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**PROBLEMATIC SUBSTANCE USE  
AND DIGITAL INTERVENTIONS:  
RESEARCHING INTERVENTION EFFICACY AMONG  
INTERNET HELP-SEEKERS,  
UNIVERSITY STUDENTS  
AND PATIENTS IN PSYCHIATRY**

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# Problematic Substance Use and Digital Interventions: Researching Intervention Efficacy among Internet Help- seekers, University Students and Patients in Psychiatry

## THESIS FOR DOCTORAL DEGREE (Ph.D.)

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Dedicated to Amelie.



## ABSTRACT

**Background:** Digital technologies are ever more present in our lives, and are being applied in numerous areas of our existence including the area of health care and health information. Problematic alcohol and drug use impose a major global burden on health, and it is of interest to find new ways of reaching out to those affected by the problem. Interventions delivered over the Internet and in the form of smartphone apps have the potential to be readily available at all times and places. Many apps are publicly available, but only a tiny proportion have been evaluated. Also, there are many evaluated self-help applications for the Internet, but research on the addition of counselor guidance over the Internet is very scarce. There is a need for scientific scrutiny before being able to either recommend or implement these applications into regular care.

**Aims:** The aims of this doctoral project were: to carry out a preliminary evaluation of an Internet-based program for problematic use with guidance among Internet help-seekers; to investigate effects of three smartphone apps, two with estimated blood alcohol concentration (eBAC) feedback and a skills-training app, among university students; and to determine the prevalence of problematic substance use in a psychiatric population receiving treatment over the Internet, and to explore whether that substance use was associated with treatment outcomes.

**Methods:** An Internet-based eight-module program was tested in a randomized controlled pilot study with 80 participants. Participants were randomized to: no guidance, guidance over secure email messaging, or choice between guidance over asynchronous secure email messaging or synchronous chat messaging (STUDY I). Effects of two smartphone apps, Promillekoll and PartyPlanner, both with real-time eBAC feedback, and one, PartyPlanner, offering the possibility to simulate a drinking event beforehand and compare afterwards to the real event, were tested in a randomized controlled trial with 1929 university students having problematic alcohol consumption. Both app groups were compared to assessment-only controls (STUDY II). The effects of offering university students with excessive drinking, already enrolled in an ongoing study similar to STUDY II, an additional app focused on skills training were investigated (STUDY III). One hundred and eighty six students were randomly assigned to either an intervention group, receiving access to the app immediately, or a wait-list group given access to the app after six weeks. Both groups were compared to each other and also to a group of assessment-only controls (n=144) from the ongoing study. In the final study, data from 1581 patients having been treated at the internet-based cognitive behavioral therapy (ICBT) clinic in Stockholm, Sweden for major depression, panic disorder or social anxiety disorder, were analyzed to identify the prevalence of problematic substance use at beginning of treatment. The association of problematic substance use with therapy outcomes was also analyzed (STUDY IV)

**Results:** Study I: The guidance group (the secure email messaging and the choice of messaging mode groups were combined) had significantly lowered their alcohol consumption

compared to the no-guidance group. Secure email messaging was the preferred mode of communication over chat for the choice group. Participants in the guidance group rated the program more favorably than participants in the no-guidance group. Study II: There were no differences between the apps and assessment-only controls on any alcohol related outcome, but one negative finding for the Promillekoll app, in that men in that group increased their drinking frequency. Study III: Both the intervention and the wait-list had lower proportions of excessive alcohol consumption compared to assessment-only controls at first follow-up. The intervention group lowered their drinking quantity at first follow-up and their drinking frequency at both follow-ups compared to controls. Study IV: Prevalence of problematic substance use was 32.4%. Exclusive problematic alcohol use was reported by 24.1%, 4.6% reported exclusive problematic drug use and 3.7% combined problematic alcohol and drug use. Problematic drug use among men and 25–34 year olds was associated with completing fewer treatment modules and combined substance use among women and 35–64 year olds negatively affected module completion. Baseline problematic substance use was not associated with worse therapy outcomes for patients treated for depression. However, hazardous alcohol use and probable dependence were associated with worse panic disorder treatment outcomes. Hazardous drug use as well as combined problematic alcohol use with either hazardous drug use or probable drug dependence were associated with worse social anxiety disorder outcomes.

**Conclusion:** Using novel communications technology is effective for reaching individuals with problematic substance use. Adding counselor guidance to a web-based relapse prevention program has beneficial effects on problematic drinking. Smartphone apps relying on eBAC feedback do not show much promise at the moment. Skills-training smartphone apps may have a beneficial effect on excessive alcohol consumption. The prevalence of problematic substance use is high in ICBT-treated psychiatric outpatients, but for a variety of levels of baseline substance use, the negative effect on therapy outcomes seems limited.





## LIST OF SCIENTIFIC PAPERS

- I. Sundström, C., **Gajecki, M.**, Johansson, M., Blankers, M., Sinadinovic, K., Stenlund-Gens, E., Berman, A. H. (2016). Guided and unguided Internet-based treatment for problematic alcohol use – a randomized controlled pilot trial. (Submitted manuscript)
- II. **Gajecki, M.**, Berman, A. H., Sinadinovic, K., Rosendahl, I., & Andersson, C. (2014). Mobile phone brief intervention applications for risky alcohol use among university students: A randomized controlled study. *Addiction Science & Clinical Practice*, 9, 11. doi:10.1186/1940-0640-9-11
- III. **Gajecki, M.**, Andersson, C., Fredriksson, M., Sinadinovic, K., Rosendahl, I., Berman, A. H. (2016). Skills training via a smartphone app for university students with excessive alcohol consumption: A randomized controlled trial. (Submitted manuscript)
- IV. **Gajecki, M.**, Berman, A. H., Sinadinovic, K., Andersson, C., Ljótsson, B., Hedman, E., Lindefors, N. (2014). Effects of baseline problematic alcohol and drug use on internet-based cognitive behavioral therapy outcomes for depression, panic disorder and social anxiety disorder. *PloS One*, 9(8), e104615. doi:10.1371/journal.pone.0104615

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## LIST OF ABBREVIATIONS

AUDIT	Alcohol Use Disorders Identification Test
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
BASICS	Brief Alcohol Screening and Intervention for College Students
CBT	Cognitive Behavioral Therapy
DALY	Disability Adjusted Life Years
DDQ	Daily Drinking Questionnaire
DSM-V	The Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition
DUDIT	Drug Use Disorders Identification Test
eBAC	Estimated Blood Alcohol Concentration
EQ-5D	EuroQoL-5 Dimensions
GAF	Global Assessment of Functioning
GEE	Generalized Estimating Equation
HADS	Hospital Anxiety and Depression Scale
ICBT	Internet-based Cognitive Behavioral Therapy
ICD-10	International Statistical Classification of Diseases and Related Health Problems - Tenth Revision
IVR	Interactive Voice Response
LSAS-SR	Liebowitz Social Anxiety Scale – Self-Rated
MADRS-S	Montgomery Åsberg Depression Rating Scale – Self-Rated
MI	Motivational Interviewing
PDSS-SR	Panic Disorder Severity Scale – Self-Rated
RCT	Randomized Controlled Trial
RCQ	Readiness to Change Questionnaire
RP	Relapse Prevention
TLFB	Timeline Follow-Back
WHOQOL-BREF	World Health Organization Quality of Life (Abbreviated)



# 1 INTRODUCTION

In many parts of the world today people's lives are more and more influenced by modern communication technology. Access to the Internet is rising, and in Sweden penetration is very high with 87% being Internet users in 2015 (1). Seventy seven percent of Swedes own mobile phones with Internet capabilities, smartphones, and 76% use them to access the Internet (2). Eight (including Sweden) of 19 countries in The World Internet Project, an international collaboration to investigate the impact of the Internet and other new technologies, report that over 80% use Internet, and all countries but one report that the majority use smartphones to access the Internet(1). It should be mentioned that this does not yet apply to developing countries where unfortunately obstacles to the growth of Internet access for citizens are more persistent than expected (3). The possibilities of computers and smartphones for communication purposes are used in many areas today: for entertainment and education, such as in books, films, interactive games and social arenas for discussion and sharing, for shopping everything from cars to groceries, and making traveling arrangements and hotel bookings, only to name a few.

Health care is also developing fast and efforts to use digital communication technologies are already in place and developing. In Sweden citizens can gain access to their local general practitioner for scheduling appointments and even for renewing medicine prescriptions. There is also a private general practice clinic that offers consultations over videoconference via computer or smartphone with licensed physicians [www.kry.se](http://www.kry.se).

An area of importance for public health is problematic alcohol use and substance use. More than 200 disease and injury conditions are connected to harmful use of alcohol, and 5.9% of all global deaths in 2012 were attributable to alcohol consumption (4). The impact on global health can also be expressed in disability adjusted life years (DALY), meaning the number of years of life lost due to premature mortality and number of years of life lost due to time lived in less than full health. Approximately 11 DALYs are lost per 1000 individuals in a population due to alcohol consumption, and approximately two DALYs per 1000 population due to illicit drug use (5).

This thesis addresses the research questions of how digital technology might be harnessed in the public health and health care contexts to reduce problematic alcohol use, and also, in a patient group utilizing digital technology for other mental health issues, how big the need might be for specific interventions addressing problematic substance use. The thesis includes studies on individuals with problematic substance use, primarily alcohol, from a variety of populations, from the general public (STUDY 1), to university students (STUDIES 2-3) and, finally, patients in Internet-based psychiatric care (STUDY 4). In this first part of the thesis some background, as well as definitions used will be given.

## **1.1 DIGITAL INTERVENTIONS – INTERNET AND APPS**

Several kinds of novel techniques have been used to address a variety of health-related problems (6, 7). In Stockholm, Sweden there is a psychiatric unit developing treatment regimes for and providing patients in regular psychiatric care with treatment over the Internet with good results (8-10). For problematic alcohol use, digital technology has also been quite widely used, including Internet-based interventions (11), interactive voice response (automated telephony) (12, 13) and short message service (or text messaging) (14, 15). The focus of this thesis is technology that is either delivered via the Internet, through a web browser, or as native smartphone apps. The advantage of web browser-based interventions over locally run programs is that content is easily updated instantly, and does not require lengthy update sequences. They are mostly reachable through the use of different types of devices, such as a laptop, desktop computer, tablet or smartphone. They can often be reached at all hours of the day, and the connectivity of a smartphone makes content readily accessible. A disadvantage is of course that reliance on connectivity sometimes interferes with access to the intervention. A smartphone app is a program designed for use in a smartphone (and sometimes tablet), which increases availability as it is run locally in a handheld format. Sometimes a native app also connects to the Internet, but depending on design the app can defer access to when there is a connection. A design concept in between web pages and smartphone apps is a “web app” somewhere in the middle; the web app is basically a web page reached through web browser technology, programmed to give the same feel as an app. Modern web technology also enables the web browser to execute program code locally in the computer or smartphone.

## **1.2 PROBLEMATIC ALCOHOL CONSUMPTION**

As mentioned above, alcohol consumption carries with it a considerable impact on global health. The theme of this thesis is the alleviation of problematic alcohol consumption, and identification of, problematic substance use. So, what is problematic alcohol consumption or use? There is no level of drinking that can be considered to be entirely risk-free, and there is not a single agreed-upon definition of problematic alcohol consumption. For the articles in this thesis the term is defined as having a score on a screening instrument over the cut-off for drinking considered risky or hazardous, or exceeding the recommendations for weekly and daily drinking, or exceeding a blood alcohol level set by the research group (see section 1.2.2 below). Although the thesis does not address individuals who have been formally diagnosed with a substance use disorder, diagnostic criteria are generally used in the research community as a definitive basis for describing the types of problems associated with substance use that is moderate or severe. Before defining the broader term of “problematic substance use” it is therefore useful to begin with a look at the diagnostic criteria for problematic alcohol use. The reader should keep in mind that a standard glass is defined as containing 12 grams of alcohol in Sweden (16).



### **1.2.1 Diagnosis of problematic alcohol consumption**

Two main systems or manuals for classification of mental diseases are in use in health care, the International Statistical Classification of Diseases and Related Health Problems - Tenth Revision (ICD-10; 17) , and the Diagnostic and Statistical Manual of Mental Disorders (DSM-V; 18). ICD-10 is a classification list of diseases in general, and DSM-V is focused specifically on mental health and psychiatry.

#### **1.2.1.1 Problematic substance use in ICD-10**

The ICD-10 has no specific alcohol-related diagnosis, but specifies two diagnoses for problematic substance use: F1x.1 Harmful use, and F1x.2 Dependence syndrome. The diagnosis of harmful use depends on the specific substance use actually having caused some kind of damage to the mental or physical health to the user. Dependence syndrome denotes a cluster of physiological, behavioral, and cognitive phenomena, where the use of the substance has overtaken the priority of things earlier having had a greater value. There are six criteria of which three or more should have been present during the last year. The criteria are: a strong desire to use the drug, loss of control over substance use, withdrawal symptoms, development of tolerance of the substance, neglect of other pleasures and interests and continuing use despite clearly harmful consequences (17).

#### **1.2.1.2 Problematic alcohol use in DSM-V**

The DSM-V specifies one diagnosis for alcohol use, namely Alcohol use disorder. This is presented as a list of 11 criteria, or symptoms: drinking more or longer than intended, inability to stop drinking, spent inordinate amounts of time or being sick, strong desire, drinking interfering with taking care of responsibilities, drinking despite causing trouble with family/friends, neglect of other important or interesting activities in favor of drinking, engaging in potentially harmful activities, drinking in spite of feeling anxiety/depression or adding to a health problem/having a memory blackout, developing tolerance to alcohol and experiencing withdrawal symptoms. The severity of the alcohol use disorder is categorized into mild, moderate or severe depending on the number of symptoms having been experienced during the past 12 months (2-3, 4-5 and 6 or more, respectively) (18).

### **1.2.2 Definitions of problematic alcohol use in this thesis**

In this thesis all populations studied have been at a distance from the researcher. Apart from e-mail contact, no direct contact during each respective study occurred with any of the individuals from the general population (STUDY 1), the university student cohorts (STUDIES 2-3) or the patients in psychiatry (STUDY 4). Assessment of the level of severity of alcohol use was therefore for pragmatic reasons limited to self-report forms. Problem severity was thus defined based on cut-offs from self-report questionnaires. A general definition of problematic use in this thesis consists of having alcohol consumption that markedly increases the risk for negative consequences.

#### 1.2.2.1 Binge drinking

Binge drinking is defined as drinking more than 4 standard glasses of alcohol at one event for women, and more than 5 for men. Drinking over this limit may lead to increased aggression and impaired judgment, and increases the risk of arrhythmia and risk factors for cardiovascular disease (16).

#### 1.2.2.2 Excessive weekly alcohol consumption

In Sweden the national recommendation for weekly alcohol consumption is to drink a maximum of 14 standard glasses per week for men and 9 standard glasses per week for women. This is based on epidemiological studies pointing to lower risk of harm under these limits (16).

#### 1.2.2.3 The Alcohol Use Disorders Test

The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item screening test developed by the World Health Organization, with cut-offs decided based upon the scores' sensitivity and specificity for respective diagnoses (19). The score ranges between 0 and 40, and there are cut-offs defined for: hazardous drinking – a pattern of alcohol consumption that increases risk of harm; harmful drinking, or a pattern of alcohol consumption causing mental or physical harm; and probable dependence, which is a cluster of behavioral, cognitive and physiological factors that typically include a strong desire to drink alcohol and difficulties in controlling its use (20). The cut-offs have been modified slightly, with lower cut-off for hazardous drinking for women (21) to consider the fact that women experience negative consequences of alcohol at lower levels of exposure than men. Negative consequences for women both occur at lower levels, and women tend to fare worse than men as a result of consuming alcohol (22). The items and scoring consider consumption, symptoms of dependence and alcohol-related harm.

#### 1.2.2.4 Blood alcohol concentration

In this thesis, a version of the so called Widmark formula for estimating blood alcohol concentration (eBAC) (23) was used. A blood alcohol concentration level of 0.08 % can be used as a cut-off for binge drinking (24), but the research group set it to a more conservative level of 0.06%, a figure close to the 0.055 % level used in the Brief Alcohol Screening and Intervention for College Students (BASICS; 25) intervention program, which has successfully been used for university students (26).

### **1.3 PROBLEMATIC DRUG USE**

The focus of this thesis is mainly problematic alcohol use, but one study explores both the prevalence of problematic drug use, and the association between having problematic drug use

when beginning Internet-based psychotherapeutic treatment, and the outcome of the treatment.

### **1.3.1 The Drug Use Disorders Identification Test**

For the purposes of defining prevalence of problematic drug use in this thesis, the Drug Use Disorders Identification Test (DUDIT) was used. DUDIT is an 11-item screening test measuring consumption of illicit drugs, dependence symptoms and drug-related harm (27). The test is scored between 0 and 44, and there are cut-off scores for hazardous drug use, harmful drug use and probable dependence. Cut-offs are based on sensitivity and specificity for drug-related diagnoses (28). In Sweden all illicit drug use is considered hazardous and therefore any score above 0 is considered problematic.

## **1.4 DIGITAL INTERVENTIONS AND PROBLEMATIC ALCOHOL CONSUMPTION**

### **1.4.1 Internet-based interventions**

Strictly speaking the term Internet refers to the globally spanning network consisting of a multitude of interconnected networks based on the communication protocols TCP/IP, and the information delivered on the Internet is not contained to a specific format. For the purposes of this thesis the term Internet-based interventions will be used to refer to interventions delivered through web browsers.

The Internet allows for the delivery of pure self-help, unguided interventions, as well as for guided interventions. Internet interventions in a pure self-help format for problematic alcohol consumption have been used successfully, with a meta-analysis from 2011 showing an effect size of  $g=0.39$  (11). The interventions delivered over the Internet range from low-intensity to high-intensity interventions, where minimal interventions are based on screening and brief interventions (29, 30) up to full-blown treatment programs, such as cognitive behavioral therapy (CBT)-based programs with several modules (31). Although the meta-analysis cited (11) indicates a moderate effect size for self-help programs, individual studies vary widely in results. For example, self-help programs seem in some cases to lead to positive effects in terms of reduced hazardous or harmful drinking (30) to somewhat equivocal effects (32), and in some cases to no discernable effects (33). It is not entirely clear what factors influence whether or not such an intervention has an effect.

#### **1.4.1.1 Guidance**

One self-help program feature recently investigated for possible additional effects is the addition of human remote guidance. So far, such research is quite scarce, with major contributions from one randomized controlled study comparing guided self-help with a wait-list group that received e-mails during the study period (34) and a second randomized controlled study comparing guided self-help with pure self-help (31). The latter study revealed a significantly greater reduction of standard drinks per week at 6-months post-randomization (but not at 3 months) for the guided group in comparison to the pure self-help

group (31). Nonetheless, a meta-analysis including both guided and unguided interventions indicated a general effect of  $g=.20$ , but no particular advantage for guided interventions (35). Evidently, the question of guidance effects warrants further research. A helpful framework for categorizing Internet-based interventions in relation to counselor guidance has been suggested by Cavanagh et al (36), who divides the interventions into pure self-help approaches with no guidance at all, “predominantly” self-help interventions with no more than 1.5 hours of guidance, “minimal contact” interventions where the therapist invests at least 1.5 hours of guidance, and “predominantly” counselor-administered interventions where the Internet intervention is a complement to ordinary face-to-face therapy. Among other research suggestions specifically focused on guidance, Cavanagh et al suggest that future research needs to identify what kind of intervention works for which kind of individual.

#### **1.4.2 Smartphone apps**

In large contrast to guided Internet-based interventions, the burgeoning field of treatment via smartphone apps shows relatively little evidence-based promise so far, at least regarding problematic alcohol consumption. Researchers have investigated publicly available apps related to alcohol consumption and found that there are many available, many encouraging drinking. Of those aiming at helping with problematic alcohol consumption, few have been evaluated scientifically (37-39). A recently published review found only 6 apps (40) that had been scientifically evaluated. Although there is huge potential in smartphone availability, packaging intervention content in an effective way appears to be quite a challenge. The question of which populations of individuals with problematic alcohol use might benefit the most from app-based interventions is also unanswered.

### **1.5 POPULATIONS AND PROBLEMATIC ALCOHOL USE**

In this thesis three different populations are explored in the studies. Each of these populations is a selected one, with a higher prevalence of problematic alcohol use than in the general population. One population consists of individuals actively seeking information on and help for their alcohol consumption. The second two populations, psychiatric patients and university students, are considered to be at a higher risk of having problematic alcohol use. Each population is briefly described below. For the sake of comparison, the reference rate of problematic alcohol consumption in the adult general population in Sweden is estimated at between 15 and 20% (41, 42). For problematic drug use, the prevalence rate is about 3% (41), with lower consumption for women compared to men.

#### **1.5.1 Help-seekers on the Internet**

As mentioned earlier, in this day and age, people seek help on health-related matters on the Internet. It is known that women tend to seek online help for health-related issues to a larger degree than do men (43). The severity of the problematic alcohol consumption among help seekers may be hard to access, due to inclusion criteria in the research, but figures indicate that severity is fairly high, with AUDIT scores over 20, suggesting probable dependence (32).

### **1.5.2 University students**

University students tend to drink more hazardously than do their non-student peers (44, 45), and they seem to establish their future adult alcohol habits during their years of higher education (46) meaning that college and university students are an important target population for alcohol interventions.. In contrast to Internet help-seekers however, college and university students who perceive worse alcohol-related problems seem to go online less for help and turn to relatives and friends instead (47). It is thus a significant challenge to convey brief interventions for reducing alcohol consumption to university students; while student health services provide interventions for problem drinking, only a small percentage of students seek such help (48).

In a recent review on electronic interventions, studies with college students showed small effects on alcohol consumption at 6-month follow-up, and diminished results at 12-month follow-up (12). Another recent review of studies on mobile interventions for reducing hazardous alcohol use among university students, covering 2012-2015, yielded seven published randomized controlled trials (RCT) using the technologies of interactive voice response (IVR), also known as automated telephony (one study), text messages (four studies) and smartphone apps (two studies) (14).

Only the study using IVR interventions reported clear positive results regarding reduced alcohol consumption (13). Three of the studies reported positive secondary results (49-51) and the remaining three studies (52-54) showed no changes over time and one showed a negative result (52).

### **1.5.3 Patients in psychiatry**

The prevalence of substance use disorders is markedly higher among those affected by psychiatric disorders. Individuals diagnosed with a psychiatric disorder run double the risk of being diagnosed with an alcohol use disorder and four times the risk of being diagnosed with a drug use disorder, compared to those without a psychiatric disorder (55).

In Sweden, about one-fourth of non-psychotic patients at psychiatric outpatient clinics have indicated problematic alcohol use (56), and almost 10% of psychotic patients have problematic drug use (57). The prevalence of substance use in a psychiatric population receiving regular treatment through novel digital technology has, as far as known, not been previously studied. Also, little is known about the influence on psychotherapeutic treatment of having problematic substance use at beginning of treatment.

## **2 AIMS OF THIS THESIS**

The overall aim of this thesis was to investigate aspects of health-supporting digital interventions, both as an arena for delivering different types of interventions for problematic

alcohol consumption and also to investigate the prevalence of, and effects of substance use in users of digital interventions in regular care.

## **2.1 STUDY I**

The specific aim of this randomized pilot study was to investigate the feasibility and effect of giving individuals seeking help with their problematic alcohol consumption on the Internet access to a self-help program, either as pure self-help or with counselor guidance. A secondary aim was to research the attractiveness of messaging with the counselor in a synchronous or asynchronous mode and effects on study retention of having a choice of messaging mode.

## **2.2 STUDY II**

The aim of this study was to evaluate the effects of two smartphone apps on problematic alcohol consumption among university students. Both apps were based on real-time alcohol consumption information with feedback on eBAC levels. One app had an additional component for planning a drinking event ahead of time with the possibility to later compare the planned event with the real event. Both app intervention groups were compared to an assessment-only control group.

## **2.3 STUDY III**

The aim of this study was to investigate the effect of giving access to an in-depth app focusing on skills training for reducing excessive weekly alcohol consumption. Subjects were university students with excessive weekly consumption already enrolled in an ongoing parallel study addressing problematic drinking, similar to STUDY II with longer follow-up measurements. Participants in STUDY III were identified as those students reporting excessive weekly alcohol consumption at six weeks into that study. The app intervention group and a wait-list group were compared to an assessment only control group.

## **2.4 STUDY IV**

This study, the only study in the thesis not investigating a digital intervention for problematic alcohol use, had an overall aim of helping assess the need of alcohol and substance use interventions in a psychiatric population already using digital interventions for psychiatric problems. The primary aim was to study the prevalence of problematic substance use among patients in regular psychiatric care for depression, panic disorder or social anxiety disorder at the internet-based cognitive behavioral therapy unit in Stockholm, Sweden. The secondary aim was to examine the effect of substance use on therapy outcomes for these patients.

## **3 THE EMPIRICAL STUDIES**

In this part, the studies in this thesis are described. For a quick overview of the studies following this part, there is a table summarizing the studies, with a short description of each study's aim, design, population, outcome measures and main findings.

### **3.1 STUDY I**

#### **3.1.1 Context and aims**

An Internet-based self-help program for individuals with problematic alcohol use developed in Holland was previously evaluated in an RCT, as a pure self-help program, and with counselor guidance (31). In that trial, guided and unguided groups showed favorable effects on alcohol-related outcomes compared to an untreated wait-list group and the guided group also had better results than the unguided group at 6 months after randomization. The purpose of STUDY I was to translate the program to Swedish and in a pilot trial in Sweden evaluate the feasibility of providing this intervention, evaluate preliminary effects of guidance on alcohol consumption and to research interest in having a choice of mode of communication with the guide, synchronous or asynchronous. A secondary aim was to investigate whether being given a choice of communication mode compared to being assigned to secure messaging would influence retention.

#### **3.1.2 Methods**

##### **3.1.2.1 Study design**

This was a three-group randomized design. Participants were randomized with the ratio 1:1:2 to one of three groups: 1. No guidance. 2. Guidance over asynchronous secure messaging. 3. Guidance with choice between synchronous and asynchronous communication. All groups were followed up post-treatment 10 weeks after randomization.

##### **3.1.2.2 Recruitment and participants**

Participants were recruited through a short information text about a study on Internet-based help for problematic alcohol use, posted on the Swedish Internet site [www.alkoholhjalpen.se](http://www.alkoholhjalpen.se), an open access website providing information and an online discussion forum for individuals seeking help for alcohol consumption. Individuals interested in joining clicked a link leading them to a web page with further information and the option to give informed consent to participate. Thereafter subjects were asked to register their age, gender and answer web versions of the AUDIT and DUDIT screening tests. They also filled out a seven-day timeline follow back (TLFB) form. Eligible for participation were individuals over 18 years of age having a score on the AUDIT indicating problematic alcohol use (AUDIT score >5 for women and > 7 for men). Participation was capped at 80 individuals, randomly allocated to no guidance (n=40), guidance over asynchronous secure messaging (n=20) or choice of guidance over chat (synchronous) or secure messaging (asynchronous) (n=20). Of the participants, 60% were female, and the mean age was 42.3 years of age.

### 3.1.2.3 Outcome measures

The primary outcome measure for measuring alcohol consumption was a seven-day web-administered version of the TLFB. Several secondary measures were used: AUDIT for additional measure of alcohol consumption, the Readiness to Change Questionnaire (RCQ) and Readiness Ruler for measuring the participants' motivation to change their drinking habits, and the Hospital Anxiety and Depression Scale (HADS) to measure anxiety and depression symptoms. Two measures were used for measuring participants' quality of life, EuroQol 5-Dimensions (EQ-5D) and World Health Organization Quality of Life – Abbreviated questionnaire (WHOQOL-BREF).

### 3.1.2.4 Intervention

All three groups received access to the same treatment program, a Swedish translation of an eight module Internet-based program for problematic alcohol use originally developed in the Netherlands, at the Jellinek clinic (31). The program modules, based on CBT and motivational interviewing (MI), were released at the rate of one module per week with exception for a three-week hiatus between modules six and ten, for a total of ten weeks. All participants could access the system and do exercises whenever they chose during the study period.

#### 3.1.2.4.1 *No guidance*

Participants in this group had access to the program portal and could read texts and do exercises with no interaction with providers. An email address was available for technical support.

#### 3.1.2.4.2 *Guidance via secure messages*

Participants in this group had the same access to the program portal as the No guidance-group, but also received messages from a counselor at least once per module. Thereto, the participants could initiate discussions and ask questions at any time related to the treatment program. Questions were to be answered by the counselor within 48 hours.

#### 3.1.2.4.3 *Choice of chat or secure messages*

Participants in this group had the same access as the No Guidance-group to the program portal, but also initially chose a mode of communication with a counselor to help guide them. The two modes of communication were: secure messaging, in the same format as in the second group, or real-time chat. If they chose the chat option, the participant and the counselor were to schedule at least one chat session per module.

### 3.1.2.5 Statistical analyses

Descriptive statistics were used to describe baseline characteristics. In order to determine baseline differences analysis of variance (ANOVA) and Student's t-test were used for continuous variables and Pearson's chi-square for categorical variables. Multiple imputation,



creating five imputed data sets, was used for missing follow-up data on outcome measures: TLFB, AUDIT, HADS, EQ5 and WHOQOL-BREF. TLFB data were square root transformed before imputation for skewed count data. General Estimated Equations (GEE) were used for outcome analyses using an unstructured working correlation matrix. For the TLFB a negative binomial model with log link was chosen, and for the other outcomes a normal model was chosen. In order to test for significance, F-tests and t-tests were done on the pooled data resulting from the GEE analyses. Analyses were done comparing all three groups, mainly to assess interest in the different communication modes and to see if choice affected retention. Analyses for outcomes were also performed, where both groups with guidance were collapsed into one large guidance group, to compare with no guidance.

### **3.1.3 Results**

At baseline, the mean alcohol consumption measured in standard glasses for the week prior to recruitment was 29.4. In the choice group 7 individuals (35%) chose to communicate via chat, and two of these chose to switch to communication via secure messages. The proportion of participants lost to follow-up (attrition) differed among the groups. The self-help group had 52.5% (n=21) attrition, the secure messages group 25% (n=5) and the choice group 15% (n=3). Combining both guidance groups, attrition in the larger guidance group was 20% (n=8). At follow-up, the guidance group had lower TLFB (M=10.8, SD=12.1) and AUDIT (M=14.4, SD=5.2) scores compared to the self-help group (M=22.6, SD=18.4; M=18.2, SD=5.9). These were significant differences, ( $t[78]=3.385$  and  $t[78]=3.037$ , respectively). Participants in the guidance group evaluated the program more favorably than did participants in the self-help group. Guidance group members reported having spoken to someone about their alcohol use more than self-help group members, while conversely the self-help group members sought more after other modes of help on the Internet.

### **3.1.4 Discussion**

This is one of, if not the first study in Sweden conducted on internet-based treatment for problematic alcohol use with counselor guidance. It was intended to be a pilot study researching feasibility of using a Swedish translated version of a Dutch program, with analyses of outcomes comparing the program as pure self-help to the program with guidance. No prior power analysis was made because of the study's pilot status. The program did show greater effects on alcohol-related outcome measures when guidance was added. Only between-group effects were analyzed, and no analysis of the magnitude of the change from baseline to follow-up was performed in the study; the within-group effects of the self-help program over time will be analyzed in other studies. For those given the choice of mode of communication with their guide, the chat option seems to have been a less compelling alternative. There is a question of whether, for some participants, scheduling times for real-time contradicts the idea of using the Internet, being able to read and interact at will, and being able to give more consideration to their replies. It seems that participants in the guidance group sought less help on the Internet than did the self-help group participants, possibly implying greater satisfaction and perhaps mirroring the more favorable opinions on

the program given by guidance group members. To summarize, the results imply that the addition of guidance is valuable.

## **3.2 STUDY II**

### **3.2.1 Context and aims**

The aim of this study was to research the effects of giving university students access to one of two smartphone apps giving real-time feedback on estimated blood alcohol concentration levels (eBAC) on risky drinking.

### **3.2.2 Methods**

#### 3.2.2.1 Study design

This was a three-group RCT. Participants were randomized with a ratio 1:1:1 to be included in one of the groups: 1. Promillekoll app; 2. Partyplanner app; 3. Assessment only control-group. All groups were followed up seven weeks after registering for the study.

#### 3.2.2.2 Recruitment and participants

The members (n=28574) of the student unions at two universities in Stockholm, Sweden were invited via email to participate in a study on smartphone apps for reducing risky alcohol consumption. Invitees were informed that participating fully would enter them in a lottery for one of three iPad units. The email contained a link to a web page with a questionnaire where participants gave informed consent and subsequently entered questions on whether they had access to a smartphone, their age, gender and weight. They also filled out online versions of the AUDIT, and Daily Drinking Questionnaire (DDQ). Eligibility for randomization in the study was dependent on having an AUDIT score indicating problematic alcohol use (AUDIT score >5 for women and > 7 for men), and having access to a smartphone running either the iOS or Android operating systems. Participants fulfilling these requirements were randomized (n=1932). Three participants were excluded from analyses because of incomplete or faulty data at baseline. The final distribution was 643 in the Promillekoll group, 640 in the PartyPlanner group and 649 in the control group. In terms of gender and age, 51.7% of participants were female and the average age was 24.7 years of age.

#### 3.2.2.3 Outcome measures

Participants filled out a seven-day version of the DDQ stating the number of standard glasses they had consumed specified for each day of a typical week during the last month. They also specified over how many hours those glasses were consumed. An additional question was added, asking how many standard glasses were consumed over how many hours during the top alcohol consumption event during the last month. There were several outcome measures for alcohol consumption in this study, all derived from the answers to the DDQ:

- Quantity – number of standard glasses consumed over the week.
- Frequency – the number of days during the week alcohol was consumed.

- Binge occasions – number of days during the week where consumption exceeded four standard glasses for women and five standard glasses for men.
- Average eBAC over the week
- Peak eBAC for the month.

#### 3.2.2.4 Interventions

##### 3.2.2.4.1 *Promillekoll app*

A publicly available app for Android and iPhone smartphones, developed by the Swedish government's alcohol monopoly, *Promillekoll* lets the user register his or her alcohol consumption in real time and calculates the user's current eBAC levels, warning the user if the eBAC will exceed 0.06 percent. The app also provides some information texts on alcohol and blood alcohol concentration.

##### 3.2.2.4.2 *PartyPlanner app*

Developed by the research group, *PartyPlanner* is a web app, accessed through a web browser. *PartyPlanner*, in addition to a similar real time registration of alcoholic consumption with eBAC feedback to that of *Promillekoll*, also offers a feature for planning ahead of an alcohol consumption event. This planned event displays how many drinks lead to what eBAC, and saves the event so that the user can compare it to the actual event afterwards.

##### 3.2.2.4.3 *Control group*

This group only filled out the assessments at registration and seven-week follow-up.

#### 3.2.2.5 Statistical analyses

Descriptive statistics were used to describe baseline characteristics. Baseline differences were tested using ANOVA for continuous variables and Pearson's chi-square test for categorical variables. Linear mixed models analyses were performed to identify changes over time in alcohol consumption outcomes: quantity, frequency, binge drinking occasions, mean eBAC and peak eBAC. These analyses were performed only for the users reporting having used the app they were assigned to, controlling for the following variables: number of reported times accessing the app, having spoken to someone about alcohol consumption and having accessed the app *Promillekoll* prior to the study.

### 3.2.3 Results

The mean AUDIT score of participants, 10.7 at baseline, indicated hazardous drinking levels. Total attrition was 29.4% and attrition was unevenly distributed among the groups, where the *PartyPlanner* group had the highest attrition rate at 39.3% compared to *Promillekoll* at 26.4% and the control group at 22.7%. Significantly more men did not complete follow-up in the *PartyPlanner* group, whereas there were no gender differences in the other groups. In the *PartyPlanner* group those not completing the follow-up had significantly higher baseline scores on alcohol consumption-related outcome variables. Fewer *PartyPlanner* participants

reported having used the *PartyPlanner* app compared to *Promillekoll* participants reporting having used the *Promillekoll* app during the study. Time-by-group interactions comparing each group to the control group revealed no significant interactions for the *PartyPlanner* group; for the *Promillekoll* group an increase in drinking frequency was significant. A secondary analysis revealed that it was the male participants in the *Promillekoll* group who increased their drinking frequency. The proportion of participants drinking over the recommended weekly limit of 8 standard glasses for women and 13 glasses for men were approximately one third at baseline, and also approximately one third at follow-up.

### **3.2.4 Discussion**

This study showed no apparent effect on drinking in any of the two intervention groups when compared to assessment-only controls, implying that pure eBAC feedback is not an effective component in a smart-phone based intervention for university students. Future studies may reveal that having eBAC feedback in combination with other components can make this a more effective intervention. There was one negative finding in the *Promillekoll* group, namely an increase in drinking frequency compared to controls. However, it is important to recognize that there were no differences in quantity, binge drinking or eBAC. This implies a somewhat difficult to integrate picture of drinking the same amount over more occasions, potentially a less harmful approach than if there been a difference in the number of binge drinking occasions. One major limitation of this study, perhaps the greatest, is the lack of objective user data. Self-reports on how many times an app was used, or even which app was used retrospectively can lead to fairly uncertain data. Also the large attrition rate, especially in the *PartyPlanner* group, may have caused the results to be skewed. In the *PartyPlanner* group men and those with higher alcohol consumption did not complete the follow-up, a finding not seen in the *Promillekoll* group. This could mean that the same increase in frequency seen in the *Promillekoll* group would have been seen among the attrited men in the *PartyPlanner* group. However, the dropout could have resulted from any number of reasons. An ethical limitation of this study that can be improved on in future studies is the lack of feedback on problematic alcohol drinking to the assessment-only-controls.

## **3.3 STUDY III**

### **3.3.1 Context and aims**

This study aimed to research the effects of giving university students already enrolled in an eBAC feedback smartphone app study, and still reporting excessive weekly alcohol consumption at first follow-up six weeks into that study, an additional app providing skills training for problematic alcohol consumption.

### 3.3.2 Methods

#### 3.3.2.1 Study design

This was a three group RCT. Participants were randomized 1:1 into either of two groups: 1. *TeleCoach app* or 2. Wait-list. For comparison, participants from the assessment-only group in the ongoing eBAC study, matched on excessive consumption, were used as a control group in this study. All groups were followed up 6 weeks and 12 weeks into the study with the exception of the *TeleCoach* group that was followed up 6 weeks and 12 weeks after receiving access to the app. Access to the app for the *TeleCoach* group was delayed by three weeks due to unforeseen technical difficulties.

#### 3.3.2.2 Recruitment and participants

University students already enrolled in an ongoing study on smartphone apps with real time eBAC feedback who reported excessive weekly alcohol consumption (n=257), i.e. 14 standard glasses or more for men and 9 standard glasses or more for women, at follow-up six weeks into that study were informed about their excessive weekly consumption and invited via email to join a study on another smartphone app. The email contained a link to a web page where participants could give informed consent. Of those invited, 186 participants gave informed consent and were randomized, 93 to the *TeleCoach* group, and 93 to the wait list. Of the assessment only controls in the ongoing study, 144 were used as a control group here, matched on excessive alcohol consumption at the six week follow up. Of the participants, 69.1% were female. Participants' average age was 25.4 years of age.

#### 3.3.2.3 Outcome measures

Baseline scores were gathered from the ongoing study's follow-up. The DDQ was used where the participant reported the number of standard glasses they had consumed for each day of a typical week during the last month. Participants also reported over how many hours those glasses were consumed. An additional question was included on the number of standard glasses consumed over a self-reported number hours, during the top consumption event during the last month. All outcome measures were derived from the answers to the DDQ. The primary outcome was the proportion of participants with excessive weekly consumption. Secondary outcomes were: Quantity – number of standard glasses consumed during seven days, Frequency – the number of days in a seven day period when alcohol was consumed, Binge occasions – the number of days in a seven day period when consumption exceeded 4 standard glasses for women and 5 standard glasses for men, Average eBAC – the average eBAC over a seven day period, Peak eBAC - within the past month.

#### 3.3.2.4 Interventions

##### 3.3.2.4.1 *TeleCoach app*

The *TeleCoach* app is a web-based app developed by the research group presenting the user with menus and options. The app has a main menu where the user either can enter their

alcohol consumption in standard glasses for each day during the last week with short feedback and a text on recommended drinking limits, or choose a skills training menu. The skills training menu offers: 1. A survey of high-risk situations where the user can identify situations where he/she is more at risk for drinking alcohol 2. Skills training on how to resist social pressure, and coping exercises for relaxation and mindfulness.

#### 3.3.2.4.2 *Wait-list*

This group was given access to the *TeleCoach* app, after having waited for six weeks.

#### 3.3.2.4.3 *Assessment-only controls*

This group completed only the assessments at the different follow-ups, and did not receive any intervention.

#### 3.3.2.5 Statistical analyses

Descriptive statistics were used to present baseline characteristics. ANOVA and Pearson's chi-squared tests were used to determine baseline differences. GEEs with an exchangeable working correlation structure were used to analyze outcome data. To estimate standard errors the semirobust Huber-White sandwich estimator was used.

### 3.3.3 Results

Eighty-seven percent of study participants responded to at least one or both of the two follow-ups, and 72.7% responded to both. At both follow-ups, the proportion of participants with excessive alcohol consumption was higher in the control group compared to both intervention and wait-list groups ( $\chi^2(2)=17.78, p<0.001$ ;  $\chi^2(2)=5.85, p=0.054$ ). Secondary outcome analyses, controlling for age and specific parameter values measured 6 weeks prior to study registration, showed that the intervention group lowered their drinking quantity more at first follow-up ( $z=-2.09, p=0.037$ ) and lowered their drinking frequency more at both first ( $z=-2.04, p=0.041$ ) and second ( $z=-2.12, p=0.034$ ) follow-ups than controls. Analyses comparing wait list and controls yielded no significant results. Across both follow-ups the odds for not having excessive alcohol consumption in the intervention group were nearly twice as high as for controls. Gender analyses, controlling for age and pre-randomization values 6 weeks before this study, revealed that men in the intervention group had a greater reduction in peak eBAC than the assessment-only controls both at first ( $z=2.32, p=0.020$ ) and second ( $z=-2.19, p=0.029$ ) follow-ups. The same was true for men in the intervention group at both follow-ups in comparison to the waitlist group ( $Z=-2.80, p=0.005$ ;  $Z=-3.24, p=0.001$ ).

### 3.3.4 Discussion

This study showed some positive results in favor of both the intervention group and wait-list group compared to controls. The proportion of excessive alcohol drinkers in both groups dropped markedly more than in the control group at first follow-up, and was still lower at second follow-up. This means that the wait-list group saw a significantly greater reduction than controls before ever having access to the app. A question arising from this result is

whether this is a result of being in a study and receiving a message explicitly stating that one is drinking excessively, or perhaps of having had access to the app from the eBAC study for a longer time. However, in favor of the intervention group is the fact that the odds for not having excessive alcohol consumption seen over both follow-ups were higher for the intervention group. Thereto, secondary analyses revealed that the intervention group saw greater reductions in quantity of drinking as well as frequency, findings not seen in the wait-list group. This means that there are positive results seen for the intervention group. A major limitation of this study is the lack of objective usage data. The self-reported data on app usage were unfortunately useless. Therefore it is hard to draw conclusions about the contribution of the TeleCoach app per se. In light of the positive results of this study, further research on the effects of providing skills-training apps to university students, as well as to other parts of the population is definitely warranted; a further reason for continued research is that there is so little research done on this ubiquitous technology.

### **3.4 STUDY IV**

#### **3.4.1 Context and aims**

In Stockholm, Sweden there is a psychiatric clinic developing and offering Internet-based cognitive behavioral therapy to patients in regular psychiatric care for major depressive disorder, social anxiety disorder and panic disorder (and after the writing of this paper also for irritable bowel syndrome) since the year 2007. At baseline patients fill out screening instruments for alcohol and drug use, but until STUDY IV was carried out, prevalence rates had not been studied, so this was the primary aim of the study. The secondary aim was to research whether drug and/or alcohol use at baseline had any influence on therapy outcomes for the patients.

#### **3.4.2 Methods**

##### **3.4.2.1 Study design**

This was a registry study based on retrospective data collected from patients in regular internet-based cognitive behavioral therapy (ICBT) care.

##### **3.4.2.2 Recruitment and participants**

Patients in regular ICBT care at the ICBT clinic at Psychiatry Southwest for major depressive disorder, social anxiety disorder or panic disorder, who had met with an intake psychiatrist between October 30, 2007 and June 16, 2010 (n=1601) were considered. Twenty individuals were excluded due to missing or faulty data, thus 1581 patients were included, and 63.1% of these were female.

### 3.4.2.3 Measures

#### 3.4.2.3.1 *Baseline measures*

For determining baseline substance use, the screening instruments AUDIT and DUDIT were used for alcohol and drugs respectively. Both were administered electronically. To gauge patient functional status, global assessment of functioning (GAF; 58) was rated by the intake psychiatrist.

#### 3.4.2.3.2 *Continuous measures*

Depression symptoms were measured at baseline and up to once a week during treatment with the Montgomery Åsberg Depression Rating Scale – self rated (MADRS-S; 59) for all patients. For patients treated for social anxiety disorder, the Liebowitz Social Anxiety Scale – Self-Rating version (LSAS-SR; 60) was administered at baseline and up to once a week for measuring social anxiety symptoms, and for patients treated for panic disorder, the Panic Disorder Severity Scale – Self Rating version (PDSS-SR; 61) was administered at baseline and up to once weekly for following panic disorder symptoms.

#### 3.4.2.4 Statistical analyses

Descriptive statistics were used to describe participant characteristics and prevalence data. For analyses of the association between baseline substance use and therapy modules completed, ANOVA tests were used with Tukey-Kramer post-hoc tests taking into account uneven sample sizes. Differences in therapy outcome by substance use category were analyzed with analysis of covariance (ANCOVA) analyses controlling for baseline values on MADRS-S, LSAS-SR and PDSS-SR depending on treatment received. Within-group effect sizes were calculated as Cohen's *d*. Additional ANCOVA analyses were conducted with therapy outcome as the dependent variable, controlling for age, gender, initial GAF score, baseline screening scores, and number of modules completed.

### **3.4.3 Results**

#### 3.4.3.1 Prevalence

Problematic substance use was reported by 32.4% at baseline, 24.1% exclusive problematic alcohol use, 4.6% exclusive problematic drug use and 3.7% combined problematic alcohol and drug use.

#### 3.4.3.2 Completion of treatment modules

Number of completed treatment modules was negatively affected by problematic drug use among men and 25–34 year olds; combined substance use negatively affected adherence for women and 35–64 year olds.



### 3.4.3.3 Treatment outcomes

Hazardous alcohol use ( $B=1.29$ ,  $p=0.034$ ) and probable alcohol dependence ( $B=5.29$ ,  $p=0.017$ ) negatively affected panic disorder outcomes, and hazardous drug use led to worse social anxiety outcomes ( $B=18.00$ ,  $p=0.002$ ). Probable dependence on drugs led to markedly worse social anxiety outcomes for the two patients in this group ( $B=41.82$ ,  $p=0.003$ ). Depression outcomes were not affected by substance use. Subsequent analyses, controlling for age, gender, initial GAF score, baseline screening score, problematic use and number of modules completed also did not show any effect of substance use on treatment outcome for those treated for depression. These analyses did show that patients treated for panic disorder with exclusive hazardous alcohol use ( $B = 1.29$ ,  $p = 0.035$ ) and patients with exclusive probable alcohol dependence ( $B = 6.35$ ,  $p = 0.005$ ) had worse outcomes on PDSS-SR than did patients without problematic substance use. For the social anxiety disorder group these subsequent analyses showed that patients with exclusive hazardous drug use ( $B = 13.70$ ,  $p = 0.039$ ), patients with combined problematic alcohol use and hazardous drug use ( $B=247.62$ ,  $p<0.001$ ) as well as patients with combined problematic alcohol use and probable drug dependence ( $B = 35.80$ ,  $p = 0.008$ ) had worse outcomes on LSAS-SR than patients with no problematic substance use.

In terms of within-group effect sizes for the different substance use categories of patients treated for depression, these ranged between  $d=0.95$  and  $d=1.45$ . For patients treated for panic disorder effect sizes ranged between  $d=0.96$  and  $d=2.80$  with the exception of patients with harmful alcohol use, with an effect size of  $d=0.56$  and probable alcohol dependence  $d=0.76$ . In the group treated for social anxiety effect sizes ranged between  $d=0.66$  and  $d=1.08$  with some exceptions, patients with harmful alcohol use  $d=0.21$ , hazardous drug use  $d=0.04$  and combined probable dependent drug use and problematic alcohol use  $d=-1.99$ . An aberrant finding was that three individuals with combined hazardous drug use and problematic alcohol use had a markedly *higher* effect size ( $d=1.92$ ).

### 3.4.4 Discussion

To my knowledge this was the first study to examine substance use among a population of patients receiving treatment in regular care at an ICBT clinic. The prevalence of substance use in this cohort was higher in this study than in earlier studies of patients in psychiatry (56, 57). In terms of outcomes there was no negative association between having problematic substance use and having worse treatment outcomes for depression. For panic disorders negative outcomes and lower effect sizes were situated in the different exclusive alcohol use categories, and for social anxiety disorders hazardous drug users, and the two individuals with probable drug dependence combined with problematic alcohol use fared worse in terms of outcomes of therapy. In most other categories, with some exceptions effect sizes for treatment in the different categories are comparable or better than for patients without substance use. This implies that with some exceptions, baseline substance use does not preclude receiving ICBT treatment. Further notice should be taken of the subgroups that seem to have worse outcomes, and alternative modes of treatment considered.

It is important to note that at the intake appointment with a psychiatrist at the clinic, patients are excluded if ICBT is deemed not suitable for them at this time. Good effects for the patients treated when having baseline substance use can definitely be an effect of appropriate inclusion and exclusion. There was no access to data on reasons for exclusion available for these analyses, and further research on this in a future study would be suggested. The prevalence study suggests that this population could benefit from treatment focused on substance use, and research on offering patients in ICBT some mode of treatment for this is warranted. Another suggestion for future studies would be to include a post-treatment measurement of substance use and research the effects of the ICBT treatment for the main diagnosis, i.e. depression, panic disorder, social anxiety disorder and irritable bowel syndrome (added to the regularly treated disorders after this study) on substance use.

## 4 SUMMARY TABLE OF STUDIES

	<b>Aim</b>	<b>Design</b>	<b>Population</b>	<b>Outcome measures</b>	<b>Main findings</b>
<b>STUDY I</b>	To study feasibility and effect of an 8-module self-help Internet intervention	Randomization into three groups:  [1] Internet self-help-program only;  [2] Internet self-help program and guidance through choice between asynchronous message or synchronous chat;  [3] Internet self-help program and guidance through asynchronous messages.	Individuals seeking help over the Internet (n=80) with problematic alcohol use.	Primary outcome:  [1] Timeline Follow Back (TLFB).  Secondary outcomes:  [2] The Alcohol Use Disorders Identification Test (AUDIT);  [3] The Drug Use Disorders Identification Test (DUDIT);  [4] The Hospital Anxiety and Depression Scale (HADS);  [5] The Readiness to Change Questionnaire (RCQ);  [6] The Readiness Ruler;  [7] EuroQol-5 dimension (EQ-5D);  [8] The World Health Organization Quality of Life Scale-abbreviated version (WHOQOL-BREF)	<i>At 10-week follow-up:</i>  Reduced TLFB and AUDIT in group 2 and 3 versus group 1.  Higher proportion would recommend the program to others in groups 2 and 3 versus group 1.
<b>STUDY II</b>	To study effects of two Swedish-language smartphone apps with real-time estimated blood alcohol concentration (eBAC) feedback in comparison to controls.	Randomization into three groups:  [1] Promillekoll - Swedish government alcohol monopoly's app  [2] PartyPlanner – app developed by the research group;  [3] Control group	University students (n=1932) with risky alcohol consumption.	Primary outcome:  [1] The Daily Drinking Questionnaire (DDQ)  Secondary outcomes:  [2] The Alcohol Use Disorders Identification Test (AUDIT);  [3] Self-reported data on [a] app usage, and [b] users' perception of the apps.	<i>At 7-week follow-up:</i>  Increased DDQ drinking occasions /week in males in group 1 versus group 3.
<b>STUDY III</b>	To evaluate the effects of offering university students with excessive alcohol	Randomization into two groups:  [1] TeleCoach –app focused on skills	University students (n=186) reporting excessive weekly alcohol consumption. A	The Daily Drinking Questionnaire (DDQ).	<i>At 6-week follow-up:</i>  Reduced quantity of drinking in group 1

	consumption, already enrolled in a parallel study on smartphone apps with real-time estimated blood alcohol concentration (eBAC) feedback, access to an additional app focused on skills training.	training, in addition to app with real-time BAC feedback.  [2] Wait list in addition to app with real-time BAC feedback.  Comparison to a third group:  [3] Untreated control group with assessment only.	control group with university students (n=144) with excessive weekly alcohol consumption and no access to any apps.	Primary outcome:  [1] Excessive weekly consumption.  Secondary outcomes  [2] Quantity of drinking  [3] Frequency of drinking	versus group 3.  <i>At 6-and 12-week follow-ups:</i>  Reduced proportions of excessive alcohol consumption in groups 1 and 2 versus group 3  Reduced frequency of drinking in group 1 versus group 3.  Odds for eliminating excessive alcohol consumption were higher in group 1 versus group 3. This was true for both men and women.
<b>STUDY IV</b>	To study prevalence and effect of patients' problematic substance use.	No comparison group.	Patients (n=1601) participating in internet-based cognitive behavioral therapy (ICBT)	[1] The Alcohol Use Disorders Identification Test (AUDIT);  [2] The Drug Use Disorders Identification Test (DUDIT);  [3] Montgomery Åsberg Depression Rating Scale –Self-rated (MADRS-S)  [4] Panic Disorder Severity Scale – Self-Rating version (PDSS-SR);  [5] Liebowitz Social Anxiety Scale – Self-Rating version (LSAS-SR)	Problematic substance use (AUDIT ≥8 for men, ≥6 for women; DUDIT ≥1) occurred among 32.4% of the patients; 24.1% only alcohol, 4.6% only drugs, and 3.7% combined alcohol and drug use.  Hazardous alcohol use and probable alcohol dependence negatively affected panic disorder outcomes.  Hazardous drug use led to worse social anxiety outcomes.  Depression outcomes were not affected by substance use.  Treatment adherence was negatively affected by problematic drug use among men and 25–34 year olds.  Combined substance use negatively affected adherence for women and 35–64 year olds.

## 5 CONCLUDING DISCUSSION

The overall aim of this thesis was to research digital interventions both when used for reducing problematic alcohol use and, also, the presence of and effects of having problematic substance on treatment outcomes of digital interventions for problems other than substance use. The focus was more specifically on using digital technology to reduce problematic alcohol consumption, and also to research a population using existent digital technology in a different area of mental health to identify prevalences of problematic substance use and any association of substance use with treatment outcomes. This latter research could assist decision-making for the future when it comes to problematic substance use in this population.

The specific aims of the studies were:

- To conduct a pilot study on the feasibility of giving individuals seeking help on the Internet for problematic alcohol use a module-based self-help program, and to perform preliminary analyses of the effects of adding guidance by a counselor.
- To evaluate the effects of giving university students with problematic drinking access to one of two smartphone apps built around the concept of real-time eBAC feedback, one app with the added functionality of planning a drinking event ahead of time.
- To investigate effects of giving access to an additional skills-training smartphone app to university students having excessive weekly alcohol consumption six weeks into a study on real-time eBAC feedback.
- To research substance use prevalence at baseline in a population of psychiatry patients in regular ICBT care for depression, social anxiety disorder and panic disorder and to study associations between baseline problematic substance and therapy outcomes.

### 5.1 PRIMARY FINDINGS

#### 5.1.1 Characteristics of participants

In the different studies, the focus was on somewhat different populations, Internet help seekers (STUDY I), university students with problematic or excessive alcohol consumption (STUDIES II & III) and psychiatry patients either self-referred via Internet or via a physician (STUDY IV). What unites them is that all participants were users of novel communication technology for health purposes. A run-through of participant characteristics over the studies follows.

##### 5.1.1.1 Alcohol use

In STUDIES I-III, inclusion and randomization was contingent on having problematic alcohol consumption, whereas in STUDY IV the prevalence of problematic consumption was investigated. The mean AUDIT score for participants in Study I was the highest, and was indicative of probable alcohol dependence (20); the reported weekly consumption at baseline of 29.4 standard glasses is far higher than the Swedish Public Health Authority's

recommendations. Participants in STUDIES II and III were university students with AUDIT scores indicative of hazardous consumption. In the first study one-third of the students drank above weekly recommendations, and also had two binge drinking events on average the preceding week. The second study, due to inclusion criteria, consisted of 100% excessive weekly drinkers, with an average of close to two binge sessions the preceding week. The focus in STUDY IV was different, but nevertheless revealed that there is a large proportion, nearly one third, of individuals with hazardous and even more severe alcohol and/or drug consumption in this digital intervention-using psychiatric population.

#### 5.1.1.2 Gender

Women were more frequently represented in all studies, except for STUDY II where gender proportions were about 50/50. It is unclear if this equal proportion reflects an interest in specifically alcohol-related interventions in the population or whether other factors, such as the iPad lottery or being enrolled in a university affected participation rates. In STUDY III, where participants were recruited from a study very similar to STUDY II, there was a higher prevalence of women. This means that of those invited due to excessive weekly alcohol use, and those willing to try another app, more were women. It is established that more women search for health information online (43). The proportion of women in STUDY III is in line with the proportions in STUDY I, consisting of online help seekers. In STUDY IV women were also represented to a higher degree. Here, the intake procedure is a little more complicated than pure self-referral, with an intake psychiatrist influencing inclusion, but perhaps the higher propensity of women to go online when searching for help is also reflected in the context of online psychiatric treatment.

#### 5.1.1.3 Age

STUDIES II and III were comprised of university students, so it is reasonable that the average age of the participants was around 25 years of age. In STUDY I the average age was the highest at 42 years of age. This is somewhat counter to the finding that younger people seek health information to a larger degree (43). The average age for STUDY IV was 36, which is in line with other studies on psychiatric populations (62, 63).

### 5.1.2 Reaching the intended population

The studies in this thesis did not explicitly examine the question of whether the participants with problematic use in the studies were individuals that would not be reached by other modes of care, or for whom other care modes would not be appropriate. What is clear from the numbers of participants and their scores on various indicators of problematic alcohol and substance use is that the studies did reach groups of affected individuals. STUDY IV, with a focus on researching the existence of a problem, also revealed that there is a potential of reaching a population affected by problematic use through an ICBT clinic.

### **5.1.3 Problematic substance use and intervention effects**

The studies in this thesis focus on different kinds of interventions, and it is not easy to summarize the results of the interventions in a short paragraph. Here is a quick summary of the various results. STUDY I showed a clear advantage of adding guidance to the eight-module self-help program, but results were not compared to an untreated control group, making it hard to draw further conclusions. The reduction in weekly consumption was high enough to warrant further research on delivering Internet interventions to individuals with problematic alcohol drinking. STUDY II did not show any improvements in alcohol-related outcomes for the eBAC smartphone interventions. One of the interventions in fact showed a heightened frequency of drinking for men, but one should bear in mind that quantity was not affected. STUDY III did show positive effects for the intervention and wait-list group, with the intervention group showing more and stronger results. In STUDY IV, no intervention was offered to reduce problematic substance use, but the effects of problematic substance use on ICBT were examined, finding no effects for participants treated for depression, but negative effects for patients treated for panic anxiety and social phobia. This suggests a need for interventions addressing problematic substance use for at least some sub-groups in the population of patients in psychiatry.

## **5.2 LIMITATIONS**

### **5.2.1 Lack of objective data**

In STUDIES II and III there was a lack of objective data collected on app usage by the participants. This is a critical loss of information due to the fact that knowledge about factual use of the smartphone app could make it possible to draw conclusions relating to the use of the app as opposed to only knowing that group members were offered access to an app. For STUDY II an additional piece of information that could help complete the puzzle is knowing what amounts of alcohol were actually entered into the apps, and the resulting eBACs. This of course would not give any information about whether or not the data entered were valid or just experimentation/play. In this study, as in all the studies in this thesis, analyses relied on self-reported data, which are known to be insecure in that substance use may be under-reported (64, 65). Then again, all instruments were administered over computer and some studies point to higher reports of consumption for computerized versions of substance use screening instruments (66, 67). Corroborating evidence in form of blood samples or a Breathalyzer test would be needed to ascertain the factual alcohol consumption. This would not have been feasible in these studies, where researchers were remote from study participants, and would call for a major overhaul of the study designs. For STUDY III information on what actual components and parts of the skills training app were actually used would help make a connection between app use, and which parts of the app would seem to influence alcohol consumption.

### **5.2.2 Lack of information on absent invitees/patients**

In STUDY II no information is available on what distinguished the 4823 individuals who decided to join study from the 23751 who never answered the invitation to participate. This means there may be implications for the generalizability of the data to university students in general. In STUDY IV no information is available about the patients who were excluded by the physician at intake. Results pointing to the limited effect of baseline substance use on therapy outcomes may to some extent be an effect of efficient patient exclusion. This does of course not contradict the finding that substance use may have a limited effect on therapy outcomes for ICBT patients, but it may be that the statement that substance use is no obstacle to effective ICBT treatment is only true for certain individuals.

### **5.2.3 Attrition**

We had attrition levels of 29.4%-37.3% in the three intervention STUDIES I-III. Attrition makes it difficult to draw conclusions on the data, since there is little chance of knowing if there is any systematic pattern behind participants' dropping out. Attrition analyses were performed based on baseline data, and in STUDY III there were no baseline differences between the attrited individuals and completers. In STUDY I, participants not responding at follow-up reported lower physical and environmental wellbeing, and in STUDY II, participants not responding in the PartyPlanner and control groups had more severe baseline levels of alcohol use on several alcohol-related measures. This difference was not seen in the Promillekoll group. Attrition was differential in STUDIES I and II. This is a threat to internal validity, since the phenomenon of individual dropout may also be a reflection of individuals' perception of the intervention or factors surrounding the presentation of it, making it more uncertain whether the differences seen are an effect of the intervention or all the possible influences causing individuals to drop out.

### **5.2.4 Follow-up times**

Follow-up times in all intervention studies (STUDIES I-III) were fairly short and ranged between seven and 12 weeks. A recent review on electronic interventions concluded that there is support for short-term effects, but little evidence for longer-term effects (12).

## **5.3 CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS**

The ubiquity, and interactive communication capabilities of smartphones and Internet access makes it easy to motivate further research on health-related interventions delivered this way. Interventions delivered this way are often grouped together as eHealth, or mHealth, as if Internet or smartphone interventions were all very similar. However, using different devices constitutes different ways of delivering content. Research on the content that can be delivered this way, how to deliver it optimally, and also deliver new types of interventions made possible by this technology still needs to be done.

As previously described, all studies managed to reach a fairly problem-laden group of individuals. The high screening and consumption scores in STUDY I meant that using a well-



known web site such as alkoholhjalpen.se for recruitment reaches a problem-laden population, and strengthens the importance of making researched intervention programs available through such a channel. Where only a small proportion of the students invited from the beginning to STUDY II and the study preceding STUDY III gave informed consent, nevertheless large numbers of individuals with problematic consumption were reached. It is easy to argue that the different paths of recruitment could be relevant for reaching individuals with problematic substance use. Determining how large a proportion of those reached belong to a group that would not be reached otherwise via ordinary healthcare, due to a variety of life circumstances such as time constraints or to avoid stigma, is an interesting avenue for future research on digital interventions.

In this thesis STUDY I revealed that there is value in continuing to research treatment over the Internet with guidance, with larger, randomized controlled methodology. Further research can compare the Internet-delivered treatment to already established face-to-face treatment. Depending on results of such future studies there may be a place for delivering treatment programs for problematic substance use in regular care over the Internet, as the Stockholm ICBT clinic successfully does for other disorders today.

When it comes to the two studies on smartphone apps, research on smartphone apps for problematic alcohol use is still in its infancy. STUDY II did not raise hopes for the effectiveness of eBAC feedback intervention apps for university students with problematic alcohol consumption. However, the way the apps were designed may not have been the optimal way of presenting this intervention. Some suggestions for future research are: combining eBAC with other components in an app, testing it with a more actively help-seeking population, and adding treatment provider contact.

STUDY III did offer positive results, but to further establish the efficacy of delivering RP skills training in the TeleCoach™ format some more research is needed. Clearer data are needed on the extent to which the intervention group actually uses the app, as well as comparing the intervention group to an untreated group receiving the same message about excessive consumption. Working in these directions would enable disentangling effects of a personal message about excessive alcohol consumption from the effects of the app and its use.

STUDY IV can be interpreted as adding support to the clinical procedure of offering ICBT treatment to most patients after the intake meeting with a psychiatrist, even when there is some problematic substance use present. STUDY IV results also suggest the need to more vigilantly follow those groups for whom baseline substance use seems detrimental to ICBT. It may be that certain groups of substance users will need to be excluded, or treatment somehow modified if the future shows that this still holds. The study opens up for more research on developing and providing brief interventions to be given as an adjunct to patients' treatment without encroaching too much further on their time. Also, future studies on ICBT treatment with post-treatment measures of substance use can enlighten the clinical research community further regarding the effects of current ICBT treatment on problematic consumption.

There is a need for longer follow-ups in future studies. Although STUDY II did not show much in the way of short-term, a longer study horizon could reveal possible effects in the longer term.

## **5.4 CONCLUSIONS**

- Using novel communications technology is an effective way to reach individuals with problematic substance use, both for the general help-seeking population who use the Internet, and for reaching out to large numbers of university students via email.
- Adding counselor guidance to a web-based RP program has beneficial effects, and participants reduce their problematic drinking.
- Smartphone apps relying on eBAC feedback do not show much promise at the moment. There are preliminary indications that skills-training smartphone apps may have a beneficial effect on excessive alcohol consumption.
- The prevalence of problematic substance use is high in ICBT-treated psychiatric outpatients. For many levels of baseline substance use, the negative effect on therapy received seems limited.

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## 7 REFERENCES

1. Center for the Digital Future. World Internet Project - International report, Sixth edition. 2016.
2. Findahl O, Davidsson P. Svenskarna och internet [The Swedes and the internet]: The Internet Foundation in Sweden; 2015. Available from: [https://www.iis.se/docs/Svenskarna\\_och\\_internet\\_2015.pdf](https://www.iis.se/docs/Svenskarna_och_internet_2015.pdf).
3. Broadband Commission. The state of broadband 2015: Broadband as a foundation for sustainable development. Geneva, Switzerland: ITU/UNESCO; 2015. Available from: <http://www.broadbandcommission.org/Documents/reports/bb-annualreport2015.pdf>.
4. World Health Organization. Global status report on alcohol and health. Geneva, Switzerland 2014. Available from: [http://www.who.int/substance\\_abuse/publications/global\\_alcohol\\_report/en/](http://www.who.int/substance_abuse/publications/global_alcohol_report/en/).
5. World Health Organization. Atlas on substance use (2010): resources for the prevention and treatment of substance use disorders. Geneva, Switzerland 2010. Available from: [http://www.who.int/substance\\_abuse/publications/Media/en/](http://www.who.int/substance_abuse/publications/Media/en/).
6. Anthes E. Mental health: There's an app for that. Nature [Internet]. 2016 20160430; 532(7597). Available from: <http://www.nature.com/news/mental-health-there-s-an-app-for-that-1.19694>.
7. Hieftje K, Edelman E, Camenga DR, Fiellin LE. Electronic media-based health interventions promoting behavior change in youth: A systematic review. JAMA Pediatrics. 2013;167(6):574-80.
8. Hedman E, Ljótsson B, Kaldø V, Hesser H, El Alaoui S, Kraepelien M, et al. Effectiveness of Internet-based cognitive behaviour therapy for depression in routine psychiatric care. J Affect Disord. 2014;155(0):49-58.
9. Hedman E, Ljótsson B, Rück C, Bergström J, Andersson G, Kaldø V, et al. Effectiveness of Internet-based cognitive behaviour therapy for panic disorder in routine psychiatric care. Acta Psychiatr Scand. 2013;128(6):457-67.
10. El Alaoui S, Hedman E, Kaldø V, Hesser H, Kraepelien M, Andersson E, et al. Effectiveness of Internet-Based Cognitive-Behavior Therapy for Social Anxiety Disorder in Clinical Psychiatry. Journal of Consulting & Clinical Psychology. 2015;83(5):902-14.
11. Riper H, Spek V, Boon B, Conijn B, Kramer J, Martin-Abello K, et al. Effectiveness of E-Self-help Interventions for Curbing Adult Problem Drinking: A Meta-analysis. J Med Internet Res. 2011;13(2).
12. Dedert EA, McDuffie JR, Stein R, McNeil JM, Kosinski AS, Freiermuth CE, et al. Electronic Interventions for Alcohol Misuse and Alcohol Use Disorders A Systematic Review. Ann Intern Med. 2015;163(3):205-+.

13. Andersson C. Comparison of WEB and Interactive Voice Response (IVR) Methods for Delivering Brief Alcohol Interventions to Hazardous-Drinking University Students: A Randomized Controlled Trial. *Eur Addict Res.* 2015;21(5):240-52.
14. Berman AH, Gajecki M, Sinadinovic K, Andersson C. Mobile Interventions Targeting Risky Drinking Among University Students: A Review. *Current Addiction Reports.* 2016:1-9.
15. Keoleian V, Polcin D, Galloway GP. Text Messaging for Addiction: A Review. *J Psychoactive Drugs.* 2015;47(2):158-76.
16. Andréasson S, Allebeck P. *Alkohol och hälsa [Alcohol and Health]: The Swedish National Institute of Public Health; 2005.*
17. World Health Organization. *The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines.* Geneva: World Health Organization; 1992.
18. American Psychiatric Association. *Diagnostic and Statistical Manual of mental Disorders (DSM-V).* 5th ed. Washington, DC: American Psychiatric Association; 2013.
19. Saunders JB, Aasland OG, Babor TF, Delafuente JR, Grant M. Development of the alcohol-use disorders identification test (AUDIT) - who collaborative project on early detection of persons with harmful alcohol-consumption-II. *Addiction.* 1993;88(6):791-804.
20. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. *AUDIT The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care.* 2 ed. Geneva: World Health Organization; 2001.
21. Bergman H, Kallmen H. Alcohol use among Swedes and a psychometric evaluation of the Alcohol Use Disorders Identification Test. *Alcohol Alcohol.* 2002;37(3):245-51.
22. Nolen-Hoeksema S. Gender differences in risk factors and consequences for alcohol use and problems. *Clin Psychol Rev.* 2004;24(8):981-1010.
23. National Highway Traffic Safety Administration. Computing a BAC estimate 1994 20131202. Available from: [http://www.craftbeer.com/attachments/0000/1170/Computing\\_a\\_BAC\\_Estimate.pdf](http://www.craftbeer.com/attachments/0000/1170/Computing_a_BAC_Estimate.pdf).
24. Fillmore MT, Jude R. Defining "binge" drinking as five drinks per occasion or drinking to a.08% BAC: Which is more sensitive to risk? *Am J Addict.* 2011;20(5):468-75.
25. Dimeff LA. *Brief Alcohol Screening and Intervention for College Students (BASICS) : a harm reduction approach.* New York: Guilford Press; 1999. xii, 200 p. p.
26. Fachini A, Aliane PP, Martinez EZ, Furtado EF. Efficacy of brief alcohol screening intervention for college students (BASICS): a meta-analysis of randomized controlled trials. *Substance Abuse Treatment, Prevention, and Policy.* 2012;7(1):1-10.
27. Berman AH, Bergman H, Palmstierna T, Schlyter F. Evaluation of the Drug Use Disorders Identification Test (DUDIT) in criminal justice and detoxification settings and in a Swedish population sample. *Eur Addict Res.* 2005;11(1):22-31.

28. Berman AH, Wennberg P, Källmén H. AUDIT och DUDIT – identifiera problem med alkohol och droger [AUDIT and DUDIT - identifying problematic use of alcohol and drugs]. Stockholm: Gothia förlag.; 2012.
29. Sinadinovic K, Berman AH, Hasson D, Wennberg P. Internet-based assessment and self-monitoring of problematic alcohol and drug use. *Addict Behav.* 2010;35(5):464-70.
30. Cunningham JA, Wild TC, Cordingley J, van Mierlo T, Humphreys K. A randomized controlled trial of an internet-based intervention for alcohol abusers. *Addiction.* 2009;104(12):2023-32.
31. Blankers M, Koeter MWJ, Schippers GM. Internet Therapy Versus Internet Self-Help Versus No Treatment for Problematic Alcohol Use: A Randomized Controlled Trial. *J Consult Clin Psychol.* 2011;79(3):330-41.
32. Sinadinovic K, Wennberg P, Johansson M, Berman AH. Targeting Individuals with Problematic Alcohol Use via Web-Based Cognitive-Behavioral Self-Help Modules, Personalized Screening Feedback or Assessment Only: A Randomized Controlled Trial. *Eur Addict Res.* 2014;20(6):305-18.
33. Wallace P, Murray E, McCambridge J, Khadjesari Z, White IR, Thompson SG, et al. On-line Randomized Controlled Trial of an Internet Based Psychologically Enhanced Intervention for People with Hazardous Alcohol Consumption. *PLoS One.* 2011;6(3).
34. Postel MG, De Haan HA, De Jong CAJ. Evaluation of an E-Therapy Program for Problem Drinkers: A Pilot Study. *Subst Use Misuse.* 2010;45(12):2059-75.
35. Riper H, Blankers M, Hadiwijaya H, Cunningham J, Clarke S, Wiers R, et al. Effectiveness of Guided and Unguided Low-Intensity Internet Interventions for Adult Alcohol Misuse: A Meta-Analysis. *PLoS One.* 2014;9(6):e99912.
36. Cavanagh K, Millings A. (Inter)personal Computing: The Role of the Therapeutic Relationship in E-mental Health. *Journal of Contemporary Psychotherapy.* 2013;43(4):197-206.
37. Crane D, Garnett C, Brown J, West R, Michie S. Behavior Change Techniques in Popular Alcohol Reduction Apps: Content Analysis. *J Med Internet Res.* 2015;17(5).
38. Cohn AM, Hunter-Reel D, Hagman BT, Mitchell J. Promoting Behavior Change from Alcohol Use Through Mobile Technology: The Future of Ecological Momentary Assessment. *Alcohol Clin Exp Res.* 2011;35(12):2209-15.
39. Weaver ER, Horyniak DR, Jenkinson R, Dietze P, Lim MSC. Let's get wasted! and other apps: Characteristics, acceptability, and use of alcohol-related smartphone applications. *J Med Internet Res.* 2013;15(6).
40. Meredith S, Alessi S, Petry N. Smartphone applications to reduce alcohol consumption and help patients with alcohol use disorder: a state-of-the-art review. *Adv Health Care Technol.* 2015;1:47-54.
41. Sinadinovic K, Wennberg P, Berman AH. Population screening of risky alcohol and drug use via Internet and Interactive Voice Response (IVR): A feasibility and psychometric study in a random sample. *Drug Alcohol Depend.* 2011;114(1):55-60.
42. Kallmen H, Wennberg P, Leifman H, Bergman H, Berman AH. Alcohol Habits in Sweden during 1997-2009 with Particular Focus on 2005 and 2009, Assessed with the AUDIT: A Repeated Cross-Sectional Study. *Eur Addict Res.* 2011;17(2):90-6.

43. Fox S, Duggan M. Health online 2013: Pew Research Center's Internet & American Life Project; 2013. Available from: <http://pewinternet.org/Reports/2013/Health-online.aspx>.
44. Johnston L, O'Malley P, Bachman J, Schulenberg J, Miech R. Monitoring the Future national survey results on drug use, 1975–2014: Volume 2, College students and adults ages 19-55. Ann Arbor: Institute for Social Research, The University of Michigan 2015.
45. Kypri K, Cronin M, Wright CS. Do university students drink more hazardously than their non-student peers? *Addiction*. 2005;100(5):713-4.
46. O'Neill SE, Parra GR, Sher KJ. Clinical relevance of heavy drinking during the college years: Cross-sectional and prospective perspectives. *Psychol Addict Behav*. 2001;15(4):350-9.
47. Buscemi J, Murphy JG, Martens MP, McDevitt-Murphy ME, Dennhardt AA, Skidmore JR. Help-Seeking for Alcohol-Related Problems in College Students: Correlates and Preferred Resources. *Psychol Addict Behav*. 2010;24(4):571-80.
48. Cellucci T, Krogh J, Vik P. Help seeking for alcohol problems in a college population. *J Gen Psychol*. 2006;133(4):421-33.
49. Bendtsen M, Bendtsen P. Feasibility and user perception of a fully automated push-based multiple-session alcohol intervention for university students: Randomized controlled trial. *J Med Internet Res*. 2014;16(6).
50. Riordan BC, Conner TS, Flett JAM, Scarf D. A Brief Orientation Week Ecological Momentary Intervention to Reduce University Student Alcohol Consumption. *J Stud Alcohol Drugs*. 2015;76(4):525-9.
51. Witkiewitz K, Kirouac M, Desai SA, Bowen S, Leigh BC, Larimer ME. Development and Evaluation of a Mobile Intervention for Heavy Drinking and Smoking Among College Students. *Psychol Addict Behav*. 2014;28(3):639-50.
52. Gajekki M, Berman AH, Sinadinovic K, Rosendahl I, Andersson C. Mobile phone brief intervention applications for risky alcohol use among university students: A randomized controlled study. *Addict Sci Clin Pract*. 2014;9:11.
53. Mason M, Benotsch EG, Way T, Kim H, Snipes D. Text messaging to increase readiness to change alcohol use in college students. *The Journal of Primary Prevention*. 2014;35(1):47-52.
54. Moore SC, Crompton K, van Goozen S, van den Bree M, Bunney J, Lydall E. A feasibility study of short message service text messaging as a surveillance tool for alcohol consumption and vehicle for interventions in university students. *BMC Public Health*. 2013;13:1011.
55. Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, et al. Comorbidity of mental-disorders with alcohol and other drug-abuse - results from the epidemiologic catchment-area (ECA) study. *J Am Med Assoc*. 1990;264(19):2511-8.
56. Eberhard S, Nordstrom G, Hoglund P, Ojehagen A. Secondary prevention of hazardous alcohol consumption in psychiatric out-patients: a randomised controlled study. *Soc Psychiatry Psychiatr Epidemiol*. 2009;44(12):1013-21.



57. Cruce G, Nordström L, Öjehagen A. Risky use and misuse of alcohol, drugs and cigarettes detected by screening questionnaires in a clinical psychosis unit. *Nordic Journal of Psychiatry*. 2007;61(2):92-9.
58. American Psychiatric Association. *Diagnostic and Statistical Manual of mental Disorders, Third edition, Revised*. Washington, DC: American Psychiatric Association; 1987.
59. Svanborg P, Asberg M. A new self-rating scale for depression and anxiety-states based on the comprehensive psychopathological rating-scale. *Acta Psychiatr Scand*. 1994;89(1):21-8.
60. Fresco DM, Coles ME, Heimberg RG, Liebowitz MR, Hami S, Stein MB, et al. The Liebowitz Social Anxiety Scale: a comparison of the psychometric properties of self-report and clinician-administered formats. *Psychol Med*. 2001;31(6):1025-35.
61. Houck PR, Spiegel DA, Shear MK, Rucci P. Reliability of the self-report version of the Panic Disorder Severity Scale. *Depress Anxiety*. 2002;15(4):183-5.
62. Eberhard S, Nordström G, Öjehagen A. Hazardous alcohol use in general psychiatric outpatients. *Journal of Mental Health*. 2015;24(3):162-7.
63. Nehlin C, Grönbladh L, Fredriksson A, Jansson L. Alcohol and Drug Use, Smoking, and Gambling Among Psychiatric Outpatients: A 1-Year Prevalence Study. *Subst Abus*. 2013;34(2):162-8.
64. Harrison LD, Hughes A. *The validity of self-reported drug use: Improving the accuracy of survey estimates* Rockville, MD: US Department of Health and Human Services, National Institutes of Health; 1997.
65. Stockwell T, Donath S, Cooper-Stanbury M, Chikritzhs T, Catalano P, Mateo C. Under-reporting of alcohol consumption in household surveys: a comparison of quantity-frequency, graduated-frequency and recent recall. *Addiction*. 2004;99(8):1024-33.
66. Kallmen H, Sinadinovic K, Berman AH, Wennberg P. Risky drinking of alcohol in Sweden: A randomized population survey comparing web- and paper-based self-reports. *Nord Stud Alcohol Drugs*. 2011;28(2):123-30.
67. Wang Y-C, Lee C-M, Lew-Ting C-Y, Hsiao CK, Chen D-R, Chen WJ. Survey of substance use among high school students in Taipei: Web-based questionnaire versus paper-and-pencil questionnaire. *J Adolesc Health*. 2005;37(4):289-95.