Medel för 2021 FO2020-00xx

Personuppgifter Namn: E-Post: Titel: Personnummer: Kön:	**Arbetsplats**
Projekttitel	
Medsökande	

Populärvetenskaplig sammanfattning av projektet

Syfte

Skadligt bruk av alkohol är en av de största orsakerna till sjukdomar och förtidig död. Ett stort problem är att alltför få söker vård för alkoholproblem, jämfört exempelvis med personer som lider av andra psykiska eller fysiska problem. Vi vet idag att behandlingsmetoder som understödjer ett kontrollerat drickande (konsumtionsnivå under gränsen för lågriskbruk) ökar andelen som söker vård, jämfört med metoder som enbart är inriktade på helnykterhet. En sådan metod är kognitiv beteendeterapi (KBT) i form av Behavior Self-Control Training (BSCT) som består av fem sessioner där patienter med alkoholproblem får hjälp med att sätta upp specifikt mål för och registrera sin konsumtion, identifiera risksituationer, måttlighetsstrategier, samt att avstå oftare från alkohol. Det saknas väsentlig kunskap kring kostnadseffektiviteten för behandlingsmetoder på alkoholområdet, inte minst studier som skattar de hälsomässiga och ekonomiska effekterna av att erbjuda metoder inriktade på kontrollerat drickande jämfört med enbart helnykterhet. Syftet med denna studie är 1) att utvärdera kostnadseffektiviteten av BSCT jämför med motivationshöjande samtal (MET) som är en annan vedertagen behandling för alkoholberoende, samt 2) att utvärdera kostnadseffektiviteten för BSCT och MET jämfört med alternativ behandling inriktad på helnykterhet. I båda delstudierna studeras vidare om kostnadseffektiviteten är relaterad till konsumtionsnivåer i samband med studiestart, målsättning för konsumtionen, samt andra relevanta aspekter som exempelvis beroendeproblemens svårighetsgrad och psykisk ohälsa. Projektet består av två kostnadseffektivitetsstudier där data extraheras från en pågående randomiserad kontrollerad prövning där effekten av BSCT jämförs med METför personer som uppfyller kriterierna för alkoholbrukssyndrom enligt DSM 5 samt från litteraturen. I projektet modelleras hälsoekonomiska effekter (Health-Related Quality of Life (HRQoL) och kostnader) i ett longitudinellt perspektiv.

Spridning

Efter avslutad studie kommer resultaten att spridas i form av vetenskaplig publikation i en välrenommerad tidskrift inom området. Resultaten kommer också att presenteras vid Svenska och internationella vetenskapliga konferenser. Vi kommer att lägga stor vikt vid att göra resultaten kända också utanför det vetenskapliga samhället, exempelvis för allmänheten och studenter på utbildningar inom området. Vi tror att kunskapen som denna studie genererar är viktig också för beslutsfattare inom politiken och hälso- och sjukvården, då det hälsoekonomiska perspektivet får allt större tyngd i samband med beslut om resurser. Vi kommer därför att sprida resultaten vid konferenser och möten där företrädare för dessa organ finns representerade, exempelvis anordnade av Sveriges kommuner och regioner (SKR). Inom forskargruppen är vi slutligen vana att arbeta aktivt med att sprida resultat från vår forskning via konferenser som vi själva anordnar samt via media - exempelvis radio, tv och dagstidningar.

Samhällsrelevans

Den analysmodell som används i projektet kommer att möjliggöra en heltäckande uppskattning av kort- och långsiktiga hälsoekonomiska effekter av alkoholbehandling. Detta gör det möjligt att applicera framtida liknande frågeställningar för andra populationer och behandlingsmodeller, vilket i sin tur kan ligga till grund för framtida hälsoekonomiska analyser och beslut på alkoholområdet. Att väga in effekt per utnyttjad resurs är avgörande för att kunna erbjuda patienter med alkoholproblem adekvat vård som också är motiverad utifrån ett samhällsekonomiskt perspektiv. Projektet bidrar till att fördjupa kunskapen kring betydelsen av att individer själva sätter målet för sin behandling, vilket är den viktigaste aspekten av så kallad patientcentrerad vård.

Datum

Underskrift huvudsökande

Underskrift prefekt eller motsv.

♦ ♦ ♦

Ansökan

Projekttitel

Projektets längd Nytt flerårigt projekt

Jag söker kategori... Fria forskningsmedel

Område A

Projektet beräknas starta (åååå-mm-dd) 2021-01-01

Projektet beräknas vara slutfört (åååå-mm-dd) 2022-06-30

Anslagsförvaltande organ

Organisationsnummer

Telefon

Adress Postadress:

Medsökande i projektet

Medsökande

Etisk prövning

Ansökan om etiskt tillstånd skall vara inskickad till granskningsmyndighet vid ansökningstillfället och diarienummer anges. Kopia på godkänd etikansökan skall vara rådet tillhanda senast 18 november för att ansökan skall tas upp till behandling på fördelningsmötet i december.

Projektet är godkänt av djuretisk eller annan etisk granskningsnämnd Ja

Ange diarienummer

Ange datum för beslut

Projektet är godkänt av Etikprövningsnämnden (EPN) Ja

Ange diarienummer xxx

Ange datum för beslut 2020-xx-xx

Om "nej" på ovanstående – motivera kort varför forskningsetisk granskning inte är relevant

Projektplan

1) Bakgrund

Harmful use of alcohol is one of the leading avoidable contributors to disease and premature death globally (1). Up to 7% of the Swedish population meets criteria for harmful use or alcohol dependency according to ICD-10 criteria (2). However, only 10-20% ever seek treatment for alcohol problems, and many of these ultimately reject or interrupt treatment when the goal of treatment is total abstinence from alcohol consumption. Conversely, the proportion of those seeking care increases when offered a treatment with controlled drinking as the main treatment goal (3,4). Providing treatments where the goal of the patient and treatment goals are compatible is therefore an important factor for both treatment initiation and treatment outcome (5,6). Controlled drinking is defined as when alcohol dependent individuals do not consume harmfully nor become completely abstinent, and without relapsing into previous high consumption (7). Matching the goals of participants with the treatment goal is an important factor when studying efficacy of treatments with an aim of controlled drinking. One psychological treatment method for controlled drinking is Behavioural Self-Control Training (BSCT), which is based on Cognitive Behavioural Therapy (CBT). BSCT is unique in that the method is based on the psychology of learning and specifically focused on skills training. There is a complete lack of studies examining the outcome of BSCT in comparison with other treatments that have a goal of controlled drinking. Another available treatment is Motivational Enhancement Therapy (MET), which has demonstrated equal or better treatment outcomes as compared with other treatment methods (8,9). MET is based on the patient's own goal of alcohol consumption and is therefore possible to use as a comparator to BSCT. In 2019, national guidelines on recommended treatments for substance abuse and addiction were released by the Swedish National Board of Health and Welfare (10). Every treatment recommended in the national guidelines is supported by scientific evidence of effectiveness. Furthermore, bearing in mind that healthcare services are a scarce resource, the ranking of recommended treatments in the national guidelines is based on the scientific evidence of cost-effectiveness of treatment alternatives (10,11). Currently, MET is one of the most recommended treatments within the Swedish healthcare system for patients with alcohol use disorder (AUD) (10). Conversely, there is a substantial lack of information on the efficacy and cost-effectiveness of BSCT. The risk of developing alcohol-induced morbidities for chronic alcohol consumers increases substantially with time. Studies have demonstrated that the relative risk of diseases such as cancer, chronic liver diseases, neuropsychiatric disorders, cardiovascular diseases, and unintentional death increases significantly with chronic harmful drinking patterns (12,13). Furthermore, the risk appears to increase linearly as consumption levels rise (12). Accordingly, reducing harmful and hazardous levels of consumption is fundamental in reducing the short- and long-term consequences and morbidities of AUD. Moreover, the consequences of high consumption levels lead to severe economic ramifications. For instance, annual costs of alcohol consumption in Sweden have been estimated at 1.3% of the Gross Domestic Product (GDP), and annual net health-related losses have been estimated at 121,800 quality-adjusted life years (QALYs) (14). A significant proportion of costs is attributable to productivity losses resulting from work absence, short- and long-term sick leave, early retirement, and mortality (14). Lastly, AUD does not only have serious health and cost consequences on consumers. Family members and close-ones to consumers have lower quality of life compared to other populations (15–17). Due to the wide-ranging consequences of alcohol consumption, economic evaluations of treatments that have the goal of reducing alcohol consumption levels should preferably undertake a long-term perspective. Specifically, estimating cost-effectiveness by focusing on health losses and healthcare costs related to the short- and long-term effects of alcohol-induced morbidities is fundamental in capturing the broad impact of AUD (1,18). AUD is a chronic disease involving, for many patients, recurring cycles of harmful consumption patterns, treatment, controlled drinking, abstinence and relapse (1,18). Recommended treatments for AUD patients should therefore have the ultimate goal of maximizing years lived in full health, whilst simultaneously minimizing long-term costs endured by society. To our knowledge, no previous studies exist that evaluated the cost-effectiveness of BSCT for AUD. A few economic evaluations have evaluated the cost-effectiveness of MET (19,20). Results have demonstrated cost-effectiveness of MET, although the strength of the evidence is unconvincing. For instance, the comparators in previous evaluations have either been treatments aiming for complete abstinence that were provided at the same time as the MET treatment (19), or a five minute consultation alternative (20) that cannot be considered an established treatment option for AUD. More importantly, these economic evaluations were limited to the relatively short follow-up time of the trials they were based on. Consequently, the evaluations were not able to analyse the long-term cost-effectiveness by including alcohol-induced morbidities and costs related to different levels of consumption, which severely hampers the current understanding of the cost-effectiveness of MET. The proposed project will thereby include two economic evaluations. Firstly, the project includes the first study to assess the long-term cost-effectiveness of BSCT compared to MET for AUD patients aiming at reducing alcohol

consumption. Secondly, the proposed project includes a study that assesses the long-term cost-effectiveness of BSCT and MET compared to alternative treatment options that aim for complete abstinence by including relevant time-lags in treatment initiation for AUD patients aiming for controlled drinking.

2) Syfte/frågeställning

The proposed project has the following aims, with aims 1 and 2 corresponding to two different studies: Aim 1: Assess the cost-effectiveness of BSCT compared to MET for patients with AUD aiming for controlled drinking. Aim 2: Assess the cost-effectiveness of BSCT and MET compared to alternative treatment options containing a goal for complete abstinence for patients with AUD aiming for controlled drinking. To provide answers to these aims, two separate cost-effectiveness studies will be conducted: Study 1. Cost-effectiveness of Behavioural Self-Control Training compared to Motivational Enhancement Therapy for AUD patients aiming for controlled drinking. The primary research question is: 1) Is BSCT cost-effective compared to MET in reducing alcohol consumption for AUD patients who aim for controlled drinking? The secondary research questions are: 2) Does the cost-effectiveness of BSCT compared to MET vary between subgroups based on initial alcohol consumption levels? 3) Does the cost-effectiveness of BSCT compared to MET vary between subgroups based on the initial goals of alcohol consumption? Study 2. An economic evaluation of Behavioural Self-Control Training and Motivational Enhancement Therapy compared to alternative treatments with a goal of complete abstinence for AUD patients aiming for controlled drinking. The primary research question is: 1) Is BSCT and/or MET cost-effective for AUD patients aiming for controlled drinking compared to alternative treatment options aiming for complete abstinence? The secondary research question is: 2) Does the cost-effectiveness of BSCT and/or MET compared to alternative treatments aiming for complete abstinence vary between subgroups based on initial alcohol consumption levels?

3) Design/urval

The proposed project will consist of two cost-effectiveness studies using an economic cohort simulation framework (i.e. a health economic model). An economic model consists of a set of mathematical equations that reflect the epidemiological transitions between the different states of a certain problem or disease being modelled. The model follows a cohort of patients as they transition between those different states, and allows for making projections over a certain length of time, based on multiple sources. Economic models can be used to incorporate all sources of evidence, and to estimate the long-term impact of interventions, which often cannot be captured in time-limited trials. Models are the main form of evaluation used by international decision-making agencies. Both studies (Study 1 and Study 2) included in this project proposal will have a common central design and methodology. We will model a cohort of patients diagnosed with alcohol use disorder (AUD) who aim for controlled drinking over a lifetime horizon and estimate the expected costs and outcomes of the interventions. The dissimilarities between the two studies will be contingent on the aforementioned aims and research questions. The model will include health states reflecting different levels of daily alcohol intake measured as grams per day, where cut-offs will be assigned according to WHO definitions (21). Moreover, health states reflecting morbidities and mortality induced by chronic levels of alcohol consumption will be included. Health-Related Quality of Life (HRQoL) weights and costs will be assigned to each health state defined in the model (i.e. to each level of alcohol consumption and to each alcohol-induced morbidity). All model states and probabilities of transitioning between states will be categorised by sex and age, since volume of alcohol intake has distinctive repercussions depending on sex and age. The health economic model will thereby provide a comprehensive representation of the short- and long-term consequences of AUD. Lastly, the model will be comparable to previous health economic evaluations that have focused on treatments for AUD and will thus allow for present and future comparisons of cost-effectiveness across populations and settings. Our model will be built with input parameters obtained from multiple sources. The input parameters are mainly efficacy outcomes of the treatments, alcohol-induced morbidities and mortalities, and relevant costs. The input parameters will be sourced from efficacy trials, previous peer-reviewed literature, epidemiological research, and national statistics. A key source for input parameters in both studies will be an ongoing two-year randomized controlled trial (RCT) conducted at the Centre for Psychiatric Research (CPF) (ISCRTN: 14539251). The RCT compares BSCT to MET for patients diagnosed with AUD, according to The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), who have a goal of controlled drinking. Principal investigator for the study is associate professor Anders Hammarberg at the Department of Clinical Neuroscience at Karolinska Institutet and Centre for Psychiatric Research. Outcome measures are gathered at inclusion (baseline), 12 weeks, 26 weeks, 52 weeks and 104 weeks post baseline. Both

treatments are set at the Stockholm Centre for Dependency Disorders (Beroendecentrum Stockholm). The RCT will henceforth be referred to as "the initial RCT" in this project proposal.

4) Metod och datainsamling/databearbetning

Input parameters Information to build the model (input parameters) will be sourced from the initial RCT as well as from previous peer-reviewed literature, epidemiological research, and national statistics (e.g. Statistics Sweden and Swedish Price Lists). 1) Input parameters from the initial RCT: A) Health Outcomes: • HRQoL weights for alcohol consumption levels states – The EQ-5D by the EuroQol group will be used to estimate base-case QALYs (22). The EQ-5D is one of the most widely used instruments for HRQoL measurement and is commonly used in economic evaluations (23). HRQoL weights will additionally be estimated using the Satisfaction with Life Scale (SWLS) (24). B) Costs: • Costs for each treatment arm – Collected from treatment logbooks and standard charges for each treatment. C) Exposure: • Alcohol consumption levels – Alcohol diary as estimated by the Timeline Followback method (TMFB) (25), where one glass represents 12 grams of alcohol. Model health states will be based on average grams consumed per day. D) Probabilities of transitioning between different states in the model: • Will be derived for each state based on changes in alcohol consumption levels for a duration of two years after treatment initiation. 2) Input parameters from previous literature, epidemiological research and national statistics: A) Health outcomes: • HRQoL weights for alcohol-induced morbidities. • HRQoL weights for alcohol consumption states derived from RCTs providing alternative treatments with goals of abstinence. B) Costs: • Resource use and costs associated with the occurrence of alcohol-induced morbidities, treatments, and mortalities will be collected from previous literature and national statistics. • Societal costs due to productivity losses, short- and long-term sick leave, etc., will be included using sources from previous literature and national statistics. C) Exposure: • Alcohol consumption levels – Consumption levels derived from previous RCTs providing abstinence treatments for patients aiming for controlled drinking. D) Probabilities of transitioning between different health states in the model: • Alcohol-induced morbidities – Previous epidemiological research based on sex, age, and consumption states. • Alcohol-induced mortality – Life tables from previous epidemiological research based on sex, age and consumption states. • Time lags in treatment initiation based on incongruent treatment goals will be included. Base case modeling analysis The base-case economic evaluation in both Study 1 and Study 2 will be cost-utility analyses, comparing costs and health outcomes between different treatment arms. The primary health outcome will therefore be the Quality-adjusted life-year (QALY), and results will be presented as costs per QALY gained. The QALY is a commonly used health outcome measure in economic evaluations of treatments and interventions, especially in Sweden and the UK (22). The QALY simultaneously captures the impact of a treatment on HRQoL, as well as the length of life, and provides a single index that can be used across different disorders, thus supporting decision-makers in making efficient choices when distributing limited resources (22,23). The economic decision model will be constructed using TreeAge Pro and Microsoft Excel 2019. Uncertainty sensitivity analyses An uncertainty sensitivity analysis will be conducted in both studies to estimate the impact of the uncertainty in model parameters on results. This will be done by attributing distributions to relevant parameters. A cost-effectiveness plane (CEP) and a cost-effectiveness acceptability curve (CEAP) will be plotted and interpreted. The CEP is a scatterplot of the joint distribution of uncertainty around the incremental cost and effect estimates between both interventions. The CEAC illustrates the probability of BSCT being cost-effective at different willingness-to-pay threshold values for a QALY gained that decision-makers would be willing to pay. Willingness to pay values for a gained QALY will be set according to national guidelines. All costs and QALYs will be discounted in line with national guidelines. Furthermore, the following deterministic sensitivity analysis will be conducted by altering individual model parameters and focusing on specific subgroups: (1) separating the modelled cohort by initial state of consumption level; (2) separating the cohort by initial treatment goals according to a standardised treatment goal-form (26); (3) separating the cohort by age categories and sex; (4) running the model for different periods of time; i.e. two years, four years, and lifetime; (5) different perspectives on costs endured by the healthcare system and society; (6) estimating QALYs using the Satisfaction with Life Scale (SWLS) instead of the EQ-5D; (7) one-way sensitivity analyses on each model parameter to investigate the impact of any single parameter on cost-effectiveness. A Tornado diagram of the results from the sensitivity analyses will be illustrated where uncertainty levels will be based on corresponding confidence intervals. Analysis of RCT data (for collection of inputs for the model) The primary statistical analysis of the data from the initial RCT will be based on the principle of intention-to-treat (ITT). A secondary analysis using a complete case (CC) analysis will be conducted for participants who complete the study according to the following criteria: Those who provided data at baseline and at 12 and 24 months vs. those who completed at least four of five BSCT and three out of four MET treatment sessions. QALYs over the trial period will be

estimated using the area under the curve (AUC) method (27). Differences in QALYs between groups will be analysed using generalised linear models (GLMs) (28). Estimations will be adjusted for baseline utility values and background covariates in the GLMs. All statistical analyses of trial data will be conducted in STATA by StataCorp. Statistical significance will be set at a p-value of $\alpha < 0.05$ for all inferential tests.

5) Förväntat resultat
We expect BSCT to yield non-inferior results when compared to MET. An interesting result will be to assess whether BSCT or MET will have higher cost-effectiveness when comparing subgroups based on initial consumption levels or based on the specific treatment goals. When focusing on a patient group with a goal of controlled drinking, we expect both BSCT and MET to demonstrate a superior long-term cost-effectiveness compared to treatments aiming for complete abstinence. The result of the studies will provide the Swedish National Board of Health and Welfare, and consequently the Swedish healthcare system and municipal services, with evidence-based knowledge on the cost-effectiveness of BSCT and MET for AUD patients aiming for controlled drinking. This knowledge will provide answers to important questions such as: Should BSCT be a recommended treatment within the Swedish healthcare system for AUD patients with a goal of controlled drinking, and for which specific patient group should BSCT or MET be a recommended treatment alternative within Swedish healthcare.

6) Referenser

Budget

Projektets beräknade totala kostnader för ansökansperioden oberoende av finansieringskällor	1 091 163
Medel som söks hos Systembolagets Alkoholforskningsråd för ansökansperioden	1 091 163

Personal som skall avlönas med sökta medel under ansökansperioden

Namn/Tjänstebenämning	Årslön	% av heltid	LKP %	Lönekostnad
Forskningsassistent och tilltänkt doktorand år 1	420 000	50	21	254 100
Forskningsassistent och tilltänkt doktorand år 2	435 000	50	21	263 175
Projektledare år 1	504 000	30	21	182 952
Projektledare år 2	504 000	40	21	243 936
Total				944 163

Övriga kostnader under ansökansperioden

Specificera övriga kostnader som material, databearbetning, resekostnader och övrigt

Typ av kostnad	Specifikation	Kostnad
Driftsmedel	Licens för modelleringsprogrammet "TreeAge", år 1	5 000
Driftsmedel	Licens för modelleringsprogrammet "TreeAge", år 2	5 000

Konferenser/publikationer	Presentation av projekt/resultat år 2 vid en svensk och en internationell konferens inklusive resa (2 pers)	35 000
Total		45 000

OH-kostnader, enligt din institution (SEK) 102 000

Total kostnad enligt ovan **1091163**

Total kostnad är summa lönekostnader, övriga kostnader och OH-kostnad under ansökansperioden

Medel från andra finansiärer under ansökansperioden

Finansiär	Sökt belopp	Erhållet belopp

Om hela det sökta beloppet ej erhålles – vilken del av ansökan kan genomföras med ett lägre belopp?
Bedömningen är att sökta medel är nödvändiga för projektets genomförande. Vid ett lägre belopp kan projektet genomföras men med väsentligt längre tidsplanering.

Publikationer

CV för huvudsökande och medsökande