



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 was launched on 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 2020. A status of the organization around the projects will also be described.

Background

With the series of 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, prevent relapse and support rehabilitation.

The Relay Study – recruiting patients to treatment

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

Purpose of the study

We hypothesized that the Relay Model would be more effective and less costly than standard methods with regard to the referral of alcohol-dependent patients from hospital to specialized treatment.

Design and original plan

In a randomized controlled design, the Relay Model was 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 (rural area), who screen positive for excessive use of or positive for alcohol dependency using the Alcohol Use Identification Test (Audit), were enrolled in the study. The primary outcome comprised the health care costs in the year following the intervention. The secondary outcome was 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 were 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 met the patient before discharge. If the patient screened positive for excessive drinking, the therapist offered a motivational talk and brief advice concerning the possibility of cutting down. If the patient screened positive for alcohol dependence, the therapist explained the significance of continuing outpatient aftercare and presented an "attendance contract." This contract included information about the prognosis for alcohol disorders and options for attending outpatient care. The patient was given an appointment at the alcohol treatment clinic and recommended to place the contract in a prominent place at home.

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

Progress of the study

A pilot study on the screening procedure was carried out on one of the participating departments at Odense University Hospital (Department O, orthopaedic Surgery) 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 at the departments of gastroenterology, and orthopaedic Surgery at Odense University Hospital ended in June 2016. The data collected from the patients was cleaned and ready for analysis in spring 2017. Data from the registers, describing costs of subsequent use of alcohol treatment, health care, social services etc., data from the National Register on Alcohol Treatment was collected in winter 2017. The data formed the basis for Anna-Sophie Schwarz' PhD-study. The first analysis was performed in 2018, and Anne-

Sophie Schwarz handed in her thesis ultimo 2018, reporting Primary and Secondary outcomes of the study. She defended her thesis in 2019. Professor Bent Nielsen, together with Research Assistant Jeppe Tryggedsson, began to make full use of the data collected and to conduct the last analyses in 2019 and 2020, including performing a three-year follow-up study. Due to the Corona pandemic, data from the national registers has, however, been delayed. This last part of the study is, thus, expected to be finalized in 2021.

Primary and secondary outcomes of the study

During the study period, a total of 6102 adult patients from the uptake areas of the alcohol treatment centers were admitted to the somatic hospital departments involved in the study; of these, 2568 patients were excluded and, thus, a total of 3534 patients completed the lifestyle questionnaire. Of those, 609 patients scored 8 points or more in the AUDIT test and were included in the study.

The treatment-as-usual (TAU) group consisted of 333 patients and the Relay group of 276 patients. Twenty-six percent of the patients (n=72) randomized to the Relay group did not receive the intervention. The alcohol therapists noted that the reasons most often were that the patients had been discharged before the alcohol therapists arrived or they were in surgery. A total of 30 patients from the TAU group and 18 from the Relay group were lost to follow-up.

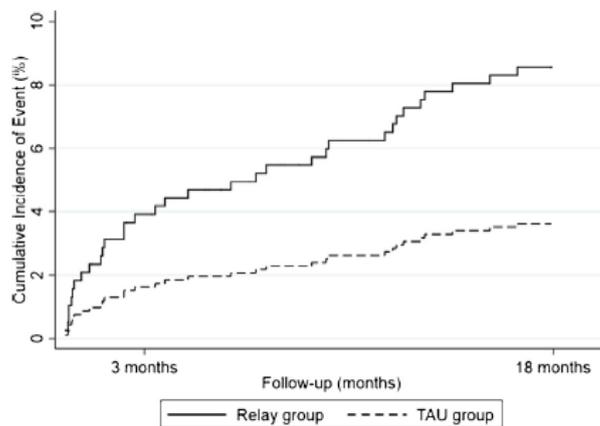
The remaining 561 patients were included in the present analysis. A significant difference in the AUDIT score groups between the Relay group and the TAU group ($p=0.011$) was found. More patients in the Relay group had AUDIT 16+ (39%) compared with the TAU group (27%). A total of 19 patients accepted a meeting contract arranging for them to attend an alcohol treatment center following discharge (it was optional). In addition, according to the alcohol therapists' notes, 18 patients wanted to arrange their own alcohol treatment visit. Everyone who received the Relay intervention received a brochure about the local alcohol treatment.

A total of 33 patients in the study sample attended outpatient treatment during the 18 months after being discharged from hospital. Of these, 22 patients (8.5% of the total number) belonged to the Relay group and 11 (3.6%) to the TAU group. The number-needed-to-treat was 20 [95% CI, 11.2;112.3]. The AUDIT scores for patients who met for treatment were significantly higher than the scores for patients who did not ($p=0.002$).

Figure 1. shows unadjusted Kaplan-Meier cumulative-event curves for attending alcohol treatment in the Relay group and the TAU group.

In the unadjusted analysis at 3 months follow-up, significantly more patients in the Relay group attended treatment (OR=4.9(1.4–7.5) $p=0.015$). After 18 months follow-up, the significant difference between the groups was still present (OR=2.5(1.2–5.2) $p=0.017$). The difference was still significant after adjusting for AUDIT scores at both 3 months (OR=3.8 (1–13.8) $p=0.04$) and 18 months (OR=2.1 (1–4.5) $p=0.05$) (Schwarz et al, 2019).

Figure 1.



The Relay group had higher mean healthcare costs than the TAU group which was mainly due to more somatic and psychiatric outpatient visits, however, we did not find a statistically significant difference in healthcare costs in the two groups at follow-up in any model ($p=0.613$). We also did not find statistically significant differences when we modelled the subgroups of health care costs separately. The difference in total social costs was also not statistically significant. No significant difference was found in productivity between the TAU and the Relay group.

We performed subgroup analysis where we looked first at the patients who scored 8-15 on AUDIT and next the patients who scored 16+. We did not find a statistically significant difference in either subgroup. In the next subgroup analysis, we looked only at the group from Odense (87% of the sample) the mean healthcare costs are much higher than for the entire group (DKR 98139 for Relay group and DKR 75852 for TAU group), but the difference was not statistically significant.

In the quantile analysis of the 10-90 percentiles of the healthcare costs we did not find any statistically significant differences at a 5 percent level (see table 5). When performing a simple regression model with health care costs as a function of treatment group we did not find a statistically significant association ($p=0.1050$), and when we controlled for AUDIT score, the p-value became even higher ($p=0.1794$) suggesting that part of the association can be explained by differences in AUDIT scores (Schwarz et al, 2020).

Spin off studies, 2nd generation studies and perspectives:

Relip-study

The data from the Relay-study created the possibility for the study *Reading between the lines – the Relip-study*. The Relip-study aims at developing algorithms that can form the basis for developing a tool for the electronic care notes at the hospital case in order to help staff address unhealthy alcohol use among the patients. The Relip-study is funded by the EU Interreg study Access& Acceleration, aims at calculating such an algorithm.

The Danish National Health Authorities, the National Data Protection Agency, and the heads of the involved hospital departments gave permission to use data from the patient records for this add-on study and thereby made the Relip-study possible. The Relip study is performed as a PhD-study, and so far, PhD-student Ali Ebrahimi, together with colleagues, have developed very promising algorithms by means of natural language processing and machine learning techniques that can identify alcohol problems with a high level of accuracy. The findings of the RELIP-study, building on data from the three departments of OUD that participated in the Relay Study, are so promising that we are currently applying for funding for up-scalation of the project. The next step will be developing similar algorithms covering all departments of the hospital and, if the findings continue to be promising, subsequently develop a software-prototype for a Decision Support Tool (DST) to be implemented in the electronic health record at the hospital. If this step also proves to be successful, at full-scale implementation study will be created together with the clinical staff in order to investigate the effectiveness of the DST.

Ali Ebrahimi's main supervisor and PI on the Relip-study is Professor Uffe Kock Wiil, Mærsk McKinney Institute, University of Southern Denmark. Professor Anette Sjøgaard Nielsen from the Unit of Clinical Alcohol Research is co-supervisor and, together with Professor Kjeld Andersen, member of the steering committee behind the study. The first step of the Relip study is expected to be finalized primo 2021.

Also, building on the Relay study and as an add-on project to the Relip-study, Research assistant Christina Oxholm performed a series of qualitative interviews among staff and patients at the somatic hospital. The aim of the interviews was both to uncover the attitude towards systematic screening for problematic alcohol use, as such, among patients and, in particular, the staff's and patients' attitude towards screening data from the Electronic Health Records (EHR) by means of an algorithm, in order to detect the alcohol problems. The hope was to uncover potential ethical dilemmas in developing and implementing a future DST in the EHR. This study was funded by the University of Southern Denmark and led by professor Anne-Marie Søndergaard from the Institute of Culture at University of Southern Denmark, in close collaboration with Professor Anette Sjøgaard Nielsen, Unit of Clinical Alcohol Research. The findings of the study have been or are currently being published.

Publications from the Relay study so far

1. Schwarz AS, Bilberg R; Bjerregaard L; Nielsen B; Sjøgaard J; Nielsen AS. **Relay model for recruiting alcohol dependent patients in general hospitals- A single-blind pragmatic randomized trial.** BMC Health Services Research, 2016; 16:132, DOI 10.1186/s12913-016-1376-8
2. Hellum R, Bjerregaard L, Nielsen AS. **Factors influencing whether nurses talk to somatic patients about their alcohol consumption.** Nordic Studies on Alcohol and Drugs, 2016;33:415-436,
3. Schwarz A-S, Nielsen B, Nielsen AS. **Lifestyle factors in somatic patients with and without potential alcohol problems.** Journal of Public Health, DOI 10.1007/s10389-017-0885-1
4. Schwarz AS, Nielsen B, Sjøgaard J, Nielsen AS, **Making a bridge between general hospital settings and community-based treatment for alcohol use disorder. A pragmatic**

randomised controlled trial. Drug and Alcohol Dependence, March 2019, DOI: 10.1016/j.drugalcdep.2018.12.017

5. Schwarz AS, Kruse M, Nielsen AS, Nielsen B, Sjøgaard J. **Health care consumption for somatic patients following a brief outreach alcohol intervention.** Nordic Journal of Health Economics, 2020; 8:1: 13-30

Spin off publications and publications, partly building on data and findings from the Relay-study (next-generation studies):

1. Ebrahimi A, Wiil UK, Mansourvar M, Shaiki GM, Naemi A, Nielsen AS. Alcohol Use Disorder Prediction Using Machine Learning: A Systematic Literature Review. Fourth International Workshop on ICT Solutions for Health (ICTS4eHealth'19). Accepted.
2. Oxholm C, Nielsen AS, Christensen A-M S. The Ethics of Algorithms in Healthcare. Cambridge Quarterly of Healthcare Ethics, Accepted.
3. Ebrahimi A, Wiil UK, Nielsen AS, Mansourvar M. A Predictive Machine Learning Model to Determine Alcohol Use Disorder. IEEE Fifth International Workshop on ICT Solutions for Health. 2020. DOI: 10.1109/ISCC50000.2020.9219685
4. Oxholm C, Christensen A-M S, Christensen R, Nielsen AS. Can we talk about alcohol for a minute? Thoughts and opinions expressed by health professionals and patients at somatic hospital. Alcohol Treatment Quarterly, 2020. <https://doi.org/10.1080/08039488.2020.1814407>.
5. Ebrahimi A, Nielsen AS, Wiil UK, Mansourvar M. The prediction of Alcohol Use Disorder: A scoping review. Proceeding, 2019 IEEE Symposium on Computers and Communications (ISCC). June 2019. DOI: [10.1109/ISCC47284.2019.8969764](https://doi.org/10.1109/ISCC47284.2019.8969764)
6. Schwarz AS, Nielsen B, Nielsen AS. Changes in profiles of patients seeking treatment and treatment outcomes in Denmark following policy changes. Journal of Public Health, DOI 10.1007/s10389-017-0841-0

Publications in progress:

Ali Ebrahimi, Uffe Koch Wiil, Marjan Mansourvar, Amin Naemi, Andersen K, Nielsen AS. Analysis of Comorbidity of Alcohol Use Disorder. ICHI2021, In review.

Oxholm C, Christensen A-M S, Wiil UK, Christensen R, Nielsen AS. Attitudes of patients and health professionals towards an algorithm screening for indications of high alcohol consumption: a qualitative study. In re-review, JMIR

Ebrahimi A, Wiil UK, Mansourvar M, Andersen K, Nielsen AS. A Deep Neural Network Application to Identify Patients with Alcohol Use Disorder Based on Historical Electronic Health Records. Conference paper submitted to 31st Medical Informatics Europe Conference (MIE2021). In review

PI, coordination of study and PhD-students in the Relay-study

Professor Bent Nielsen (UCAR) (PI)

Assistant Professor Randi Bilberg (coordination)

Research Assistant Rikke Hellum (after having assisted on the Relay-study, Ms Hellum is now a PhD-student)

Research Assistant Jeppe Tryggedsson (after having assisted on the Relay-study, Mr Tryggedsson is now a PhD-student)

Professor Jes Sjøgaard (supervisor)

PhD student Anne-Sophie Schwarz. After having received her PhD, Ms Schwarz is now employed at Sundhedsdatastyrelsen.

Professor Anette Sjøgaard Nielsen (supervisor)

The Elderly Study – individualized treatment

The **Elderly Study** aimed to improve the prognosis for a particular patient group by tailoring treatment to match individual needs.

Purpose of the study

The study evaluated new methods for treating 60+ year old patients with alcohol use disorders.

Design

The Elderly study was designed as a randomized controlled trial with two arms and conducted in three different countries with 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 the US (Albuquerque), were enrolled in the study. The patients were randomized to either (A) *Standard treatment* or (B) *Extended treatment*.

Interventions

(A) *Standard Treatment* comprised four sessions of Motivational Enhancement Therapy over four weeks. This intervention was likely to be offered, typically, in general practice, or possibly to the intervention offered at specialized treatment centres, which lack experience with this patient group. In the present study, the intervention in this arm was considered standard treatment, although the intervention was far briefer than treatment typically offered alcohol dependent patients seeking treatment in specialized treatment institutions.

(B) *Extended treatment* was the experimental intervention in the present study and comprised 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 for seniors, CRA-S). The CRA-S encouraged sobriety by helping the patient create routines and activities that were meaningful to the patient and rewarded staying sober. Particular focus was to establish sober social networks and to coping with aging.

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

Primary outcome

Percentage of patients with abstinence or controlled use (maximum daily alcohol intake equivalent to BAC \leq 0.05%) in the last 30 days at 6 months after start of treatment

Hypothesis

1. Fifty percent of the patients randomly assigned to a brief outpatient behavior therapy program (Standard treatment; 4 sessions of MET) would show a clinically significant improvement of their drinking pattern between onset, end of treatment and 6-month follow-up.
2. Patients randomly assigned to a more intensive outpatient behavior therapy (Extended treatment, MET plus CRA-S) would show greater improvement of their drinking pattern between onset, end of treatment and 6-month follow-up. A clinically significant difference in outcome was defined as at least a 10% greater rate of abstinence or drinking in a controlled manner in treatment group 2 compared to group 1.

Progress and conclusions of the study

Intervention and data collection

The Danish site began enrolling patients in the pilot study mid-January 2014. The German and US site began enrolling patients on 1st of March 2014. The enrolment of patients ended on the 31st of March 2016 at the German sites, at the US site, and in Copenhagen and Aarhus. Enrolment ended on the 30th of April 2016 in Odense, and the interventions offered to the last participants ended in August 2016. All the follow up interviews were finalized in autumn 2017. Data were cleaned in winter 2017. During the data cleaning process of baseline data, we realized that information on some of the DSM V criteria was missing for some of the patients enrolled in the early stages of the study. Regrettably, this led to the exclusion of 11 patients, for whom it was not possible to give a DSM V diagnosis. In 2019, the primary outcome was published. Analysis of data will continue during 2020 and 2021 due to the vast amount of data collected in the study, in addition to data from registers that supplement the data on the Danish participants. Analyses and future publications will be performed by PhD-students and senior researchers.

Findings

Table 1 presents a few baseline data from each country. The data suggested a few interesting differences between cultures, although some of the differences may be explained by differences in recruitment procedures. Although statistically significant differences were found, some of the differences were not big in absolute terms and, therefore, deemed not clinically relevant.

Table 1	Danish site N=341	American site N=149	German site N=203	p-value *
Males (%)	64,2	59,7	52,2	0,02
Mean age, years (SD)	65,1 (4.1)	65,2 (5.2)	66,5 (4.8)	<0.01
Marital status:				
Married/partner (%)	44.6	39.9	56.7	<0.01
Separated/single (%)	46.3	54.4	32.5	
Widower (%)	9.1	6.7	10.1	0.42
Employment status:				
Full/part time work (%)	15.3	28,2	23.7	<0.01
Retired (%)	62.8	50.3	71.4	<0.01
Alcohol measures				
Number of drinking days, mean¹, (SD)	14.9 (10.5)	21.0 (10.5)	22.7 (9.1)	<0.01
Days with binge drinking, mean¹, (SD)	11.8 (10.2)	15.0 (12.0)	15.6 (12.2)	<0.01
Alcohol Dependence, mean (SD)²	12.2 (5.9)	12.2 (7.2)	6.1 (3.8)	
Major depressive episode (%)⁵	9.7	8.7	4.9	NS
Social phobia (%)⁵	1.2	1.3	0	NS

¹ Last 30 days prior to treatment start, binge drinking defined as drinking more than 60 grams of pure alcohol per day

² Alcohol Dependence Scale, missing information on 15 participants

³ PEN-scale, missing information on this scale from 3 participants

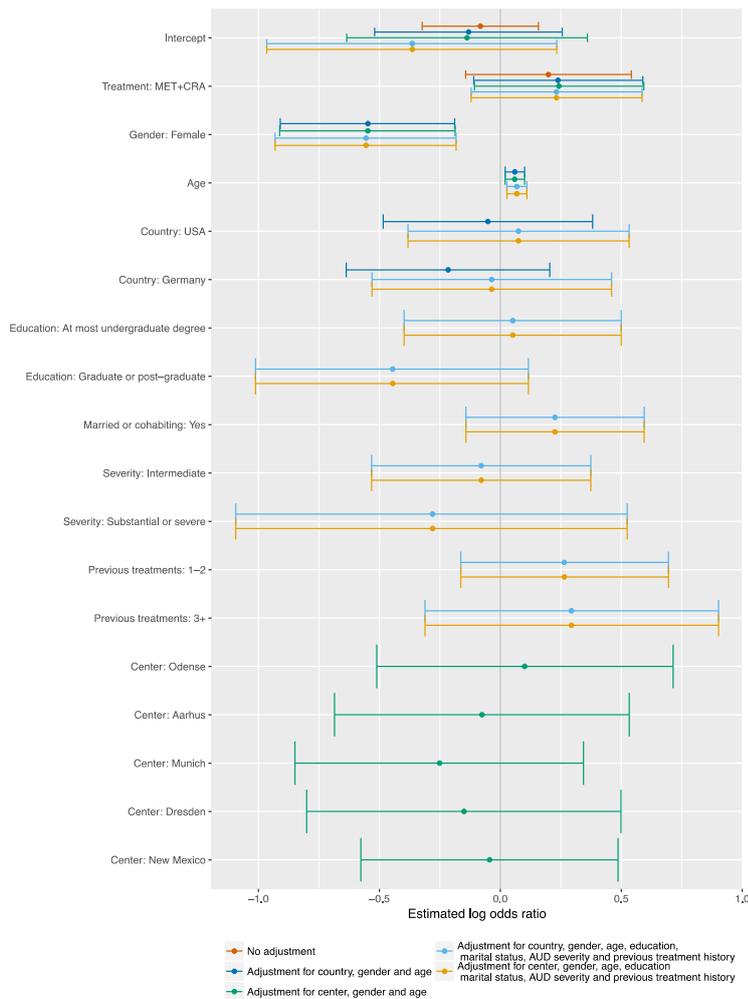
⁴ Drinker Inventory of Consequences -2R, sum of all items except control item 5, 15, 25, 35 and 45. Total score may range between 0 and 135. Missing information on this scale from 32 participants

⁵ Screening positive according to MINI

* Fisher's exact test when comparing proportions, and Kruskal-Wallis equality-of-populations rank test when comparing equality of median. Means are reported in the table for easier reading.

At 26 weeks following inclusion in the study, 48.3% among the patients randomized to Standard treatment (4 sessions, MET) met the criteria for treatment success, compared to 52.3% among the patients randomized to extended treatment (4 sessions MET + 8 sessions CRA-S). Hence, the clinically relevant difference between the two treatment options at minimum 10% points was not achieved. As can be seen from the full model, shown in figure 1, not only were there no differences in outcome between treatment methods, but neither between countries.

Figure 1



The only factor in the model with significant impact on treatment outcome was gender. When controlling for all other factors, women had a significantly worse prognosis than men. This finding was rather surprising. The overall conclusion of the Elderly study is that relatively brief treatment is possible with good and comparable results in both Europe and USA.

Sub-studies within the Elderly-Study (Postdoc studies, PhD-studies and pre-graduate studies)

A PhD-study was carried out at the Danish site by Jakob Emiliussen, focusing on why some elderly start drinking late in life. The PhD-study recruited informants among the Danish participants in the Elderly Study. Participants, who did not start drinking excessively until after the age of 60, were asked for an extra qualitative interview. The main findings were that after a lifelong unproblematic (at times heavy) use of alcohol, it seemed that using alcohol as a coping strategy was one of the main factors in very late-onset alcohol use disorder among the participants. The participants expressed how they experienced a marked loss of identity when they had no activities to fill up their time after retirement. Social activities involving alcohol were also closely related to very late-onset alcohol use disorder. The study concludes that loss of identity, coping with physical and psychological problems, an overarching societal and social culture surrounding alcohol and the interrelationship between social life, alcohol use and heavy drinking are important factors that need to be addressed clinically and preventively, and specifically for individuals experiencing very late-onset alcohol use disorder (Emiliussen, Andersen & Nielsen, 2017). Jakob Emiliussen defended his thesis, based on qualitative data from the Elderly Study, in spring 2017.

The Postdoc Study *Psycho-pathology among elderly alcohol dependent patients who seek treatment (working title)* focusing on symptoms and severity of the mental disorders, including the alcohol use disorders among the participants in the Elderly study, began when the data was collected. The main researcher on the study is Silke Behrendt from the Dresden site of the study, where she functioned as the local project manager. In 2018, dr. Behrendt moved to Denmark to continue her work as a postdoc on the Elderly data. In the Autumn 2019, dr. Behrendt became Associate Professor at the Institute of Psychology at the University of Southern Denmark. So far, two publications have been published, and further three publications are in review.

The PhD-study *Factors influencing the effect of therapy for alcohol use disorders – a study of duration, quality of treatment and research assessments*, focusing on the general factors of treatment and their impact of treatment outcome, was initiated in 2016. PhD-student Lotte Kramer defended her thesis in May 2019. Three publications from this sub-study have been published.

The PhD-study *Epidemiology of older adults with problematic drinking habits* will, by means of register-data on the Danish participants in the Elderly study and on healthy controls, explore the sociodemographic background of older adults, to understand which subgroups, if any, have a higher risk of heavy drinking and AUD, and what effect heavy drinking has on morbidity and mortality rates. In addition, the PhD-study will investigate the prognosis of older adults suffering from alcohol use disorder, compared to older heavy drinkers and to older adults, who perform sensible drinking. The study was initiated in 2017, and part-time PhD-student Anna Mejldal is expected to defend her thesis in June 2021. So far, five publications from this sub-study have been published.

The PhD-study *Alcohol Use Disorder: self-reported alcohol intake – elucidating characteristics on outpatients aged 60 years and older who underreport alcohol intake* will assess the association between underreporting alcohol consumption and effect of treatment for alcohol use disorders, and identify parameters associated with increased risk of underreporting patients based on hair analysis and collected data from the Elderly study. The study was initiated in 2017, and PhD-student Dorthe Grüner Nielsen is expected to finalize the study primo 2022. All the hair samples have been analysed in collaboration with the Department of Chemical Engineering, Biotechnology and Environmental Technology, and the data analysis is being performed. So far, a systematic review from this sub-study has been published, and one publication is in review.

The PhD-study *Understanding gender differences in treatment outcome among a clinical sample of 60+ year old individuals seeking treatment for AUD* will examine gender differences related to the distribution of problems at treatment start and subsequent choice of psychosocial skills training modules during the treatment phase, examine gender differences in the association between the Personal Happiness Form (PHF) and Quality of Life (QoL), and examine gender differences related to treatment compliance and alcohol related and quality of life-related outcome of treatment, taking the findings described above into consideration, including choice of treatment modules. The PhD-study was initiated on 1st of January 2021 and PhD-student Jeppe Tryggedsson is expected to finalize the study ultimo 2023. The study is co-funded by SDU and the Psychiatric Research Foundation in Region of Southern Denmark.

The pre-graduate study *Elderly with relief/reward drinking patterns: characteristics and treatment outcomes* will compare the effect of MET to MET+CRA, among elderly individuals (60+ years) with a relief or reward-driven drinking pattern, differentiated into clinical subgroups. Thus, the study investigated whether treatment outcomes vary per differentiated subgroups regarding two different treatment approaches. Pre-graduate student Peter Schøler finalized the first part of the study in the late summer of 2018. After having concluded his KBU, Peter Schøler and colleagues are finalizing and submitting the publication in 2021.

*Spin-off studies and 2nd generation studies, building on or inspired by the Elderly-study
Elderly Wellbeing and Alcohol: A Tricky Cocktail.*

The project is a natural next step from the Elderly Study. During observations and qualitative interviews with staff, elderly and their significant others, the project identifies, describes and develops strategies to solve the ethical dilemmas and problems arising in relation to alcohol and elderly in nursing homes and elderly with assisted living at home. The project group consists of Professor Søren Harnow Klausen (PI) from the Institute of Cultural Science (IKV), Anette Søgård Nielsen from the Unit of Clinical Alcohol Research (UCAR), Jakob Emiliussen (UCAR), Regina Christiansen (IKV & UCAR) and Søren Engelsen (IKV). The Velux Foundation granted the project DKR 5.020.680 in 2017, of which 1.300.000 is a subgrant for the Unit of Clinical Alcohol Research.

Narratives of older treatment-seeking drinkers

This study, which is part of Narrative Medicine on SDU, is being performed by Postdoc Jakob Emiliussen and Professor Anette Sjøgaard Nielsen, Unit of Clinical Alcohol Research, in collaboration with Associate Professor Cindie Aagaard and Assistant Professor Anita Wohlmann, Institute of Culture, University of Southern Denmark. In addition to performing a systematic review of the scientific literature in order to identify master-narratives on how older patients explain development of their alcohol use disorder, the study also builds on data collected as part of the Elderly-study. A narrative analysis of a random sample of the recordings of first encounters between therapists and patients participating in the Danish part of the Elderly study is being performed. This additional study is supported by a grant from the University of Southern Denmark, the Human-Health grant. The first publication from this sub-study is currently in review.

Kodningslab.dk.

During the Elderly-study, the research unit developed a high level of expertise in monitoring, fidelity assessment and giving feedback to staff on their performance of psychosocial treatment sessions, based on recordings of the sessions. After having finalized her PhD on this topic, dr. Kramer Schmidt applied for and received a research grant from Trygfonden to develop a sustainable coding lab that can assist future research studies and help clinicians staying attuned when they perform psychosocial interventions, building on these experiences. The grant allowed the development of a safe and smooth infra-structure of the coding lab in submission and coding processes of recordings. So far, the coding-lab can assess the quality of sessions based on Motivational Interviewing and deliver feedback to staff. Projects on how to best train staff and secure the quality of psychosocial interventions are currently being planned.

Publications from the Elderly study so far

1. Mejdal A, Andersen K, Behrendt S, Bilberg R, Christensen AI, Lau CJ, Möller S, Nielsen AS. History of health care use and disease burden in older adults with different levels of alcohol use. A register-based cohort study. *Alcoholism: Clinical and Experimental Research*. 2021; 45:3:638-649. DOI: 10.1111/acer.14562.
2. Nielsen DG, Andersen K, Nielsen AS, Juhl C, Mellentin AI. Consistency between self-reported alcohol consumption and biological markers among alcohol use disorder patients – a systematic review. *Neuroscience and Biobehavioral Reviews*, 2021. DOI: 10.1016/j.neubiorev.2021.02.006
3. Mejdal A, Andersen K, Behrendt S, Bilberg R, Bogenschutz M, Braun B, Bühringer G, Nielsen AS. Treatment of seniors suffering from alcohol use disorders: WHO Drinking Risk Levels Reductions following treatment and their relation to quality of health and DSM-5 symptoms. *Alcoholism: Clinical and Experimental Research*. 2021. DOI: 10.1111/acer.14562
4. Schmidt LK, Andersen K, Nielsen AS. Differences in the delivery of Motivational Interviewing across three Countries. *Journal of Ethnicity in Substance Abuse*. 2020.

5. Behrendt S, Kuerbis A, Bilberg R, Braun B, Mejldal A; Bühringer G, Bogenschutz M, Andersen K, Nielsen AS. Impact of comorbid mental disorders on outcomes of brief outpatient treatment for DSM-5 alcohol use disorder in older adults. *Journal of Substance Abuse Treatment*, 2020. DOI: 10.1016/j.jsat.2020.108143
6. Mejldal A, Andersen K, Behrendt S, Bilberg R, Christensen AI, Lau CJ, Möller S, Nielsen, AS. Twenty years socioeconomic trajectories in older adults with varying alcohol use: A register-based cohort study. *Alcohol and Alcoholism*. 2020. DOI: 10.1093/alcalc/agaa019
7. Mejldal A, Andersen K; Bilberg R, Möller S; Nielsen AS. DSM-5 latent classes of alcohol users among treatment seeking older adults. *Substance Use & Misuse*, 2020, 55:8, 1214-1222. doi.org/10.1080/10826084.2020.1731546.
8. Mejldal A; Braun B, Bilberg R, Bühringer G, Bogenschutz M, Nielsen AS, Andersen K, Behrendt S. The Alcohol Dependence Scale and DSM-5 Alcohol Use Disorder: Severity ratings correspond insufficiently in older patients. *International Journal of Methods in Psychiatric Research*. 2019 Dec 5:e1811. doi: 10.1002/mpr.1811.
9. Andersen K, Behrendt S, Bilberg R, Bogenschutz M, Buehringer G, Braun B, Ekstrøm CT, Mejldal A, Petersen AH, Nielsen AS. Evaluation of adding the Community Reinforcement Approach to Motivational Enhancement Therapy for Adults Aged 60 Years and Older with DSM-5 Alcohol Use Disorder: A Randomised Controlled Trial. *Addiction*, 2020; 115(1):69-81 <https://doi.org/10.1111/add.14795>
10. Schmidt LK, Nielsen AS, Moyers TB, Andersen K. Is Motivational Interviewing fidelity associated with alcohol outcomes in treatment seeking 60+ year old citizens?" *Journal of Studies on Alcohol and Drugs*, 2019, 101, 1-11. <https://doi.org/10.1016/j.jsat.2019.03.004>
11. Emiliussen J, Andersen K, Nielsen AS, Braun B, Bilberg R. What do elderly problem drinkers aim for? Choice of goal for treatment among elderly treatment seeking alcohol dependent patients. *Nordic Journal on Alcohol and Drugs*, 2019, <https://doi.org/10.1177/1455072519852852>.
12. Schmidt LK, Nielsen AS, Andersen K, Moyers T. Lessons learned from measuring fidelity with the Motivational Interviewing Treatment Integrity code (MITI4). *Journal of Substance Abuse Treatment*, 2018, <https://doi.org/10.1016/j.jsat.2018.11.004> .
13. Behrendt S, Braun B, Bilberg R, Bühringer G, Bogenschutz M, Nielsen AS; Mejldal A, Andersen K. DSM-5 alcohol use disorder features among treatment-seeking older adults. *SUCHT*, 2018; 64:185-196. <https://doi.org/10.1024/0939-5911/a000550>.
14. Schmidt LK, Bojesen AB, Nielsen AS, Andersen K. Duration of therapy – does it matter? A systematic review and meta-analysis of the duration of psychosocial treatment for alcohol use disorders. *Journal of Substance Abuse Treatment* 2018:84 57–67

15. Nielsen AS, Bilberg R, Andersen K. Self-assessed stress level among elderly seeking treatment for alcohol use disorder. A descriptive study. *Alcohol* 2017, 60, May, (Supplement S19)
16. Emiliussen J, Nielsen AS, Andersen K. Identifying Risk Factors for Late-Onset (50+) Alcohol Use Disorder and Heavy Drinking: A Systematic Review, *Substance Use & Misuse*, 2017; DOI: 10.1080/10826084.2017.1293102
17. Emiliussen J, Nielsen K, Nielsen AS. Why do some older adults start drinking excessively late in life? - results from an Interpretative Phenomenological, Study. *Scandinavian Journal of Caring Sciences*, 2017, doi: 10.1111/scs.12421.
18. Emiliussen J, Nielsen AS, Andersen K. How do older adults with very late-onset alcohol use disorder define alcohol problems? - *Results from an interpretative phenomenological study.*, *Alcoholism Treatment Quarterly*. 2017;32(2):151-164. Tilgængelig fra, DOI: 10.1080/07347324.2017.1288480
19. Emiliussen J, Andersen K, Nielsen AS. How does family pressure, health and ambivalence factor into entering alcohol treatment? Results from an interpretative phenomenological inquiry into the experiences of people aged 60 and older with alcohol use disorders. *Nordic Studies on Alcohol and Drugs*. 2017;34(1):28-42.
20. Nielsen AS, Nielsen B, Andersen K, Roessler KK, Sjøgaard 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*, 2016;22:306–317
21. Andersen K, Bogenschutz MP, Bühringer G, Behrendt S, Bilberg R, Braun B, Ekstrøm CT, Forchimes 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.

Publications submitted and in review

1. Behrendt S, Braun B, Bilberg R, Bühringer G, Bogenschutz M, Mejdal A, Andersen K, Nielsen AS. Post-treatment alcohol use disorder symptoms predict disadvantageous long-term treatment outcomes in seniors with DSM-5 AUD
2. Ismaeeli ARP; Andersen K, Behrendt S; Bilberg R, Braun B; Bogenschutz M; Bühringer G; Nielsen AS; Mejdal A. Achieving treatment goal and quality of life outcome in alcohol dependent patients. Re-Submitted, *Alcohol & Alcoholism*.

Spin off publications, partly building on findings from the Elderly-study (next-generation studies):

1. Emiliussen J, Maagaard CA, Wohlmann A, Nielsen AS. How do patients narrate their perceptions of alcohol problems? Systematic review of medical and psychological research

literature. JSAD, submitted.

2. Harnow SH, Engelsen S, Christiansen R, Emiliussen J. Elderly Well-being and Alcohol: A tricky Cocktail. A study protocol. *International Journal of Qualitative Studies*. 2020, doi.org/10.1177/1609406920931687
3. Rettie H, Emiliussen J. Practical impressions of interpretative phenomenological analysis from the novice's standpoint. *Nurse Researcher* 2018; 26(2). DOI: [10.7748/nr.2018.e1589](https://doi.org/10.7748/nr.2018.e1589)
4. Emiliussen J, Morrison AD. Alcohol use and generational masculinity: An interdisciplinary approach. *Nordic Studies on Alcohol and Drugs* 2017; 34(4):314-329

Book chapters

1. Nielsen AS, Andersen K. Alkohol på godt og ondt. In: Emiliussen, J. og Klausen, S. H (eds). *Ældrevelværd – Samtidsperspektiver på aldring og det gode liv*. Aalborg Universitetsforlag. In press.

PhD- and pre-graduate students within the Elderly Study

Jakob Emiliussen, Phycologist. Thesis defended in 2017. Currently in a postdoc and clinical position.
Lotte Kramer Schmidt, MD. Thesis defended in 2019. Currently in a combined postdoc and clinical position.

Anna Mejldal, MSc. Part-time PhD-study in progress. Expected to defend her thesis in June 2021

Dorthe Grüner Nielsen, MD. PhD-study in progress. Expected to defend her thesis medio 2022

Jeppe Tryggedsson, M.Sci. PhD-study in progress. Expected to defend his thesis ultimo 2023

PIs, coordination of study, senior researchers in "the Elderly-group"

Professor Kjeld Andersen, UCAR (PI, Danish site and PI, overall),

Professor Michael Bogenschutz, NYU Langone Medical Center and MD (PI, US site)

Professor Gerhard Bühringer, Technische Universität, Dresden/Institut für Therapieforschung (PI, German site). Adjunct Professor at the Unit of Clinical Alcohol Research, SDU.

Professor Anette Søgaard Nielsen (Danish site and overall coordinator of RESCueH)

Project leader, PhD Randi Bilberg (DK)

Associate Professor Silke Behrendt (G, DK)

Postdoc Barbara Braun (G)

Inspiration and sparring for the project 2020

Associate Professor Alexis Kuerbis has collaborated on specific publications, Professor Katie Witkiewitz has discussed and given feedback on a sub-study.

The Self-Match Study – involving patients in treatment decisions

The **Self-Match Study** is 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

Consecutive patients aged 18-60 years who, either at presentation or after detoxification, wish to start treatment at the Alcohol Treatment Clinic in Odense, were offered participation in the study. The Alcohol Treatment Clinic had five psychosocial treatment options: Contract therapy, cognitive behavioural therapy, family therapy, supportive therapy and environmental therapy. In the Self-Match Study, patients, who accepted participation, were randomized to: (A) an experimental arm, involving patient choosing one of the five treatment options themselves, or (B) treatment as usual, involving expert assignment to one of the five treatment options, based on an algorithm.

The patients were interviewed at baseline and 6 months after treatment start. Enrolment of patients was concluded in spring 2019, and follow-up data collected ultimo 2019.

Hypothesis

We expected that patients, who chose their own treatment method, would drink significantly less alcohol one year after treatment initiation than those who were assigned treatment as usual, by means of a research-based algorithm (expert matching). We hypothesized that this would be due to improved adherence to the treatment programme among patients, who chose their own treatment.

Progress of the study

Procedure

When seeking treatment at the alcohol treatment center, all patients received treatment as usual and were, thus, offered pharmaceutical treatment for withdrawal symptoms if needed and had 1-3 sessions of Motivational Interviewing (MI) before the assessment and initiation of one of the five treatment options. At this point, patients were invited to participate in the study by a research assistant, who was not part of the clinical staff. If they agreed to participate, they were randomized to either self-matching to treatment (Informed Choice) or allocation to treatment as usual by an algorithm (TAU).

The algorithm was developed based on follow-up studies from locally performed trials and previously found to increase the overall outcome of treatment, compared to a historic control group, where patients were allocated to treatment based on the expertise of the therapist only. The algorithm is based on a composite score from the seven problem areas derived from the Addiction Severity Index (ASI): medical health, employment, alcohol and drug use, illegal activity, social problems, family relations, and psychiatric problems, and then patients are matched to the degree of structure of the treatment options.

After randomization, the research staff showed the patients in the self-match group a video presentation of the five treatment options, and based on that information, the patients chose the treatment they preferred. The algorithm matches patients' characteristics to the structure of the treatment, hence, the focus in the video presentation was on providing information on the structure of the treatment options. The treatment options were shown in random sequence to avoid selection bias. To ensure that the patients' decisions were not affected by others, they were asked to choose their treatment after seeing the videos and before they left. The vast majority of patients chose immediately after seeing the videos, and only a few had additional questions, wished to see the videos one more time, or needed to think for some minutes before they chose their treatment.

After having been either chosen or assigned to treatment option, the patients received treatment according to the manuals and standard procedures for the particular treatment option. A treatment course would typically last three months.

Initiation of the study

The study began to enrol patients in May 2017. At the end of 2018, 340 patients were enrolled. Only very few patients have refused to participate in the study. Enrolment continued until 402 patients had accepted participation and concluded in May 2019. Patients were followed up six months after enrolment in the study. A total of 78 (20%) were lost to follow-up.

Findings

The Self-Match group chose supportive therapy twice as much as it was offered in the TAU group, and, in contrast, the TAU group was assigned to contract treatment more often than was chosen by the Self-Match group. There was no difference between Self-Match and TAU-group in how many patients received cognitive therapy, family therapy, and environmental therapy. Because of this difference, treatment type was adjusted for in the primary and secondary outcome analyses.

In the Self-Match group, 53 (28%) chose the same treatment options as the algorithm would have assigned them to. On all the outcome measures there were no significant differences between those who chose the same treatment as the algorithm prescribed, and those who did not.

There was no significant difference between Self-Match group and TAU regarding treatment satisfaction: In both the Self-Match group and the TAU group, three out of four patients were satisfied or very satisfied with the treatment they had received. There was, however, a significant difference (p -value <0.001) regarding satisfaction on whether the patient got the opportunity to choose. 120 (80%) in the Self-Match group were satisfied with being randomized to self-matching whereas only 43 (25%) in the TAU group were satisfied with being randomized to expert matching.

Both groups showed great reduction in number of heavy drinking days. The Self-Match group reduced number of heavy drinking days during the last month from 17.14 (SD 10.60) to 3.43 (SD 6.63) and the TAU group reduced mean number of heavy drinking days from 15.45 (SD 10.88) to 3.58 (SD 7.02). There were no significant differences between Self-Match and TAU.

All four QOL domains were improved after treatment, but there was no statistically significant difference between Self-Match and TAU. Further, the secondary drinking outcomes also improved

overall, but there was no statistical difference between Self-Match and TAU. Likewise, there was no statistical significance on retention.

Spin-off and 2nd generation studies, building on the Self-Match study

Morten Hell has applied the Psychiatric Research Foundation for funding of a post-doc project, aimed at investigating the implementation of shared decision-making in a Psychiatric Department.

Publications from the study so far

1. Hell M, Miller WR, Nielsen B, Nielsen AS. The impact of free choice in alcohol treatment. Primary outcomes of the Self-Match study, Drug and Alcohol Dependence. 2021. 10.1016/j.drugalcdep.2021.108587 .
2. Hell M, Nielsen AS. Does patient involvement in treatment planning improve adherence, enrolment and other treatment outcome in alcohol addiction treatment? A systematic review. *Addiction Research & Theory* (IART). 2019, <https://doi.org/10.1080/16066359.2020.1723083>.
3. Hell ME, Nielsen B, Miller WR, Nielsen AS. Is treatment outcome improved if patients match themselves to treatment options? Study protocol for a randomized controlled trial. BMC Trials. 2018;19:219. <https://doi.org/10.1186/s13063-018-2592-9>
4. Nielsen AS, Ellermann AE. Need to know and wish to know: What individuals 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*, 2016;33;2:123-137

Publications currently in preparation

1. Hell M, Nielsen B, Nielsen AS. Personality Traits and Alcohol Consumption: Secondary Analysis of the Self-Match Study. Submitted.

Staff at the Self-Match study

Principal Investigator: Professor Anette Søgaard Nielsen

PhD student Morten Hell. Defended his thesis in March 2021 and continues in a combined clinical and postdoc position.

Supervisor: Professor WR Miller.

Professor Bent Nielsen

Interviewer: Birgit Jensen.

The Cue Exposure Study – preventing relapse after treatment

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

Design

The study was a randomized controlled trial with three arms, of which two were 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 smartphone 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 May 2015 till Medio 2017, were offered participation and enrolled in the study. The patients were interviewed at baseline, just before aftercare treatment, and at 8 and 26 weeks after initiation of aftercare. Data collection included relevant questionnaires and interview instruments.

Interventions

(A) Aftercare comprising therapist-led CET: The patients in this group participated in four 2-weekly group sessions, delivered by a therapist without the use of a smartphone.

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

(C) Standard aftercare: The patients in this group attended an individual follow-up session 8 weeks after discharge from treatment. This session contained no CET.

Hypothesis

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

Progress of the study

The application for the smartphone was finalized in 2014 and presented to patients and therapists in order to receive feedback. After that, it was adjusted and tested again. Training of the therapist was performed at the beginning of 2015, and Dr Bodil Andersen was attached as supervisor for the therapist throughout the study.

Patients, who started primary treatment after the 1st of February 2015, were offered participation in the study when they were 3 months into their treatment course and planned termination of treatment. Patients, who agreed to participate in the Cue Exposure aftercare study, were randomized to either CET-based aftercare in groups, to CET by means of the application for smartphone, or aftercare as usual. Hence, the first patients were enrolled in May 2015.

The last patients offered participation in Cue Exposure Aftercare study were individuals starting primary treatment on the 30th of April 2017. They concluded their primary treatment in July and were after that offered participation in the Cue Exposure Aftercare study. Hence, enrolment of the patients in the Cue Exposure study was concluded at the end of July 2017. A total of 164 patients were enrolled in the study. 153 (93%) patients completed the post-treatment assessment 8 weeks after beginning aftercare treatment, and the last 6 months follow-up data was be collected primo 2018.

Challenges

Throughout the study, fewer patients than expected sought treatment for alcohol problems; a tendency that was seen not only in Odense, but in Danish society as such. Furthermore, the refusal rate for participation in the study was higher than expected. Relatively many patients did not want aftercare treatment since they felt that they finalized treatment and were ready to try out the strategies they had learned through treatment by themselves.

Findings

During the inclusion period, a total of 323 patients, fulfilling the eligibility criteria, finalized primary treatment, and were offered to participate in the Cue Exposure aftercare study. A total of 159 declined to participate, and 164 (51%) were enrolled in the study and completed pre-aftercare assessment.

Approximately 70% of the participants in the Cue Exposure study were relatively well-educated having completed either vocational training, a bachelor's degree at vocational academies or university colleges (≤ 4 years education) or a university degree or other higher education (> 4 years education) after finishing elementary school or high school. In addition, for approximately 50% of the sample, the source of revenue was employment income, and 10% were students receiving grants, state loans and employment income. Around 35% were pensioned, mainly due to retirement, and the rest of the sample was temporarily out of employment, on sickness benefits, unemployment benefits or cash assistance. A total of 153 (93%) individuals completed the post-aftercare assessment 8 weeks after beginning aftercare: 94% ($n=51$) in the CET in groups-arm, 91% ($n=49$) in the CET Smartphone-arm, and 95% ($n=53$) in the aftercare as usual- arm.

No differences in the trajectories were found between the experimental groups (CET GA and SAA) compared to AAU on drinking- and craving outcomes over time. Both the CET in groups-arm (Est.= 5.99, SE 2.59, $z=2.31$, $p= 0.021$) and the CET Smartphone arm (Est.=4.90, SE= 2.26, $z=2.31$, $p= 0.021$) showed increased use of the USCS compared to AAU at post-treatment, but the effect attenuated at the 6-month follow-up. Finally, no differences were detected between the experimental groups on any outcomes.

The conclusion of the Cue Exposure study is that neither CET with USCS delivered via group session, nor a smartphone application as aftercare, increased the effectiveness of primary treatment.

Spin-off and next-generation studies

After finalizing her phd-study, Angelina Mellentin continued to work as postdoc on the Cue Exposure study, performing sub-studies and analyzing the large amount of data collected in the Cue Exposure study. In 2020, Angelina Mellentin has initiated further studies of neuropsychological interventions and is expected to be granted a position as Associate Professor at the Research Unit in 2021.

Publications from the study so far

1. Mellentin AI, Nielsen B, Nielsen AS, Yu F, Nielsen DG, Mejdal A, Stenager E. A smartphone application featuring cue exposure therapy as aftercare for alcohol use disorders: a randomized controlled trial. JMIR mHealth and uHealth, 2019, <http://dx.doi.org/10.2196/13793>
2. Mellentin AI, Nielsen B, Nielsen AS, Fei Yu, Stenager EN. A randomized controlled study of exposure therapy as aftercare for alcohol use disorder: study protocol. BMC Psychiatry, 2016;16:112. DOI 10.1186/s12888-016-0795-8
3. Mellentin AI; Stenager E; Nielsen B; Nielsen AS; Yu F. A smarter pathway for delivering cue exposure therapy? The design and development of a smartphone application targeting alcohol use disorder. JMIR Mhealth And Uhealth, 2017 ;5(1):e5) DOI:[10.2196/mhealth.6500](https://doi.org/10.2196/mhealth.6500).
4. Mellentin AI, Skøtt L, Nielsen B, Juhl C, Nielsen AS, Schippers G, Stenager E. Cue Exposure Therapy for the Treatment of Alcohol Use Disorders: A systematic Review and Meta-analysis, Clinical Psychology Review, 2017. DOI: [10.1016/j.cpr.2017.07.006](https://doi.org/10.1016/j.cpr.2017.07.006).

Publications currently in review

1. Eriksen LS, Larsen MB, Mejdal A, Sibbersen C, Stenager E, Nielsen AS, Nielsen B. Mellentin AI. Relapse prevention for alcohol use disorders: combined cue exposure and acamprostate therapy as aftercare. Submitted

Spin off publications, partly building on findings from the Cue Exposure -study (next-generation studies):

1. Mistarz N, Andersen K, Nielsen AS, Goudriaan AE, Mitchel TM, Skøtt L, Nielsen DG, Mellentin AI. Pharmacological Enhancing Agents Targeting Neurocognitive Dysfunctions in Patients with Alcohol-Induced Neuropsychiatric Disorders: A Systematic Review. Neuroscience and Biobehavioral Reviews, 2021, <https://doi.org/10.1016/j.neubiorev.2021.02.038>
2. Mellentin AI, Nielsen AS; Ascone L; Wirtz J; Samochowiec J; Kucharska-Mazur J; Schadow F; Lebiecka Z; Skoneczny T; Mistarz N; Bremer T; Kühn S. A randomized controlled trial of a virtual reality based, approach-avoidance training program for alcohol use disorder: a study protocol. BMC Psychiatry, 2020, DOI: 10.1186/s12888-020-02739-1

Staff at the Cue Exposure study

Principal investigator: Professor Bent Nielsen, UCAR.

Supervisors (study): Professor Elsebeth Stenager, Professor Anette Søggaard Nielsen

Supervisor (clinical): MD Bodil Andersen

Technical development of the application: Associate Professor Arne Bilberg, Associate Professor Fei Yu.

Postdoc Angelina Mellentin (was granted the young researcher award in 2017 and defended her thesis in 2018)

Interviewer Birgit Jensen

Medical Student Lene Stryhn

Medical Student Mathias Larsen

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

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

Design

The study was 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, starting treatment at 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.

Hypothesis

We hypothesized that adding physical exercise of moderate-intensity to treatment as usual for AUD would yield significant clinical improvements regarding the amount and frequency of alcohol intake, such that exercising patients would have significantly lower consumption than non-exercising patients.

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 increased each week as the patients' fitness level improved. The exercise programme was 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 summer 2012. 10 patients participated in the pilot study. The pilot study showed that 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 mid-May 2013 and stopped enrolment in February 2015. 175 patients were enrolled, of which 62 were randomized by urn randomization into training in groups, 60 to individual training and 53 to control group. 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 57% (100 patients).

Findings

Primary outcome: Alcohol intake

The primary outcome measure was defined as the proportion of patients who did not drink excessively six months after treatment start. Not drinking excessively was defined as being either abstinent or drinking moderately during the last 30 days prior to the follow up interview. Moderate drinking was defined as drinking a maximum of 14 and 21 standard units of alcohol per week for women and men, respectively, and a maximum of 5 standard units of alcohol on a drinking day (Recommendations of the Danish Health Authority), again during the last 30 days prior to follow up.

At the time for the six-month follow-up, all three groups showed a highly significant reduction in alcohol intake. No differences between the groups were found in the proportion of patients who

drank excessively. Participants allocated to exercise, and participants allocated to the control group were not significantly different from each other in relation to drinking outcome measured as consumed units of alcohol per month at follow-up. The number of days abstinent was increased, while the number of drinks per drinking day was decreased across the total sample.

A dose-response effect of exercise was found. The amount of alcohol intake in the intervention groups decreased by 4% [95% CI: 0.03 – 6.8%], $p=0.015$, for each increased exercising day. That is, the more days participants registered their exercise, the less alcohol they consumed at follow-up.

Secondary outcome: Physical fitness

At baseline, women had a mean age, height, weight and VO_{2max} of 51 ± 11 years, 1.65 ± 0.09 m, 68.3 ± 12 kg and 28.2 ± 6.8 $mlO_2 \text{ min}^{-1}kg^{-1}$, while men had 43 ± 12 years, 1.79 ± 0.07 m, 83.1 ± 12.3 kg and 38.0 ± 9.3 $mlO_2 \text{ min}^{-1}kg^{-1}$. Physiological parameters measured during maximal treadmill running were: Treadmill running time (T_{max}), maximal heart rate (HR_{max}), maximal blood lactate concentration (BL) and respiratory exchange ratio (RER), Rate of Perceived Exertion (RPE) and VO_{2max} for the subgroup of patients completing both tests.

In the subgroup presenting for test of physical fitness, the individual group (IND) had changed their VO_{2max} after 6 months training by 5.7% ($p<0.05$), while there was no change in the other two groups (group training GR and control C) ($p>0.05$); however, all groups had decreased their alcohol intake highly significantly ($p<0.0001$). When using the definition of “excessive drinking” per the Danish Board of Health in terms of an average weekly consumption exceeding 14 and 21 units for women and men, respectively, the reduction in alcohol use implied that only 39 and 36% of the patients, respectively, from the group condition and individual condition were still presenting “excessive drinking” after the intervention, while there were 57% in C. The training intensity was $78.2\pm 6.9\%$, and time per training unit was 37.8 ± 9.6 min with no difference between IND and GR ($p>0.05$). Assuming data coming from patients using and downloading data from heart rate monitors, veridically reflected frequency in training, the average frequency was four or five times a month during the first month of the intervention, dropping to once or twice a month during the following 5 months ($p<0.05$).

Secondary outcome: Interpersonal problems

Another secondary outcome was the level of interpersonal problems, and the question whether the patients differed from the normal population at baseline. When comparing the participating patients with a healthy population, the patients achieved a significantly higher score on four of the eight subscales. The subscales, where the AUD-patients perceived to have significantly more interpersonal problems, were: vindictive ($p = <0.0001^{**}$), cold ($p = <0.0001^{**}$), socially avoidant ($p = <0.0001^{**}$) and non-assertive ($p = 0.048^*$).

Perspectives and spin-off

In particular, we learned from the Healthy Lifestyle study that interventions aimed at improving general lifestyle (and thereby improve health in the long run) need to be developed and planned together with the users of the interventions, i.e., the patients. Thus, first stage of a study aimed at preventing cardiovascular diseases among patients suffering from alcohol use disorders or severe mental illness has been performed, **The Psychiatric Cardiovascular Participatory Study**. This study involves patients in all stages, from the development of interventions to the design of study and the interpretations of results. So far, the interventions have been developed and funding for pilot

testing is being applied for. Professor Bent Nielsen was the PI of the development part of the study, and Professor Kjeld Andersen will be the PI for the following stages, i.e., testing and evaluation.

Inspiration and sparring group for the Healthy Lifestyle study

The project group behind Healthy Lifestyle study 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 Dr. Kirsten K. Roessler, Department of Psychology, SDU.

Project co-supervisor: Assistant professor Randi Bilberg

PhD student: Sengül Sari. Defended thesis in May 2017.

Pre-graduate student: Martin Mau

Publications from the study so far

1. Bilberg R, Roessler KK, Nielsen AS. Saying yes or no to physical activity – A comparative cohort analysis of patient seeking treatment for Alcohol Use Disorder. *Addictive Behaviors Reports*, 2019; 9, [100180]. <https://doi.org/10.1016/j.abrep.2019.100180>
2. Sari S, Bilberg R, Nielsen AS, Roessler KK. The effect of exercise as adjunctive treatment on quality of life for individuals with alcohol use disorders: a randomized controlled trial. *B M C Public Health*. 2019 jun 11;19. 727. <https://doi.org/10.1186/s12889-019-7083-8>
3. Mau M, Muller A, Roessler KK. Alcohol relapse and near-relapse experiences show that relapse models need to be updated. *Alcoholism Treatment Quarterly*, October 2018. DOI:10.1080/07347324.2018.1532775
4. Jensen K, Nielsen C, Ekstrøm C, Roessler KK. Physical exercise in the treatment of alcohol use disorder (AUD) patients affects their drinking habits: A randomized controlled trial. In press, *Scandinavian Journal of Public Health* (in press)
5. Roessler, KK, Mau, M, Ekstrøm, C Interpersonal Problems of Alcohol Use Disorder Patients undergoing a Physical Exercise Intervention – a Randomised Controlled trial. *Nordic Psychology*. 2018. Available from <https://doi.org/10.1080/19012276.2017.1418414>
6. Roessler KK, Bilberg R, Nielsen AS, Jensen K, Ekstrøm CT, Sari S. Exercise as adjunctive treatment for alcohol use disorder: Results of a randomized controlled trial. *PLoS ONE* 2017;12(10): e0186076. <https://doi.org/10.1371/journal.pone.0186076>.
7. Sari S, Muller AE, Roessler KK. Exercising alcohol patients don't lack motivation but struggle with structures, emotions and social context: a qualitative dropout study. *B M C Family Practice*. 2017;18. 45. Available from DOI: 10.1186/s12875-017-0606-4

8. Sari S, Bilberg RM, Nielsen AS, Jensen K, Larsen JP, Roessler KK. Physical Activity Patterns in Patients with Alcohol Use Disorder. *Open Access Journal of Exercise and Sports Medicine*. 2017;1(1).
9. Roessler KK, Bramsen RH, Dervisevic A, Bilberg RM. Exercise based interventions for alcohol use disorder: A comment on motivational aspects of participation. *Scandinavian Journal of Psychology*. 2016;58(1):23-28. Available from DOI: 10.1111/sjop.12334.
10. Roessler, KK. (2016). Emotional experiences and interpersonal relations in physical activity as health prevention and treatment: a psychodynamic group approach. I M. Raab, P. Wylleman, R. Seiler, A-M. Elbe, & A. Hatzigeorgiadis (eds.), *Sport & Exercise Psychology Research: From Theory to Practice*. (s. 461-486). Kapitel 21. London: Elsevier Inc. DOI: 10.1016/B978-0-12-803634-1.00021-2
11. Roessler, KK, Bilberg R, Jensen K, Kjaergaard AS, Dervisevic A, Nielsen B. Exercise as treatment for Alcohol Dependence – A pilot study. *Sports Science Review*. 2013; 22(3-4). Available from <https://doi.org/10.2478/ssr-2013-0010>
12. Sari S, Bilberg R, Jensen K, Nielsen AS, Nielsen B, Roessler KK. Physical exercise as a supplement to outpatient treatment of alcohol use disorders – a randomized controlled trial. *BMC Psychology* 2013, 1:23, <http://www.biomedcentral.com/2050-7283/1/23>

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 have been established. The International Advisory Board consisted of: Dean Ole Skøtt (SDU) (chair), CEO Kim Brixen (OUH), Research Vice Director Sissel Vorstrup/Lars Torup (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) and Dr. Gillian Tober (Leeds Addiction Unit).

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

The Advisory Board and the Steering Committee held their fifth and last meetings in 2018. The research-period for the RESCueH-studies is extended till ultimo 2020, but it was agreed that no meetings are needed in 2019 and 2020.

Overview of staff at the RESCueH studies (Danish Site, employed or associated), 2020

Professor Anette Sjøgaard Nielsen (UCAR, SDU)
Research secretary Annemette Munk Svensson (UCAR, SDU)
Professor Bent Nielsen (UCAR, SDU)
Professor Kjeld Andersen (UCAR, SDU)
Professor Jes Sjøgaard, (UCAR, SDU)
Adjunct Professor Gerhard Bühringer
Project leader, PhD Randi Bilberg (UCAR, SDU)
Associate Professor Silke Behrendt
Postdoc Angelina Mellentin (UCAR, SDU)
Postdoc Jakob Emiliussen (UCAR, SDU)
PhD-student/Postdoc Lotte Kramer, (UCAR, SDU)
PhD-student Morten Hell (UCAR, SDU) (part time)
PhD-student Anna Mejldal (UCAR, SDU) (part time)
PhD-student Dorthe Grüner Nielsen (UCAR, SDU)
Interviewer and coder Birgit Jensen (UCAR, SDU)
Research Assistant Jeppe Tryggedsson, (UCAR, SDU)
Research assistant Peter Schøler (UCAR, SDU)
Medical Student Augustus Ismaeeli
Medical Student Lene Stryhn
Student Aid Ayse Corap (UCAR, SDU)
Student Aid Klara Capelle (UCAR, SDU)
Student Aid Ayat Allah Alnabhan
Student Aid Anders Müller
Student Aid Camilla Olsen

Collaborating Danish treatment institutions in 2019 (RESCueH-studies, only)

The Alcohol Treatment Centre in Odense participating in all five studies: Relay Study, Elderly Study, Self-Match Study, Cue Exposure Study and Healthy Lifestyle Study.

The Alcohol Treatment Centre in Aarhus and the Alcohol Treatment Centre in Copenhagen, participating in Elderly Study.

The Alcohol Treatment Centre in Aabenraa, participating in Relay Study.

Gastrointestinal, neurological and orthopaedic departments at Odense University Hospital and Aabenraa Hospital, participating in Relay Study.

International collaborators in The RESCueH studies in 2020

The Elderly study:

Professor Gerhard Buehringer: Principal Investigator for the German site in the Elderly Study, and his team. The study intervention at the German site was 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 was conducted in the First Choice Family Practice Clinics, New Mexico.

Associate professor Teresa Moyers, CASAA, University of New Mexico, who was supervising, training and monitoring treatment fidelity in the Elderly Study, co-supervised phd-student Lotte Kramer Schmidt, and supervised Lotte during her research stay at CASAA.

Associate Professor Alexis Kuerbis, Silberman School of Social Work at Hunter College, USA, collaborated on the analysis of data

The Self-Match study:

Professor William R. Miller, CASAA, Albuquerque, co-supervised PhD-student Morten Hell.

New and future projects and studies, initiated or planned at UCAR in 2017-2020, and building on the RESCueH-studies:

Derivative studies within the rationale: Better recruitment of patients to treatment, as only a minority of alcohol-dependent drinkers currently receive treatment:

Alternatives to nagging, pleading, and threatening: A study on strategies to get loved ones to seek treatment for alcohol dependence. Like the Relay study, this study focuses on how to increase the likelihood that patients seek specialized treatment. The study is a cluster randomized controlled trial on methods to empower the relatives of problem drinkers, who are reluctant to seek treatment, and help them motivate their drinking family member to change. Project group: Randi Bilberg (coordinator), Anette Søgaard Nielsen (PI), Kjeld Andersen, Claus Ekstrøm and Bent Nielsen. In 2017, the study was granted DKR 2,000,000 from Trygfonden in addition to a research year for the PhD-student from the Region Southern Denmark Psychiatric Research Foundation, and another research year for the PhD-student from University of Southern Denmark. Primary outcomes from the study will be published before long.

Feasibility study of the 15-method in General Practice. Professor Sven Andreasson in Stockholm and his group have developed an easily learned and implemented strategy to be used in General Practice to identify and treat patients with mild to moderate alcohol use disorder. The method has been tested in a randomized design in Stockholm, however, only with patients directly referred to and asking for the intervention (thus lacking the identification part). Together with Trygfonden, and the research Unit for General Medicine at University of Southern Denmark, the Unit of Clinical Alcohol Research currently investigates the feasibility of the 15-method among Danish GPs. If feasible, the method will be investigated in a randomized controlled trial involving patients, identified by the GPs themselves among their patients. The study is funded by Trygfonden (DKK 1,300,000).

The Respect-campaign – does it work? The study investigates if the mass media campaign called *the Respect campaign* reduces stigma and leads to more individuals seeking treatment for alcohol use disorder. The study is funded by Trygfonden (DKK 728,000)

Derivative studies within the rationale: Matching treatment to individual needs, reflecting the heterogeneity of alcohol-dependent patients:

Elderly Wellbeing and Alcohol: A Tricky Cocktail. The project was a natural next step from the Elderly Study. During observations and qualitative interviews with staff, elderly and their significant others, the project identifies, describes and develops strategies to solve the ethical dilemmas and

problems arising in relation to alcohol and elderly in nursing homes and elderly with assisted living at home. The project group consists of Professor Søren Harnow Klausen (PI) from the Institute of Cultural Science (IKV), Anette Sjøgaard Nielsen from the Unit of Clinical Alcohol Research (UCAR), Jakob Emiliussen (UCAR), Regina Christiansen (IKV & UCAR) and Søren Engelsen (IKV). The Velux Foundation granted the project DKR 5.020.680 in 2017, of which 1.300.000 is a subgrant for the Unit of Clinical Alcohol Research.

Psych-ID. Patients suffering from both alcohol use disorder and depression or anxiety are common in the outpatient treatment for alcohol use disorder, offered by the local governments, and just as mentioned above, the treatment of depression and anxiety is the responsibility of general practices and the regional governments. Hence, the patients are relatively more difficult to treat effectively, compared to patients suffering from alcohol use disorder only. The present study tests and aim at being able to recommending a screening instrument that can be used effectively in the alcohol treatment institutions, in order to identify patients suffering from depression or anxiety (phase 1). Next step will be developing and testing a shared-care model that includes treatment of both depression or anxiety *and* alcohol use disorder in an integrated treatment course (phase 2). Trygfonden granted the study DKR 240.000 in 2018 to perform phase 1 of the study.

Derivative studies within the rationale: Greater patient involvement in treatment, as active involvement in treatment decision processes is essential for compliance:

Blend-A. In the Blend-A, we investigate whether compliance in treatment increases, if patients are more actively involved in the treatment process by blending face-to-face treatment with internet-based modules. Hence, the Blend-A Study will evaluate effectiveness and compliance in a therapist-supported online intervention for alcohol use disorder blended with face-to-face consultations. Blend-A will be evaluated in alcohol treatment institutions in 18 municipalities in Denmark, in a stepped-wedge randomized controlled design, allowing for comparison with face-to-face outpatient treatment as usual (TAU) by means of both current and historical controls. Blend-A will be led by the Unit of Clinical Alcohol Research and performed in collaboration with the Centre for Telepsychiatry the Research Unit, and Sundhed.dk. Phase 1 was initiated in autumn 2017 and consists of translating the online intervention from Dutch to Danish as well as adjusting and pilot testing it. Phase 1 was funded by the Centre for Telepsychiatry, Odense University Hospital, Sundhed.dk, UCAR and the alcohol treatment institutions in Kolding, Svendborg, and Haderslev. Phase 1 was performed in 2018, and the study is granted 5.000.000 from Trygfonden, allowing phase 2 to be performed in 2020 and the years to come.

The Psychiatric Cardiovascular Participatory Study. Due to the extremely high mortality rate among individuals suffering from alcohol dependency, psychiatric illness and, in particular, both conditions simultaneously, there is a need for effective interventions for this patient group. So far, no attempts

have been successful. By means of a user participatory design and the highest level of user involvement, this study develops treatment strategies and interventions, that makes it possible for the patient group to receive relevant and sufficient treatment. The study is the first step in a longer series of studies. So far, the interventions have been developed, supported by a grant from the Psychiatric Research Fund in Region South Denmark. Currently, funding for pilot testing the interventions is currently being applied for at Trygfonden, the Psychiatric Research Foundation in the Region of Southern Denmark, at Jascha Fonden, and Hjerteforeningen.

Derivative studies within the rationale: Preventing relapse, as return to harmful drinking is a common problem:

Use of Virtual Reality in treatment for alcohol dependency. WP in the Baltic Sea Programme Project, Baltic Game Industry. This study builds on the experiences from the Cue Exposure study. In 2016, UCAR was invited to be a partner in an EU-Interreg grant application, more specifically in WP4 on the use of Virtual Reality (VR) in the treatment of alcohol dependence. The application was granted funding by the EU in 2017, and the WP4 on the use of VR was initiated in the spring of 2018. Within this work package, partners collaborate closely to develop a clinical tool in VR with the goal to reduce relapse rates in alcohol addicted patients. The PI on the study is Prof. Simone Kühn, Universitätsklinikum Hamburg-Eppendorf (UKE), and Max Planck Institute, Berlin. UCAR was granted 104.025 € as a Danish partner. The study on the use of VR in treatment for alcohol use disorder was a natural next step from the Cue Exposure Study, is performed as a postdoc study at UCAR, and includes patients referred to treatment at the inpatient treatment institution Ringgården in Middelfart. So far, two thirds of the number of patients needed have been enrolled in the study.

Attentional control training for treating alcohol use disorders among younger adults. The study will investigate if treatment can be enhanced by implementing a gamified ACTP smartphone application as an add-on to treatment as usual for younger AUD patients. The study is an RCT of A: a gamified ACTP smartphone application + treatment as usual (TAU) versus B: a gamified ACTP sham-control application + TAU, or versus C: only TAU. Angelina Isabella Mellentin (PI), Javad Fadardi (co-investigator), Anette Sjøgaard Nielsen (co-investigator), & W. Miles Cox (co-investigator). Funding: Trygfonden, DKK 5,530,380.

Brain+ AlcoRecover. The study will investigate the effect of adding training by means of a gamified smartphone application, Brain+ Recover, to treatment as usual. The application includes various cognitive training games. The aim of the study is, first, to examine the feasibility of smartphone-based multi-cognitive training with gamified elements as part of conventional outpatient treatment for AUD, and second, to perform an RCT, investigating the effect of adding the gamified training program to treatment for AUD as usual. Angelina Mellentin (PI), Anneke Goudriaan (co-investigator), Kjeld Andersen (co-investigator), Tanja Sheldrick-Michel (co-investigator), Anette Sjøgaard Nielsen (co-investigator), Nicolaj Mistarz (PhD-student). Funding: Psychiatric Research Foundation in Region of Southern Denmark, DKK 1,031,300 for feasibility and pilot testing.

Creative Writing workshops as a means to cognitive remediation. Creative writing is a cognitive process characterized by decisions, high hierarchical organization, and goal-directed thinking. Adding creative writing workshops to treatment for AUD may, thus, be a novel, fun and motivating way of training brain functions, impaired after years of drinking. A research protocol is currently being developed. Anette Søgaaard Nielsen (PI), Kjeld Andersen (co-investigator), Angelina Mellentin (co-investigator), Anders Juhl Langscheiden Rasmussen (co-investigator), Tanja Sheldrick-Michel (co-investigator). Funding: will be applied for.

Online social cognitive training program for alcohol use disorder patients with and without psychiatric comorbidity. The first aim of this project is to develop an online social cognitive training program that can (a) identify emotional bias and recognition deficits in AUD patients, and determine whether differences exist between those with and without psychiatric comorbidity; and (b) ameliorate the identified dysfunctions using ABM techniques. The second aim is to test the effectiveness of online social cognitive training as add-on to conventional evidenced-based AUD treatment compared to treatment as usual (TAU). A protocol is currently under development. Angelina Mellentin (PI), Kjeld Andersen (co-investigator), Anette Søgaaard Nielsen (co-investigator), Tanja Sheldrick-Michel (co-investigator). Funding: will be applied for.

Transcranial magnetic stimulation. The study will investigate if HF rTMS as add-on therapy can increase the effectiveness of AUD treatment as usual for AUD patients with and without comorbid MDD. The study is a randomized controlled trial. A protocol is currently under development. Angelina Mellentin (PI), Erik Roj (co-investigator), Kjeld Andersen (co-investigator), Tanja Sheldrick-Michel (co-investigator). Funding: will be applied for.

Research publications (UCAR) and other research and dissemination activity in 2020

Peer reviewed research publications in 2020

1. Mejdal A, Andersen K, Behrendt S, Bilberg R, Christensen AI, Lau CJ, Möller S, Nielsen AS. History of health care use and disease burden in older adults with different levels of alcohol use. A register-based cohort study. *Alcoholism: Clinical and Experimental Research*. 2021; 45:3:638-649. DOI: 10.1111/acer.14562.
2. Ebrahimi A, Wiil UK, Andersen A, Mansourvar M, Nielsen AS, A Predictive Machine Learning Model to Determine Alcohol Use Disorder, 2020 IEEE Symposium on Computers and Communications (ISCC), Rennes, France, 2020, pp. 1-7, doi: 10.1109/ISCC50000.2020.9219685.
3. Niclasen BV, Johansen ELR, Becker U, Nielsen AS. Negative life events and risk of homelessness in a Greenlandic population of individuals seeking treatment for substance use disorders. *Nordic Journal of Psychiatry*, <https://doi.org/10.1080/08039488.2021.1912171>.
4. Nielsen AS, Becker U. Det kommunale alkoholbehandlingstilbud. *Ugeskrift for Læger*. 2020;182:V11200848.
5. Hell M, Miller WR, Nielsen B, Nielsen AS. The impact of free choice in alcohol treatment. Primary outcomes of the Self-Match study, *Drug and Alcohol Dependence*. 2021. 10.1016/j.drugalcdep.2021.108587 .
6. Mejdal A, Andersen K, Behrendt S, Bilberg R, Bogenschutz M, Braun B, Bühringer G, Nielsen AS. Treatment of seniors suffering from alcohol use disorders: WHO Drinking Risk Levels Reductions following treatment and their relation to quality of health and DSM-5 symptoms. *Alcoholism: Clinical and Experimental Research*. 2021; 45:3:638-649. DOI: 10.1111/acer.14562
7. Schmidt LK, Andersen K, Nielsen AS. Differences in the delivery of Motivational Interviewing across three Countries. *Journal of Ethnicity in Substance Abuse*. 2020. DOI: 10.1080/15332640.2020.1824838
8. Niclasen BV, Flyger J, Becker U, Nielsen B, Nielsen AS. Implementation of AUDIT in the treatment planning process for alcohol disorder in Greenland. *Nordic Journal of Psychiatry*. 2020. DOI: 10.1080/08039488.2020.1814407
9. Oxholm C, Christensen A-M S, Christensen R, Nielsen AS. Can we talk about alcohol for a minute? Thoughts and opinions expressed by health professionals and patients at somatic hospital. *Alcohol Treatment Quarterly*, 2020. <https://doi.org/10.1080/08039488.2020.1814407>.
10. Behrendt S, Kuerbis A, Bilberg R, Braun B, Mejdal A; Bühringer G, Bogenschutz M, Andersen K, Nielsen AS. Impact of comorbid mental disorders on outcomes of brief outpatient treatment for DSM-5 alcohol use disorder in older adults. *Journal of Substance Abuse Treatment*, 2020. DOI: 10.1016/j.jsat.2020.108143
11. Mellentin AI, Nielsen AS; Ascone L; Wirtz J; Samochowiec J; Kucharska-Mazur J; Schadow F; Lebiecka Z; Skoneczny T; Mistarz N; Bremer T; Kühn S. A randomized controlled trial of a virtual reality based, approach-avoidance training program for alcohol use disorder: a study protocol. *BMC Psychiatry*,

2020, DOI: 10.1186/s12888-020-02739-1

12. Schwarz AS, Kruse M, Nielsen AS, Nielsen B, Søgaard J. Health care consumption for somatic patients following a brief outreach alcohol intervention. *Nordic Journal of Health Economics*, 2020, DOI: 10.5617/njhe.6470
13. Mejdal A, Andersen K, Behrendt S, Bilberg R, Christensen AI, Lau CJ, Möller S, Nielsen, AS. Twenty years socioeconomic trajectories in older adults with varying alcohol use: A register-based cohort study. *Alcohol and Alcoholism*. 2020. DOI: 10.1093/alcalc/agaa019
14. Hansen EM, Mejdal A, Nielsen AS. Predictors of Readmission following Outpatient Treatment for Alcohol Use Disorder. *Alcohol and Alcoholism*. 2020. doi: 10.1093/alcalc/agaa018
15. Mejdal A, Andersen K; Bilberg R, Möller S; Nielsen AS. DSM-5 latent classes of alcohol users among treatment seeking older adults. *Substance Use & Misuse*, 2020, 55:8, 1214-1222. doi.org/10.1080/10826084.2020.1731546.

Books and book chapters in 2020, peer-reviewed

1. Nielsen AS, Emiliussen J. Hvorfor drikker Jeppe? Narrativer om alkoholmisbrug in Rasmussen AJ, Mai A-M, Hansen HP (eds). *Narrativ medicin i uddannelse og praksis*. Gads Forlag. In press.
2. Nielsen AS, Andersen K. Alkohol på godt og ondt. In: Emiliussen, J. og Klausen, S. H (eds). *Ældrevelværd – Samtidsperspektiver på aldring og det gode liv*. Aalborg Universitetsforlag. In press.
3. Nielsen AS, Hesse M, Andersen K, Schippers G. *Substance Use Disorder*. In: Pedersen SS, Pouwer F, Roessler KK, Andersen TE (eds): *Applied Medical Psychology: A Multi-Disciplinary Approach*. Southern Denmark University Press (in press).
4. Nielsen AS, Rasmussen AJ. *Kan der findes evidens for effekten af kreative skriveværksteder inden for en sundhedsfaglig kontekst?* In: Jespersen MR, Gammelgaard LR, Ulbjerg S (eds). *Skrivning og Sundhed*. Aarhus Universitetsforlag. ISBN: 978 87 7184 993 6.
5. Marshall C, Nielsen AS. *Motivational Interviewing for Leaders in the Helping Professions: Facilitating Change in Organizations*. Guilford, New York, 2020. (250 sider). ISBN: 978-1-4625-4382-3

Submitted 2020, still in review or accepted in 2020

1. Ebrahimi A, Wiil UK, Mansourvara M, Andersen K, Nielsen AS. A Deep Neural Network Application to Identify Patients with Alcohol Use Disorder Based on Historical Electronic Health Records. Conference paper submitted to 31st Medical Informatics Europe Conference (MIE2021). Accepted
2. Oxholm C, Nielsen AS, Christensen A-M S. The Ethics of Algorithms in Healthcare. *Cambridge Quarterly of Healthcare Ethics*, Accepted.

3. Stryhn L, Larsen M, Mejdal A, Sibbersen C, Nielsen D, Nielsen B, Nielsen AS, Stenager E, Mellentin A. Combined acamprosate and Cue Exposure Therapy as relapse prevention for alcohol use disorders. *Alcohol and Alcoholism*, in review.
4. Emiliussen J, Maagaard CA, Wohlmann A, Nielsen AS. How do patients narrate their perceptions of alcohol problems? Systematic review of medical and psychological research literature. *JSAD*, in review.
5. Ali Ebrahimi, Uffe Koch Wiil, Marjan Mansourvar, Amin Naemi, Andersen K, Nielsen AS. Analysis of Comorbidity of Alcohol Use Disorder. *ICHI2021*, in review.
6. Ismaeeli A, Andersen K, Nielsen AS, Bilberg R, Mejdal A. Achieving treatment goal and quality of life outcome in alcohol dependent patients. *Alcohol and Alcoholism*. In re-review.
7. Tarp K, Sari S, Nielsen AS. Reasons for not seeking alcohol use disorder treatment. *Nordic Studies of Alcohol and Drugs*, in review.
8. Hellum R, Bilberg R, Nielsen AS. He is lovely and awful. The challenges of being close to an individual with alcohol problems. *Nordic Studies of Alcohol and Drugs*. In re-review.
9. Oxholm C, Christensen A-M S, Wiil UK, Christensen R, Nielsen AS. Attitudes of patients and health professionals towards an algorithm screening for indications of high alcohol consumption: a qualitative study. In re-review, *JMIR*
10. Tarp KH, Rasmussen J, Mejdal A, Folker MP, Nielsen AS. Development and Implementation Lessons Learned from a Blended Alcohol Treatment Trial (the BLEND-A Study). In re-review, *JMIR*.
11. Behrendt S, Kuerbis A, Braun-Michl B, Bilberg R, Bühringer G, Bogenschutz M, Mejdal A, Andersen K, Nielsen AS. Residual alcohol use disorder symptoms after treatment predict disadvantageous long-term drinking outcomes in seniors with DSM-5 alcohol use disorder. In re-review.
12. Ebrahimi A, Wiil UK, Mansourvar M, Andersen K, Nielsen AS. Clinical Factor Identification for Alcohol Use Disorder from Electronic Health Records using Feature Selection Methods. *IEEE Journal of Biomedical and Health Informatics*. In review.
13. Hell M, Nielsen B, Nielsen AS. Personality Traits and Alcohol Consumption: Secondary Analysis of the Self-Match Study. In review.
14. Christiansen R, Nielsen A.S. Bring Me My Alcohol! – on the continuum of pleasure and pain. *Nursing Philosophy*, In review.
15. Behrendt S, Kuerbis A, Becker U, Mejdal A, Andersen K, Nielsen AS, Tolstrup J, Elisassen MH. Distinct health-related risk profiles among middle-aged and older adults with risky alcohol use from the Danish general population. *Drug and Alcohol Dependence*. In re-review.

Dissemination in general in 2020

Teaching and training

Nielsen AS. Teaching on the National Health Authorities' Alcohol Therapist Course (post graduate course), Denmark.

Nielsen AS. Teaching, Post graduate Course, General Practitioners

Nielsen AS is teaching on the National Health Authorities' Alcohol Therapist Course (post graduate course), Greenland.

Other engagements, relevant for dissemination and implementation

Anette Sjøgaard Nielsen is member of the Network of managers of alcohol treatment institutions in Denmark and informs about the research findings on a regular basis.

UCAR supplies the newsletters from Alcohol and Society and from Alkopedia.dk with research findings to be distributed to the clinical world.

Newsletters

UCAR sends out newsletters from the RESCueH-studies to practitioners and everyone else who have an interest. UCAR also sends out messages on LinkedIn and Facebook.

Website

www.sdu.dk/ucar

www.alkopedia.dk (in collaboration with Alcohol & Society, and Trygfonden).

Masters dissertations in 2020

Graduate student of medicine Augustus Rebar Panawandi Ismaeeli

Graduate student of medicine Marie Korsgaard Voss

Graduate student of medicine Emmanuel Mangkornkaew Hansen

Graduate students of medicine Daniel Ramstad

Graduate students of medicine Jan Ramstad

Graduate student of Psychology Freja Bjerck-Amundsen

Graduate student of Public Health Tina Marie Olsson

Graduate student of medicine Lene Stryhn Eriksen

Graduate student of medicine Mathias Bach Larsen

Graduate student of medicine Peter Bernhard Tramm

Graduate student of medicine Hans Christian Bang

Graduate students of medicine Didde Christiansen

Graduate students of medicine Sharmake A. Maxamed

Graduate students of medicine Svanlaug Àrnadóttir

Graduate student of medicine Jonna Molly Blendberg

Post-graduate specialization, psychologist Alena Hansen

Appointments etc.

Bent Nielsen was appointed advisor to the National Health Authorities, Greenland, in the planning of treatment for alcohol use disorder in Greenland (2016-2019).

Anette Sjøgaard Nielsen is appointed member of the reference group for BRUS (a large, multi-site project aimed at supporting children and adolescents in families with problems with alcohol and substance)

Anette Sjøgaard Nielsen was Chair of Alcohol & Society since 2011.