# Self-help applications for problematic alcohol use in primary care: a systematic review

Jonas Laenens, Catholic University of Leuven

Dries Munters, Catholic University of Leuven

Promotor: Van Nuland Marc, Catholic University of Leuven

Master of Family Medicine

Masterproef Huisartsgeneeskunde

Academiejaar: [2021 – 2022]

*Deze masterproef is een examendocument dat niet werd gecorrigeerd voor eventueel vastgestelde fouten. Zonder voorafgaande schriftelijke toestemming van zowel de promotor(en) als de auteur(s) is overnemen, kopiëren, gebruiken of realiseren van deze uitgave of gedeelten ervan verboden. Voor aanvragen tot of informatie i.v.m. het overnemen en/of gebruik en/of realisatie van gedeelten uit deze publicatie, wendt u tot de universiteit waaraan de auteur is ingeschreven.*

*Voorafgaande schriftelijke toestemming van de promotor(en) is eveneens vereist voor het aanwenden van de in dit afstudeerwerk beschreven (originele) methoden, producten, schakelingen en programma's voor industrieel of commercieel nut en voor de inzending van deze publicatie ter deelname aan wetenschappelijke prijzen of wedstrijden.*

# Table of contents


ABSTRACT ..... 4

ABSTRACT – DUTCH ..... 5

ABBREVIATION LIST ..... 6

INTRODUCTION ..... 7

METHODS ..... 10

RESULTS ..... 12

STUDY SELECTION ..... 12

STUDY SETTING AND PARTICIPANT RECRUITMENT ..... 14

POPULATION CHARACTERISTICS ..... 14

INTERVENTION AND COMPARISON TREATMENT ..... 15

STUDY DURATION AND LOSS OF FOLLOW-UP ..... 16

OUTCOME MEASURES ..... 16

EFFICACY OF MCBT INTERVENTIONS IN COMPARISON TO TREATMENT AS USUAL ..... 17

STUDY QUALITY ..... 19

DISCUSSION ..... 22

ACKNOWLEDGEMENTS ..... 25

REFERENCES ..... 26

APPENDIX ..... 35

APPENDIX 1: SEARCH STRATEGY ..... 35

APPENDIX 2: WEB OF SCIENCE COLLECTIONS ..... 40

APPENDIX 4: LOGBOOK ..... 44

APPENDIX 5: SELF-REFLECTION ..... 45

# Abstract

Problematic alcohol use remains an important source of morbidity and mortality in current society. Despite the availability of evidence-based treatments, a lot of patients don't get the help they need. mHealth is a promising tool to close this treatment gap with substantial evidence in various health challenges. While online brief interventions (BI) for alcohol misuse have been investigated more thoroughly, research on mHealth using cognitive behaviour therapy (CBT) is however limited, especially in primary care. In this systematic review we want to investigate the efficacy of mobile applications or websites using CBT-techniques for problematic alcohol use in comparison to treatment as usual in a western primary-care setting. We searched for RCT's from 2010 onwards. Studies including participants under the age of 16 or requiring specific comorbidities were excluded. We carried out a literature search on 7 May 2021 in the following 4 databases: PubMed, Embase, Web of Science and Cochrane Library. A total of 3437 articles were independently screened by the two reviewers. The eight included articles were independently evaluated for bias using the ROB-2 tool. Due to heterogeneity in our included studies we decided to elaborate a narrative review. Our review shows a small but inconsistent effect in favour of mCBT in comparison to a waiting list or online BI. However, data is sparse, most studies recruited participants in the general population and non-inferiority to a face-to-face BI in a general practitioner's (GP) office could not be demonstrated. To make more robust statements about the effectiveness of mCBT interventions in a GP's office, more research is needed in a primary care setting involving general practises in Western countries.

This review was realised with support from the Catholic University of Leuven. Approval was granted by the ethical commission for medical research of the University Hospital of Leuven. No other funding or relevant conflicts of interest are worth mentioning.

# Abstract – Dutch

Problematisch alcoholgebruik blijft een belangrijke bron van morbiditeit en mortaliteit in onze samenleving. Ondanks de beschikbaarheid van wetenschappelijk-onderbouwde behandelingen vinden vele patiënten momenteel de weg naar de zorg niet. mHealth is een veelbelovende instrument om deze kloof te overbruggen en is reeds onderzocht bij vele andere aandoeningen. Terwijl online korte interventies bij problematisch alcoholgebruik reeds beter zijn onderbouwd, hinkt het onderzoek naar mHealth op basis van cognitieve gedragstechnieken (CGT) nog achterop, zeker in de eerste lijn. In deze systematische review onderzoeken we de effectiviteit van mobiele applicaties of websites die gebruikmaken van CGT-technieken bij problematisch alcoholgebruik in vergelijking met de gebruikelijke zorg in de westerse eerste lijn. We zochten naar gerandomiseerde gecontrolleerde studies vanaf 2010. We excludeerden studies die patiënten onder 16 jaar includeerden of die specifieke comorbiditeiten vereisten. We voerden onze zoekopdracht uit op 7 mei 2021 in de volgende 4 databanken: PubMed, Embase, Web of Science en Cochrane Library. De twee reviewers screenden de 3437 artikels onafhankelijk van elkaar. Hierna evalueerden ze op onafhankelijke wijze de acht geïncludeerde artikels op bias, door gebruik te maken van de ROB-2 tool. We kozen ervoor om een narratieve review te schrijven omwille van de heterogeniteit in onze geïncludeerde artikels. Onze resultaten tonen een klein maar inconsistent effect in het voordeel van mCBT in vergelijking met een wachtlijst of online korte interventies. Echter, de gegevens zijn beperkt, het merendeel van de studies includeerde patiënten uit de algemene populatie en gelijkwaardige effectiviteit t.o.v. face-to-face korte interventie bij de huisarts kon niet worden aangetoond. Om een duidelijk conclusie te kunnen trekken over de effectiviteit van mCBT interventies in de huisartsenpraktijk, is meer onderzoek nodig.

Deze review werd gerealiseerd met ondersteuning van de Katholieke Universiteit van Leuven. Ethische goedkeuring werd verleend door de ethische commissie voor medisch onderzoek van het Universitair ziekenhuis van Leuven. Er zijn geen verdere belangenvermenging of gegevens over financiering te vermelden.

# Abbreviation list

| Abbreviation | Meaning |
|---|---|
| App | Application |
| AUDIT | Alcohol Use Disorder Identification Test |
| AUDIT-C | Alcohol Use Disorder Identification Test-Consumption |
| B | Beta weight |
| BAC | Blood alcohol concentration |
| BI | Brief intervention |
| CBT | Cognitive behavioural therapy |
| CI | Confidence interval |
| d | Cohen's d |
| DALY | Disability-adjusted life year |
| DrInC | Drinker Inventory of Consequences |
| e-booklet | Electronic booklet |
| F | F-test |
| FAST | Fast Alcohol Screening Test |
| GP | General practitioner |
| HIV | Human immunodeficiency virus |
| HIVA | Onderzoeksinstituut voor Arbeid en Samenleving |
| ICBT | Internet cognitive behavioural therapy |
| IT | Information technology |
| ITT | Intention to treat |
| KU Leuven | Katholieke Universiteit Leuven |
| M | Median |
| mCBT | Mobile cognitive behavioural therapy |
| MD | ModerateDrinking.com |
| mHealth | Mobile health |
| MM | Moderation management |
| P | P-value |
| PDA | Percentage days of abstinence |
| PICO | Patient Intervention Comparison Outcome |
| PP | Per protocol |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| PTSD | Post-traumatic stress disorder |
| QOL | Quality of life |
| RCT | Randomised controlled trial |
| ROB 2 tool | Version 2 of the Cochrane risk-of-bias tool for randomized trials |
| SAO | Self-help alcohol online |
| SD | Standard deviation |
| t | t-test |
| TAU | Treatment as usual |
| USA | United States of America |
| WL | Waiting list |
| WHO | World Health Organisation |

# Introduction

The use of alcohol is deeply embedded in Belgian culture. According to the 2018 Belgian Health Interview Survey, 77% of Belgians drink alcohol occasionally, whereas 10% drink daily (1). Although alcohol use may be acceptable to some level, excessive alcohol use frequently causes problems for the individual, their direct environment and for society at large. In Belgium, problematic alcohol use remains an important problem. When the definition of 14 units per week for women and 21 for men is used for problematic alcohol use, 6% of the Belgian population older than 15 years drinks excessive amounts of alcohol. When using the cut-off of 10 units per week, this percentage rises to 14%. Binge drinking occurs in 11% of the population, whereof 7% monthly and 4% weekly (1). As expected, problematic alcohol use is a prevalent problem in primary care. A study based on data from six European countries estimates the prevalence of alcohol use disorders at 11,8% (2). In general practices in Flanders data on problematic alcohol use varies between 5 and 15% (3).

The adverse effects of alcohol use can be physical, psychological, or social in nature. The most important physical consequences are susceptibility to infections, physical harm (e.g., during falls), obesity, gastritis, pancreatitis, and liver diseases, neoplastic, neurological, or cardiovascular diseases (4). Psychological adverse effects of alcohol use can consist of mood disorders, sleep disorders, an increased risk of suicide, hallucinations, and early-onset dementia (3). Moreover, alcohol can also affect the environment of the user (e.g., domestic violence, divorce, aggression, traffic accidents) (5). In one study, 18-79% of responders report experiencing negative consequences from the drinking behaviour of others (6–8). Worldwide, the consequences from harmful use of alcohol are estimated at 3 million deaths in 2016 (5,3% of total mortality) and 132,6 million disability-adjusted life years (DALY's) (5,1% of total DALY's in 2016). In Europe, the relative impact of alcohol is even greater with alcohol accounting for 10,1% of deaths and 10,8% of total DALY's (4). Finally, the economic burden of alcohol use is considerable. The Research Institute for Work and Society (HIVA), a multidisciplinary research institution at KU Leuven, calculated the cost of alcohol use for the population over a period from 1999 to 2001 at 4,5 billion euros yearly. The majority of cost originates from light and moderate alcohol usage (9).

The treatment of problematic alcohol use takes place at different levels and in different settings. In primary care, the main goal is to detect the problem, estimate its severity and start a treatment or refer to specialized care. Usually, the treatment in primary care consists of evidence-based brief interventions (BI) (10–12). Cognitive behavioural therapy (CBT) on the other hand, is an evidence-based approach that is often used in specialized settings (13). However, despite the availability of evidence-based treatments, a lot of patients don't get the help they need. In Belgium there is an average of 18 years between onset of symptoms and help-seeking behaviour and eventually only 61% of patients will seek help (14). Common barriers include fear for stigma, lack of insight, unawareness of and lack of confidence in available treatments (14–16). Furthermore, in some subgroups financial and language barriers exist (17). An interesting evolution that may help with this treatment gap is the implementation of mHealth. mHealth is defined by the WHO as the usage of mobile or wireless technology (e.g., smartphones, tablets) to achieve health related goals (18). Possible advantages include the low cost, resolution of language barriers and possibility of 'just in time feedback and support', e.g., administering an intervention when entering a pub or night shop (19–21). mHealth is also readily available, since 80% of adults have access to a mobile phone and 90% have access to the internet (22–24).

Research on mHealth is being conducted for various health challenges e.g., diabetes, obesity, compliance of therapy in HIV (25–28). Next to somatic diseases, mHealth is also being studied in psychiatric conditions like depression, anxiety, PTSD, schizophrenia and addiction to tobacco and other drugs (29–36). Regarding alcohol abuse, we found several reviews investigating technology-delivered interventions (30,37–40). In these systematic reviews the addition of self-help apps to care as usual had possible positive effects on the outcome. However, the effect sizes were small. A potential cause for the small effect sizes that were obtained in previous reviews, is the varying quality of mHealth apps, websites or other software used in therapy. Information on scientific background and underlying methodology are hard to find for a lot of these applications.

Because of the extensive evidence and widespread use in treatment of alcohol use disorders we chose to focus on CBT-based interventions specifically. The evidence on face-to-face CBT can obviously not be readily translated to CBT delivered through mobile platforms. Reviews have been conducted comparing technology-delivered CBT to treatment as usual (face-to-

face treatment, waiting list, placebo pills etc.) in a variety of psychiatric disorders (anxiety disorders, depression, PTSD etc.). These reviews indicate that technology-delivered CBT is an effective treatment for these conditions (41–43). For problematic alcohol use, two reviews have been conducted about CBT-based technology-delivered interventions (23,44). In primary care, we only found two reviews supporting the effectiveness of technology-based interventions for alcohol abuse (45,46). But to our knowledge, a systematic review investigating the efficacy of CBT delivered through smart phone (mCBT) for problematic alcohol use in primary care has not been conducted yet. To fill in this gap, we will investigate the effectiveness of mHealth interventions using CBT-techniques in comparison to usual care in a Western primary care setting.

# Methods

We conducted a systematic review following the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA) guidelines (47). We included randomized controlled trials of adults and/or adolescents (age ≥16 years) with problematic alcohol use in the general population or presenting in primary care. Furthermore, the study had to be conducted in a Western country (Western-Europe, USA, Canada or Australia). Articles were excluded when they investigated problematic alcohol use in combination with one specific comorbidity (e.g., depression) or when they took place in a specialized setting or non-Western country. We only considered studies investigating the comparison of mobile interventions, available through smartphone (mobile applications or websites) and using CBT-techniques, with usual care. Digital interventions using other methods were excluded. We included studies reporting qualitative as well as quantitative outcome data. Also, we excluded articles before 2010, because they might not be applicable due to the evolutions in smartphones and mobile internet. At last, we only included articles written in English, French or Dutch.

We carried out a literature search in the following four databases: PubMed, Embase, Web of Science and Cochrane Library. We chose these databases because of their relevance for medical subjects and their availability through our association with KU Leuven. We drew up the strategy together with biomedical reference librarians of the KU Leuven Libraries. No grey literature was consulted. We searched all the databases on 7 May 2021 without applying any filter. The complete search strategy is mentioned in appendix 1. In Web of Science, we searched in a part of the Core Collection. All included editions are mentioned in appendix 2. We uploaded all the articles to the reference manager Mendeley and removed duplicates (48). Then, the two reviewers screened title and abstract independently using the tool of Rayyan Systems Inc. (49). Later, we assessed full text articles for eligibility. After this independent assessment, the two reviewers resolved conflicts until a definite decision was made. The process of study selection can be seen in Figure 1.

The two reviewers collected data independently from the selected reports using a data extraction form, adapted from Cochrane data extraction forms (50). We collected data regarding conflicts of interests, study and population characteristics, inclusion and exclusion criteria, primary and secondary outcomes, follow-up, intervention and comparison treatment. A

summarised sheet is presented in appendix 3. Next, the two authors assessed risk of bias independently for all the included studies, using the ROB-2 tool, the revised Cochrane risk of bias tool for randomized trials (51). We will conduct a meta-analysis if feasible. Otherwise, we will carry out a narrative review of the available results, describing and critically evaluating the study setting, population characteristics, intervention- and comparison treatment, outcome measures, follow-up, efficacy of mCBT-interventions and study quality of all included studies.

# Results

## Study selection

We screened 3437 articles of which 2690 were excluded based on abstract and 22 after reading the full text article. With 'article not matching search terms' we mean that the article does not meet multiple inclusion criteria. After the selection process eight articles were included. The process of study selection can be seen in Figure 1. An overview of the included studies can be found in Table 1. As we noticed a lot of heterogeneity regarding study population, intervention tool, comparison treatment and outcome parameters, a meta-analysis didn't seem feasible. Therefore, we decided to elaborate a narrative review.

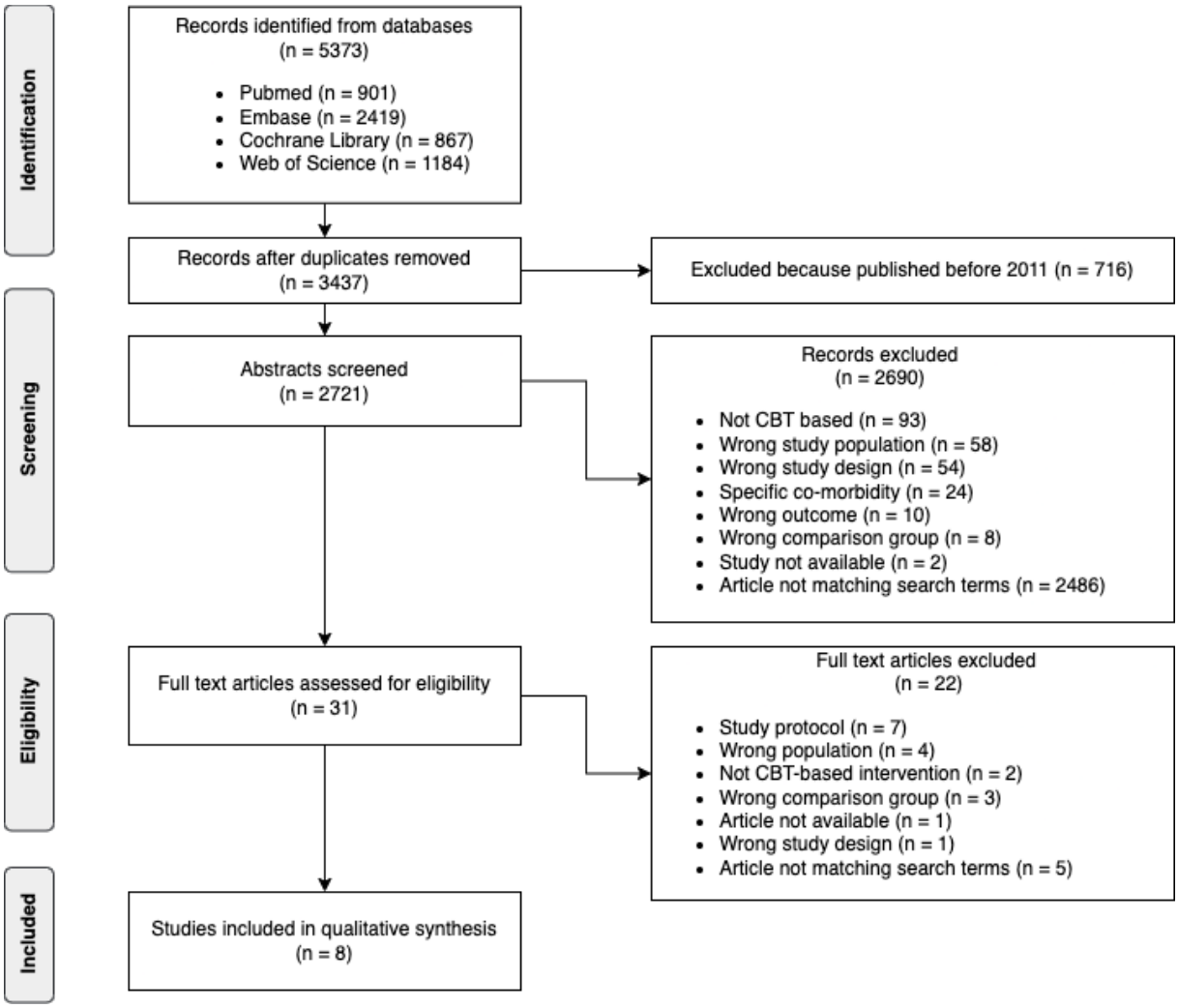



FIGURE 1. PRISMA FLOWCHART

| Author (year of publication) (ref.) | Setting | Participant selection method | Intervention (n) | Control (n) | Primary outcome measures |
|---|---|---|---|---|---|
| Hester R. et al. (2011) (52) | General population; America, Albuquerque | Newspaper advertisement | ModerateDrinking.com combined with access to the website moderation.org (40) | moderation.org (44) | Percentage of abstinence days, log units per day, log mean BAC, DrInC Recent Total score |
| Blankers M. et al. (2011) (53) | Internet help seekers; Netherlands | Online recruitment on website of substance abuse treatment centre | Internet based therapy: therapy alcohol online (68) | Waiting list (69) | Units consumed last week, percentage of weeks within safe drinking guidelines |
| Cunningham J. et al. (2012) (54) | General population; Canada | Newspaper advertisements | Online CBT program: AlcoholHelpCenter.net (83) | Online BI: checkyourdrinking.net (87) | Units consumed in typical week, highest number of drinks on one occasion in last 6 months, Audit-C |
| Brendryen H. et al. (2013) (55) | General population; Norway | Banner advertisements on online newspapers | Online BI + intensive online CBT intervention (125) | Online BI + e-booklet (119) | Self-reported alcohol consumption in previous week |
| Sinadinovic K. et al. (2014) (56) | Internet help seekers; Sweden | Ads on alcohol and drug-related websites and Google Ads | Online CBT program: Alkoholhjalpen.se (114) | Waiting list (210) / eScreen.se (152) | Total Audit-C at 3, 6 and 12 months |
| Wallace P. et al. (2017) (57) | Primary care / GP facilitated; Italy | Selection by general practitioner | Feedback on drinking behaviour and CBT program: Thinking drinking record (347) | Face-to-face BI (416) | Proportion AUDIT ≥ 8 after 3 months |
| Brendryen H. et al. (2017) (58) | Workplace; Norway | Intranet newsfeed in four companies and recruitment emails | Online BI + intensive online CBT intervention (43) | Online BI + e-booklet (42) | Self-reported alcohol consumption in previous week |
| Boß et al. (2018) (59) | Employed general population; Germany Lüneburg | Announcement on magazines and website of health insurance companies and newspaper articles | Online CBT modules with or without adherence focus guidance (146/144 resp.) | Waiting list (144) | Self-reported alcohol consumption in previous week (timeline follow back) |

TABLE 1: OVERVIEW OF INCLUDED STUDIES

## Study setting and participant recruitment

Participants were recruited by multiple methods. The first method was recruitment through online newspaper advertisements. Four studies used this method to recruit participants in the general population (52,59–61). One of these also included announcements on magazines and websites of health insurance companies (59).

Secondly, announcements on alcohol and drug-related websites (including websites of treatment centres for substance abuse disorders) were used in two studies (53,56). Hereby, they presumably targeted patients autonomously searching for therapy on the internet. One study recruited their participants in the workplace setting. Employees were informed through the intranet and mailing system of four participating companies (58).

Lastly, only in the study of Wallace et al., a general practitioner (GP) recruited participants in a primary care setting (57). A trained GP handed over brochures that encouraged patients to access the trial website. There, they were asked to complete the short Alcohol Use Disorders Identification Test (AUDIT). Those scoring above the cut points received a personalized online message from their GP stating that their drinking patterns were putting them at risk and encouraging them to take part in the study.

## Population characteristics

The mean age of participants in our included studies varied between 39 and 50 years old (SD 10 -13y). Only the study of Wallace et al. included an older population (mean age >50 years) (57). Five studies included socio-economic data on participants (52–54,57,59). The level of education was described as high (>55% of participants completed tertiary education) in all but one study (only 19%) (57). The employment rate exceeded 75% in two studies (53,59), while in Cunningham et al. the employment rate was only 55% (60), and In Wallace et al. and Hester et al. there was no information on employment rate (52,57). Only one study gave information on current and previous psychotherapy or health training (59). No other information of medical history was provided in any of the included studies.

The severity of alcohol usage in participants was measured with scoring systems like AUDIT and fast alcohol screening test (FAST). An alternative method was the measurement of total amount of standard units of alcohol in the last week.

The AUDIT-score, a screening tool for harmful alcohol use in clinical practice, was used in all but three studies. A total score of 8 or more indicates hazardous or harmful alcohol use. In women, and men over the age of 65 the cut-off is lowered to 7 (62). The mean audit scores in all but one of the studies varied between 17,7 and 21. In the study of Wallace et al., the mean audit score was 5,5 with only 28,6% of participants scoring 8 or higher (57). The two included studies of Brendryen et al. used the FAST-score, an abbreviated version of the AUDIT, which they adapted to Norwegian official guidelines. Mean scores on this test ranged from 4.6 to 6.3 (55,58). Besides the scoring systems, seven studies also measured the number of standard units in the last week. The usage of participants in these studies varied from 19 to 45 units per week.

### Intervention and comparison treatment

All our included studies used an online CBT-based program, and none used a smartphone application. In the two trials of Brendryen et al. the same intervention was used together with an online BI (55,58). The six remaining trials all used different mCBT interventions. All programs consisted of modules concerning topics as motivation, goal setting, relapse prevention, monitoring alcohol consumption, coping strategies etc. Besides CBT, the modules included other psychological interventions as well, e.g., social support and psychoeducation.

Since we were interested in interventions suitable for GP practices, studies examining guided online CBT programs were excluded. However, one program included the possibility for GP's to develop personalized online messages for patients at four key points in the program (57). Furthermore, one trial examined two intervention groups, one with and one without adherence guidance (59).

In some programs the modules were made available gradually over time in a predetermined order (55,58,59) while in other programs all modules were available from the beginning. Some of these suggest daily engagement (53), others suggest usage at least one time per week (52) and some studies didn't mention any recommendations regarding exposure time at all (56,57,60).

The comparison treatment varied between studies. In four studies, the comparison treatment consisted of an online BI. The group of Brendryen et al. conducted two studies comparing the experimental intervention to an online BI in combination with an informative e-booklet (55,57). In Cunningham et al. participants allocated to the control group were referred to checkyourdrinking.net, an 18-item brief screener, providing personalized normative feedback after completion (60). Lastly, one arm of the three-armed study of Sinadinovic et al. also consisted of an online BI and diary, namely escreen.se (56). The third arm of the latter consisted of a waiting list. The RCT's of Blankers and Boß et al. also compare the mCBT intervention to a waiting list group (53,59). Additionally, one study provided access to the website moderation.org, providing an online mutual-help community, face-to-face meetings and written materials describing the Moderation Management program of behavioural change (52). Lastly, only in the study of Wallace et al., the comparison treatment was fully equivalent to treatment as usual in a GP's office in Flanders (57). This trial compared the mCBT-intervention to a face-to-face BI conducted by a GP.

### Study duration and loss of follow-up

The follow-up duration varied between 6 to 12 months with one to three data collection moments after baseline assessment. The loss of follow-up was high in the study of Sinadinovic et al. with 62% loss of follow-up after 3m, 65% after 6m and 55% after 12m (56). In five studies the attrition rate was average with loss of follow-up ranging from 21,6% to 40%. Only in two studies the amount of attrition was lower with a total of 10% after 6 months in the study of Cunningham et al. (60) and 8,5% after 3 months and 18,8% after 12 months in the study of Wallace et al. (57).

### Outcome measures

We can identify four categories of outcome measures in the included studies. The first group consists of the measurements of consumption. All studies except one had at least one measure of consumption (57). Four studies used the timeline follow-back method, a standardized method to measure the alcohol consumption in the last week (53,55,58,59), while one study used the consumption in a typical week (54). Three studies used the AUDIT-C and/or AUDIT-score (53,56,63).

The second group is measures of 'treatment response'. In Wallace et al., the researchers looked at the proportion of hazardous or harmful drinkers as defined by a score of ≥8 points on the AUDIT questionnaire (57). In the study of Sinadinovic et al. they looked at the percentage of participants that reduced their alcohol use to a non-problematic or a clinically lower level, predefined with the AUDIT-score (56). In the study of Blankers et al. the response was mainly based on the British Medical Association's (1995) guidelines for safe drinking (53,64). The third group consists of alcohol-related problems, as measured with the DrInC questionnaire in Hester et al. (52). The last group are QOL-questionnaires. Wallace et al. used the EQ-5D (57), whereas Blankers et al. used the EQ-5D and the QOLS (53).

## Efficacy of mCBT interventions in comparison to treatment as usual

The study of Wallace et al. comparing an online CBT program with a BI carried out by a GP showed non-inferiority with reduction of the number of participants with an AUDIT score ≥8 from 95 (27.5%) to 85 (26.8%) at three months, while those in the BI group increased from 123 (20.6%) to 141 (37%) (57). At 12 months, the intervention group rose to 88 (26.3%) and the control group dropped to 71 (24.9%). However, the non-inferiority was not supported with additional analyses that consider the bias in the response to AUDIT question 10 ("Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested you cut down?"), which led to the high observation at three months for the BI group.

The group of Brendryen et al. conducted two studies comparing the mCBT intervention + online BI to an online BI + informative e-booklet (55,58). The first study, conducted in the general population, showed a statistically significant effect of the experimental intervention on the alcohol consumption in the last week at six months, but not at two months [B = 2.96; 95% confidence interval (CI) = 0.02–5.90; P = 0.049]. At six months, the participants in the intervention group drank three drinks fewer than the participants of the control group with a Cohen's d of 0,20. The second study, conducted in a workplace setting, showed no statistical difference between interventions at two or six months using the baseline observation carried forward strategy.

The study of Cunningham et al. compared an online CBT intervention to an online BI (54). Multivariate analysis of variance showed a significant interaction between time and condition (F3,163 = 2.7, P = .046, partial eta squared = 0.05), indicating a significantly higher reduction in drinking among participants in the experimental group after six months. In the study of Sinadinovic et al, the CBT intervention was compared to an online BI and to a waiting list (56). Only in the 'per protocol'-analysis (PP), there was a statistically significant lower AUDIT-C score at 6 months follow-up for participants in the online CBT intervention in comparison to the BI (p = 0.048). There were no significant differences between any of the groups at any other time point and the 'intention to treat'-analysis (ITT) showed no statistically significant difference.

Two studies also compared an mCBT intervention with a waiting list. The first one, conducted in a working population by Boß et al., combined the data from the unguided and guided arm because there was no statistical difference between the groups (59). Their data showed that the intervention group reduced their weekly drinking on average by 4,9 units compared to controls after six weeks [B=4.85, 95% confidence interval (CI)= 7.02 to 2.68, P < 0.001] and on average by 5,7 after six months (B= 5.72, 95% CI= 7.71 to 3,73, P < 0.001). The second study, carried out by Blankers et al. targeting internet help seekers, showed a significant difference in weekly alcohol units at 3 months in favour of the CBT intervention [WL M = 35,5 vs. SAO M = 27,0; t(135) = 2,04; p = 0,03; one-tailed, d = 0,36] (53). In the experimental arm, the consumption was reduced from M = 43,6 to M = 27. In the waiting list arm, it was reduced from M = 47,2 to M = 35,5. The difference between these two arms was not examined at six months, as the waiting list group was offered a treatment after the first follow-up session.

At last, the study of Hester et al. examined the effectiveness of their web-based protocol ModerateDrinking.com (MD) combined with access to the website Moderation.org (MM), in comparison to MM alone (52). The data showed a statistically significant differential effect between the groups on percentage days of abstinence (PDA). The change of the means of PDA from baseline to the average of the three follow-ups at 3,6 and 12 months was greater in the MD + MM condition (28.6) than in the MM only condition (7,8), F(1, 55) = 9,22; p = 0,004, yielding a between-groups effect size of d = 0,65 (95% CI [0,12; 1,16]). There was no

significant difference in the log mean blood alcohol concentration per drinking day and the log mean drinks per day.

## Study quality

We have no concerns regarding the randomization process in the studies. The allocation to the different groups was randomized, mostly by using online tools, the randomization sequence was concealed and there were no important baseline differences between the groups.

As described above, the most common method to measure outcome was the measurement of consumptions the last week or in a typical week and the AUDIT(-C). Because these methods are appropriate in this context, we concluded to have 'no concerns' regarding bias in measurement of the outcome. However, we do acknowledge that it's not an ideal way of measuring outcome as it relies on recall and is prone to errors. The outcome data were measured digitally mostly, while two studies used research assistants that were possibly (52) or certainly (54) aware of the intervention the participants received. Some studies only used a blinded research assistant if participants didn't respond after two emails.

We express some concerns regarding the reported results in the study of Brendryen at al. as they add a second and third regression model, as well as a baseline observation carried forward approach, which were not specified in the original protocol (58). It was added during the review process of a companion trial published elsewhere. However, it is not clear whether outcome data were already available at that time and the third model was the only one statistically significant. For the other studies we have no concerns in this regard as the outcome measurements and statistical analysis were done as described in the methods and the statistical plan. However, we were not able to find a protocol for all the included studies.

In one study outcome data were available for nearly all participants randomized (>90%), raising no concerns regarding bias due to missing outcome data (54). In the other studies however, missing outcome data were abundant and only two of those studies provide evidence that the results nevertheless were not biased (53,59). The other studies do raise some concerns, because we judge that it is possible but unlikely that missingness depends on the true value of the outcome (52,56–58). For one study we express high concerns as there were big

differences in the proportions of missing outcome data between the intervention groups (55).

All studies used ITT analysis and one used ITT as well as PP analysis. Regarding bias due to deviations from intended interventions we deem that five studies are at low risk. In four of them, the participants were probably not aware of the intervention they received, while in one study participants were probably aware of their allocation to the control group (waiting list). However, the number of deviations were low and balanced between the interventions (58). In four of them, the interventions are delivered by technology, so there are also no concerns regarding personnel undermining the trial comparisons by implementing non-protocol interventions or failing to implement the protocol interventions (54,55,58,59). In the fifth, the people explaining the participants about the assigned interventions were aware of the assignment, but we judged there were probably no deviations because of the trial context (52). Two studies raise some concerns as in one, participants in the control group were probably aware of their assignment as they were put on a waiting list and in the other, there is no blinding. But there is no information on whether deviations arose because of the trial context (53,57). The study of Sinadinovic et al. is at high risk for bias as participants in the control group were probably aware of their assignment (waiting list) and some controls and eScreen.se users also used the Alkoholjalpen.se website (56).

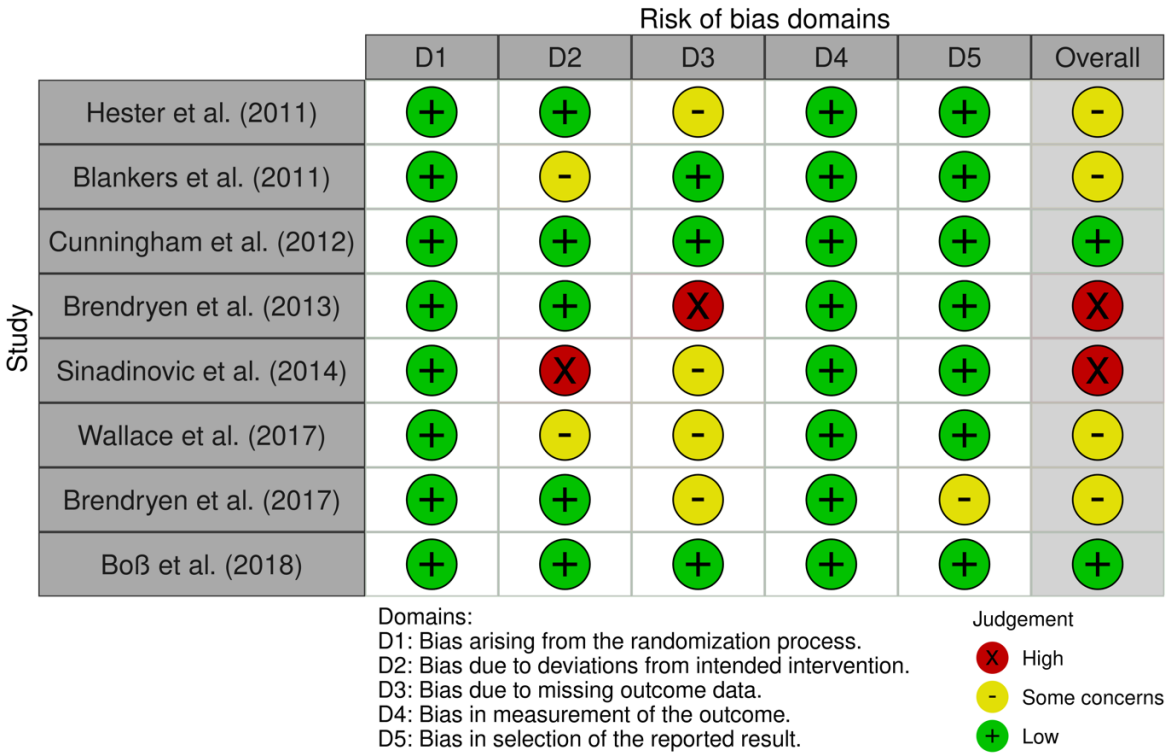



TABLE 2: RISK OF BIAS ANALYSIS – TRAFFIC LIGHT PLOT

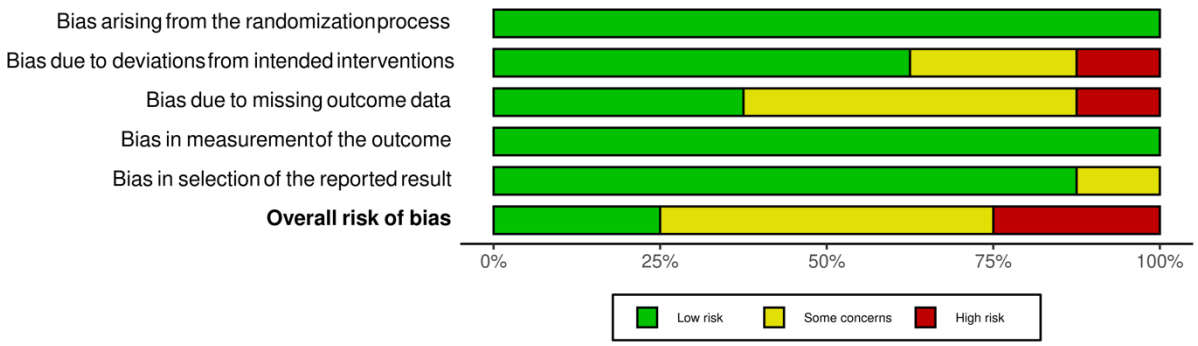



FIGURE 2: RISK OF BIAS – SUMMARY PLOT

# Discussion

The goal of this review was to investigate the effectiveness of mHealth interventions using CBT-techniques in comparison to usual care in a Western first-line setting. We found one study conducted in a GP's office, comparing mCBT with a BI, which could not demonstrate non-inferiority with post-hoc analysis considering the response bias that distorted the primary analysis (57). One study in the general population showed that the mCBT intervention was more effective in reducing alcohol consumption than an online BI (54). However, this was not confirmed by another study showing no intervention effect (58). When comparing a mCBT intervention to a waiting list, we found a treatment effect in favour of the mCBT intervention in two studies targeting the working population or internet help seekers (53,59). While in another study, mCBT was not more effective in reducing alcohol consumption (56). When investigating the effect of adding an mCBT intervention to an online BI, one study in the general population showed an additional effect, while another in the working population did not confirm this (55,58). At last, one study examining their intervention to online mutual support groups, showed a differential effect supporting mCBT on percentage days of abstinence, but not on other outcome measures (52).

So, although there are indications that mCBT interventions are equally or more effective than treatment as usual (i.e., face-to-face or online BI, waiting list, online support groups) in a non-specialized setting, the evidence is sparse and inconsistent in the studies we examined. This is in line with the findings of two reviews that have been carried out in a non-primary care setting showing a small favourable effect for therapist guided ICBT in comparison to a waiting list or as addition to usual care in specialized psychiatric settings (23,44). Based on two medium-sized RCTs, one review also suggests that therapist guided ICBT would be superior to self-guided ICBT (44). Comparably, there is evidence supporting the superior efficacy of ICBT in comparison with controls (i.e., TAU, waiting list) for other psychiatric disorders such as depression, anxiety disorders, PTSD and OCD (65–67). However, these reviews didn't investigate the effectiveness in a primary care population. Although data are limited in primary care, one review examining non-specific technology-based alcohol interventions in

this setting, did show mostly beneficial results with outcomes enhanced by provider involvement and an implementation strategy. Promising is also the growth of studies in primary care regarding this topic with nearly a tripling in the last decade (45).

Important strengths of our review are the focus on mCBT specifically and the attempt to investigate these interventions in a primary care setting for the first time. We also consider our exclusion of psychiatric comorbidities as a strength as most guidelines for GP's do recommend referring these patients for specialised care (3,68). Also, we followed the PRISMA guidelines to improve reporting of our systematic review and used the RoB-2 tool to assess the bias in our included RCT's. Additionally, the two authors screened the articles and analysed their bias independently and to improve the sensitivity and specificity of our search strategy, we worked together with biomedical reference librarians of the KU Leuven Libraries. Our review also has some limitations. Firstly, we often couldn't access the interventions used and had to rely on the description in the article to assess whether the intervention could be classified as a mCBT intervention. Next, we included studies in a non-specialised setting, incorporating studies in the general population or in a workplace setting. These populations don't necessarily represent the population in a GP's office. At last, our review doesn't include a meta-analysis as this didn't seem feasible due to heterogeneity.

Besides our review process, the included studies also revealed multiple limitations of the evidence. Firstly, the method of recruiting participants has several implications. By using advertisement-based and work-based announcements researchers already select for a help-seeking, technology-adept population. This manifests in our included studies as a well-educated population with an extensive alcohol usage. This deviates from the population a GP would encounter, where a more preventive approach also includes patients who are still in the early stages of behavioural change or have a less extensive alcohol problem. This makes it difficult to extrapolate the results to a primary care population. An exception is the study of Wallace et al. (57) where participants are recruited by a GP, resulting in a less-educated population with lower alcohol usage. Additionally, an older population was selected, presumably by excluding people under the legal age of drinking and by recruiting through advertisements on newspapers or in the workplace.

Secondly, there is a lack of standardization in intervention treatment with only two studies using the same CBT intervention (58,61). This is a problem in research related to self-help apps for alcohol dependence in general. Furthermore, we did not find any studies investigating mobile applications as we primarily intended. As a result, the possible advantages of mobile health, such as continuous availability to the patient or 'just in time feedback and support' as described above, are not used to their full potential. Analogous to the intervention, there was a lot of variability in comparison treatment. This limits our review as we primarily wanted to compare an mCBT intervention to the current recommended treatment i.e., face-to-face BI.

The third limitation is the lack of objective outcome measures in determining the efficacy of the intervention. The usage of self-reported measures decreases the accuracy of the outcome data, among other things due to recall bias or personal expectations in follow-up measurements. Fourthly, our follow-up is limited to a maximum of 12 months. As such, we have no long-term data. The question remains if the online intervention has a lasting impact on health and quality of life.

Lastly, the quality of the included studies was mediocre. The risk of bias is high in two studies, while we have some concerns about bias in four of the eight studies. Most problematic is the high attrition rate, varying between 20-55% for most studies. There were two studies with a pronounced low attrition rate, presumably due to a more personalized approach (57) or monetized incentives (54). While some studies do provide evidence that the results were nevertheless not biased, for other studies it is possible that missingness could depend on the true value of the outcome. Another recurring problem is possible bias due to deviations from the intended interventions in the studies comparing mCBT to a waiting list. As people are probably aware that they aren't receiving an intervention, they might feel unlucky and seek other treatments. This is demonstrated in the study of Sinadinovic et al. where some controls also used the website containing the CBT-intervention (55).

From a clinical point of view our opinion is reserved. The question remains if these results are applicable in the primary care setting. The participants in the studies are older, better educated and have more substantial alcohol problems then we would expect in primary care. To make more robust statements about the effectiveness of mCBT interventions in a

GP's office, more research is needed in a primary care setting involving GP practises in Western countries. Preferably, a working group involving GP's, psychiatrists, psychologists, IT specialists could develop an application containing CBT techniques which is then tested in clinical trials. Before implementation in practices in Flanders there is need for a mobile app in the native language of the patient, as no mCBT interventions were found in Dutch. An interesting population to target should be adolescents or young adults, as they presumably are particularly susceptible for interventions delivered through smartphones. However, besides the question of efficacy of these applications, research should also focus on the feasibility and acceptability in general practitioners and patients with problematic alcohol use as this could also affect the efficacy outside a trial context.

## Acknowledgements

We wish to thank our promotor, prof. dr. Marc Van Nuland for the support and coaching during the process. We would also like to thank Thomas Vandendriessche, Krizia Tuand and Kristel Paque, the biomedical reference librarians of the KU Leuven Libraries - 2Bergen - Learning Centre Désiré Collen (Leuven, Belgium), for their help in conducting the systematic literature search.

# References


1. Gisle L. Gezondheidsenquete België 2018 - Gebruik van alcohol. 2018;
2. Manthey J, Gual A, Jakubczyk A, Pieper L, Probst C, Struzzo P, et al. Alcohol use disorders in Europe: A comparison of general population and primary health care prevalence rates. http://dx.doi.org.kuleuven.e-bronnen.be/103109/1465989120151063719 [Internet]. 2016 Sep 2 [cited 2021 Dec 7];21(5):478–84. Available from: https://www-tandfonline-com.kuleuven.e-bronnen.be/doi/abs/10.3109/14659891.2015.1063719
3. Problematisch Alcoholgebruik. Aanpak van de Huisarts. | Domus Medica [Internet]. [cited 2021 Dec 7]. Available from: https://www.domusmedica.be/richtlijnen/problematisch-alcoholgebruik-aanpak-van-de-huisarts
4. Hammer JH, Parent MC, Spiker DA, World Health Organization. Global status report on alcohol and health 2018 [Internet]. Vol. 65, Global status report on alcohol. 2018. 74–85 p. Available from: http://www.who.int/substance_abuse/publications/global_alcohol_report/msbgsruprofiles.pdf%0Ahttp://www.ncbi.nlm.nih.gov/pubmed/29355346
5. Navarro HJ, Doran CM, Shakeshaft AP. Measuring costs of alcohol harm to others: a review of the literature. Drug Alcohol Depend [Internet]. 2011 Apr 1 [cited 2021 Dec 7];114(2–3):87–99. Available from: https://pubmed.ncbi.nlm.nih.gov/21193271/
6. Gell L, Ally A, Buykx P, Meier P, Hope A. Alcohol's Harm to Others. 2015.
7. Connor J, Casswell S. Alcohol-related Harm to Others in New Zealand: Evidence of the Burden and Gaps in Knowledge - PubMed [Internet]. The New Zealand medical journal. 2012 [cited 2020 Jul 7]. Available from: https://pubmed.ncbi.nlm.nih.gov/22932651/
8. Navarro HJ, Doran CM, Shakeshaft AP. Measuring costs of alcohol harm to others: A review of the literature [Internet]. Vol. 114, Drug and Alcohol Dependence. Drug Alcohol Depend; 2011 [cited 2020 Jul 7]. p. 87–99. Available from: https://pubmed.ncbi.nlm.nih.gov/21193271/
9. Doncker J de, Donder E de, Möbius D. Dossier Alcohol VAD. 2015;118.

10. O'donnell A, Anderson P, Newbury-Birch D, Schulte B, Schmidt C, Reimer J, et al. The Impact of Brief Alcohol Interventions in Primary Healthcare: A Systematic Review of Reviews. 2013 [cited 2020 Jul 7]; Available from: http://creativecommons.

11. NICE. Screening and Brief Interventions for Prevention and Early Identification of Alcohol Use Disorders in Adults and Young People. 2010;(February 2015):6–424.

12. Jonas DE, Garbutt JC, Brown JM, Amick HR, Brownley K a, Council CL, et al. Screening, Behavioral Counseling, and Referral in Primary Care To Reduce Alcohol Misuse. Comparative Effectiveness Review [Internet]. 2012 [cited 2020 Jul 7];(64):1–87. Available from: http://www.ncbi.nlm.nih.gov/books/NBK99199/

13. Magill M, Ray LA. Cognitive-behavioral treatment with adult alcohol and illicit drug users: A meta-analysis of randomized controlled trials. Journal of Studies on Alcohol and Drugs [Internet]. 2009 [cited 2020 Jul 7];70(4):516–27. Available from: https://pubmed.ncbi.nlm.nih.gov/19515291/

14. Mistiaen P, Kohn L, Mambourg F, Ketterer University of Liege F, of General Practice D, Medicine F, et al. Reduction of the treatment gap for problematic alcohol use in Belgium – Synthesis. [cited 2021 Dec 7]; Available from: www.kce.fgov.be

15. TUCKER JA. Predictors of help-seeking and the temporal relationship of help to recovery among treated and untreated recovered problem drinkers. Addiction (Abingdon, England) [Internet]. 1995 [cited 2021 Dec 7];90(6):805–9. Available from: https://pubmed.ncbi.nlm.nih.gov/7633297/

16. McNeely J, Kumar PC, Rieckmann T, Sedlander E, Farkas S, Chollak C, et al. Barriers and facilitators affecting the implementation of substance use screening in primary care clinics: a qualitative study of patients, providers, and staff. Addiction science & clinical practice [Internet]. 2018 Dec 27 [cited 2021 Dec 7];13(1). Available from: https://pubmed.ncbi.nlm.nih.gov/29628018/

17. Szaflarski M, Klepinger DH, Cubbins LA. Alcohol use/abuse and help-seeking among U.S. adults: The role of racial-ethnic origin and foreign-born status. J Ethn Subst Abuse [Internet]. 2019 Apr 3 [cited 2021 Dec 7];18(2):183–210. Available from: https://pubmed.ncbi.nlm.nih.gov/28678640/

18. Marsch LA, Carroll K m, Kiluk BD. Technology-Based Interventions for the Treatment & Recovery. Journal of Substance Abuse Treatment. 2014;46(1):1–7.

19. Suffoletto B, Scaglione S. Using Digital Interventions to Support Individuals with Alcohol Use Disorder and Advanced Liver Disease: A Bridge Over Troubled Waters. Alcohol Clin Exp Res [Internet]. 2018 Jul 1 [cited 2021 Dec 7];42(7):1160–5. Available from: https://pubmed.ncbi.nlm.nih.gov/29750368/

20. The Use of Emerging Technologies in Alcohol Treatment.: EBSCOhost [Internet]. [cited 2021 Dec 7]. Available from: https://web-p-ebscohost-com.kuleuven.e-bronnen.be/ehost/pdfviewer/pdfviewer?vid=1&sid=33859b02-c77f-4c35-9b59-017f39199f52%40redis

21. Gustafson DH, McTavish FM, Chih MY, Atwood AK, Johnson RA, Boyle MG, et al. A smartphone application to support recovery from alcoholism: a randomized clinical trial. JAMA Psychiatry. 2014 May;71(5):566–72.

22. Oosterveen E, Tzelepis F, Ashton L, Hutchesson MJ. A systematic review of eHealth behavioral interventions targeting smoking, nutrition, alcohol, physical activity and/or obesity for young adults. Prev Med (Baltim) [Internet]. 2017 Jun 1 [cited 2021 Dec 14];99:197–206. Available from: https://pubmed.ncbi.nlm.nih.gov/28130046/

23. Kiluk BD, Ray LA, Walthers J, Bernstein M, Tonigan JS, Magill M. Technology-Delivered Cognitive-Behavioral Interventions for Alcohol Use: A Meta-Analysis. Alcoholism: Clinical and Experimental Research [Internet]. 2019 Nov 30;43(11):2285–95. Available from: https://onlinelibrary.wiley.com/doi/10.1111/acer.14189

24. Milward J, Day E, Wadsworth E, Strang J, Lynskey M. Mobile phone ownership, usage and readiness to use by patients in drug treatment. Drug and Alcohol Dependence [Internet]. 2015;146(1):111–5. Available from: http://dx.doi.org/10.1016/j.drugalcdep.2014.11.001

25. Bakken S, Jia H, Chen ES, Choi J, John RM, Lee NJ, et al. The Effect of a Mobile Health Decision Support System on Diagnosis and Management of Obesity, Tobacco Use, and Depression in Adults and Children. J Nurse Pract [Internet]. 2014 Nov 1 [cited 2021 Dec 14];10(10):774. Available from: /pmc/articles/PMC4376009/

26. Gerber BS, Stolley MR, Thompson AL, Sharp LK, Fitzgibbon ML. Mobile phone text messaging to promote healthy behaviors and weight loss maintenance: a feasibility study. Health Informatics J [Internet]. 2009 [cited 2021 Dec 14];15(1):17–25. Available from: https://pubmed.ncbi.nlm.nih.gov/19218309/

27. Pal K, Eastwood S v., Michie S, Farmer A, Barnard ML, Peacock R, et al. Computer-based interventions to improve self-management in adults with type 2 diabetes: a systematic review and meta-analysis. Diabetes Care [Internet]. 2014 [cited 2021 Dec 14];37(6):1759–66. Available from: https://pubmed.ncbi.nlm.nih.gov/24855158/

28. Catalani C, Philbrick W, Fraser H, Mechael , Patricia, Israelski DM. mHealth for HIV Treatment & Prevention: A Systematic Review of the Literature. Open AIDS J [Internet]. 2013 Aug 21 [cited 2021 Dec 14];7(1):17–41. Available from: https://pubmed.ncbi.nlm.nih.gov/24133558/

29. Karyotaki E, Ebert DD, Donkin L, Riper H, Twisk J, Burger S, et al. Do guided internet-based interventions result in clinically relevant changes for patients with depression? An individual participant data meta-analysis. Clin Psychol Rev [Internet]. 2018 Jul 1 [cited 2021 Dec 14];63:80–92. Available from: https://pubmed.ncbi.nlm.nih.gov/29940401/

30. Patton R, Deluca P, Kaner E, Newbury-Birch D, Phillips T, Drummond C. Alcohol Screening and Brief Intervention for Adolescents: The How, What and Where of Reducing Alcohol Consumption and Related Harm Among Young People. Alcohol and Alcoholism (Oxford, Oxfordshire) [Internet]. 2014 Mar [cited 2021 Dec 14];49(2):207. Available from: /pmc/articles/PMC3932830/

31. Sijbrandij M, Kunovski I, Cuijpers P. EFFECTIVENESS OF INTERNET-DELIVERED COGNITIVE BEHAVIORAL THERAPY FOR POSTTRAUMATIC STRESS DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS. Depress Anxiety [Internet]. 2016 Sep 1 [cited 2021 Dec 14];33(9):783–91. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27322710

32. Ben-Zeev D, Brenner CJ, Begale M, Duffecy J, Mohr DC, Mueser KT. Feasibility, acceptability, and preliminary efficacy of a smartphone intervention for schizophrenia. Schizophr Bull [Internet]. 2014 Nov 1 [cited 2021 Dec 14];40(6):1244–53. Available from: https://pubmed.ncbi.nlm.nih.gov/24609454/

33. Riley W, Obermayer J, Jean-Mary J. Internet and mobile phone text messaging intervention for college smokers. J Am Coll Health [Internet]. 2008 Sep 1 [cited 2021 Dec 14];57(2):245–8. Available from: https://pubmed.ncbi.nlm.nih.gov/18809542/

34. Tait RJ, Spijkerman R, Riper H. Internet and computer based interventions for cannabis use: a meta-analysis. Drug Alcohol Depend [Internet]. 2013 Dec 1 [cited 2021 Dec 14];133(2):295–304. Available from: https://pubmed.ncbi.nlm.nih.gov/23747236/

35. Bickel WK, Christensen DR, Marsch LA. A Review of Computer-Based Interventions Used in the Assessment, Treatment, and Research of Drug Addiction. Subst Use Misuse [Internet]. 2011 Jan [cited 2021 Dec 14];46(1):4. Available from: /pmc/articles/PMC3092368/

36. Sugarman DE, Campbell ANC, Iles BR, Greenfield SF. Technology-Based Interventions for Substance Use and Comorbid Disorders: An Examination of the Emerging Literature. Harv Rev Psychiatry [Internet]. 2017 [cited 2021 Dec 14];25(3):123–34. Available from: https://pubmed.ncbi.nlm.nih.gov/28475504/

37. White A, Kavanagh D, Stallman H, Klein B, Kay-Lambkin F, Proudfoot J, et al. Online Alcohol Interventions: A Systematic Review. JOURNAL OF MEDICAL INTERNET RESEARCH. 2010;12(5).

38. Rooke S, Thorsteinsson E, Karpin A, Copeland J, Allsop D. Computer-delivered interventions for alcohol and tobacco use: a meta-analysis. Addiction (Abingdon, England) [Internet]. 2010 Aug [cited 2021 Dec 14];105(8):1381–90. Available from: https://pubmed.ncbi.nlm.nih.gov/20528806/

39. Dedert EA, McDuffie JR, Stein R, McNiel JM, Kosinski AS, Freiermuth CE, et al. Electronic Interventions for Alcohol Misuse and Alcohol Use Disorders: A Systematic Review. Ann Intern Med [Internet]. 2015 Aug 4 [cited 2021 Dec 14];163(3):205–14. Available from: https://pubmed.ncbi.nlm.nih.gov/26237752/

40. Sundström C, Blankers M, Khadjesari Z. Computer-Based Interventions for Problematic Alcohol Use: a Review of Systematic Reviews. International Journal of Behavioral Medicine [Internet]. 2017 Oct 1 [cited 2021 Dec 14];24(5):646. Available from: /pmc/articles/PMC5608865/

41. Andersson G, Cuijpers P, Carlbring P, Riper H, Hedman E. Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. World Psychiatry [Internet]. 2014 Oct 1 [cited 2021 Dec 14];13(3):288–95. Available from: https://pubmed.ncbi.nlm.nih.gov/25273302/

42. Andrews G, Basu A, Cuijpers P, Craske MG, McEvoy P, English CL, et al. Computer therapy for the anxiety and depression disorders is effective, acceptable and practical health care: An updated meta-analysis. J Anxiety Disord [Internet]. 2018 Apr 1 [cited 2021 Dec 14];55:70–8. Available from: https://pubmed.ncbi.nlm.nih.gov/29422409/

43. Sijbrandij M, Kunovski I, Cuijpers P. EFFECTIVENESS OF INTERNET-DELIVERED COGNITIVE BEHAVIORAL THERAPY FOR POSTTRAUMATIC STRESS DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS. Depression and Anxiety [Internet]. 2016 Sep 1 [cited 2021 Dec 14];33(9):783–91. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/da.22533

44. Hadjistavropoulos HD, Mehta S, Wilhelms A, Keough MT, Sundstrom C. A systematic review of internet-delivered cognitive behavior therapy for alcohol misuse: study characteristics, program content and outcomes. COGNITIVE BEHAVIOUR THERAPY. 2020 Jul;49(4):327–46.

45. Ramsey AT, Satterfield JM, Gerke DR, Proctor EK. Technology-Based Alcohol Interventions in Primary Care: Systematic Review. J Med Internet Res. 2019 Apr;21(4):e10859.

46. Nair NK, Newton NC, Shakeshaft A, Wallace P, Teesson M. A Systematic Review of Digital and Computer-Based Alcohol Intervention Programs in Primary Care. Curr Drug Abuse Rev. 2015;8(2):111–8.

47. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ [Internet]. 2021 Mar 29 [cited 2021 Dec 7];372. Available from: https://www.bmj.com/content/372/bmj.n71

48. Mendeley - Reference Management Software & Researcher Network [Internet]. [cited 2021 Dec 7]. Available from: https://www.mendeley.com/?interaction_required=true

49. Rayyan – Intelligent Systematic Review [Internet]. [cited 2021 Dec 7]. Available from: https://www.rayyan.ai/

50. Data extraction forms | Cochrane Developmental, Psychosocial and Learning Problems [Internet]. [cited 2021 Dec 14]. Available from: https://dplp.cochrane.org/data-extraction-forms

51. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ [Internet]. 2019 [cited 2022 Mar 22];366. Available from: https://pubmed.ncbi.nlm.nih.gov/31462531/

52. Hester RK, Delaney HD, Campbell W. ModerateDrinking.com and Moderation Management: Outcomes of a randomized clinical trial with non-dependent problem drinkers. J Consult Clin Psychol [Internet]. 2011 Apr [cited 2022 Mar 29];79(2):215. Available from: /pmc/articles/PMC3066281/

53. 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 Jun;79(3):330–41.

54. Cunningham JA. Comparison of Two Internet-Based Interventions for Problem Drinkers: Randomized Controlled Trial. J Med Internet Res 2012;14(4):e107 https://www.jmir.org/2012/4/e107 [Internet]. 2012 Aug 1 [cited 2022 Mar 15];14(4):e2090. Available from: https://www.jmir.org/2012/4/e107

55. Brendryen H, Lund IO, Johansen AB, Riksheim M, Nesvåg S, Duckert F. Balance--a pragmatic randomized controlled trial of an online intensive self-help alcohol intervention. Addiction (Abingdon, England). 2014 Feb;109(2):218–26.

56. 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.

57. Wallace P, Struzzo P, della Vedova R, Scafuri F, Tersar C, Lygidakis C, et al. Randomised controlled non-inferiority trial of primary care-based facilitated access to an alcohol reduction website. BMJ Open. 2017 Nov;7(11):e014576.

58. Brendryen H, Johansen A, Duckert F, Nesvåg S. A Pilot Randomized Controlled Trial of an Internet-Based Alcohol Intervention in a Workplace Setting. Int J Behav Med. 2017 Oct;24(5):768–77.

59. Boß L, Lehr D, Schaub MP, Paz Castro R, Riper H, Berking M, et al. Efficacy of a web-based intervention with and without guidance for employees with risky drinking: results of a three-arm randomized controlled trial. Addiction (Abingdon, England). 2018 Apr;113(4):635–46.

60. Cunningham JA. Comparison of two internet-based interventions for problem drinkers: Randomized controlled trial. Journal of Medical Internet Research. 2012;14(4):24–30.

61. Brendryen H, Lund IO, Johansen AB, Riksheim M, Nesvåg S, Duckert F. Balance--a pragmatic randomized controlled trial of an online intensive self-help alcohol intervention. Addiction (Abingdon, England) [Internet]. 2014;109(2):218–26. Available from: https://www.embase.com/search/results?subaction=viewrecord&id=L603636007&from=export

62. Campbell CE, Maisto SA. Validity of the AUDIT-C screen for at-risk drinking among students utilizing university primary care. Journal of American College Health. 2018 Nov;66(8):774–82.

63. Hester RK, Delaney HD, Campbell W, Handmaker N. A web application for moderation training: Initial results of a randomized clinical trial. J Subst Abuse Treat [Internet]. 2009 Oct [cited 2022 Mar 15];37(3):266. Available from: /pmc/articles/PMC2739257/

64. Sensible Drinking The Report of an Inter-Departmental Working Group. 1995;

65. Andrews G, Basu A, Cuijpers P, Craske MG, McEvoy P, English CL, et al. Computer therapy for the anxiety and depression disorders is effective, acceptable and practical health care: An updated meta-analysis. J Anxiety Disord [Internet]. 2018 Apr 1 [cited 2022 Apr 5];55:70–8. Available from: https://pubmed.ncbi.nlm.nih.gov/29422409/

66. Sijbrandij M, Kunovski I, Cuijpers P. EFFECTIVENESS OF INTERNET-DELIVERED COGNITIVE BEHAVIORAL THERAPY FOR POSTTRAUMATIC STRESS DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS. Depress Anxiety [Internet]. 2016 Sep 1 [cited 2022 Apr 5];33(9):783–91. Available from: https://pubmed.ncbi.nlm.nih.gov/27322710/

67. Dèttore D, Pozza A, Andersson G. Efficacy of technology-delivered cognitive behavioural therapy for OCD versus control conditions, and in comparison with therapist-

administered CBT: meta-analysis of randomized controlled trials. Cogn Behav Ther [Internet]. 2015 May 4 [cited 2022 Apr 5];44(3):190–211. Available from: https://pubmed.ncbi.nlm.nih.gov/25705787/

68. Problematisch alcoholgebruik | NHG-Richtlijnen [Internet]. [cited 2022 Apr 19]. Available from: https://richtlijnen.nhg.org/standaarden/problematisch-alcoholgebruik

# Appendix

## Appendix 1: Search strategy

**Pubmed**

*Concept 1: mHealth*

"Internet-Based Intervention"[Mesh] OR "Telemedicine"[Mesh:NoExp] OR "Therapy, Computer-Assisted"[Mesh:NoExp] OR "Mobile Applications"[Mesh] OR "Mobile Health"[tiab] OR Telehealth[tiab] OR "tele health"[tiab] OR mhealth[tiab] OR ehealth[tiab] OR telepsychiatr*[tiab] OR "tele psychiatr*"[tiab] OR "e health"[tiab] OR "m health"[tiab] OR telemedicine[tiab] OR "tele medicine"[tiab] OR ("self care"[tiab] AND software[tiab]) OR ((internet[tiab] OR web[tiab] OR computerized[tiab] OR "computer based"[tiab] OR "computer assisted"[tiab] OR "technology based"[tiab] OR "technology assisted"[tiab] OR "self guided"[tiab] OR online[tiab]) AND (therap*[tiab] OR intervention*[tiab] OR treatment*[tiab] OR "self help"[tiab] OR "self care"[tiab] OR "Self Care"[Mesh:NoExp])) OR ((app[tiab] OR apps[tiab] OR website[tiab] OR "portable software"[tiab] OR application*[tiab]) AND ("Smartphone"[Mesh] OR smartphone*[tiab] OR phone*[tiab] OR tablet[tiab] OR android[tiab] OR iphone[tiab] OR iOS[tiab] OR internet*[tiab] OR web[tiab] OR digital[tiab] OR online*[tiab] OR mobile[tiab] OR device*[tiab] OR "Web Browser"[Mesh]))

*Concept 2: primary care*

"Primary Health Care"[Mesh:NoExp] OR "primary health*"[tiab] OR "primary care*"[tiab] OR "Physicians, Primary Care"[Mesh] OR "first line care"[tiab] OR "primary medical care*"[tiab] OR "family practi*"[tiab] OR "family doctor*"[tiab] OR "family medi*"[tiab] OR "Physicians, Family"[Mesh] OR "family physician*"[tiab] OR "Ambulatory Care"[Mesh:NoExp] OR "Ambulatory Care Facilities"[Mesh] OR outpatient*[tiab] OR "ambulatory care"[tiab] OR "clinic visit*"[tiab] OR "extramural care"[tiab] OR "office visit*"[tiab] OR "General Practice"[Mesh] OR "General Practitioners"[Mesh] OR "general practi*"[tiab] OR "general medical practi*"[tiab] OR "general physi*"[tiab] OR gp[tiab] OR GPs[tiab] OR "health center*"[tiab] OR "community mental health*"[tiab] OR "Self Care"[Mesh:NoExp] OR "self care"[tiab] OR selfcare[tiab] OR "self help"[tiab] OR selfhelp[tiab] OR selfmanagement[tiab] OR "self management"[tiab] OR selftreatment[tiab] OR "self treatment"[tiab]

*Concept 3: alcohol*

"Drinking Behavior"[Mesh] OR "Alcoholic Beverages"[Mesh:NoExp] OR "Alcoholism"[Mesh] OR "Alcoholic Intoxication"[Mesh] OR "Alcohol-Related Disorders"[Mesh:NoExp] OR "Binge Drinking"[Mesh] OR drinking[tiab] OR alcohol*[tiab] OR abstinence[tiab] OR “harmful use"[tiab] OR "hazardous use"[tiab] OR ethyl[tiab] OR drink[tiab]

**Embase**

*Concept 1: mHealth*

'web-based intervention'/exp OR 'telemedicine'/de OR 'telepsychiatry'/exp OR 'telehealth'/de OR 'computer assisted therapy'/de OR 'mhealth'/exp OR 'mobile application'/exp OR ‘self-care software’/exp OR ‘self help’/exp OR ‘mobile health’:ti,ab,kw OR ‘telehealth’:ti,ab,kw OR ‘tele health’:ti,ab,kw OR ‘mhealth’:ti,ab,kw OR ‘ehealth’:ti,ab,kw OR ‘telepsychiatr*’:ti,ab,kw OR ‘tele psychiatr*’:ti,ab,kw OR ‘e health’:ti,ab,kw OR ‘m health’:ti,ab,kw OR ‘telemedicine’:ti,ab,kw OR ‘tele medicine’:ti,ab,kw OR ((‘self care’ NEAR/6 ‘software’):ti,ab,kw) OR ((‘internet’:ti,ab,kw OR ‘web’:ti,ab,kw OR ‘computerized’:ti,ab,kw OR ‘computer based’:ti,ab,kw OR ‘computer assisted’:ti,ab,kw OR ‘technology based’:ti,ab,kw OR ‘technology assisted’:ti,ab,kw OR ‘self guided’:ti,ab,kw OR ‘online’:ti,ab,kw) AND (‘therap*’:ti,ab,kw OR ‘intervention*’:ti,ab,kw OR ‘treatment*’:ti,ab,kw OR ‘self help’:ti,ab,kw OR ‘self care’:ti,ab,kw)) OR ((‘app’:ti,ab,kw or ‘apps’:ti,ab,kw OR 'website'/exp OR ‘website’:ti,ab,kw OR ‘portable software’:ti,ab,kw or ‘application*’:ti,ab,kw) AND ('smartphone'/exp OR ‘smartphone*’:ti,ab,kw OR ‘phone*’:ti,ab,kw OR ‘tablet’:ti,ab,kw OR ‘android’:ti,ab,kw OR ‘iphone’:ti,ab,kw OR ‘iOS’:ti,ab,kw OR ‘internet*’:ti,ab,kw OR ‘web’:ti,ab,kw OR 'web'/exp OR ‘digital’:ti,ab,kw OR ‘online*’:ti,ab,kw OR ‘mobile’:ti,ab,kw OR 'web browser'/exp OR 'iphone'/exp OR 'android'/exp OR 'devices'/exp OR ‘device*’:ti,ab,kw))

*Concept 2: Primary care*

'primary health care'/exp OR 'primary health*':ti,ab,kw OR 'primary care*':ti,ab,kw OR 'primary medical care':ti,ab,kw OR 'first line care':ti,ab,kw OR 'family practi*':ti,ab,kw OR 'family doctor*':ti,ab,kw OR 'family medi*':ti,ab,kw OR 'family physician*':ti,ab,kw OR 'ambulatory

care'/de OR 'ambulatory care':ti,ab,kw OR 'outpatient department'/exp OR 'outpatient*':ti,ab,kw OR 'extramural care':ti,ab,kw OR 'office visit*':ti,ab,kw OR 'clinic visit*':ti,ab,kw OR 'general practitioner'/exp OR 'general practice'/exp OR 'general practi*':ti,ab,kw OR 'general medical practi*':ti,ab,kw OR 'gp':ti,ab,kw OR 'GPs':ti,ab,kw OR 'general physi*':ti,ab,kw OR 'health center'/exp OR 'community mental health center'/exp OR 'community mental health service'/de OR 'health center*':ti,ab,kw OR 'community mental health*':ti,ab,kw OR 'self care'/de OR 'selfcare':ti,ab,kw OR 'self care':ti,ab,kw OR 'self help'/exp OR 'self help':ti,ab,kw OR 'selfhelp':ti,ab,kw OR 'selfmanagement':ti,ab,kw OR 'self management':ti,ab,kw OR 'selftreatment':ti,ab,kw OR 'self treatment':ti,ab,kw

*Concept 3: Alcohol*

'drinking behavior'/exp OR 'alcohol abstinence'/exp OR 'alcohol abuse'/exp OR 'alcoholic beverage'/de OR 'alcoholism'/exp OR 'alcohol related problem'/exp OR 'drinking':ti,ab,kw OR 'alcohol*':ti,ab,kw OR 'abstinence':ti,ab,kw OR 'harmful use':ti,ab,kw OR 'hazardous use':ti,ab,kw OR 'ethyl*':ti,ab,kw OR 'drink':ti,ab,kw

**Web of Science**

*Concept 1: mHealth*

TS=("mobile health" OR "telehealth" OR "tele health" OR "mhealth" OR "ehealth" OR "telepsychiatr*" OR "tele psychiatry*" OR "e health" OR "m health" OR "telemedicine" OR "tele medicine" OR ("self care" AND "software") OR (("internet" OR "web" OR "computerized" OR "computer based" OR "computer assisted" OR "technology based" OR "Technology assisted" OR "self guided" OR "online") AND ("therap*" OR "intervention*" OR "treatment*" OR "self help" OR "self care")) OR (("app" OR "apps" OR "website" OR "portable software" OR "application*") AND ("smartphone*" OR "phone*" OR "tablet" OR "android" OR "iphone" OR "iOS" OR "internet*" OR "web" OR "digital" OR "online*" OR "mobile" OR " device*")))

*Concept 2: Primary care*

TS = ("primary health*" OR "primary care*" OR "first line care" OR "primary medical care*" OR "family practi*" OR "family doctor*" OR "GP" OR "GPs" OR "family medi*" OR "family physician*" OR "outpatient*" OR "ambulatory care" OR "clinic visit*" OR "extramural care"

OR “office visit*” OR “general practi*” OR “general medical practi*” OR “general physi*” OR “health center*” OR “community mental health*” OR “self care” OR “selfcare” OR “self help” OR “selfhelp” OR selfmanagement OR "self management" OR selftreatment OR "self treatment")

*Concept 3: Alcohol*

TS=(“drinking” OR “alcohol*” OR “abstinence” OR “harmful use” OR “hazardous use” OR “ethyl” OR “drink”)

**Cochrane**

*Concept 1: mHealth*

#1: ([mh "Internet-Based Intervention"] OR [mh ^"Telemedicine"] OR [mh ^"Therapy, Computer-Assisted"] OR [mh "Mobile Applications"])

#2: ("Mobile Health" OR Telehealth OR “Tele health” OR mhealth OR ehealth OR telepsychiatr* OR (tele NEXT psychiatry*) OR "e health" OR "m health" OR telemedicine OR “tele medicine” ):ti,ab,kw

#3: ("self care" AND software):ti,ab,kw

#4: (internet OR web OR computerized OR "computer based" OR "computer assisted" OR "technology based" OR "technology assisted" OR "self guided" OR online):ti,ab,kw)

#5: [mh ^"Self Care"]

#6: (therap* OR intervention* OR treatment* OR "self help" OR "self care"):ti,ab,kw

#7: #5 OR #6

#8: #4 AND #7

#9: (app OR apps OR website OR "portable software" OR application*):ti,ab,kw

#10: [mh "Smartphone"] OR [mh "Web Browser"]

#11: (smartphone* OR phone* OR tablet* OR android OR iphone OR iOS OR internet* OR web OR digital OR online* OR mobile OR device*):ti,ab,kw

#12: #10 OR #11

#13: #9 AND #12

#14: #1 OR #2 OR #3 OR #8 OR #13

*Concept 2: Primary care*

#15: ([mh ^"Primary Health Care"] OR [mh "Physicians, Primary Care"] OR [mh "Physicians, Family"] OR [mh ^"Ambulatory Care"] OR [mh "Ambulatory Care Facilities"] OR [mh "General Practice"] OR [mh "General Practitioners"] OR [mh ^"Self Care"])

#16: ((primary NEXT medical NEXT care*) OR (primary NEXT health*) OR (primary NEXT care*) OR "first line care" OR (family NEXT practi*) OR (family NEXT doctor*) OR (family NEXT medi*) OR (family NEXT physician*) OR outpatient* OR "ambulatory care" OR (clinic NEXT visit*) OR "extramural care" OR (office NEXT visit*) OR (general NEXT practi*) OR (general NEXT physi*) OR gp* OR (health NEXT center*) OR (community NEXT mental NEXT health*) OR "self care" OR selfcare OR "self help" OR selfhelp OR selfmanagement OR "self management" OR selftreatment OR "self treatment"):ti,ab,kw

#17: #15 OR #16

*Concept 3: Alcohol*

#18: ([mh "Drinking Behavior"] OR [mh ^"Alcoholic Beverages"] OR [mh "Alcoholism"] OR [mh "Alcoholic Intoxication"] OR [mh ^"Alcohol-Related Disorders"] OR [mh "Binge Drinking"])

#19: (drinking OR alcohol* OR abstinence OR "harmful use" OR "hazardous use" OR ethyl OR drink):ti,ab,kw

#20: #18 OR #19

#21: #17 AND #20 AND #14

## Appendix 2: web of science collections

**Web of science core collection**:

- Science citation index Expanded -1955 to present
- Social Sciences Citation Index – 156 to present
- Conference Proceedings citation index – science – 1990 to present
- Conference proceedings citation index – social science and humanities – 1990 to present
- Emerging sources citation index – 2005 to present

## Appendix 3: Extraction sheet

| Study identification | | | | Trial info | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Author | Year | Title | Journal | Study goal | Inclusion criteria | Exclusie criterion | Partici-pant fol-low-up | Selection of participants | Geo-graphic location | Ratio of female partici-pants in popula-tion | Average age (SD) interven-tion/control | Standard units per week (SD) intervention/con-trol | Severity of use disorder (SD) intervention/con-trol | Loss of follow-up |
| **Hester R. et al.** | 2011 | ModerateDrink-ing.com and Moderation Management: Outcomes of a randomized clin-ical trial with non-dependent problem drinkers | Journal of Substance Abuse Treat-ment | To evaluate the effectiveness of both the Moderate Drink-ing (MD) web application as an adjunct to participation in the online activities offered by moderation management | Audit >7; 10+ standard drinks per week; Not currently abstain-ing; Interest in moderating their consumption; Minimum age 21; A computer with Internet access at home. | History of treatment for substance abuse | 12 months | Newspaper advertisement | Amer-ica, Al-buquer-que | 0,56 | 48,7 (?)/52,1 (?) | 33 (?) /35,4 (?) | AUDIT: 17,7 (?)/ 18,3 (?) | 27% after 12 months |
| **Blankers M. et al.** | 2011 | Internet therapy versus internet self-help versus no treatment for problematic al-cohol use: A ran-domized con-trolled trial | Journal of Consulting and Clinical Psychology | To compare the effectiveness of Internet-based therapy (therapy alcohol online) with Internet-based self-help (self-help alcohol online) for prob-lematic alcohol users. | between 18 and 65 y/o; resident of the Nether-lands with health care insurance; Internet access at home; AUDIT > 8; >14 standard drinks per week | Prior substance abuse treatment; history of alcohol delirium or a drug overdose; a se-vere coronary or in-testinal disease; schizophrenia, epi-lepsy, or suicidal tendencies in the last 12 months | 6 months | Online recruit-ment on web-site of sub-stance abuse treatment cen-tre | Nether-lands | 0,5 | 41.1 (9.6) / 43.7 (9.3) | 43.4 (24.0) / 45.4 (28.9) | AUDIT: 19,6 (5,6) / 20.1 (4,9) | 40% after 12 months |
| **Cunning-ham J. et al.** | 2012 | Comparison of two internet-based interven-tions for prob-lem drinkers: randomized con-trolled trial | Journal of Medical Inter-net Research | To evaluate the added benefit of providing access to an ex-tended Internet-based inter-vention in problematic drink-ers | AUDIT-C ≥ 8 | < 19 y/o; AUDIT-C < 8; not having home access to the Internet | 6 months | Newspaper advertise-ments | Canada | 0,41 | 45.2 (12.2) (only info on to-tal group) | 32.6 (17.9) / 30.8 (19.2) (typical weekly consump-tion) | AUDIT-C: 9.0 (1.5) / 8.6 (2.0) | 10% after 6 months |
| **Brendryen H. et al.** | 2013 | Balance--a prag-matic random-ized controlled trial of an online intensive self-help alcohol in-tervention | Addiction | To compare two versions of the online intervention 'Bal-ance': the brief intervention-only versus the full version comprising both the brief and intensive self-help. | FAST ≥3; ≥18 y/o; complete the baseline assess-ment with no missing items | No valid e-mail ad-dress and Norwegian mobile telephone number | 6 months | Banner adver-tisements on online news-papers | Norway | 0,43 | 39 (14) / 37 (13) | 19,8 (14) / 19,4 (12,8) | FAST: 6,3(3,0) / 6,2 (2,8) | 38% after 6 months |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sinadinovic K.** | 2014 | Targeting individuals with problematic alcohol use via Web-based cognitive-behavioural self-help modules, personalized screening feedback or assessment only: a randomized controlled trial | European addiction research | To compare an online normative feedback intervention to an online CBT program | >15 y/o; Audit-C >8 for men or 6 for women | Use of other drugs; absence of computer skills | 12 months | Ads on alcohol and drug-related websites and Google Ads | Sweden | 0,56 | 43,8 (11,9) /44,1 (12,1) | ? | AUDIT: 20,1 (?) / 20,9 (?) | 55% after 12 months |
| **Wallace P. et al.** | 2017 | Randomised controlled non-inferiority trial of primary care-based facilitated access to an alcohol reduction website | BMJ open | To compare a facilitated access to an interactive alcohol reduction website to a face-to-face brief intervention in reducing hazardous and harmful drinking | ≥18 y/o; Audit-C > 5 for men 4 for women | Severe psychiatric disorder; serious visual impairment or terminal illness; inadequate command of the Italian language | 12 months | Selection by general practitioner | Italy | 0,38 | 49 (?) / 50 (?) | ? | AUDIT-10 5 (?) / 6 (?) | 18,8% after 12 months |
| **Brendryen H. et al.** | 2017 | A pilot randomized controlled trial of an Internet-based alcohol intervention in a workplace setting. | International journal of behavioural medicine | To compare the effectiveness of a brief and an intensive self-help alcohol intervention and to assess the feasibility of recruiting to such interventions in a workplace setting | Employed; at-risk drinker based on FAST; ≥18 y/o; complete the baseline assessment with no missing items | No valid e-mail address and Norwegian mobile phone number | 6 months | Intranet newsfeed in 4 companies and recruitment emails | Norway | 0,44 | 43 (11) / 43 (11) | 17.0 (6.4) /17.3 (8.7) | FAST: 4,8 (2,1) /4,6 (2,1) | 26% after 6 months |
| **Boß et al.** | 2018 | Efficacy of a web-based intervention with and without guidance for employees with risky drinking: results of a three-arm randomized controlled trial. | Addiction | To test the efficacy of a web-based alcohol intervention named ‘GET.ON Clever weniger trinken’ ( be smart – drink less) in employees with a problematic drinking pattern | Audit ≥15 | <3 ICD-criteria; <18 y/o | 6 months | Announcement on magazines and website of health insurance companies and newspaper articles | Germany, Lüneburg | 0,59 | 47.6 (9.3) / 47.3 (10.3) | 30.26 (16.11) / 28.99 (13.38) | ? | 27,4% after 6 months |

| Study identification | | | Intervention group | | Control group | | Outcome | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Author | Year | Title | Treatment | Numer of participants | Treatment | Number of participants | Outcome measures | Outcome intervention population (SD) | Outcome control population (SD) | Conclusion |
| Hester R. et al. | 2009 | A web application for moderation training: Initial results of a randomized clinical trial | ModerateDrinking.com combined with access to the website www.moderation.org | 40 | moderation.org | 44 | Percentage of abstinence days, log units per day, log mean BAC, DrInC Recent Total score | 14.7% baseline to 43.9% at 12m (PDA) | 14.8% at baseline to 22.6% at 12m (PDA) | Both groups reduced their consumption and alcohol-related problems. The experimental group showed a greater reduction in consumption. |
| Blankers M. et al. | 2011 | Internet therapy versus internet self-help versus no treatment for problematic alcohol use: A randomized controlled trial | Internet based therapy: therapy alcohol online | 68 | Waiting list | 69 | Units consumed last week, percentage of weeks within safe drinking guidelines | 43,6 (23,8) at baseline to 27 (24,8) at 3m; 28% at 3m | 47,2 (28,2) at baseline to 35,5 (23,6) at 3m; 16% at 3m | After 6 months the Internet-based therapy did show larger reductions than Internet-based self-help. |
| Cunningham J. et al. | 2012 | Comparison of two internet-based interventions for problem drinkers: randomized controlled trial | Online CBT program: AlcoholHelpCenter.net | 83 | Online brief intervention: checkyourdrinking.net | 87 | Units consumed in typical week, highest number of drinks on one occasion in last 6 months, Audit-C | 32,6 (17,9) at baseline to 26,3 (20,7); 13,9 (7,3) at baseline to 10,3 (5,4); 13,9 (7,3) at baseline to 10,3 (5,4) | 30,8 (19,2) at baseline to 25,9 (18,7); 13,1 (7) at baseline to 11,5 (6,1); 13,1 (7) at baseline to 11,5 (7,3) | A small but significant additional reduction in drinking was found among participants who were provided with access to the extended Internet-based intervention |
| Brendryen H. et al. | 2013 | Balance--a pragmatic randomized controlled trial of an online intensive self-help alcohol intervention | Online brief intervention + intensive online CBT intervention | 125 | Online brief intervention + e-booklet | 119 | Self-reported alcohol consumption in previous week | 19,8 (14) at baseline to 16.3 (13.5) at 2m and 15.4 (13.6) at 6m | 19.4 (12.8) at baseline to 18.1 (13.4) at 2m and 17.9 (15.7) at 6m | This study provides partial evidence for the benefit of intensive self-help over and above traditional, brief interventions online. |
| Sinadinovic K. | 2014 | Targeting individuals with problematic alcohol use via Web-based cognitive-behavioural self-help modules, personalized screening feedback or assessment only: a randomized controlled trial | Online CBT program: Alkoholhjalpen.se | 114 | Waiting list<br>eScreen.se | 210<br>152 | Total Audit-C at 3, 6 and 12 months | 8,0 (7,7-8,2) at baseline to 6.7 (6.4–7.0) at 3m, 6.7 (6.3–7.0) at 6m and 6,6 (6,3-6,9) at 12m | 8,2 (7,9-8,4) at baseline to 6.8 (6.5–7.1) at 3m, 6.8 (6.5–7.1) at 6m and 6.7 (6.4–7.0) at 12m (waiting list) | Cognitive-behavioural extended self-help in combination with other interventions was more effective in changing alcohol use than online brief intervention or assessment only. |
| Wallace P. et al. | 2017 | Randomised controlled non-inferiority trial of primary care-based facilitated access to an alcohol reduction website | Feedback on drinking behaviour and CBT program: Thinking drinking record | 347 | Face-to-face brief intervention | 416 | Proportion AUDIT ≥ 8 after 3 months | 27.5% at baseline to 24,9% | 29,6% at baseline to 26,3% | Analysis of all prespecified outcome measures demonstrated evidence of non-inferiority for facilitated access versus face-to-face BI. Not after correcting for bias. |
| Brendryen H. et al. | 2017 | A pilot randomized controlled trial of an Internet-based alcohol intervention in a workplace setting. | Online brief intervention + intensive online CBT intervention | 43 | Online brief intervention + e-booklet | 42 | Self-reported alcohol consumption in previous week | 17,0 (6,4) at baseline to 13.7 (10.7) at 2m and 13.4 (7.5) at 6m | 17,3 (8,7) at baseline to 16.1 (9.4) at 2m and 14.6 (9.4) at 6m | No clear evidence supporting the hypothesis at 6 months after baseline was found. The complete case analyses, tended to support the hypothesis, indicating a better effect for the intensive condition. |
| Boß et al. | 2018 | Efficacy of a web-based intervention with and without guidance for employees with risky drinking: results of a three-arm randomized controlled trial. | Online CBT modules with or without adherence focus guidance | 146/144 | Waiting list | 144 | Self-reported alcohol consumption in previous week (timeline follow back) | 30.26 (16.11) at baseline to 17.89 (12.16) (unguided) | 28.99 (13.38) at baseline to 24.04 (13.18) | The intervention ‘GET.ON Clever weniger trinken’ is effective at reducing weekly alcohol consumption, whether offered with or without additional guidance. |

## Appendix 4: Logbook

| Datum | Activiteit | Betrokkenen | Afspraken/taakverdeling |
|---|---|---|---|
| 11/19 | Onderwerp + type masterproef | Dries, Jonas | Beiden: systematic review (SR) over selfhelp apps bij GGZ |
| 12/19-01/20 | Bepaling onderzoeksvraag SR | Dries, Jonas | Beiden: verkennend literatuuronderzoek: huidige stand van zaken? |
| 14/01/20 | Meeting met promotor | Promotor, Dries, Jonas | SR mCBT interventies bij problematisch alcoholgebruik |
| 3/3/20 | Opleidingssessie SR | Promotor, Dries, Jonas | |
| 3/20-7/20 | Protocol opstellen | Dries, Jonas | Jonas: inleiding deel 1 schrijven, PICO met begrippenlijst opstellen<br>Dries: inleiding deel 2 schrijven, data-extractieformulier opstellen<br>Beiden: methodesectie (inclusie/exclusie, zoekstrategie) en tijdslijn, feedback op elkaars werk. |
| 29/07/20 | Meeting met promotor | Promotor, Dries, Jonas | Review zal geschreven worden in het Engels<br>Samenwerken met bibliothecaris voor zoekstrategie |
| 08/20 | Aanvraag ethische commissie | Dries | |
| 15/08/20 | Opladen protocol | Dries, Jonas | |
| 9/20-12/20 | Selectie artikels | Dries, Jonas | Beiden: onafhankelijk artikels selecteren o.b.v. inclusie/exclusie criteria |
| 19/01/21 | Meeting met promotor | Promotor, Dries, Jonas | Herwerken zoekstrategie (bibliothecaris, cf. andere reviews)<br>Risk of bias analyse includeren in extractie formulier |
| 01/20-05/20 | Selectie artikels | Dries, Jonas, bibliothecaris | Beiden: herwerken strategie en selecteren artikels |
| 25/05/21 | Meeting met promotor | Promotor, Dries, Jonas | Starten met data-extractie en bias-analyse onafhankelijk van elkaar<br>Evalueren of meta-analyse mogelijk is, dan wel narratieve review |
| 05/21-10/21 | Data-extractie, bias-analyse | Dries, Jonas | Beiden: onafhankelijk data-extractie en bias-analyse studies |
| 2/11/21 | Meeting met promotor | Promotor, Dries, Jonas | Meta-analyse niet mogelijk owv heterogeniteit<br>Onderzoeksartikel schrijven en geen klassieke thesis |
| 11/21-12/21 | Draft: Inleiding en methoden | Dries en Jonas | Beiden: herlezen en aanpassen van inleiding en methode sectie |
| 01/22 – 03/22 | Draft: resultatensectie | Dries en Jonas | Beiden: brainstormen, effectiviteit CBT, feedback op elkaars werk<br>Dries: populatiekenmerken, studieduur, follow-up, eindpunten<br>Jonas: studie selectie, setting/rekrutering, interventies, kwaliteit studies |
| 04/22 | Draft: discussiesectie | Dries en Jonas | Beiden: brainstormen, feedback op elkaars werk<br>Dries: sterktes/limitaties evidentie, implicaties voor de praktijk<br>Jonas: resultaten in context, sterktes/limitaties review, verder onderzoek |
| 12/04/22 | Afwerken thesis | Dries en Jonas | Dries: abstract in Engels en Nederlands<br>Jonas: lijst met afkortingen, feedback op abstract<br>Beiden: nalezen en aanpassen van gehele thesis na feedback promotor |
| 04/22 | Zelfreflectie | Dries en Jonas | Beiden: onafhankelijke zelfreflectie over het leerproces |
| 01/22-04/22 | Feedback | Promotor | Constructieve feedback op voorlopige versies van thesis |
| 01/05/2022 | Indienen manuscript | Dries en Jonas | Beiden |
| 05/22 | Opstellen powerpoint | Dries en Jonas | Beiden: onafhankelijk powerpoint presentatie maken |
| 16/05/2022 | Indienen powerpoint | Dries en Jonas | Beiden |
| 21/05/2022 | Verdediging masterthesis | Dries en Jonas | Beiden: onafhankelijk mondeling presenteren en thesis verdedigen |

## Appendix 5: self-reflection

Het proces in het schrijven van de masterproef starte bij het selecteren van een onderwerp. Ik was op zoek naar een onderwerp met de volgende kenmerken. Ten eerste zochten ik naar een onderwerp met voldoende relevantie in de klinische praktijk, om zo dingen op te pikken die ik kon toepassen in mijn toekomstige huisartsenprakijk. Verder heb ik een interesse in psychologische en psychiatrische problematieken zoals slaapstoornissen, verslavingsproblematieken, angst en depressie. Ten laatste zocht ik een onderwerp dat een verschil zou kunnen veroorzaken in de manier van praktijkvoeren, zoals het gebruik van nieuwe technologieën, een verandering in aanpak of een nieuwe diagnostische test. Na het doorlopen van de verschillende thesisonderwerpen, voorzien door het icho, viel mijn oog op eHealth. Deze nieuwe beweging is een veelbelovende, maar tot nu toe weinig toegepaste, technolgie die een belanrijke inpakt kan hebben op de manier van prakijkvoeren. Jonas had gelijkaardige verwachtingen van de masterproef, dus besloten samen dit traject op te starten. Na een exploratieve literatuurstudie bekwamen Jonas en ik problematisch alcoholgebruik als onderzoeksgebied, gezien het beperkte aantal systematische reviews en toch al degelijke hoeveelheid randomised controlled trials beschikbaar over het onderwerp.

Onze volgende mijlpaal werd het opstellen van een onderzoeksvraag, een onderzoeksprotocol en een bijhorende zoekstring voor onze databases. Gezien we in onze explorerende literatuurzoektocht een zeer varrierende kwaliteit van self-help apps tegenkwamen, wilden we in ons onderzoek de nadruk leggen op een bepaalde kwaliteit. Dit deden we door de gebruikte omkadering, gebruikt als basis voor de apps, vast te leggen in de vorm van cognitieve gedragstherapie. Op basis hiervan, en in combinatie met de doelen die we voorop hadden gesteld, stelden we onze onderzoeksvraag en onderzoeksprotocol op. Hierin werden we geholpen door een oriënterende sessie mede georganiseerd door onze promotor. Een eerste zoektocht in de databases werd uitgevoerd. Helaas volgden hier na selectie beperktere resultaten dan gehoopt. Een verbeterde versie van onze zoekstring werd opgesteld met hulp van de medewerkers van het leercentrum Désiré Collen (medische bibliotheek te UZ Gasthuisberg). Hierdoor was de opbrengst van onze zoekstring sterk verbeterd en konden we verder met de definitieve selectie van onze artikels.

De selectie van onze artikels gebeurde onafhankelijk van elkaar, gebruik makend van de methodiek zoals vastgelegd in de PRISMA guidelines. Hiervoor gebruikten we de, door onze

promotor gessugereerde tool, Rayyan tool voor. Eens een onafhankelijke selectie was voltooid werden de resultaten samengelegd en vergeleken. De verschillen werden weggewerkt na overleg. Ook de data-extractie en bias analyse werden onafhankelijk van elkaar uitgevoerd. We stelden samen een data-extractie formulier op. Na een zoektocht in de literatuur en overleg met onze promotor gebruikten we de ROB-2 tool voor de bias analyse. Ook hier werden tegenstellende resultaten vergeleken en weggewerkt na overleg.

In het schrijven van ons artikel hebben we gekozen om de verschillende onderdelen van de tekst te verdelen en zo een eerste versie op te stellen. Deze werd nadien nagelezen door de andere partij en indien nodig gecorrigeerd. De tekst werd nadien verder geïntegreerd in de rest van de tekst.

In het samenwerken met Jonas heb ik geen problemen ervaren. Naar mijn gevoel waren we beiden gemotiveerd, afspraken konden worden gemaakt en werden nagekomen. Ik denk ook dat we elkaar goed aanvulde in onze kwaliteiten. Zo heeft Jonas een sterkere schrijfstijl, en is hij beter in plannen. Ik ben zelf meer behendig met de computer en had meer ervaring in het opstellen van een zoekstring. Hierdoor hebben we elk in verschilllende onderdelen van het proces het voortouw genomen. Op het vlak van verdeling van de workload voelt dit voor mij gelijkwaardig aan. Ingebakken in de methodiek van een systematische review zit sowieso een groot gedeelte van onafhankelijke screening en evaluatie. Het op elkaar afstemmen gebeurde nadien zonder problemen en met goede argumentatie. De analyses die we elk uit de bekomen resultaten bekwamen vulden elkaar mooi aan.

Qua betekenis van de resultaten van onze paper blijft mijn mening gereserveerd. Aan de ene kant lijkt lijkt mHealth een interessante aanvulling op de huidige klinische praktijk, zowel in alcoholproblematieken als in heel wat andere problematieken waar het momenteel in wordt onderzocht. Ik vermoed dat we nog veel van deze technologie gaan zien in de nabije toekomst. Mogelijk heeft de invloed van de corona-crisis hier ook wel wat losgemaakt in de algemene visie op telehealth. Maar tot op heden blijf ik, in het gebruik van mijn eigen praktijkvoeren, nog weg van het gebruik hiervan. Ik heb nog steeds mijn twijfels bij de kwaliteit van vele apps, zowel in de wetenschappelijke onderbouwing van de verschillende tools, maar ook in de veiligheid naar wat betreft privacy en bewaren van patiëntengegevens. Momenteel lijkt de technologie, zeker in de eigen taal, nog onvoldoende ontwikkeld. In onze

literatuurstudie bewkamen we bijvoorbeeld geen enkele app in het Nederlands. Een essentiële vereiste voor mij voor het gebruik ervan in de praktijk.

Ik denk dat verder onderzoek en grotere finaciering nodig zijn voordat deze technologie gebruikt kan worden in de klinische praktijk.