



RESCueH

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

Anette Søgaard Nielsen, PhD
(Program Director)



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Introduction

The RESCueH Alcohol Research Program was launched 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 2017. 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** tests a new model for referring patients. It is a multicentre study involving hospitals in both urban and rural areas and was conducted in hospital departments that have a high number of patients with alcohol-related diseases.

Purpose of the study

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

Design and original plan

In a randomized controlled design, the Relay Model is 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), are enrolled in the study. The primary outcome comprises the health care costs in the year following the intervention. The secondary outcome is social costs, and criminal justice cost, and the number of patients beginning specialized treatment for alcohol use disorder after discharge from the general hospital. Data are collected from registers and databases and merged using the Danish Civil Registration system.

Interventions

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

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

Progress of the study

A pilot study on the screening procedure was carried out on one of the participating departments at Odense University Hospital (Department O) during October 2013, and the full study was initiated on all five participating departments 1st of November 2013. Enrolment of patients from the rural hospital ended in October 2015. Enrolment at the departments of gastroenterology, and orthopaedic Surgery at Odense University Hospital ended in June 2016. The data collected from the patients has been cleaned and is 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 first analysis was performed in 2018. Anne-Sophie Schwarz handed in her thesis ultimo 2018, reporting Primary

and Secondary outcomes of the study, and professor Bent Nielsen will together with Research Assistant Jeppe Tryggedsson make full use of the data collected and conduct the last analyses during 2019.

The data from Relay-study will from 2019 also be used in the Relip-study, funded by EU Interreg study Access& Acceleration, to develop algorithms to be used on patient-records from somatic hospitals to detect alcohol problems among patients. The National Health Authorities, the National Data Protection Agency, and the heads of the involved hospital departments have given their permission to use data from the patient records for this add-on study.

Findings so far (primary and secondary outcomes)

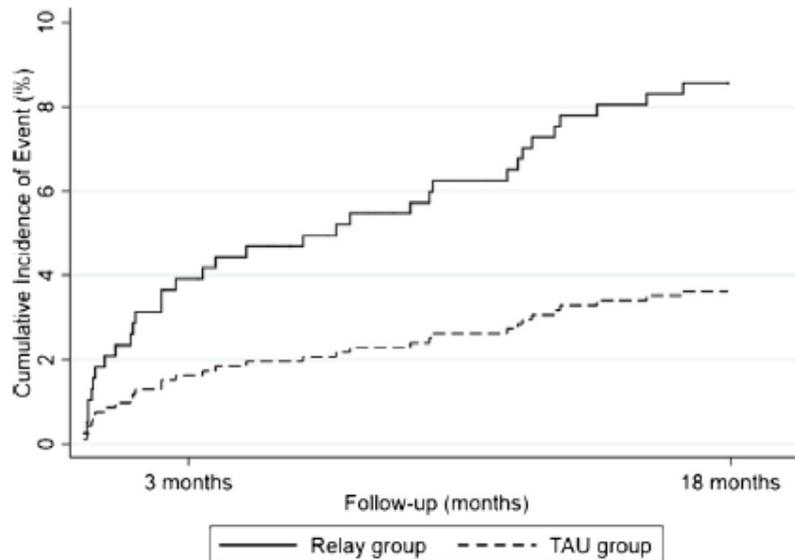
During the study period, a total of 6102 adult patients from the uptake areas of the alcohol treatment centers were admitted to the somatic hospital departments involved in the study; of these, 2568 patients were excluded, and thus a total of 3534 patients completed the lifestyle questionnaire. Of those, 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. Since we do not know if any patients from the TAU group also received different treatment than normal, these 72 patients in the Relay group were not excluded from the analysis. 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 used 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 show up at alcohol treatment centers 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%) 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 ($p=0.002$).

The figure below 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).

The Relay group had higher mean health care 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 health care 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 percent of the sample) the mean health care costs are much higher than for the entire group (DKR 98139 for Relay group and DKR 75852 for TAU group), but the difference was also not statistically significant.

In the quantile analysis of the 10-90 percentiles of the health care costs we did not find any statistically significant differences at a 5 percent level (see table 5). However, for the 90% percentile the p-value was 0.1158 and thus the difference here was the closest to being statistically significant. When performing a simple regression model with health care costs as a function of treatment group we also 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, in review).

Publications from the study so far

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

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,

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

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

Spin off publications:

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

In review:

Schwarz AS, Kruse M, Nielsen AS, Nielsen B, Sjøgaard J. **Health care consumption for somatic patients following a brief outreach alcohol intervention.** In review

Presentations in 2018:

Anne Sophie Schwarz. **Lifestyle factors in somatic patients with and without potential alcohol problems,** EASAR conference, Vienna

PI, coordination of study and PhD-students

Professor Bent Nielsen (UCAR)

Assistant Professor Randi Bilberg (coordination)

Research Assistant Rikke Hellum

Research Assistant Jeppe Tryggedsson

Professor Jes Sjøgaard (supervisor)

PhD student Anne-Sophie Schwartz

Associate Professor Anette Sjøgaard Nielsen (supervisor)

The Elderly Study – individualized treatment

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

Purpose of the study

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

Design

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

Interventions

(A) *Standard Treatment* comprises four sessions of Motivational Enhancement Therapy over four weeks. This intervention is likely to be 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 is considered to be standard treatment, although the intervention is far briefer than treatment typically offered alcohol depended patients seeking treatment in specialized treatment institutions.

(B) *Extended treatment* is the experimental intervention in the present study and comprises four sessions of Motivational Enhancement Therapy over 4 weeks, followed by up to 8 sessions of Community Reinforcement Approach specifically designed to target the needs of elderly (CRA-Elderly). The CRA-Elderly encourages sobriety by helping the patient create routines and activities that are meaningful to the patient and reward staying sober. Particular focus is given to establishing sober social networks and to coping with aging.

All patients are 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

We expected that 50% of patients in MET treatment and 60% of patients in the MET+CRA will have a good clinical outcome as defined in the hypothesis by the end of treatment.

1. Fifty percent of the patients randomly assigned to a brief outpatient behavior therapy program (Standard treatment; 4 sessions of MET) will 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) will show greater improvement of their drinking pattern between onset, end of treatment and 6-month follow-up. A clinically significant difference in outcome is

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 of the study

Intervention and data collection

The Danish site began enrolling patients in the pilot study mid-January 2014. The German site and the US site began enrolling patients 1st of March 2014. The enrolment of patients ended on the 31st of March 2016 at the German sites, at the US site and in Copenhagen and in 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 was cleaned winter 2017. We realized during the data cleaning process of baseline data, that information on all 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. Hence, the final number of participants in the study is 693. In 2018, data was analysed, and findings published. This work will continue during 2019 and 2020 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.

Findings so far

Table 1 presents a few baseline data from each country. The data suggest a few interesting differences between cultures, although some of the differences may be explained by differences in recruitment procedures. In contrast, although statistically significant differences are found, some of the differences are not big in absolute terms and may therefore not be 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, mean ¹ , (SD)	14.9 (10.5)	21.0 (10.5)	22.7 (9.1)	<0.01
Days with binge drinking, mean ¹ , (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

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

⁴Drinker 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.

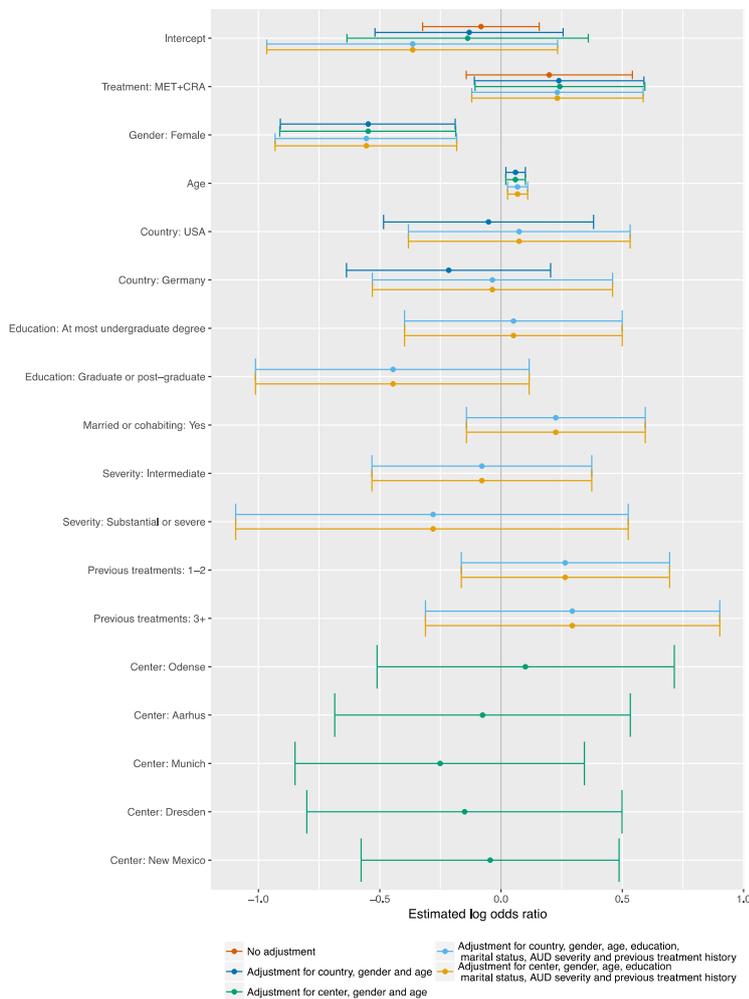
Missing information on this scale from 32 participants

⁵Screening 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 it can be seen from the full model, shown in figure 1, there are not only 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 is gender. When controlling for all other factors, women have a significantly worse prognosis than men. This finding is rather surprising, and we are currently planning further studies to learn more about the impact of gender in relation to treatment outcome.

The overall conclusion of the Elderly study is that relatively brief treatment is possible with good and comparable results in both Europe and USA. The primary outcome paper is currently in review.

Sub-studies in the Elderly-Study:

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.

So far, five additional sub-studies are initiated within the Elderly Study as Postdoc studies, PhD-studies and pre-graduate studies:

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 Postdoc Silke Behrendt from the Dresden site of the study, where she functioned as the local project manager. Silke recently moved to Denmark and now are working with the data on Unit of Clinical Alcohol Research at SDU, and so far, one publication has been published.

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 has submitted her thesis ultimo February 2019. So far, two publications from the thesis has been accepted, in addition to one being currently in review and one submitted.

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 PhD-student Anna Mejldal is expected to finalize the study in 2020.

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 in 2020.

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 first part of the study in the late summer 2018, and a publication is ready for submission primo 2019

Publications from the Elderly study so far

Behrendt S, Braun B, Bilberg R, Bühringer G, Bogenschutz M, Nielsen AS; Mejdal 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>.

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>

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

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

Emiliussen J, Morrison A. **Alcohol use and generational masculinity:: An interdisciplinary approach.** Nordisk Alkohol- & Narkotikatidskrift. 2017;34(4):314-329. Tilgængelig fra, DOI: 10.1177/1455072517709654

Emiliussen J. **Commentary on Halonen et al. (2017): Pondering the latent class trajectories of retiring older adults.** Addiction. 2017;112(7):1171–1172. Tilgængelig fra, DOI: 10.1111/add.13848

Nielsen AS, Bilberg R, Andersen K. **Self-assessed stress level among elderly seeking treatment for alcohol use disorder. A descriptive study.** Conference paper. Conference: Volterra conference. Alcoholism and Stress - Alcoholism and Stress. A framework for future treatment strategies. Maj, 2017

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

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.

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. DOI: 10.1080/07347324.2017.1288480

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.

Petersen AH, Ekstrøm CE. **dataMaid: your assistant for documenting supervised data quality screening in R**. Journal of Statistical Software, in review.

Schmidt LK, Moyers TB, Nielsen AS, Andersen K. **Is fidelity to motivational interviewing associated with alcohol outcomes in treatment-seeking 60+ year-old citizens?** Journal of Substance Abuse Treatment. 2019;101:1-11. <https://doi.org/10.1016/j.jsat.2019.03.004>

Publications submitted and in review

Andersen K, Behrendt S, Bilberg R, Bogenschutz M, Braun B, Bühringer G, Ekstrøm CT, Mejldal A, Petersen AH, Nielsen AS. **Brief alcohol treatment for individuals aged 60 and older proves effective. Findings from a randomized clinical multisite trial in Denmark, Germany, and USA**. Addiction (in re-review).

Jakob Emiliussen, 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 Studies on Alcohol and Drugs (in re- review)*

Publications prepared and ready for submission, but awaiting the publication of the primary outcome paper:

Mejldal A, Nielsen AS, Andersen K, Møller S. **DSM-5 latent classes of alcohol users among treatment seeking older adults**.

Behrendt S, Braun B, Bilberg R, Bühringer G, Bogenschutz M, Nielsen AS, Mejldal A, Andersen K. **Alcohol use intensity at treatment entry but not alcohol use disorder severity predicts DSM-5 alcohol use disorder treatment outcome among adults aged 60+**

Nielsen AS, Behrendt S, Bilberg R, Bogenschutz M, Braun B, Bühringer G, Andersen K. **Self-perceived stress and social support among treatment seeking +60 year old individuals, suffering from Alcohol Use Disorder: Exploring the alcohol-stress link**.

Behrendt S, Braun B, Bilberg R, Bühringer G, Bogenschutz M, Andersen K, Mejdal A, Nielsen AS. **Post-treatment but not pre-treatment alcohol use disorder symptoms predict negative long-term treatment outcomes in seniors with DSM-5 AUD**

Publications in preparation

Tarp KH, Nielsen B, Andersen K, Nielsen AS. **The impact of severity on treatment outcome among older female alcohol use disorder outpatients: A naturalistic case-control follow-up study**

Braun B, Behrendt S, Bilberg R, Piontek D, Kraus L, Bühringer G, Bogenschutz M, Nielsen AS, Andersen K. **The individual treatment goal influences drinking quantity after treatment in older persons with alcohol use disorder: results of the randomized controlled Elderly-study**

Schøler PN, Braun B, Behrendt S, Bilberg R, Bühringer G, Bogenschutz M, Nielsen AS, Andersen K. **Elderly with relief/reward drinking patterns: characteristics and treatment outcomes**

Presentations in 2018

Plenary presentation of the Elderly Study at the Annual meeting of the Danish Association of Psychiatry (invited). Presenters: Kjeld Andersen, Lotte Kramer Schmidt, Jakob Emiliussen and Peter Schøler. Chair: Anette Sjøgaard Nielsen.

Anna Mejdal: **DSM-5 latent classes among an elderly population in alcohol use disorder treatment: Results from the Danish part of the Elderly-Study.** EASAR conference, Vienna

Lotte Kramer Schmidt, **Treatment fidelity and effect of treatment,** EASAR conference, Vienna

Barbara Braun. **The individual treatment goal influences drinking quantity after treatment in older persons with alcohol use disorder.** Results of the randomized controlled Elderly-Study, EASAR conference, Vienna.

Peter Schøler, **Alcohol and drug use among patients in a psychiatric emergency ward: characteristics and course of hospitalization,** EPA, NICE

PhD- and pre-graduate students within the Elderly Study

Jakob Emiliussen, Phycologist. Thesis defended in 2017.

Lotte Kramer Schmidt, MD. Thesis submitted primo 2019.

Anna Mejdal, MSc. PhD-study in progress.

Dorthe Grüner Nielsen, MD. PhD-study in progress.

Inspiration and sparring for the project

Primo 2018, Professor David Nutt visited the Unit of Clinical Alcohol Research, University of Southern Denmark.

Primo 2018, Professor Marcin Wojnar visited the Unit of Clinical Alcohol Research, University of Southern Denmark.

Medio 2018, Professor Karl Mann visited the Unit of Clinical Alcohol Research, University of Southern Denmark

PIs, coordination of study, senior researchers and PhD-students

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

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

Snehal Bhatt, New Mexico School of Medicine (US site)

Professor Gerhard Bühringer, Technische Universität, Dresden/Institut für Therapieforschung (PI, German site).

Associate professor and director Anette Søgaard Nielsen (Danish site and overall coordinator)

Assistant professor Randi Bilberg (DK)

Senior Researcher Silke Behrendt (G)(DK from 2018)

Postdoc Barbara Braun (G)

Project coordinator Christine Lizzaraga (US)

PhD-student Jakob Emiliussen, Phycologist. Thesis defended in 2017.

PhD-student Lotte Kramer Schmidt, MD. Thesis submitted primo 2019.

PhD-student Anna Mejldal, MSc. PhD-study in progress.

PhD-student Dorthe Grüner Nielsen, MD. PhD-study in progress.

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

The study is a randomized controlled study with two arms: (A) an experimental arm, involving patient self-matching to treatment, and (B) treatment as usual, involving expert assignment to treatment. Consecutive patients aged 18-60 years who, either at presentation or after detoxification, wish to start treatment at the Alcohol Treatment Clinic in Odense, will be enrolled. The patients will be interviewed at baseline and 6 months after treatment start. Enrolment of patients is expected to begin in spring 2017.

Expected results

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

Progress of the study

Information material

Based on knowledge from a survey at the Danish alcohol treatment institutions and in collaboration with the staff from the Alcohol Treatment Center in Odense, the information material to be used by the patients as a foundation for the choice of treatment was developed and tested ultimo 2016 and primo 2017. The information material consists of both video presentations and written information.

Initiation of the study

The study began to enrol patients in May 2017. At the end of 2018, 340 patients were enrolled. So far, only very patients have refused to participate in the study. Enrolment is expected to continue until 400 patients are included and conclude April 2019.

Publications from the study so far

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>

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

Hell ME, Miller WR, Nielsen B, Nielsen AS. Does Shared Decision Making improve adherence, retention and treatment outcome in alcohol addiction treatment? A systematic review.

Inspiration and sparring group for the project

In the end of 2017 and early 2018, the PhD-student on the Self-Match study had a two-month research stay in the USA, visiting Palo Alto Medical Center, San Francisco, California and San Diego State University, School of Social Work, San Diego, California.

Staff at the Self-Match study

Principal Investigator: Associate Professor Anette Søgaard Nielsen

PhD student Morten Hell

Supervisor: Professor WR Miller.

Interviewer: Birgit Jensen.

The Cue Exposure Study – preventing relapse after treatment

The **Cue Exposure Study** compares 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 is a randomized controlled trial with three arms, of which two are experimental: (A) an experimental aftercare comprising 4 group sessions of CET (one session every two weeks), (B) an experimental aftercare comprising 1 individual session with instruction for a CET 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, are offered participation and enrolled in the study. The patients are interviewed at baseline just before aftercare treatment and at 8 and 26 weeks after initiation of aftercare. Data collection includes relevant questionnaires and interview instruments.

Interventions

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

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

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

Expected results

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

Progress of the study

The application for the smart phone was finalized in 2014 and presented to patients and therapists in order to receive feedback. Thereafter 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 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 thereafter 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 data will 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.

After finalizing her phd-study, Angelina Mellentin continues to work as postdoc on the study, performing sub-studies and analyzing the large amount of data collected in the Cue Exposure study.

Publications from the study so far

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

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).

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

Mellentin AI, Nielsen AS, Fei Y, Nielsen B, Stenager E. **A smartphone application featuring cue exposure therapy as aftercare for alcohol use disorders: a randomized controlled trial.** JMIR, in review.

Staff at the Cue Exposure study

Principal investigator: Professor Bent Nielsen, UCAR.

Supervisors (study): Professor Elsebeth Stenager, Associate Professor Anette Søgaard Nielsen

Supervisor (clinical): MD Bodil Andersen

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

Postdoc Angelina Mellentin (previously phd-student on the study)

Interviewer Birgit Jensen

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

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

Design

The study 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.

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

The study is expected to be followed up by further studies using other kinds of physical activity and a more flexible approach regarding physical activity.

Conclusion of PhD-study

Sengül Sari defended her thesis, based on the Healthy Lifestyle study, in 2017

Inspiration and sparring group for the project

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.

Pregraduate student: Martin Mau

Publications from the study so far

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

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)

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>

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>.

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

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).

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.

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 (red.), 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

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>

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>

Publications in review

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.** BMC Public Health. In re-review.

Bilberg R, Nielsen AS, Roessler, KK. **Saying yes or no to physical activity – A comparative cohort analysis of patient seeking treatment for Alcohol Use Disorder.** Addictive Behaviors Reports. In re-review.

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 consists 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.

Research Office

Director Anette Sjøgaard Nielsen (UCAR, SDU)
Professor Bent Nielsen (UCAR, SDU)
Professor Kjeld Andersen (UCAR, SDU)
Professor Jes Sjøgaard (UCAR, SDU)
Research secretary Annemette Munk Svensson (UCAR, SDU)

Overview of staff at the RESCueH studies (Danish Site, employed or associated), 2018

Director Anette Sjøgaard Nielsen (UCAR, SDU)
Research secretary Annemette Munk Svensson (UCAR, SDU)
Professor Bent Nielsen (UCAR, SDU)
Professor Kjeld Andersen (UCAR, SDU)
Professor Kirsten Kaya Roessler (Department of Psychology, SDU)
Professor Claus Ekstrøm (Section of Biostatistics, IFSV, KU)
Professor Jes Sjøgaard, (UCAR, SDU)
Assistant Professor Randi Bilbjerg (UCAR, SDU)
Postdoc Angelina Mellentin (UCAR, SDU)
Postdoc Jakob Emiliussen (UCAR, SDU)
PhD-student Lotte Kramer, (UCAR, SDU)
PhD-student Anne-Sophie Schwartz (UCAR, SDU)
PhD-student Morten Hell (UCAR, SDU)
PhD-student Anna Mejldal (UCAR, SDU)
PhD-student Dorte Grøner Nielsen (UCAR, SDU)
Interviewer and coder Birgit Jensen (UCAR, SDU)
Pre-graduate student Peter Schøler (UCAR, SDU)
Student Ayse Corap (UCAR, SDU)
Student Klara Capelle (UCAR, SDU)
Student Louise Bundsgaard (UCAR, SDU)

Student Jeppe Tryggedsson, (UCAR, SDU)

Collaborating Danish treatment institutions in 2018 (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 2018

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 Bogenschütz: 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.

Relay study:

Professor Simon Coulton supervised PhD-student Anne-Sophie Schwarz during her research stay at Kent University

The Self-Match study:

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

New and future projects and studies, initiated at UCAR in 2017-2018:

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

Reading between the lines in the patient case-notes (RELIP) is a study that builds on data from the Relay study, and by means of them investigates whether it is possible to develop algorithms that can search in the patient records from in the somatic hospital and based on the information already in the records can identify patients with a harmful consumption of alcohol. The algorithms will form the basis for development of software that can serve as reading assistance for hospital staff, and hopeful help remove the barrier for talking about alcohol with patients. The study is a phd-study and supported by funding from EU Interreg programme where it is part of the Access & Acceleration program.

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 Sjøgaard 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.

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 is a natural next step from the Elderly Study. During observations, and qualitative interviews with staff, elderly and their significant others, the project will identify, describe and develop 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 Institute of Cultural Science (IKV), Anette Sjøgaard Nielsen from Unit of Clinical Alcohol Research (UCAR), Jakob Emiliussen (UCAR), Regina Christiansen (IKV & UCAR) and Søren Engelsen (IKV). Velux Foundation granted the project DKR 5.020.680 in 2017, of which 1.300.000 is a sub grant for Unit of Clinical Alcohol Research.

ForensAlc: Patients suffering from both mental diseases and alcohol use disorder are both common and difficult to treat effectively, and the research in the field, performed so far, is limited. The National Clinical Guidelines suggest that both conditions are treated simultaneously, but since

the treatment of alcohol use disorder is the responsibility of the local governments and the treatment of mental disorder is the responsibility of the regional governments, the treatment coordination is complicated. The present study will investigate the effect of adding elements from alcohol treatment, more specifically CRA-modules, to forensic psychiatric treatment. Hence, the ForensAlc study will tailor existing strategies to a new, specific and challenging patient group by integrating modules for treating alcohol use disorder in forensic psychiatric treatment. As with the Elderly study, the study will also develop relevant CRA-modules relevant to dual diagnosis patients. Both patients and staff will be involved in this process. In 2017, the study was first granted DKR 216,000 from the Psychiatric Research Foundation in Region of Southern Denmark to writing protocol and full application, and later in 2018 the full study was supported with DKR 376.000, also from the Psychiatric Research Foundation, and 300.000 from Helsefonden. The full grant application is currently under review in Jascha Fonden.

Psych-Alc. 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 practice 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 will first test and choose a screening instrument that effectively can be used in the alcohol treatment institutions in order to identify patients suffering from depression or anxiety (phase 1) and develop and test a shared-care model that include 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 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 Unit of Clinical Alcohol Research and performed in collaboration with Telepsychiatric Department and Research Unit and Sundhed.dk. Phase 1 was initiated in autumn 2017 and consists of translating the online intervention from Dutch to Danish, adjusting and pilot testing it. Phase 1 is funded by Tele-psychiatric department, 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 2019 and the years to come.

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 will be building on the experiences from the Cue Exposure study. In 2016, UCAR was invited to be partner in a in an EU-Interreg grant application, more specifically in WP4 on use of Virtual Reality (VR) in the treatment of alcohol dependence. The application was granted funding from the EU in 2017, and the WP4 on use of VR will be initiated in the spring of 2018. Within this work package partners will 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 Danish partner. The study on use of VR in treatment for alcohol use disorder is a natural next step from the Cue Exposure Study and will be performed as a postdoc study at UCAR.

Derivative studies within the rationale: Encouraging a healthy lifestyle, which will improve compliance in treatment and prevent relapse:

Creative Writing workshops – a Southern Denmark University Lighthouse project. The medical school at University of Southern Denmark has, in collaboration with Odense University Hospital, given priority to narrative medicine to increase the medical staff's ability to communicate with patients. However, narrative medicine also includes uses of literature and creative writing workshops as supplementary means to rehabilitation. Therefore, after a successful pilot test (Phase 1), UCAR, together with Institute of Cultural Science, University of Southern Denmark, applied SDU Lighthouse for funding to develop and further test the use of creative writing workshops as a rehabilitating supplement to treatment for alcohol dependence to prevent relapse, and to increase the individuals' quality of life (Phase 2). The Lighthouse application was granted DKR 499.400 in 2017, and the phase 2 study on creative writing workshops will be initiated in 2018. The project group behind the project is currently applying Trygfonden for additional funding of the study (in re-rereview).

A new, additional focus area, within the rationale: Sufficient treatment of co-occurring somatic illnesses may increase the survival rate among patients suffering from alcohol use disorder alone or in combination with mental disorders

Psychiatric Cardiovascular Screening trial. Due to the extremely high mortality rate among individuals suffering from alcohol dependency, psychiatric illness and, in particular, both conditions, this study will identify individuals among these patient groups at high risk for cardiovascular diseases and liver diseases and initiate preventive medical treatment. Furthermore, the study will identify patients with a high oxidative stress level and identify treatment methods (oxidative matching). The study is in its planning phase. A full grant application was submitted to Trygfonden in the spring 2019, in addition to an application for funding of a pilot study that was sent to the Psychiatric Research Fund in Region South Denmark.

Research publications (UCAR) and other research and dissemination activity

Published in 2018

1. Mellentin A, Ellermann AE, Nielsen B, Mejdal A, Møller S, Nielsen AS. **The prognosis of outpatient alcohol treatment among parents with childcare responsibility.** *BJPsych Open*, 2018, DOI:10.1192/bjo.2018.69
2. Rettie, H., & Emiliussen, J. (2018). **Practical impressions of interpretative phenomenological analysis from the novice's standpoint.** *Nurse Res*, 26(2), 46-49.
3. Christiansen, R., Christensen, A. S., Bilberg, R., & Emiliussen, J. (2018). **Conceptualizing moral responsibility related to alcohol use disorder.** *Alcoholism Treatment Quarterly*
4. 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>
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9. 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>
10. Nielsen AS, Nielsen B. **Outreach visits as a means to ease the transition from inpatient detoxification at a mental health hospital to outpatient treatment for alcohol use disorder. A randomized controlled trial.** *Nordic Journal of Psychiatry*, 2018, <https://doi.org/10.1080/08039488.2018.1451557> .
11. Schwarz A-S, Nielsen B, Nielsen AS. **Lifestyle factors in somatic patients with and without potential alcohol problems.** *Journal of Public Health*, 2018, <https://doi.org/10.1007/s10389-017-0885-1>
12. Nielsen AS, Nielsen B. **Improving Outpatient Alcohol Treatment Systems: Integrating focus on motivation and Actuarial Matching.** *Alcoholism Treatment Quarterly*, 2018, <https://doi.org/10.1080/07347324.2018.1424592> .
13. 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

Accepted in 2018

1. Ghani AMAG, Faiz E, Nielsen AS, Bilberg R. **What is the cause of death, when alcohol dependent persons die prematurely?** *Drug and Alcohol Dependence*, Accepted
2. Schwarz AS, Nielsen B, Sogaard 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*, Accepted
3. Hellum R, Nielsen AS, Nielsen B, Ekstrøm CT, Bischoff G, Andersen K, Hesse M, Bilberg R. **Community Reinforcement and Family Training (CRAFT) - design of a cluster randomized controlled trial comparing individual, group and self-help interventions.** *BMC Public Health*, Accepted

Submitted 2018 and in review

1. Ailenei S, Nielsen AS, Bilberg R. **Batterers And Alcoholics: Typologies. In Search For A Theory For Understanding Alcohol-Related IPV.** *Trauma, Violence, & Abuse*, in re-review.
2. 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*, in review.

3. Schwarz AS, Kruse M, Nielsen AS, Nielsen B, Søggaard J. **Health care consumption for somatic patients following a brief outreach alcohol intervention.** In review.
4. Mellentin A et al. **The degree of multi-dimensional severity of alcohol use disorder among treatment-seeking patients. Is there an additive effect of parental alcohol use disorder?** *European Addiction*, in re-review.
5. 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.** Submitted, *Journal of studies on Alcohol and Drugs*, in re-review.
6. Andersen K, Behrendt S, Bilberg R, Bogenschutz M, Buehringer G, Braun B, Ekstrøm CT, Mejdal A, Petersen AH, Nielsen AS. **Brief alcohol treatment for individuals aged 60 and older proves effective. Findings from a randomized clinical multisite trial in Denmark, Germany, and USA.** *Addiction*, in re-review.
7. Sari S, Nielsen AS, Bilberg R, Roessler KK. **The Effect of Exercise as Adjunctive Treatment on Quality of Life for Individuals with Alcohol Use Disorders: a randomized controlled trial.** *BMC Public Health*, in re-review.
8. Ebrahimi A, Wiil UK, Mansourvar M, Nielsen AS. **Prediction of Alcohol Use Disorder: A Scoping Review.** Submitted MedInfo 2019
9. Schmidt LK, Nielsen AS, Moyers TB, Andersen K. **Is Motivational Interviewing fidelity associated with alcohol outcomes in treatment seeking 60+ year old citizens?** Submitted.

Books and book chapters in 2018

Nielsen AS. **Alkoholbehandling i praksis. - redskaber i den ambulante, psykosociale alkoholbehandling.** Lærebog og standardværk. 2. opdaterede udgave. Hans Reitzels Forlag, 2018. (401 sider). ISBN 9788741272566

Oral presentations at workshops, conferences and meetings in 2018

Nielsen AS. **Alkoholforskningen aktuelt.** FLORs annual meeting, Middelfart, 2018.

Regina Christensen. **Elderly Wellbeing and Alcohol – a tricky cocktail, I,** EASAR conference, Vienna

Jakob Emiliussen. **Elderly Wellbeing and Alcohol – a tricky cocktail, II.** EASAR conference, Vienna

Anne Sophie Schwarz. **Lifestyle factors in somatic patients with and without potential alcohol problems,** EASAR conference, Vienna

Kristine Tarp. **Blend-A – blended treatment for alcohol use disorder.** EASAR conference, Vienna

Morten Hell. **The Self-Match Study,** EASAR conference, Vienna.

Barbara Braun. **The individual treatment goal influences drinking quantity after treatment in older persons with alcohol use disorder.** Results of the randomized controlled Elderly-Study, EASAR conference, Vienna.

Peter Schøler, **Alcohol and drug use among patients in a psychiatric emergency ward: characteristics and course of hospitalization,** EPA, NICE

Kjeld Andersen, Jakob Emiliussen, Lotte Kramer Schmidt, Peter Schøler, Kristine Tarp, Angelina Mellentin, Anette Sjøgaard Nielsen: **Alcohol dependency**. Annual meeting, Danish Association on Psychiatry, Nyborg.

Research stays

Phd-student Anne-Sophie Schwarz stayed at University of Kent, UK, in January/February

PhD-student Lotte Kramer from UCAR stayed at CASAA, Albuquerque, US, two weeks in July.

Assisting Professor Randi Bilberg from UCAR stayed at CASAA, Albuquerque, US, three weeks in September.

PhD-student Morten Hell from UCAR stayed at two Universities in California for 3 weeks in January.

PhD-student Anna Mejldal from UCAR stayed for a week at the Technische University of Dresden in November.

Dissemination in general in 2018

Teaching and training

Mellentin A, Nielsen B, Nielsen AS, Andersen K, Bilberg R, Mejldal A. One day conference in the alcohol treatment institution in Odense: Preliminary findings of the RESCueH studies.

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.

Nielsen AS. A presentation on Alcohol problems on the Open House arrangement, open for the public, at department of Psychiatry, Odense.

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 news letters 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 2018

Louise Amalie Knopp Andersen & Sarah Græsbøll Munk: What treatment should be offered to indigenous people suffering from alcohol use disorder? (Master of medicine)

Emil Bjerring Ahmad-Nielsen, Nicolai Gundtoft Andersen. Characteristics and addiction severity of treatment-seeking outpatients with alcohol use disorder (AUD), comparing patients with none, one or both parents having an AUD history. (Master of medicine)

Camilla May. Barriers for seeking treatment for alcohol use disorder (Master of medicine)

Ali Mohamad Abdul Ghani, Edris Faiz: What is the cause of death, when alcohol dependent persons die prematurely? (Master of medicine)

Daniel Meng. Selvhjælpsgrupper til personer med OCD: En gennemgang og kritisk vurdering af litteraturens aktuelle status. (Master of Psychology)

Dorthe Rubak. Kan koder for ICF "Core-set" for arbejdsrettet rehabilitering genfindes i den socialmedicinske udredning? (Master of rehabilitation)

Nina Bache. Opioidbehandling til mennesker med vedvarende/kroniske smerter, set i et organisatorisk perspektiv (Master of rehabilitation)

Peter Schøler Elderly with relief/reward drinking patterns: characteristics and treatment outcomes (Master of Medicine)

Silvia Helen Kasin, Rebekka Loftsson. Barriers clinicians experience when they screen for alcohol use disorder among patients. (Master of Medicine)

Sharmake Abdulahi Maxamed. The association between the use of alcohol and psychotropic drugs. (Master of Medicine)

Dines Jamil. Prevention of Wernicke - Korsakoff syndrome after alcohol abuse. (Master of Pharmacy)

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 is Chair of Alcohol & Society since 2011.