RESCueH

– A research programme addressing challenges critical to the quality of care for patients with alcohol use disorders

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Introduction

The RESCueH Alcohol Research Program opened 3rd of June 2013. This annual report from the Unit of Clinical Alcohol Research (UCAR), University of Southern Denmark, describes the progress and results from Research Program, achieved in 2015. A status on the organization around the projects will also be described.

Background

With the series studies in the **RESCueH** Alcohol Research Program, we aim to improve the prognosis for patients with alcohol use disorders by developing strategies to identify, treat and reduce relapse in patients with alcohol problems:

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

2. **The Elderly Study**
   Rationale: Matching treatment to individual needs, reflecting the heterogeneity of alcohol-dependent patients.

3. **The Self-Match Study**
   Rationale: Greater patient involvement in treatment, as active involvement in treatment decision processes is essential for compliance.

4. **The Cue Exposure Study**
   Rationale: Preventing relapse, as return to harmful drinking is a common problem.

5. **The Healthy Lifestyle Study**
   Rationale: Encouraging a healthy lifestyle, which will improve compliance in treatment and prevent relapse.

The Relay Study – recruiting patients to treatment

The **Relay Study** tests a new model for referring patients. It is a multicentre study involving hospitals in both urban and rural areas and will be conducted in hospital departments that have a high number of patients with alcohol-related diseases.

Purpose of the study

We hypothesize that the Relay Model is more effective and less costly than standard methods with regards to referral of alcohol-dependent patients from hospital to specialized treatment.

Design and original plan

In a randomized controlled design, the Relay Model will be compared with Referral as Usual over a follow-up period of one year. Consecutive patients admitted to the departments of gastroenterology, neurology and orthopaedic Surgery at Odense University Hospital (urban area) and Aabenraa Hospital, Sygehus Sønderjylland (rural area), who screen positive for excessive use of or positive for alcohol dependency using the Alcohol Use Identification Test (Audit) will be enrolled in the study. The primary outcome comprises the health care costs in the year following the intervention. The secondary outcome is social costs, and criminal justice cost, and the number of patients beginning specialized treatment for alcohol use disorder after discharge from the general hospital. Data will be collected from registers and databases and merged using the Danish Civil Registration system.

Interventions

The Relay Model: In the experimental intervention, a therapist from the alcohol treatment clinic meets the patient before discharge. If the patient has screened positive for excessive drinking, the therapist will offer a motivational talk and brief advice concerning the possibility of cutting down. If the patient has screened positive for alcohol dependence, the therapist explains the significance of continuing outpatient aftercare and presents an "attendance contract". This contract includes information about prognosis for alcohol disorders and options for attending outpatient care. The patient is given an appointment at the alcohol treatment clinic and is recommended to place the contract in a prominent place at home.

Referral as Usual: In the standard intervention, the hospital staffs encourage the patient to cut down or seek treatment for alcohol use disorder after discharge. The hospital personnel call the alcohol treatment clinic, and the patient is given an appointment and a meeting card. Standard intervention is intervention as usual.

Progress of the study

A pilot study on the screening procedure was carried on one of the participating departments at Odense University Hospital (Department O) during October 2013, and the full study was initiated on all five participating departments 1st of November 2013. Enrolment of patients from the rural hospital ended in October 2015. Enrolment will continue until June 2016 at the departments of gastroenterology, and orthopaedic Surgery at Odense University Hospital in order to secure enrolment of as many patients as possible. Data from January 2014 – December 2015 showed that on average 17,7 % of the hospitalized patients score 8 or more on the Audit.

Organisation
The project-coordinator meets with the PI every second week. The project-coordinator meets with the out-going staff from the Alcohol Clinics every two month, - and there are quarterly meetings with the hospital departments. The project coordinator sends out a bi-weekly newsletter about the study and the progress to everybody involved. A full day status meeting with both staffs from the Alcohol Clinics, hospital departments and the research group was held in the autumn of 2015.

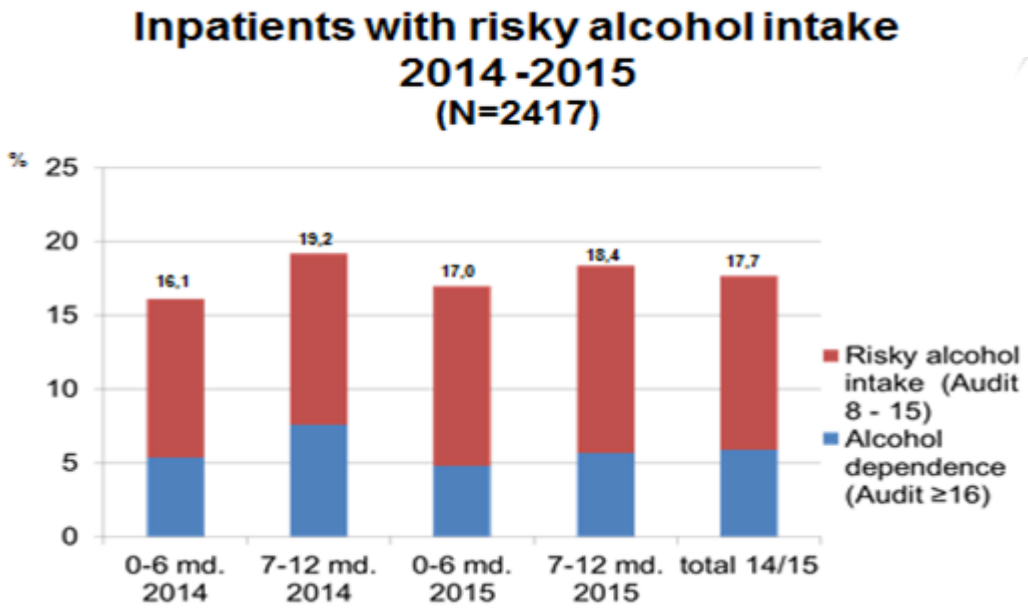
Qualitative aspects
The staffs from the Alcohol Treatment Clinics have been engaged and enthusiastic about the study. They have still not met resistance from the patients when they showed up at the hospital. The patients are willing to talk about their alcohol habits with the staff from the Alcohol Clinics, when they are approached.

The staffs at the hospital departments at Odense University Hospitals are also engaged in and positive towards the study. The data discipline will keep being monitored carefully.

Preparations of the health economic analysis to come
A PhD-protocol was prepared in 2015, and Anne-Sophie Schwarz was enrolled as PhD-student in the end of 2015. As a preparation for the analysis to come, Anne-Sophie Schwarz wrote her masters' thesis on "Giver overforbrug af alkohol meromkostninger i sundhedsvæsenet?" earlier in 2015.

Preliminary findings
In figure 1 it can be seen how many patients, who screened positive for risky alcohol intake or alcohol dependence in 2014 and 2015.

Figure 1.



Publications from the study in 2015
Schwarz AS, Bilberg R; Bjerregaard L; Nielsen B; Søgaard J; Nielsen AS. **Relay model for recruiting alcohol dependent patients in general hospitals- A single-blind pragmatic randomized trial.** BMC Health Services Research (accepted)

PI, coordination of study and PhD-students
Professor Bent Nielsen (UCAR)
Assistant Professor Randi Bilberg (coordination)
Professor Jes Søgaard (supervisor)
PhD student Anne-Sophie Schwartz
Associate professor Anette Søgaard Nielsen (supervisor)

The Elderly Study – individualized treatment

The **Elderly Study** aims to improve the prognosis for this patient group by tailoring treatment to match individual needs.

Purpose of the study
The study will evaluate new methods for treating elderly patients with alcohol use disorders.

Design
The Elderly study is designed as a randomized controlled trial with two arms and conducted in three different drinking cultures. Consecutive patients, aged 60+ years, seeking treatment for alcohol use disorders at three facilities in Denmark (Odense, Aarhus and Copenhagen), two facilities in Germany (Dresden and Munich) and a single treatment facility in US (Albuquerque) will be enrolled in the study. The patients will be randomized to either *(A) Standard treatment* or *(B) Extended treatment.*

Interventions
(A) Standard Treatment comprises four sessions of Motivational Enhancement Therapy over four weeks. This intervention is likely to be similar to that typically offered in general practice, or possibly to the intervention offered at specialized treatment centres which lack experience with this patient group. The intervention in this arm is considered to be basic care.

(B) Extended treatment is the experimental intervention and comprises four sessions of Motivational Enhancement Therapy over 4 weeks, followed by up to 8 sessions of Community Reinforcement Approach specifically designed to target the needs of elderly (CRA-Elderly). The CRA-Elderly 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 and to coping with aging.

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

Progress of the study
Treatment manual
A treatment manual was developed in the autumn 2013, partly on the basis of the Combine Manual (eds. WR Miller). The new manual is called the CRAS manual (Community Reinforcement Approach for Seniors). The manual describes both the Standard Treatment and the Extended Treatment.

The Standard Treatment consists of one session of Motivational Interviewing, one session of Personalized Feedback, one session with a functional analysis and one session allocated to development of a change plan (standard treatment) or treatment plan (extended treatment). At the fourth session, a supporting significant other is supposed to participate together with the patient.

The Extended treatment builds on the Standard Treatment and offers up to 8 sessions, working with modules of the patient's choice. There are five modules to choose between: a module on coping with craving, a module on social recreational activities, a module on mood management, a module on building a sober network and finally a module on coping with aging. A module can cover several sessions.

The manual was compiled by Alyssa Forcehimes and Teresa Moyers from the US site and Anette Søgaard Nielsen from the Danish site on the side-line. The manual was divided into two manuals in spring 2014, one for Standard and one for Extended Treatment, and slightly adjusted in summer 2014.

Progress of the study

The Danish site began enrolling patients in the pilot study Mid-January 2014. The German site and the US site began enrolling patients 1st of March 2014. The pilot study continued to late May 2014. The pilot phase was evaluated on meeting in the Elderly Research Group that took place in the end of April 2014 in Odense. The evaluation showed that all procedures worked well and that the invited patients accepted to participate and most strayed in treatment as expected. No major changes were made in relation to the study procedures, and it was agreed that pilot patients would be included in the final group under study. The full study was initiated at the 1st of June 2014 at all sites and stops enrolling patients at the 31st of March 2016.

Monitoring treatment fidelity

All treatment sessions are recorded. At the end of the study, a sample of 10% randomly picked sessions will be analysed in order to estimate fidelity to the treatment manuals. A team of coders has been appointed at each site. Professor Moyers and one of her students started training the coders in the autumn 2015, and the coding for treatment fidelity will take place in May-June 2016. Professor Theresa Moyers will coordinate and overlook the process of coding for treatment fidelity.

Data managing

A collaboration agreement between Unit of Clinical Alcohol Research and Odense Patient data Explorative Network (OPEN) was signed in the summer 2013. Data manager Lars Søgaard finalized developing databases for the study in OPEN in November 2014. In order to secure the possibility of data entering via the internet directly into the database in OPEN, it was decided to make use of REDCap (Research Electronic Data Capture). REDCap is a browser-based, metadata-driven EDC software solution and workflow methodology for designing clinical and translational research databases. It is widely used in the academic research community.

Sharing documents

In order to carry out version control of documents, a web based SharePoint was established. All final versions of forms, the treatment manual, work descriptions and minutes of meetings are placed at the SharePoint and can be reached from all sites. The sharepoint also includes a complete list of changes made during the study – and the changes' implications for the anticipated results. No change so far is expected to affect the results.

Supervision

All recordings of treatment sessions are stored locally. In Denmark, the sessions are stored on a safe sharepoint to which recordings can be uploaded directly from the participating treatment centres. A procedure has been developed that involved the Danish supervisor listen to the recordings either at random or to specific recordings if the therapists specifically ask for supervision in relation to a certain patient. In the end of 2015, the Danish supervisor has listened to and given feedback based on 115 Danish recordings. Feedback on the recordings is mailed to the therapists, and if a recording show satisfying treatment manual fidelity, it is also copied into a library of Golden Standards. All Danish therapists are encouraged to listen to the Golden Standards in addition to reading the treatment manual again and again. Similar procedures are developed locally at the foreign sites in ways that fit the local structures.

Video-conference systems

So far, all meetings between sites – except two face-to-face meetings in 2014 – have been carried out by the means of skype.

Hair tests

As it is described in the protocol, hair samples of the participants are collected at the 6 months follow up. The hair samples will be analysed in order to validate the data on self-reported alcohol consumption. Collaboration between UCAR and professor Tine Kold Jensen and Senior Scientist Flemming Nielsen, Environmental Medicine, SDU was thus initiated in 2015. Tine Kold Jensen and Flemming Nielsen will carry out the analysis in 2016 and 2017 when all hair samples are collected.

Challenges

The cultural differences between the sites are obvious. These include differences in how the treatment for alcohol problems is organized and how the patients seek treatment. In addition, the enrolment of patient at the sites has been slightly slower than expected. Several initiatives have been tried in order to make the project visible, including initiating articles in the newspapers, advertising, distributing leaflets and hanging up poster, and informing relevant staff categories that are in contact with senior citizens. The rate of inclusion is carefully monitored and information about number of included participants is send to the sites every Friday afternoon, adding the last week to the total picture. An example on the information provided to the sites is shown in figure 2, below.

Figure 2: **information on number of patients randomized at the sites in the last weeks of 2015.**

	Week 30	Week 31	Week 32	Week 33	Week 34	Week 35	Week 36	Week 37	Week 38	Week 39	Week 40	Week 41	Week 42	Week 43	Week 44	Week 45	Week 46	Week 47	Week 48	Week 49	Week 50	Week 51	Week 52	Week 53
Copenhagen	97	98	98	101	103	105	105	106	109	109	112	114	116	116	119	122	122	122	125	128	128	129	130	131
Odense	60	61	62	63	63	63	64	65	66	67	67	68	70	71	72	73	77	78	79	79	80	82	85	86
Aarhus	71	71	72	73	74	78	79	79	80	80	80	81	82	82	85	85	86	87	88	89	91	93	93	93
Totally in Denmark:	228	230	232	237	240	246	248	250	255	256	259	263	268	269	276	280	285	287	292	296	299	304	308	310
Munich	76	78	81	83	85	85	85	85	85	86	87	90	90	90	90	90	90	92	94	97	98	99	100	100
Dresden	79	79	79	79	79	79	82	82	83	83	83	84	85	85	85	85	85	87	89	89	89	89	89	89
Totally in Germany:	155	157	160	162	164	164	167	167	168	169	170	174	175	175	175	175	175	179	183	186	187	188	189	189
New Mexico	110	110	110	110	114	119	120	120	120	121	122	129	130	130	130	130	130	133	136	137	137	139	139	139
Totally in Elderly-study	493	497	502	509	518	529	535	537	543	546	551	566	573	574	581	585	590	599	611	619	623	631	636	638
Included in this week:	7	4	5	7	9	11	6	2	6	3	5	15	7	1	7	4	5	9	12	8	4	8	5	2

End of enrolment
We expect to have included a total of 720 patients in the end of March 2016 and will then stop enrolment.

Organisation
The PI group and the overall coordinator have met via Skype every 2 weeks since May 2013, and included the local coordinators in the biweekly skype meetings from October 2013. This routine continued to take place throughout 2015.

The supervisors have met with professor Terri Moyers on skype every two weeks during the first half of 2015, and the interviewers have met with associate professor Roberta Chavez on skype every 3 month in order to secure data quality across sites.

At the Danish site, the PI, the overall coordinator and the local coordinator have met regularly throughout 2015. The overall coordinator and the Danish therapists have met every second month face-to-face in order to secure fidelity to the treatment manual, in addition to the individual supervision, based on the recordings. Furthermore, the overall coordinator, the local coordinator and the managers from the treatment institutions have met every 6 months in order to secure implementation of the study, including help to put focus on the study and attract patients.

Since October 2013, the local project coordinator has send out biweekly newsletters from the Elderly study to all managers and staffs in the alcohol treatment centres in Odense, Aarhus and Copenhagen in order to inform and describe progress of the study.

Data and safety monitoring plan
In 2015, all descriptions and procedures in relation to data and safety monitoring, were reviewed, discussed and finally compiled into one document. The document can be seen in Annex 1.

Change of PI at the US site
Professor Michael Bogenshutz changed position in 2015, and is now professor in Psychiatry at the Langone Medical Center in New York. Professor Bogenschutz continues in the Elderly Research Group, but in order to secure the ongoing execution of the Elderly project at the University of New Mexico, Dr. Snehal Bhatt was appointed as PI and took over the formal responsibilities from professor Bogenschutz. Dr. Snehal Bhatt is addiction psychiatrist, medical director of the addiction treatment programs at UNM, and director of the addictions division in the department of psychiatry.

Preliminary findings
We have not yet analysed the data from the baseline interviews, but in June 2015, we described the participants enrolled so far, at the ICTAB conference, based on preliminary data. We found that the participants from the German, US and Danish sites were strikingly alike in relation to gender-distribution and level of education. Preliminary Danish data on gender and level of education, based on the first 123 participants, can be seen in figure 3 and 4.

Figure 3: gender distribution, Danish site (preliminary findings)

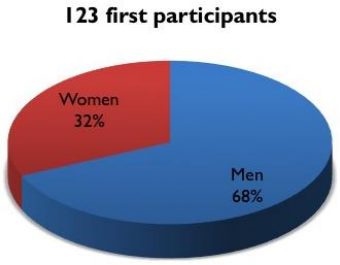
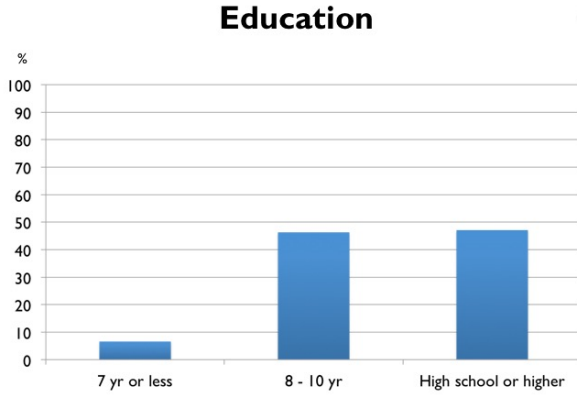


Figure 4: level of education, Danish site (preliminary findings)



As it can be seen from the preliminary findings, shown in figure 4, the level of education is rather high, compared to the rest of the Danish population in that age group.

Publications from the study in 2015

Andersen K, Bogenschutz MP, Bühringer G, Behrendt S, Bilberg R, Braun B, Ekstrøm CT, Forcehimes A, Lizarraga C, Moyers TB, Nielsen AS. **Outpatient treatment of Alcohol Use Disorders among subjects 60+ years. Design of a randomized controlled trial conducted in three countries (Elderly-study).** BMC Psychiatry (2015) 15:280 DOI 10.1186/s12888-015-0672-x.

PIs, coordination of study and PhD-students

Principal Investigators: Professor Kjeld Andersen, UCAR (Danish site), Professor Michael Bogenschutz, NYU Langone Medical Center and MD Snehal Bhatt, New Mexico School of Medicine (US site), Professor Gerhard Bühringer, Technische Universität Dresden and Institut für Therapieforschung (German site).

Overall coordination: director Anette Søgaard Nielsen.

Local Coordinators: Randi Bilberg (DK), Silke Behrendt (G), Barbara Braun (G), Christine Lizzaraga (US)

PhD-students: Jakob Emiliussen (DK), Anne Kohlman (G), Lotte Kramer Schmidt (DK)

The Self-Match Study – involving patients in treatment decisions

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.

Purpose of the study

The study will compare the effects of patient-led versus expert-led treatment choice in terms of compliance in the treatment programme, alcohol consumption and patient satisfaction with treatment for alcohol use disorder.

Design

The study is a randomized controlled study with two arms: (A) an experimental arm, involving patient self-matching to treatment, and (B) treatment as usual, involving expert assignment to treatment. 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. Enrolment of patients is expected to begin in the spring 2017.

Expected results

We expect that patients who choose their own treatment method will drink significantly less alcohol one 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.

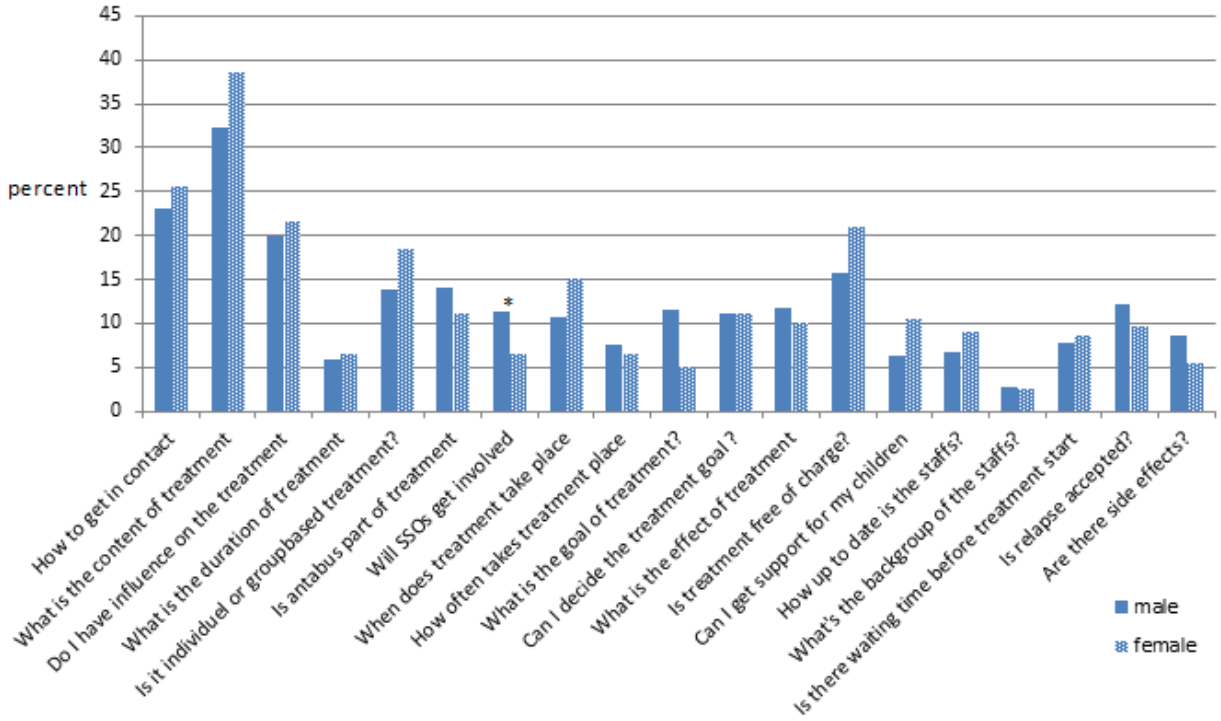
Progress of the study

Planning phase

As a foundation for developing the information material to be used by the patients in order to choose treatment, a survey was carried out in 2014. All public treatment institutions in Denmark were invited to participate in the survey, and half of the institutions agreed, a total of 25 treatment institutions. Both big and smaller treatment institutions participated. In a specific week, the survey was carried out among patients at the treatment institutions, who had an appointment that week. A questionnaire with 20 questions was used. The patients were asked to fill out the questionnaire anonymously before leaving the institution, and 704 patients did so. Most questions introduced a topic and asked the patient to rate whether or not it was important to receive information about this topic before treatment start or whether it should wait till later. All patients were also asked what information it was most important to make available before treatment start.

Figure 5 shows what topics were considered the *most* important to be informed about before treatment start, if the patients were to prioritize the three most important topics on the list. Information about the content of treatment was given priority by far the most respondents, regardless of gender (38.5% female versus 32.3% male, NS). Information about how to contact the treatment centers (via mail, phone or face-to-face) was given priority by about a quarter of the respondents, closely followed by information about the influence the patients themselves might have on the treatment content, and information about treatment being free of charge.

Figure 5: Percent male and female patients in treatment for alcohol dependence stating the topic of information to be one of the three most important topics to have information on before treatment start (N=704. Missing information from 35 patients)



** p < 0,05*

The knowledge from the survey will be used to qualify the information material to be used by the patients as a foundation for the choice of treatment. All treatment methods will be described by using the same headlines. The information material will be presented to patients, both in focus groups and to individuals. The patients will be encouraged to express all thoughts they may have when they see and read the material. When the patients express that they feel informed by the material to a level that feels safe in order to choose between the methods, the material will be considered ready for use in a randomized controlled trial, focused on testing the effect of choosing own treatment.

Initiation of the study
The study is expected to begin enrolling patients primo 2017. A PhD-student will be appointed in 2016.

Publications from the study in 2015
Nielsen AS, Ellermann AE. **Need to know and wish to know: What clients find important to know about treatment for alcohol problems in order to be able to decide whether to start treatment or not.** Nordic Studies on Alcohol and Drugs (accepted)

PI, coordination of study and PhD-students
Principal Investigator: Director Anette Søgaard Nielsen
PhD student NN
Supervisor: Professor WR Miller.

The Cue Exposure Study – preventing relapse after treatment

The **Cue Exposure Study** will compare aftercare based on cue exposure treatment (CET) delivered either by a therapist or through a smart phone application with standard aftercare, with the aim of preventing relapse to harmful drinking.

Design

The study is a randomized controlled trial with three arms, of which two are experimental: (A) an experimental aftercare comprising 4 group sessions of CET (one session every two weeks), (B) an experimental aftercare comprising 1 individual session with instruction for a CET smart phone application + one individual follow-up session 8 weeks after discharge, (C) aftercare as usual comprising one individual follow-up session 8 weeks after discharge only, i.e. no CET. Consecutive patients aged 18-60 years, who finish standard treatment at the Alcohol Treatment Centre in Odense from the period 1st of Mai 2015 till ultimo 2016/primo 2017, 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.

Interventions

(A) Aftercare comprising therapist-led CET: These patients will participate in four 2-weekly group sessions, delivered by a therapist without the use of a smart phone.

(B) Aftercare based on a smart phone CET application: At the start of aftercare, these patients will attend an individual session where they will be instructed in the use of the smart phone software, and a further individual session after 8 weeks. The patients will be asked to practice their skills for reducing cue reactivity on a regular basis.

(C) Standard aftercare: These patients will attend an individual follow-up session 8 weeks after discharge from treatment. This session contains no CET.

Expected results

We expect that alcohol consumption 8 and 26 weeks after discharge from treatment will be lower in the experimental groups (A & B) than in the control group (C). We explore whether the experimental intervention (B) will be more cost-effective than the other interventions.

Progress of the study

Planning phase

The application for the mobile phone was finalized in 2014, and presented to patients and therapists in order to receive feedback, be adjusted, and tested again.

Data collection plan and software was developed in 2014 and early 2015. The study was approved by the Scientific Ethical Committee, and the therapists selected. Training of the therapist was performed in the beginning of 2015, and Dr Bodil Andersen, who is one of the most experience Danish trainers in Cognitive Behavioural Therapy, was attached as supervisor for the therapist throughout the study.

The first 3 months after start of enrolment of patients or until 30 patients were enrolled in the study was decided to be considered pilot phase.

Initiation of the study
Patients who started treatment after 1st of February 2015 were (and are) offered participation in the study when they are 3 month into their treatment course and plan termination of treatment. Patients, who agree to participate in the Cue Exposure aftercare study, are randomized to either CET based aftercare in groups, to CET by the means of the application for smartphone, or aftercare as usual. Hence, the first patients were enrolled in May 2015. Ultimo 2015, 35 patients were enrolled. The pilot phase was evaluated in November 2015. It was obvious from the pilot phase that recruitment is a problem, since one third of the patients tend to drop out of treatment before they finalize treatment, hence will not be informed about of the Cue Exposure study during the last session in the ordinary treatment phase, - and since less than 50% of the patients who do finalize treatment agree to participate in the Cue Exposure study.

Adjustments
When evaluating the pilot phase, it was therefore decided to adjust and strengthen the logistics of the study, for instance by informing the patients about the Cue Exposure study already in the early stages of treatment by the means of leaflets and additionally by having the therapist inform the patients about the aftercare project during the last sessions of the ordinary treatment, and letting the therapist introduce the research assistant a couple of weeks before treatment closure. It was also decided to prolong the expected period of enrolment.

The decided changes of the logistics lead to increased number of patients who accepted enrolment in the study. In the end of February 2016 50 patients were enrolled in the Cue Exposure study.

Further challenges
When evaluating the pilot phase and during the regular meeting with the therapists in the study, it became clear that the patients do not seem to experience high levels of craving when exposed to the interventions. It was considered to change the intervention and add visualisation (cognitive induced cues) to the cue exposure. However, when seeking advice about this question from a member of the Advisory Board, we were advised against making changes in the treatment manual, partly in order to prevent the study and not make changes that would make it difficult to interpret the results, but also because we do not have neither own data or data from other studies that suggest that high level of craving is needed in order to make the interventions work. It may be so that the interventions work absolutely fine with rather low levels of craving, and the interventions thus prevent relapse nevertheless. Hence, the research group behind the Cue Exposure Study decided to make no changes of the aftercare manual, and keep on inducing craving by the means of cues only.

The research group also decided to carry out a safety analysis when 60 patients have been followed up at 26 weeks. An independent statistician will be asked to open the blinding and analyse data on the first 60 patients in order to make sure that no unexpected safety problems occur.

Expected results
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.

Publications from the study in 2015
Mellentin A.I., Nielsen B., Nielsen A.S., Yu F., & Stenager E. Study protocol: **A randomized controlled study of exposure therapy as aftercare for alcohol use disorder.** *BMC Psychiatry*, accepted

PI, coordination of study, PhD-students
Principal investigator: Professor Bent Nielsen, UCAR.
Supervisors (study): Professor Elsebeth Stenager, Associate Professor Anette Søgaard Nielsen
Supervisor (clinical): MD Bodil Andersen
Technical development of the application: Associate professor Arne Bilberg, associate professor Fei Yu.
PhD student Angelina Mellentin

The Healthy Lifestyle Study – it isn't enough to just remove alcohol

The **Healthy Lifestyle Study** tests whether the addition of moderate physical training to standard treatment for alcohol dependency will increase compliance with alcohol treatment.

Design

The study is a randomized controlled trial with three arms: (A) Standard treatment + physical exercise on an individual basis, (B) Standard treatment + physical exercise in groups, or (C) Standard treatment alone. Consecutive patients, aged 18-60 years, presenting to the Alcohol Treatment Centre in Odense were enrolled in the study. The patients were interviewed and tested at baseline, and after 6 and 12 months.

Interventions

All patients received standard outpatient treatment at the Alcohol Treatment Centre. The exercise programme was conducted 2 days a week for a total of 24 weeks. The programme consisted of brisk walking or running, where the duration and intensity of the exercise increases each week as the patients' fitness level improved. The exercise programme were be led by a physical trainer. It was either carried out on an individual basis (experimental arm A) or in a group setting (experimental arm B). The third arm served as control.

Progress of the study

A pilot study was carried out in the summer 2012. 10 patients participated in the pilot study. The pilot study showed that at 6 out of the 10 patients receiving treatment for alcohol dependence were willing and able to run in groups on a regular basis, supported by running instructors. (Roessler et al., 2013). The randomized controlled trial started enrolling patients in medium May 2013, and stopped enrolment in February 2015. 175 patients were enrolled of which 62 were randomized into training in groups, 60 to individual training and 53 to control group.

Challenges

Throughout the study, fewer patients than expected sought treatment for alcohol problems; a tendency that as seen not only in Odense, but in the Danish society as such. Furthermore, the refusal rate for participation in the study was higher than expected. In the end of enrolment, 345 consecutive patients had been introduced to the study, and 175 patients had accepted. The reasons for refusing to participate were mostly health problems.

Follow up data

During 2015, the main tasks in the study was collection of follow up data and preparation of analyses and publications, based on the baseline data and on the qualitative data collected among patients who dropped out of the study. The follow up rate at 6 months (collection of data for primary outcome) was 79% (137 patients) and 12 months follow up and 12 months 56% (98 patients). The follow up rate at 12 months may still increase since the data collection in this wave has not closed yet.

Data Cleaning
Baseline data and data from the 6 months follow up has been entered in the database, cleaned and prepared for analysis.

Results and publications
Currently, the paper presenting the primary outcome of the study is under preparation. Professor Kirsten Kaya Roessler, Professor Claus Ekstrøm, and PhD-student Sengül Sari are working on the analyses. In addition, a series of papers on the qualitative data and the baseline data are under preparation or have been submitted.

The baseline characteristics of the participants in the Healthy Lifestyle Study can be seen in the table below.

TABLE 1: Baseline characteristics of the sample

	Group training	Individual training	Control	Total
	N=62	N=60	N=53	N=175
Age (mean, SD)	44.8 (11.3)	44.4 (10.9)	47.2 (11.6)	45.4 (11.2)
Male (%)	58	78	74	70
Education (%)				
None	31	29	25	28
Skilled worker	41	46	47	45
college < 3 yrs	5	3	2	3
college > 2 yrs	23	22	27	23
Marital status (%)				
married/cohabiting	31	22	52	34
Employment (%)				
full time	41	53	47	47
TLFB (mean, SD)				
drinks/month	217.1 (210.3)	329.4 (240.4)	243.2 (239.3)	263.6 (233.6)

Perspective
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.

Inspiration and sparring group for the project
The project group behind Healthy Lifestyle study has developed a strong collaboration with researchers from Oslo, in particular Prof. Egil Martinsen, Medicinsk Institut, Oslo Universitet (http://www.med.uio.no/klinmed/personer/vit/egilwm/), Prof. Thomas Clausen, Institute of Clinical Medicine, Oslo Universitet, SERAF Norwegian Centre for Addiction Research, (http://www.med.uio.no/klinmed/english/people/aca/thclause/), and Ashley Muller, Medicinsk

Institut, Oslo Universitet, SERAF SERAF Norwegian Centre for Addiction Research (http://www.med.uio.no/klinmed/english/people/aca/ashleym/).

PI, coordination of study and PhD-students
Principal Investigator and project coordinator: Professor Kirsten K. Roessler, Institute of Psychology, SDU.
Project co-supervisor: Assistant professor Randi Bilberg
PhD student: Sengül Sari

The organization of the RESCueH-studies/UCAR

Steering committee and International Advisory Group
A Steering Committee, a Research Office and an International Scientific Advisory Board has been established. The International Advisory Board consists of: Dean Ole Skøtt (SDU) (chair), CEO Kim Brixen (OUH), Research Vice Director Sissel Vorstrup (Lundbeckfonden), Research Director Anders Hede (Trygfonden), Medical Director Anders Meinert (Region of Southern Denmark), Professor WR Miller (CASAA, UNM), Professor Gerard Schippers (Amsterdam Institute for Addiction Research), Dr. Gillian Tober (Leeds Addiction Unit).

The Steering committee consists of: Dean Ole Skøtt (SDU) (chair), CEO Kim Brixen (OUH), Research Vice Director Sissel Vorstrup (Lundbeckfonden), Research Director Anders Hede (Trygfonden), Medical Director Anders Meinert (Region of Southern Denmark).

Research Office
Director Anette Søgaard Nielsen (UCAR, SDU)
Professor Bent Nielsen (UCAR, SDU)
Research secretary Jena Weber(UCAR, SDU)

Overview of staff at the RESCueH studies (Danish Site), 2015
Director Anette Søgaard Nielsen (UCAR, SDU)
Research secretary Jena Weber (UCAR, SDU)
Professor Bent Nielsen (UCAR, SDU)
Professor Kjeld Andersen (UCAR, SDU)
Professor Kirsten Kaya Roessler (Department of Psychology, SDU)
Professor Claus Ekstrøm (Section of Biostatistics, IFSV, KU)
Professor Jes Søgaard, (Clinical Medicine, AU)
Assistant professor Randi Bilbjerg (UCAR, SDU)
Data manager Lars Søgaard (OPEN, SDU)
PhD student Angelina Mellentin (UCAR, SDU)
PhD student Jakob Emiliussen (UCAR, SDU)
PhD student Sengül Sari (Institute of Psychology, SDU)
PhD-student Lotte Kramer, (UCAR, SDU)
PhD-student Anne-Sophie Schwartz (UCAR, SDU)
Research assistant Birgit Jensen (UCAR, SDU)
Research assistant Rikke Hellum (UCAR, SDU)
Student Martin Mau (Department of Psychology, SDU)
Student Josefine Pilegaard (Department of Psychology, SDU)
Dr. Kurt Jensen (Department of Sports Science)
Student Karoline Mathiasen (Department of Psychology, SDU)
Student Ann Jessen (Department of Psychology, SDU)
Student Charlotte Nielsen (Department of Psychology, SDU)
Student Camilla Sødekvist (Department of Psychology, SDU)
Student Sine Østergaard (Department of Psychology, SDU)
Student Nina Burmester, (UCAR, SDU)

Student Ayse Corab (UCAR, SDU)
Student Emil Hvidberg (UCAR, SDU)
Student Klara Capelle (UCAR, SDU)
Student Louise Bundsgaard (UCAR, SDU)
Student Sibel Yilmaz (UCAR, SDU)

Collaborating Danish treatment institutions in 2015

The Alcohol Treatment Centre in Odense who participates in all five studies: the Relay Study, the Elderly Study, the Self-Match Study, the Cue Exposure Study and the Healthy Lifestyle Study.
The Alcohol Treatment Centre in Aarhus and the *Alcohol Treatment Centre in Copenhagen*, who participates in the Elderly Study.
The Alcohol Treatment Centre in Aabenraa, who participates in the Relay Study.
Gastrointestinal, neurological and orthopaedic departments at Odense University Hospital and *Aabenraa Hospital,* who participate in the Relay Study.

International collaborators in 2015

The Elderly study:
Professor Gerhard Buehringer: Principal Investigator for the German site in the Elderly Study, and his team. The study interventions at the German site will be conducted in the (1) Chair of Addiction Research, Technische Universität Dresden, and (2) Institut für Therapieforschung, Munich.
Professor Michael Bogenschutz: Principal Investigator for the US site in the Elderly Study, and his team. Dr. Snehal Bhatt took over the formal position as PI in the summer 2015. The study intervention at the US site is conducted in the First Choice Family Practice Clinics, New Mexico.
Associate professor Teresa Moyers, CASAA, University of New Mexico, who is supervising, training and monitoring treatment fidelity in the Elderly Study.
Program operations director Roberta Chavez, CASAA, New Mexico, who is training and supervising the interviewers in the use of FORM90 in the Elderly Study.

Spin off projects and collaborations in 2015

- **Phase One Application** for receiving status as Excellent Psychiatric Clinical Research Unit in the Region of Southern Denmark. Application submitted December 2015 and currently under review.
- **Grant application: The RELIP-project: development of an algoritm for screening for alcohol problems in electronic hospital records** (in preparation, based on data from the Relay-study). Project group, Danish site: Anette Søgaard Nielsen (UCAR), Professor Uffe Kock Wiil (Mærsk-McKinney Institute, SDU), professor Anders Søgaard (Center of Language Technology, KU, Claus Duedal Petersen (CIMT, SDU), and professor Aleksander Krag (OUH). Currently in preparation and to be submitted to the Innovation Foundation May 2016.
- **Grant application: Alternatives to nagging, pleading, and threatening: A study on strategies to get loved ones to seek treatment for alcohol dependence.** A cluster randomized controlled trial on methods to empower the relatives of problem drinkers who are reluctant to seek treatment. Project group: Randi Bilberg (coordinator), Anette Søgaard

Nielsen (PI), Kjeld Andersen, Claus Ekstrøm, Bent Nielsen. Application re-submitted to Trygfonden, December 2015.

- **A qualitative study of the assessment instrument MATE (measurements in the addictions for triage and evaluation).** Project group: Morten Hell (coordinator), Kjeld Andersen (PI), Anette Søgaard Nielsen - in collaboration with Professor Gerard Schippers and Theo Broekman, Holland. Granted 872.000,- from The Psychiatric Research Foundation in Region of Southern Denmark.
- **Grant application: Blended care in treatment for alcohol problems.** Development and evaluation of a therapist-supported Internet-based treatment for alcohol use disorder blended with face-to-face sessions, aimed at improving compliance and structure in out-patient treatment. In collaboration with the Center of Telepsychiatry, and Arkin Institute, Amsterdam and Sundhed.dk. Anette Søgaard Nielsen (UCAR) (PI), Marie Paldam Folker (co-investigator). In preparation and to be submitted to Trygfonden, September 2016.
- **Grant application: Psych-id study.** A cluster randomized study testing the outcome of systematic screening and treatment of anxiety and depression in alcohol-dependent patients. Bent Nielsen (PI). In preparation. Funding: To be determined and applied for.
- **Alcohol and Culture.** Interdisciplinary alcohol studies. A network consisting of researchers from the humanities, epidemiology and the clinical world held a workshop in November 2015. The network is currently writing a special edition of the Nordic Journal of Alcohol and Drug about Alcohol Culture to be published in 2017. Funding: Nice Welfare, University of Southern Denmark. Professor Anne-Marie Mai and Associate Professor Anette Søgaard Nielsen (eds)

Dissemination of project, results and alcohol treatment related topics in 2015

Research publications

Published in 2015

Andersen K, Bogenschutz MP, Bühringer G, Behrendt S, Bilberg R, Braun B, Ekstrøm CT, Forcehimes A, Lizarraga C, Moyers TB, Nielsen AS. **Outpatient treatment of Alcohol Use Disorders among subjects 60+ years. Design of a randomized controlled trial conducted in three countries (Elderly-study).** BMC Psychiatry (2015) 15:280 DOI 10.1186/s12888-015-0672-x.

Bæksgaard Hansen M, Kolster S, Danquah IH, Nielsen AS, Becker U, Tjørnhøj-Thomsen T, Tolstrup JS. **I may suspect a welfare recipient of drinking, but as long as he does as told – he can drink himself to death. A qualitative analysis of Alcohol and Employment, a randomized controlled trial**. BMC Public Health, 2015, DOI: 10.1186/s12889-015-1620-x.

Mellentin, AI, Nielsen B, Stenager E. Nielsen AS. **The effect of co-morbid depression and anxiety on the course and outcome of alcohol outpatient treatment: a prospective cohort study.** Nordic Journal of Psychiatry 2015;69(5):1-8. (doi:10.3109/08039488.2014.981857)

Nielsen AS, Nielsen B. **Implementation of a Clinical Pathway Improves Alcohol Treatment Outcome**. Addiction Science & Clinical Practice, 2015; 10:7 (7 March 2015), DOI 10.1186/s13722-015-0031-8

Accepted in 2015 and primo 2016:

Nielsen AS, Ellermann AE. **Need to know and wish to know: What clients find important to know about treatment for alcohol problems in order to be able to decide whether to start treatment or not.** Nordic Studies on Alcohol and Drugs, accepted

Schwarz AS, Bilberg R; Bjerregaard L; Nielsen B; Søgaard J; Nielsen AS. **Relay model for recruiting alcohol dependent patients in general hospitals- A single-blind pragmatic randomized trial.** BMC Health Services Research, accepted

Mellentin A.I., Nielsen B., Nielsen A.S., Yu F., & Stenager E. Study protocol: **A randomized controlled study of exposure therapy as aftercare for alcohol use disorder.** *BMC Psychiatry*, accepted

Submitted in 2015 and primo 2016

Tarp KHH, Nielsen AS. **When Alcohol Treatment via videoconferencing makes sense: A qualitative semi-structured interview study on patient perspectives.** International Journal on Behavioural Medicine. (Submitted)

Sari S, Müller AE, Roessler KK. **Exercising alcohol patients don't lack motivation – but struggle with structures, emotions and social context.** British Journal of Health Psychology (Submitted)

Hansen MB, Nielsen AS, Becker U, Tolstrup JS. **Alcohol and Employment – a pragmatic randomised controlled trial among unemployed individuals with problematic alcohol consumption.** Journal of Studies on Alcohol and Drugs (Submitted)

Schmidt LK, Bojesen AB, Nielsen AS, Andersen K. **Does Time and intensity Matter? A Systematic Review and Meta-Analysis of the Duration of Psychosocial Treatments for Alcohol Use Disorders**. (Submitted)

Hellum R, Bjerregaard L, Nielsen B, Nielsen AS. **Factors influencing whether nurses talk to somatic patients about alcohol consumption.** Nordic Studies on Alcohol and Drugs (Submitted)

Nielsen AS, Nielsen B, Andersen K, Roessler KK, Søgaard J, Bühringer G, Bogenschutz M, Ekstrøm CT. **The RESCueH programme: Testing new non-pharmacologic interventions for Alcohol Use Disorders: Rationale and methods.** European Addiction Research (Submitted)

Emiliussen J, Nielsen AS, Andersen K. **Causes for late onset alcohol use disorder - a systematic review.** Addiction Research & Theory. (Submitted)

Sari S, Bilberg R, Jensen K, Pilegaard J, Roessler KK. **Physical activity patterns in patients with alcohol use disorder.** BMC Public Health (Submitted)

Nielsen AS, Nielsen B. **Improving Outpatient Alcohol Treatment Systems: Integrating focus on motivation and Actuarial Matching.** Patient Preference and Adherence (Submitted)

Roessler KK, Bramsen, Dervisevic A, Bilberg R. **Exercise based interventions for alcohol use disorder. A comment on motivational aspects of participation.** (Submitted)

Mellentin, A. I., Brink, M., Andersen, L., Bjerregaard, L. B. L., Stenager, E., Erlangsen, A. & Christiansen, E. **The Risk of Offspring Developing Substance Use Disorders when Exposed to One versus Two Parents with Alcohol Use Disorder: A Nationwide, Register-based Cohort Study.** *Journal of Psychiatric Research.* (Submitted)

In preparation in 2015 - 2016

Schwarz AS, Kruse M, Søgaard J, Nielsen B, Søgaard Nielsen A. **Does excessive alcohol use lead to increase in health costs?** (working title, in preparation)

Mellentin AI, Nielsen B, Hellum R, Bojesen AB, Nielsen AS. **The impact of social phobia on alcohol treatment outcomes among outpatients: A naturalistic follow-up study.** (working title, in

preparation)

Nielsen B, Nielsen AS **Outrearch visits to psychiatric department** (working title, in preparation)

Bilberg R, Nielsen B, Nielsen AS. **Treatment for alcohol dependence: The impact of living with children.** (working title, in preparation)

Sari, S. & Roessler, K.K. **The challenges of adding physical activity to alcohol treatment – a qualitative interview study on motivation and drop-out patients.** (working title, in preparation)

Mellentin AI, Yu F, Nielsen B, Nielsen AS, Stenager E**. Mental healthcare applications targeting alcohol use disorder: a systematic review and meta-analyses** (working title, in preparation)

Nautrup Andersen C, Andersen K, Nielsen AS. **Early and late onset of alcohol dependence among men and women** (working title, in preparation)

Posters, 2015
Behrendt S, Braun B, Kohlmann A, Hergert J, Bogenschutz M, Nielsen AS, Andersen K, Bühringer G. **Drinking patterns and alcohol use disorder characteristics in senior citizens with DSM-5 alcohol use disorder entering an outpatient short-term intervention: results from a randomized clinical trial.** First European conference on addictive behaviours and dependencies, Lisbon

Emiliussen J, Nielsen AS, Andersen K. **Causes for Late onset Alcohol Use Disorder: a Critical Systematic Review.** International Conference on Treatment of Addictive Behaviours (ICTAB), Odense.

Ellermann AE, Nielsen AS. **What kind of information do I as a patient want, before I start treatment for alcohol abuse?** ICTAB, Odense

Sari S, Bilberg R. Roessler KK. **Alcohol patients on a treadmill – how fit are they?** ICTAB, Odense.

Tarp KHH, Nielsen B, Nielsen AS. **Analysis of participation refusal within a randomized controlled study of alcohol treatment via videoconference.** ICTAB, Odense.

Bilberg R, Andersen K, Behrendt S, Bogenschutz M, Braun B, Bühringer G, Lizarraga C, Nielsen AS. **Study management – process experiences from The Elderly Study** ICTAB, Odense.

Bilberg R, Roessler KK. **Psychological distress among people with an alcohol use disorder in a physical activity treatment**, ICTAB, Odense.

Mellentin, A. I., Brink, M., Andersen, L., Bjerregaard, L. B. L., Stenager, E., Erlangsen, A, Christiansen, E. **The risk of offspring developing substance use disorders when exposed to parental alcohol use disorder: a register-based prospective cohort study.** ICTAB, Odense.

Schmidt LS, Nielsen AS, Andersen K. **Does the duration matter? A systematic review of psychosocial interventions for AUD – initial results**. ICTAB, Odense

Books and book chapters in 2015
Nielsen AS. **Oversigt over behandlingsforløb. In: Nina Brunes, Bjarne Elholm, Nanna Kappel (eds) Mennesker med Alkoholproblemer**. Nyt Nordisk Forlag, 2015. ISBN-13 9788717042353

Nielsen AS. **Alkoholafhængighed.** In Alkohol – et sundhedsfagligt problem af Ulrik Becker og Janne S. Tolstrup (eds). Munksgaards Forlag, in press.

Nielsen AS. **Psykosocial behandling**. In Alkohol – et sundhedsfagligt problem af Ulrik Becker og Janne S. Tolstrup (eds). Munksgaards Forlag, in press.

Nielsen AS. **Familierelateret behandling**. In Alkohol – et sundhedsfagligt problem af Ulrik Becker og Janne S. Tolstrup (eds). Munksgaards Forlag, in press.

Nielsen AS. **Betydningen af alt det andet, der påvirker behandlingen: Behandlingsformen, struktur i behandlingen og efterbehandling.** In Alkohol – et sundhedsfagligt problem af Ulrik Becker og Janne S. Tolstrup (eds). Munksgaards Forlag, in press.

Hesse M, Thylstrup B, Nielsen AS. **Matching patients to treatments or matching interventions to needs.** In: Handbook of drug and alcohol studies – social science perspectives. Eds Torsten Kolind, Betsy Thom & Geoffrey Hunt SAGE (in press)

Translations in 2015
Nielsen AS. Danish Translation of **Motivational Interviewing Treatment Integrety (MITI) 4.2. Coding Manual**.

Oral presentations at workshops, conferences and meetings in 2015
Bilberg R, Andersen K, Bogenschutz M, Bühringer G, Lizarraga C, Behrendt S, Braun B, Nielsen AS. **Treating Alcohol Problems in the Elderly (+60 years),** European Association of Substance Abuse Research (EASAR), Wales

Schmidt LS, Nielsen AS, Andersen K. **Treatment of Alcohol Use Disorder. Does the duration of the intervention matter? A systematic review.** EASAR, Wales.

Emiliussen J. **Præsentation af resultater fra et systematisk review om ældre personer med sent påbegyndt alkoholproblemer.** EASAR, Wales.

Sari S. **Exercise in alcohol treatment – a relapse prevention strategy.** EASAR, Wales

Nielsen AS, Bjerregaard L. **Hospitalized patients and their lifestyle.** International Conference on Treatment of Addictive Behaviour (ICTAB). Odense.

Andersen K, Bogenschutz M, Bühringer G, Behrendt S, Braun B, Forcehimes A, Bilberg R, Lizzarago C, Nielsen AS. **Introduction to the Elderly study: Treatment for alcohol problems among 60+ year**

persons. ICTAB, Odense

Andersen K. **A description of the group of patient +60 who have sought treatment so far at the Danish site, and the conditions, under which treatment is sought and given.** ICTAB, Odense,

Forcehimes A, Bogenschutz M, **A description of the group of patient +60 who have sought treatment so far at the US site, and the conditions, under which treatment is sought and given.** ICTAB, Odense.

Braun B, Bühringer G. **A description of the group of patient +60 who have sought treatment so far at the German sites, and the conditions, under which treatment is sought and given.** ICTAB, Odense.

Roessler K. **Interpersonal problems of alcohol patients undergoing an exercise intervention.** ICTAB, Odense.

Roessler KK, P**roject Healthy Lifestyle.** Malmø.

Emiliussen J. **Arbejdsliv i psykiatrien: Den PhD-studerendes plads i forskningen. SDU**

Bilberg R, Andersen K, Nielsen AS. **Elderly-studiet: Sammenhængen mellem psykologiske lidelser, alder, køn og drikkemønstre**. Psykiatriens forskningsdag, Fredericia

Hellum, R. **Factors influencing whether nurses will talk to somatic patients about alcohol consumption.** Psykiatriens forskningsdag, Fredericia

Emiliussen, J **Hvad er problemet i at søge behandling? Resultater fra en kvalitativ undersøgelser med personer over 60 år, med alkoholproblemer** Psykiatriens forskningsdag, Fredericia

Schmidt LS, Bojesen AB, Nielsen AS, Andersen K. **Systematisk review og meta analyse af varigheden af de ambulante psykosociale behandlingstilbud til mennesker, der lider af "Alcohol Use Disorders**. **Forskningsinterview viser sig at have en signifikant indflydelse på effekt af behandlingen.** Psykiatriens forskningsdag, Fredericia.

Sari S. **Hvor fysisk aktive er alkoholafhængige?** Psykiatriens forskningsdag, Fredericia.

Dissemination in general in 2015
Nielsen AS, Andersen K. **Drikker din patient? Fokus på alkohol i almen praksis – det er ikke så svært.** Practicus, 2015;24:30-31

Newsletters
UCAR sends out newsletters from the RESCueH-studies to practitioners and everybody else who have an interest.

Website
www.sdu.dk/ucar

Other routes of dissemination of findings
www.alkopedia.dk (in collaboration with Alcohol & Society, and Trygfonden).

UCAR arrangements (conferences, symposia and large meetings) in 2015

Symposium on Assessment Instruments and Strategies. Odense. Key Note speakers: professor Gerard Schippers, Associate professor Angela Buchholz, Professor Mads Uffe Pedersen, Associate professor Anette Søgaard Nielsen. (One day). Odense, 20th of January.

13th International Conference of Treatment of Addictive Behaviours (ICTAB) in close collaboration with CASAA, University of New Mexico. Conference director: Anette Søgaard Nielsen. Conference Co-director: Barbara McCrady. Odense, 31th of Mai – 4th of June. Furthermore, RESCueH-researchers gave the following symposia on ICTAB:

- Andersen K (chair and organizer): Symposium on **Alcohol Dependence among the Elderly**. ICTAB, Odense.
- Roessler KK (chair and organizer): Symposium on **Physical Activity and Alcohol Use Disorder.** ICTAB, Odense.
- Nielsen B (chair and organizer): Symposium on **Bridges between Mental Health and Addictions.** ICTAB, Odense.
- Nielsen AS. (Organizer): Symposium on **Somatic Hospitals and prevention of Alcohol problems,** ICTAB, 2015

Interviews, television, newspaper articles and the like in 2015
Roessler KK. Motionsafhængighed skal erstatte alkoholmisbrug. Kristeligt Dagblad, 27.7. 2015
Roessler KK. Fysisk aktivitet og bevægelse hjælper alkoholpatienterne. Helse, 17. august 2015.

Masters dissertations in 2015
Elisabeth Everest (Psykologi): **Analyse af CMD-SQ data fra Healthy Lifestyle.** Supervisor: Kaya Roessler.
Christian Nautrup Andersen (Medicine): **Early and late onset of alcohol dependence**. Supervisors: Kjeld Andersen & Anette Søgaard Nielsen
Mia Kuni (Medicine) **Differences in alcohol dependents who have and haven't been sexually abused.** Supervisors: Kjeld Andersen & Anette Søgaard Nielsen
Gitte Rasmussen (Medicine) **Differences between male and female alcohol dependent patients**. Supervisors: Kjeld Andersen & Anette Søgaard Nielsen

Appendix 1.

DATA AND SAFETY MONITORING PLAN for the Elderly Study

General Considerations

The risks of the interventions used in this study are minimal. The data and safety monitoring plan is therefore mainly designed to monitor study progress, including recruitment, retention, data quality, and adherence to the protocol.

Institutional Reviews

All study procedures have been approved by the Ethical Committees in the involved countries prior to beginning the study. These follow local guidelines, which in Denmark and US implies that the ethics committee monitors the safety of participants. In Denmark and in US, this is achieved by the committee approves a yearly report on adverse events to ensure that all safety procedures are followed according to protocol and no one is not harmed in any way due to participation in the study.

Data Safety

The data collected throughout the study will be entered and stored in a secure database by the means of the software program REDCAP, located at OPEN at University of Southern Denmark, Institute of Clinical Research:
http://www.sdu.dk/en/om_sdu/institutter_centre/klinisk_institut/forskning/forskningsenheder/open.

The databases in OPEN can only be accessed by limited staffs groups who have been appointed direct authority to handle the data. All accesses to the databases are monitored and logged. The databases in OPEN are under the inspection of the Danish Data Monitoring Authorities.

When enrolled in the study each participant will receive a unique participation number. The link between this participation number and information identifying the participant is at all times kept locally at the research sites. The data entered in the database in OPEN are only entered under this participation number. Only the Danish participants have name and address entered in REDCAP. It is impossible to identify any non-Danish individual in the database.

The local project coordinators have access to read, opportunity to change and export own data in OPEN. The project coordinator on the Danish site (Randi Bilberg) has, together with the main principal researcher, Kjeld Andersen reading and export access to data from all sites, except on information that can identify non-Danish participants.

Data monitoring

When randomized, all patients receive a participation number. When the participation number is entered in the database, a data account for the particular participation number is generated. The Data Manager (Lars Søgaard) at OPEN will together with Randi Bilberg, the Danish study coordinator, monitor the flow of data on an ongoing basis and report recruitment to the local site-leaders, coordinators and principal investigators every week. The data delivered from the Lars

Søgaard and Randi Bilberg on recruitment, missing data etc., will (can) only be based on aggregated data or on the participation number. The link between these data and a participant can only be made locally.

During the study, data on the participants are collected on paper or entered directly in REDCAP, depending on whether or not interviewers have access to internet when interviewing the participant or not. Hence, the local coordinators are responsible for monitoring data storage and secure data completeness during the project of patient enrollment and follow up. The local procedures are as follows:

Denmark: At the Danish research site, all data are collected and stored either directly in REDCAP during the interview with the participants or collected on paper and entered into REDCAP shortly after the interview. The research coordinator browses through data regularly in order to monitor data completeness, missing follow-ups etc. The Danish interviewers meet with the local coordinator every month and ensure consistency in the data collection process.

Germany (Munich): At the Munich research site, all data are collected and stored either directly in REDCAP during the interview with the participants or collected on paper and entered into REDCAP shortly after the interview. The research coordinator browses through data regularly in order to monitor data completeness, missing follow-ups etc. Interviewers are supervised and monitored regularly.

Germany (Dresden): At the Dresden research site, all data are collected and stored either directly in REDCAP during the interview with the participants or collected on paper and entered into REDCAP shortly after the interview. The research coordinator browses through data regularly in order to monitor data completeness, missing follow-ups etc. Interviewers are supervised and monitored regularly.

US:
At US research site, all data are collected and stored either directly in REDCAP during the interview with the participants whenever possible. Data are collected on paper and entered into REDCAP shortly after the interview. The research coordinator browses through data regularly in order to monitor data completeness, missing follow-ups etc. Interviewers are supervised and monitored regularly. Research coordinator meets with the research team frequently to continue to assess the progress of data entry and the needs of the project.

The project coordinators monitor the data collection locally and have regular Skype meetings to ensure consistency across sites.

From 1st of January 2016 all sites shall secure that data are entered in REDCAP either during the interview with the participant or within a week after at the latest. From 1st of January 2016, Randi Bilberg and Lars Søgaard will send out a status on data completeness every month.

Data cleaning

Professor Claus Ekstrøm is overall responsible for the data cleaning process. All baseline data on patients enrolled before 31st of December 2015 will be checked and cleaned by the following procedure:

Start date	End date	Action
1-1-2016		Baseline data for "green" participants eligible for cleaning ("Green" participants = participants with all baseline data entered in REDCap)
15-1-2016	15-2-2016	Generation of frequency tables and distributed to all countries
16-2-2016	15-3-2016	Each site assess their "own" tables (and may look at the data from the other countries) Based on this assessment of tables: discussion and definition of outliers (Skype meetings) Decision of "rules of corrections" will be documented
16-3-2016	15-4-2016	Corrections will be made based on "rules of corrections" and documented Data for these participants are locked The last participants enrolled are entered in REDCap (baseline-data)
16-4-2016	15-5-2016	The procedure is repeated for the remaining participants: Frequency tables Correction of outliers The whole data set (baseline data) is locked and ready for analyses.
1-6-2016		The absolute last date! – for locking the baseline data set

Similar procedures will be carried out for follow up data.

Procedures for Monitoring and Reporting Adverse Events.

Adverse events (AEs) will be collected according to the sites' national legal procedures in relation to patient safety, when they come to the awareness of study staff. In addition, information on adverse events will be captured in the study data system as follows:

Adverse Events: For the purpose of this study, information on the following events is collected and reported in the data system:

- Alcohol Use Events, including
  - Worsening of alcohol use
  - Need for higher level of care
  - Signs and symptoms of withdrawal
  - Alcohol craving
  - Admission for detoxification and/or residential treatment
  - Medical events that are directly related to alcohol use
  - Diagnosis of dependence and drinking >= 60 gram (men) or 30 gram (women) per day

Serious Adverse Events: For the purpose of this study, the following SAEs is collected and recorded in the data system. According to the local ethical guidelines they will be reported to the ethical committees only if they are both unexpected and probably study-related.

- Admission to a hospital or freestanding residential facility for drug detoxification.
- Inpatient hospital admission for a psychiatric event (i.e. suicidality, depression).
- Any suicidality (independent of hospitalization) reported at any time during participation in the study.

Adherence to the treatment manual

The treatment in the study consists of Motivational Enhancement Therapy and Community reinforcement Approach, adjusted to elderly. The therapy described in details in the treatment manual. Local on-site trainers will trained by Theresa Moyers during a 4-days train-the trainers course.

All treatment sessions will be recorded and therapist adherence to manual will be monitored and supervised. Overall fidelity to the manual will be calculated, based on at least 10% randomly chosen recordings of treatment session. All audiotapes are only identified by participation number, therapist conducting the therapy, session number and date.

The group of local treatment supervisors meet with Theresa Moyers every second week during the first two project years, receive supervision and discuss potential discrepancies across sites. Potential changes to treatment manual are documented on the common secure sharepoint, and it is noted if the decided change has impact on the data.

Adherence to interview procedures.

All interviewers and local coordinators will be trained in Form 90 by Roberta Chavez. The group of interviewer coordinators meet on skype with Roberta Chavez every second month throughout the project period, receive supervision and discuss potential discrepancies across sites.

Adherence to the protocol.

The project coordinators and the PIs (the so-called operations group in the Elderly Study) meet face-to face at least every year during the first years of the study, and every week on skype throughout the whole study. Potential changes decided for are documented in a file on the common secure sharepoint, and it is noted if the decided change has impact on the data.

Independent Interim Analysis.

Independent Interim analyses are not required in studies like The Elderly Study.