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# BMJ Open

## The influence of hazardous drinking on psychological functioning, stress and sleep during and after treatment in patients with mental health problems; a randomized controlled trial

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4 **The influence of hazardous drinking on psychological**  
5 **functioning, stress and sleep during and after treatment in**  
6 **patients with mental health problems; a randomized**  
7 **controlled trial**  
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11 **Short title** – Hazardous drinking in treatment of mental health problems  
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## ABSTRACT

### Objectives

Hazardous drinking could negatively affect health and lead to alcohol use disorders, but it is unclear how hazardous drinking affects treatment outcomes of depression and anxiety and stress-related mental health problems.

The aims of this study were to examine whether hazardous drinking, measured by AUDIT-C, influence the outcomes of repeated assessments of psychological functioning (OQ-45), stress (PSS) and sleep (KSQ) during and after treatment in patients with mental ill-health.

### Methods

The study was conducted within REGASSA, a randomized controlled trial aimed at comparing Internet-based CBT and physical exercise with treatment as usual on primary care patients with mental ill-health. The study involved 871 participants who completed Alcohol Use Disorders Identification Test at baseline and who were assessed repeatedly during and after treatment on psychological function, stress and sleep by Interactive Voice Response (IVR), a computerized, automated telephone technology.

### Results

At baseline hazardous drinkers were more depressed and had lower scores for psychological functioning than non-hazardous drinkers, while there were no differences for stress and sleep. During the follow-ups, hazardous drinking negatively influenced perceived stress, i.e. hazardous drinkers seemed to have less treatment effect on stress and the results remained after controlling for depression. There were no differences during the follow-ups regarding psychological functioning and sleep.

## Conclusions

Hazardous drinking negatively influenced perceived stress. The study findings emphasize the importance of screening for alcohol habits in mental ill-health patients, since risky drinking may affect the outcomes of treatment.

## Trial registration

The REGASSA study was 2015/06/10 retrospectively registered in German clinical trials DRKS00008745, but it was 2011/02/10 originally registered with KTA CT20110063.

**Key words:** Hazardous drinking, mental health problems, primary care, psychological functioning, stress, sleep, IVR, repeated assessments, Internet-based CBT, physical exercise

## STRENGTHS AND LIMITATIONS

- The randomized controlled study design is a strength in the study
- The large sample of primary care patients is also a strength
- Repeated assessments by automated technology was an easy way of following a large sample of participants
- The high attrition in the repeated assessments was a limitation
- The analyze model was a strength compensating for the attrition in the study

## INTRODUCTION

Hazardous or risky alcohol consumption is common in patients seeking primary care, but is often not sufficiently examined at the medical visit,[1-2] and only some patients with risky consumption are advised to reduce their alcohol use,[3]. Hazardous drinking, both the number of drinks consumed weekly and on a single occasion, binge drinking, is considered an alcohol drinking pattern that could lead to negative effects on health and to development of alcohol use disorders,[4-5]. Screening for alcohol use is a recommended intervention for patients in routine care, and patients reporting a pattern of hazardous drinking should be given advice on how to change this pattern and offered brief interventions. Patients with alcohol use disorder or dependence should be referred for treatment,[6-8].

Several studies have shown higher prevalence rates for hazardous drinking in patients with common mental health problems compared to the general population,[6, 9-11]. However, only a few studies have examined whether concomitant hazardous drinking affects treatment outcome of mental health problems. In an extensive review by Sullivan and colleagues (2005), it could not be established whether hazardous drinking or alcohol use disorders influenced recovery from or relapse in depression, although the review only involved one study examining risk drinking. In that study hazardous drinking did not affect recovery from depression,[12]. Gajecki and co-workers (2014) examined whether problematic substance use affected on Internet-based cognitive behaviour therapy for depression and anxiety disorders, and found no differences in effect between hazardous and non-hazardous drinkers on depression, but hazardous drinkers showed less treatment effect for panic disorder,[13]. In another study on treatment of anxiety, alcohol use severity had no impact on treatment effect, although, baseline hazardous alcohol use was associated with more anxiety and depression symptoms at long-term follow-up,[14]. Haynes and colleagues (2007) showed little evidence that hazardous drinking is a risk factor in non-recovery from common mental disorders, but

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3 binge-drinking may be a potential risk,[5]. Consequently few studies have been conducted on  
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5 the impact of hazardous alcohol use on treatment effects and the findings are inconsistent,  
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7 which justifies further research.  
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10 The present study was performed within the framework of REGASSA, a multicenter  
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12 randomized controlled trial (RCT) conducted in primary care on patients with mild to  
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14 moderate depression, anxiety, and stress-related mental health problems. The objectives of  
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16 REGASSA were to study the effects of Internet-based cognitive behaviour therapy (ICBT)  
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18 and physical exercise (PE) compared to treatment as usual (TAU) on work-ability and sick-  
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20 leave as primary outcome measures, and depression as secondary outcome. Other secondary  
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22 outcome measures were used, including repeated assessments of psychological functioning,  
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24 perceived stress and sleep. Data was collected by automated telephone technique, Interactive  
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26 Voice Response (IVR) which enabled frequent follow-ups during and after treatment. In a  
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28 previous analysis of REGASSA using these secondary outcomes, we found that ICBT and PE  
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30 were more effective than TAU on psychological functioning and sleep, but on perceived  
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32 stress no differences were found, all three treatment groups improved,[15].  
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37 In the present study, we wanted to examine hazardous alcohol use in relation to the outcome  
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39 measures of sleep, psychological functioning and stress, factors that might be influenced by  
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41 hazardous alcohol consumption. To the best of our knowledge, the relationship between  
42  
43 hazardous drinking and the secondary variables of REGASSA has previously only been  
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45 studied with less frequent follow-ups, or has not been studied at all.  
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48 Stress is known to be linked with sleeping problems and mood disorders,[16-18]. In a  
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50 previous primary care study, high levels of stress were commonly reported in association with  
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52 symptoms of anxiety and depression,[19] and high levels of perceived stress have been shown  
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54 to be associated with less antidepressant treatment effect,[20].  
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3 In an epidemiological study of over 30.000 individuals, Dawson et al,[21] found that stress  
4 resulted in increased quantities of alcohol consumption on specific drinking occasions, rather  
5 than more frequent drinking. According to Scher et al whether alcohol reduces perceived  
6 stress is unclear, and is likely to be influenced by both individual and situational factors,[22].  
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12 Vinson and colleagues conducted a study in primary care on sleep and alcohol consumption  
13 and found no associations between hazardous drinking and sleeping problems,[23]. To the  
14 best of our knowledge, how hazardous drinking may affect change in psychological  
15 functioning (Outcome Questionnaire-45, OQ-45) has not yet been studied.  
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21 At baseline, patients in REGASSA completed the Alcohol Use Disorders Identification Test  
22 (AUDIT), which was developed for early detection of individuals with hazardous or harmful  
23 alcohol drinking,[24]. A previous study of REGASSA showed that the total AUDIT scores  
24 and the scores of AUDIT-C were higher among REGASSA patients compared to the general  
25 population,[25].  
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31 This study aimed to examine whether hazardous drinking at baseline influences the outcomes  
32 of repeated assessments of psychological functioning, stress and sleep collected by IVR  
33 during and after treatment in REGASSA.  
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## 39 40 **METHODS**

### 41 42 **Study design**

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44 Study design, participants and measurements are presented in more detail in an earlier  
45 study,[15], and only a brief description is given here. REGASSA was carried out in primary  
46 care in six health care regions in Sweden between 2011 and 2014. After given written  
47 informed consent, patients were randomized to one of three treatment alternatives, ICBT, PE  
48 and TAU, for a 12-week intervention. At baseline, participants completed a battery of  
49 questionnaires, including measures of depression (MADRS) and alcohol use (AUDIT), and  
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3 follow-ups were conducted 3 and 12 months after baseline. Secondary outcomes of  
4 psychological functioning, stress and sleep were continually collected by IVR during and  
5 after treatment.  
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10 IVR is an automated telephone system programmed to administer various questionnaires and  
11 to follow a large population over time. At baseline the patients in REGASSA registered their  
12 personal mobile number and answered the 55 questions included in IVR using touch-tone  
13 technology. The automated system then called the patients on six measurement occasions, two  
14 during treatment, one at the end of treatment, and three after treatment until 12 months after  
15 baseline. The drop-out in IVR showed varying but decreasing levels over the 12-month study  
16 period. For example, at 3-month follow-up 54 % completed the questionnaires, but this had  
17 fallen to 25 % at the final 12-month follow-up.  
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## 28 **Participants**

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30 Participants were primary care patients with light to moderate depression, anxiety and stress-  
31 related mental ill-health. The inclusion criteria were  $\geq 10$  points on the Patient Health  
32 Questionnaire (PHQ9), a short depression scale and, Swedish language skills due to the ICBT  
33 programme, which was only delivered in Swedish. REGASSA included 945 patients, of  
34 which 879 completed the IVR baseline assessments and of these 879 patients, 871 also  
35 completed AUDIT at baseline. Patients with a primary substance use disorders were excluded.  
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43 The CONSORT diagram (Figure 1) shows the flow of participants in the study.  
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## 46 **Measures at baseline**

### 47 **AUDIT**

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49 AUDIT is a ten- item scale for measuring alcohol consumption and alcohol-related problems.  
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51 The test is validated in primary care and has shown acceptable psychometric properties,[24].  
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55 AUDIT is divided in two parts, items 1-3 measuring alcohol consumption (AUDIT-C), and  
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3 items 4-10 measuring alcohol problems (dependency and harm combined). In this study, we  
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5 only used the abbreviated consumption subscale AUDIT-C, since the three questions in OQ-  
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7 45 on negative consequences of drinking behaviour would otherwise interfere with questions  
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9 4-10 in AUDIT. The items in AUDIT-C are (1) *How often do you drink alcohol?* (2) *How*  
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11 *many glasses do you drink on a typical day when you drink alcohol?* (3) *How often do you*  
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13 *have six or more drinks on one occasion?* The scores range from 0-4 and maximum negative  
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15 score is 12. AUDIT-C has shown high specificity and sensitivity in screening for risky  
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17 alcohol habits,[26-27]. The cut-off score for hazardous drinking in this study was set to  $\geq 5$   
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19 for women and  $\geq 6$  for men in accordance with Swedish guidelines,[28]. These cut-offs are  
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21 higher than in previous studies where the cut-off scores have been set to  $\geq 3-4$  for women and  
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23  $\geq 4-5$  for men, but it is recommended that cut-off scores be determined empirically in  
24  
25 different cultures, since drinking frequency varies largely between countries,[6, 26-27].  
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29 When studying the question of binge drinking separately, the cut- off was set to *at least on a*  
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31 *monthly basis* for both women and men.  
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#### 34 MADRS

35 In earlier REGASSA studies, MADRS was used as an outcome measure for depression but, in  
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37 this study, it was used as a baseline measurement and only for controlling results obtained  
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39 with AUDIT-C. MADRS is a well-used measure for depression that has shown good  
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41 psychometric properties. It consists of ten items with six response alternatives,[29].  
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#### 45 Gender

46 We analyzed whether there were any gender differences between in terms of hazardous  
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48 drinking and its influence on the outcome measures of psychological functioning, sleep and  
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50 stress.  
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## Outcome measurements in IVR

### Outcome Questionnaire-45

The repeated assessments of psychological functioning were measured by Outcome Questionnaire-45 (OQ-45). OQ-45 was developed by Lambert and colleagues to measure psychotherapy effects,[30]. It consists of 45 questions with a score range of 0-180, where 180 is the maximum negative score. OQ-45 captures the patient's psychological functioning through questions about symptoms, interpersonal problems and social role function. Both the original and the Swedish version of OQ-45 have shown good psychometric properties,[30-32].

### Perceived Stress Scale

Stress was repeatedly assessed by the Perceived Stress Scale (PSS), originally a ten-item scale measuring how the patient copes with stress. In this study, we used a shortened 4-item version of this scale that has proved suitable for telephone assessments,[33]. The scores range from 0-4 and the maximum total negative score is 16.

### Karolinska Sleep Questionnaire

A short version of the Karolinska Sleep Questionnaire assessed the sleep outcome. The questionnaire comprises four items with scores ranging from 1-6, and the maximum negative score was 24. KSQ has shown good validity, reliability and sensitivity in various studies,[34].

## Statistics

Differences between hazardous drinkers and non-hazardous drinkers were calculated on continuous baseline measurements using independent samples t-tests, and differences in proportions of hazardous drinkers in discrete variables were examined with chi-square tests. To examine how alcohol consumption (AUDIT-C) at baseline affected the course and outcome for psychological functioning, stress and sleep, we conducted three separate analyses with linear mixed-models with first order auto-regressive heterogeneous rho covariance structure. Mixed-models include all measures that are available at each assessment, and were

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3 therefore considered suitable for this study. We assumed that missing observations were  
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5 unrelated to the observed value, i.e. missing at random. Each model included six follow-ups  
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7 called assessments 1, 2, 3, 4, 5 and 6, the assigned treatment groups ICBT, PE and TAU,  
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9 gender and two baseline measures, i.e. hazardous drinking (AUDIT-C) and the baseline  
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11 scores of one of the three outcome measures (OQ-45, PSS, KSQ). All variables were  
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13 modelled as fixed effects. The outcome measures baseline scores were used as continuous  
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15 covariate and the control variable hazardous drinking (AUDIT-C) and gender as categorical  
16  
17 covariates. AUDIT-C was a dichotomous variable where 0 was defined as non-hazardous  
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19 drinking and 1 hazardous drinking. MADRS was used as a continuous covariate for  
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21 controlling for depression if AUDIT-C showed significant influence on the outcome  
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23 measures. Assessment data was nominal, i.e. each measurement occasion was separate and  
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25 time was not a continuous linear regressor in the model. The analyses began with a full model  
26  
27 with interaction effects of AUDIT-C x Treatment group x Assessment and was simplified to  
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29 main group effects if no significant interaction effects were found. Before the results were  
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31 analysed the residuals were examined and showed a normal distribution. A test for robustness  
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33 showed similar results as the mixed-models analysis. All statistics were performed in the  
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35 SPSS for Windows 22.0.  
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## 39 40 **RESULTS**

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42 The average age of patients was 43 and 62 % had a high level of education. Most of the  
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44 patients were working and only 5 % were on sick-leave. In Table 1, different descriptions of  
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46 baseline measurements for hazardous drinkers and non-hazardous drinkers are presented.  
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**Table 1.**

Baseline scores for hazardous drinkers and non-hazardous drinkers on sociodemographic data, depression (MADRS) psychological function (OQ-45), stress (PSS) and sleep (KSQ) and the three treatment conditions, Internet- based cognitive behaviour therapy (ICBT), Physical exercise (PE) and treatment as usual (TAU)

<b>Variables</b>	<b>Non-Hazardous</b>	<b>Hazardous</b>
Age M( $\pm$ SD)	43.4 (12.0)	40.7 (13.1)
Gender %		
Male	25	35
Education %		
Low	4	5
Medium	35	38
High	61	57
Employment %		
Employed/study	81	82
Pension	4	3
Unemployed	10	3
Sick-leave	5	12
Civil state %		
Living alone	37	43
MADRS M ( $\pm$ SD)	21.3 (7.1)	23.0 (6.9)
Depression level %		
No depression	9	4
Mild depression	33	27
Moderate depression	55	65
Severe depression	3	4
OQ-45 M ( $\pm$ SD)	83.7 (19.6)	89.0 (17.9)
PSS M ( $\pm$ SD)	8.9 (2.5)	9.3 (2.5)
KSQ M ( $\pm$ SD)	14.7 (4.4)	14.6 (4.4)
Allocation %		
ICBT	35	29
PE	33	38
TAU	32	34

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3 The proportion of hazardous drinkers at baseline measured by AUDIT-C was 14 %, and the  
4 proportion was significantly higher in men, 18 % compared to 12 % for women,  $\chi^2 = 5.23$   $p =$   
5 0.022. The proportions of binge drinkers measured by item 3 in AUDIT-C was 13 %, and the  
6 overlap between hazardous and binge drinkers was high; of the 122 hazardous drinkers, 90  
7 were also binge drinkers, and of the total of 110 binge drinkers 90 were hazardous drinkers,  
8 so our analysis focused solely on the summarised score in AUDIT-C as a measure of  
9 hazardous drinking. The baseline average depression score (MADRS) showed moderate  
10 depressive problems and hazardous drinkers were more depressed  $t(853) = -2.31$ ,  $p = 0.021$   
11 and had lower psychological functioning (OQ-45)  $t(871) = -2.85$ ,  $p = 0.004$  than non-  
12 hazardous drinkers. There were no baseline differences between the treatment alternatives for  
13 perceived stress, sleep or age, education level, civil state and employment.  
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27 The results of the linear mixed- models showed that hazardous alcohol consumption at  
28 baseline influenced the outcome for perceived stress (PSS). The patients with hazardous  
29 drinking had a higher average score on PSS throughout the assessments, which might indicate  
30 less treatment effect for perceived stress compared to non-hazardous drinkers. To test whether  
31 this effect could be due to depression, since hazardous drinkers were more depressed than  
32 non-hazardous, we carried out a new analysis with MADRS and AUDIT-C as baseline  
33 covariates, and both MADRS  $p = 0.003$  and AUDIT-C  $p = 0.022$  were significant, i.e. the  
34 effects of hazardous drinking remained. In the full model, we included interaction effects  
35 between hazardous alcohol consumption and treatment alternatives and hazardous alcohol  
36 consumption and the IVR-assessments, but no significant interaction effects were found. The  
37 model was reduced to main effects of group, including a control for differences at baseline  
38 between hazardous and non-hazardous drinkers; the results are presented in Table 2.  
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**Table 2.**

The influence of alcohol consumption on repeated assessments of perceived stress as main effect of group presented in average change scores.

Variables	Average change	<i>df</i>	<i>t</i>	95 % CI
Assessment 1	0			
Assessment 2 <sup>a</sup>	-.43	725.65	-4.39***	[-.63, -.24]
Assessment 3 <sup>a</sup>	-1.02	707.27	-9.00***	[-1.25, -.80]
Assessment 4 <sup>a</sup>	-1.06	621.12	-8.52***	[-1.30, -.81]
Assessment 5 <sup>a</sup>	-1.28	601.23	-9.78***	[-1.53, -1.02]
Assessment 6 <sup>a</sup>	-1.49	319.69	-9.79***	[-1.79, -1.19]
Gender <sup>b</sup>	.32	642.18	1.78	[-.03, .66]
AUDIT-C <sup>c</sup>	.61	668.58	2.65***	[.16, 1.06]

Note. AUDIT C = Alcohol Use Disorders Identification Test-Consumption.

Assessment 1 is set to zero because it is a redundant.

<sup>a</sup> A negative score means a reduction from Assessment 1.

<sup>b</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in women as compared to men.

<sup>c</sup> A positive score means that the average score of Assessments 1-6 shows larger reduction from Assessment 1 in non-hazardous as compared to hazardous drinkers.

\* $p < .05$ , \*\* $p < .01$ , \*\*\*  $p < .001$

The main effect of group occurred after baseline, i.e. during and after treatment so hazardous drinkers probably had less treatment effect even if no differences in how hazardous drinking influenced stress were found between the treatment alternatives. The average changes on PSS over the assessments for patients with and without hazardous drinking are presented in Figure 2. The differences in stress between hazardous drinkers and non-hazardous drinkers were higher at the follow-ups conducted after the end of treatment, but these figures should be treated with some caution because of the large attrition.

The results of the linear mixed-models on psychological functioning (OQ-45) and sleep (KSQ) were not significantly influenced by the level of hazardous alcohol consumption at baseline although there was a tendency ( $p = 0.064$ ) for higher average scores on OQ-45 for hazardous drinkers compared to non-hazardous drinkers (Tables 3 and 4). Since the main

effect of group was not significant on OQ-45 and KS interaction effects between hazardous drinking and treatment group or hazardous drinking and assessments were not examined.

**Table 3.**

The influence of alcohol consumption on repeated assessments of Outcome Questionnaire-45 as main effect of group presented in average change scores.

Variables	Average change	df	t	95 % CI
Assessment 1	0	0	0	
Assessment 2 <sup>a</sup>	-4.00	724.13	-7.19***	[-5.09, -2.91]
Assessment 3 <sup>a</sup>	-8.50	694.62	-11.52***	[-9.95, -7.05]
Assessment 4 <sup>a</sup>	-9.87	579.86	-11.15***	[-11.61, -8.13]
Assessment 5 <sup>a</sup>	-10.07	497.79	-10.28***	[-12.00, -8.15]
Assessment 6 <sup>a</sup>	-11.83	291.60	-10.05***	[-14.14, -9.51]
Gender <sup>b</sup>	2.62	605.08	1.79	[-.25, 5.48]
AUDIT-C <sup>c</sup>	3.50	627.39	1.86	[-.20, 7.21]

Note. AUDIT C = Alcohol use disorder identification test-consumption.

Assessment 1 is set to zero because it is a redundant.

<sup>a</sup> A negative score means a reduction from Assessment 1.

<sup>b</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in women as compared to men.

<sup>c</sup> A positive score means that the average score of Assessments 1-6 shows larger reduction from Assessment 1 in non-hazardous drinkers as compared to hazardous.

\*p < .05, \*\*p < .01, \*\*\* p < .001



**Table 4.**

The influence of alcohol consumption on repeated assessments of sleep as main effect of group presented in average change scores.

Variables	Average change	df	t	95 % CI
Assessment 1	0			
Assessment 2 <sup>a</sup>	-.44	710.76	-3.49***	[-.69, -.19]
Assessment 3 <sup>a</sup>	-1.02	759.76	-6.47***	[-1.33, -.71]
Assessment 4 <sup>a</sup>	-1.05	649.15	-5.78***	[-1.41, -.70]
Assessment 5 <sup>a</sup>	-1.02	632.79	-5.76***	[-1.36, -.67]
Assessment 6 <sup>a</sup>	-1.31	338.53	-5.88***	[-1.74, -.87]
Gender <sup>b</sup>	.14	635.91	.53	[-.37, .65]
AUDIT-C <sup>c</sup>	.49	660.12	1.46	[-.17, 1.15]

*Note.* AUDIT-C = Alcohol use disorder identification test-consumption.

Assessment 1 is set to zero because it is a redundant.

<sup>a</sup> A negative score means a reduction from Assessment 1.

<sup>b</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in women as compared to men.

<sup>c</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in non-hazardous as compared to hazardous drinkers.

\*p < .05, \*\*p < .01, \*\*\* p < .001

## DISCUSSION

The aim of this study was to examine whether hazardous alcohol consumption influences the outcome for psychological functioning, perceived stress and sleep, over a twelve-month assessment period. The results showed that stress was influenced by hazardous drinking, but psychological functioning and sleep were not. Patients with hazardous drinking had a higher level of stress during the follow-ups compared with non-hazardous drinkers, while not initially and these results remained after controlling for depression. In a previous study in REGASSA,[15] we reported that the treatment had positive effect on perceived stress, and all treatment groups showed improvements. The present study adds that the improvement was negatively influenced by hazardous drinking i.e. hazardous drinkers improved less than non-hazardous drinkers irrespective of treatment alternative.

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3 Dawson and co-workers, who separated binge drinking from other consumption measures,  
4 found that stress was associated with binge drinking and not with frequency of drinking,[21].  
5  
6 In our study, binge drinking was a part of hazardous drinking in the summarized measure of  
7  
8 AUDIT-C, which might explain our results that hazardous drinking was associated with  
9  
10 higher levels of stress. Hazardous drinkers seemed to get less treatment effects on stress  
11  
12 which is not in line with the assumption that alcohol could reduce stress. Although it is  
13  
14 uncertain whether alcohol reduces stress, its effect on stress seems to depend on several  
15  
16 factors,[22]. The focus in the present study was on the effect of hazardous alcohol  
17  
18 consumption which may not reduce stress. The influence of alcohol use on stress seems  
19  
20 unclear and further investigations are required.  
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25 The fact that hazardous drinking did not affect sleep is in line with an earlier study conducted  
26  
27 in primary care,[23] but contradicts other findings that risky alcohol use affects sleep  
28  
29 quality,[35].  
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32 When comparing the baseline scores of OQ-45 in our sample of depressed patients with  
33  
34 samples of patients with alcohol use disorders, the patients in our sample showed lower  
35  
36 psychological functioning and that applied for both hazardous and non-hazardous  
37  
38 drinkers,[31, 36]. Hazardous drinkers had a significantly higher score on OQ-45 at baseline  
39  
40 but, during follow-ups, these differences were no longer significant although a tendency  
41  
42 towards higher scores remained. In summary, results of our analyses were unclear about the  
43  
44 way hazardous drinking affects psychological functioning, and more research is needed.  
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48 Several studies have concluded that alcohol use patterns should be screened in health care,  
49  
50 and the AUDIT-C has been recommended as a suitable screening test,[6-7, 26]. The patients  
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52 in REGASSA turned out to have higher proportions of hazardous drinking and alcohol  
53  
54 problems than the general population,[25] which emphasizes the need to examine patterns of  
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3 alcohol use among patients with mental ill-health. The results in our study also confirm the  
4 importance of screening for drinking habits in primary care, to identify risky consumption that  
5 may have an impact on treatment effects on perceived stress for patients with common mental  
6 health problems.  
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### 10 11 12 **Strengths and limitations**

13  
14 The large sample of mental ill-health patients in primary care is an advantage and strengthens  
15 the results. The randomized controlled study design and the repeated assessments collected by  
16 IVR are also strengths that enabled us to make reliable comparisons and to follow the patients  
17 throughout the study. The analysis model is a strength compensating for the high attrition in  
18 IVR, which is otherwise a limitation. However, conclusions about differences on stress  
19 between hazardous drinkers and non- hazardous in later follow-ups should be drawn with  
20 caution.  
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### 30 31 **Conclusion**

32 This study showed that hazardous drinkers were more depressed and had lower psychological  
33 functioning at baseline and higher level of stress during and after treatment. These results add  
34 to previous studies on the importance of screening for alcohol consumption in mental ill-  
35 health patients seeking primary care since hazardous drinking may influence some treatment  
36 effects. Further research is needed on how hazardous drinking affects different treatment  
37 outcomes in patients with common mental health problems.  
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## List of abbreviations

AUDIT	Alcohol Use Disorder Identification Test
AUDIT-C	Alcohol Use Disorder Identification Test - Consumption
GP	General practitioner
ICBT	Internet-based Cognitive behavioral therapy
ITT	Intention to treat
IVR	Interactive Voice Response
KSQ	Karolinska Sleep Questionnaire
MADRS	Mongomery Åsberg Depression Rating Scale
M.I.N.I.	Mini-International Psychiatric Interview
OQ-45	Outcome Questionnaire-45
PE	Physical exercise
PHQ-9	Patient Health Questionnaire-9
PSS	Perceived Stress Scale
RCT	Randomized controlled trial
TAU	Treatment as usual

## DECLARATION

### Ethics approval and consent to participate

The REGASSA study was approved by the regional ethical review board at Karolinska Institutet in Stockholm (Dnr 2010/1779-31/4) and retrospectively registered in German clinical trials DRKS00008745. Before allocation a written informed consent was obtained from each patient.

### Consent for publication

Consent for publication was not applicable in this study.

### **Availability of data and material**

The datasets generated and/or analyzed during the current study are not publicly available due to that there is no permission granted for this from the ethical review board, but are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare that they have no competing interest.

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### **Authors' contributions**

CS was involved in the data collecting process, made major contributions to the data analysis and was a major contributor in writing the manuscript. CA was involved in the study design and the data collecting process, made contributions to the data analysis and writing process. AH was vice director for the REGASSA study and was involved in the study design, made contributions to the data analysis and the writing process. All authors read and approved the final manuscript.

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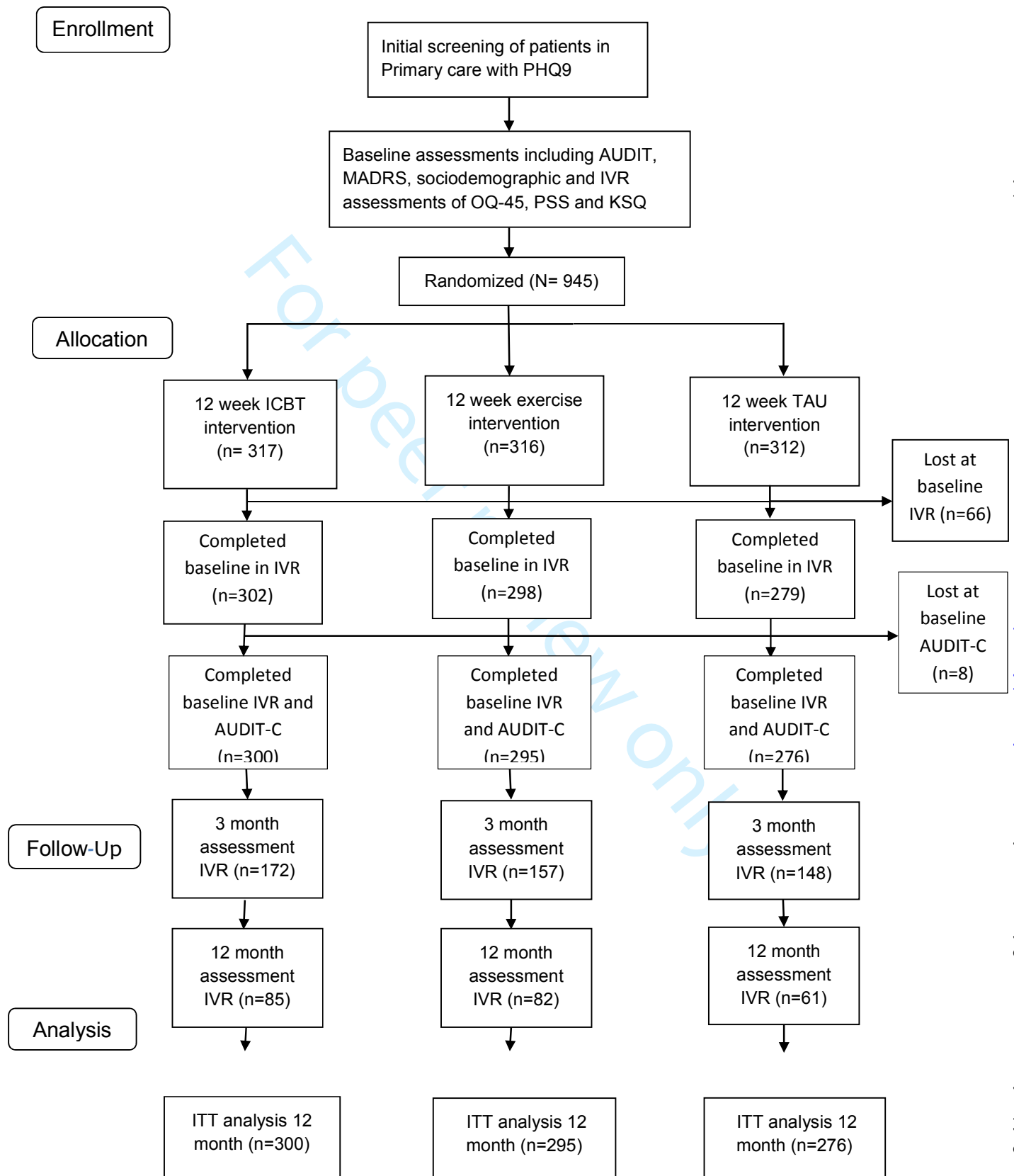
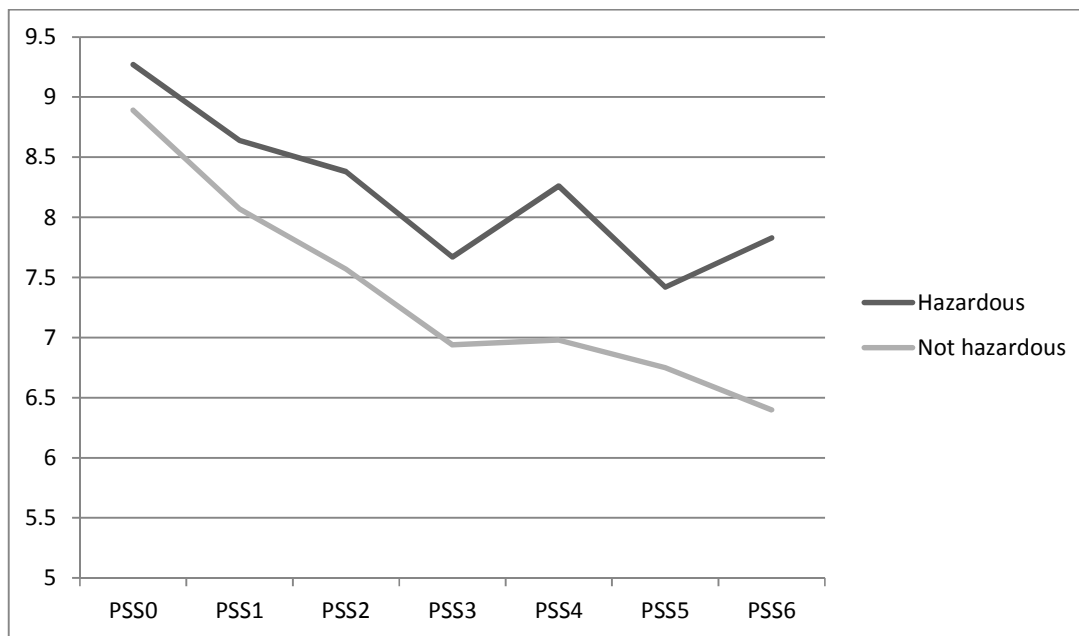
**Figure 1** The Participant's Flow Through the Study

Figure 2 Course on Perceived stress for patients with and without hazardous drinking at baseline



PSS0-PSS6 are measure points where PSS0 is baseline measure and PSS1-PSS3 are during and directly after treatment and PSS4-PSS6 are follow ups

# BMJ Open

## The influence of hazardous drinking on psychological functioning, stress and sleep during and after treatment in patients with mental health problems; a secondary analysis of a randomized controlled intervention study

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Keywords:	AUDIT, MENTAL HEALTH, Depression & mood disorders < PSYCHIATRY, Substance misuse < PSYCHIATRY, Clinical trials < THERAPEUTICS

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4 **The influence of hazardous drinking on psychological**  
5 **functioning, stress and sleep during and after treatment in**  
6 **patients with mental health problems; a secondary analysis of**  
7 **a randomized controlled intervention study**  
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11 **Short title** – Hazardous drinking in treatment of mental health problems  
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14 **Catharina Strid<sup>1</sup>, Claes Andersson<sup>2</sup> and Agneta Öjehagen<sup>3</sup>**  
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## ABSTRACT

### Objectives

Hazardous drinking could negatively affect health and lead to alcohol use disorders, but it is unclear how hazardous drinking affects treatment outcomes of depression and anxiety and stress-related mental health problems.

The aim of this study was to examine whether hazardous drinking, measured by AUDIT-C, influences the outcomes of repeated assessments of psychological functioning (OQ-45), stress (PSS) and sleep (KSQ), during and after treatment in patients with mental ill-health.

### Methods

The study was conducted within REGASSA, a randomized controlled trial aimed at comparing Internet-based CBT and physical exercise with treatment as usual on primary care patients with mental ill-health. The study involved 871 participants who completed the Alcohol Use Disorders Identification Test at baseline and who were assessed repeatedly during and after treatment on psychological function, stress and sleep by Interactive Voice Response (IVR), a computerized, automated telephone technology.

### Results

At baseline, hazardous drinkers were more depressed and had lower scores on psychological functioning than non-hazardous drinkers, while there were no differences on stress and sleep. During the follow-ups, hazardous drinking negatively influenced perceived stress, i.e. hazardous drinkers seemed to have less treatment effect on stress, and the results remained after controlling for depression. There were no differences during the follow-ups regarding psychological functioning and sleep.

## Conclusions

Hazardous drinking negatively influenced perceived stress. The findings of the study emphasize the importance of screening for alcohol habits in mental ill-health patients, since risky drinking may affect the outcomes of treatment.

## Trial registration

On 2015/06/10 the REGASSA study was retrospectively registered in German clinical trials DRKS00008745, but it had been originally registered with KTA CT20110063 on 2011/02/10.

**Key words:** Hazardous drinking, mental health problems, primary care, psychological functioning, stress, sleep, IVR, repeated assessments, Internet-based CBT, physical exercise

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is a secondary analysis of RCT data and not a prospectively designed RCT, which was a limitation.
- However, the large sample of primary care patients was a strength.
- Another strength, was the repeated assessments collected by automated technology, which was a convenient way of monitoring a large sample of participants.
- The high attrition in the repeated assessments was a limitation, although the analysis model compensating for the attrition was a strength and the proportion of hazardous drinkers remained almost the same.
- The AUDIT-C cut-off scores have not been validated in a population of mental health problems, which was a limitation.

## INTRODUCTION

Hazardous or risky alcohol consumption is common in patients seeking primary care, but is often not adequately examined at the medical visit,[1-2], and only some of the patients with risky consumption, are advised to reduce their alcohol use,[3]. Hazardous drinking, including both the number of drinks consumed weekly and on a single occasion, ‘binge drinking’, is considered an alcohol drinking pattern that could lead to negative effects on health and to development of alcohol use disorders,[4-5]. Screening for alcohol use is a recommended intervention for patients in routine care, and patients reporting a pattern of hazardous drinking should be given advice on how to change this pattern and offered brief interventions. Patients with alcohol use disorder or dependence should be referred for treatment,[6-8].

Several studies have shown higher prevalence rates for hazardous drinking in patients with common mental health problems compared to the general population,[6, 9-11]. Eberhard and colleagues (2009) found a prevalence of 21 % in a population of psychiatric outpatients, and Nehlin and co-workers (2011) showed a proportion of 19 %,[6, 10] which was higher than that in the Swedish general population at the time, (15 %). However, only a few studies have examined whether concomitant hazardous drinking affects treatment outcome of mental health problems. In an extensive review by Sullivan and colleagues (2005), it could not be established whether hazardous drinking or alcohol use disorders influenced recovery from or relapse in depression, although the review only involved one study examining risk drinking. In that study hazardous drinking did not affect recovery from depression,[12]. Gajecki and co-workers (2014) examined whether problematic substance use affected an Internet-based cognitive behavior therapy for depression and anxiety disorders, and found no differences in effect between hazardous and non-hazardous drinkers on depression, but hazardous drinkers showed less treatment effect for panic disorder,[13]. In another study on treatment of anxiety, alcohol use severity had no impact on treatment effect, although, baseline hazardous alcohol

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3 use was associated with more anxiety and depression symptoms at long-term follow-up,[14].  
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5 Haynes and colleagues (2007) found little evidence that hazardous drinking is a risk factor in  
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7 non-recovery from common mental disorders, but binge-drinking may be a potential risk,[5].  
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9 Consequently, few studies have addressed the impact of hazardous alcohol use on treatment  
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11 effects, and the findings are inconsistent, which justifies further research.  
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14 The present study is a secondary analysis performed within the framework of REGASSA, a  
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16 multicenter randomized controlled trial (RCT) conducted in primary care on patients with  
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18 mild to moderate depression, anxiety, and stress-related mental health problems. The  
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20 objectives of REGASSA were to study the effects of Internet-based cognitive behavior  
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22 therapy (ICBT) and physical exercise (PE) compared to treatment as usual (TAU) on work-  
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24 ability and sick-leave as primary outcome measures, and depression as secondary outcome.  
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26 Other secondary outcome measures used were repeated assessments of psychological  
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28 functioning, perceived stress and sleep. Data were collected by automated telephone  
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30 technique, Interactive Voice Response (IVR), which enabled frequent follow-ups during and  
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32 after treatment. In a previous analysis of REGASSA using these secondary outcomes, we  
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34 found that ICBT and PE were more effective than TAU on psychological functioning and  
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36 sleep, no differences were found on perceived stress, all three treatment groups  
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38 improved,[15].  
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43 In the present study, we wanted to explore whether hazardous alcohol use could predict the  
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45 outcomes of sleep, psychological functioning and stress, factors that may be influenced by  
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47 hazardous alcohol consumption. To the best of our knowledge, the relationship between  
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49 hazardous drinking and the secondary variables of REGASSA has previously only been  
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51 studied with less frequent follow-ups, or has not been studied at all.  
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3 Stress is known to be linked with sleeping problems and mood disorders,[16-18]. In a  
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5 previous primary care study, high levels of stress were commonly reported in association with  
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7 symptoms of anxiety and depression,[19] and high levels of perceived stress have been shown  
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9 to be associated with less antidepressant treatment effect,[20].  
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12 In an epidemiological study of over 30.000 individuals, Dawson et al,[21] found that stress  
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14 resulted in increased quantities of alcohol consumption on specific drinking occasions, rather  
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16 than more frequent drinking. Scher et al. reported no clear results whether alcohol reduces  
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18 perceived stress, and concluded that stress is likely to be influenced by both individual and  
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20 situational factors,[22].  
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23 Vinson and colleagues conducted a study in primary care on sleep and alcohol consumption  
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25 and found no associations between hazardous drinking and sleeping problems,[23]. To the  
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27 best of our knowledge, how hazardous drinking may affect change in psychological  
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29 functioning (Outcome Questionnaire-45, OQ-45) has not yet been studied.  
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33 At baseline, patients in REGASSA completed the Alcohol Use Disorders Identification Test  
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35 (AUDIT), which was developed for early detection of individuals with hazardous or harmful  
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37 alcohol drinking,[24]. A previous cross-sectional study of REGASSA showed that the total  
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39 AUDIT score, the scores of AUDIT-C and the proportions of hazardous drinkers, 22 %, were  
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41 higher among REGASSA patients compared to the general population, 15 % [25].  
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45 This study aimed to examine whether hazardous drinking at baseline predicts the outcomes of  
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47 repeated assessments of psychological functioning, stress and sleep collected by IVR during  
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49 and after treatment in REGASSA.  
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## METHODS

### Study design

Study design, participants and measurements are presented in more detail in an earlier study,[15], and only a brief description is given here. REGASSA was carried out in primary care in six health care regions in Sweden between 2011 and 2014. After giving written informed consent, patients were randomized to one of three treatment alternatives, ICBT, PE and TAU, for a 12-week intervention. At baseline, participants completed a battery of questionnaires, including measures of depression (MADRS) and alcohol use (AUDIT), and follow-ups were conducted 3 and 12 months after baseline. Secondary outcomes of psychological functioning, stress and sleep were continually collected by IVR during and after treatment.

IVR is an automated telephone system programmed to administer various questionnaires and to follow a large population over time. At baseline the patients in REGASSA registered their personal mobile number and answered the 55 questions included in IVR using touch-tone technology. The automated system then called the patients on six measurement occasions, two during treatment, one at the end of treatment, and three after treatment until 12 months after baseline. The attrition in IVR showed varying but decreasing levels over the 12-month study period (Table 1). The proportion of responders at 3-month follow-up was 54 %, at 6-month 47 %, at 9-month 47 %, and at the final 12-month follow-up the proportion of responders had fallen to 25 %. The proportion of hazardous drinkers remained almost constant, 15 % at 3-month follow-up, 13 % at 6-months, 14 % at 9-months and 15 % at 12-month follow-up. The number of responders is presented in Figure 1.

## Participants

Participants were primary care patients with light to moderate depression, anxiety and stress-related mental ill-health. The inclusion criteria were  $\geq 10$  points on the Patient Health Questionnaire (PHQ9), a short depression scale and, Swedish language skills due to the ICBT program, being only delivered in Swedish. REGASSA included 945 patients, of which 879 completed the IVR baseline assessments and, of these 879 patients, 871 also completed AUDIT at baseline. Patients with a primary substance use disorder were excluded. The CONSORT diagram (Figure 1) shows the flow of the participants and the number of responders at each follow-up for hazardous and non-hazardous drinkers.

## Measures at baseline

### AUDIT

AUDIT is a ten- item scale for measuring alcohol consumption and alcohol-related problems. The test is validated in primary care and has shown acceptable psychometric properties,[24]. AUDIT is in two parts, items 1-3 measuring alcohol consumption (AUDIT-C), and items 4-10 measuring alcohol problems (dependency and harm combined). In this study, we only used the abbreviated consumption subscale AUDIT-C, since the three questions in OQ-45 on negative consequences of drinking behavior would otherwise interfere with questions 4-10 in AUDIT. The items in AUDIT-C are (1) *How often do you drink alcohol?* (2) *How many glasses do you drink on a typical day when you drink alcohol?* (3) *How often do you have six or more drinks on one occasion?* The scores range from 0-4 and maximum negative score is 12. AUDIT-C has shown high specificity and sensitivity in screening for risky alcohol habits,[26-27]. The cut-off score for hazardous drinking in this study was set to  $\geq 5$  for women and  $\geq 6$  for men in accordance with Swedish guidelines,[28]. These cut-offs are higher than in previous studies where the cut-off scores have been set to  $\geq 3-4$  for women and

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3  $\geq 4$ -5 for men, but it is recommended that cut-off scores are determined empirically in  
4 different cultures, since drinking frequency varies largely between countries,[6, 11, 26-27].  
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8 When studying the question of binge drinking separately, the cut-off was set to *at least on a*  
9 *monthly basis* for both women and men.  
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### 11 12 13 MADRS

14 In earlier REGASSA studies, MADRS was used as an outcome measure for depression but, in  
15 this study, it was used as a baseline measurement and only for controlling results obtained  
16 with AUDIT-C. MADRS is a commonly used measure for depression that has shown good  
17 psychometric properties. It consists of ten items with six response alternatives,[29].  
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### 23 24 Gender

25 We analyzed whether there were any gender differences in terms of hazardous drinking and  
26 its influence on the outcome measures of psychological functioning, sleep and stress.  
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### 30 31 **Outcome measurements in IVR**

#### 32 Outcome Questionnaire-45

33 The repeated assessments of psychological functioning were measured by Outcome  
34 Questionnaire-45 (OQ-45). OQ-45 was developed by Lambert and colleagues to measure  
35 psychotherapy effects,[30]. It consists of 45 questions with a score range of 0-180, where 180  
36 is the maximum negative score. OQ-45 captures the patient's psychological functioning  
37 through questions about symptoms, interpersonal problems and social role function. Both the  
38 original and the Swedish version of OQ-45 have shown good psychometric properties,[30-  
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#### 50 Perceived Stress Scale

51 Stress was repeatedly assessed by the Perceived Stress Scale (PSS), originally a ten-item scale  
52 measuring how the patient copes with stress. In this study, we used a shortened 4-item version  
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of this scale that has proved suitable for telephone assessments,[33]. The scores range from 0-4 and the maximum total negative score is 16.

### Karolinska Sleep Questionnaire

A short version of the Karolinska Sleep Questionnaire assessed the sleep outcome. The questionnaire comprises four items capturing sleep quality, with scores ranging from 1- 6, and the maximum negative score was 24. KSQ has shown good validity, reliability and sensitivity in various studies,[34].

### Statistics

Differences between hazardous drinkers and non-hazardous drinkers were calculated on continuous baseline measurements using independent samples t-tests, and differences in proportions of hazardous drinkers in discrete variables were examined with chi-square tests. Differences in attrition between non-hazardous and hazardous drinkers were calculated with Fisher`s exact test. To examine how alcohol consumption (AUDIT-C) at baseline affected the course and outcome for psychological functioning, stress and sleep, we conducted three separate analyses with linear mixed-models with a first-order auto-regressive, heterogeneous rho covariance structure. Mixed-models include all measures that are available at each assessment, and were therefore considered suitable for this study. We assumed that missing observations were unrelated to the observed value, i.e. missing at random. Each model included six follow-ups called assessments 1, 2, 3, 4, 5 and 6, the assigned treatment groups ICBT, PE and TAU, gender, and two baseline measures, i.e. hazardous drinking (AUDIT-C) and the baseline scores of one of the three outcome measures (OQ-45, PSS, KSQ). All variables were modelled as fixed effects. The outcome measure baseline scores were used as continuous covariate and the control variable hazardous drinking (AUDIT-C) and gender as categorical covariates. AUDIT-C was a dichotomous variable where 0 was defined as non-hazardous drinking and 1 hazardous drinking. MADRS was used as a continuous covariate for

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3 controlling for depression if AUDIT-C showed significant influence on the outcome  
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5 measures. Assessment data was nominal, i.e. each measurement occasion was separate and  
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7 time was not a continuous linear regressor in the model. The analyses began with a full model  
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9 with interaction effects of AUDIT-C x Treatment group x Assessment and was simplified to  
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11 main group effects if no significant interaction effects were found. Before the results were  
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13 analysed, the residuals were examined and showed a normal distribution. A test for robustness  
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15 showed similar results as the mixed-models analysis. All statistics were performed in the  
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17 SPSS for Windows 22.0.  
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## 20 21 **RESULTS**

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23 The average age of patients was 43, and 62 % had a high level of education. Most of the  
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25 patients were working and only 5 % were on sick-leave. In Table 1, different descriptions of  
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27 baseline measurements for hazardous drinkers and non-hazardous drinkers and attrition  
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29 during the follow-ups, are presented.  
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**Table 1.** Baseline scores for non-hazardous drinkers and hazardous drinkers on sociodemographic data, depression (MADRS), psychological function (OQ-45), stress (PSS), and sleep (KSQ), the allocation in each three-treatment condition, Internet- based cognitive behavior therapy (ICBT), Physical exercise (PE) and Treatment as usual (TAU), and the attrition in the follow-ups.

Variables	Non-Hazardous n = 749	Hazardous n = 122
Age M ( $\pm$ SD)	43.4 (12.0)	40.7 (13.1)
Gender %		
Male	25	35
Education %		
Low	4	5
Medium	35	38
High	61	57
Employment %		
Employed/study	81	82
Pension	4	3
Unemployed	10	3
Sick-leave	5	12
Civil state %		
Living alone	37	43
MADRS M ( $\pm$ SD)	21.3 (7.1)	23.0 (6.9)
Depression level %		
No depression	9	4
Mild depression	33	27
Moderate depression	55	65
Severe depression	3	4
OQ-45 M ( $\pm$ SD)	83.7 (19.6)	89.0 (17.9)
PSS M ( $\pm$ SD)	8.9 (2.5)	9.3 (2.5)
KSQ M ( $\pm$ SD)	14.7 (4.4)	14.6 (4.4)
Allocation		
ICBT	35	29
PE	33	38
TAU	32	34
Attrition %		
3 month	45	50
6 month	52	61
9 month	52	59
12 month	74	76

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3 The proportion of hazardous drinkers at baseline measured by AUDIT-C was 14 %, with a  
4 significantly higher proportion in men, (18 %) compared to women (12 %),  $\chi^2 = 5.23$   $p =$   
5 0.022. The proportions of binge drinkers measured by item 3 in AUDIT-C was 13 %, and the  
6 overlap between hazardous and binge drinkers was high; 90 out of the 122 hazardous  
7 drinkers, were also binge drinkers, and 90 of the 110 binge drinkers were hazardous drinkers,  
8 so our analysis focused solely on the summarized score in AUDIT-C as a measure of  
9 hazardous drinking. The baseline average depression score (MADRS) showed moderate  
10 depressive problems, and hazardous drinkers were more depressed  $t(853) = -2.31$ ,  $p = 0.021$   
11 and had lower psychological functioning (OQ-45)  $t(871) = -2.85$ ,  $p = 0.004$  than non-  
12 hazardous drinkers. There were no baseline differences between the treatment alternatives,  
13 perceived stress, sleep or age, education level, civil state and employment. The Fisher's exact  
14 test showed no differences in attrition between non-hazardous and hazardous drinkers at any  
15 follow-up and there were no differences between the treatment alternatives.  
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31 The results of the linear mixed-models showed that hazardous alcohol consumption at  
32 baseline predicted the outcome for perceived stress (PSS). The patients with hazardous  
33 drinking had a higher average score on PSS throughout the assessments, which might indicate  
34 less treatment effect for perceived stress compared to non-hazardous drinkers. To test whether  
35 this effect could be due to depression, since hazardous drinkers were more depressed than  
36 non-hazardous, we carried out a new analysis with MADRS and AUDIT-C as baseline  
37 covariates, and both MADRS  $p = 0.003$  and AUDIT-C  $p = 0.022$  were significant, i.e. the  
38 effects of hazardous drinking remained. In the full model, we included interaction effects  
39 between hazardous alcohol consumption and treatment alternatives and hazardous alcohol  
40 consumption and the IVR-assessments, but no significant interaction effects were found. The  
41 model was reduced to main effects of group, including a control for differences at baseline  
42 between hazardous and non-hazardous drinkers; the results are presented in Table 2.  
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**Table 2.**

The influence of alcohol consumption on repeated assessments of perceived stress as main effect of group presented in average change scores.

Variables	Average change	<i>df</i>	<i>t</i>	95 % CI
Assessment 1	0			
Assessment 2 <sup>a</sup>	-.43	725.65	-4.39***	[-.63, -.24]
Assessment 3 <sup>a</sup>	-1.02	707.27	-9.00***	[-1.25, -.80]
Assessment 4 <sup>a</sup>	-1.06	621.12	-8.52***	[-1.30, -.81]
Assessment 5 <sup>a</sup>	-1.28	601.23	-9.78***	[-1.53, -1.02]
Assessment 6 <sup>a</sup>	-1.49	319.69	-9.79***	[-1.79, -1.19]
Gender <sup>b</sup>	.32	642.18	1.78	[-.03, .66]
AUDIT-C <sup>c</sup>	.61	668.58	2.65***	[.16, 1.06]

*Note.* AUDIT C = Alcohol Use Disorders Identification Test-Consumption.

Assessment 1 is set to zero because it is a redundant.

<sup>a</sup> A negative score means a reduction from Assessment 1.

<sup>b</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in women as compared to men.

<sup>c</sup> A positive score means that the average score of Assessments 1-6 shows larger reduction from Assessment 1 in non-hazardous as compared to hazardous drinkers.

\**p* < .05, \*\**p* < .01, \*\*\* *p* < .001

The main effect of group occurred after baseline, i.e. during and after treatment, so hazardous drinkers probably had less treatment effect even if no differences in how hazardous drinking predicted stress were found between the treatment alternatives. The average changes on PSS over the assessments for patients with and without hazardous drinking are presented in Figure 2. The differences in stress between hazardous drinkers and non-hazardous drinkers were higher at the follow-ups conducted after the end of treatment, but these figures should be treated with some caution because of the large attrition, even if there were no differences in attrition between the two groups.

The results of the linear mixed-models on psychological functioning (OQ-45) and sleep (KSQ) were not significantly influenced by the level of hazardous alcohol consumption at

baseline, although there was a tendency ( $p = 0.064$ ) for higher average scores on OQ-45 for hazardous drinkers compared to non-hazardous drinkers (Tables 3 and 4). Since the main effect of group was not significant on OQ-45 and KSQ, interaction effects between hazardous drinking and treatment group or hazardous drinking and assessments were not examined.

**Table 3.**

The influence of alcohol consumption on repeated assessments of Outcome Questionnaire-45 as main effect of group presented in average change scores.

Variables	Average change	<i>df</i>	<i>t</i>	95 % CI
Assessment 1	0	0	0	
Assessment 2 <sup>a</sup>	-4.00	724.13	-7.19***	[-5.09, -2.91]
Assessment 3 <sup>a</sup>	-8.50	694.62	-11.52***	[-9.95, -7.05]
Assessment 4 <sup>a</sup>	-9.87	579.86	-11.15***	[-11.61, -8.13]
Assessment 5 <sup>a</sup>	-10.07	497.79	-10.28***	[-12.00, -8.15]
Assessment 6 <sup>a</sup>	-11.83	291.60	-10.05***	[-14.14, -9.51]
Gender <sup>b</sup>	2.62	605.08	1.79	[-.25, 5.48]
AUDIT-C <sup>c</sup>	3.50	627.39	1.86	[-.20, 7.21]

Note. AUDIT C = Alcohol use disorder identification test-consumption.

Assessment 1 is set to zero because it is a redundant.

<sup>a</sup> A negative score means a reduction from Assessment 1.

<sup>b</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in women as compared to men.

<sup>c</sup> A positive score means that the average score of Assessments 1-6 shows larger reduction from Assessment 1 in non-hazardous drinkers as compared to hazardous.

\* $p < .05$ , \*\* $p < .01$ , \*\*\*  $p < .001$

**Table 4.**

The influence of alcohol consumption on repeated assessments of sleep as main effect of group presented in average change scores.

Variables	Average change	df	t	95 % CI
Assessment 1	0			
Assessment 2 <sup>a</sup>	-.44	710.76	-3.49***	[-.69, -.19]
Assessment 3 <sup>a</sup>	-1.02	759.76	-6.47***	[-1.33, -.71]
Assessment 4 <sup>a</sup>	-1.05	649.15	-5.78***	[-1.41, -.70]
Assessment 5 <sup>a</sup>	-1.02	632.79	-5.76***	[-1.36, -.67]
Assessment 6 <sup>a</sup>	-1.31	338.53	-5.88***	[-1.74, -.87]
Gender <sup>b</sup>	.14	635.91	.53	[-.37, .65]
AUDIT-C <sup>c</sup>	.49	660.12	1.46	[-.17, 1.15]

Note. AUDIT-C = Alcohol use disorder identification test-consumption.

Assessment 1 is set to zero because it is a redundant.

<sup>a</sup> A negative score means a reduction from Assessment 1.

<sup>b</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in women as compared to men.

<sup>c</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in non-hazardous as compared to hazardous drinkers.

\*p < .05, \*\*p < .01, \*\*\* p < .001

## DISCUSSION

The aim of this study was to examine whether hazardous alcohol consumption predicts the outcome for psychological functioning, perceived stress and sleep, over a twelve-month assessment period. The results showed that hazardous drinking predicted stress, but not psychological functioning and sleep. Patients with hazardous drinking had a higher level of stress during the follow-ups compared with non-hazardous drinkers, but not at baseline, and these results remained after controlling for depression. In a previous study in REGASSA,[15], we reported that the treatment had positive effect on perceived stress, and all treatment groups showed improvements. The present study adds that the improvement was negatively

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3 influenced by hazardous drinking, i.e. hazardous drinkers improved less than non-hazardous  
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5 drinkers irrespective of treatment alternative.  
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8 Dawson and co-workers, who separated binge drinking from other consumption measures,  
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10 found that stress was associated with binge drinking and not with frequency of drinking,[21].  
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12 In our study, binge drinking was a part of hazardous drinking in the summarized measure of  
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14 AUDIT-C, which might explain our results that hazardous drinking was associated with  
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16 higher levels of stress. Hazardous drinkers seemed to get less treatment effects on stress,  
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18 which is not in line with the assumption that alcohol could reduce stress. Although it is  
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20 uncertain whether alcohol reduces stress, its effect on stress seems to depend on several  
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22 factors,[22]. The focus in the present study was on hazardous alcohol consumption, which  
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24 may not reduce stress. The influence of alcohol use on stress seems unclear and further  
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26 investigations are required.  
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30 The finding that hazardous drinking did not affect sleep quality is in line with an earlier study  
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32 conducted in primary care,[23], but contradicts other findings where risky alcohol users have  
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34 reported lower sleep quality,[35].  
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38 When comparing the baseline scores of OQ-45 in our sample of depressed patients with  
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40 samples of patients with alcohol use disorders, the patients in our sample showed lower  
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42 psychological functioning, and this applied for both hazardous and non-hazardous  
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44 drinkers,[31, 36]. Hazardous drinkers had a significantly higher score on OQ-45 at baseline  
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46 but, during follow-ups, these differences were no longer significant, although a tendency  
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48 towards higher scores remained. In summary, results of our analyses were unclear about the  
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50 way hazardous drinking affects psychological functioning, and more research is needed.  
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54 Several studies have concluded that alcohol use patterns should be screened in health care,  
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56 and the AUDIT-C has been recommended as a suitable screening test,[6-7, 26]. A common  
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3 barrier for addressing alcohol habits in health care is lack of time, so a short screening tool  
4 such as the AUDIT-C could be a facilitator,[1, 7], as well as automated technology. The  
5 patients in REGASSA turned out to have higher proportions of hazardous drinking and  
6 alcohol problems than the general population,[25], which emphasizes the need to examine the  
7 alcohol patterns and increase the amount of advice on alcohol consumption given to patients  
8 with mental ill-health. Systematic screening for alcohol use in primary care has been shown to  
9 increase the detection of hazardous drinkers, and facilitate brief interventions,[7]. The results  
10 in our study confirm the importance of screening for drinking habits in primary care, to  
11 identify risky consumption that may have an impact on treatment effects on perceived stress  
12 for patients with common mental health problems.  
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### 25 **Strengths and limitations**

26 The large sample of mental ill-health patients in primary care is an advantage and strengthens  
27 the results. However, the present design, a secondary analysis of RCT data, examining the  
28 prediction of alcohol consumption on psychological function, stress and sleep, is not powered  
29 to fully answer the question, which is a limitation. The chosen cut-off scores of AUDIT-C,  
30 which are recommended by the Swedish national guidelines, have not been validated in a  
31 population of patients with mental health problems, which is a limitation. The repeated  
32 assessments collected by IVR is a strength that enabled us to make reliable comparisons and  
33 to follow the patients throughout the study. The analysis model is a strength compensating for  
34 the high attrition in IVR, which is otherwise a limitation. Conclusions about differences on  
35 stress between hazardous drinkers and non-hazardous in later follow-ups, should be drawn  
36 with caution due to attrition, although the attrition was not higher among hazardous drinkers  
37 during the follow-ups.  
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## Conclusion

This study showed that hazardous drinkers were more depressed and had lower psychological functioning at baseline and higher level of stress during and after treatment. These results add to previous studies on the importance of screening for alcohol consumption in mental ill-health patients seeking primary care, since hazardous drinking may influence some treatment effects. Further research is needed on how hazardous drinking affects different treatment outcomes in patients with common mental health problems.

## List of abbreviations

AUDIT	Alcohol Use Disorder Identification Test
AUDIT-C	Alcohol Use Disorder Identification Test - Consumption
GP	General practitioner
ICBT	Internet-based cognitive behavior therapy
ITT	Intention to treat
IVR	Interactive Voice Response
KSQ	Karolinska Sleep Questionnaire
MADRS	Montgomery Åsberg Depression Rating Scale
M.I.N.I.	Mini-International Psychiatric Interview
OQ-45	Outcome Questionnaire-45
PE	Physical exercise
PHQ-9	Patient Health Questionnaire-9
PSS	Perceived Stress Scale
RCT	Randomized controlled trial
TAU	Treatment as usual

## DECLARATION

### Ethics approval and consent to participate

The REGASSA study was approved by the regional ethical review board at Karolinska Institutet in Stockholm (Dnr 2010/1779-31/4) and retrospectively registered in German clinical trials DRKS00008745. Before allocation, a written informed consent was obtained from each patient.

### Consent for publication

Consent for publication was not applicable in this study.

### Availability of data and material

The datasets generated and/or analyzed during the current study are not publicly available, since the ethical review board has not granted permission for this, but are available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interest.

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### Authors' contributions

CS was involved in the data collecting process, made major contributions to the data analysis, and was a major contributor in writing the manuscript. CA was involved in the study design

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3 and the data collecting process, made contributions to the data analysis and writing process.  
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5 AH was vice director for the REGASSA study and was involved in the study design, made  
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7 contributions to the data analysis and the writing process. All authors read and approved the  
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9 final manuscript.  
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13  
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15  
16 Lundh at the Department of Psychology, Lund University for valuable comments on the  
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18 manuscript.  
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22 **Figure 1** The CONSORT diagram shows the participants' flow through the study  
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25 **Figure 2** The graph shows the course of stress during and after treatment for patients with and  
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27 without hazardous drinking at baseline  
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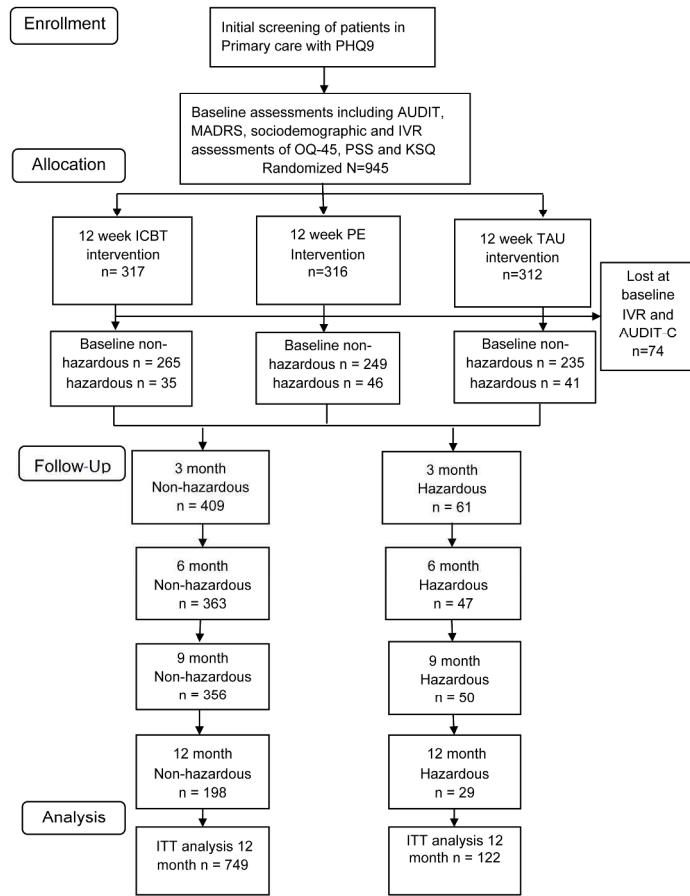
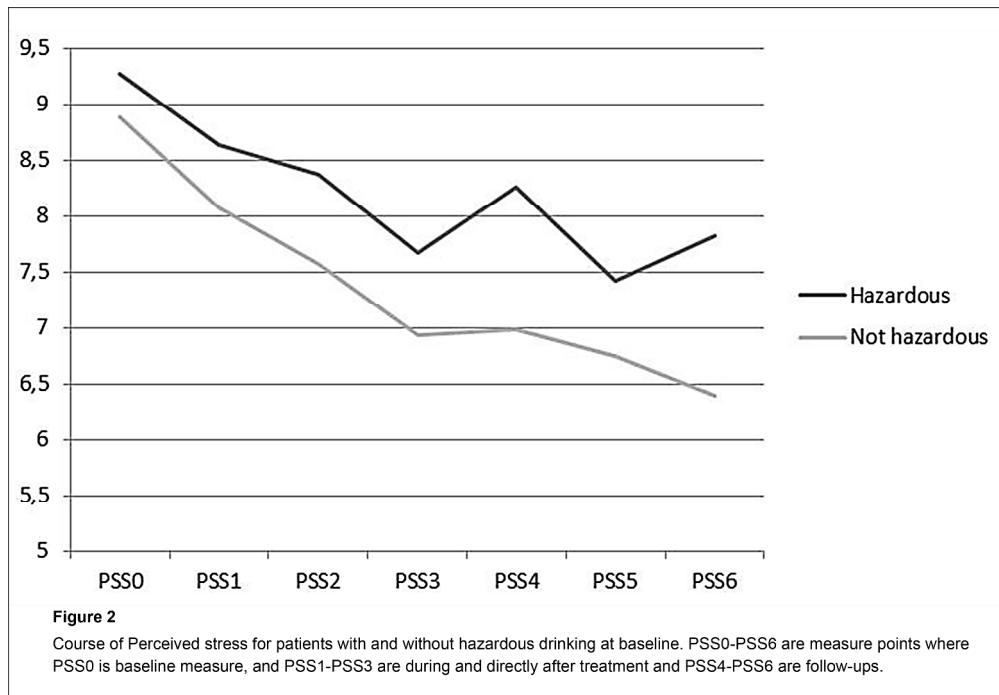


Figure 1 The Participant's Flow Through the Study

CONSORT diagram showing the participants flow through the study

209x297mm (300 x 300 DPI)



The graph shows the course of perceived stress during and after treatment for patients with and without hazardous drinking at baseline

304x210mm (300 x 300 DPI)

# BMJ Open

## The influence of hazardous drinking on psychological functioning, stress and sleep during and after treatment in patients with mental health problems; a secondary analysis of a randomized controlled intervention study

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4 **The influence of hazardous drinking on psychological**  
5 **functioning, stress and sleep during and after treatment in**  
6 **patients with mental health problems; a secondary analysis of**  
7 **a randomized controlled intervention study**  
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## ABSTRACT

### Objectives

Hazardous drinking could negatively affect health and lead to alcohol use disorders, but it is unclear how hazardous drinking affects treatment outcomes of depression and anxiety and stress-related mental health problems.

The aim of this study was to examine whether hazardous drinking, measured by AUDIT-C, influences the outcomes of repeated assessments of psychological functioning (OQ-45), stress (PSS) and sleep (KSQ), during and after treatment in patients with mental ill-health.

### Methods

The study was conducted within REGASSA, a randomized controlled trial aimed at comparing Internet-based CBT and physical exercise with treatment as usual on primary care patients with mental ill-health. The study involved 871 participants who completed the Alcohol Use Disorders Identification Test at baseline and who were assessed repeatedly during and after treatment on psychological function, stress and sleep by Interactive Voice Response (IVR), a computerized, automated telephone technology.

### Results

At baseline, hazardous drinkers were more depressed and had lower scores on psychological functioning than non-hazardous drinkers, while there were no differences on stress and sleep. During the follow-ups, hazardous drinking negatively influenced perceived stress, i.e. hazardous drinkers seemed to have less treatment effect on stress, and the results remained after controlling for depression. There were no differences during the follow-ups regarding psychological functioning and sleep.



## Conclusions

Hazardous drinking negatively influenced perceived stress. The findings of the study emphasize the importance of screening for alcohol habits in mental ill-health patients, since risky drinking may affect the outcomes of treatment.

## Trial registration

On 2015/06/10 the REGASSA study was retrospectively registered in German clinical trials DRKS00008745, but it had been originally registered with KTA CT20110063 on 2011/02/10.

**Key words:** Hazardous drinking, mental health problems, primary care, psychological functioning, stress, sleep, IVR, repeated assessments, Internet-based CBT, physical exercise

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is a secondary analysis of RCT data and not a prospectively designed RCT, which was a limitation.
- However, the large sample of primary care patients was a strength.
- Another strength, was the repeated assessments collected by automated technology, which was a convenient way of monitoring a large sample of participants.
- The high attrition in the repeated assessments was a limitation, although the analysis model compensating for the attrition was a strength and the proportion of hazardous drinkers remained almost the same.
- The AUDIT-C cut-off scores have not been validated in a population of mental health problems, which was a limitation.

## INTRODUCTION

Hazardous or risky alcohol consumption is common in patients seeking primary care, but is often not adequately examined at the medical visit,[1-2], and only some of the patients with risky consumption, are advised to reduce their alcohol use,[3]. Hazardous drinking, including both the number of drinks consumed weekly and on a single occasion, ‘binge drinking’, is considered an alcohol drinking pattern that could lead to negative effects on health and to development of alcohol use disorders,[4-5]. Screening for alcohol use is a recommended intervention for patients in routine care, and patients reporting a pattern of hazardous drinking should be given advice on how to change this pattern and offered brief interventions. Patients with alcohol use disorder or dependence should be referred for treatment,[6-8].

Several studies have shown higher prevalence rates for hazardous drinking in patients with common mental health problems compared to the general population,[6, 9-11]. Eberhard and colleagues (2009) found a prevalence of 21 % in a population of psychiatric outpatients, and Nehlin and co-workers (2011) showed a proportion of 19 %,[6, 10] which was higher than that in the Swedish general population at the time, (15 %). However, only a few studies have examined whether concomitant hazardous drinking affects treatment outcome of mental health problems. In an extensive review by Sullivan and colleagues (2005), it could not be established whether hazardous drinking or alcohol use disorders influenced recovery from or relapse in depression, although the review only involved one study examining risk drinking. In that study hazardous drinking did not affect recovery from depression,[12]. Gajecki and co-workers (2014) examined whether problematic substance use affected an Internet-based cognitive behavior therapy for depression and anxiety disorders, and found no differences in effect between hazardous and non-hazardous drinkers on depression, but hazardous drinkers showed less treatment effect for panic disorder,[13]. In another study on treatment of anxiety, alcohol use severity had no impact on treatment effect, although, baseline hazardous alcohol

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3 use was associated with more anxiety and depression symptoms at long-term follow-up,[14].  
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5 Haynes and colleagues (2007) found little evidence that hazardous drinking is a risk factor in  
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7 non-recovery from common mental disorders, but binge-drinking may be a potential risk,[5].  
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9 Consequently, few studies have addressed the impact of hazardous alcohol use on treatment  
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11 effects, and the findings are inconsistent, which justifies further research.  
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14 The present study is a secondary analysis performed within the framework of REGASSA, a  
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16 multicenter randomized controlled trial (RCT) conducted in primary care on patients with  
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18 mild to moderate depression, anxiety, and stress-related mental health problems. The  
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20 objectives of REGASSA were to study the effects of Internet-based cognitive behavior  
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22 therapy (ICBT) and physical exercise (PE) compared to treatment as usual (TAU) on work-  
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24 ability and sick-leave as primary outcome measures, and depression as secondary outcome.  
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26 Other secondary outcome measures used were repeated assessments of psychological  
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28 functioning, perceived stress and sleep. Data were collected by automated telephone  
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30 technique, Interactive Voice Response (IVR), which enabled frequent follow-ups during and  
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32 after treatment. In a previous analysis of REGASSA using these secondary outcomes, we  
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34 found that ICBT and PE were more effective than TAU on psychological functioning and  
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36 sleep, no differences were found on perceived stress, all three treatment groups  
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38 improved,[15].  
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43 In the present study, we wanted to explore whether hazardous alcohol use could predict the  
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45 outcomes of sleep, psychological functioning and stress, factors that may be influenced by  
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47 hazardous alcohol consumption. To the best of our knowledge, the relationship between  
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49 hazardous drinking and the secondary variables of REGASSA has previously only been  
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51 studied with less frequent follow-ups, or has not been studied at all.  
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3 Stress is known to be linked with sleeping problems and mood disorders,[16-18]. In a  
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5 previous primary care study, high levels of stress were commonly reported in association with  
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7 symptoms of anxiety and depression,[19] and high levels of perceived stress have been shown  
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9 to be associated with less antidepressant treatment effect,[20].  
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12 In an epidemiological study of over 30.000 individuals, Dawson et al,[21] found that stress  
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14 resulted in increased quantities of alcohol consumption on specific drinking occasions, rather  
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16 than more frequent drinking. Scher et al. reported no clear results whether alcohol reduces  
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18 perceived stress, and concluded that stress is likely to be influenced by both individual and  
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20 situational factors,[22].  
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23 Vinson and colleagues conducted a study in primary care on sleep and alcohol consumption  
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25 and found no associations between hazardous drinking and sleeping problems,[23]. To the  
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27 best of our knowledge, how hazardous drinking may affect change in psychological  
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29 functioning (Outcome Questionnaire-45, OQ-45) has not yet been studied.  
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32 At baseline, patients in REGASSA completed the Alcohol Use Disorders Identification Test  
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34 (AUDIT), which was developed for early detection of individuals with hazardous or harmful  
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36 alcohol drinking,[24]. A previous cross-sectional study of REGASSA showed that the total  
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38 AUDIT score, the scores of AUDIT-C and the proportions of hazardous drinkers, 22 %, were  
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40 higher among REGASSA patients compared to the general population, 15 % [25].  
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43 This study aimed to examine whether hazardous drinking at baseline predicts the outcomes of  
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45 repeated assessments of psychological functioning, stress and sleep collected by IVR during  
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47 and after treatment in REGASSA.  
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## METHODS

### Study design

Study design, participants and measurements are presented in more detail in an earlier study,[15], and only a brief description is given here. REGASSA was carried out in primary care in six health care regions in Sweden between 2011 and 2014. After giving written informed consent, patients were randomized to one of three treatment alternatives, ICBT, PE and TAU, for a 12-week intervention. At baseline, participants completed a battery of questionnaires, including measures of depression (MADRS) and alcohol use (AUDIT), and follow-ups were conducted 3 and 12 months after baseline. Secondary outcomes of psychological functioning, stress and sleep were continually collected by IVR during and after treatment.

IVR is an automated telephone system programmed to administer various questionnaires and to follow a large population over time. At baseline the patients in REGASSA registered their personal mobile number and answered the 55 questions included in IVR using touch-tone technology. The automated system then called the patients on six measurement occasions, two during treatment, one at the end of treatment, and three after treatment until 12 months after baseline. The attrition in IVR showed varying but decreasing levels over the 12-month study period (Table 1). The proportion of responders at 3-month follow-up was 54 %, at 6-month 47 %, at 9-month 47 %, and at the final 12-month follow-up the proportion of responders had fallen to 25 %. The proportion of hazardous drinkers remained almost constant, 15 % at 3-month follow-up, 13 % at 6-months, 14 % at 9-months and 15 % at 12-month follow-up. The number of responders is presented in Figure 1.

## Participants

Participants were primary care patients with light to moderate depression, anxiety and stress-related mental ill-health. The inclusion criteria were  $\geq 10$  points on the Patient Health Questionnaire (PHQ9), a short depression scale and, Swedish language skills due to the ICBT program, being only delivered in Swedish. REGASSA included 945 patients, of which 879 completed the IVR baseline assessments and, of these 879 patients, 871 also completed AUDIT at baseline. Patients with a primary substance use disorder were excluded. The CONSORT diagram (Figure 1) shows the flow of the participants and the number of responders at each follow-up for hazardous and non-hazardous drinkers.

## Measures at baseline

### AUDIT

AUDIT is a ten- item scale for measuring alcohol consumption and alcohol-related problems. The test is validated in primary care and has shown acceptable psychometric properties,[24]. AUDIT is in two parts, items 1-3 measuring alcohol consumption (AUDIT-C), and items 4-10 measuring alcohol problems (dependency and harm combined). In this study, we only used the abbreviated consumption subscale AUDIT-C, since the three questions in OQ-45 on negative consequences of drinking behavior would otherwise interfere with questions 4-10 in AUDIT. The items in AUDIT-C are (1) *How often do you drink alcohol?* (2) *How many glasses do you drink on a typical day when you drink alcohol?* (3) *How often do you have six or more drinks on one occasion?* The scores range from 0-4 and maximum negative score is 12. AUDIT-C has shown high specificity and sensitivity in screening for risky alcohol habits,[26-27]. The cut-off score for hazardous drinking in this study was set to  $\geq 5$  for women and  $\geq 6$  for men in accordance with Swedish guidelines,[28]. These cut-offs are higher than in previous studies where the cut-off scores have been set to  $\geq 3-4$  for women and

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3  $\geq 4$ -5 for men, but it is recommended that cut-off scores are determined empirically in  
4 different cultures, since drinking frequency varies largely between countries,[6, 11, 26-27].  
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8 When studying the question of binge drinking separately, the cut-off was set to *at least on a*  
9 *monthly basis* for both women and men.  
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### 11 12 13 MADRS

14 In earlier REGASSA studies, MADRS was used as an outcome measure for depression but, in  
15 this study, it was used as a baseline measurement and only for controlling results obtained  
16 with AUDIT-C. MADRS is a commonly used measure for depression that has shown good  
17 psychometric properties. It consists of ten items with six response alternatives,[29].  
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### 23 24 Gender

25 We analyzed whether there were any gender differences in terms of hazardous drinking and  
26 its influence on the outcome measures of psychological functioning, sleep and stress.  
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### 30 31 **Outcome measurements in IVR**

#### 32 Outcome Questionnaire-45

33 The repeated assessments of psychological functioning were measured by Outcome  
34 Questionnaire-45 (OQ-45). OQ-45 was developed by Lambert and colleagues to measure  
35 psychotherapy effects,[30]. It consists of 45 questions with a score range of 0-180, where 180  
36 is the maximum negative score. OQ-45 captures the patient's psychological functioning  
37 through questions about symptoms, interpersonal problems and social role function. Both the  
38 original and the Swedish version of OQ-45 have shown good psychometric properties,[30-  
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#### 50 Perceived Stress Scale

51 Stress was repeatedly assessed by the Perceived Stress Scale (PSS), originally a ten-item scale  
52 measuring how the patient copes with stress. In this study, we used a shortened 4-item version  
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of this scale that has proved suitable for telephone assessments,[33]. The scores range from 0-4 and the maximum total negative score is 16.

### Karolinska Sleep Questionnaire

A short version of the Karolinska Sleep Questionnaire assessed the sleep outcome. The questionnaire comprises four items capturing sleep quality, with scores ranging from 1- 6, and the maximum negative score was 24. KSQ has shown good validity, reliability and sensitivity in various studies,[34].

### Statistics

Differences between hazardous drinkers and non-hazardous drinkers were calculated on continuous baseline measurements using independent samples t-tests, and differences in proportions of hazardous drinkers in discrete variables were examined with chi-square tests. Differences in attrition between non-hazardous and hazardous drinkers were calculated with Fisher's exact test. To examine how alcohol consumption (AUDIT-C) at baseline affected the course and outcome for psychological functioning, stress and sleep, we conducted three separate analyses with linear mixed-models with a first-order auto-regressive, heterogeneous rho covariance structure. Mixed-models include all measures that are available at each assessment, and were therefore considered suitable for this study. We assumed that missing observations were unrelated to the observed value, i.e. missing at random. Each model included six follow-ups called assessments 1, 2, 3, 4, 5 and 6, the assigned treatment groups ICBT, PE and TAU, gender, and two baseline measures, i.e. hazardous drinking (AUDIT-C) and the baseline scores of one of the three outcome measures (OQ-45, PSS, KSQ). All variables were modelled as fixed effects. The outcome measure baseline scores were used as continuous covariate and the control variable hazardous drinking (AUDIT-C) and gender as categorical covariates. AUDIT-C was a dichotomous variable where 0 was defined as non-hazardous drinking and 1 hazardous drinking. MADRS was used as a continuous covariate for



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3 controlling for depression if AUDIT-C showed significant influence on the outcome  
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5 measures. Assessment data was nominal, i.e. each measurement occasion was separate and  
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7 time was not a continuous linear regressor in the model. The analyses began with a full model  
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9 with interaction effects of AUDIT-C x Treatment group x Assessment and was simplified to  
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11 main group effects if no significant interaction effects were found. Before the results were  
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13 analysed, the residuals were examined and showed a normal distribution. A test for robustness  
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15 showed similar results as the mixed-models analysis. All statistics were performed in the  
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17 SPSS for Windows 22.0.  
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## 20 21 **RESULTS**

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23 The average age of patients was 43, and 62 % had a high level of education. Most of the  
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25 patients were working and only 5 % were on sick-leave. In Table 1, different descriptions of  
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27 baseline measurements for hazardous drinkers and non-hazardous drinkers and attrition  
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29 during the follow-ups are presented.  
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**Table 1.** Baseline scores for non-hazardous drinkers and hazardous drinkers on sociodemographic data, depression (MADRS), psychological function (OQ-45), stress (PSS), and sleep (KSQ), the allocation in each three-treatment condition, Internet- based cognitive behavior therapy (ICBT), Physical exercise (PE) and Treatment as usual (TAU), and the numbers (%) still in follow-up.

Variables	Non-Hazardous n = 749	Hazardous n = 122
Age M ( $\pm$ SD)	43.4 (12.0)	40.7 (13.1)
Gender %		
Male	25	35
Education %		
Low	4	5
Medium	35	38
High	61	57
Employment %		
Employed/study	81	82
Pension	4	3
Unemployed	10	3
Sick-leave	5	12
Civil state %		
Living alone	37	43
MADRS M ( $\pm$ SD)	21.3 (7.1)	23.0 (6.9)
Depression level %		
No depression	9	4
Mild depression	33	27
Moderate depression	55	65
Severe depression	3	4
OQ-45 M ( $\pm$ SD)	83.7 (19.6)	89.0 (17.9)
PSS M ( $\pm$ SD)	8.9 (2.5)	9.3 (2.5)
KSQ M ( $\pm$ SD)	14.7 (4.4)	14.6 (4.4)
Allocation		
ICBT	35	29
PE	33	38
TAU	32	34
Numbers still in follow-up %		
3 month	55	50
6 month	48	39
9 month	48	41
12 month	26	24

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3 The proportion of hazardous drinkers at baseline measured by AUDIT-C was 14 %, with a  
4 significantly higher proportion in men, (18 %) compared to women (12 %),  $\chi^2 = 5.23$   $p =$   
5 0.022. The proportions of binge drinkers measured by item 3 in AUDIT-C was 13 %, and the  
6 overlap between hazardous and binge drinkers was high; 90 out of the 122 hazardous  
7 drinkers, were also binge drinkers, and 90 of the 110 binge drinkers were hazardous drinkers,  
8 so our analysis focused solely on the summarized score in AUDIT-C as a measure of  
9 hazardous drinking. The baseline average depression score (MADRS) showed moderate  
10 depressive problems, and hazardous drinkers were more depressed  $t(853) = -2.31$ ,  $p = 0.021$   
11 and had lower psychological functioning (OQ-45)  $t(871) = -2.85$ ,  $p = 0.004$  than non-  
12 hazardous drinkers. There were no baseline differences between the treatment alternatives,  
13 perceived stress, sleep or age, education level, civil state and employment. The Fisher's exact  
14 test showed no differences in attrition between non-hazardous and hazardous drinkers at any  
15 follow-up and there were no differences between the treatment alternatives.  
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31 The results of the linear mixed-models showed that hazardous alcohol consumption at  
32 baseline predicted the outcome for perceived stress (PSS). The patients with hazardous  
33 drinking had a higher average score on PSS throughout the assessments, which might indicate  
34 less treatment effect for perceived stress compared to non-hazardous drinkers. To test whether  
35 this effect could be due to depression, since hazardous drinkers were more depressed than  
36 non-hazardous, we carried out a new analysis with MADRS and AUDIT-C as baseline  
37 covariates, and both MADRS  $p = 0.003$  and AUDIT-C  $p = 0.022$  were significant, i.e. the  
38 effects of hazardous drinking remained. In the full model, we included interaction effects  
39 between hazardous alcohol consumption and treatment alternatives and hazardous alcohol  
40 consumption and the IVR-assessments, but no significant interaction effects were found. The  
41 model was reduced to main effects of group, including a control for differences at baseline  
42 between hazardous and non-hazardous drinkers; the results are presented in Table 2.  
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**Table 2.**

The influence of alcohol consumption on repeated assessments of perceived stress as main effect of group presented in average change scores.

Variables	Average change	<i>df</i>	<i>t</i>	95 % CI
Assessment 1	0			
Assessment 2 <sup>a</sup>	-.43	725.65	-4.39***	[-.63, -.24]
Assessment 3 <sup>a</sup>	-1.02	707.27	-9.00***	[-1.25, -.80]
Assessment 4 <sup>a</sup>	-1.06	621.12	-8.52***	[-1.30, -.81]
Assessment 5 <sup>a</sup>	-1.28	601.23	-9.78***	[-1.53, -1.02]
Assessment 6 <sup>a</sup>	-1.49	319.69	-9.79***	[-1.79, -1.19]
Gender <sup>b</sup>	.32	642.18	1.78	[-.03, .66]
AUDIT-C <sup>c</sup>	.61	668.58	2.65***	[.16, 1.06]

*Note.* AUDIT C = Alcohol Use Disorders Identification Test-Consumption.

Assessment 1 is set to zero because it is a redundant.

<sup>a</sup> A negative score means a reduction from Assessment 1.

<sup>b</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in women as compared to men.

<sup>c</sup> A positive score means that the average score of Assessments 1-6 shows larger reduction from Assessment 1 in non-hazardous as compared to hazardous drinkers.

\**p* < .05, \*\**p* < .01, \*\*\* *p* < .001

The main effect of group occurred after baseline, i.e. during and after treatment, so hazardous drinkers probably had less treatment effect even if no differences in how hazardous drinking predicted stress were found between the treatment alternatives. The average changes on PSS over the assessments for patients with and without hazardous drinking are presented in Figure 2. The differences in stress between hazardous drinkers and non-hazardous drinkers were higher at the follow-ups conducted after the end of treatment, but these figures should be treated with some caution because of the large attrition, even if there were no differences in attrition between the two groups.

The results of the linear mixed-models on psychological functioning (OQ-45) and sleep (KSQ) were not significantly influenced by the level of hazardous alcohol consumption at

baseline, although there was a tendency ( $p = 0.064$ ) for higher average scores on OQ-45 for hazardous drinkers compared to non-hazardous drinkers (Tables 3 and 4). Since the main effect of group was not significant on OQ-45 and KSQ, interaction effects between hazardous drinking and treatment group or hazardous drinking and assessments were not examined.

**Table 3.**

The influence of alcohol consumption on repeated assessments of Outcome Questionnaire-45 as main effect of group presented in average change scores.

Variables	Average change	<i>df</i>	<i>t</i>	95 % CI
Assessment 1	0	0	0	
Assessment 2 <sup>a</sup>	-4.00	724.13	-7.19***	[-5.09, -2.91]
Assessment 3 <sup>a</sup>	-8.50	694.62	-11.52***	[-9.95, -7.05]
Assessment 4 <sup>a</sup>	-9.87	579.86	-11.15***	[-11.61, -8.13]
Assessment 5 <sup>a</sup>	-10.07	497.79	-10.28***	[-12.00, -8.15]
Assessment 6 <sup>a</sup>	-11.83	291.60	-10.05***	[-14.14, -9.51]
Gender <sup>b</sup>	2.62	605.08	1.79	[-.25, 5.48]
AUDIT-C <sup>c</sup>	3.50	627.39	1.86	[-.20, 7.21]

Note. AUDIT C = Alcohol use disorder identification test-consumption.

Assessment 1 is set to zero because it is a redundant.

<sup>a</sup> A negative score means a reduction from Assessment 1.

<sup>b</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in women as compared to men.

<sup>c</sup> A positive score means that the average score of Assessments 1-6 shows larger reduction from Assessment 1 in non-hazardous drinkers as compared to hazardous.

\* $p < .05$ , \*\* $p < .01$ , \*\*\*  $p < .001$

**Table 4.**

The influence of alcohol consumption on repeated assessments of sleep as main effect of group presented in average change scores.

Variables	Average change	df	t	95 % CI
Assessment 1	0			
Assessment 2 <sup>a</sup>	-.44	710.76	-3.49***	[-.69, -.19]
Assessment 3 <sup>a</sup>	-1.02	759.76	-6.47***	[-1.33, -.71]
Assessment 4 <sup>a</sup>	-1.05	649.15	-5.78***	[-1.41, -.70]
Assessment 5 <sup>a</sup>	-1.02	632.79	-5.76***	[-1.36, -.67]
Assessment 6 <sup>a</sup>	-1.31	338.53	-5.88***	[-1.74, -.87]
Gender <sup>b</sup>	.14	635.91	.53	[-.37, .65]
AUDIT-C <sup>c</sup>	.49	660.12	1.46	[-.17, 1.15]

*Note.* AUDIT-C = Alcohol use disorder identification test-consumption.

Assessment 1 is set to zero because it is a redundant.

<sup>a</sup> A negative score means a reduction from Assessment 1.

<sup>b</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in women as compared to men.

<sup>c</sup> A positive score means that the average score of Assessments 1-6 shows a larger reduction from Assessment 1 in non-hazardous as compared to hazardous drinkers.

\*p < .05, \*\*p < .01, \*\*\* p < .001

## DISCUSSION

The aim of this study was to examine whether hazardous alcohol consumption predicts the outcome for psychological functioning, perceived stress and sleep, over a twelve-month assessment period. The results showed that hazardous drinking predicted stress, but not psychological functioning and sleep. Patients with hazardous drinking had a higher level of stress during the follow-ups compared with non-hazardous drinkers, but not at baseline, and these results remained after controlling for depression. In a previous study in REGASSA,[15], we reported that the treatment had positive effect on perceived stress, and all treatment groups showed improvements. The present study adds that the improvement was negatively

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2  
3 influenced by hazardous drinking, i.e. hazardous drinkers improved less than non-hazardous  
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5 drinkers irrespective of treatment alternative.  
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8 Dawson and co-workers, who separated binge drinking from other consumption measures,  
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10 found that stress was associated with binge drinking and not with frequency of drinking,[21].  
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12 In our study, binge drinking was a part of hazardous drinking in the summarized measure of  
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14 AUDIT-C, which might explain our results that hazardous drinking was associated with  
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16 higher levels of stress. Hazardous drinkers seemed to get less treatment effects on stress,  
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18 which is not in line with the assumption that alcohol could reduce stress. Although it is  
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20 uncertain whether alcohol reduces stress, its effect on stress seems to depend on several  
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22 factors,[22]. The focus in the present study was on hazardous alcohol consumption, which  
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24 may not reduce stress. The influence of alcohol use on stress seems unclear and further  
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26 investigations are required.  
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30 The finding that hazardous drinking did not affect sleep quality is in line with an earlier study  
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32 conducted in primary care,[23], but contradicts other findings where risky alcohol users have  
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34 reported lower sleep quality,[35].  
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38 When comparing the baseline scores of OQ-45 in our sample of depressed patients with  
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40 samples of patients with alcohol use disorders, the patients in our sample showed lower  
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42 psychological functioning, and this applied for both hazardous and non-hazardous  
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44 drinkers,[31, 36]. Hazardous drinkers had a significantly higher score on OQ-45 at baseline  
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46 but, during follow-ups, these differences were no longer significant, although a tendency  
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48 towards higher scores remained. In summary, results of our analyses were unclear about the  
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50 way hazardous drinking affects psychological functioning, and more research is needed.  
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54 Several studies have concluded that alcohol use patterns should be screened in health care,  
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56 and the AUDIT-C has been recommended as a suitable screening test,[6-7, 26]. A common  
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3 barrier for addressing alcohol habits in health care is lack of time, so a short screening tool  
4 such as the AUDIT-C could be a facilitator,[1, 7], as well as automated technology. The  
5 patients in REGASSA turned out to have higher proportions of hazardous drinking and  
6 alcohol problems than the general population,[25], which emphasizes the need to examine the  
7 alcohol patterns and increase the amount of advice on alcohol consumption given to patients  
8 with mental ill-health. Systematic screening for alcohol use in primary care has been shown to  
9 increase the detection of hazardous drinkers, and facilitate brief interventions,[7]. The results  
10 in our study confirm the importance of screening for drinking habits in primary care, to  
11 identify risky consumption that may have an impact on treatment effects on perceived stress  
12 for patients with common mental health problems.

### 24 25 **Strengths and limitations**

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27 The large sample of mental ill-health patients in primary care is an advantage and strengthens  
28 the results. However, the present design, a secondary analysis of RCT data, examining the  
29 prediction of alcohol consumption on psychological function, stress and sleep, is not powered  
30 to fully answer the question, which is a limitation. The chosen cut-off scores of AUDIT-C,  
31 which are recommended by the Swedish national guidelines, have not been validated in a  
32 population of patients with mental health problems, which is a limitation. The repeated  
33 assessments in collected by IVR is a strength that enabled us to make reliable comparisons  
34 and to follow the patients throughout the study. The analysis model is a strength  
35 compensating for the high attrition in IVR, which is otherwise a limitation. Conclusions about  
36 differences on stress between hazardous drinkers and non-hazardous in later follow-ups,  
37 should be drawn with caution due to attrition, although the attrition was not higher among  
38 hazardous drinkers during the follow-ups.



## Conclusion

This study showed that hazardous drinkers were more depressed and had lower psychological functioning at baseline and higher level of stress during and after treatment. These results add to previous studies on the importance of screening for alcohol consumption in mental ill-health patients seeking primary care, since hazardous drinking may influence some treatment effects. Further research is needed on how hazardous drinking affects different treatment outcomes in patients with common mental health problems.

## List of abbreviations

AUDIT	Alcohol Use Disorder Identification Test
AUDIT-C	Alcohol Use Disorder Identification Test - Consumption
GP	General Practitioner
ICBT	Internet-based cognitive behavior therapy
ITT	Intention to treat
IVR	Interactive Voice Response
KSQ	Karolinska Sleep Questionnaire
MADRS	Montgomery Åsberg Depression Rating Scale
M.I.N.I.	Mini-International Psychiatric Interview
OQ-45	Outcome Questionnaire-45
PE	Physical exercise
PHQ-9	Patient Health Questionnaire-9
PSS	Perceived Stress Scale
RCT	Randomized controlled trial
TAU	Treatment as usual

## DECLARATION

### Ethics approval and consent to participate

The REGASSA study was approved by the regional ethical review board at Karolinska Institutet in Stockholm (Dnr 2010/1779-31/4) and retrospectively registered in German clinical trials DRKS00008745. Before allocation, a written informed consent was obtained from each patient.

### Consent for publication

Consent for publication was not applicable in this study.

### Availability of data and material

The datasets generated and/or analyzed during the current study are not publicly available, since the ethical review board has not granted permission for this, but are available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interest.

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### Authors' contributions

CS was involved in the data collecting process, made major contributions to the data analysis, and was a major contributor in writing the manuscript. CA was involved in the study design

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2  
3 and the data collecting process, made contributions to the data analysis and writing process.  
4  
5 AH was vice director for the REGASSA study and was involved in the study design, made  
6  
7 contributions to the data analysis and the writing process. All authors read and approved the  
8  
9 final manuscript.  
10

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16 Lundh at the Department of Psychology, Lund University for valuable comments on the  
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18 manuscript.  
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22 **Figure 1** The CONSORT diagram shows the participants' flow through the study  
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25 **Figure 2** The graph shows the course of stress during and after treatment for patients with and  
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27 without hazardous drinking at baseline  
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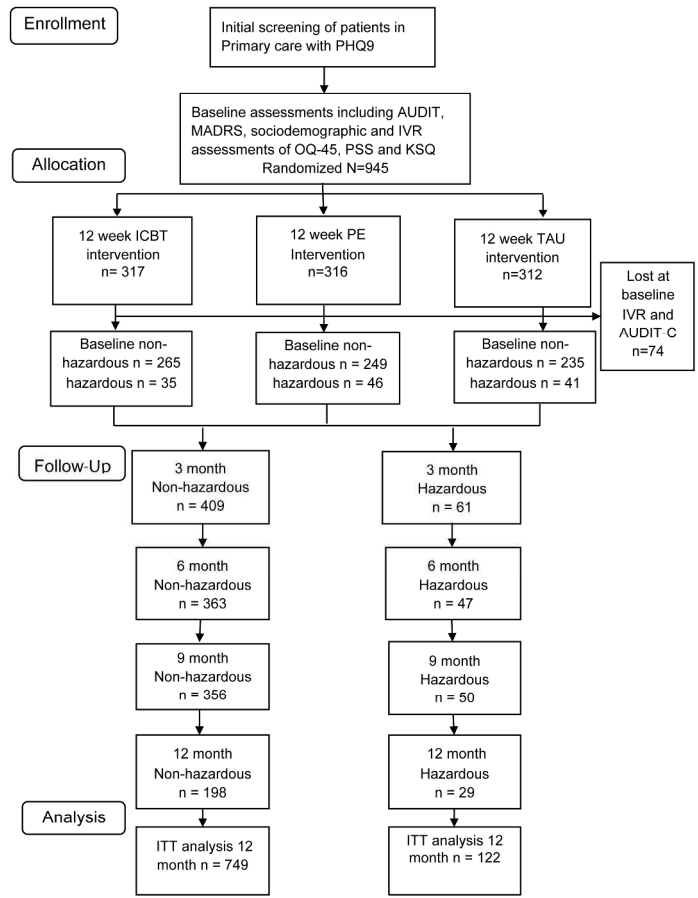
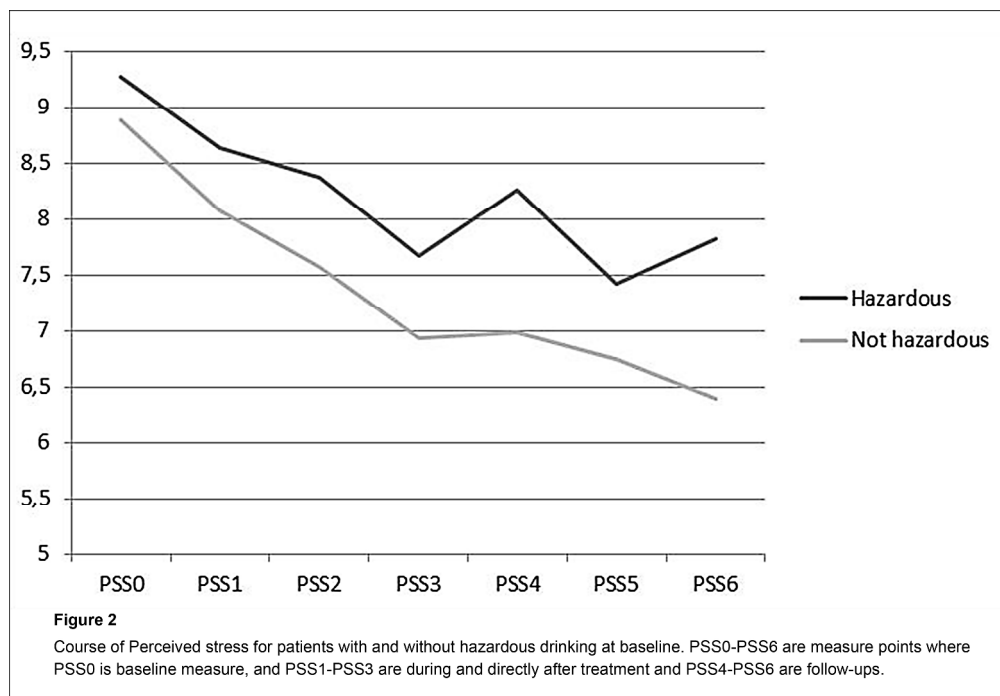


Figure 1 The Participant's Flow Through the Study

CONSORT diagram showing the participants flow through the study

209x297mm (300 x 300 DPI)



The graph shows the course of perceived stress during and after treatment for patients with and without hazardous drinking at baseline

304x210mm (300 x 300 DPI)