

Internet-based psychological interventions for alcohol use disorder

Treating addiction and supporting concerned significant others

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*På fel sida räcket efter julfesten
du räckte mig handen drog tillbaks mig
i sista stund
ifrån den stora John Blund
man kan ta livet av sig
man kan också ta en cigarett
man kan tänka på allt som går över
man kan tänka på allt som inte är lätt
men ring mig nästa gång
istället för piller i badkaret
leva livet
tar livet av oss
allt vi vill ha mer av
är inget vi mår bra av
leva livet
tar livet av oss*

– Prinsen av Peking

Abstract

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Alcohol use disorder (AUD) is a common problem in both Sweden and many parts of the world. Approximately 3 million people die every year due to alcohol consumption, making it the third largest cause of death in the world. Alcohol consumption has a causal effect on more than 60 different diseases, and also has a high level of comorbidity with other psychiatric disorders, such as depression, bipolar disorder, hypomania, panic syndrome, personality disorders, and schizophrenia. Despite the major illness burden that often accompanies AUD, there are estimations that as few as 10–20% of people with problematic alcohol use ever enter treatment. Internet treatment could make it easier to seek treatment for those who otherwise would not seek help.

The overall aim of the three studies included in this thesis was to investigate the efficacy of three internet-based interventions for alcohol problems: (1) *high-intensity internet treatment (ePlus)* compared to (2) an *unguided low-intensity internet treatment (eChange)* and waiting list (WL) conditions, for people with AUD (**Study I**, with a long-term follow-up in **Study II**), and (3) an *internet-based version of the Community Reinforcement and Family Training program (iCRAFT)* for concerned significant others (CSOs) to individuals with AUD (**Study III**).

Data was collected via self-reported questionnaires and telephone interviews. The primary outcomes in **Study I** and **Study II** were two measures of the participants' alcohol consumption: number of standard drinks per week and number of heavy drinking days (HDDs) per week. The primary outcome in **Study III** was treatment engagement, as expressed in the IPs' initiative to seek treatment.

In Study I (N = 166), a significant reduction was seen in number of standard drinks as well as HDDs for both the ePlus and the eChange group compared to the WL group at post-treatment. The reduction in standard drinks per week was more or less maintained after 6 months compared to pre-treatment for both intervention groups. These results align with findings in previous studies on both traditional Cognitive Behavioral Therapy (CBT) and guided internet interventions. There was no statistically significant difference between ePlus and eChange in number of standard drinks, but participants in the ePlus program had significantly fewer HDDs compared to participants in the eChange program at post-treatment, but this difference was no longer seen at 6-month

follow-up. Participants in the ePlus program displayed greater treatment satisfaction than did participants in the eChange program.

The results in **Study II** (N = 143) showed that, compared to pre-treatment, both treatment groups had lower alcohol consumption at both long-term follow-ups (12 and 24 months). These long-term follow-up results are in line with previous research regarding long-term internet interventions for anxiety and depression, with maintained symptom reductions compared to pre-treatment. Compared to post-treatment, there was increased alcohol consumption in the ePlus group on both follow-up occasions, but lower alcohol consumption in the eChange group. Although one group had increased and the other group had decreased consumption at the 12-month follow-up compared to the end of treatment, comparisons of the two groups at both long-term follow-ups showed no statistically significant differences between them.

In **Study III** (N = 94), the results showed that although twice as many CSOs in the iCRAFT condition reported IP treatment engagement, this difference was not statistically significant. The rate of treatment seeking reported for CSOs in the iCRAFT group was lower compared with previous studies.

In summary, the results in **Study I** indicate that ePlus is effective in reducing both number of standard drinks per week and HDDs compared to WL conditions; moreover, compared to eChange, ePlus is more effective in reducing HDDs immediately after treatment. **Study II** showed that participation in both ePlus and eChange seemed to be associated with maintained low alcohol consumption at long-term follow-up compared to pre-treatment, and that there were no significant differences between the two treatments. Both interventions may have potential as alternatives to traditional treatment forms, and their different structures (long vs. short, human guidance vs. no human guidance) open up for possibilities for clinics and patients to choose what suits them best. Results in **Study III** were unexpected, as previous research on Community Reinforcement Approach and Family Training (CRAFT) using a face-to-face approach has shown substantial effects. The lack of statistically significant effects can possibly be due to an underpowered study, but also points to a need to further develop the program.

Keywords: alcohol use disorder, internet-based treatment, Cognitive Behavioral Therapy, relapse prevention, Community Reinforcement and Family Training

Swedish summary

Alkohol har varit en del av människans historia i tusentals år, på både gott och ont. Idag dricker den genomsnittlige svensken 9 liter ren alkohol per år, och uppskattningsvis har 780 000 personer i Sverige så pass allvarliga problem med alkoholkonsumtion, så att denne skulle behöva gå i behandling för sina problem. Diagnosen vid alkoholproblem som används i denna avhandling följer DSM-5, "alkoholbrukssyndrom" ("alcohol use disorder", AUD). Utöver att vara ett vanligt problem i Sverige och stora delar av världen, så har alkoholbrukssyndrom en enorm sjukdomsbörda, och ungefär 3 miljoner personer dör varje år på grund av alkohol, vilket gör den till den tredje största dödsorsaken i världen. Alkoholkonsumtion har en orsakverkan på fler än 60 olika sjukdomar, där ökad alkoholkonsumtion redan från första glaset i de flesta fall innebär större risk att få sjukdomen. Alkoholkonsumtion har också en hög komorbiditet med andra psykiatriska sjukdomar, såsom depression, bipolär sjukdom, hypomani, paniksyndrom, personlighetsstörningar, schizofreni och suicid. Trots den stora sjukdomsbörda som ofta följer med alkoholbrukssyndrom, så är det uppskattningsvis så få som 10–20 % som söker behandling. Detta kan bero på olika anledningar, såsom oro att behandlingen inte ska vara effektiv, en önskan om att själv ta hand om problemet, förnekande att ha problem samt att det är förenat med skam och stigma att ha alkoholproblem. Internetbehandling kan vara en väg in till behandling för de som annars inte hade sökt hjälp.

Det övergripande syftet med de tre studierna som ingår i denna avhandling var att undersöka effekten av två internetbaserade insatser för alkoholproblem. Data samlades in delvis via självrapporterade frågeformulär som administrerades genom behandlingsplattformen, och dels via telefonintervjuer.

I **Studie I** undersöktes en högintensiv internetbehandling (kallad ePlus) för personer med alkoholbrukssyndrom. Syftet med studien var att jämföra behandlingen med en lågintensiv internetbehandling med liknande innehåll (eChange) och med en väntelista. Data samlades in från 166 deltagare (81 män, 85 kvinnor). Det antogs att deltagare i ePlus skulle minska sin alkoholkonsumtion, mätt i antal standardglas och antal högkonsumtionsdagar, mer än deltagarna både i eChange och väntelista. Ett sekundärt syfte var att utvärdera de negativa effekterna av hög- och lågintensiv internetbehandling för alkoholbrukssyndrom. Resultaten visade en statistiskt signifikant minskning i antalet standardglas såväl som högkonsumtionsdagar för deltagarna i både ePlus- och eChange-gruppen jämfört med deltagarna som stod på väntelistan direkt efter behandlingsavslut. Minskningen av alkoholkonsumtion bibehölls mer eller mindre efter 6 månader jämfört med vid behandlingsstart för båda

interventionsgrupperna. Dessa resultat överensstämmer med resultat i tidigare studier om både traditionell kognitiv beteendeterapi (KBT) och internetbehandling. Däremot visade resultaten att det inte fanns någon statistiskt signifikant skillnad mellan ePlus och eChange gällande antal standardglas, men däremot en signifikant skillnad i antal högkonsumtionsdagar för ePlus-gruppen jämfört med eChange-gruppen mätt i samband med behandlingsavslut, där deltagare i ePlus hade färre antal högkonsumtionsdagar. Denna skillnad mellan de två interventionsgrupperna uppmättes däremot inte vid 6-månadersuppföljningen. Deltagare i ePlus-tillståndet visade däremot större behandlingsnöjdhet än deltagare i eChange-gruppen.

I **Studie II** utfördes en långtidsuppföljning av Studie I, tolv respektive 24 månader efter att deltagarna hade slumpats till sin respektive grupp. Väntelistan som var med i Studie I följdes inte upp, då de hade fått en behandling direkt efter sin väntetid, och därmed inte längre räknades som en väntegrupp. Deltagarna svarade både på formulär och blev intervjuade per telefon, där bland annat diagnos kring alkoholbrukssyndrom kunde ställas. Det var tre huvudsakliga syften med studien: att vid långtidsuppföljning undersöka dels om deltagarnas alkoholkonsumtion var fortsatt lägre jämfört med när behandlingarna började, dels om alkoholkonsumtionen var på fortsatt samma nivå som när behandlingarna avslutades, och slutligen att undersöka om det fanns några skillnader mellan de två grupperna. Resultaten blev att jämfört med början av behandlingen, så hade deltagarna i båda behandlingarna lägre alkoholkonsumtion både vid tolv och 24-månadersuppföljningarna. Dessa resultat är jämförbara med tidigare forskning gällande internetbehandlingar för ångest och depression – som är de områden som är mest beforskade inom internetbehandlingar. Jämfört med behandlingsavslut var det en ökad alkoholkonsumtion i ePlus-gruppen vid båda uppföljningstillfällena, men en lägre alkoholkonsumtion i eChange-gruppen jämfört med vid behandlingsavslut vid tolv månadersuppföljningen. Trots att ena gruppen ökade och andra gruppen minskade vid tolv månadersuppföljningen jämfört med behandlingsavslut, visade det sig vid jämförelser av de båda grupperna vid båda långtidsuppföljningar, att det inte fanns några statistiskt signifikanta skillnader dem emellan.

I **Studie III** undersöktes en internetbaserad version av Community Reinforcement and Family Training-programmet (iCRAFT) för ”berörda viktiga andra” (engelska ”concerned significant others” eller förkortat CSOs) till personer med alkoholbrukssyndrom (engelska ”identified person”, förkortat IP). Även här samlades data in dels via självrapporterade frågeformulär som administrerades genom behandlingsplattformen, och dels via telefonintervjuer. Syftet med Studie III var att utvärdera iCRAFT jämfört med en väntelista. Hypotesen var att deltagare som fick iCRAFT skulle öka IPs behandlingsengage-

mang. Sekundära syften var att undersöka om iCRAFT hade ökat CSOs livskvalitet och minskat IPs alkoholbruk. I studien ingick 94 deltagare (2 män, 92 kvinnor). Det primära resultatet i studie III var behandlingsengagemang, dvs IPs egna initiativ att söka behandling för sina alkoholproblem. Resultaten visade att även om dubbelt så många CSO i iCRAFT-gruppen rapporterade att deras närstående hade sökt behandling, så var denna skillnad inte statistiskt signifikant.

Sammanfattningsvis indikerar resultaten i **Studie I** att ePlus är effektiv för att minska både standardglas per dag och antal högkonsumtionsdagar jämfört med väntelista, och jämfört med eChange är det också effektivt att minska högkonsumtionsdagar på kort sikt, det vill säga omedelbart efter behandlingen. Långtidsuppföljningen i **Studie II** visade att deltagarna i både ePlus och eChange hade fortsatt låg alkoholkonsumtion vid långtidsuppföljning jämfört med när de påbörjade behandlingen, men jämfört med när behandlingen avslutades hade deltagarna i ePlus ökat en del av sin konsumtion medan deltagarna i eChange hade fortsatt sänkt sin konsumtion, men vid jämförelse av de båda behandlingarna mot varandra fanns det inte några statistiskt signifikanta skillnader. Det faktum att båda behandlingarna både verkar vara fortsatt effektiva vid långtidsuppföljningarna och att de är olika varandra till karaktär (långa kontra korta texter, med kontra utan stöd från behandlare) öppnar upp för möjligheten att både kliniker och patienter kan välja den behandling som de tror passar dem bäst. Resultaten i **Studie III** var oväntade, eftersom tidigare forskning om CRAFT ansikte-mot-ansikte har visat betydande effekter. Bristen på statistiskt signifikant effekt kan eventuellt bero på att det var för få deltagare i studien, men också ett behov av vidareutveckling av programmet.

Preface

This thesis consists of a summary and the following three papers, which are referred to by their Roman numerals:

- I Sundström C., Eék N., Kraepelien M., Fahlke C., Gajecki M., Jakobson M., Beckman M., Kaldó V., Berman A.H. (2020) High- versus low-intensity internet interventions for alcohol use disorders: Results of a three-armed randomized controlled superiority trial. *Addiction* **115**: 863–874.
- II Eék N., Sundström C., Kraepelien M., Lundgren J., Kaldó V., Berman A.H. High- versus low-intensity internet interventions for alcohol use disorders (AUDs): A 2-year follow-up of a single-blind randomized controlled trial. (Submitted)
- III Eék N., Romberg K., Siljeholm O., Johansson M., Andreasson S., Lundgren T., Fahlke C., Ingesson S., Bäckman L., Hammarberg A. (2020) Efficacy of an internet-based Community Reinforcement and Family Training program to increase treatment engagement for AUD and to improve psychiatric health for CSOs: A randomized controlled trial. *Alcohol and Alcoholism* **55**: 187–195.

Abbreviations

AASES	Alcohol Abstinence Self-Efficacy Scale
AAQ	Acceptance and Action Questionnaire
ADHD	attention deficit hyperactivity disorder
Al-Anon	Alcoholics Anonymous
App	computer application
ARISE	Albany–Rochester Sequence for Engagement
AUD	alcohol use disorder
AUDIT	Alcohol Use Disorders Identification Test
B	Bayes factor
B5	Big Five personality traits
CBT	Cognitive Behavioral Therapy
CI	confidence interval
COMBINE	Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence
COS	core outcome set
CRA	Community Reinforcement Approach
CRAFT	Community Reinforcement Approach and Family Training
CSO	concerned significant other
CSQ-8	Client Satisfaction Questionnaire-8
DASS 42	Depression, Anxiety and Stress Scales
DSM	Diagnostic and Statistical Manual of Mental Disorders
EQ-5D	Euroqol-5D
GABA	gamma aminobutyric acid
GAD	generalized anxiety disorder
GAD-7	Generalized Anxiety Disorder Scale
GEE	generalized estimating equations
HDD	heavy drinking day
HIII	high-intensity internet intervention
iCBT	internet-based Cognitive Behavioral Therapy
ICD	International Statistical Classification of Diseases and Related Health Problems
iCRAFT	internet-based Community Reinforcement Approach and Family Training
IOGT–NTO	Independent Order of Good Templars in collaboration with the National Templar Order
IP	identified person
ITT	intention-to-treat

LII	low-intensity internet intervention
MADRS-S	Montgomery-Åsberg Depression Rating Scale – Self-report
MATCH	Matching Alcoholism Treatments to Client Heterogeneity
MCAR test	Missing Completely at Random test
MET	Motivational Enhancement Therapy
MI	Motivational Interviewing
MINI	M.I.N.I. International Neuropsychiatric Interview
OR	odds ratio
PACS	Penn Alcohol Craving Scale
QoL	quality of life
RCT	randomized controlled trial
RDL	risk drinking level
RHS	Relationship Happiness Scale
RP	relapse prevention
SBNT	Social Behavior Network Therapy
SCID-I	Structured Clinical Interview for DSM-IV axis I disorders
SD	standard deviation
SE	standard error
SUD	substance use disorder
SWLS	Satisfaction with Life Scale
TCI	Temperament and Character Inventory
TLFB	Timeline Followback
WHO	World Health Organization
WL	waiting list

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Niels Eék
Ödsmål, mars 2022

The purpose of this thesis has been to explore a new and modern approach to deal with a very old problem – problematic alcohol use. To give a perspective, this thesis starts with a general history of alcohol consumption.

Alcohol consumption – then and now

Humans have been drinking alcohol for thousands of years, and the discovery of 10 000-year-old beer containers demonstrates that we have fermented alcoholic beverages since the late Stone Age. Alcohol has played an important role in the history of humanity. Besides being consumed to quench thirst, it has sometimes given us hard-to-obtain nutrients and energy, also providing medical, antiseptic, and analgesic benefits. Furthermore, alcohol has played an important role in religion; it can make it easier to relax and socialize and it can make food taste better. It has given us pharmacological and psychological benefits and, when taken in moderation, it can enhance pleasure and quality of life (QoL), albeit only in the short term (Hanson, 2013).

The very first alcohol beverages were probably made from honey and berries. With the introduction of grain farming in the Near East, beer brewing was introduced and beer became a basic source of nourishment. Winemaking started in China a thousand years later, around 7000 BC, and later in the area of Caucasus, Iran, and Egypt. By 2000 BC, winemaking had reached Greece. At public festivities, all participants were given the same amount of wine, and from this it is said that democracy was born (Hanson, 2013). Both in Greece and in Rome, moderate drinking was promoted and hence became the norm, but with the spread of the Roman Empire around 400 BC, people started drinking more heavily, and alcohol misuse became more common. This misuse of alcohol consumption reached its peak around 50 BC, at which point even several Roman emperors had been known for abusive drinking. But this trend turned down again with the introduction of Christianity, as drunkenness was disapproved of. The Bible condemns intoxication (e.g., Isaiah 5:11 King James Version) and recommends total abstinence for those who cannot drink in moderation. Moderate drinking, as well as drinking alcohol for medicinal purposes, was approved of, in particular wine. The Bible mentions wine no less than 165 times (Courtwright, 2009; Hanson, 2013).

Depending on local conditions, different kinds of alcoholic beverages were developed and consumed as a source of nourishment, e.g., beer, mead, and fruit wines in northern Europe. Beer was a less polluted drink than water, with lower risk for pathogenic bacteria. In England between 1000 and 1500 AD, both men and women and even children drank ale for breakfast and dinner

and before bedtime. Drinking beer instead of water was also common in Swedish cities and towns, during times when there was no clean water (Husberg, 1994). The water used in beer is boiled, and pathogenic microorganisms cannot survive due to the presence of various inhibitory factors, such as ethanol, hops, low pH, carbon dioxide, the lack of nutritive substances, and so forth (Menz, Aldred, & Vriesekoop, 2008). For an adult, 4 liters of beer (with low alcohol content) per day was not uncommon. In Sweden, the beer consumption during the Middle Ages may have been 40 times higher than in contemporary Sweden (Hanson, 2013).

In the 18th century, the agricultural revolution made it possible to produce alcohol in large quantities at low cost. At the same time, transportation was also improved, which in combination resulted in increased availability so that even the common workers could afford to drink various types of alcoholic beverages in high amounts. In the 19th century, the industrial society had higher demands for a sober workforce. Alcohol consumption was seen as the cause of an increase in crime, poverty, and high infant mortality (De Bejczy, 2016; Hanson, 2013). Various temperance movements began. In Sweden, this occurred towards the end of the 19th century with the Order of Good Templars, which today is called the “Independent Order of Good Templars in collaboration with the National Templar Order (IOGT–NTO).”

In Sweden, legislation aimed to reduce the availability of alcoholic beverages came into force in 1917. The legislation known as the “Bratt System” was named after its main progenitor Ivan Bratt. Every citizen allowed to consume alcohol was given a booklet called “*motbok*”, in which a stamp was added each time an alcoholic purchase was made – with the exception of wine which was considered less dangerous. In 1922, a referendum was announced on a total ban on alcohol consumption. In the vote, the “No” side won by 51%, and the sale of alcohol continued to be legal. Soon thereafter, the shortcomings of the Bratt System were realized. Admittedly, and a bit contradictorily, alcohol abuse decreased, but the overall consumption increased, and smuggling and illicit production became commonplace. The Bratt System was abolished in 1955, and instead the state-owned retail monopoly (*Systembolaget*) was established. With the abolishment of the Bratt System, alcohol consumption increased for some time, but soon decreased again to its former levels.

The current total yearly alcohol consumption in Sweden is estimated to be 9 liters of pure alcohol per capita for individuals 15 years and older (Trolldal & Leifman, 2018), which can be compared to the estimated European consumption of 9.8 liters per capita (World Health Organization, 2018). Four out of five adults in the Swedish population are estimated to drink alcohol during a 30-day period. Young people (17–29 years old) tend to drink a higher

amount of alcohol on fewer occasions compared to older people. Older people have increased their alcohol consumption since 2004, whereas younger people have lowered their consumption – but younger people still drink the highest volumes. During the 10-year period between 2008 and 2017, there was an 8% decline in total consumption (Trolldal & Leifman, 2018). Men tend to drink more than women in terms of both total consumption and heavy drinking days (HDDs), defined as five or more standard units for men and four or more standard units for women (where one unit equals to 12 grams of alcohol) consumed on one occasion (Guttormsson & Gröndahl, 2017b).

Alcohol Use Disorder

Definitions

Problematic alcohol use used to be diagnosed as either alcohol abuse or alcohol dependence. Alcohol dependence was seen as a “somatic disorder” since dependence primarily indicated withdrawal symptoms and repeated failure to quit; while alcohol abuse was seen as a “social disorder” as abuse primarily indicated a use causing harm to self or others. With the update of the Diagnostic and Statistical Manual of Mental Disorders (DSM), fourth edition (DSM-IV), to the fifth edition (DSM-5), these two diagnoses were integrated into the new diagnosis of alcohol use disorder (AUD). People with AUD have impaired control over their alcohol consumption and continue drinking despite serious adverse consequences. Alcohol use disorder is defined as a dimensional diagnosis with eleven criteria. The more criteria are met and the more symptoms there are, the more severe the AUD. Presence of two to three symptoms is considered to constitute mild AUD, whereas four or five symptoms are considered to be moderate AUD, and six or more symptoms constitute severe AUD.

In this thesis, abuse of and dependence on alcohol will be addressed as AUD, since that is the DSM-5 nomenclature (American Psychiatric Association, 2013). The other main diagnostic manual, the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) (World Health Organization, 1992) from 1990, still uses the terms “alcohol abuse” and “alcohol dependence.” The main difference between these two manuals is that the DSM-5 is mainly used in research, whereas the ICD-10 is mainly used in health care.

Prevalence

In 2011, initiated by the Swedish government, the public report on addiction and its treatments titled “*Missbruksutredningen*” was published, which estimated that around 780 000 people (8.3% of the population) in Sweden over 18 years of age had an ongoing AUD (SOU, 2011). Three years later, a more in-depth national report was published which estimated the prevalence rate at 5.9% (7.6% of men, 4.3% of women). This translates to a total of 446 000 people with AUD – 285 000 men and 161 000 women (Ramstedt, Sundin, Landberg, & Raninen, 2014). The difference between the two estimations is that, in “*Missbruksutredningen*” (SOU, 2011), the estimations were made in only five of Sweden’s 21 counties, and only using the Alcohol Use Disorders

Identification Test (AUDIT) (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993) as an indirect measure of alcohol abuse and dependence. By contrast, Ramstedt et al. (2014) used an extensive survey in a randomized sample from the whole country.

Sweden lacks official guidelines to define risk consumption. “Risk consumption” is broadly defined as occurring when alcohol consumption increases the risk of social and/or medical problems, but when there is no AUD present (SOU, 2011). A definition suggested in a report from 2005 is often used (Andréasson & Allebeck, 2005), defining a weekly consumption above nine standard units (12 grams of alcohol) for women and above 14 units for men as “risk consumption” (Guttormsson & Gröndahl, 2017a). Lately, there has been a suggestion for a new recommendation of a weekly maximum of nine standard units for both women and men (Allebeck et al., 2018), but this suggestion is still not widely accepted.

The World Health Organization (WHO) estimated in 2018 that 11.0% of the Swedish population have AUD or harmful alcohol use, compared to the global prevalence of 5.1% and the European prevalence of 8.8%. Alcohol use disorder is more prevalent in high income countries (World Health Organization, 2018). As a comparison, in an extensive survey with face-to-face interviews among US citizens (N = 36 309), the 12-month prevalence of AUD was 13.9%, whereas the lifetime prevalence was 29.1% (Grant et al., 2015). We can conclude that the estimations of AUD prevalence in Sweden vary somewhere between 5.9% and 11%. There are several reasons for this variation, such as different measures used, the timing of the research, and whether it was a cross-sectional or longitudinal study.

It is not only the individuals with AUD who are affected by their excessive drinking, but also their relatives and concerned significant others (CSOs) including close friends. It has been reported that 30% of the Swedish population are estimated to be a CSO to someone who drinks alcohol excessively, and 15% have experienced negative consequences of a relative’s or friend’s high alcohol consumption in the last 12 months (Ramstedt et al., 2014).

Last but not least, only 10–20% of individuals suffering from AUD enter treatment (Cunningham & Breslin, 2004; Degenhardt et al., 2017; Grant et al., 2015; Probst, Manthey, Martinez, & Rehm, 2015; Stinson et al., 2005). A recent study conducted in a primary care setting in six different European countries found that only one in five people with current alcohol dependence had received professional help for their alcohol problems (Rehm et al., 2015). There are various reasons for this, e.g., a concern that the treatment will not be effective, a wish to be able to deal with the problem on their own, and/or a denial altogether of having a problem (Grant, 1997). Furthermore, AUD is severely stigmatized (Keyes et al., 2010; Kilian et al., 2021), provoking more

social rejection and negative emotions than other psychiatric conditions (Schomerus et al., 2011).

Not infrequently, recovery from AUD occurs spontaneously, without any formal treatment, so-called “natural recovery” (Blomqvist, 2009). There are a number of reasons why people with AUD recover without any formal treatment. Cross-sectional studies have shown that natural recovery occurs in a few percent to 30% of persons with AUD per year and longitudinal studies have shown even greater numbers, around 50% per year, but this may be an overestimation because usually not everyone is included, e.g., individuals who are deceased or in too bad a shape. Blomqvist and colleagues also point out that there are considerable problems in defining both “AUD” and “recovery,” which makes all estimates imprecise (Blomqvist, Cunningham, Wallander, & Collin, 2007).

Alcohol-related consequences

The impact of AUD on morbidity and mortality among individuals with AUD is estimated to account for a substantial part of worldwide alcohol-related harm (Rehm et al., 2010). In particular, the risk of premature death from somatic diseases such as liver cirrhosis, cancer, and cardiovascular disease is several times higher among people with an AUD (Balldin, Berglund, Berggren, Wennberg, & Fahlke, 2018; O’Keefe, Bhatti, Bajwa, DiNicolantonio, & Lavie, 2014). Harmful use of alcohol accounts for 5.3% of all deaths worldwide, or about 3 million deaths annually (World Health Organization, 2018), which makes alcohol the third leading contributor to the global disease burden, preceded by hypertension and tobacco smoking (Lim et al., 2012). There is a causal link between alcohol and more than 60 medical conditions, and most of those have a direct dose–response relationship, with risk of the disease increasing with higher alcohol volume. Among diseases linked to alcohol consumption are different kinds of cancer such as oesophageal cancer, mouth and oropharyngeal cancers, liver cancer and breast cancer, some cardiovascular disorders, neuropsychiatric disorders such as epilepsy, but also injuries, both intentional and unintentional (Rehm, 2011; Room, Babor, & Rehm, 2005). There is a common view that low to moderate alcohol consumption might protect against some diseases, cardiovascular disease in particular, which has been supported by some previous research (O’Keefe et al., 2014), but this claim has been called into question in recent years (Chikritzhs et al., 2015). No health benefit has been seen in people who engage in binge drinking (World Health Organization, 2018); quite on the contrary, any alcohol consumption increases the risk of certain cancers, and higher levels of consumption further increase those risks (Andréasson et al., 2017). There is also a positive correlation between alcohol consumption in the population as a whole

and harm regarding, e.g., liver cirrhosis mortality, suicide, injuries, assaults, and driving under the influence, as shown in Swedish studies (Norström & Ramstedt, 2005; 2018). This implies that the risk for negative consequences related to alcohol consumption does not only stem from individuals with AUD.

Alcohol-related comorbidity

There are several psychiatric conditions that are associated with AUD, such as major depression, dysthymia, bipolar disorder, hypomania, panic disorder, phobias, generalized anxiety disorder (GAD), personality disorders, any drug use disorder, and schizophrenia. Other aspects of mental ill health, such as increased risk for suicidal ideation and suicide, are also associated with AUD. Likewise, psychiatric comorbidity is associated with greater severity of alcohol-related symptoms (Cargiulo, 2007; Grant et al., 2015).

Alcohol-related harm for concerned significant others

Research has shown that adult CSOs' QoL suffers in the process of chronically dealing with stressors that are associated with the substance [or alcohol] [ab]use of an identified person (IP) close to them (Ryan et al., 1997). The stressors typically include violence, verbal aggression, financial problems, marital conflict, disrupted relationships with the children, and social embarrassment (Jacob, Krahn, & Leonard, 1991; Leonard & Eiden, 2007; O'Farrell & Birchler, 1987). Concerned significant others have been shown to often respond to these stressors with depression, anxiety, complaints of physically illness, and low self-esteem (Ray, Mertens, & Weisner, 2007; 2009; Ryan et al., 1997; Spear & Mason, 1991).

Theoretical explanations for alcohol use disorder

The development and maintenance of AUD has been theoretically understood and described from different perspectives. The main perspective which the interventions in the studies in this thesis are based on are learned behavior, and, more specifically, conditioning. Classical and operant conditioning are described below, followed by other perspectives.

Classical conditioning

Classical conditioning (also known as "Pavlovian" or "respondent conditioning") is the first learning principle, and is best known from the characteristic experiments by physiologist Ivan Pavlov whose dogs heard a chime every time they got fed. In other words, the previously neutral stimulus of the sound of

the chime was paired (or conditioned) with eating, and in time the dogs started to drool every time they heard the conditioned sound, even when they no longer got fed. The behavior of dogs to drool when they are about to eat is an unconditioned reflex of evolutionary origin, but a conditioned response, that is, the behavior to start drooling because of a learned sound, is based on individual experience. Likewise, certain cues, or relapse triggers, can form paired associations between a certain behavior, e.g., passing by a bar, socializing with friends who usually drink alcohol, or perhaps just thinking about summer (examples of three specific stimuli), and consuming alcohol and so, a conditioned response is created. Just as in the case of Pavlov's dogs, the conditioned response (the desire to drink alcohol) follows regardless of whether the conditioned stimuli (cues or triggers) lead to consuming alcohol or not (Kadden & Cooney, 2005; Onken, Blaine, & Boren, 1993).

Operant conditioning

Operant conditioning is the second learning principle, described by psychologist B.F. Skinner. Every behavior has a consequence, and this learning occurs as a result of the cause and effect relationship between the two. The behaviors can be reinforced or extinguished depending on the consequences. Reinforcement means that the consequences of behavior increase the likelihood that the behavior will be repeated. Positive effects of consuming alcohol lead to increased likelihood that even more alcohol is consumed, more frequently, or in higher quantities. Reinforcement is divided into positive and negative reinforcement, where the former occurs when the consequence, e.g., feeling relaxed or joyful, is appreciated by the consumer and the latter occurs when the consequence of the behavior is removing something that is not appreciated, e.g., removing a headache or social anxiety. Alcohol consumption is reinforcing for most people in the short term; the exception is, e.g., when someone has a genetic predisposition for immediate punishing consequences. In the long term, as the person develops AUD, the consequences usually change from being positively reinforcing to being negatively reinforcing, i.e., they change from bringing something appreciated or desired, to removing something unwanted or undesired. Then it can be harder to link the behavior of alcohol consumption to the long-term consequences, e.g., negative emotions, worse sleep quality, and getting less family quality time. The transition from positively to negatively reinforced behavior makes it harder to discontinue the behavior of alcohol consumption, since it is harder for the brain to make that link between cause and effect (Kadden & Cooney, 2005; Meyers & Smith, 1995). Behavior that stop having reinforcing consequences will eventually discontinue, this is called extinction.

Other perspectives

There are also other theoretical explanations for AUD. For instance, there is evidence that genetic disposition may predispose some individuals to develop AUD (Volkow & Koob, 2015). Other perspectives are the pharmacology of the substance, personality, different neuropsychiatric factors, social impact, and availability. None of these models can on its own explain the full complex picture of AUD. The conventional view among researchers today is that a multifactorial explanation model best explains the disorder.

The biopsychosocial model was first introduced by George Engel (1977; Blomqvist, 2012) in response to the prevailing view that mental diseases were solely of medical origin. The biopsychosocial model is, in short, an interdisciplinary model that links biology, psychology, and socioenvironmental factors, and these three perspectives must all be considered when assessing and treating diseases.

Although there is a significant amount of research that suggests that a multifactorial explanation best explains AUD, disciplines such as psychology and medicine often have their own models. A few prominent samples of different perspectives follow below.

Biological models concern brain chemistry and brain structure and emphasize the importance of genetics and genetic abnormalities and the risk to develop AUD. According to a meta-analysis of twin and adoption studies, the heritability of AUD, i.e., the combined genetic risk of developing AUD, is estimated to explain approximately 50% of the disease risk (Verhulst, Neale, & Kendler, 2015). According to previous research (e.g., McGue, Pickens, & Svikis, 1992; Prescott & Kendler, 1999), men are more prone to develop AUD because of genetic factors than women, but according to Verhulst et al. (2015), there is no support for this claim. As for the medical perspective, a biomedical explanation model is that addiction is best understood as a brain disease. In 2015, Nora Volkow and George Koob argued that prefrontal and striatal deregulation leads to loss of control and compulsive alcohol or drug intake when the person takes the substance or is exposed to conditioned cues (Volkow & Koob, 2015).

Excessive alcohol consumption is associated with changes in the midbrain, the limbic system, the prefrontal cortex, and the amygdala – regions that are related to execution of motivated behaviors, and also to control of stress and emotionality (Koob, 2003; Koob & Volkow, 2016). Related to operant conditioning as described above, different neurotransmitters affect neurons in different ways depending on the type of reinforcement, i.e., positive or negative reinforcement. When alcohol consumption is positively reinforced, such as when it leads to joy or feeling relaxed, which in turn leads to more alcohol consumption, the neurotransmitters dopamine, opioid peptides, serotonin,

gamma aminobutyric acid (GABA), and endocannabinoids are recruited. On the other hand, when alcohol consumption is negatively reinforced, such as when it leads to more consumption because something experienced as negative is removed, such as anxiety or somatic pain, corticotropin-releasing factor and glutamatergic systems are recruited and downregulation of GABA transmission is induced (Koob & Volkow, 2016). As the person develops AUD in the long term, when the consequences usually change from being positively reinforced to being negatively reinforced, adaptive changes occur in several neurotransmitters, such as GABA, glutamate, and norepinephrine.

A large American survey examined the risks of transition from different substance uses (including alcohol) to dependence, following almost 29 000 respondents using alcohol over a 13-year period (Lopez-Quintero et al., 2011). The cumulative probability estimate that alcohol users would transcend to alcohol dependence was 22.7%. According to this study, there are several risk factors for developing AUD – early debut, being of male gender, other substance use, unemployment, and never having been married, as well as mental disorder and a family history of alcoholism, but not education or income level. Children who see their role models consume alcohol can learn from their behavior, but different individuals react differently to growing up with a parent with AUD. Some limit their consumption because of aversion, while others consume more alcohol (Slutske et al., 2008).

Studies exploring the longitudinal association between both personality disorders and personality traits and later onset of AUD show that antisocial personality disorder and borderline personality disorder generally precede AUD (Cloninger, Sigvardsson, & Bohman, 1988; Newton-Howes, Horwood, & Mulder, 2015). One hypothesis posits that individuals with antisocial and impulsive traits have lower thresholds to deviant behaviors, which in turn favors the engagement in early alcohol use and development of AUD (Verheul & van den Brink, 2000). In the late 1980s, Robert Cloninger and colleagues, using data from previously assessed 11-year-old children reassessed at the age of 27, showed that four personality traits were associated with excessive alcohol consumption and later AUD, namely, impulsivity and disinhibition, novelty seeking, harm avoidance, and reward dependence (Cloninger et al., 1988). A later review examined Cloninger's personality model Temperament and Character Inventory (TCI) with different psychiatric disorders, including AUD, but failed to link AUD with any of the TCI dimensions (Miettunen & Raevuori, 2012).

An alternative personality model to Cloninger's TCI is the five factor model Big Five personality traits (B5), developed using factor analysis. Two meta-analyses (Lui, Chmielewski, Trujillo, Morris, & Pigott, 2022; Malouff,

Thorsteinsson, & Schutte, 2005) have shown that a higher level of extraversion predicts increased alcohol consumption, and high neuroticism, low agreeableness, and low conscientiousness predict more negative consequences stemming from high alcohol consumption. Openness was unrelated to alcohol use.

As for the psychological perspectives, Gerhard Bühringer et al. in 2008 introduced the theory that addiction reflects an imbalance between an automatic “impulsive” system and a higher order “reflective” system (much like Daniel Kahneman’s cognitive System 1 and System 2 in cognitive neuroscience (Kahneman, 2011)). According to this, impairments in higher order control functions play a role in substance use disorders (SUDs) such as AUD, in that the impairments are a vulnerability factor or proximal risk factor for the onset of addiction and an important moderator in cessation processes (Bühringer, Wittchen, Gottlebe, Kufeld, & Goschke, 2008).

Another psychological perspective on addiction comes from Kadden (2001), and states that AUD is a maladaptive way of coping with problems or meeting needs. When a person prone to developing AUD (which is true for some but not all people who develop AUD) experiences either the reinforcing effects of alcohol or expectations regarding its effects, or imitates role models, then AUD has the potential to develop as a set of learned behaviors acquired through experience. Thus, if alcohol has had reinforcing effects on repeated occasions, it may become the preferred way of achieving those effects.

Alcohol Use Disorder Treatment

Alcohol use disorder, as well as other disease-related disorders, should be treated with evidence-based interventions (Öst, 2016). There are several treatments for AUD that have been shown to be effective in both research and regular care. Meta-analyses of alcohol treatments show mixed effect sizes, depending on type of intervention and if they have been compared with waiting list (WL) or an active treatment. Motivational interviewing have shown small effect sizes (Lundahl, Kunz, Brownell, Tollefson, & Burke, 2010), and other CBT-based brief interventions have shown moderate, sometimes large effect sizes (Bertholet, Daeppen, Wietlisbach, Fleming, & Burnand, 2005; Magill et al., 2019). Pharmaceuticals for AUD show a similar pattern with low to moderate effect sizes (Maisel, Blodgett, Wilbourne, Humphreys, & Finney, 2013). The Swedish national guidelines for care and support in addiction (Socialstyrelsen, 2019) recommend both pharmacological and psychological/psychosocial treatments for AUD.

The recommended psychological and psychosocial treatments for AUD are Motivational Enhancement Therapy (MET), Cognitive Behavioral Therapy (CBT), relapse prevention (RP), the Community Reinforcement Approach (CRA), the twelve-step program, and Social Behavior Network Therapy (SBNT) (Socialstyrelsen, 2019). These methods have the best proven efficacy, and when administered in group format they also show favorable health economic properties, except for MET which is low cost even when administered individually. The national guidelines also mention internet-based treatment and recommend that it can be used within research and development (Socialstyrelsen, 2019). The RP program is of theoretical relevance to this thesis and is presented below.

The recommended pharmaceuticals are disulfiram (known under its trade name "Antabuse"), acamprosate, and naltrexone. Disulfiram is well documented and tested, with good effect in open non-blinded studies, and is suitable when the aim of the treatment is total abstinence (Mutschler, Grosshans, Soyka, & Rösner, 2016). Acamprosate has shown efficiency when the aim was reduced alcohol consumption and a reduction in number of relapses (see, e.g., Sass, Soyka, Mann, & Zieglgänsberger, 1996; Tempesta, Janiri, Bignamini, Chabac, & Potgieter, 2000), while naltrexone mainly results in fewer HDDs (Carmen, Angeles, Ana, & María, 2004).

There are a few different self-help programs for relatives. The Community Reinforcement Approach and Family Training (CRAFT) support program has

been used in this thesis, but there are also others, such as Alcoholics Anonymous (Al-Anon), the Johnson Intervention, and the Albany–Rochester Sequence for Engagement (ARISE), to mention a few. The Al-Anon approach is recommended by the Swedish national guidelines and is based on the premise that the relative without drinking problems should detach from responsibility for altering their relative’s drinking problem.

Relapse prevention

Relapse prevention is based on CBT, which was developed during the 1970s to be used in alcohol treatment. Since the 1970s, CBT has also been applied to a wider range of problem behaviors, such as gambling, eating disorders, and sexual risk behaviors. When applied to alcohol problems, the primary focus of treatment lies on identifying the needs currently being met by drinking alcohol, and developing coping skills that provide alternative ways of meeting those needs (Larimer, Palmer, & Marlatt, 1999; Marlatt & Donovan, 2005). The RP approach has generally been shown to be effective for alcohol problems (Irvin, Bowers, Dunn, & Wang, 1999; Magill et al., 2019). The theory is that when the patient meets those needs without using alcohol, the risk of relapsing to alcohol decreases.

Community Reinforcement Approach and Family Training

For several decades, relatives of someone with AUD were seen as “codependents” and were consequently pathologized (Miller, Forcehimes, & Zweben, 2019). The CRAFT program, recommended by the Swedish national guidelines (Socialstyrelsen, 2019), offers an alternative approach to the view of “codependence.” The program was developed as an extension of the CRA, which is a treatment that uses operant conditioning, where the patient learns what triggers drinking behaviors and how to avoid and/or cope with those triggers. The CRAFT program, which is the CRA with a “Family Training” addition, is a support program for CSOs to IPs (i.e., persons with AUD) based on core principles used in behavioral therapy. Behavioral therapy stems from learning theory, in which learned behaviors, and how the environment influences those behaviors, are core principles. The CSO helps the IP by rewarding behaviors that lead to increased sobriety, and not reinforcing behaviors that lead to increased alcohol consumption. Just like in CRA, the method is based on operant conditioning, where CSOs are taught how to improve sobriety by offering alternatives to consuming alcohol, and how to positively reinforce these alternatives, e.g., through activities the IP used to enjoy but no longer performs.

The CRAFT program is usually delivered in an open care setting during eight to twelve sessions, over a maximum 6-month period. The support program is often administered either individually or in a group format, led by health care professionals often with a 3-day introductory course in CRAFT.

The program has the following main aims: (1) to increase CSOs' QoL by encouraging them to engage in recovering activities; (2) to decrease IPs' alcohol use by teaching CSOs how to change their own behavior in order to minimize the positive consequences of alcohol use for IPs, to increase the positive consequences of IPs' sober and healthy activities, and to communicate in a clear and positive way; and (3) to increase IPs' treatment engagement by developing CSOs' skills in proposing treatment seeking (Smith & Meyers, 2007). In addition to AUD, the CRAFT program has also been shown to be efficient in treating drug abuse (Meyers, Miller, Hill, & Tonigan, 1998) and problem gambling (Nayoski & Hodgins, 2016). Concerning CSOs to individuals suffering from AUD, the CRAFT has been shown to improve rates of treatment engagement for IPs, compared to other support programs, while at the same time improving CSOs' physical and mental health status and QoL (Bischof, Iwen, Freyer-Adam, & Rumpf, 2016; Miller, Meyers, & Tonigan, 1999).

Long-term follow-up of Alcohol Use Disorder treatments

Long-term follow-up on Cognitive Behavioral Therapy

Long-term follow-ups of randomized controlled trials (RCTs), here defined as 2 years and longer, are rare in the field of face-to-face CBT. It is known that face-to-face CBT can yield long-term effects (Hollon, Stewart, & Strunk, 2006), and that long-term effects of face-to-face CBT can be superior to those achieved with medication (Cuijpers et al., 2013). The few published studies have mainly concerned depression and anxiety (Gibby, Casline, & Ginsburg, 2017; Hollon et al., 2006; Nadiga, Hensley, & Uhlenhuth, 2003), with a few exceptions, e.g., attention deficit hyperactivity disorder (ADHD) (Ginsberg, Långström, Larsson, & Lindefors, 2015), dental fear (Hakeberg, Berggren, Carlsson, & Gröndahl, 1993), and schizophrenia (Turkington et al., 2008).

Long-term follow-up on Cognitive Behavioral Therapy for alcohol use disorder

Likewise, long-term follow-up studies in the field of CBT for people with AUD are scarce. One recent study based on data from the Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence (COMBINE)

study (N = 694) and the Matching Alcoholism Treatments to Client Heterogeneity project (Project MATCH) (N = 806) indicated that alcohol consumption reductions were mostly maintained at a 3-year follow-up (Witkiewitz et al., 2021), measured as WHO risk drinking levels (WHO RDLs). Participants in the COMBINE study mostly received pharmacological interventions, while participants in Project MATCH were randomized to either CBT, MET, or twelve-step facilitation – but none of these were performed online.

Long-term follow-up on Cognitive Behavioral Therapy-based internet interventions

Cognitive Behavioral Therapy-based internet interventions have included long-term follow-ups to a seemingly rather large extent compared to non-internet-based interventions. A recent review included 14 long-term follow-up studies (≥ 2 years) published between 2007 and 2014 with altogether 902 participants, regarding depression and different kinds of anxiety (panic disorder, social anxiety disorder, GAD, obsessive compulsive disorder, and mixed anxiety and depression), but also pathological gambling, stress, and chronic fatigue (Andersson, Rozental, Shafran, & Carlbring, 2018). Long-term within-group effect sizes varied greatly, with mean Hedge's $g = 1.52$. One recurrent weakness in long-term follow-up studies of internet interventions, however, is that they generally lack documentation of treatment seeking in the interim period between the completed intervention and the follow-up, making it difficult to determine whether the effect sizes derive from the internet intervention, or from additional help sought by participants.

Long-term follow-up on Cognitive Behavioral Therapy-based internet interventions for alcohol use disorder

Little data is available regarding long-term follow-up of internet interventions for AUD. A meta-analysis from 2018 (Riper et al., 2018) examined 19 different internet interventions for adult problem drinking, but usually with a short-term follow-up of 6 months. A few studies have been identified that have investigated long-term effects of internet interventions for AUD, but even these were limited to a follow-up of maximum 12 months (Bischof et al., 2008; Sinadinovic, Wennberg, Johansson, & Berman, 2014), showing no differences in drinking outcomes between different interventions. To our knowledge, there have been no follow-ups of 2 years or more in studies based solely on internet interventions for AUD.

Internet-based Treatment

Internet-based Cognitive Behavioral Therapy

Internet-based treatments of psychiatric disorders have been studied since 1997, with the advent of the Dutch program Interapy (Lange, 2001). In Sweden, internet-based treatment started soon thereafter, in 1998 (Hedman, Carlbring, Ljótsson, & Andersson, 2014).

Internet-based treatment can be divided into two different traditions: the clinical tradition and the public health tradition. The clinical tradition sees internet interventions primarily as a development and extension of clinical alternatives aside regular face-to-face therapy (Hedman, 2014). These interventions, frequently referred to as “internet-based Cognitive Behavioral Therapy (iCBT),” often have extensive manuals and a therapist guiding the user through the intervention, with so-called “minimal guidance” (approximately 10–15 minutes per week). Diagnostic assessments prior to the treatment are a prerequisite and clinical generalizations are essential (Andersson et al., 2008).

The public health tradition, on the other hand, sees internet interventions as an avenue for secondary prevention, with the potential to attract people in the general population who may not yet realize that they have a problem, or who for some reason are reluctant to seek help within the health care system. In this later tradition, the texts are briefer, diagnostic assessments are not relevant as the interventions are not intended to be used in clinic, and therapists are not involved in the delivery (Andersson, 2009).

Treatment with minimal guidance from an active therapist has shown effects equivalent to traditional CBT (Andersson, 2016). The treatments are usually structured around the participants to implement different steps, so-called “modules.” Each module has homework assignments, e.g., in the form of different exercises, which are reported in worksheets on the same platform. At different stages of treatment, participants answer questionnaires that can be used in evaluation and monitoring.

Cognitive Behavioral Therapy interventions administered via the internet, following the clinical tradition described above, are provided in a highly structured format, making it easy for both the therapist and the participant to adhere to certain specific techniques. This also facilitates the possibility of reviewing all contact between the patient and the therapist to check that the treatment rationale is followed. In traditional psychological treatment, there is always a difficulty in controlling and measuring exactly what a therapist communicates with the person being treated. The contents of a self-help

manual and also the contents of the written interaction during the course of treatment can be controlled to a much greater extent. This makes internet-based treatment a very interesting option, when treatments with different content are being compared to each other.

When new treatments are investigated, negative effects should also be explored. This is usually done when investigating new pharmacological treatments; however, for psychological equivalents, it has been rarely done, especially in internet-based interventions (Rozenal et al., 2014; Rozenal, Magnusson, Boettcher, Andersson, & Carlbring, 2017).

Therapist guidance in internet-based treatment programs

Internet-based treatments are self-help programs, but often they provide minimal guidance from an active therapist. The role of the therapist is to give feedback on homework and exercises, to regularly encourage the participants to proceed in times of difficulties, and to help them with problem solving, both of technical problems (e.g., problems logging in) and treatment-related issues. A secure built-in message system in both treatment platforms enables synchronous or asynchronous interaction between the participant and the therapist.

Advantages and disadvantages of internet-based treatment

There are advantages and disadvantages to internet-based treatments. The first advantage is that the world is connected to the internet; in particular in Sweden a substantial majority of the population, 97.7%, are online (IWS, 2021). Secondly, internet-based treatments generally have strong evidence of being effective, with hundreds of RCTs to support this claim (Carlbring, Andersson, Cuijpers, Riper, & Hedman-Lagerlöf, 2018). Thirdly, internet-based treatments could be a way to radically increase the availability of effective psychological treatment. This applies in particular to conditions where people tend to hesitate to seek treatment for various reasons (Hedman et al., 2014) or when living far away from the health care facility, as is common especially in northern Sweden. A number of advantages of internet-based treatment, such as the possibility for the patient to access quality-assured health care, the flexibility to participate in the treatment when and where it best suits the patient, and the possibility to repeat chosen parts of the treatment content and to get fast feedback from the therapist have been listed (Andersson, Titov, Dear, Rozenal, & Carlbring, 2019; Vernmark & Bjärehed, 2013; Vernmark, Dahlin, & Andersson, 2021). Furthermore, the advantages for the therapist include the possibility to help more patients (in terms of both

time and tools), having a clear focus and structure since manual-based treatment is guaranteed, and that the risk of therapist drift is minimized. The possibility for increased compliance, i.e., that patients read the associated texts, answer the questionnaires, and do the homework, is also greater as it is easier to monitor the progress of the patients. Lastly, advantages for clinics are increased availability, quality-assured care, the possibility to treat more patients who otherwise would not seek treatment, easier evaluation of the treatments, and less therapist time spent per treatment (Andersson et al., 2019; Vernmark & Bjärehed, 2013; Vernmark et al., 2021).

Some of the disadvantages that have been observed (Vernmark & Bjärehed, 2013; Vernmark et al., 2021) are the potential problem that, as more and more information between health care providers and patients is delivered over the internet, the risk of confusing evidence-based treatments with other information, recommendations, and non-evidence-based treatments may arise. This makes it even more important to review internet-based treatments before they are delivered to the patients. Another risk is that of administration or technical failures, where patient data could be leaked. A third risk is that internet-based treatment may be perceived as complicated and hard to grasp for the patient. In combination with the fact that the personal contact with the therapist is less frequent; this could lead to dropouts or insufficient help. A fourth risk is that it may be too easy for health care providers to let patients start with internet-based treatment, and in combination with giving the patients insufficient therapist support and/or “social pressure,” this problem may also lead to dropouts. Other risks are that patients may feel excluded and lonely because they are being offered internet-based treatment; also, more advanced techniques in themselves may be a barrier and the therapist may feel like a controller instead of a therapist. Lastly, there are also cultural and language barriers as most internet-based treatments are developed in the Western world and for Western populations.

Using the Internet to reach people with problematic alcohol use

The first computer-based intervention for alcohol problems saw the light of day back in 1989, with a “microcomputer-based” approach to prevent drug and alcohol abuse among adolescents. This intervention mainly assessed users’ attitudes to drug and alcohol information delivered via a computer (Moncher et al., 1989). With the explosion of internet use around the world in general, and in Sweden in particular, it can almost be seen as a natural development to start administering internet-based (and not only local computer-based) interventions. Today there are several different online and mo-

bile interventions for problematic alcohol use, based on motivational or cognitive behavioral theoretical approaches. Several reviews mostly show short-term decreases in alcohol consumption (Giroux, Goulet, Mercier, Jacques, & Bouchard, 2017; Kaner et al., 2017; Kiluk, 2019; Nesvåg & McKay, 2018; Riper et al., 2018; Sundström, Blankers, & Khadjesari, 2017).

Studies I and II in this thesis are based on previous research on the treatment programs eChange and ePlus. eChange has been explored in a large internet-based intervention in naturalistic settings including almost 4 000 participants, but with a high attrition rate at follow-up (73%). The study showed a statistically significant decrease in alcohol consumption (within-group effect size for change in alcohol consumption, $d = 0.74$) (Johansson et al., 2017). ePlus has previously been investigated in a pilot study showing large, statistically significant within-group effect sizes (pre-post $d = 0.76$, pre-3-month follow-up $d = 0.79$) (Sundström, Kraepelien, et al., 2017).

As mentioned previously, only 10–20% of those who suffer from AUD enter treatment. Internet-based treatments may be an alternative for some individuals who hesitate to seek help within regular services. Aside from the obvious advantages of radically increasing access and eliminating geographical barriers, these interventions could hypothetically circumvent the stigma associated with physically visiting a clinic.

ePlus

ePlus treatment is an internet-based treatment (Sundström, Kraepelien, et al., 2017) based on CBT and RP for people with AUD. The treatment is described in detail under “Summary of the Studies.” In brief, it consists of 14 modules to be administered over 12 weeks with minimal guidance from an active therapist on the platform. The main aim of the treatment is to lower alcohol consumption, measured as standard drinks and HDDs.

eChange

The eChange program is an internet-based treatment (Blankers, Koeter, & Schippers, 2011) with a similar purpose and content as ePlus, but with fewer modules and also fewer pages of text than ePlus. Also, the treatment is administered with no human guidance. More information on this treatment can be found in “Summary of the Studies.”

iCRAFT

iCRAFT is an internet-based support program for CSOs who live, or have close contact, with an IP who suffers from AUD. The treatment is described in detail in “Summary of the Studies.” In short, the program consists of five modules

to be administered over 5–6 weeks. The program is based on the CRAFT (Community Reinforcement Approach and Family Training) method (Meyers & Smith, 1997), and the main aim of the program is to motivate the IP to seek treatment for his or her AUD. The participant has minimal guidance (i.e., 10–15 minutes per patient per week) from a therapist on the platform.

Aims of the Thesis

Main aim

The main aim of this thesis was to investigate the efficacy of three internet-based interventions for alcohol-related problems: (1) a high-intensity internet treatment, ePlus, for people with AUDs; (2) a low-intensity internet treatment, eChange, for people with AUDs; and (3) an internet-based version of the iCRAFT program for CSOs to individuals with AUD. In a broader perspective, in-depth knowledge about internet-based treatments can increase the availability of psychological treatments, both for people with AUDs, and for CSOs to alcohol-dependent IPs.

In **Study I**, the aim was to evaluate the high-intensity internet treatment ePlus in people with AUD. This treatment was compared with a low-intensity internet treatment (eChange) and with being on a waiting list (WL). It was hypothesized that participants of ePlus would reduce their alcohol consumption significantly more than would participants both in eChange and on the WL. A secondary aim was to evaluate any negative psychological effects of high- and low-intensity internet treatment for AUD.

The aims of **Study II** were threefold. The first aim was to investigate if participants in the ePlus and eChange programs had long-term lower alcohol consumption compared to pre-treatment measures. The second aim was to investigate if ePlus and eChange achieved a statistically significant change in alcohol consumption compared to post-treatment measures. The third and final aim was to explore whether there were any differences between the two groups at long-term measurements.

The original hypothesis was that the ePlus program would yield greater reductions over time than the eChange program in the primary outcomes of drinks per week and HDDs. As the analysis of short-term outcomes could not discriminate between the two interventions, with participants in both trial arms reducing their use of alcohol, the hypothesis for the current analysis of long-term follow-ups was therefore revised to state that there would be a statistically significant change in alcohol consumption over time in both groups.

In **Study III**, the aim was to evaluate an internet-based version of CRAFT (iCRAFT) compared to WL conditions. It was hypothesized that, for CSOs receiving iCRAFT, IPs' treatment engagement would be increased compared to being on a WL. Secondary aims were to investigate whether iCRAFT increased CSOs' QoL and decreased IPs' alcohol use in our study population.

Summary of the Studies

Methods – Studies I and II

Brief description of the two programs that were compared

ePlus (Studies I and II)

ePlus is a treatment program for people with AUD, which was developed by our research group led by Associate Professor Anne H Berman at Karolinska Institute, Stockholm, in Sweden (Sundström, Kraepelien, et al., 2017). In Studies I and II, ePlus was considered a high-intensity internet intervention (HIII). ePlus is an extended internet-based treatment program for AUD, with 13 text-based modules, comprising about 80 pages in total, in contrast to the nine modules in eChange (described in detail below). Each module includes educational texts, practical exercises, quizzes, and worksheets. Table 1 presents the content of the treatment modules. As well as the 13 modules, the treatment program consists of an alcohol diary.

The aim when developing the ePlus program was to produce an AUD treatment manual that was more in line with other internet-based treatments, which usually have more psychoeducational content, including knowledge-based quizzes and additional homework tasks. All modules were newly written, although some of the modules have content that overlaps with eChange. In Study I, the treatment was delivered over 12 weeks, with modules 2 and 3 delivered in the same week. Unlike with eChange, the participants had an active therapist.

Table 1. Overview of the treatment modules in ePlus, modified from Sundström, Kraepelien et al. (2017).

<i>Module</i>	<i>Purpose of module</i>	<i>Homework assignment</i>
Module 1 Alcohol education	To learn about the effects of alcohol on the body and mind, and about tolerance and abstinence	– Questions pertaining to the text
Module 2 Pros and cons of drinking	To help the participant reflect about the pros and cons of drinking	– Make a decisional balance sheet
Module 3 Goals and values	To learn the difference between goals and values, and why these are important to establish at the beginning of treatment	– Set an alcohol consumption goal during treatment (abstinence/moderate drinking) – Explore/formulate core values in life
Module 4 Analyzing risk situations	To learn what risk situations are, and how to analyze them	– Complete a behavioral analysis of own risk situations

Table 1 continued

Module 5 Dealing with craving	To learn about craving and ways of dealing with it	<ul style="list-style-type: none"> – Make notes on how to deal with craving: Who can you call when you feel craving? What can you do to distract yourself?
Module 6 Dealing with thoughts about alcohol	To learn about what thoughts commonly occur to people who have just begun changing their alcohol habits	<ul style="list-style-type: none"> – Make notes on which thoughts about alcohol occur most frequently – Make a situational analysis and choose which specific coping strategies to use when the thoughts appear
Module 7 Dealing with social situations	To learn about why it can be hard to say “no” to alcohol in social situations	<ul style="list-style-type: none"> – Practice saying “no” with a friend or in front of a mirror – Write down answers to specific situations presented in the text
Module 8 Finding other activities	To learn about the “reward trap” (using alcohol as a reward) and the importance of finding other meaningful activities	<ul style="list-style-type: none"> – List activities to engage in that do not include alcohol – Draw up a time schedule for doing them
Module 9 Problem solving	To learn about stress and how it is sometimes associated with alcohol use, and about problem solving as a technique	<ul style="list-style-type: none"> – In steps, apply problem solving in at least one situation
Module 10 Negative thoughts and interpretation traps	To learn about negative thoughts and about coping strategies to deal with them, such as cognitive restructuring and other cognitive therapy skills	<ul style="list-style-type: none"> – Complete a behavioral analysis of negative thoughts and challenge these thoughts
Module 11 Seemingly irrelevant decisions	To learn about the importance of identifying small, seemingly irrelevant decisions that could lead to drinking	<ul style="list-style-type: none"> – Make notes about a situation where irrelevant decisions were involved in drinking
Module 12 Relapse plan	To learn about the concept of relapse, and predict situations that could make it harder to resist drinking	<ul style="list-style-type: none"> – Formulate a relapse plan
Module 13 Life without alcohol problems	To summarize the treatment and look towards the future	<ul style="list-style-type: none"> – Review the initial alcohol consumption goal formulated in Module 3 – Set goals for the future
Optional module About relapses and setbacks	To reflect on the situation in which the relapse/setback occurred (for participants reporting a setback during treatment to the therapist)	<ul style="list-style-type: none"> – Make a situational analysis and prepare for how to cope with a similar situation in the future

eChange (comparative treatment intervention in Studies I and II)

eChange is a Swedish adaptation of the treatment program “Therapy Online,” which was originally developed at the Trimbos Instituut in Utrecht, the Netherlands, and evaluated in an RCT by Blankers et al. (2011). eChange has been evaluated in an RCT (Sundström et al., 2016) and a naturalistic study (Johansson et al., 2017) as well as compared to face-to-face interventions (Johansson et al., 2021). The content is based on RP, i.e., a cognitive behavioral approach with a focus on identifying and preventing high-risk situations and developing skills to cope with these (Larimer et al., 1999; Marlatt & Donovan, 2005). The unguided self-help program from the original RCT by Blankers et al. (2011) is still in use (www.zelfhulpalcohol.nl), whereas the guided version has evolved into a blended CBT/Motivational Interviewing (MI) intervention over the past years, which is now the standard outpatient treatment modality at the Trimbos Instituut (M. Blankers, personal communication, November 13th, 2018).

The program consists of nine modules. Each module consists of written text (one to two pages), a homework assignment, and a worksheet, and it takes approximately 1 week for the participant to complete each module. The program is intended to be used without therapist guidance. In Studies I and II, eChange was termed a “low-intensity internet intervention (LIII).” The treatment was delivered over 12 weeks, and during weeks 8–11, the participants received no new modules, but instead were sent weekly text messages as a reminder to log in and answer the weekly assessment.

Both ePlus and eChange have similar content, but eChange lacks modules covering “alcohol education,” “finding other activities,” “problem solving,” “negative thoughts and interpretation traps,” “seemingly irrelevant decisions,” and an optional module regarding relapses and setbacks. On the other hand, eChange has a module covering self-control skills, which is not included in ePlus.

In Studies I and II, both eChange and ePlus were delivered through a technical platform with encrypted traffic and an authentication/login function to guarantee participant confidentiality. The platform was provided by the Internet Psychiatry Clinic in Stockholm, Sweden.

Participants

To be eligible, participants needed to fulfill the following criteria: (1) aged 18 or over; (2) ≥ 14 points (women) and ≥ 16 points (men) on the AUDIT (Saunders et al., 1993); (3) a weekly consumption of eleven or more (women) or ≥ 14 (men) standard drinks of alcohol; and (4) having an AUD, defined as two or more positive criteria for AUD, according to the DSM-5.

Exclusion criteria were insufficient skills in Swedish, significant reading and writing difficulties, concurrent psychological treatment, severe depression, acute suicidal ideation, drug use problems, contraindicated psychiatric or somatic condition (e.g., bipolar disorder, psychosis, and posttraumatic stress disorder), and recently initiated use of medication for alcohol or other psychiatric disorder.

Participants were recruited from across Sweden through Google Adwords and the Remente mental wellbeing smartphone application (App) (www.remente.com). Recruitment occurred between January 2016 and February 2017, with a 6-month follow-up completed in August 2017.

Procedure

Interested persons registered on the study's secure website and completed online screening. Potentially suitable participants underwent a telephone-based structured psychiatric interview with a licensed clinical psychologist (69% of the interviews) or with a clinical psychology Master student under supervision (31%). All interviewers had undergone basic training in structured diagnostic interviewing.

Participants were randomized without stratification by an independent third party, using an online tool with a random number generator function (randomizer.org). As we were aiming for a small WL (≤ 25) to contrast with the two treatment groups, initial participants were randomized at a 1:1:1 ratio (ePlus:eChange:WL) until the desired number of participants had been reached for the WL. Remaining participants were randomized at a 1:1 ratio (ePlus:eChange). Participants randomized to either of the treatments were blinded to the treatment allocation (ePlus/eChange) and were not informed about the study's hypotheses.

The long-term follow-up measures (Study II) were conducted at 12 and 24 months post-randomization, i.e., at 6 and 18 months after the 6-month follow-up mentioned previously. Follow-up data for the analyses were collected between May 1st, 2017, and August 11th, 2019.

Measures

The Structured Clinical Interview for DSM-IV axis I disorders (SCID-I) was used (Kranzler, Kadden, Babor, Tennen, & Rounsaville, 1996) in order to establish a diagnosis of AUD. To conform to the changes in the DSM-5 (American Psychiatric Association, 2013), the SCID-I was updated, i.e., we added a question about craving for alcohol. To determine the presence of other comorbid psychiatric disorders, the M.I.N.I. International Neuropsychiatric Interview (MINI) was used (Sheehan et al., 1998).

Two primary outcomes were aggregated: (1) total number of drinks; and (2) number of HDDs, where “HDD” was defined as five or more (men) or four or more (women) standard drinks on a single day. These outcomes were measured using the Timeline Followback (TLFB) (Sobell & Sobell, 1996). Participants were asked about number of standard drinks (12 grams of pure alcohol) consumed during each of the preceding 7 days at all major assessment points in this study.

Secondary outcomes were other alcohol problems, other psychiatric states, and QoL. For secondary outcomes, three alcohol-related questionnaires were used: the AUDIT (Saunders et al., 1993) to assess alcohol problems, the Alcohol Abstinence Self-Efficacy Scale (AASES) (DiClemente, Carbonari, Montgomery, & Hughes, 1994) to assess self-efficacy, and the Penn Alcohol Craving Scale (PACS) (Flannery, Volpicelli, & Pettinati, 1999) to assess cravings. The Montgomery–Åsberg Depression Rating Scale – Self-report (MADRS-S) (Svanborg & Åsberg, 2001) was used to assess depression, the Generalized Anxiety Disorder Scale (GAD-7) was used to assess anxiety (Spitzer, Kroenke, Williams, & Löwe, 2006), and the Euroqol-5D (EQ-5D) (Herdman et al., 2011) was used to assess QoL. All participants completed outcome measures six times: online at screening, pre-treatment (primary outcome only), monthly (i.e., twice) during treatment (primary outcome only), post-treatment, and 6 months after randomization.

Negative effects were assessed halfway through the treatment and immediately post-treatment with the open question “During the treatment, have you encountered any unwanted event that you think was a result of the treatment or have you experienced any undesired effect of the treatment?” Where they answered in the affirmative, participants were then asked to describe the event/effect. The participants also answered the Client Satisfaction Questionnaire-8 (CSQ-8) (Larsen, Attkisson, Hargreaves, & Nguyen, 1979) post-treatment, complemented with other evaluation questions, to assess treatment satisfaction.

The long-term follow-up in Study II used the same measures as in Study I, except for questionnaires not directly measuring treatment effectivity, such as client satisfaction (CSQ-8) and negative effects. The EQ-5D measuring QoL was also not used, primarily for technical reasons as one item was mistakenly left out, which made the questionnaire insufficient. Semi-structured diagnostic telephone interviews were conducted at both 12- and 24-month follow-ups. The MINI and parts of the SCID-I, adapted to DSM-5 criteria, were used in the diagnostic interviews to assess comorbid psychiatric disorders, AUD diagnosis, and changes in AUD criteria number and severity over time.

Statistical analyses, Study I

The study was powered to detect a medium differential effect size in terms of number of standard drinks between intervention groups (Cohen's $d = 0.5$). Power calculations were based on results from previous trials of ePlus (Sundström, Kraepelien, et al., 2017) and eChange (Sundström et al., 2016). A sample size of 72 per group was deemed required for 80% power with a two-sided 5% significance level. A large differential effect size was expected between the ePlus and WL groups, and for this reason, a small WL (≤ 25) was considered sufficient. All participants randomized were included in the outcome analysis according to intention-to-treat (ITT) principles. Missing data was deemed missing at random with Little's Missing Completely at Random (MCAR) test ($p = 0.263$).

Generalized estimating equations (GEE) with an unstructured working correlation matrix and a 3 (intervention) \times 5 (pre-treatment, mid-treatment 1, mid-treatment 2, post-treatment, 6-month follow-up) design were used to assess interaction effects on primary outcomes with the screening measure included as a covariate. To evaluate effects on secondary outcomes, a 3 (intervention) \times 3 (screening, post-treatment, 6-month follow-up) design was used. For primary outcomes, a negative binomial model with log link was used, while a normal model was used for secondary outcomes. Planned two-sided contrast tests were used to test between-group differences.

In addition, Bayes factors (B) were calculated to assess strength of evidence of primary outcomes (number of drinks and HDDs). A B of 3 or more indicates evidence for the alternative hypothesis (H1) over the null hypothesis (H0); a B below 1/3 indicates evidence for H0 over H1, while B between 1/3 and 3 indicates insensitive data. Furthermore, BH [0, standard deviation (SD)] refers to a Bayes factor in which the predictions of H1 are modeled as a half-normal distribution with a peak at 0 (indicating no effect) and an SD equal to the expected effect size.

Statistical analyses, Study II

In the long-term follow-up study, we continued to use GEE, but missing data was not imputed. The reason for not imputing missing data was that attrition was high, especially at the 24-month follow-up where attrition was 53%, which is above the 40% rule of thumb presented in the literature (e.g., Jakobsen, Gluud, Wetterslev, & Winkel, 2017). The details in the analysis are otherwise mostly the same, but with two more time points (namely, the 12- and 24-month follow-up), i.e.: GEE with an unstructured working correlation matrix, using a negative binomial model with log link (Horton, Kim, & Saitz, 2007) and a 2 (intervention) \times 8 (screening, pre-treatment, two measures

mid-treatment (“mid1” and “mid2”), post-treatment, 6-, 12- and 24-month follow-ups) design was used to assess interaction effects on primary outcomes. The same GEE analysis was used to calculate within-group effects on primary outcomes, comparing pre- and post-treatment levels to long-term follow-ups. In addition, GEE was also used to evaluate effects on secondary outcomes, but with a normal model instead of the negative binomial model, since the secondary outcomes were normally distributed, in contrast to alcohol consumption.

Other analyses of secondary outcomes involved mainly descriptive statistics, such as number of AUD criteria and number of psychiatric comorbidities.

In a sensitivity analysis, AASES scores and the total number of anxiety disorders at screening were included as covariates, as these variables correlated highly with both alcohol consumption change over time and “missingness,” i.e., the tendency for data to be missing, at the long-term follow-ups. This increased the GEE model’s ability to perform estimations despite missing data.

A dropout analysis was performed by comparing number of standard drinks at the very first screening between those participants who were active and those who were non-active at the 12- and 24-month follow-up.

Methods – Study III

Brief description of the program

Internet-based Community Reinforcement Approach and Family Training (Study III)

The iCRAFT program is an internet-based version of CRAFT (Meyers et al., 1998). The CRAFT (and iCRAFT) program is not a treatment program per se, since it targets family members and close friends of individuals with AUD who refuse to get treatment. The internet-based version was developed to meet the need for CRAFT availability in Sweden, since face-to-face CRAFT was, and still is, rare, being available mainly in the bigger cities, whereas iCRAFT has the technical possibility to be administered without geographical boundaries, and also to give CSOs the possibility to receive help without the stigma of visiting the local addiction clinic. The iCRAFT program was developed by our research group, inspired by a book titled *Motivating Substance Abusers to Enter Treatment: Working with Family Members* written by Smith and Meyers (2007), and contains the same basic elements as CRAFT. It consists of five

modules (see Table 2), with the first follow-up at 6 weeks. Each module consists of a text (equaling about eight pages), videos, homework assignments, and a final report. The program has a built-in message system where the participant and therapist can write messages to each other, either synchronously or asynchronously. The program was delivered through a technical platform provided by the Stockholm Center for Dependency Disorders.

Table 2. Overview of the treatment modules in the internet-based Community Reinforcement Approach and Family Training (iCRAFT) program.

<i>Module</i>	<i>Purpose of module</i>	<i>Homework assignment</i>
Module 1 (1) Introduction and rationale; and (2) Own QoL, part 1	(1) To learn about the CRAFT method and strengthen the motivation of the CSO; and (2) strategies for CSOs to improve their own mental health	– Implementing a planned change for the CSO’s own goal
Module 2 (1) To have the Talk, part 1; and (2) Communication	(1) Strategies to improve the likelihood of a positive response when asking the IP to seek treatment; and (2) positive communication skills training	– Practicing eight helpful communication skills
Module 3 The Interaction Chain	Contingency management of the IP’s drinking behavior	– Analyzing the IP’s drinking behavior in a functional analysis
Module 4 Encourage change	Positive reinforcement of abstinence	– Formulating a plan for positive consequences – Practicing rewarding sober behavior
Module 5 (1) Negative consequences; (2) Own QoL, part 2; (3) To have the Talk, part 2	(1) Not interfering with negative consequences of drinking, and removal of planned reinforcers in situations where the IP drinks; (2) strategies for CSOs to improve their own mental health; (3) strategies to improve the likelihood of a positive response when asking IPs to seek treatment	– Removing previous rewards when the IP is drinking – Having a talk with the IP – Relapse plan

CRAFT = Community Reinforcement Approach and Family Training; CSO = concerned significant other; IP = identified person.

Participants

To be eligible, participants had to meet the following criteria: (1) ongoing relation with an IP having the DSM-IV diagnosis of alcohol dependence or abuse; (2) (both the CSO and the IP) aged at least 18; (3) spending time with the IP at least 3 days per week in the last 90 days (with no planned future change in this respect); (4) confirming any alcohol consumption for the IP during 30 of the last 90 days; (5) having a goal of engaging the IP to enter treatment if possible; (6) consenting to participate in the study. All assessments of eligibility based on the inclusion criteria were made on the basis of CSO reports.

Exclusion criteria were: (1) CSO statements that the IP would agree to seek alcohol-related treatment if asked; (2) alcohol-related treatment for the IP in the last 6 months; (3) major psychiatric or somatic illness of the CSO or IP; (4) CSO's description of the IP as meeting the DSM-IV diagnosis of substance (not alcohol or nicotine) dependence or abuse; (5) insufficient skills in Swedish; (6) participation in a CSO support program (e.g., Al-Anon) during the last 12 months; and (7) risk for domestic violence from the IP.

Participants were recruited nationwide in Sweden through advertisements through Google AdWords, information posts on Facebook, the Remente mental wellbeing smartphone App, and the website "Alkoholhjälpen.se" (*alkoholhjälpen* = "Alcohol Help"), and, on one occasion, in a newspaper distributed free of charge in the Stockholm metro area.

Recruitment occurred between May 2015 and December 2016, with the last 24-week follow-up completed in June 2017.

Procedure

Individuals who were interested in participating registered on the study's secure website and completed a short online screening. A licensed clinical psychologist performed a telephone-based structured interview to assess individuals' eligibility for participation in the study. All interviewers had undergone basic training in structured diagnostic interviewing.

Concerned significant others who were eligible for inclusion were randomized in blocks of ten with a 1:1 allocation using an automated and concealed procedure in the online platform. There was no blinding to study allocation. Participants were instructed that randomization would be done following completion of baseline assessments.

Measures

All primary and secondary measures were based on CSO reports. To establish a diagnosis of both AUD and other comorbid psychiatric disorders, the MINI was used (Sheehan et al., 1998).

All assessments of outcome measures were completed online. The primary outcome, proportion of IPs seeking treatment during the 24-week follow-up period, was measured at weeks 6, 12, and 24. The IPs' alcohol consumption was assessed weekly. All other assessments were conducted at inclusion, and again at 6, 12, and 24 weeks after inclusion.

Secondary outcomes were IP alcohol consumption, the CSO's mental health (depression, anxiety, and stress), QoL, and relational satisfaction. The IPs' alcohol consumption was measured using the TLFB technique (Sobell & Sobell, 1996). Mental health of CSOs was measured using the GAD-7 (Spitzer

et al., 2006), MADRS–S (Svanborg & Åsberg, 1994), Depression, Anxiety and Stress Scales (DASS 42) (Lovibond & Lovibond, 1995), and Acceptance and Action Questionnaire (AAQ) (Bond et al., 2011; Lundgren & Parling, 2017). Quality of life of CSOs was measured using the Satisfaction with Life Scale (SWLS) (Pavot & Diener, 2008; Pavot, Diener, Colvin, & Sandvik, 1991). Relational satisfaction of CSO was measured using the Relationship Happiness Scale (RHS) (Azrin, Naster, & Jones, 1973) (one item concerning affection/sex was excluded to enable use in different types of relationships).

Statistical analyses

The primary outcome, i.e., treatment initiation, was analyzed using Cox regression. Exact partial likelihood was used to account for the discrete data time points. As a test of overall significance considering proportion of treatment seekers in the iCRAFT vs. the WL group, chi-square statistics were calculated.

The secondary outcomes were alcohol consumption of the IP and mental health of the CSO. The first of these was analyzed using logistic mixed models (any alcohol consumption) and a Poisson mixed model (number of standard glasses). The second was viewed as a normal continuous mixed model.

Main Findings and Conclusions

Study I

Participants in Study I were 81 men and 85 women, mean age 52.9 (SD = 10.7) years. Seventy-five percent of participants had severe AUD. Altogether 44% had a psychiatric comorbidity. Depression was the most common psychiatric comorbidity (25.5%), followed by agoraphobia (13.3%) and GAD (10.3%).

Generalized estimating equations analysis for each group (ePlus, eChange, and WL) indicated reduced alcohol consumption from pre-treatment to post-treatment in each group (see Table 3). For more details, see Sundström et al. (2020).

At post-treatment, participants in the ePlus group had a significantly greater reduction, compared to the WL group, both in number of standard drinks and in the number of HDDs per week, and so did participants in eChange. There was no significant difference between ePlus and eChange in number of standard drinks, but participants in the ePlus program had significantly fewer HDDs compared to participants in the eChange program. At 6-month follow-up, there were no significant differences between ePlus and eChange, either in number of standard drinks or in number of HDDs (see Table 3).

Table 3. Primary outcomes across time by group for the groups allocated to ePlus, eChange, and waiting list (WL) control conditions. Modified from Sundström et al. (2020).

	<i>ePlus</i>		<i>eChange</i>		<i>Waiting list</i>		<i>Effect size (Cohen's d)</i>		
	<i>Mean</i>	<i>SE</i>	<i>Mean</i>	<i>SE</i>	<i>Mean</i>	<i>SE</i>	<i>ePlus vs. eChange</i>	<i>ePlus vs WL</i>	<i>eChange vs WL</i>
Standard drinks									
Pre-treatment	22.3	1.4	22.9	1.6	22.6	2.9			
Post-treatment	10.9	1.4	14.2	1.5	20.6	2.7	0.29	0.78*	0.48*
6-month follow-up	16.6	1.5	14.5	1.5	n/a	n/a	0.17	–	–
Heavy drinking days									
Pre-treatment	2.57	0.14	2.51	0.19	2.43	0.32			
Post-treatment	1.22	0.16	1.69	0.17	2.51	0.30	0.34*	0.92**	0.57*
6-month follow-up	1.77	0.17	1.66	0.19	n/a	n/a	0.07	–	–

* $p \leq 0.05$; ** $p \leq 0.01$.

Measures of alcohol consumption before and after treatment as well as at 6 months post-randomization in the ePlus and eChange groups are shown in Figure 1. Since the participants in the WL group received the ePlus condition after 12 weeks, there was no follow-up at 6 months for this group (i.e., they were no longer on a WL).

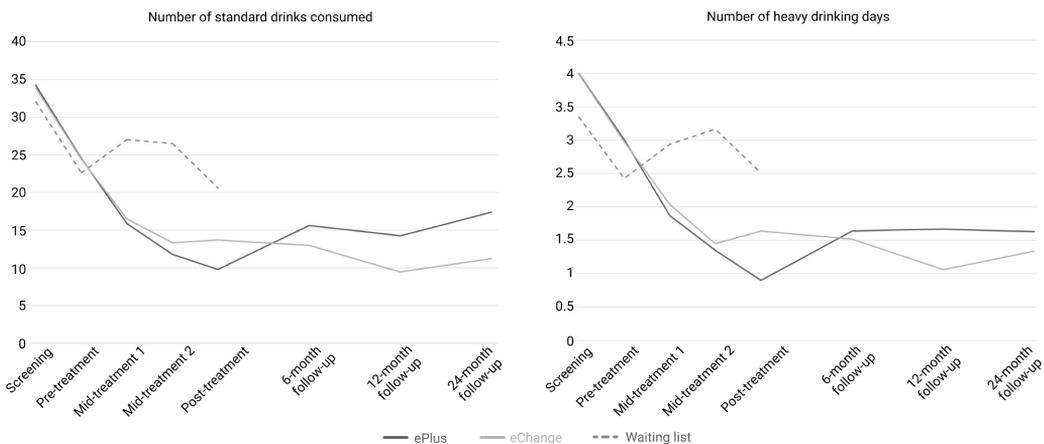


Figure 1 Number of estimated standard drinks consumed (left panel) and number of estimated heavy drinking days (HDDs) (right panel) from Studies I and II, at screening, 1 calendar week before, and during and after treatment, and at the long-term follow-ups.

The results for the secondary measures showed that, post-treatment, participants in ePlus had reduced their AUDIT and MADRS–S scores statistically significant compared to the WL participants, but there were no significant differences between any other groups or measures. At the 6-month follow-up, there were no significant differences between the intervention groups. For a further overview, see Table 4 below.

Table 4. Overview of between-group effect sizes of secondary outcomes between the three study groups. Effect sizes in Cohen’s, *d*. Modified from Sundström et al. (2020).

	<i>Post-treatment</i>			<i>6 month follow-up</i>
	<i>ePlus–eChange</i>	<i>ePlus–WL</i>	<i>eChange–WL</i>	<i>ePlus–eChange</i>
AUDIT	0.17	0.51*	0.32	0.14
Self-efficacy (AASES)	0.07	0.12	0.17	0.20
Craving (PACS)	0.11	0.17	0.05	0.14
Depression (MADRS-S)	0.05	0.49*	0.45	0.09
Anxiety (GAD-7)	0.09	0.23	0.31	0.16
Quality of life (EQ-5D)	0.09	0.21	0.28	0.20
Quality of life scale (EQ-5D VAS)	0.37	0.12	0.25	0.30

AASES = Alcohol Abstinence Self-Efficacy Scale; AUDIT = Alcohol Use Disorders Identification Test; EQ-5D = Euroqol-5D; GAD-7 = Generalized Anxiety Disorder Scale; MADRS-S = Montgomery–Åsberg Depression Rating Scale – Self-report; PACS = Penn Alcohol Craving Scale; VAS = visual analog scale; WL = waiting list; * $p \leq 0.05$.

Negative effects during treatment

There were few reports of negative effects of treatment. Six participants in the ePlus program (9.5%) and five in eChange (8.3%) reported a negative effect post-treatment. These numbers were lower than at the mid-treatment assessment, when negative effects were reported by ten participants in the ePlus program (13.8%) and 14 participants in the eChange program (19.7%). Four categories of negative effects emerged in the analysis: (1) alcohol-related changes, such as craving, intense thoughts about alcohol, and increased alcohol consumption; (2) negative social consequences; (3) feelings of distress and depression; and (4) somatic issues, such as headache and sleeping problems.

Study II

In Study II, 143 people were included, mean age 52.8 (SD = 11.1) years; 47% were male. Unlike in Study I, WL participant data was not analyzed. No significant differences were found between the two intervention groups regarding baseline characteristics.

Attrition was defined as not participating in the online self-reported follow-up questionnaires. Attrition rates at the 12- and 24-month follow-ups for ePlus and eChange were 36% and 53%, respectively, with no significant difference between the two intervention groups at the 12-month follow-up ($\chi^2 = 0.13$, $p = 0.911$). However, a significant difference was found between the two groups at the 24-month follow-up, where ePlus had a 43% attrition rate, and eChange had a 63% attrition rate ($\chi^2 = 5.93$, $p = 0.015$).

Primary outcomes

Figure 1 presents changes in weekly consumption of standard drinks and number of HDDs across all assessment points for both intervention groups, measured using the TLFB.

To test whether the two internet interventions were associated with lower alcohol consumption in the long term compared to pre-treatment, within-group differences over time, from pre-treatment measurement to long-term follow-ups, were examined. The analyses showed that ePlus and eChange both had statistically significant alcohol reductions in drinks per week and HDDs, at both the 12- and the 24-month follow-up, see Table 5.

Table 5. Generalized estimating equations (GEE) analysis showing estimated means of the primary outcomes of number of standard drinks of alcohol consumed and heavy drinking days (HDDs) in the previous week. Differences and effect sizes within groups between pre-treatment and the 12- and 24-month follow-ups are shown. No WL group was used.

<i>Primary outcomes</i>		<i>Pre-treatment</i>	<i>12/24-month follow-up</i>	<i>Significance, 12/24 months</i>	<i>Effect size, 12/24 months</i>
Drinks per week	ePlus, m (SE)	24.51 (2.33)	14.24 (2.01)/ 17.37 (2.77)	$p < 0.001$ / $p = 0.021$	$g = 0.59$ / $g = 0.38$
	eChange, m (SE)	24.39 (1.99)	9.47 (1.57)/ 11.23 (1.87)	$p < 0.001$ / $p < 0.001$	$g = 1.04$ / $g = 0.89$
Heavy drinking days	ePlus, m (SE)	3.01 (0.26)	1.67 (0.27)/	$p < 0.001$ /	$g = 0.65$ /
			1.63 (0.32)	$p < 0.001$	$g = 0.65$
	eChange, m (SE)	2.98 (0.29)	1.02 (0.21)/ 1.34 (0.29)	$p < 0.001$ / $p < 0.001$	$g = 0.94$ / $g = 0.75$

g = effect size according to Hedge's g ; m = mean; SE = standard error.

To investigate if participants maintained their post-treatment alcohol consumption at the long-term follow-ups, within-group differences were analyzed over time, from the post-treatment measurement to the long-term follow-ups. Results showed that participants in the ePlus program had significantly increased alcohol consumption at the long-term follow-ups, compared to the end of treatment, in terms of both number of drinks per week and HDDs. Participants in the eChange program, on the other hand, had statistically significantly further decreased alcohol consumption in both these measures at the 12-month follow-up. However, this decrease was no longer significant at the 24-month follow-up, see Table 6.

Table 6. Generalized estimating equations (GEE) analysis showing estimated means of the primary outcomes standard drinks of alcohol consumed and heavy drinking days (HDDs) in the previous week. Differences and effect sizes within groups, between post-treatment and the 12- and 24-month follow-up, respectively.

Primary outcomes		Post-treatment	12/24-month follow-up	Significance, 12/24 months	Effect size, 12/24 months
Drinks per week	ePlus, m (SE)	9.77 (1.37)	14.24 (2.01)/ 17.37 (2.77)	$p = 0.026/$ $p = 0.001$	$g = -0.37/$ $g = -0.52$
	eChange, m (SE)	13.69 (1.84)	9.47 (1.57)/ 11.23 (1.87)	$p = 0.018/$ $p = 0.178$	$g = 0.33/$ $g = 0.19$
Heavy drinking days	ePlus, m (SE)	0.9 (0.17)	1.67 (0.27)/ 1.63 (0.32)	$p = 0.002/$ $p = 0.021$	$g = -0.49/$ $g = -0.46$
	eChange, m (SE)	1.64 (0.24)	1.06 (0.20)/ 1.34 (0.29)	$p = 0.014/$ $p = 0.284$	$g = .035/$ $g = 0.17$

g = effect size according to Hedge's g; m = mean; SE = standard error.

Finally, to examine if there were any differences between the interventions at long-term follow-up, between-group differences over time were analyzed at the 12- and 24-month follow-ups. No statistically significant differences were found long-term between the two groups in either of the primary outcome measures, see Table 7.

Table 7. Generalized estimating equations (GEE) analysis showing pairwise comparisons of estimated means of the primary outcomes standard drinks of alcohol consumed and heavy drinking days (HDDs) in the previous week between the ePlus and eChange groups across all time points.

Primary outcomes		Screening	Pre	Mid1	Mid2	Post	6-month	12-month	24-month
Drinks per week	ePlus, m (SE)	34.24 (2.02)	24.51 (2.33)	15.86 (2.10)	11.78 (1.50)	9.77 (1.37)	15.62 (1.86)	14.24 (2.01)	17.37 (2.77)
	eChange, m (SE)	33.85 (1.94)	24.39 (1.99)	16.48 (1.65)	13.31 (1.84)	13.69 (1.84)	12.99 (1.90)	9.47 (1.57)	11.23 (1.87)
	Significance	$p = 0.889$	$p = 0.970$	$p = 0.815$	$p = 0.521$	$p = 0.087$	$p = 0.323$	$p = 0.062$	$p = 0.066$
	Effect size	$g = -0.02$	$g = -0.01$	$g = 0.04$	$g = 0.14$	$g = 0.31$	$g = -0.19$	$g = -0.39$	$g = -0.41$
Heavy drinking days	ePlus, m (SE)	4.00 (0.23)	3.01 (0.26)	1.87 (0.24)	1.35 (0.22)	0.90 (0.17)	1.64 (0.26)	1.67 (0.27)	1.63 (0.32)
	eChange, m (SE)	3.99 (0.25)	2.98 (0.29)	2.04 (0.24)	1.45 (0.30)	1.64 (0.24)	1.52 (0.27)	1.06 (0.20)	1.34 (0.29)
	Significance	$p = 0.967$	$p = 0.941$	$p = 0.631$	$p = 0.804$	$p = 0.013$	$p = 0.739$	$p = 0.072$	$p = 0.507$
	Effect size	$g = -0.01$	$g = -0.01$	$g = 0.09$	$g = 0.06$	$g = 0.46$	$g = -0.06$	$g = -0.38$	$g = -0.16$

g = effect size according to Hedge's g; m = mean; SE = standard error.

Secondary outcomes

Number of AUD criteria and a short list of comorbidities are displayed in Table 8. The psychiatric comorbidities consisted of depression, agoraphobia, GAD, and social phobia, and also “Other psychiatric comorbidity” including bipolar disorder, panic disorder, obsessive compulsive disorder, post-traumatic stress disorder, psychosis, anorexia nervosa, bulimia nervosa, and antisocial personality disorder. Only “other psychiatric comorbidity” showed a significant change between ePlus and eChange treatment at screening (ePlus = 3 (4.2%); eChange = 10 (14.3%); $\chi^2 = 4.370$; $p = 0.037$). These statistically significant changes were no longer present at the 12- or 24-month follow-up. For a more extensive Table, see the corresponding article (see Appendix, Study II).

Table 8. Number of alcohol use disorder (AUD) criteria and comparison of psychiatric diagnosis between ePlus and eChange treatment at baseline and at the long-term follow-ups, as obtained from diagnostic telephone interviews.

		<i>Screening</i>	<i>12-month</i>	<i>24-month</i>
Number of AUD criteria	ePlus, m (SD)	6.6 (1.83)	4.7 (3.13)	3.4 (3.19)
	eChange, m (SD)	6.6 (2.10)	3.8 (2.74)	3.1 (2.90)
<i>Psychiatric comorbidity (MINI)</i>		<i>Screening</i>	<i>12-month</i>	<i>24-month</i>
Any psychiatric comorbidity	ePlus, n (%)	28 (38.9)	6 (26.1)	6 (31.6)
	eChange, n (%)	30 (42.9)	4 (19.0)	4 (26.7)
	χ^2	0.231	0.310	0.097
	Significance level	$p = 0.631$	$p = 0.578$	$p = 0.755$
Other	ePlus, n (%)	3 (4.2)	2 (8.7)	3 (15.8)
	eChange, n (%)	10 (14.3)	2 (9.5)	4 (26.7)
	χ^2	4.370	0.009	0.607
	Significance level	$p = 0.037$	$p = 0.924$	$p = 0.436$

Other psychiatric comorbidity = bipolar disorder, panic disorder, obsessive compulsive disorder, post-traumatic stress disorder, psychosis, anorexia nervosa, bulimia nervosa, and antisocial personality disorder.

m = mean; MINI = M.I.N.I. International Neuropsychiatric Interview; SD = standard deviation.

Alcohol use disorder severity

Alcohol use disorder is classified into three severity categories: mild (where the person meets two to three criteria), moderate (four to five criteria), or severe (six or more criteria, maximum eleven). At baseline, most participants (n = 104; 73.2%) were classified as having a severe AUD, with the remaining participants falling into the moderate (n = 25; 17.6%) and mild (n = 13; 9.2%) categories. The proportion of participants in each severity category did not significantly differ by treatment assignment. Changes in AUD severity over time are displayed in Figure 2, which shows the percentage of participants categorized as having mild, moderate, and severe AUD at screening, and at the 12-month and 24-month follow-up. Most participants (70%) achieved at least one level of reduction in AUD severity and almost half (48%) achieved two levels of reduction in severity, as measured at the 24-month follow-up.

Of the 34 participants who participated in the diagnostic telephone interview at 24-month follow-up, the majority achieved at least one level of reduction in severity compared to their baseline screening level (n = 23; 70%; ePlus = 68%; eChange = 71%). Half achieved at least two levels of reduction (n = 15; 48%; ePlus = 47%; eChange = 50%). Changes in level of AUD severity from screening to the 24-month follow-up are displayed in Figure 3. Of those participants categorized as having severe AUD at screening, 25 (18%; ePlus = 18%; eChange = 17%) participated in the interview at the 24-month follow-up. Of these, nine (36%; ePlus = 39%; eChange = 33%) remained in the severe category at the 24-month follow-up; three (12%; ePlus = 8%; eChange = 17%) had declined to a moderate severity level; four (16%; ePlus = 15%; eChange = 17%) had declined to a mild severity level; and nine (36%; ePlus = 39%; eChange = 33%) no longer met the criteria for AUD. Of the 25 (18%; ePlus = 21%; eChange = 14%) participants meeting the criteria for moderate severity AUD at screening, only seven (5%; ePlus = 8%; eChange = 1%) were interviewed at the 24-month follow-up, where one from the ePlus group remained at moderate severity, three had reduced to mild severity, and two no longer met the criteria for AUD; in the eChange group, one participant had deteriorated to a severe category by the 24-month follow-up.

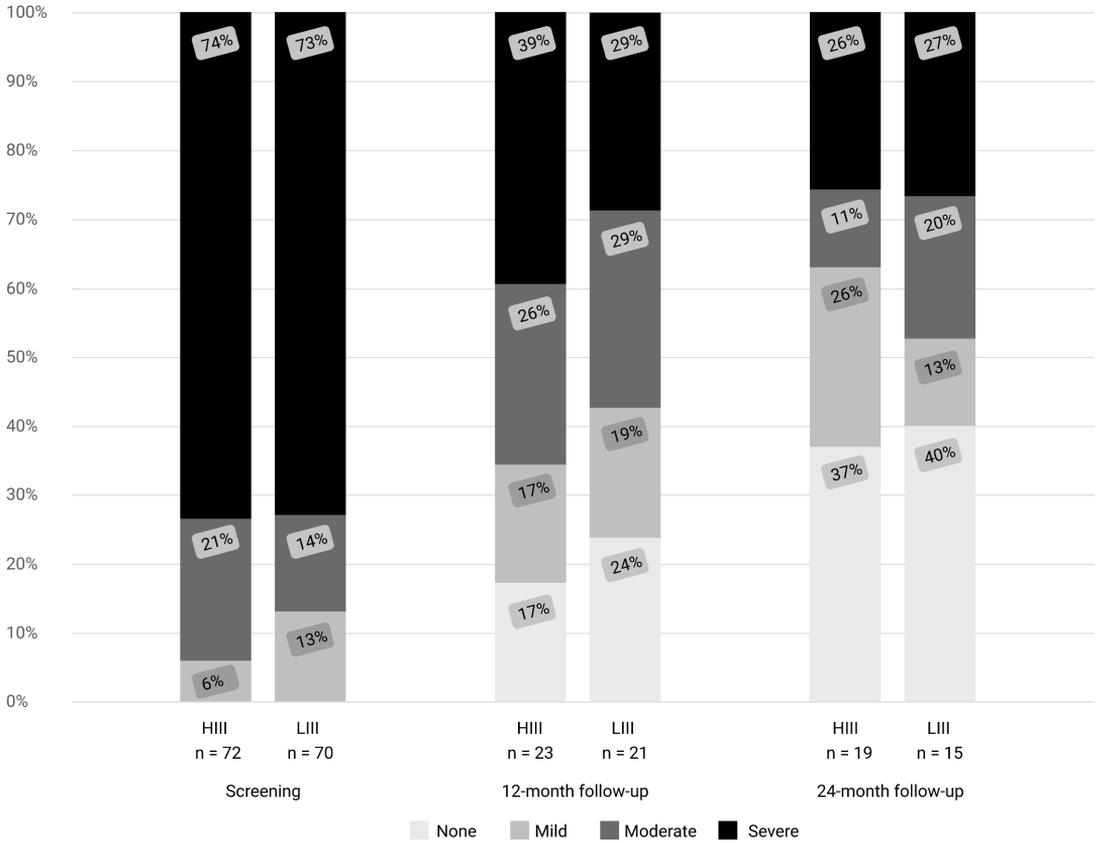


Figure 2. Percentage of participants in each alcohol use disorder (AUD) severity category at each time point, in both intervention groups. Mild = meeting two to three criteria; moderate = four to five criteria; severe = six or more (maximum eleven) criteria. HIII = high-intensity internet intervention (ePlus); LIII = low-intensity internet intervention (eChange).

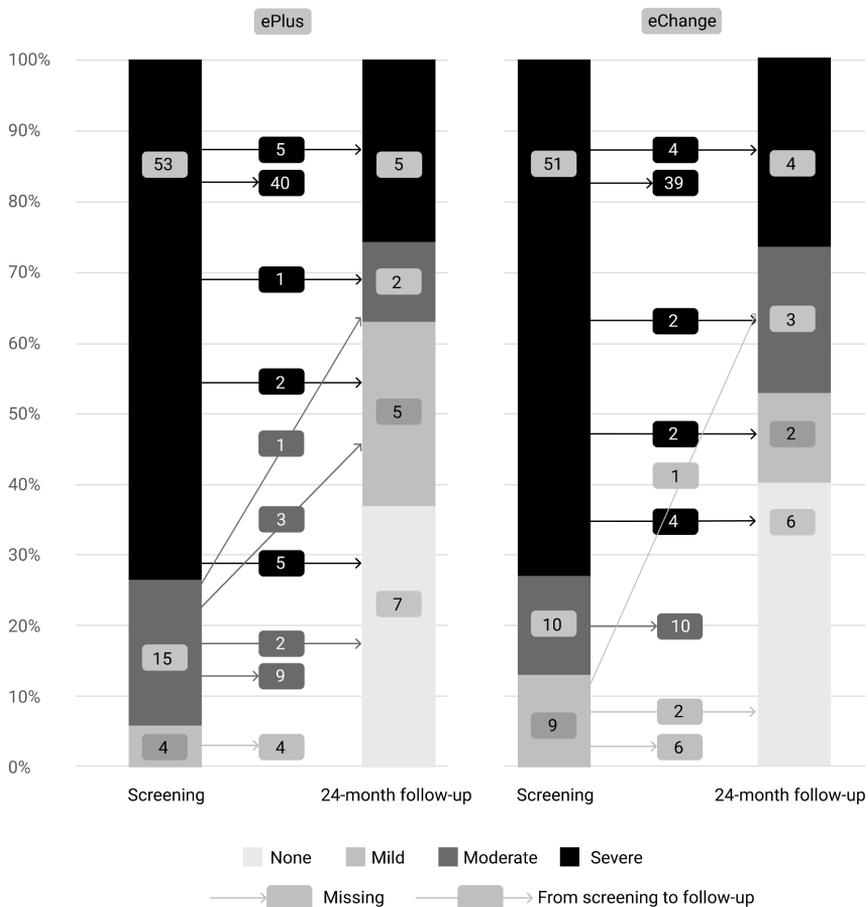


Figure 3. Change in level of alcohol use disorder (AUD) severity for participants in the ePlus and eChange groups from screening to 24-month follow-up. Mild = meeting two to three criteria; moderate = four to five criteria; severe = six or more (maximum eleven) criteria.

Online questionnaires

Regarding secondary outcomes in terms of online questionnaires, at the 12-month follow-up, participants in the eChange program had reduced their levels of craving (PACS) and depression (MADRS-S) to a significantly greater extent compared to those in the ePlus program (PACS: ePlus = 10.28 vs. eChange = 6.70, $p = 0.006$, $g = 0.578$; MADRS-S: ePlus = 10.80 vs. 7.43, $p = 0.018$, $g = 0.494$). These differences did not appear in any other measure or at any other time point. At the 24-month follow-up, participants in the eChange program had lower AUDIT scores compared to participants in ePlus (ePlus = 12.61 vs.

eChange = 8.88, $p = 0.018$, $g = -0.52$); again, this difference only appeared at this time point.

Receiving other treatments

A secondary analysis of treatments in the period between post-treatment and the 24-month follow-up showed that about one-fifth of participants in both intervention groups accessed other treatment, 22.4% ($n = 33$) in the ePlus group and 21.3% ($n = 30$) in the eChange group ($\chi^2 = 0.058$, $p = 0.81$). There were no differences in number of other treatments accessed between the two intervention groups, either at the 12-month or at the 24-month follow-up.

Study III

Participants included in this study were two men and 92 women. The mean age of the participants was 46.8 (SD = 12.3) years, and 86.2% were in a partner relationship with the IP. Of the IPs, 94.7% had alcohol dependence and 23.4% had major depression.

The primary outcome in Study III was treatment engagement, i.e., the IP's initiative to seek treatment, according to the CSO's reports, see Table 9. In the iCRAFT condition, ten (21.3%) CSOs reported that their IP initiated treatment at least once, while in the WL condition, five (10.6%) CSOs reported that an IP took the initiative to seek treatment. This difference between conditions in proportion of treatment-seeking IPs was, however, not statistically significant (odds ratio (OR) = 2.47 (0.96–6.39), $p = 0.062$).

Table 9. Data on a selection of statistically significant primary and secondary outcomes at the specified time points by condition (iCRAFT vs. waiting list): (1) treatment seeking of the identified person (IP), according to concerned significant others (CSOs); (2) predicted mean Montgomery–Åsberg Depression Rating Scale – Self-report (MADRS–S) score; (3) predicted mean Depression, Anxiety and Stress Scales (DASS) Depression score. Modified from Eék et al. (2020).

	Condi- tion	Baseline	6 weeks	12 weeks	24 weeks
(1) IP treatment seeking (accu- mulated)	iCRAFT	0	6	9	10
	Wait- ing list	0	5	5	5
(2) Mean MADRS–S score for CSO	iCRAFT	12.2 (10.6– 13.8)	9.1 (7.3– 10.9)	9.2 (7.3– 11.1)	9.6 (7.5– 11.6)
	Wait- ing list	12.1 (10.5– 13.7)	14.1 (12.2– 16.0)	10.4 (8.5– 12.2)	11.0 (9.1– 12.8)
(3) Mean DASS Depression score for CSO	iCRAFT	7.2 (5.6– 8.8)	5.4 (3.6– 7.2)	5.9 (4.0– 7.7)	7.6 (5.5–9.6)
	Wait- ing list	7.5 (5.9– 9.1)	8.3 (6.4– 10.1)	7.4 (5.6– 9.3)	6.6 (4.7–8.4)

Confidence intervals for all mean values are given in parentheses. iCRAFT = internet-based Community Reinforcement Approach and Family Training.

The results for the secondary outcomes showed a common pattern in that CSOs indicated short-term improvements in mental health, but this difference was not sustained over time (Table 9 (2)–(3)). Firstly, the iCRAFT group had decreased symptoms of depression at the 6-week follow-up, as measured by MADRS–S (Table 9 (2)), compared to the WL group (coefficient = 4.99, 95% confidence interval (CI) 2.45–7.53, $p = 0.0002$). This difference was, however, no longer apparent at the follow-up at 12 and 24 weeks. The same pattern was visible on the Depression subscale of DASS (Table 9 (3)), where CSOs in the iCRAFT condition reported a reduced depression score compared to WL at 6 weeks’ follow-up (coefficient = 2.89, 95% CI 0.36–5.42, $p = 0.0276$) while there were no significant differences between groups at 12 and 24 weeks post-inclusion in the study.

Other secondary outcomes, such as days with alcohol intake for the IP, and scores in DASS subscales Anxiety and Stress for the CSO, showed a general trend towards a reduction in symptoms for iCRAFT compared to the WL condition at certain time points, but this did not reach statistical significance. For more details, see Appendix, Study III.

General Discussion

Alcohol consumption is culturally and socially accepted in Sweden and many parts of the world – and alcohol consumption is also generally high. For some individuals, alcohol use goes beyond the limit of what is socially and culturally acceptable, with alcohol consumption at such levels that may lead to several health and social consequences, and subsequently they need treatment. Although there has been a general decline in total consumption over the 10-year period from 2008 to 2017, the treatment gap between the number of individuals who need treatment and the number who are offered or who seek evidence-based treatment is substantial, which is partly explained by stigma. This thesis shows that internet-based interventions (ePlus and eChange, Studies I and II) based on behavior principles in CBT and RP can be an alternative for individuals who are unable or do not prefer, to seek conventional treatment.

As previously mentioned, most individuals with problematic alcohol use never seek treatment, which is a problem also for their close ones. In Study III, iCRAFT was developed and studied to help those who live close to individuals with alcohol consumption problems. The study shows there are still improvements to be made before iCRAFT can be effective as an internet-based support program.

The overall aim of this thesis was to examine the efficacy of the three internet-based interventions ePlus, eChange, and iCRAFT. The first, ePlus, an internet-based therapy manual created for Study I, was proven effective in reducing both number of standard drinks per week and HDDs, compared to the WL condition. The comparative treatment, eChange, was also effective in reducing number of standard drinks per week both in the short term, that is, immediately after treatment, and at 6-month follow-up. Participants in the ePlus program had significantly fewer HDDs compared to participants in the eChange program at post-treatment, but this difference between the two active treatments was not sustained at 6 months' follow-up. However, participants in ePlus displayed significantly greater treatment satisfaction compared to participants in the eChange group. It might have been expected that the results at the 6-month follow-up would persist over time, since the few long-term follow-up studies on anxiety have reported that iCBT effects are maintained for as long as 5 years post-treatment (Hedman et al., 2011).

At long-term follow-up (Study II), i.e., 12 and 24 months post-randomization (6 and 18 months after the 6-month follow-up), alcohol consumption was still low compared to pre-treatment for both ePlus and eChange participants. However, compared to post-treatment, the ePlus group had a rise in alcohol

consumption at long-term both time points. The eChange group, on the other hand, had a further decline in alcohol consumption at the 12-month follow-up (while the seemingly low alcohol consumption for eChange at the 24-month follow-up was non-significant). There were no significant differences between ePlus and eChange at the long-term follow-ups.

The short-term results in Study I align with findings in previous studies: Meta-analyses of alcohol treatments generally show effect sizes in the small (Lundahl et al., 2010) to moderate range (Bertholet et al., 2005; Magill et al., 2019). Guided internet interventions tend to be more effective than both unguided internet interventions and WL conditions, with small, and medium to large, differential effect sizes, respectively (Blankers et al., 2011; Postel, de Haan, ter Huurne, Becker, & de Jong, 2010; Sundström et al., 2016). However, the 6-month follow-up results, with no significant difference in alcohol consumption between the two intervention groups differ from previous studies. Notably, differences between guided and unguided interventions were larger in a previous pilot trial (Sundström et al., 2016). The source of this discrepancy is that the unguided group in the present trial reduced their alcohol consumption to a much greater degree compared to the unguided group in the previous trial, despite the fact that the two groups received the same program (eChange). Although this may reflect a selection effect, as slightly different inclusion criteria were used in these two trials, another likely explanation is that the comprehensive inclusion process in this study (diagnostic interview) increased motivation among those randomized to the low-intensity intervention. The phenomenon of assessment reactivity (Clifford, Maisto, & Davis, 2007; French et al., 2021) is well documented in the alcohol treatment literature and diagnostic assessment has been associated with pre-treatment change (Epstein et al., 2005). This explanation is supported by evaluation questions confirming that participants perceived the diagnostic interview as therapeutic, and by the fact that all groups reduced their alcohol consumption significantly immediately after the interview, an effect that also could be explained by high motivation among the participants pre-treatment. Therefore, an unexpected but clinically relevant finding of this trial is that assessment-related, human contact may augment effects of an LIII over the longer term.

The long-term follow-up results in Study II are partly in line with previous research regarding internet interventions for anxiety and depression, with maintained symptom reductions (Andersson et al., 2018). The difference is that the within-group effect sizes are lower than long-term follow-up research on anxiety and depression. This could be statistically explained by the fact that anxiety and depression are usually measured with questionnaires with a limited number of answers (e.g., zero to six in MADRS-S). By contrast,

alcohol consumption is usually measured in number of drinks per week, with virtually an infinite number of answers, where especially outliers have a potential to give a larger variation and, hence, larger SDs, which in turn results in lower effect sizes. It is more difficult to compare the results to long-term internet interventions for AUD, since they are so scarce. The closest to a long-term follow-up treatment study (2 years or longer) on AUD in previous literature is the research based on the COMBINE study and Project MATCH (Witkiewitz et al., 2021). Worth stating is that the COMBINE study was mostly based on pharmaceutical interventions and Project MATCH was based on MET, twelve-step facilitation, and CBT, making it less relevant to compare since two-thirds of the interventions were non-CBT-based. Nevertheless, the results of Witkiewitz et al. (2021) showed that decreased WHO RDLs were maintained long-term compared to post-treatment.

One noteworthy finding is that participants in ePlus reported an increase in alcohol consumption at long-term follow-ups, including 6-month follow-up, compared to post-treatment, while participants in eChange reported decreased alcohol consumption at the 12-month follow-up. A speculation is that ePlus' therapist guidance functioned as an effective motivation booster, which for some participants resulted in relapse when the guidance eventually ended (Baumeister, Reichler, Munzinger, & Lin, 2014). The majority of individuals with AUD relapse within the first year (Miller, Walters, & Bennett, 2001), and continuing care, i.e., regular checkups on patients after treatment, have a demonstrable effect on alcohol consumption (McLellan, McKay, Forman, Cacciola, & Kemp, 2005). This does, however, not explain why the participants in eChange group remained at the same level at long-term follow-up. It might have been expected that the results at the long-term follow-ups would persist over time, since the few long-term follow-up studies on anxiety have reported that iCBT effects are maintained for as long as 5 years post-treatment (Hedman et al., 2011). Another plausible reason may be the Hello-Goodbye effect, where a patient may sometimes exaggerate his or her symptoms to receive therapy and at the end of treatment, may minimize or underreport his or her symptoms to please the clinician (Salkind, 2007). This effect may partly explain why participants in ePlus, who received human guidance, measured lower alcohol consumption at post-treatment, which at follow-up bounced back to, if this effect is accurate, more valid levels. A final possible explanation is that the attrition rate was higher in the eChange group at 24-month follow-up, and the participants who had dropped out may have been the same participants who had increased their alcohol consumption.

In Study III, there were no statistically significant differences in reported treatment seeking behavior between CSOs in the iCRAFT condition compared

to CSOs in the WL condition. One plausible explanation as to why the difference was not statistically significant is that the study was probably underpowered. Due to time constraints, the number of participants was decreased from 140 to 94 participants, following an interim analysis of the primary outcome measure.

The finding that there were no differences in treatment seeking between CSOs in the iCRAFT and the WL condition was unexpected, since previous research on CRAFT using a face-to-face approach has shown substantial effects (Bischof et al., 2016; Manuel et al., 2012; Miller et al., 1999). It should be noted that there were no substantial differences in CSOs' sociodemographic characteristics between the iCRAFT group and face-to-face research using CRAFT. There may be several explanations as to why there was no effect. One explanation may be a possible overconfidence in the validity of CSOs' self-reports of IP treatment engagement. The IPs could have sought treatment without informing the CSO, resulting in an underestimation of the number of IPs seeking treatment. Another explanation could have to do with unequal access to treatment depending on geographical location. Previous CRAFT studies have generally been conducted with participants residing in specific regions (Bischof et al., 2016; Miller et al., 1999), but the present study was a nationwide study. The research group could not ensure access to treatment across the whole country, which may have resulted in unequal access to treatment depending on where the participants lived.

The iCRAFT intervention was developed by our research group modelled on the CRAFT intervention program as described by Smith and Meyers (2007). One possible explanation for the lack of effect could be that the original CRAFT manual may not have been sufficiently adapted for the internet-based version. Also, it is possible that some parts of the program do not easily function in an internet-based format. Firstly, in order to avoid a high rate of drop-outs due to the treatment period being too long – a feature seen in internet studies from other fields (e.g., Christensen, Griffiths, & Farrer, 2009) – the number of treatment sessions was reduced from between ten and twelve sessions to five. In treatments for AUD, the length and intensity of treatment have been shown to be of less importance. Brief treatment programs in general show comparable efficacy compared to more extensive programs (Hammarberg, Wennberg, Beck, & Franck, 2004; Project MATCH Research Group, 1998). The median number of completed modules for iCRAFT participants was four out of five. This completion rate can be considered as high (e.g., Johansson et al., 2017). But for CSOs to acquire an adequate level of competence in skills involved in the task of inducing behavior change (i.e., treatment seeking or a reduction in alcohol consumption) in a third party (in

the case of CRAFT, the IP) may require a longer time period of specific skills training than was offered within the iCRAFT program.

Limitations

Some limitations need to be considered when interpreting the results. Firstly, data in the studies relied on self-reports, which is a limitation related to internal validity. It could be argued that this may reflect recall bias and/or social desirability, especially given that the participants were answering questions about one of the most stigmatized mental health disorders in the Western world (Kilian et al., 2021). Although self-report measures are commonly used in alcohol treatment trials, using these measures in combination with more objective ways of measuring alcohol consumption (e.g., blood tests such as Peth or CDT (Socialstyrelsen, 2019), especially in Studies I and II) would strengthen future evaluations.

Secondly, the inclusion of diagnostic assessment interviews in both studies may have sorted out less motivated persons at an early stage. Thirdly, the recruitment process of the trials may have introduced a selection bias worth considering when attempting generalizations to a clinical population. Participants were recruited by self-referral and may have had high initial motivation. Fourthly, the design of the studies did not allow for follow-up of outcomes in the WL conditions following treatment entry, which would have enabled consideration of the WL participants as their own controls in the studies.

Most studies on internet-based treatments have not used active control groups (Carlbring et al., 2018). One explanation for this could be that the research field of internet-based treatments is still young. It is easier to start with a WL only as a comparator, when you are still figuring out how to set up the treatment online, especially if the therapy manual is new. This limitation is true for Study III. However, Studies I and II had an active control group, with the same basic elements as in the ePlus condition.

Two limitations apply specifically to Study I. The first concerns participants in the WL, who first decreased their alcohol consumption after the interview, but then increased it again after having been randomized to the WL. This pattern may reflect disappointment after participants realized that they had been randomized to a WL, rather than to an active treatment condition. The second is that Study I used eleven or more (for women) and ≥ 14 (for men) standard drinks of alcohol in the preceding week as an inclusion criterion, but there is no evidence that this level of risk is realistic. It has almost become customary to set a nine or more (women) and ≥ 14 (men) drink risk limit (and as inclusion/exclusion criteria in alcohol treatment trials); however, new research points out that there is a linear relationship, i.e., an increasing risk in

the form of dose response (Griswold et al., 2018). One solution in future studies would be to include levels of diagnosis from DSM instead of sharp cutoff points. Another solution would be to include primary outcome measures such as core outcome set (COS) for alcohol (Shorter et al., 2021), which consists of ten different outcomes that measure several aspects of alcohol problem, as opposed to only alcohol consumption.

In Study II, the long-term follow-up study using telephone interviews and, in eChange, online questionnaires for long-term follow-up, the attrition rate was substantial at 24-month follow-up, and therefore we should be cautious in interpreting these results. A simple dropout analysis was performed to examine if participants in the eChange program who responded to long-term follow-up had different alcohol consumption at screening compared to participants who did not respond to long-term follow-ups. The analysis did not show any differences.

A last limitation concerns Study III. The WL design with no active control group implied weaknesses that have been addressed in several contexts (Patterson, Boyle, Kivlenieks, & Van Ameringen, 2016). However, since no established and validated support program (including internet-based programs) for CSOs exists in Sweden, including an active comparison group would have introduced uncertainties in interpreting the results.

Clinical implications

This thesis has covered three internet-based interventions that all have the potential to have direct clinical implications. The first, ePlus, seems effective, acceptable, and safe and may have potential as an alternative to traditional treatment forms for the large group of people with AUD who for varying reasons are reluctant or unable to visit a clinic. Low-intensity interventions such as eChange may possibly be a promising treatment alternative, at least when administered after a comprehensive inclusion process with a diagnostic interview. Further research is needed to elucidate the differential contributions of ePlus vs. eChange to recovery from AUD.

Since only 10–20% of individuals suffering from AUD enter treatment, there is an urgent need for programs that concomitantly increase motivation to seek treatment while at the same time addressing the stress and strain experienced by CSOs. Access to face-to-face delivered CRAFT is scarce in large parts of Sweden as well as internationally. Developing new modes of administering CRAFT would enable public health authorities and clinical treatment providers to reach a larger proportion of those in need of support.

Ethical considerations

Both Study I and Study III used WL control conditions. Previous research points out that participants allocated to a WL may “postpone” any changes while awaiting the intervention (Cunningham, Kypri, & McCambridge, 2013). They are told to wait for the intervention, and that is exactly what they do – wait. There is need for caution regarding the ethics of assigning participants who are actively ready to change to a WL control condition.

In Studies I and II, the treatment program for AUD, the research group took several responsibilities, such as to provide practical support to participants who felt worse during treatment due to abstinence symptoms. A part of the first module was to inform participants about what abstinence is and what the risks are, what signs to look out for, and when individuals should consider seeking help for detoxification. Through the platform itself, the research group had the possibility to automatically “flag” participants who scored high on the MADRS–S depression scale, on the item reflecting suicidal thoughts. All participants were obliged to answer the questions on MADRS–S on a weekly basis. When the therapist logged in, he or she was informed about this and was able to take some form of action.

Another important ethical aspect was that the research group referred participants to other treatment if this was deemed necessary when acute problems arose. Several help-seeking individuals were excluded during telephone screening. They were assisted to establish contact with relevant health care providers. The research group were committed to offering help to participants in treatment, e.g., if they felt that they were in need of some other form of help, to get in touch with relevant health care providers – but no participants asked for or were deemed in need of such other treatment. Negative effects, only explored in Study I, were reported by six individuals in the ePlus and five individuals in the eChange group. The negative effects mostly consisted of disappointment with the progress made during treatment. These results are similar to other internet-based interventions in both content and prevalence (Rozental et al., 2014).

In Study III, which used the support program for CSOs to people with AUD, the research group also took special responsibilities. Concerned significant others who were found ineligible were guided to relevant help individually tailored to their needs. During screening (sign up and telephone interview), all interviewed persons were asked about domestic violence. In cases where risk of violence was identified, CSOs were referred to a national support helpline primarily aimed at women exposed to threats and violence but also inviting men to call, or if necessary, consult appropriate health care services. The technical platform providing iCRAFT did not offer an automatic warning sys-

tem, such as when the participant scored high on suicidal thoughts in the Depression scale of the MADRS–S, and the only measure used on a weekly basis was the IP’s alcohol consumption. Even though this study was aimed at CSOs and did not directly target the IP and therefore potentially involved lower suicidal risk, there could have been CSO participants with suicidal thoughts. Since internet-based interventions usually have the benefit of automatic warning flag systems, these should always be used when appropriate. If there is no such technical benefit, there should at least be a manual examination of critical variables (such as suicidal thoughts, increased depression score, increased alcohol consumption, and so on) by the therapists on a weekly basis.

Conclusions and future directions

The high-intensity ePlus intervention was more effective in reducing HDDs compared to the low-intensity eChange intervention in the short term. Treatment satisfaction was high and negative effects were few. Long-term follow-up showed that participants in both the ePlus and the eChange programs maintained low alcohol consumption compared to pre-treatment and there were no differences between the two groups. The field is ready for trials conducted in clinical settings, and more non-inferiority trials such as the RCT by Johansson et al. (2021) showing non-inferiority between internet-based CBT and face-to-face CBT for AUD are needed. Future studies examining both treatment credibility (how do health care organizations and patients choose between long vs. short content and human guidance vs. no guidance?) and more treatment effectivity trials in clinical settings are also needed.

Considering iCRAFT, this is the first study investigating CRAFT delivered over the internet for CSOs to IPs with AUD. The results did not give us evidence that iCRAFT in its present form is sufficient to increase treatment seeking behavior among IPs. Future studies should investigate the optimal design for an internet-based version of CRAFT.

As AUD is one of the most common public health diseases, it is important to start offering internet-based treatments as alternative treatments to hard-to-reach people with AUD. At the same time as internet-based interventions are offered as regular care, it is equally important to conduct research on those treatments, including meticulous documentation and recurring follow-ups, preferably annually.

Internet-based treatments have the advantage that participants can easily answer questionnaires online. This fact can be used to add other instruments that measure other aspects of health as primary outcome, rather than just asking about number of standard drinks per week. If the risks and consequences of AUD are multifactorial (according to Engel’s biopsychosocial model (Engel, 1977)), we also need to develop primary outcome measures

that do measure this multifactorial model. This would open up the possibility to measure whether the biopsychosocial aspects have improved. One attempt at doing this has been a newly developed and recently evaluated index consisting of a number of indicators, so-called recommended “core outcome sets (COSs)” (Shorter et al., 2021). Using such outcomes in future studies would be a way to try to capture the vast meaning of AUD, and not just describe the disorder in terms of drinking too much alcohol.

AUD is strongly linked to morbidity and mortality, and only a fraction of individuals with alcohol problems seek treatment. We need to reach those individuals who otherwise would not enter treatment and offer them treatments that suits their needs. The research described in this thesis is a contribution to take another step in approaching that goal.

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