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

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Table of contents

ABSTRACT 5

ABSTRACT – DUTCH 6

ABBREVIATION LIST 7

INTRODUCTION 8

METHODS 11

RESULTS 13

STUDY SELECTION 13

STUDY SETTING AND PARTICIPANT RECRUITMENT 15

POPULATION CHARACTERISTICS 15

INTERVENTION AND COMPARISON TREATMENT 16

STUDY DURATION AND LOSS OF FOLLOW-UP 17

OUTCOME MEASURES 17

EFFICACY OF MCBT INTERVENTIONS IN COMPARISON TO TREATMENT AS USUAL 18

STUDY QUALITY 20

DISCUSSION 23

ACKNOWLEDGEMENTS 26

REFERENCES 27

APPENDIX 36

APPENDIX 1: SEARCH STRATEGY 36

APPENDIX 2: WEB OF SCIENCE COLLECTIONS 41

APPENDIX 3: EXTRACTION SHEET 42

APPENDIX 4: LOGBOOK 45

APPENDIX 5: SELF-REFLECTION 46

APPENDIX 6: ETHICAL APPROVAL **49**

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.

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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.

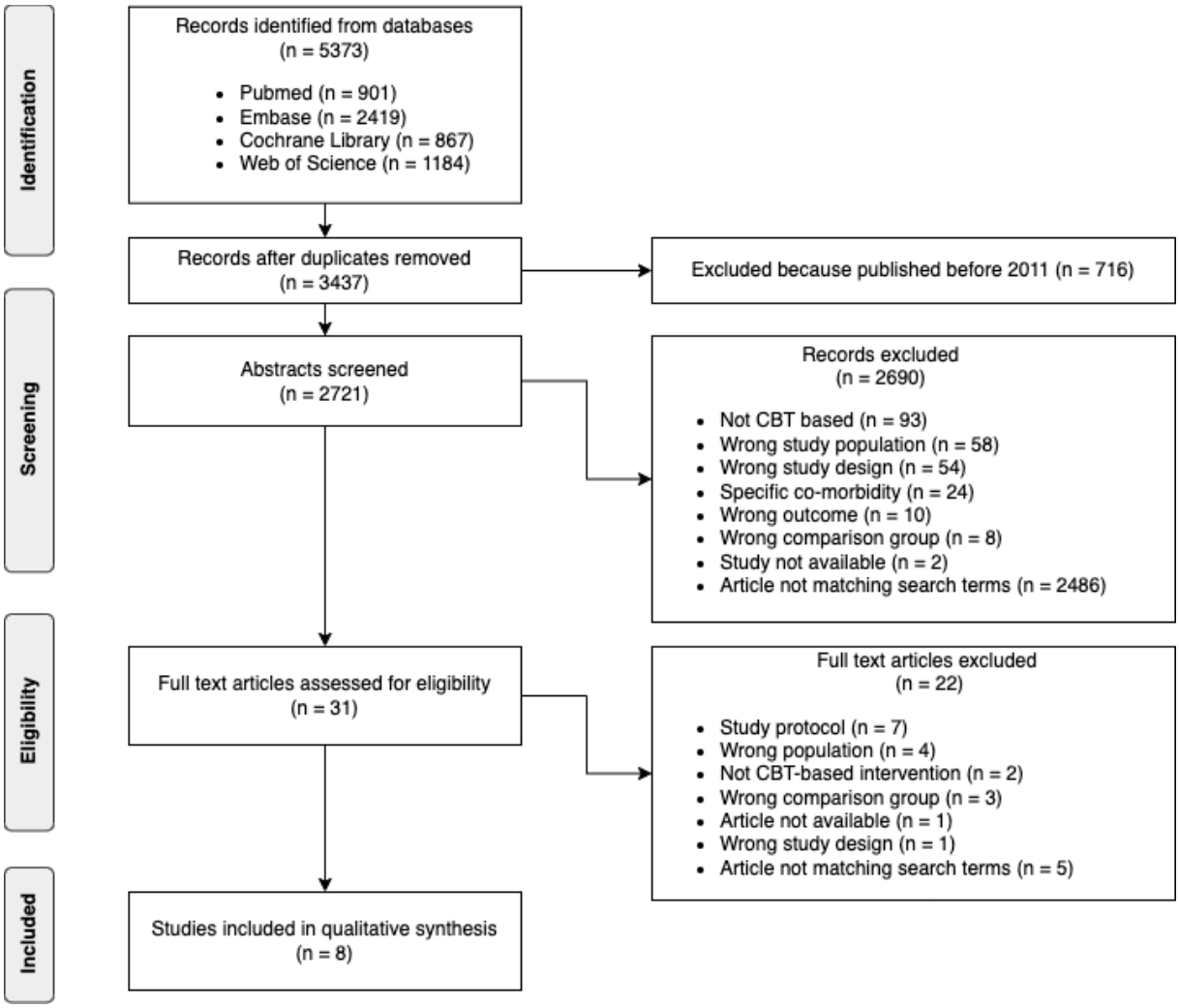


FIGURE 1. PRISMA FLOWCHART

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). An overview of the risk of bias in all included studies can be seen in Table 2 and Figure 2.

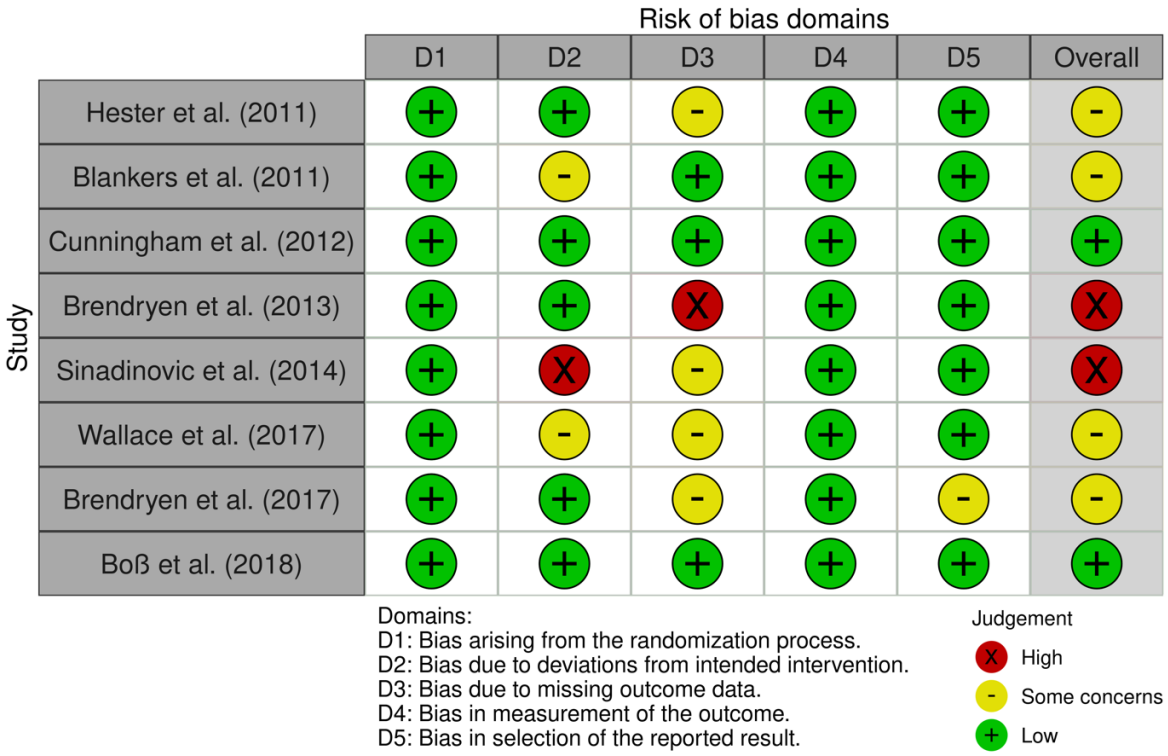


TABLE 2: RISK OF BIAS ANALYSIS – TRAFFIC LIGHT PLOT

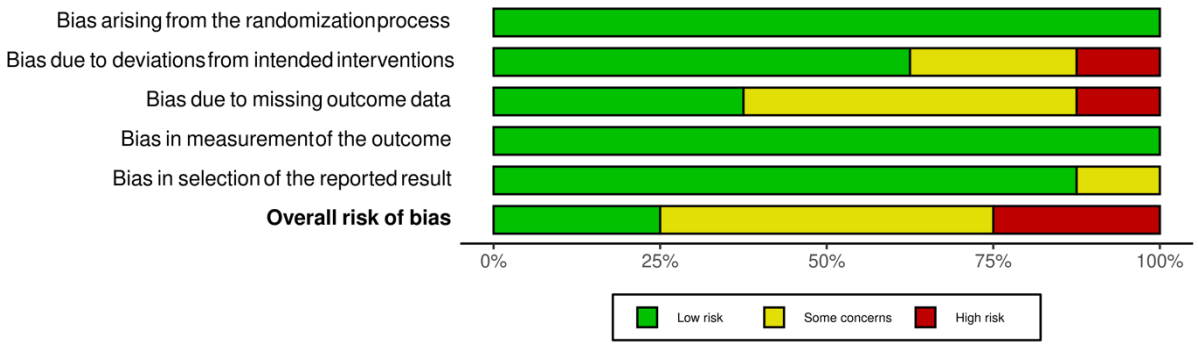


FIGURE 2: RISK OF BIAS – SUMMARY PLOT

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 (56). 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.

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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 'tele-health'/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 ‘tele-health’: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 ‘computer-ized’: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 ‘treat-ment*’: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 ‘ap-plication*’: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 ‘inter-net*’: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 'pri-mary 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 eScreen.se	210 152	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 Dries: inleiding deel 2 schrijven, data-extractieformulier opstellen 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 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) 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 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 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 Dries: populatiekenmerken, studieduur, follow-up, eindpunten Jonas: studie selectie, setting/rekrutering, interventies, kwaliteit studies
04/22	Draft: discussiesectie	Dries en Jonas	Beiden: brainstormen, feedback op elkaars werk Dries: sterktes/limitaties evidentie, implicaties voor de praktijk Jonas: resultaten in context, sterktes/limitaties review, verder onderzoek
12/04/22	Afwerken thesis	Dries en Jonas	Dries: abstract in Engels en Nederlands Jonas: lijst met afkortingen, feedback op abstract 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

Tijdens mijn opleiding tot huisarts werkte ik van oktober 2019 tot en met april 2022 samen met Dries Munters aan ons gezamenlijk project rond mobiele applicaties bij problematisch alcoholgebruik. Naar aanleiding van deze masterproef schrijf ik dit persoonlijk reflectieverslag om na te denken over het verloop van het groepsproces, over mijn persoonlijk aandeel en mijn leerproces en anderzijds om mijn persoonlijke visie over wat het werk betekent voor het werkveld weer te geven.

Aangezien zowel Dries als ikzelf geïnteresseerd zijn in de geestelijke gezondheidszorg (GGZ) en we in de praktijk regelmatig geconfronteerd worden met de uitdagingen van problematisch alcoholgebruik, kwamen we na raadpleging van de voorgestelde onderwerpen tot de beslissing om een thesis te schrijven rond smartphone applicaties bij GGZ problematieken. In de keuze van het type masterproef werden we tijdens de introductiesectie gestuurd richting een systematische review. Hoewel ik tevreden ben met onze keuze, denk ik dat een kwalitatief onderzoek met peiling naar de meningen en attituden rond deze interventies bij huisartsen en patiënten ook erg waardevolle inzichten had kunnen verschaffen.

Vanaf de start met het oriënterend literatuurnazicht en de formulering van de onderzoeksvraag tot aan het laatste nazicht van ons definitief werk, kijk in terug op een vlotte en vruchtbare samenwerking met Dries. We hebben beiden nauwgezet en op een systematische manier gewerkt aan het project en naar mijn gevoel in gelijke mate bijgedragen aan het uiteindelijke product. Hierbij hebben we zowel een aantal taken kunnen verdelen, alsook andere taken beiden onafhankelijk of juist samen uitgevoerd. Zo hebben we de selectie van de artikels op basis van de vooraf vastgelegde inclusie- en exclusie criteria, de analyse van de bias en de data extractie - conform de richtlijnen - onafhankelijk van elkaar uitgevoerd. Het verkennend literatuuronderzoek, het brainstormen, het opstellen van de zoekstrategie en het schrijven van de methodesectie daarentegen gebeurden tezamen. Hiernaast heb ik door de taakverdeling vooral bijgedragen aan de volgende delen: PICO en begrippenlijst in het protocol, het eerste deel van de inleiding (epidemiologie, gevolgen van alcoholgebruik) en de discussie (interpretatie van de resultaten in de context van andere evidentie, sterktes en limitaties van de review), de delen over studieselectie, studiesetting en rekrutering, de toegepaste interventies, de effectiviteit van mCBT en de

kwaliteit van de geïncludeerde studies in de resultatensectie . De taakverdeling kan ook teruggevonden worden in het logboek. Tijdens het schrijfproces werden deze delen uiteraard ook door de andere auteur nagelezen en eventueel gecorrigeerd en/of aangevuld, waardoor we alle onderdelen als een gezamenlijk product kunnen beschouwen.

Naast de evenredige taakverdeling kijk ik ook tevreden terug op onze systematische manier van werken. Hoewel we onze vooraf opgestelde tijdslijn enkele keren hebben moeten aanpassen, zijn we toch vlot op tijd klaar geraakt. Door bij elke samenkomst goede afspraken te maken, deadlines op te stellen en de volgende vergaderingen reeds in te plannen, bleven we continu met het project bezig, op een aantal korte onderbrekingen na. Ook onze promotor, prof. Van Nuland, heeft hiertoe bijgedragen door telkens een verslag te laten maken, door aan te sturen op minstens 2 overlegmomenten per jaar en door doelstellingen te formuleren voor de volgende ontmoeting. Hiernaast gaf hij ook steeds snel feedback op onze voorlopige versies.

Hoewel ik zelf geen carrière ambieer in wetenschappelijk onderzoek, heeft dit project mij toch een aantal belangrijke leermomenten opgeleverd. Voor mijn toekomstige rol als huisarts zijn met name de kritische evaluatie van de RCT's alsook het evalueren van de sterktes en limitaties van de eigen review leerrijk geweest. Er moet rekening gehouden worden met tal van potentiële bias en het proces van kritische evaluatie kost tijd en alertheid om grondig uit te voeren. Dit zal ik zeker meenemen bij het evalueren van artikels als huisarts in de toekomst. Hiernaast heb ik ook geleerd dat bij een systematische review het opstellen van een goede zoekstrategie uitermate belangrijk is. Na het uitvoeren van een eerdere versie van onze zoekstrategie bekwamen we slechts ongeveer 5 artikels na screenen van titel en abstract. Met de zoekstrategie die we ontwikkelden in samenwerking met de bibliothecaris steeg dit aantal tot 31. Bovendien was de overlap van bekomen artikels met beide zoekstrengen zeer laag, dus zowel de sensitiviteit alsook de specificiteit ging beduidend naar omhoog.

Bij de aanvang van ons onderzoeksproject had ik gehoopt dat ik na afloop één of meerdere mobiele applicaties had kunnen voorstellen en aanbevelen voor huisartsen als aanvulling op korte interventies. Hoewel ik denk dat mobiele applicaties met o.a. gebruik van CBT-technieken zeker een potentieel hebben in de aanpak van problematisch alcoholgebruik door de huisarts, kan ik o.b.v. onze onderzoeksresultaten heden geen evidence-based mCBT

interventie aanbevelen voor in de huisartsenpraktijk. Hoewel er volgens onze review indicaties zijn dat deze interventies even effectief of effectiever zijn in vergelijking met een wachtlijst of een online korte interventie, kunnen we deze beperkte evidentie niet extrapoleren naar de huisartsenpraktijk. In de meeste studies werden participanten gerekruteerd uit de algemene bevolking en betreft het een relatief oude, hoogopgeleide populatie met eerder extensief alcoholgebruik. Bovendien kon de enige studie in een éérstelijns setting geen niet-inferioriteit ten opzichte van een face-to-face korte interventie aantonen. We stellen met onze review dus met name ook vast dat er op dit moment quasi geen gerandomiseerde gecontroleerde klinische studies uitgevoerd zijn in Westerse huisartsenpraktijken. Om correcte uitspraken te doen over de effectiviteit zouden er meer kwalitatieve studies in deze setting moeten uitgevoerd worden. Naast effectiviteitsstudies lijkt het me ook zinvol om kwalitatief onderzoek te verrichten naar de meningen en attituden bij huisartsen en patiënten om in te schatten of deze interventies geschikt zijn voor de huisartsenpraktijk.

Appendix 6: Ethical approval

Selfhelp apps op basis van CBT technieken bij alcoholmisbruik in eerste lijn

Dossiernr.: MP016966
[[[Stage/Masterproef/Keuzevak]]]: Masterproef I HAIO, 2019-2022
Faculteit/opleiding: Faculteit Geneeskunde - Master in de huisartsgeneeskunde
Studiefase: eerste fase
Academiejaar: 2020-2021

Korte omschrijving / abstract:

Achtergrond
Alcoholgebruik is sterk genormaliseerd in de Belgische cultuur. Volgens de gezondheidsenquête van Sciensano uit 2018 drinkt 77% van de Belgische bevolking alcohol en drinkt 10% het dagelijks (1). Dit alcoholgebruik kan aanvaardbaar zijn, indien men gematigd en verantwoord drinkt, geïntegreerd in de samenleving. Helaas veroorzaakt alcoholgebruik vaak problemen zowel voor het individu en zijn directe omgeving, als voor de maatschappij.
Onder problematisch alcoholgebruik verstaan we zowel riskant als schadelijk alcoholgebruik. Riskant alcoholgebruik is een drinkpatroon met een verhoogd risico op schadelijke gevolgen zonder dat er reeds alcohol gerelateerde schade is opgetreden (2). Het gaat in dit geval bijvoorbeeld over het occasioneel overmatig alcoholgebruik waarbij een bepaalde norm wordt overschreden. Het Vlaams expertisecentrum Alcohol en andere Drugs schuift de norm van 10 standaardeenheden per week naar voren, naast een aantal andere criteria (3). Hiernaast beschouwen we drinken op niet geschikte tijdstippen of situaties en piekdrinken ook als riskant alcoholgebruik. Onder piekdrinken verstaan we het binnen 2 uur opdrinken van 4 standaardeenheden voor een vrouw en 6 voor een man (1). Wanneer er alcohol gerelateerde schade optreedt op fysiek, psychisch of sociaal vlak spreken we van schadelijk alcoholgebruik (2).
Problematisch alcoholgebruik is in België een belangrijk probleem. Indien men de definitie hanteert van meer dan 14E/w voor vrouwen en meer dan 21 E/w voor mannen, drinkt 6% van de Belgische bevolking ouder dan 15 jaar overmatige hoeveelheden alcohol. Vanuit het standpunt van maximum 10 alcoholische dranken per week, vormt het gebruik van alcohol mogelijks een gevaar voor 14% van de bevolking. Verder komt piekdrinken regelmatig voor bij 11% van de inwoners van België, 7% geeft aan dit maandelijks te doen, 4% zelfs wekelijks (1). Ook in de huisartsenpraktijk is problematisch alcoholgebruik prevalent. Een studie uitgevoerd in 6 Europese landen toonde aan dat bij 11,8% van de patiënten in de eerstelijnsgezondheidszorg een stoornis in alcoholgebruik voorkwam (4). In de Vlaamse huisartsenpraktijk variëren de cijfers van problematisch alcoholgebruik tussen 5 en 15% (5).
Problemen die gepaard gaan met het alcoholgebruik, kunnen van fysieke, psychische of sociale aard zijn. De belangrijkste alcohol gerelateerde fysieke aandoeningen zijn infectieziekten, gastritis, pancreatitis, leveraandoeningen, kankers, cardiovasculaire aandoeningen, neurologische aandoeningen, overgewicht en verwondingen (6). Hiernaast heeft alcohol ook gevolgen voor de sociale omgeving van de drinker (7). Het gaat hierbij o.a. om huiselijk geweld, scheidingen, agressie en schade door verkeersongevallen. In onderzoek meldt 18-79% van de respondenten dat ze ervaring hebben met de negatieve gevolgen van het alcoholgebruik van iemand anders (8–10). Schadelijk alcoholgebruik leidde in 2016 tot een schatting van 3 miljoen doden (5,3% van alle doden) en een ziektelast van 132,6 miljoen DALY's (5,1% van alle DALY's in 2016) wereldwijd. In de Europese regio van de WHO waren de proportie door alcohol veroorzaakten doden en DALY's het hoogste, met 10,1% en 10,8% respectievelijk(6).
Ten slotte zijn ook de maatschappelijke kosten aanzienlijk. Het Hoger Instituut voor de Arbeid (HIVA) deed in 1999-2001 een studie over de kosten en baten van alcoholgebruik in België (2). Uit deze studie bleek dat de totale netto jaarlijkse kost voor de overheid in België 4,5 miljard euro bedraagt. Deze kosten zouden voornamelijk afkomstig zijn van licht en matig alcoholgebruik (11).
De aanpak van problematisch alcoholgebruik gebeurt op verschillende niveaus en in verschillende settings. In de eerstelijnszorg is het voornamelijk belangrijk om problematisch alcoholgebruik te detecteren, het probleem in te schatten en hierna zelf een behandeling op te starten of door te verwijzen naar de gespecialiseerde hulpverlening. De behandeling in een huisartsenpraktijk bestaat meestal uit een kortdurende interventie, waarvan de effectiviteit reeds veelvuldig is aangetoond (12–14) en die door de Vlaamse huisartsenvereniging Domus Medica wordt aanbevolen (5). Er bestaan verschillende invalshoeken voor zorgverleners om alcoholproblematiek aan te pakken. Een van deze modaliteiten is de cognitieve gedragstherapie, waarvan de effectiviteit bij alcoholproblematiek reeds is aangetoond (15)
Ondanks de grote ziektelast en andere problemen gepaard gaande met alcoholgebruik wordt een groot percentage van patiënten met een alcoholproblematiek momenteel laat of niet bereikt. Volgens Europese gegevens zou gemiddeld 8% van deze patiënten (gaande van 3,8% tot 23,3% medische hulp hebben gezocht in het laatste jaar (16,17). België zou het hierin iets beter doen dan het Europees gemiddelde met 12,8%. Ook in België blijft er een grote vertraging bestaan van mediaan 18 jaar tussen het opkomen van de klachten en het zoeken van hulp. Uiteindelijk zou 61% van de patiënten met een alcoholproblematiek hulp vinden. Vroegere interventies zouden een groot verschil kunnen betekenen in de mortaliteit en morbiditeit van deze aandoening (16).
Oorzaken van dit lage percentage en deze vertraging in het vinden van behandeling zijn zowel te vinden bij de patiënt als in het gezondheidssysteem. Een eerste bepalende factor is het hulp-zoekend-gedrag van de patiënt. Dit gedrag wordt beïnvloed door verschillende factoren waarvan angst voor stigma, beperkt ziekte-inzicht, niet bekend zijn met mogelijke therapieën en weinig vertrouwen in de beschikbare therapieën de belangrijkste zijn (16,18,19). In bepaalde subgroepen is een beperkte toegang tot het gezondheidssysteem door een taalbarrière of financiële redenen ook een belangrijk element (20). Een andere bepalende factor is de implementatie van alcohol-gerelateerde zorg in eerste lijn. Zo wordt tijdens een consult bij de huisarts maar een beperkt gedeelde (41,7%) van de patiënten met een alcoholproblematiek ontdekt (16). Onvoldoende training en kennis van de behandeling, schrik om patiënten te labelen en geloof dat de patiënten niet eerlijk zouden antwoorden op vragen over het drinkgedrag worden door artsen benoemd als voornaamste barrières in de diagnose van een alcoholproblematiek (16,19,21). Daarnaast bestaan er ook verschillende sociale, culturele en maatschappelijke factoren, zoals het stigma rond alcoholproblemen en de alomtegenwoordige aanwezigheid van alcohol in de maatschappij die de barrière tot behandeling vergroten.
Een mogelijke technologie die de barrière tot de behandeling kan verkleinen of als aanvulling aan de huidige behandeling kan worden toegevoegd is mHealth (22). mHealth wordt door de WHO gedefinieerd als het gebruik van mobiele en draadloze technologie om gezondheidsdoelen te bereiken. In de praktijk betekent dit het inzetten van mobiele telefoons, smartphones of tablets voor het verbeteren van de gezondheid. Meestal in de vorm van berichten, videochat, telefoon-applicaties of websites.
Er zijn verschillende mogelijke voordelen van mHealth. Zo wordt het mogelijk om met wetenschappelijk onderbouwde strategieën op een systematische manier een breed publiek te bereiken. En dit op een goedkope en makkelijk toegankelijke manier voor de patiënt. Daarnaast is de patiënt niet gebonden aan de tijdsbeperkingen van hulpverleners, zowel op het vlak van beschikbaarheid van de hulpverlener als op het vlak van tijd per consult. De patiënt heeft zo continu toegang tot interventies, ook op onverwachte momenten waar een interventie nodig is. De patiënt hoeft zich niet te verplaatsen voor interventies. Mogelijke taalbarrières kunnen worden weggewerkt. Met de huidige technologie is het zelfs mogelijk om context-specifieke interventies op basis van locatie uit te voeren op het moment dat deze het meest nodig zijn. Bijvoorbeeld een interventie voor de patiënt bij het binnenwandelen in een café of nachtwinkel (de zogenaamde 'just in time feedback and support') (23–25).
Gezien de grote toename van internet- en mobiele telefoongebruik over de laatste jaren wordt mHealth ook een zeer toegankelijke technologie. 80% van volwassenen heeft toegang tot een mobiele telefoon en 57% tot een smartphone. Ongeveer 90% van de volwassenen heeft ook toegang tot het internet. In de groep van 18 tot 29-jarigen zijn deze cijfers zelfs nog hoger. Maar socio-economische factoren spelen wel een belangrijke rol, waardoor bepaalde groepen mogelijk wel beperkte toegang hebben. (26–28)
MHealth wordt reeds gebruikt en onderzocht op verschillende domeinen. Zo wordt er reeds onderzoek uitgevoerd op verschillende somatische problematieken zoals diabetes, overgewicht en bij de therapietrouw van medicatie bij bijvoorbeeld HIV of diabetes. (29-32) Ook bij psychiatrische problematieken wordt het reeds onderzocht zoals depressie, angststoornissen, PTSD en schizofrenie. (33-36) Daarnaast wordt mHealth ook reeds onderzocht bij andere verslavingsproblematieken zoals roken en druggebruik. (37-40)
In de context van alcohol-gerelateerde ziekten wordt mHealth ook reeds bestudeerd. Er werden al verschillende systematische reviews uitgevoerd bij verschillende subpopulaties zoals bijvoorbeeld bij jongeren (34,41,42). Ook over de eerste lijn werden reeds onderzoeken uitgevoerd. Hierin werd aangetoond dat self-help-apps als toevoeging op de standaard therapie mogelijk een positief effect kunnen hebben. Mogelijk wordt een betere therapietrouw bekomen over een langere periode. De effectgroottes zijn helaas klein. Tot noch toe werd het voordeel van alleen staande mHealth therapie tov standaard therapie nog niet aangetoond. (43–45)
Een mogelijke oorzaak van deze kleine effectgroottes is de wisselende kwaliteit van de verschillende apps, websites of programma's die gebruikt worden in dergelijke therapie. Bij vele van deze applicaties is er weinig info over de ondersteunende methodiek of wetenschappelijke onderbouwing die gebruikt wordt. Momenteel bestaan er weinig systematische reviews die zich toespitsen op één zo'n methode. Wel vonden we één systematische review die zich toespitste op cognitieve gedragstherapie bij zware alcoholproblematieken. Ook hier vinden we maar een klein, maar significant verschil bij toevoeging van mHealth interventies aan de standaard therapie, ook na 12 maanden. (26)

Studiedoel
Met onze studie zullen wij trachten een antwoord te bieden op de volgende onderzoeksvragen:

• Leidt associatie van CBT-mHealth interventie aan de gebruikelijke zorg bij patiënten met problematisch alcoholgebruik in de Westerse eerstelijnszorg tot meer reductie in drinkgedrag dan de gebruikelijke zorg alleen?

• Wat is de effectiviteit van CBT-mHealth interventie in vergelijking met de gebruikelijke zorg bij patiënten met problematisch alcoholgebruik in de Westerse eerstelijnszorg?

• (Wat is de effectiviteit van CBT-mHealth interventie in vergelijking met intensievere behandeling bij patiënten met problematisch alcoholgebruik in het Westen?)

Begrippen:

Self-help mHealth interventie: Een digitaal platform dat continu beschikbaar is voor de patiënt (website, mobiele applicatie), waarbij de arts niet actief bijdraagt (dus niet email, sms, teleconsult, videoconsult…) en dat gebruik maakt van elementen van cognitieve gedragstherapie.

CBT: cognitieve gedragstherapie

Gebruikelijke zorg (care as usual): Hiermee bedoelen we voornamelijk de kortdurende interventies (brief intervention), korte sessies waarin duidelijk en gestructureerd advies wordt gegeven, met feedback op maat van de patiënt over diens individuele verantwoordelijkheid om zijn gewoonten te veranderen. Daarbij worden veranderingsstrategieën aangeboden en wordt de nadruk gelegd op het stimuleren van het zelfvertrouwen van de patiënt in zijn slaagkansen om te veranderen. Er wordt een onderscheid gemaakt tussen kort advies ('simple brief intervention of brief advice') en een korte interventie ('extended brief intervention')
Problematisch alcoholgebruik: Hieronder verstaan we zowel riskant als schadelijk alcoholgebruik.
• Riskant alcoholgebruik (hazardous use) is een drinkpatroon met een verhoogd risico op schadelijke gevolgen zonder dat er reeds alcoholgerelateerde schade is opgetreden. Het gaat in dit geval bijvoorbeeld over het occasioneel overmatig alcoholgebruik waarbij een bepaalde norm wordt overschreden. Het Vlaams expertisecentrum Alcohol en andere Drugs schuift de norm van 10 standaardeenheden per week naar voren, naast een aantal andere criteria. Hiernaast beschouwen we drinken op niet geschikte tijdstippen of situaties en piekdrinken binge drinking) ook als riskant alcoholgebruik. Onder piekdrinken verstaan we het binnen 2 uur opdrinken van 4 standaardeenheden voor een vrouw en 6 voor een man.
• Schadelijk alcoholgebruik (harmful use) is alcoholgebruik met reeds alcoholgerelateerde schade op fysiek, psychisch of sociaal vlak.

Westers: West-Europa, Australië, VS, Canada

Eerstelijnszorg: makkelijk toegankelijke zorg die als eerste contact beschikbaar is voor een medisch probleem, waar zorg continuïteit gegarandeerd is en de verdere zorg, indien nodig, gecoördineerd wordt. Zoals zorg bij de huisarts, psycholoog, tandarts of apotheker.

Methode
Zoekstrategie
We voeren een zoekopdracht uit op 4 verschillende databanken: pubmed, embase, web of science en Cochrane Library. We hebben deze databanken gekozen omwille van hun relevantie bij medische onderwerpen en omdat we via de Katholieke Universiteit van Leuven toegang krijgen tot de volledige artikels.

We baseren onze zoekstrategie op de volgende zoektermen:
• P: Alle patiënten met problematisch alcoholgebruik in de Westerse eerstelijnszorg.
• I: CBT-mHealth interventie geassocieerd aan de gebruikelijke zorg of als alleenstaande therapie.
• C: Gebruikelijke zorg (bv kortdurende interventie) of intensievere behandeling.
• O: Drinkgedrag We includeren zowel studies die drinkgedrag kwalitatief als kwantitatief beoordelen.

Vanuit deze zoektermen werd een zoekstrategie opgemaakt voor zowel pubmed, embase als web of science:
• Pubmed:
  ◦ ((mhealth[tiab] OR eHealth[tiab] OR "Smartphone"[Mesh] OR smartphone*[tiab] OR smart-phone*[tiab] OR android[tiab] OR iphone[tiab] OR iOS[tiab] OR internet*[tiab] OR web[tiab] OR "Internet-Based Intervention"[Mesh] OR online*[tiab] OR app[tiab] OR "Mobile Applications"[Mesh] OR application*[tiab] OR digital[tiab])
AND
("General Practitioners"[Mesh] OR general-practi*[tiab] OR "Physicians, (Family"[Mesh] OR family-physician*[tiab] OR "Primary Health Care"[Mesh] OR primary-health*[tiab] OR primary-care[tiab] OR community[tiab] OR GP[tiab])
AND
("Drinking Behavior"[Mesh] OR "Alcohol Abstinence"[Mesh] OR Abstinence[tiab] OR "Alcohol Drinking"[Mesh] OR consumption[tiab] OR "Binge Drinking"[Mesh] OR binge-drink*[tiab] OR "Alcoholic Beverages"[Mesh] OR alcohol*[tiab] OR "Alcoholism"[Mesh] OR intoxica*[tiab])

• Embase:
  ◦ 'mhealth'/exp OR 'mhealth':ti,ab,kw OR
'smartphone'/exp OR 'smartphone':ti,ab,kw OR
'mobile application'/exp OR 'app':ti,ab,kw OR 'application':ti,ab,kw OR
'iphone'/exp OR 'iphone':ti,ab,kw OR 'ios':ti,ab,kw
'android'/exp OR 'android':ti,ab,kw OR
'web-based intervention'/exp OR 'web':ti,ab,kw OR 'internet':ti,ab,kw
AND
'general practitioner'/exp OR 'family physician*':ti,ab,kw OR 'GP':ti,ab,kw or 'general practitioner':ti,ab,kw OR
'primary health care'/exp OR 'primary care':ti,ab,kw OR 'primary health care':ti,ab,kw OR
'community dwelling person'/exp OR 'community dwelling':ti,ab,kw
AND
'drinking behavior'/exp OR 'drink':ti,ab,kw OR
'alcohol abstinence'/exp OR 'abstinence':ti,ab,kw OR
'binge drinking'/exp OR 'binge':ti,ab,kw OR
'alcoholic beverage'/exp OR 'alcohol':ti,ab,kw OR 'intoxication':ti,ab,kw OR 'alcoholism'

• Web of science:
  ◦ AB= (mhealth OR eHealth OR smartphone* OR "smart phone*" OR smart-phone* OR android OR iphone OR iOS OR internet* OR web* OR "Internet-Based"* OR online* OR app OR application* OR digital)
AND
AB= ("General Practitioners" OR "general practi"* OR "family physician"* OR "Primary Health" OR "health care"* OR "primary care"* OR "GP" OR "community")
AND
AB= (drink* OR abstinence OR alcohol* OR consumption OR binge* OR beverage OR intoxica*)

• Cochrane Library
  ◦ Concept 1:
    ▪ #1: [mh "smartphone"] OR [mh "Internet-Based Intervention"] OR [mh "Mobile Applications"]
    ▪ #2: ("mhealth" OR "eHealth" OR smartphone* OR (smart NEXT phone*) OR "android" OR "iphone" OR "IOS" OR internet* OR "web" OR online* OR "app" OR application* OR "digital"):ti,ab,kw
    ▪ #3: #1 OR #2
  ◦ Concept 2:
    ▪ #4: [mh "General Practitioners"] OR [mh "Physicians, Family"] OR [mh "Primary Health Care"]
    ▪ #5: ((general NEXT practi*) OR (family NEXT physician*) OR (primary NEXT health*) OR "primary care"):ti,ab,kw
    ▪ #6: #4 OR #5
  ◦ Concept 3:
    ▪ #7: [mh "Drinking Behavior"] OR [mh "Alcohol Abstinence"] OR [mh "Alcohol Drinking"] OR [mh "Binge Drinking"] OR [mh "Alcoholic Beverages"] OR [mh "Alcoholism"]
    ▪ #8: ("Abstinence" OR "consumption" OR binge-drink* OR alcohol* OR intoxica*):ti,ab,kw
    ▪ #9: #7 OR #8
    ▪ #10: #3 AND #6 AND #9

Alternatieve bronnen worden in onze studie niet aangewend voor het vinden van artikels.
Selectie artikels
De zoekresultaten van de verschillende databanken worden gecombineerd in een citatie manager (Mendeley) en duplicaten worden geregistreerd en verwijderd.

Vanuit de verschillende zoekmachines wordt een email-alarm opgesteld om ook de meest recent gepubliceerde artikels te kunnen screenen. Tot 2021 worden nog artikels geanalyseerd.

Van hieruit starten we individueel de selectie van artikels.

Als inclusiecriteria voor onze studie gelden:
• Artikels die voldoen aan onze zoektermen, zoals hierboven vermeld
• Gepubliceerd in de laatste 10 jaar (2011 tot 2021)
• Artikels met als studieontwerp randomized Controlled Trials
• Participanten van >16j
• Uitgevoerd in een Westerse land (West-Europa, Verenigde staten, Canada en Australië).
• Uitgevoerd in een eerstelijns setting
• Geschreven in het Engels, Frans of Nederlands
Als exclusiecriteria voor onze studie gelden:
• Artikels die niet voldoen aan onze zoektermen, zoals hierboven vermeld.
• Gepubliceerd voor 2011
• Studieontwerp geen Randomized controlled trial.
• Studies over participanten met één specifieke psychiatrische co-morbiditeit
• Artikel zonder peer-review, enkel studies gepubliceerd in een wetenschappelijk tijdschrift worden geïncludeerd.
• Geschreven in een andere taal dan Engels, Frans of Nederlands.

De studieselectie zal worden uitgevoerd op basis van titel en abstract door gebruik te maken van de Rayyan QCRI webapp. De artikels worden door beide onderzoekers individueel gescreend. Nadien worden verschillen besproken en weggewerkt. Hierna wordt de 2e fase van de screening uitgevoerd op de volledige artikels. Verder verloopt deze screeningsfase gelijk aan de eerste.
Data extractie
Van onze geselecteerde artikels wordt op basis van een vooraf opgesteld data-extractie-formulier de volgende gegevens geëxtraheerd:
• Auteurs, affiliatie auteurs (universiteit, onderzoeksgroep) en contactgegevens auteurs
• Identificatiegegevens van het artikel (jaar van uitgave, titel, PMID, DOI, URL)
• Studiegegevens (Studiedesign, studiedoel, PICO, in- en exclusiecriteria, mate en methode van blindering, periode van gegevensverzameling, geografische locatie)
• Gegevens van de interventie- en controlegroep (aantal participanten, verdeling m/v, leeftijd van de populatie, informatie over comorbiditeiten en medische voorgeschiedenis, socio-economische gegevens, gegevens over het alcoholgebruik voor interventie)
• Gegevens van de outcome van de studie (definiëring van outcome, methode van bepalen van de outcome, outcome voor de interventie- en controlegroep, eventuele subgroepen die besproken zijn, en de conclusie van het artikel)
• Zowel vermelde als niet vermelde limieten in de studie
• Vermelding van ethische goedkeuring
Kwaliteitsassessment
Op de geselecteerde artikels voeren we een kwaliteitsanalyse uit. Voor het bepalen van de kwaliteit van de studie worden de volgende elementen in rekening genomen (46,47):

• Is er een duidelijk studieontwerp, een duidelijk doel van de studie met een duidelijk afgebakende interventie- en controle groep? Een duidelijke outcomes-maat en beschrijving hiervan?
• Is het studieopzet geschikt om deze wetenschappelijke vraag te beantwoorden? Is de gekozen outcome een goede maat voor het aantonen van deze wetenschappelijke vraag?
• Is er duidelijkheid over het proces van toewijzing in de interventie- en controle groep? Zijn de verschillen bij de start van het onderzoek tussen de controle- en interventiegroep waarschijnlijk door toeval? Hebben deze effect op de outcome?
• Wisten de behandelaars de interventie de participanten kregen? Hadden deze een mogelijk effect op de outcome?
• Werd bij het bepalen van de outcome voldoende blindering van de evaluator voorzien? Heeft dit mogelijk effect op de outcome van het onderzoek?
• Zijn er mogelijke confounders die de outcome kunnen beïnvloeden?
• Werden voldoende participanten opgevolgd tot het einde van de studie? Zijn er gegevens over voldoende participanten? Heeft de duur van follow-up en outcome mogelijk een verband met elkaar (vb. goede/slechte outcome geeft meer drop-outs)? Heeft het aantal drop-outs mogelijk effect op de outcome?
• Werd de data geanalyseerd aan een vooraf bepaald plan? Werd de outcomes-maat (uit verschillende opties) mogelijk laat in het analyseproces gekozen? Werd 1 analyse uitgevoerd of meerdere?
• Is het resultaat van deze studie toepasbaar op de bredere populatie?
• Is het resultaat van deze studie relevant in de klinische praktijk?
• Is er een mogelijke belangenvermenging in deze studie?
• Selective reporting bias: Komen outcome-maten vermeld in de methodesectie overeen met de outcome-maten in de resultatensectie? en indien een protocol beschikbaar is, komen de outcome-maten in het protocol overeen met de outcome-maten van het gepubliceerde artikel?

Analyse
Indien de gevonden artikels zowel statistisch als in methodiek voldoende homogeen zijn wordt een meta-analyse uitgevoerd met de bekomen gegevens. Indien de gegevens te heterogeen zijn zal een narratieve review worden uitgevoerd met de resultaten.

Toegepaste technieken:	literatuuronderzoek, systematic review
Key publication:	1. Gisle L, S. Demarest S, Drieskens S. Gezondheidsenquête 2018: Gebruik van alcohol. Brussel, België; 2018. 2. De Doncker J, De Donder E, Möbius D. Dossier Alcohol. 2016. 3. Geirnaert M. Een nieuwe richtlijn voor alcoholgebruik - VAD. 2016; 4. 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. J Subst Use [Internet]. 2016;21(5):478–84. Available from: http://dx.doi.org/10.3109/14659891.2015.1063719 5. Michels J, Hoeck S, Dom G, Goossens M, Van Hal G, Van Roye P. Problematisch alcoholgebruik. Aanpak door de huisarts. 2011. 6. 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. 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Trefwoorden:	Alcohol use primary care CBT mHealth
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De verstrekte informatie toont aan dat het onderzoek in het kader van de masterproef een zuivere literatuurstudie betreft en dat er op geen enkele wijze gebruik wordt gemaakt van proefdieren, proefpersonen of menselijk lichaamsmateriaal.

Dit type onderzoek vereist geen goedkeuring van een gemachtigde commissie voor medische ethiek.

Onder voorbehoud van de volledigheid en correctheid van de door u verstrekte gegevens, krijgt u hierbij het akkoord om het onderzoek in het kader van de masterproef te starten. Deze mail dient als bewijs van goedkeuring mocht u uw onderzoek wensen te publiceren.

Wij willen u erop attent maken dat u zelf verantwoordelijk blijft voor uw onderzoek. Bovendien doet elke wijziging aan de door u verstrekte gegevens omtrent de onderzoeksopzet deze goedkeuring vervallen. U dient in dat geval een amendement te maken aan uw huidig dossier.