow-up data, have been collected, and the analysis has begun. Findings of the study are expected to be published later this year.

Program Schedule

UCAR is responsible for implementing the RESCueH programme. UCAR has an established record of conducting alcohol treatment research of high clinical relevance. The RESCueH programme will be carried out in active treatment environments, that is, alcohol treatment clinics and hospital departments. The timetable for implementing the RESCueH programme is shown in figure 1.

Expected Results and Perspectives

In the Relay Study, we expect healthcare costs during the 12 months after hospital discharge to be significantly lower in the experimental group than in the standard referral group. We also expect that the number of patients initiating treatment at the specialized treatment clinic within 2 weeks after discharge will be higher in the experimental Relay Model than in the control group.

If the new referral approach is found to be successful, it is likely that the intervention could be implemented more widely.

The elderly patients assigned to a brief motivational intervention followed by a programme to enhance the quality of life and pleasure from sober living will have significantly reduced alcohol consumption and healthcare use at follow-up, compared to patients assigned the brief motivational intervention alone. It is hypothesized that these findings will be similar across drinking cultures.

If the brief motivational intervention plus CRA-Senior intervention is more successful than motivational intervention alone, the approach will be recommended to clinicians in specialized alcohol treatment institutions. Should the brief motivational intervention alone be as good as the extended intervention, it will be recommended for use in other settings, such as general practice or somatic hospitals. Besides improving treatment for AUDs among the elderly, we expect this study to make a significant contribution to a better understanding of the interpretation and comparison of study results from different countries.

In the Self-match Study, we expect that patients who choose their own treatment method will drink significantly less alcohol 1 year after treatment initiation than those who are assigned treatment by a clinical expert. We hypothesize that this will be due to improved adherence to the treatment programme among self-matched patients.

This study will contribute to knowledge about how to involve the patient in treatment, with the aim of improving adherence with treatment. If self-matching of treatment proves to be successful, it will be a useful strategy for clinicians. It would require a more collaborative approach to working with patients, but should not impose extra costs.

In the Cue Exposure Study, we expect that alcohol consumption 8 and 26 weeks after discharge from treatment will be lower in the experimental groups (A and B) than in the control group (C). We also expect that the smartphone intervention will be more cost-effective than the other interventions.

Besides increasing our knowledge about the effectiveness of various methods of aftercare, this study will be the first in a series to incorporate new technology that will give the patient ready access to learned strategies in daily life after discharge. Such technology-based strategies are likely to be particularly useful for younger patients.

In the Healthy Lifestyle Study, we expect that alcohol consumption 6 months after starting the treatment will be lower in the experimental groups than in the control group. We also expect compliance during treatment to be better in the experimental groups than in the control group. Furthermore, we expect less anxiety and depression and better fitness in the experimental groups than in the control group.

If a physical exercise programme proves to be beneficial in the treatment of alcohol problems, it will be recommended to clinicians in the alcohol treatment field as a low-cost strategy to improve the outcome of treatment. The study is expected to be followed up by further studies using other kinds of physical activity and by nutrition studies.

Discussion

If you want to ensure an improved treatment of people with AUD in everyday practice, we believe there is a need for a research strategy which seeks to bridge the gap between efficacy trials and effectiveness trials. In 5 studies of the RESCueH programme, we have sought to combine features from the 2 designs with the main objective being to develop methods which in daily life ensure a better treatment for so many AUD patients representative of everyday clinical practice.

Scientific Implications

We expect the findings of the RESCueH programme to make a significant contribution to the body of knowledge about treatment for AUDs. The programme will also provide information of a more general nature that will extend much further than the specific research questions studied. The Elderly Study will allow us to study differences between US and European findings, which will in turn help us to interpret results from previous and future treatment studies.

The findings of the RESCueH programme are expected to lead to a new generation of studies. A positive outcome in the Healthy Lifestyle Study will stimulate further studies on aspects of patient lifestyle, such as nutrition. Successful recruitment strategies in the Relay Study will generate studies testing implementation of similar strategies in other settings, such as general practice. A positive outcome in the Self-match Study may result in further investigation of patient empowerment and involvement in treatment, such as consideration of subjective experiences from drinking alcohol. Successful strategies for preventing relapse in the Cue Exposure Study are likely to inspire further research into the use of new technologies in controlling craving and in the treatment of AUDs more generally.

Clinical Implications

The RESCueH research programme addresses specific clinical problems in the treatment of AUDs. The studies will be conducted in active treatment settings, and the resulting new methods and approaches should be feasible to implement in these settings. The participation of the 2 largest Danish public alcohol treatment institutions increases the likelihood that the interventions will be implemented if they prove effective. Dissemination of study findings will be further aided by the close dialogue that the Unit for Clinical Alcohol Research has with the Danish Network of Alcohol Treatment Institution Managers.

Ethics

In all the studies, the patients will receive oral and written information. It will be emphasized that declination of participation will not in any way have an impact on subsequent treatment offered to the patient. Likewise, acceptance of participation can at any point in time be withdrawn, again with no impact on the treatment offered.

No information is collected before the patient has accepted participation by an informed consent declaration.

All information obtained in the study will be dealt with confidentially. Participants will be allocated a respondent number. No analysis or publications will contain any information that can identify any individual patient.

Data collected in the study will be stored locally. Each center will ensure data quality and data security according to guidelines across centers. Furthermore, all data management must apply with all local guidelines and regulations, which may differ from center to center.

Adverse events will be handled according to local guidelines as specified for each participating center, which again may differ from center to center, but will not differ from how any other adverse event is handled at that particular center.

The Elderly Study, the Cue Exposure Study and the Healthy Lifestyle Study have been approved by the local ethics committees. The Relay Study has been presented to the local Ethics Committee who decided that the study did not need approval. The Self-match Study will be approved by the local Ethics Committee before initiation. All guidelines for data protection are followed. All procedures in the study are in accordance with the second Declaration of Helsinki.

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Disclosure Statement

The authors declare no conflict of interests.

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