



Effects of Baseline Problematic Alcohol and Drug Use on Internet-Based Cognitive Behavioral Therapy Outcomes for Depression, Panic Disorder and Social Anxiety Disorder

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Abstract

Purpose: Patients' problematic substance use prevalence and effects were explored in relation to internet-based cognitive behavioral therapy (ICBT) outcomes for depression, panic disorder and social anxiety disorder.

Methods: At baseline and treatment conclusion, 1601 ICBT patients were assessed with self-rated measures for alcohol and drug use (AUDIT/DUDIT), depressive symptoms (MADRS-S), panic disorder symptoms (PDSS-SR) and social anxiety symptoms (LSAS-SR).

Results: Problematic substance use (AUDIT ≥ 8 for men, ≥ 6 for women; DUDIT ≥ 1) occurred among 32.4% of the patients; 24.1% only alcohol, 4.6% only drugs, and 3.7% combined alcohol and drug use. Hazardous alcohol use and probable alcohol dependence negatively affected panic disorder outcomes, and hazardous drug use led to worse social anxiety outcomes. Depression outcomes were not affected by substance use. Treatment adherence was negatively affected by problematic drug use among men and 25–34 year olds; combined substance use negatively affected adherence for women and 35–64 year olds.

Conclusion: Problematic substance use does not preclude ICBT treatment but can worsen outcomes, particularly problematic alcohol use for panic disorder patients and hazardous drug use for social anxiety patients. ICBT clinicians should exercise particular caution when treating men and younger patients with problematic drug use, and women or older patients with combined substance use.

Citation: Gajecki M, Berman AH, Sinadinovic K, Andersson C, Ljótsson B, et al. (2014) Effects of Baseline Problematic Alcohol and Drug Use on Internet-Based Cognitive Behavioral Therapy Outcomes for Depression, Panic Disorder and Social Anxiety Disorder. PLoS ONE 9(8): e104615. doi:10.1371/journal.pone.0104615

Editor: Gabriele Fischer, Medical University of Vienna, Austria

Received: February 4, 2014; **Accepted:** July 15, 2014; **Published:** August 14, 2014

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Funding: This study was funded by the Stockholm Center for Dependency Disorders (http://www.sls.sll.se/SLPOtemplates/SLPOPage1____6639.aspx), Psychiatry Southwest (http://www.sls.sll.se/slpotemplates/slpopage1____4432.aspx) and Vinnova (<http://www.vinnova.se/>), grant number 2009-00192. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

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Introduction

Considerable evidence indicates an association between psychiatric disorders and problematic substance use. Individuals diagnosed with a psychiatric disorder run double the risk of being diagnosed with an alcohol use disorder and four times the risk of being diagnosed with a drug use disorder, compared to those without a psychiatric disorder [1]. In a US national survey, the 12-month prevalence level of a diagnosed alcohol use disorder among individuals with a mood disorder was 17.3% and 6.9% for a drug use disorder. Among individuals with an anxiety disorder, 12-month prevalences were 13.0% and 4.6% respectively. In comparison, prevalences in the general population were lower – 8.5% for diagnosed alcohol and 2% for drug use disorders. Among

those seeking treatment for major depressive disorder, panic disorder with agoraphobia, panic disorder without agoraphobia and social anxiety disorder the 12-month prevalences for an alcohol use disorder were 16.8%, 15.4%, 13.7% and 16.0% respectively. The corresponding numbers for a drug use disorder were 7.5%, 9.7%, 5.1% and 8.2% [2].

In Sweden, about one-fourth of non-psychotic patients at psychiatric outpatient clinics have indicated problematic alcohol use [3], and almost 10% of psychotic patients have problematic drug use [4], higher levels than among the general population, where 21.1% show problematic alcohol use, and 2.8% indicate problematic drug use [5]. The causes of increased substance use among patients with psychiatric disorders are not well studied, but

one explanation could be self-medication [6–8]. Accordingly, studies have shown that development of common psychiatric disorders such as social anxiety disorder typically precedes the onset of substance abuse [9–11]. Initial substance use can conversely induce psychiatric disorders [12–14].

Surprisingly, little research seems to have been conducted about the effects of problematic substance use on psychotherapeutic treatment outcomes. A search for studies specifically examining how substance use affects the outcome of psychotherapeutic treatment for depression returned no results. In the area of anxiety disorders, a naturalistic 12-year study showed that concurrent alcohol or other SUDs did not affect social anxiety disorder and panic disorder outcomes [15]. In another study, pre-treatment problematic alcohol use levels did not predict treatment outcomes for social anxiety disorder or panic disorder; however, lower pre-treatment drinking levels led to greater improvement in social interaction anxiety [16]. A systematic review of predictors for dropout and treatment outcomes following CBT for social anxiety disorder examined alcohol and general substance use as predictors for treatment outcomes without finding any association [17].

A recent development in the psychiatric treatment of mental disorders is internet-based cognitive behavioral therapy (ICBT). ICBT has shown effect sizes similar to traditional therapy ($d = 0.91$; 95% confidence interval (CI) 0.68–1.14) for affective as well as anxiety disorders of mild or moderate severity [18,19]. Although research on treatment outcomes for internet-delivered psychotherapy for various diagnostic categories has increased exponentially over the past few years [20–22], a literature search using the terms “online therapy, e-therapy, alcohol, substance use, alcoholism, drug abuse, drug usage and effect” yielded no research about SUD effects on internet-based psychotherapy treatment outcomes. The little published research available from disparate studies suggests that SUDs do not seem to affect psychiatric treatment outcomes, running counter to standard psychiatric recommendations for integrated treatment for concurrent psychiatric and SUDs, at least for severe mental illness [23]. Furthermore, empirical evidence concerning the prevalence of SUD among patients seeking treatment with ICBT for depression, panic disorder and social anxiety disorder is scarce.

To the best of our knowledge, this is the first study investigating the effects of problematic substance use on ICBT outcomes. We first explored the prevalence of problematic alcohol and drug use among patients treated for depression, panic disorder and social anxiety disorder at an ICBT unit within ordinary psychiatric care in Sweden and, secondly, assessed the effects of problematic substance use on therapy outcomes for these patients.

Subjects, Materials and Methods

Ethics statement

All data analyzed in this study came from existing patient registries. After intake, ICBT patients were sent written information that their data might be used in future research regarding treatment effectiveness. The information stated explicitly that the patient could ask for their individual data to be withdrawn from the patient registry. No informed consent form was signed by patients at this time. The study was granted ethical approval by the Stockholm Regional Ethics Review Board, ref nr 2011/1029-31/5, August 18, 2011. The Board thus considered the patient information procedure ethically adequate for this study.

Setting

The ICBT clinic at Psychiatry Southwest in Stockholm-Huddinge (www.internetpsykiatri.se) specializes in the develop-

ment and delivery of ICBT within regular health and psychiatric care. Analyses have shown large within-group effect sizes for patients treated for major depressive disorder [24] panic disorder [25], and social anxiety disorder (El Alaoui, S., personal communication 22 October 2013) and maintenance of improvements 6 months after treatment. Baseline screening data on substance use are collected for all patients but the unit has not offered any internet-based treatment specifically for problematic substance use. Treatment at the ICBT unit includes self-assessment and 10–15 diagnosis-specific psycho-educational treatment modules, via a web-based communication platform with online therapist support.

Recruitment and treatment procedure

Patients are referred for treatment at the ICBT unit by a general practitioner or other physician, or self-referred. They complete web-based screening with diagnosis-specific screening instruments (see under Measures below) and are offered an intake appointment with a resident or specialist psychiatrist for further clinical assessment and diagnosis with the Mini-International Neuropsychiatric Interview (MINI) [26]. All individuals who met with an intake psychiatrist between October 30, 2007 and June 16, 2010, and who went on to initiate treatment, were included in this study. Patients included either had an ongoing unipolar depression, panic disorder (with or without agoraphobia) or social anxiety disorder. At the intake appointment, a joint decision is made by the assessing psychiatrist and the patient on whether or not to begin ICBT treatment. In cases of comorbidity the psychiatrist and the patient jointly decide on which of the offered treatment programs is most suitable for the patient at the time. Patients are informed that participating in other concurrent psychotherapeutic treatment will make them ineligible to receive ICBT. Also, if patients are on medication, their medication needs to be stabilized for one month prior to initiating ICBT. Patients are referred elsewhere if they fulfill any of the following conditions rendering them unable to benefit adequately from the treatment: insufficient knowledge of Swedish, suffering from psychosis or bipolar disorder, substance use so severe it interferes with their ability to participate, or suicidal ideation to a degree that makes other, alternative treatment, more suitable. Approximately 40% of referred patients did not initiate ICBT treatment.

All patients participating in ICBT treatment were given access to an ICBT program with therapist contact via an online asynchronous communication system for a period of 12–15 weeks. The therapists were all clinical psychologists. Patients were instructed to work with one module per week and to contact the therapist at least once every week. Patients could contact their therapist at any time and expect a reply within 48 hours on weekdays. The depression and panic disorder treatments comprised ten modules spanning over 12 weeks. The social anxiety disorder treatment was initially given in 15 modules over 15 weeks, but this was changed after the first year in regular care. The reason for this was that it is clinically more practical to administer a program over 12 weeks in order to avoid longer vacation periods in Sweden when patients are likely to be away (the summer months and winter holidays). In addition, in the original social anxiety disorder treatment, the final three modules were fairly light in content and it was possible to easily compress these into fewer modules with an expected maintained effect. The final format, with 12 modules over 12 weeks, is the one currently used. Moving on to the next treatment module was contingent on completing exercises and answering module-specific questions. Access to therapist support was terminated after 12/15 weeks but access to the text modules was open for additional six months. The

treatment context has been described in more detail elsewhere [24,25].

Addressing suicidal ideation

All patients complete the Montgomery Åsberg Depression Rating Scale – Self-rated (MADRS-S) weekly. An algorithm alerts the internet therapist, if the patient scores 4 or above on the suicidal ideation item (question 9) and the patient is contacted for in-person assessment. An automated alert is also sent out to the therapist if the patient stops interacting with the system for a period of seven days. The psychologist has access to the patient's phone number, and calls the patient if s/he stops communicating with the platform. The psychologist can also refer the patient for an emergency psychiatric appointment if deemed necessary. For acute circumstances, every patient has also provided the contact details of a close relative.

Study population

This study used retrospective data collected from ICBT patients in regular psychiatric care, and included 1601 patients screened for problematic alcohol and drug use, treated for depression ($n = 770$), panic disorder ($n = 483$), or social anxiety disorder ($n = 347$; 170 were offered 15 treatment modules and 177 were offered 12 modules). Twenty patients were excluded from analysis, one due to incorrect information on the number of treatment modules completed and 19 for whom screening data on the Alcohol Use Disorders Identification Test (AUDIT) and the Drug Use Disorders Identification Test (DUDIT) were missing, leaving a total population of 1581.

Baseline measures

The AUDIT [27] in Swedish translation [28,29], with well-established reliability and validity, was used to measure alcohol consumption and alcohol-related problems (total score range 0–40). In this study the term problematic alcohol use includes hazardous use (6–15 points for women [28] and 8–15 for men), harmful use (16–19) and probable dependence (20–40) [30]. The DUDIT, also with proven reliability and validity, measured illicit use of drugs and drug-related problems (total score range 0–44). In this study, problematic drug use includes hazardous use (1 for women and 1–5 for men), harmful use (2–24 for women and 6–24 for men) as well as probable dependence (25–44) [29,31]. The GAF (Global Assessment of Functioning) [32], with demonstrated adequate validity and reliability [33], was used by the intake psychiatrist to rate patients' functional status (total score range 0–100).

Continuous measures

MADRS-S (Montgomery Åsberg Depression Rating Scale – Self-rated) [34] was used to measure symptoms and severity of depression. MADRS-S is the self-rating version of MADRS [35], with a total score range of 0–54 [36] and good psychometric properties [37].

PDSS-SR (Panic Disorders Severity Scale – Self-Rating version) [38] was used to measure symptoms of panic disorder. The PDSS-SR is the self-rating version of the PDSS [39] and has a score range of 0–28 [40].

LSAS-SR (Liebowitz Social Anxiety Scale – Self-Rating version) [41] was used to measure social anxiety symptoms and severity. LSAS-SR is the self-rating version of LSAS [42] with a total score range of 0–144 [43].

All patients completed the MADRS-S at baseline and up to once a week during treatment to measure depression severity. In

parallel and at the same intervals, patients treated for panic disorder also completed the PDSS-SR and patients treated for social anxiety disorder completed the LSAS-SR.

Imputation of missing values and statistical analyses

Missing values at baseline for MADRS-S, PDSS-SR and LSAS-SR were imputed such that missing values were replaced by the first observation carried backward. Post-treatment missing values were replaced by the last prior observation carried forward.

Descriptive statistics were used for participant characteristics and prevalence data. The number of treatment modules completed by gender, age, diagnosis and problematic substance use were evaluated with ANOVA tests. To examine pairwise differences between groups in the analyses of variance, the Tukey-Kramer post-hoc test was used, taking into consideration unequal sample sizes, and controlling for mass significance [44]. Differences in therapy outcome by gender, age, diagnosis and levels of problematic substance use were tested using analyses of variance (ANOVA) and analyses of covariance (ANCOVA).

For purposes of comparison, the number of treatment modules for the social anxiety disorder treatment groups were adjusted to fit a scale of 0–10, and this adjusted number was used in all reported means and analyses.

To simplify interpretation of therapy outcomes over time, within-group effect sizes were calculated as Cohen's d by dividing the mean difference between pre- and post-measures by their pooled standard deviation. Comparisons between effect sizes were based on visual inspection. Interactive effects between treatment outcome and number of modules completed, GAF-scores, gender, age and diagnostic categories were analyzed using analysis of covariance (ANCOVA). All ANCOVA analyses used a reference group of individuals without problematic substance use, who were in the same category (e.g., gender or age). The IBM SPSS Statistical Package version 20 (IBM Corp, Armonk, NY, USA) for MacOS was used for all analyses.

Results

Participant characteristics

Table 1 shows participant characteristics by diagnosis for gender, mean age, mean GAF score and number of completed treatment modules, with specified levels of problematic substance use.

Substance use prevalence

Among the population of 1581 patients, problematic substance use was reported by 32.4%, with 24.1% indicating problematic alcohol use only, 4.6% reporting problematic drug use only and 3.7% indicating combined problematic alcohol and drug use, with a total of 8.3% indicating problematic drug use with or without alcohol. The age range was 17 to 79. Patients treated for depression were slightly older than the population mean, whereas panic disorder and social anxiety disorder patients were younger. The mean GAF-score indicated moderate to mild symptoms of difficulty in social, occupational or school functioning. A higher proportion of women than men were receiving ICBT treatment, particularly for depression and panic disorder. More men than women had harmful alcohol use, probable alcohol dependence and hazardous drug use as well as hazardous drug use combined with problematic alcohol use as measured with AUDIT and DUDIT respectively. In contrast, for harmful drug use the proportion of women was larger as well as for harmful drug use in combination with problematic alcohol use.

Table 1. ICBT patient population characteristics by gender, age, global assessment of functioning (GAF) ratings, number of modules completed, and mutually exclusive sub-categories of non-problematic and problematic substance use.

	All	Non-Problematic Use			Alcohol Use Categories			Drug Use Categories			Drug Use Categories+Problematic Alcohol Use		
		N (%)	Mean age (sd)	Mean Initial GAF ^a (sd)	Hazardous	Harmful	Probable Dependence	Hazardous	Harmful	Probable Dependence	Hazardous	Harmful	Probable Dependence
Total	1581(100)	1069(67.6)	321(20.3)	40(2.5)	20(1.3)	44(2.8)	28(1.8)	23(1.5)	34(2.2)	2(0.001)			
Women (%)	998(63.1)	709(66.3)	207(64.5)	16(40.0)	2(10.0)	11(25.0)	24(85.7)	2(8.7)	27(79.4)	0.0(0.0)			
Mean age (sd)	36.1(11.6)	37(11.6)	34.6(11.4)	33.7(12.0)	35.6(10.0)	35.4(13.6)	35.7(11.3)	31(11.0)	29.1(7.8)	24(2.8)			
Mean Initial GAF ^a (sd)	62.2(8.0)	62.3(8.0)	62.4(8.8)	63.2(6.3)	59.8(6.2)	61.1(5.7)	59.9(6.8)	61.7(6.3)	61.8(8.2)	60(0.0)			
Mean Completed Modules (sd)	6.9(3.1)	7.2(3.0)	6.8(3.1)	6.2(3.0)	5.1(3.4)	5.7(3.3)	6.5(3.6)	5.3(3.4)	5.8(3.1)	2.7(0.9)			
Depression	762(100)	508(66.7)	160(21.0)	24(3.1)	11(1.4)	14(1.8)	15(2.0)	10(1.3)	20(2.6)	0(0.0)			
Women (%)	505(66.3)	358(70.5)	104(65.0)	8(33.3)	1(9.1)	6(42.9)	11(73.3)	0(0.0)	16(80.0)	0(0.0)			
Mean age (sd)	38.4(12.1)	39.1(12.0)	37.2(12.1)	36.4(13.1)	38.2(9.6)	44.1(13.8)	37.1(11.1)	32.2(11.8)	31.6(8.4)	-			
Mean Initial GAF ^a (sd)	62.7(7.1)	62.6(7.2)	63.8(6.8)	65.0(6.0)	56.9(5.9)	61.6(6.2)	59.6(6.8)	62.8(8.8)	62.9(7.4)	-			
Mean Completed Modules (sd)	7.1(3.1)	7.3(3.1)	7.2(3.2)	6.8(2.6)	6.4(3.4)	6.8(3.6)	6.5(3.3)	4.7(3.7)	6.3(3.0)	-			
Panic Disorder	475(100)	339(71.4)	80(16.8)	8(1.7)	5(1.1)	18(3.8)	11(2.3)	10(2.1)	4(0.8)	0(0.0)			
Women (%)	299(62.9)	221(65.2)	54(67.5)	4(50.0)	0(0.0)	4(22.2)	11(100.0)	0(0.0)	4(100.0)	0(0.0)			
Mean age (sd)	34.8(10.6)	35.6(10.1)	32.7(11.2)	31.8(12.3)	30.0(12.1)	34.9(13.3)	34.3(12.4)	31.7(11.8)	28.3(6.4)	-			
Mean Initial GAF ^a (sd)	60.7(9.5)	61.1(9.3)	58.7(12.2)	60.4(7.4)	61.3(1.5)	60.2(6.7)	58.8(5.5)	61.2(5.2)	66.0(12.2)	-			
Mean Completed modules (sd)	7.1(2.9)	7.4(2.8)	6.8(2.9)	5.8(3.9)	4.0(3.7)	6.3(3.0)	6.6(3.9)	6.5(3.3)	5.3(3.7)	-			
Social Anxiety disorder	344(100)	222(64.5)	81(23.5)	8(2.3)	4(1.2)	12(3.5)	2(0.6)	3(0.9)	10(2.9)	2(0.6)			
Women (%)	194(56.4)	130(58.6)	49(60.5)	4(50.0)	1(25.0)	1(8.3)	2(100.0)	0(0.0)	7(70.0)	0(0.0)			
Mean age (sd)	32.7(10.8)	34.3(11.8)	31.4(8.8)	27.6(3.2)	35.5(7.1)	26.0(6.2)	32.5(12.0)	24.7(3.2)	24.6(4.5)	24.0(2.8)			
Mean Initial GAF ^a (sd)	63.1(7.4)	63.3(7.5)	63.2(7.6)	61.0(4.4)	66.3(5.1)	61.7(3.4)	75.0(-)	60.0(0.0)	58.3(8.0)	60.0(0.0)			
Mean Completed Modules (sd) ^b	6.2(3.1)	6.6(3.0)	6.1(3.0)	5.0(3.4)	2.9(1.3)	3.4(2.1)	5.4(6.5)	3.4(1.4)	5.0(3.1)	2.7(0.9)			

^aFor the total population, GAF values are based on n = 1327; for Depression, n = 634, for Panic disorder, n = 403, and for Social anxiety disorder n = 290.

^bThe number of modules completed for patients in social anxiety disorder treatment was rescaled from 12 or 15 treatment modules to a range of 0–10 modules for comparison purposes within the social anxiety disorder group, as well as between diagnostic groups. Ten treatment modules were offered to all patients treated for depression and panic disorder.
doi:10.1371/journal.pone.0104615.t001

Number of treatment modules completed

The number of treatment modules completed was analyzed by gender, age and diagnostic category across mutually exclusive categories of substance use: non-problematic use, problematic alcohol use, problematic drug use and combined drug and problematic alcohol use. See Table 2.

Tukey-Kramer post-hoc tests showed that men with problematic drug use completed, on average, 1.4 fewer treatment modules than men without problematic substance use ($p = 0.049$). Among women, only those with combined problematic drug and alcohol use completed significantly fewer treatment modules (1.6 fewer modules) compared to patients without problematic substance use ($p = 0.018$).

Among 25 to 34-year-olds, those with problematic drug use completed an average of 1.94 fewer treatment modules than those without problematic substance use ($p = 0.008$). In the group of 35 to 64-year-olds, those with combined problematic alcohol and drug use completed, on average, 2.08 fewer modules than those without problematic substance use ($p = 0.036$).

In the group treated for social anxiety disorder, an average of 2.96 fewer treatment modules were completed by patients with problematic drug use ($p = 0.002$), as well as 2.30 fewer treatment modules among those with combined problematic alcohol and drug use ($p = 0.023$), compared to patients without problematic substance use. In the group treated for panic disorder, which showed significantly fewer completed treatment modules for problematic substance users overall, the post-hoc tests did not show any significant differences.

Therapy outcomes

A general overview of therapy outcomes for the total population by diagnostic category across mutually exclusive substance use categories is shown in Table 3. Within-group effect sizes (Cohen's d) show effects over time for each problematic use category, and B -values based on ANCOVA analyses, controlled for MADRS-S, PDSS-SR and LSAS-SR baseline values, show mean differences in therapy outcome between problematic users in different categories, compared to non-users who serve as the reference category throughout.

Overall within-group effect sizes for MADRS-S were high. While effect sizes were generally high for patients treated for depression, they were nominally lower among those who had concurrent harmful drug use as well as hazardous drug use combined with problematic alcohol use. In contrast, higher within-group effect sizes occurred among hazardous alcohol users as well as hazardous drug users who were treated for depression. Among patients treated for panic disorder, effect sizes according to the PDSS-SR ranged between fair and very high. Patients with harmful alcohol use and those with probable dependence on alcohol showed lower effect sizes. Again in contrast, higher effect sizes were identified in the panic disorder group for harmful drug users and those combining harmful drug use with problematic alcohol use. Effect sizes for patients treated for social anxiety disorder ranged from below zero to very high on the LSAS-SR, where patients with harmful alcohol use and hazardous drug use had lower effect sizes and the two patients who showed probable drug dependence in combination with problematic alcohol use had negative effect sizes. In the social anxiety disorder group, higher effect sizes were found for those with either probable dependence on alcohol or combined hazardous drug use with problematic alcohol use.

The ANCOVA analyses showed that individuals with harmful drug use combined with problematic alcohol use negatively affected overall depression outcomes in the entire study popula-

tion, with an average of 3.5 points post-treatment higher scores on the MADRS-S (not shown). However, among patients treated for depression, substance use did not affect improvement in depressive symptoms. In contrast, panic disorder patients with hazardous use of alcohol (1.29 points higher on the PDSS-SR) or probable dependence (5.29 points higher on the PDSS-SR) and social anxiety disorder patients with hazardous drug use (18 points higher on the LSAS-SR and 5.03 points higher on the MADRS-S) had worse therapy outcomes than non-using patients within their respective diagnostic categories. The two individuals with probable dependence on drugs combined with problematic alcohol use in the social anxiety disorder groups differed highly significantly from the non-users in the same diagnostic category.

Effects of problematic use on therapy outcomes, controlling for gender, age, baseline GAF and screening scores and number of completed modules

Separate ANCOVA analyses were conducted with therapy outcome as the dependent variable, controlling for age, gender, initial GAF score, baseline MADRS-S score, problematic use, treatment group and number of modules completed. Due to missing data on GAF, the number of individuals in the sample was 1316.

For the group treated for depression, problematic alcohol and drug use did not affect MADRS-S outcomes. However, GAF ($B = -0.14$, $p = 0.003$), baseline MADRS-S scores ($B = 0.42$, $p < 0.001$) and number of completed modules ($B = -1.14$, $p < 0.001$) significantly affected MADRS-S outcomes in the depression group. For the group treated for panic disorder, controlling for PDSS-SR baseline values and analyzing PDSS-SR outcomes, GAF ($B = -0.08$, $p = 0.001$), baseline PDSS-SR scores ($B = 0.32$, $p < 0.001$) and number of completed modules ($B = -0.59$, $p < 0.001$) significantly affected outcomes, and individuals with problematic alcohol use ($B = 1.55$, $p = 0.008$) had worse outcomes than those without problematic substance use. An in-depth analysis of the substance use subcategories in the panic disorder group showed that patients with exclusive hazardous alcohol use ($B = 1.29$, $p = 0.035$) and patients with exclusive probable alcohol dependence ($B = 6.35$, $p = 0.005$) had worse outcomes on PDSS-SR than patients without problematic substance use. For the social anxiety disorder group, GAF ($B = -0.36$, $p = 0.046$), baseline LSAS-SR scores ($B = 0.67$, $p < 0.001$) and the number of modules completed ($B = -1.48$, $p < 0.001$) affected outcomes and individuals with problematic drug use had significantly worse outcomes than patients in this group without problematic substance use ($B = 12.431$, $p = 0.053$). An in-depth analysis of the substance use subcategories in the social anxiety disorder group showed that patients with exclusive hazardous drug use ($B = 13.70$, $p = 0.039$), patients with combined problematic alcohol use and hazardous drug use ($B = -47.62$, $p < 0.001$) as well as patients with combined problematic alcohol use and probable drug dependence ($B = 35.80$, $p = 0.008$) had worse outcomes on LSAS-SR than patients without problematic substance use.

Discussion

Generally, according to GAF scores, patients in this study consisted of fairly highly functioning individuals, regardless of substance use severity. The overall prevalence of problematic substance use in the patient population was 32%, with 28% problematic alcohol use and 8% problematic drug use, levels higher than in previous studies of patients in psychiatry [3,4] as well as the general population [5]. A larger proportion of patients overall were women, but we found more men in the categories of

Table 2. Number of completed treatment modules^a by gender, age, diagnosis and problematic substance use category.

	Non-problematic users (n = 1069)		Problematic alcohol users (n = 381)		Problematic drug users (n = 72)		Combined problematic alcohol and drug users (n = 59)		F	df	P
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)					
Gender											
Men (n = 583)	6.6(3.2)	6.2(3.1)	6.2(3.1)	5.2(3.1)	5.2(3.3)	4.1	3,579	0.007			
Women (n = 998)	7.4(2.9)	7.0(3.1)	6.7(3.6)	6.7(3.6)	5.8(3.1)	4.1	3,994	0.007			
Age											
18–24 (n = 228)	6.2(3.2)	6.1(3.2)	4.2(3.0)	4.2(3.0)	5.4(3.4)	1.9	3,224	0.129			
25–34 (n = 599)	7.1(3.1)	6.7(3.0)	5.1(3.2)	5.1(3.2)	5.6(3.2)	4.9	3,595	0.002			
35–64 (n = 720)	7.5(2.9)	6.9(3.2)	7.6(3.1)	7.6(3.1)	5.4(3.2)	3.8	3,716	0.010			
65+ (n = 34)	7.9(2.9)	7.3(3.3)	6.0(–)	6.0(–)	–(–)	0.3	2,31	0.774			
Diagnosis											
Depression (n = 762)	7.3(3.1)	7.1(3.1)	6.6(3.4)	6.6(3.4)	5.8(3.3)	2.5	3,758	0.057			
Panic disorder (n = 475)	7.4(2.8)	6.6(3.0)	6.4(3.3)	6.4(3.3)	6.1(3.3)	2.9	3,471	0.034			
Social anxiety disorder (n = 344)	6.6(3.0)	5.9(3.0)	3.7(2.7)	3.7(2.7)	4.3(2.7)	7.1	3,340	<0.001			

a. Ten treatment modules were offered to all patients treated for depression and panic disorder. The number of modules completed for patients in social anxiety disorder treatment was rescaled from 12 or 15 treatment modules to a range of 0–10 modules for comparison purposes within the social anxiety disorder group and between diagnostic groups.
doi:10.1371/journal.pone.0104615.t002

Table 3. Therapy outcomes among ICBT patients by treatment group and problematic substance use categories.

	No Problematic Use	Alcohol Use Categories			Drug Use Categories			Drug Use Categories and Problematic Alcohol Use		
		Hazardous	Harmful	Probable Dependence	Hazardous	Harmful	Probable Dependence	Hazardous	Harmful	Probable Dependence
Depression n=762	508	160	24	11	14	15	0	10	20	0
MADRS-pre, mean (SD)	24.2(6.5)	25.5(6.6)	25.8(6.9)	29.9(6.9)	25.8(5.5)	25.5(5.9)	-	26.3(5.1)	25.5(5.8)	-
MADRS-post, mean (SD)	13.8(9.0)	14.2(9.2)	16.0(9.1)	18.4(10.5)	15.6(8.7)	17.3(10.7)	-	18.7(10.8)	18.0(8.6)	-
Within-groups effect size, <i>d</i>	1.33	1.42	1.24	1.36	1.45	0.98	-	0.95	1.05	-
B ^a	-0.22	1.39	1.66	1.66	0.98	2.86	-	3.84	3.52	-
<i>p</i> -value	0.779	0.435	0.524	0.524	0.675	0.201	-	0.159	0.071	-
Panic Disorder n=475	339	80	8	5	18	11	0	10	4	0
PDSS-pre, mean (SD)	12.0(5.5)	12.4(5.3)	9.1(3.8)	16.2(3.4)	12.5(5.8)	14.0(6.2)	-	12.3(5.8)	11.0(3.5)	-
PDSS-post, mean (SD)	5.6(5.1)	7.0(6.0)	7.3(3.0)	12.4(7.1)	6.3(5.1)	6.0(5.7)	-	6.4(4.2)	5.0(0.0)	-
Within-groups effect size, <i>d</i>	1.21	0.96	0.56	0.76	1.17	1.41	-	1.24	2.80	-
B ^a	1.29	2.73	5.29	5.29	0.58	-0.30	-	0.97	-0.21	-
<i>p</i> -value	0.034	0.121	0.017	0.017	0.626	0.840	-	0.557	0.942	-
Social Anxiety Disorder n=344	222	81	8	4	12	2	0	3	10	2
LSAS-pre, mean (SD)	75.9(25.5)	70.0(21.6)	76.9(22.0)	81.0(17.6)	78.7(25.0)	49.0(7.1)	-	84.0(31.2)	82.4(24.1)	91.5(14.9)
LSAS-post, mean (SD)	57.7(27.2)	54.9(24.5)	71.9(29.5)	55.3(34.7)	77.8(22.5)	41.5(17.7)	-	42.0(21.6)	63.0(23.6)	111.0(12.7)
Within-groups effect size, <i>d</i>	0.69	0.66	0.21	1.08	0.04	0.79	-	1.92	0.86	-1.99
B ^a	1.52	13.44	-6.21	-6.21	18.00	3.51	-	-21.66	0.51	41.84
<i>p</i> -value	0.550	0.056	0.527	0.527	0.002	0.800	-	0.056	0.935	0.003

a. B-values describe mean differences in specific outcomes between groups based on ANCOVA analyses, where patients with no problematic substance use serve as the reference category. doi:10.1371/journal.pone.0104615.t003

more severe alcohol use and hazardous drug use. Our finding that severe alcohol use was more prevalent among men than among women is consistent with earlier studies [5,45]. The total prevalence of problematic substance use by diagnostic group was lowest among patients treated for panic disorder (29%), followed by depression (33.4%) and social anxiety disorder (35.5%).

Treatment outcomes for the total population in terms of depression ratings were good, with large effect sizes (Cohen's d 0.81 to 1.09) regardless of problematic use. This implies that concurrent problematic substance use is not an obstacle to obtaining good effects from ICBT treatment, with a clear exception in the two individuals in the social anxiety disorder group who had combined problematic alcohol use and probable drug dependence. In terms of specific diagnoses, treatment outcomes for depression were not affected by problematic substance use. However, among patients treated for panic disorder, hazardous drug use (80 individuals) and probable alcohol dependence (5 individuals) did negatively affect specific outcomes. For social anxiety disorder, the 12 individuals with hazardous drug use and the two with probable drug dependence combined with problematic alcohol use had worse specific treatment outcomes. It is worth noting that some substance use categories in each treatment group seemed to fare better in terms of within-group effect sizes than non-problematic users. In the social anxiety disorder group, those with probable alcohol dependence and hazardous drug use combined with problematic alcohol use did better than the non-problematic users. These particular findings would be in conflict with the theoretical view that alcohol and drug use function as safety behaviors for persons dealing with social anxiety, serving to protect the individual from dreaded exposure to anxiety. Not experiencing the feared situation in a sober state could hinder patients from disconfirming erroneous beliefs about the consequences of anxiety in social situations, therefore hampering therapeutic progress [46].

In the depression group, better effect sizes occurred for hazardous alcohol *or* hazardous drug users, but not for those with combined use. Finally, in the panic disorder group patients with probable dependence on alcohol or combined hazardous drug use with problematic alcohol use did better in therapy than non-problematic users. The cause of the improved therapeutic outcomes in these groups is not clear from our data, and further investigation into when substance use and therapy have a synergistic effect, and the possible mechanisms behind this could be warranted. What is clear is that these results are well in line with the argument that ICBT seems to have good results in presence of problematic substance use for these groups.

Problematic substance use negatively affected the number of completed treatment modules to a certain extent, with some gender and age effects. Problematic substance use seems not to have affected the number of modules completed in patients under 25 years of age. Among those older, there were effects of either problematic drug use alone (25–34 years) or the combination of problematic alcohol and drug use (35–64 years). Interpreting data on the number of completed treatment modules presents some challenges. In the ICBT unit's experience, completing more treatment modules is associated with better outcomes, but an exact defining point regarding the need for individuals to complete a certain number of modules is elusive: some patients benefit the most early on and subsequently lessen their activity in the program without prejudicing good outcomes. Thus there is great variability between individuals regarding the effects of quitting treatment early on therapy outcomes. Nonetheless, the significant overall association between number of modules completed and positive

outcome justifies the ambition of ensuring a high rate of completed modules among patients.

Strengths and limitations

To our knowledge this is the first study of substance use in a population receiving psychotherapeutic treatment over the Internet in regular care. Major strengths of this study are that the data were collected in a non-experimental naturalistic clinical setting, and the sizes of the treatment groups studied were large with nearly complete data sets. These factors suggest high external validity for our findings. Also, the study used well validated measures of substance use and symptom severity.

At the same time, the retrospective design led to several limitations that should be noted. First, our analyses were limited to data that had already been collected at the clinic, thus omitting potentially vital data for this type of study. For instance, no data were collected on the types of drugs used by patients. We were thus unable to establish any connection between type of drug use and therapy outcomes. A substance that is of relevance to the study, but was not addressed in the substance use screening, is nicotine. There is a known connection between nicotine and psychiatric comorbidity [47], particularly affective disorders [48,49]. Nicotine use would therefore constitute a valuable observation in relation to patient outcomes. Second, the data did not include any information on simultaneous medication parallel to ICBT treatment, nor on access to other treatment providers. What we did know was that psychiatric medication needed to be stable for one month prior to beginning ICBT and that patients receiving concurrent psychotherapy were not eligible for ICBT. Simultaneous complementary (e.g., substance use) or alternative treatment access could significantly affect patient outcomes, and lack of this information could bias our conclusions. Third, no data were available on individuals who were referred for ICBT treatment but never began therapy.

An additional limitation is that clinical exclusion of patients with severe substance use may have affected population characteristics and led to results biased for better functioning patients with less severe substance use problems. At the same time, in this study we were limited to using self-reported data on substance use, and research has shown that self-report data may be subject to bias in form of underreporting actual use [50,51], so consumption levels may have been higher than we knew. Indeed, if the self-reported substance use in this study was underreported by the patients, this would lend further strength to the conclusion that ICBT is effective even at slightly higher levels of problematic use. Of course, this reasoning is only speculative. Nonetheless, some studies have shown that respondents report higher consumption of substances when filling out self-report instruments on a computer in comparison to paper questionnaires, so actual use may have been reported relatively correctly [52,53]. In any case, in the absence of corroborative measures of substance use, for example biological markers, we were not able to evaluate the validity of the level of substance use reported by patients. A further limitation concerned the classification of patients in categories of mutually exclusive types of substance use, which in some cases led to very small groups. It is unclear whether these would be representative of future patient populations, even if the our patients did constitute the entire population of patients at the ICBT unit during the time period studied. A final limitation is the fact that the substance use categories defined were based on baseline measures, since the naturalistic study design did not include follow-up measures of substance use. This makes it impossible to know whether changes in initial substance use categories occurred during treatment and how this in turn might have affected treatment outcome.

Future research

Future research should use a prospective design, where important data that were missing in this study could be included. Information on types of substances and concurrent medication used by the participating parties would make for analyses providing more information on the actual effects on therapy and also a more detailed prevalence description. A more in-depth study of substance use and therapy progress during the actual treatment period could investigate why certain user categories seem to do better in therapy than their non-problematic counterparts. Data on reasons for exclusion gathered by admitting psychiatrists would further add knowledge about the patient group studied and add information on generalizability to a psychiatric population.

Conclusion

The results indicate that problematic substance use generally does not affect the outcome of ICBT. In most cases, problematic substance use had no discernible detrimental effect on outcomes, suggesting no obstacle to providing individuals with ICBT based on problematic substance use. It should be noted, however, that

particular subgroups of individuals in specific categories of substance use did differ in outcome from their counterparts without problematic substance use. At the same time, increased severity of substance use neither worsened nor improved outcomes; neither did it reduce the number of treatment modules completed in any linear correlation. This made it difficult to evaluate the exact effects of substance use on outcomes and treatment completion.

Notwithstanding the above, we conclude that the worse outcomes and fewer treatment modules completed among men and younger adult patients (25–34 years old) with problematic drug use, as well as women and older patients (35–64 years old) with combined problematic drug and alcohol use, do give cause for further attention to these groups. These individuals' substance use might need to be addressed concurrently with treatment for their primary psychiatric diagnosis.

Author Contributions

Conceived and designed the experiments: AHB MG BL NL CR. Analyzed the data: MG KS CA AHB. Contributed reagents/materials/analysis tools: BL CR NL. Wrote the paper: MG AHB KS CA BL EH CR NL.

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