

## Chapter 4

### **Effectiveness of a web-based guided self-help intervention in treating subthreshold depression**

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# **Abstract**

## **Background**

Research on the effectiveness of treatments for sub-threshold depression (sD) is still scarce. The aim was to evaluate the efficacy of a web-based guided self-help intervention (i.e. GET.ON Mood Enhancer) in the treatment of sD.

## **Methods**

Participants with sD (N = 406) recruited from the general population via i.e. a large health insurance company were randomly allocated to a web-based cognitive behavioural intervention or to enhanced care-as-usual. The primary outcome was the reduction in depressive symptom severity as measured with the Center for Epidemiologic Studies Depression Scale at post-treatment and 6-month follow-up.

## **Results**

Participants in the intervention group showed a significantly greater pre-post reduction in depressive symptom severity ( $d = 1.06$ ; 95% CI 0.86 - 1.27) as compared to the control condition ( $d = 0.29$ ; 95% CI 0.10 - 0.49). The corresponding between-group effect size was  $d = 0.69$  (95% CI 0.49 - 0.89). At 6-month follow-up the effect was reduced to  $d=0.28$  (95% CI 0.09 - 0.48) but was still statistically significant [ $F(1, 403) = 9.240$ ;  $p = .003$ ].

## **Conclusions**

This study lends support to the idea that problem-solving coupled with behavioural activation is an effective treatment for sD. In addition, the delivery of this intervention over the Internet might be a promising strategy for the dissemination of psychological interventions for sD on a large scale.

## Background

Sub-threshold depression (sD) is commonly defined by the existence of significant symptoms of depression that fail to meet criteria for a full-blown depressive disorder by a small margin (1). sD is a highly prevalent condition (2), associated with increased mortality (3), poorer quality of life (4), increased use of health care services (5), and with substantial economic costs (6). Additionally, sD has been identified as a significant predictor of major depression (7).

However, in contrast to MDD, there are only a few studies on the efficacy of treatments for sD. Studies indicate that antidepressants and benzodiazepines are unlikely to have a clinical advantage over placebos in treating sD (8). A recent meta-analysis showed small to moderate effect sizes of psychological interventions on depressive symptom severity at post-treatment compared to care-as-usual ( $g = 0.35$ , 95% CI 0.23 - 0.47) (1). However, studies conducted in this field vary in methodological quality owing to not using intention-to-treat analyses or selective outcome reporting. Moreover, most of the studies were based on comparatively small and likely underpowered samples.

Besides, psychological face-to-face interventions have some limitations (i.e., limited manpower and health care resources to deliver such interventions to the community en masse (9, 10) or low participation rates (11)). Using the Internet to offer psychological interventions may help to overcome some of the limitations of traditional services. Web-based interventions are less resource-intensive and could reduce travel time and costs for participants (12, 13). In addition, web-based interventions have shown to be feasible (14) and as low-threshold services, such interventions may serve as initial interventions in stepped care models (15).

While there is ample evidence available that web-based interventions are effective in treating depressive disorders (16, 17) and enhancing long-term outcome of inpatient psychotherapy (18), research into their effectiveness in sD is still scarce. To the best of our knowledge, only one study has evaluated the potential of a web-based intervention to reduce depressive symptom severity in a clearly defined subclinical sample (19). However, this study was directed at elderly people only. Thus, the aim of the present study was to further clarify the effectiveness of psychological interventions for sD by evaluating the effectiveness of a newly developed web-based guided self-help intervention in a large scale randomised controlled trial.

## Methods

### Study population and recruitment

Participants were recruited from March 2013 to March 2014 from the general population via a large German health insurance company, through newspaper articles, on-air media, and related

websites. Participants did not need to be referred by their GP or other mental health care specialist. This open recruitment strategy was chosen as it mimics the (future) clinical practice thus enhancing the study's ecological validity. After all, it is very likely that we attracted the population in this study that will be attracted for web-based interventions in the future. Individuals interested in participation could apply online on the research website by providing the research team with their e-mail address or by sending directly an e-mail to the research team.

Applicants were asked to complete an online screening questionnaire to assess whether they (a) suffered from sD (Centre for Epidemiologic Studies Depression Scale (CES-D)  $\geq 16$ ) (7), (b) were aged 18 and above, (c) had Internet access, (d) were not currently receiving psychotherapy for any kind of mental health problem, (e) were not on a waiting list for psychotherapy, (f) had not received psychotherapy for any kind of mental health disorder in the past six months, and (g) did not show a notable suicidal risk (BDI item 9  $> 1$ ).

Potentially eligible participants were scheduled for a semi-structured clinical interview (SCID) conducted by telephone by trainees in psychotherapy to assess final eligibility. Participants were eligible if they met the following criteria: not meeting DSM-IV criteria for (a) a major depressive episode, (b) bipolar disorder, (c) psychotic disorder, and (d) not having a history of a major depressive disorder in the past six months (based on Kupfer (20)). To maximise the external validity of the findings, there were no further exclusion criteria. Full details of the study have been described in the study protocol (21).

## **Procedure**

Participants who provided informed consent and completed the baseline assessment were randomly assigned to either the intervention or control condition. Randomisation took place at an individual level and was conducted centrally by an independent researcher not otherwise involved in the study using an automated computer-generated random numbers table. Block randomisation, of size two, was used to ensure similar sample sizes across conditions. Participants received an e-mail alert referring to the follow-up assessments six weeks and six months after randomisation. Participants received an incentive of €10 for completing the follow-up assessment. All procedures involved in the study were consistent with generally accepted standards of ethical practice (22) and were approved by the Ethics Committee of the University of Marburg (No. 2012-35K). The trial was registered at the German Clinical Trial Registry DRKS00004709.

## **Interventions**

All study participants had unrestricted access to care-as-usual (CAU) in routine care. In the German health care system, psychological interventions (i.e. CBT-based psychotherapy) are not provided to people suffering from sD. CAU for sD mainly includes visits to the GP and the GP might inform the patient about the nature of depressive complaints and treatment options if depressive symptoms deteriorate. If symptoms worsen, CAU will be offered in accordance with the German S3-Guideline/National Disease Management Guideline Unipolar Depression for treating major depressive disorder (23). These guidelines involve basic interventions (i.e. psycho-education) stepped up to more intensive interventions (i.e. psychotherapy, prescription of medication) when required. CAU is likely to be heterogeneous but that is a reflection of clinical practice. In our pragmatic trial, we did neither interfere nor protocolised CAU, but took it as it was. However, health care consumption was measured in the context of an economic evaluation meaning that all types of medical help received were monitored so that an accurate description of CAU can be produced (21).

### **Web-based cognitive behavioural intervention**

The web-based intervention consists of six 30-minute interactive sessions. However, the duration of sessions might vary among users. Sessions include text, exercises, testimonials, and interactive elements such as audio and video clips. Audio sequences introduce relaxation exercises, whereas video clips are used to explain theoretical frameworks in a user-friendly way. Participants were advised to do two sessions a week if possible but at least a minimum of one. Consequently, it took participants 3 to 6 weeks to complete the training.

The intervention is based on behaviour therapy (BT) and problem-solving therapy (PST). The content of the training has been described in detail elsewhere (21). A strong emphasis was placed on homework assignments in order to integrate the newly acquired coping strategies into daily life. As an optional component, participants could choose to receive a set of about 42 standardised text-messages supporting them in integrating the learned techniques into their everyday life. During the training, participants were supported by an online trainer, who provided written feedback after each session. The online trainer and participants communicated with each other through the internal messaging function of the intervention. The total time a trainer spent per participant was approximately two hours. Trained and supervised graduate students and health care professionals provided guidance.

### **Control condition**

Participants in the control condition got access to a web-based psycho-educational intervention. Psycho-educational interventions have been shown to be effective in reducing depressive

symptoms and might serve as initial interventions in primary care (24). In the current study, the psycho-educational intervention was based on the German S3-Guideline/National Disease Management Guideline for Unipolar Depression (23). It informed participants about the nature and evidence-based treatments of depression including information about symptoms and sources of help. By offering the web-based psycho-educational intervention, we thus mimicked and enhanced usual care as we systematically offered information that patients might not always receive from their GP. Participants could go through the material as often as they wanted to. However, we did not monitor the uptake of the intervention. In this study, the psycho-educational intervention neither required participants to do homework assignments nor was any support by an online-trainer offered to participants.

## **Outcomes**

All measures were based on self-report and were collected using a secured online-based assessment system (AES, 256-bit encrypted). The SCID interviews to assess final eligibility before entering the study were conducted by telephone.

### **Primary outcome**

#### ***Depressive symptom severity***

The primary outcome is the difference between the groups in the pre-post change in depressive symptom severity. Depressive symptoms were assessed with the German version of the Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is a self-reporting scale consisting of 20 items, each scored 0 - 3. The total score ranges from 0-60, with a higher score indicating more severe depressive symptoms. The CES-D is a widely used instrument in comparable studies (25-29). The reliability of the CES-D has been shown to be good (30). Cronbach's  $\alpha$  in the present study was .73.

### **Secondary outcomes**

#### ***Functional impairment***

Functional impairment was assessed with the SF-12v1 Health Survey (31). The SF-12v1 has 12 items covering eight health aspects (physical functioning, role functioning (physical and emotional), bodily pain, general health, vitality, social functioning, and mental health). The SF-12 generates summary scores for physical and mental health.

#### ***Anxiety***

Anxiety was measured with the German version of the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A) (32, 33). The anxiety subscale consists of seven questions and each is scored from 0 - 3 such that the total score ranges from 0 - 21 where a score between 0-

7 indicates no anxiety, between 8 and 10 possible anxiety, and above 11 or 12 a clinical anxiety disorder. Psychometric properties are well-established with Cronbach's  $\alpha$  ranging from .63 to .93 (34) and being .77 in the present study.

### ***Problem-solving skills***

Problem-solving ability was measured with two subscales of the Social Problem-Solving Inventory-Revised (SPSI-R) (35). The positive problem orientation (PPO) subscale represents a constructive dimension whereas the negative problem orientation (NPO) subscale is viewed as a dysfunctional dimension. Both subscales have displayed strong validity and reliability in former studies (35). In this study, Cronbach's alpha for the NPO subscale was .88 whereas the alpha for the PPO subscale was .78.

### ***Behavioural activation***

Participants' increase in engaging in pleasant activities and their reduction of avoidance behaviours was measured with the BADS-Short Form (BADS-SF) (36). The BADS-SF entails 9 items comprising two subscales (activation and avoidance). The items are rated on a 7-point Likert-type scale. Higher scores indicate that the individual scores high on the area of interest. The BADS-SF has good psychometric properties (36). In this study, Cronbach's  $\alpha$  was .78.

### ***Mastery (internal locus of control)***

Internal locus of control was measured with the Pearlin Mastery Scale (37). The Pearlin Mastery Scale consists of 7 items and each is rated on a 4-point Likert scale. The higher the score, the higher is the individual's sense of control over situations (internal mastery). A lower score indicates that the individual has the feeling that events are out of his or her control. The psychometric properties of this scale are well established (37). In this study, the alpha was .80.

### ***Worrying***

Worrying was assessed with the ultra-brief version of the Penn State Worry Questionnaire (PSWQ) (38). The ultra-brief version consists of 3 items arising from the standard version, with each item being rated on a 7-point scale. The total score ranges from 0 - 18 with higher scores indicating more worry. The ultra-brief version shows similar psychometric properties compared to the standard version (Cronbach's  $\alpha$  = .85). In this study, the alpha was .87.

### ***Insomnia severity***

Insomnia severity was assessed with the Insomnia Severity Index (ISI) (39). The ISI measures the nature, severity, and impact of insomnia. It consists of 7 items; each is rated on a 5-point Likert scale resulting in a total score ranging from 0 to 28. Higher scores indicate more severe

insomnia. The ISI is a valid and reliable instrument for detecting cases of insomnia in a population-based sample (40). In this study, we found a Cronbach's  $\alpha$  of .89.

### ***Treatment credibility/patient expectancy***

The intervention's credibility and participants' expectations about improvement were measured with the credibility and expectancy questionnaire (CEQ). The CEQ consists of six items, which are rated on a 9- or 10-point Likert scale. The psychometric properties of the instrument are well-established (41). In our study, the alpha was .70.

### ***Users' satisfaction with the intervention***

User satisfaction was measured with a self-designed questionnaire that is based on the Satisfaction with Psychotherapy Questionnaire (ZUF-8) (42), the German version of the Client Satisfaction Questionnaire (CSQ-8) (43). This self-reporting measure consists of 8 items, which are rated on a 4-point Likert scale measuring overall client satisfaction with the web-based training. Previous research indicated a high internal consistency (Cronbach's  $\alpha$  = .91) (44). In this study, the alpha was .94.

### **Sample size**

With  $N = 203$  per condition, the study had a power of 0.90 to detect a standardised effect size of 0.33 (or larger) in a test with  $\alpha = 0.05$  (2-sided). Accordingly,  $d > 0.33$  would correspond with the lower bound of a medium effect size according to the conventions proposed by Cohen (45).

### **Data analyses**

All analyses are reported according to the CONSORT statement (46). Analyses were based on the intention-to-treat (ITT) principle. Missing data were imputed using a Markov Chain Monte Carlo multivariate imputation algorithm (missing data module in SPSS 22) with 10 estimations per missing value. In addition, per protocol analyses were conducted based on the sample of participants who adequately adhered to the intervention protocol by completing at least five out of six intervention sessions.

We used analysis of covariance (ANCOVA) to compare outcomes between groups at post-treatment and at 6-month follow-up adjusting for baseline scores. We also included concurrent drug use as covariate into the model. As the use of antidepressants was not a predictor of the outcome, we excluded it from the final model. Results were reported as mean within- and between-group difference and as Cohen's  $d$  effect sizes (and their 95% CIs according to Hedges and Olkin (47)).

To assess improvements of the primary outcome (depressive symptom severity) at individual level, we examined the number of participants who displayed treatment response defined by a reliable change from baseline to post-treatment according to the reliable change index (RCI) of Jacobson and Truax (48). Participants were defined as reliably improved if their CES-D-score declined from baseline to post-treatment with a RCI greater than 1.96, while taking into account the reliability of the CES-D to compensate for measurement error (corresponding to a change of at least 7.06 points in the CES-D). In addition, we examined how many participants reached a close to symptom-free status at post-treatment and 6-month follow-up as indicated by a CES-D score < 16. We also calculated the number needed-to-treat (NNT) and 95% CIs accordingly to achieve one additional treatment response and close to symptom-free status, respectively (49). All analyses were performed with IBM SPSS v. 22. All reported p-values are two-sided with a significance level of 0.05.

## Results

### Participants

Figure 1 illustrates the flow of participants through the study. A total of 406 participants were enrolled in the study. At post-treatment, n = 366 participants completed the assessment (attrition rate 9.9%), n = 325 completed the 6-month follow-up (attrition rate 19.9%). There were no relevant baseline differences between participants completing the follow-up assessments and those who were lost-to-follow-up.

Participant characteristics at baseline are shown in Table 1. Participants were predominately female (73.9%), with an average age of 45 years (SD = 11.9), an above average level of education (A-level or higher: 81.5%), and employed (82.5%). At baseline, 44 participants (21.6%) in the control group and 50 participants (24.8%) in the intervention group used antidepressants. During the 6-month follow-up period, 40 participants (19.6%) in the control and 32 participants (15.8%) in the intervention group took antidepressants. Only 96 participants (23.6%) had participated in any kind of healthcare training (i.e. stress management training) prior to the study. Nearly half of participants had at some point in their lives received psychotherapy (n = 176; 43.3%). In the intervention group, only eight participants (4.0%) received professional help (i.e. cognitive behavioural psychotherapy) during follow-up whereas this was the case for 29 participants (14.2%) in the control group. There were no clinically important differences between treatment conditions in terms of any baseline characteristic indicating that randomisation was successful.

## Primary intervention outcome

Table 2 depicts means, standard deviations, and between-group effect sizes of the clinical outcomes at follow-up assessments based on the intention-to-treat sample. The intervention and control groups showed both statistically significant reductions in depressive symptom severity indicated by changes in baseline to post-treatment scores on the CES-D. In the intervention group, we found a mean reduction of 8.73 points on the CES-D [ $t(200) = 13.50, p < .001$ ] corresponding to a large within-group Cohen's  $d$  effect size ( $d = 1.06, 95\% \text{ CI } 0.86 - 1.27$ ). In the control condition, the mean reduction on the CES-D was 2.81 points [ $t(202) = 4.57, p < .001$ ] reflecting a small within-group effect size ( $d = 0.29, 95\% \text{ CI } 0.10 - 0.49$ ). There was a statistically significant between-group difference in CES-D scores at post-treatment in favour of the intervention group [ $F(1, 403) = 54.104, p < .001$ ]. This difference corresponded to a medium effect size of 0.69 (95% CI 0.49 - 0.89). Per protocol analyses revealed that intervention completers differed significantly from non-completers regarding CES-D scores at post-treatment [ $F(1, 199) = 5.944, p = .016$ ]. In the intervention completers group, we found a pre- to post improvement effect size of 1.14 (95% CI 0.89 - 1.38), which was 0.84 (95% CI 0.44 - 1.24) among non-completers. Between-group differences reflected a medium effect size of 0.41 (95% CI 0.09 - 0.73).

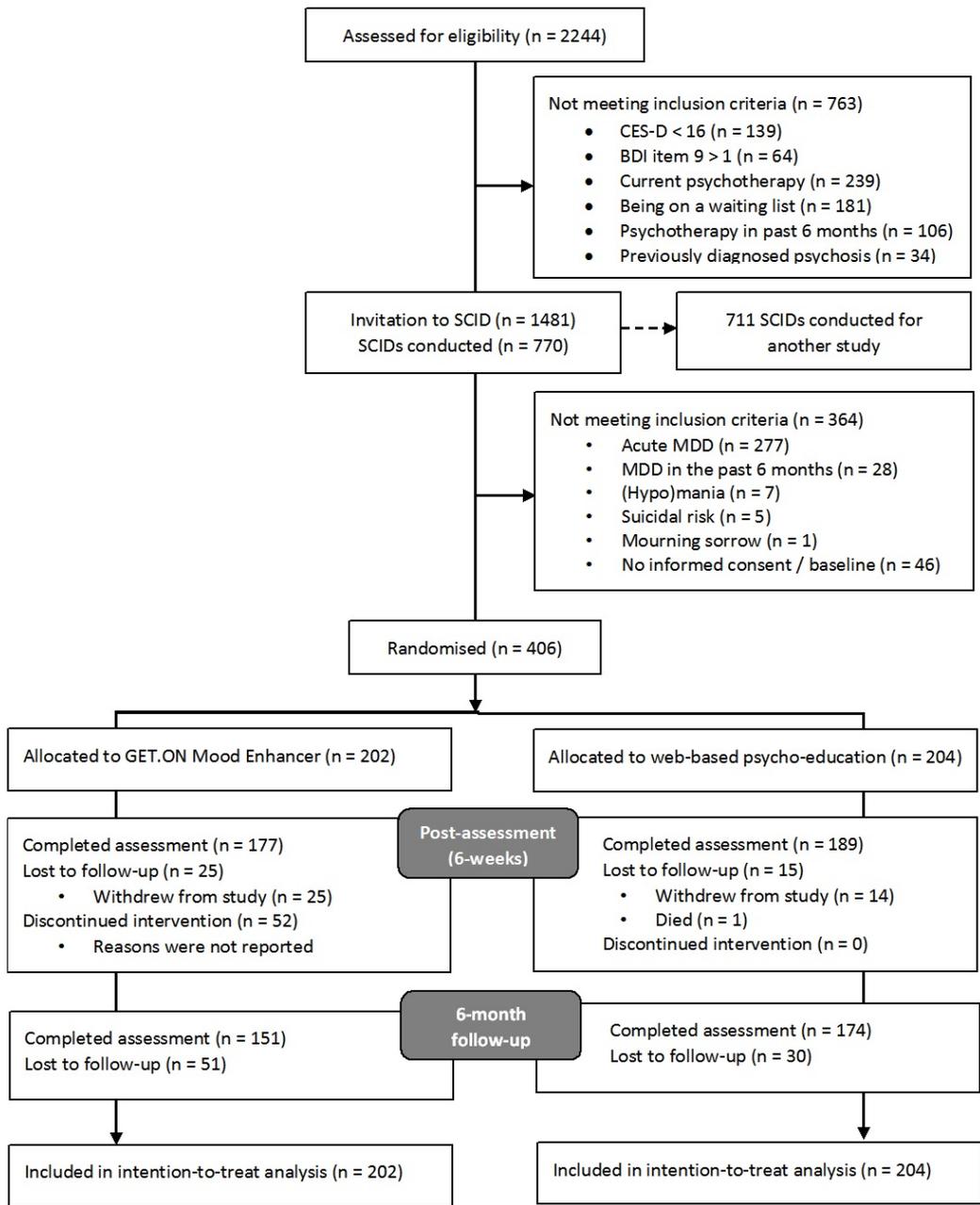


Figure 1. Study flow

**Table 1.** Baseline characteristics per study group

<b>Characteristic</b>	<b>Intervention group (n = 202)</b>	<b>Control group (n = 204)</b>	<b>Total sample (N = 406)</b>
<b>CES-D score, mean (SD)</b>	26.25 (7.85)	26.42 (7.99)	26.34 (7.91)
<b>Age, mean (SD)</b>	45.71 (11.93)	44.38 (11.84)	45.04 (11.89)
<b>Gender, n (%)</b>			
<b>Male</b>	53 (26)	53 (26)	106 (26.1)
<b>Female</b>	150 (74)	150 (74)	300 (73.9)
<b>Relationship, n (%)</b>			
<b>Single</b>	62 (30.7)	67 (32.8)	129 (31.8)
<b>Married/cohabiting</b>	102 (50)	107 (52.9)	209 (51.5)
<b>Divorced/separated</b>	37 (18.3)	25 (12.3)	62 (15.3)
<b>Widowed</b>	2 (1)	4 (2)	6 (1.5)
<b>Ethnicity, n (%)</b>			
<b>Caucasian</b>	165 (81.2)	174 (85.8)	339 (83.5)
<b>Afro-American</b>	1 (0.5)	0	1 (.2)
<b>Latin American</b>	0	1 (0.5)	1 (.2)
<b>Not reported</b>	37 (18.3)	28 (13.7)	65 (16)
<b>Level of education, n (%)</b>			
<b>Low</b>	7 (3.5)	8 (3.9)	15 (3.7)
<b>Middle</b>	54 (26.2)	57 (28.4)	111 (27.3)
<b>High</b>	142 (70.3)	138 (67.6)	280 (69)
<b>Employment status, n (%)</b>			
<b>Full time working</b>	105 (52)	106 (52)	211 (52)
<b>Part time working</b>	65 (32.2)	59 (28.9)	124 (30.5)
<b>Non-working</b>	26 (12.4)	28 (14.2)	54 (13.3)
<b>Unemployed/seeking work</b>	4 (2)	8 (3.9)	12 (3)
<b>On sick leave</b>	3 (1.5)	2 (1)	5 (1.2)
<b>Income in Euro, n (%)</b>			
<b>Low (&lt; 10.000)</b>	16 (7.9)	25 (12.3)	41 (10.1)
<b>Middle (10 - 60.000)</b>	145 (71.8)	149 (73)	294 (72.4)
<b>High (&gt; 60.000)</b>	26 (12.9)	12 (5.9)	38 (9.4)
<b>Not reported</b>	18 (8.8)	15 (7.4)	33 (8.1)
<b>Experience, n (%)</b>			
<b>Health training</b>	51 (25.2)	45 (22.1)	96 (23.6)
<b>Psychotherapy</b>	88 (43.6)	88 (42.2)	176 (43.4)

Abbreviations: CES-D, Center for Epidemiologic Depression Scale; SD, standard deviation

## Treatment response

A reliable change from baseline to post-treatment in depressive symptom severity was seen in significantly more participants in the intervention group (113/202 = 55.9%) as compared to the control condition [58/204 = 28.4%;  $\chi^2$  (1, n = 406) = 31.507,  $p < .001$ ]. This resulted in a NNT of 3.64 to achieve one additional treatment response as compared to the control group (95% CI 2.72 - 5.47). The likelihood of seeing a treatment response was twice as high in the intervention group as compared to the control condition (likelihood ratio (LR) = 1.97; 95% CI 1.53 - 2.53). Significantly less participants in the intervention group (n = 7/202; 3.5%) experienced a reliable deterioration in CES-D symptom severity (post-treatment CES-D > 7.06 above the baseline CES-D score) as compared to 21 participants in the control group [10.3%;  $\chi^2$  (1, n = 406) = 7.371,  $p = .007$ ].

## Close to symptom-free status

In the intervention group, significantly more participants achieved a close to symptom-free status (CES-D < 16) at post-treatment (n = 91/202; 45.0%) as compared to the control condition [n = 42/204; 20.6%;  $\chi^2$  (1, n = 406) = 27.571,  $p < .001$ ]. The NNT to achieve one additional close to symptom-free status as compared to the control group was 4.09 (95% CI 3.00 - 6.40).

## Secondary outcomes

There were significant between-group differences for all secondary outcomes favouring the intervention group. Corresponding effect sizes were small to moderate or even large ranging from  $d = 0.20$  (95% CI 0.001 - 0.39) for the positive problem orientation subscale of the SPSI to  $d = 0.75$  (95% CI 0.54 - 0.95) for behavioural activation (Table 2). Effects on the SF-12 physical health subscale and negative problem-orientation subscale of the SPSI were smaller than  $d = 0.20$  and non-significant.

## Longer-term effects

The reduction in depressive symptom severity found at post-treatment in the intervention group was sustained at 6-month follow-up [ $t(201) = -0.909$ ,  $p = .365$ ]. The control group showed a significant improvement in depressive symptom severity from post-treatment to 6-month follow-up [ $t(203) = 5.06$ ,  $p < .001$ ]. There was a statistically significant between-group difference in CES-D scores at 6-month follow-up favouring the intervention group [ $F(1, 403) = 9.240$ ,  $p = .003$ ]. This difference corresponded to a small effect size of 0.28 (95% CI 0.09 - 0.48). Significantly more participants in the intervention group still showed a treatment response (n = 108/202; 53.5%) and a close to symptom free-status (85/202 = 42.1%) at 6-month follow-up compared to the control condition (response: n = 89/204; 43.6%;  $\chi^2$  (1, n = 406) = 3.933,  $p =$

.047; symptom free-status:  $n = 65/204$ ; 31.9%;  $\chi^2 (1, n = 406) = 4.548, p = .033$ ; NNT = 9.79, 95% CI 5.11 - 114.07]. Less participants in the intervention group as compared to the control group experienced a symptom deterioration at 6-month follow-up, although this difference was not significant [ $n = 8/202$  vs.  $n = 16/204$ ;  $\chi^2 (1, n = 406) = 2.751, p = .097$ ].

In the intervention group, effects on all secondary outcomes remained stable at 6-month follow-up as compared to the post-assessment. Participants in the control condition showed improvements from post-assessment to 6-month follow-up on all secondary outcomes except for the physical health summary score of the SF-12. At 6-month follow-up, between-group differences favouring the intervention group were still significant for behavioural activation, anxiety symptoms, and the mental health summary score of the SF-12. Corresponding effect sizes were small to moderate (Table 2).

### **Adherence to and satisfaction with the intervention**

The average treatment duration was 5.84 weeks (SD = 4.37). Out of the 202 participants who were initially assigned to the intervention, 150 (74.3%) were intervention completers. Of those, 138 (92%) adhered to all six sessions. On average, participants completed 4.93 sessions. Of the 52 participants (25.7%) not completing 80% of the intervention, four participants never started the intervention (2%). Compared to completers, non-completers did not differ with regard to their baseline depressive symptom severity [ $t(199) = 0.79, p = .428$ ] or their expectancy for improvement [ $t(199) = 0.56, p = .575$ ].

The overall client satisfaction with the training was high (range: 0 - 28; mean = 26.27; SD = 5.32;  $n = 175$ ) with 88% ( $n = 154$ ) being satisfied overall with the intervention. The majority of participants perceived the training as being of high quality ( $n = 165$ ; 94.3%). Four fifths of participants said they received the kind of training they wanted to receive, perceived that their needs were met ( $n = 145$ ; 82.8%), were satisfied with the amount of help they got ( $n = 143$ ; 81.7%), and would use it again should the need arise ( $n = 146$ ; 83.4%). Almost 90% of participants reported that the training helped them to deal effectively with their problems ( $n = 151$ ; 86.3%). Of the participants, 90.3% ( $n = 158$ ) would recommend the intervention to a friend.

**Table 2.** Means, SD, and between-group effect sizes for each outcome measure and measurement based on the intention-to-treat sample (N = 406)

	n	Pre-assessment		Post-assessment		6-month FU		Between-group effect size Cohen's d (95% CI)	
		mean	SD	mean	SD	mean	SD	pre-post	pre-6-month FU
<b>CES-D</b>									
<b>INT</b>	202	26.26	7.85	17.52	8.69	17.86	8.36	0.69 (0.49 - 0.89)	0.28 (0.09 - 0.48)
<b>CTR</b>	204	26.42	8.0	23.61	9.74	20.34	9.15		
<b>SF-12 MCS</b>								0.57 (0.37 - 0.77)	0.48 (0.28 - 0.68)
<b>INT</b>	202	31.45	7.31	40.55	9.26	42.40	9.23		
<b>CTR</b>	204	30.77	7.83	35.16	9.68	37.94	9.43		
<b>SF-12 PCS</b>								0.13 (-0.06 - 0.33)	0.13 (-0.07 - 0.32)
<b>INT</b>	202	47.47	9.71	49.13	8.21	46.79	9.35		
<b>CTR</b>	204	47.83	9.13	48.04	8.09	47.91	8.57		
<b>HADS-A</b>								0.52 (0.32 - 0.72)	0.32 (0.12 - 0.52)
<b>INT</b>	202	9.59	3.27	7.01	3.33	7.10	3.30		
<b>CTR</b>	204	9.59	3.20	8.77	3.43	8.22	3.70		
<b>BADS-SF</b>								0.75 (0.54 - 0.95)	0.35 (0.15 - 0.54)
<b>INT</b>	202	25.45	7.80	33.83	8.12	33.46	7.75		
<b>CTR</b>	204	24.62	7.56	27.78	8.10	30.64	8.46		
<b>SPSI-NPO</b>								0.16 (-0.04 - 0.35)	0.09 (-0.10 - 0.29)
<b>INT</b>	202	7.00	4.47	5.93	4.20	5.54	3.98		
<b>CTR</b>	204	6.99	4.66	6.61	4.41	5.94	4.49		
<b>SPSI-PPO</b>								0.20 (0.001 - 0.39)	0.01 (-0.19 - 0.20)
<b>INT</b>	202	9.12	3.94	10.53	3.64	10.87	3.67		
<b>CTR</b>	204	9.18	3.64	9.84	3.47	10.84	3.66		
<b>PSWQ</b>								0.53 (0.33 - 0.73)	0.15 (-0.05 - 0.34)
<b>INT</b>	202	9.44	4.04	6.46	3.90	6.75	3.93		
<b>CTR</b>	204	9.76	3.91	8.62	4.23	7.31	3.79		
<b>ISI</b>								0.26 (0.07 - 0.46)	0.11 (-0.08 - 0.31)
<b>INT</b>	202	12.00	5.81	9.15	5.54	8.96	5.53		
<b>CTR</b>	204	11.70	5.92	10.64	5.82	9.56	5.17		

**Table 2.** Means, SD, and between-group effect sizes for each outcome measure and measurement based on the intention-to-treat sample (N = 406) (continued)

	n	Pre-assessment		Post-assessment		6-month FU		Between-group effect size Cohen's d (95% CI)	
		mean	SD	mean	SD	mean	SD	pre-post	pre-6-month FU
<b>PSMS</b>									
<b>INT</b>	202	19.11	3.45	20.45	3.53	20.59	3.32	0.29 (0.10 - 0.49)	0.12 (-0.08 - 0.31)
<b>CTR</b>	204	19.22	3.00	19.41	3.41	20.21	3.39		

Abbreviations: INT, intervention group; CTR, control group; SD, Standard deviation; FU, follow-up; CI, confidence interval; CES-D, Center for Epidemiologic Depression Scale; SF-12 MCS, SF-12 Health Survey Mental Health Composite Subscale; SF-12 PCS, SF-12 Health Survey Physical Health Composite Subscale; HADS-A, Hospital Anxiety and Depression Scale; BADS, Behavioural Activation for Depression Scale Short Form; SPSI-NPO, Social Problem-Solving Inventory - negative problem orientation; SPSI-PPO, Social Problem-Solving Inventory - positive problem orientation; PSWQ, Penn State Worrying Questionnaire (ultra brief version); ISI, insomnia Severity Index; PSMS, Pearlin Mastery Scale

## Discussion

We evaluated the effectiveness of a web-based cognitive behavioural intervention in a sample of adults suffering from sub-threshold depression (sD). The results indicated a greater reduction in depressive symptom severity in the intervention group as compared to the control group at post-treatment. Effects were sustained at 6-month follow-up. Almost 60% of participants in the intervention group exhibited a positive treatment response meaning that for approximately every four individuals suffering from sD and treated with the intervention, one treatment response can be expected. In addition, results suggest that the intervention increased behavioural activity, reduced anxiety symptoms, and improved mental functioning as compared to the control condition in the long-term. No effects were found for negative problem-orientation and the physical health summary score of the SF-12.

To the best of our knowledge, this is the largest and sufficiently powered study that has been conducted so far evaluating the effectiveness of a psychological intervention in a subclinical depressive sample. The observed between-group effect size in this trial ( $d = 0.69$ , 95% CI 0.49 - 0.89) is superior to the results from a recent meta-analysis on psychological interventions for the treatment of sD showing a small to moderate effect size at post-treatment ( $g = 0.35$ , 95% CI 0.23 - 0.47) (1). This might be explained by the high heterogeneity in the meta-analysis with respect to target groups, treatment, and type of control group. Most of the studies included in the meta-analysis evaluated the effectiveness of a psychological intervention in older adults and pregnant women, respectively (i.e. (50, 51)). Those studies including an adult population (18 - 65 years) showed similar effect sizes as found in the present trial ranging from  $d = 0.69$  to  $0.80$  (i.e. (52, 53)). The observed within-group effect size in the intervention group ( $d = 1.06$ , 95% CI 0.86 - 1.27) is also comparable to the pre- to post-improvement effect size in the only published study on an Internet-based treatment for sD in adults aged 50 and older ( $d = 1.00$ ) (19). However, in the study by Spek and colleagues (19), no professional support was offered to participants in the Internet-based cognitive-behavioural intervention. Future studies should evaluate, therefore, the amount of guidance needed to achieve an optimal outcome while using as few resources as possible.

The observed reduction in depressive symptom severity in the control condition at 6-month follow-up is in line with previous research. Evidence suggests that one could expect a decrease of approximately 10 - 15% on average in depressive symptomatology if left untreated (54).

The present study has important implications for clinical research and practice. Firstly, it adds to the growing body of literature indicating that psychological interventions for sD could result in substantial and clinically significant effects. The post-treatment effect size found in the

present study was as great as those disclosed in a meta-analysis on face-to-face psychotherapy for major depression (MDD) (55). The treatment effect was sustained at 6-month follow-up. Thus, in contrast to recommendations of current clinical guidelines (i.e. (23, 56, 57)) we found strong evidence for offering psychological interventions to individuals with sD.

Secondly, while the majority of non-web-based psychological interventions for sD evaluated so far consist of 10 or more sessions (i.e. (51, 52, 58)), in the present study similar effect sizes were achieved with a briefer intervention consisting of six sessions. This does not only permit treating more individuals for the same or lesser costs, it also reduces opportunity costs for participants (i.e. their time investment). This makes the intervention potentially more attractive for people with sD. More attractive and less burdensome interventions are needed as the majority of individuals suffering from depressive symptoms do not seek help (59), and participation rates in face-to-face interventions for sD are low (11).

Thirdly, the current study showed that psychological interventions could be successfully delivered via the Internet. For approximately 60% of participants, it was their first time taking part in a psychological intervention indicating that web-based interventions do attract people who may not make use of traditional face-to-face mental health services. Providing low-intensity evidence-based interventions over the Internet may be a promising strategy to reach individuals at an early stage and may thus help to prevent the transition from sub-threshold to a full-blown depressive disorder or relapses in recurrent depressive disorder (60).

Fourthly, although treatment response rates in the present trial were considerable it needs to be acknowledged that about half (i.e. 44%) of the participants failed to achieve a reliable change. This is in line with results of other studies for sD (i.e. (19, 61)) and also of studies on psychotherapy in MDD (62). Lack of treatment response may lead to various negative consequences. One particular adverse effect could be that participants become less motivated to engage in other, more intensive psychological treatments. Thus, future studies should evaluate potential negative effects of web-based interventions, especially in non-responders (63).

There are several limitations to the study including the exclusive use of self-reports to assess depressive symptom severity. In addition, there is evidence that the CES-D does not specifically measure depression as the utility of the CES-D for detecting MDD is approximately equal to its utility for detecting generalized anxiety disorder (64). Future studies should therefore include an independent outcome evaluation, such as observer-based ratings of depressive symptom severity to clearly distinguish depression from related constructs such as anxiety or demoralization syndrome (65, 66). Moreover, participants in our study were better educated than the general population and predominately female. Hence, conclusions from the

present study may not generally apply to i.e. lower educated people and populations recruited by different recruitment strategies (i.e. patients recruited from a mental health clinic). However, this is a common finding in web-based interventions trials (67) indicating that results may generally apply to a population that is interested in this kind of treatment delivery. Additionally, not all individuals may benefit from this particular web-based intervention to the same extent (i.e. participants with low Internet literacy). Thus, future studies should investigate potential effect modifiers. Finally, given that the potential of psychological interventions very much depends on the acceptance in the target population, future studies should focus on evaluating the willingness to use such innovative approaches and strategies to overcome barriers of acceptance (68).

In summary, this trial has shown that GET.ON Mood Enhancer is effective in treating sD. Our study adds to the growing body of literature that psychological interventions for sD are effective, can result in clinical meaningful changes also in the long-term and that such interventions can be successfully delivered using the Internet. Web-based interventions might be a complement to face-to-face mental health services in the treatment of sD. Guided self-help interventions require less therapist time and may be a very efficient approach in treating sD. Web-based interventions are more easily disseminated on a large scale, implying that only a small increase in therapeutic resources is needed for reaching a greater proportion of the eligible population using these interventions.

## References

1. Cuijpers P, Koole SL, van Dijke A, Roca M, Li J, Reynolds CF, 3rd. Psychotherapy for subclinical depression: meta-analysis. *Br J Psychiatry*. 2014; 205(4): 268-74.
2. Cuijpers P, de Graaf R, van Dorsselaer S. Minor depression: risk profiles, functional disability, health care use and risk of developing major depression. *Journal of Affective Disorders*. 2004; 79(1-3): 71-9.
3. Cuijpers P, Vogelzangs N, Twisk J, Kleiboer A, Li J, Penninx BW. Differential mortality rates in major and subthreshold depression: meta-analysis of studies that measured both. *Br J Psychiatry*. 2013; 202(1): 22-7.
4. Rucci P, Gherardi S, Tansella M, Piccinelli M, Berardi D, Bisoffi G, et al. Subthreshold psychiatric disorders in primary care: prevalence and associated characteristics. *J Affect Disord*. 2003; 76(1-3): 171-81.
5. Goldney RD, Fisher LJ, Dal Grande E, Taylor AW. Subsyndromal depression: prevalence, use of health services and quality of life in an Australian population. *Soc Psychiatry Psychiatr Epidemiol*. 2004; 39(4): 293-8.
6. Cuijpers P, Smit F, Oostenbrink J, de Graaf R, Ten Have M, Beekman A. Economic costs of minor depression: a population-based study. *Acta Psychiatr Scand*. 2007; 115(3): 229-36.
7. Cuijpers P, Smit F. Subthreshold depression as a risk indicator for major depressive disorder: a systematic review of prospective studies. *Acta Psychiatr Scand*. 2004; 109(5): 325-31.
8. Barbui C, Cipriani A, Patel V, Ayuso-Mateos JL, van Ommeren M. Efficacy of antidepressants and benzodiazepines in minor depression: systematic review and meta-analysis. *Br J Psychiatry*. 2011; 198(1): 11-6, sup 1.
9. Morgan AJ, Jorm AF, Mackinnon AJ. Email-based promotion of self-help for subthreshold depression: Mood Memos randomised controlled trial. *Br J Psychiatry*. 2012; 200(5): 412-8.
10. Christensen H, Griffiths KM. The prevention of depression using the Internet. *Med J Aust*. 2002; 177 Suppl: S122-5.
11. Cuijpers P, van Straten A, Warmerdam L, van Rooy MJ. Recruiting participants for interventions to prevent the onset of depressive disorders: possible ways to increase participation rates. *BMC Health Serv Res*. 2010; 10: 181.
12. Lin J, Ebert DD, Lehr D, Berking M, Baumeister H. [Internet based cognitive behavioral interventions: state of the art and implementation possibilities in rehabilitation]. *Rehabilitation (Stuttg)*. 2013; 52(3): 155-63.
13. Ebert DD, Lehr D, Boss L, Riper H, Cuijpers P, Andersson G, et al. Efficacy of an internet-based problem-solving training for teachers: results of a randomized controlled trial. *Scandinavian journal of work, environment & health*. 2014; 40(6): 582-96.
14. Herbst N, Voderholzer U, Thiel N, Schaub R, Knaevelsrud C, Stracke S, et al. No talking, just writing! Efficacy of an Internet-based cognitive behavioral therapy with exposure and response prevention in obsessive compulsive disorder. *Psychother Psychosom*. 2014; 83(3): 165-75.
15. Cheng SK, Dizon J. Computerised cognitive behavioural therapy for insomnia: a systematic review and meta-analysis. *Psychother Psychosom*. 2012; 81(4): 206-16.

16. Richards D, Richardson T. Computer-based psychological treatments for depression: A systematic review and meta-analysis. *Clin Psychol Rev.* 2012; 32(4): 329-42.
17. Arnberg FK, Linton SJ, Hultcrantz M, Heintz E, Jonsson U. Internet-delivered psychological treatments for mood and anxiety disorders: a systematic review of their efficacy, safety, and cost-effectiveness. *PLoS One.* 2014; 9(5): e98118.
18. Ebert D, Tarnowski T, Gollwitzer M, Sieland B, Berking M. A transdiagnostic internet-based maintenance treatment enhances the stability of outcome after inpatient cognitive behavioral therapy: a randomized controlled trial. *Psychother Psychosom.* 2013; 82(4): 246-56.
19. Spek V, Nyklicek I, Smits N, Cuijpers P, Riper H, Keyzer J, et al. Internet-based cognitive behavioural therapy for subthreshold depression in people over 50 years old: a randomized controlled clinical trial. *Psychol Med.* 2007; 37(12): 1797-806.
20. Kupfer DJ. Long-term treatment of depression. *J Clin Psychiatry.* 1991; 52 Suppl: 28-34.
21. Buntrock C, Ebert DD, Lehr D, Cuijpers P, Riper H, Smit F, et al. Evaluating the efficacy and cost-effectiveness of web-based indicated prevention of major depression: design of a randomised controlled trial. *BMC Psychiatry.* 2014; 14: 25.
22. Eysenbach G. CONSORT-EHEALTH: improving and standardizing evaluation reports of Web-based and mobile health interventions. *J Med Internet Res.* 2011; 13(4): e126.
23. Bundesärztekammer, Bundesvereinigung K, Fachgesellschaften AdWM. German S3-Guideline/National Disease Management Guideline Unipolar Depression. 2011. <http://www.depression.versorgungsleitlinien.de/>.
24. Donker T, Griffiths KM, Cuijpers P, Christensen H. Psychoeducation for depression, anxiety and psychological distress: a meta-analysis. *BMC Med.* 2009; 7: 79.
25. Bot M, Pouwer F, Ormel J, Slaets JP, de Jonge P. Predictors of incident major depression in diabetic outpatients with subthreshold depression. *Diabet Med.* 2010; 27(11): 1295-301.
26. Lara MA, Navarro C, Navarrete L. Outcome results of a psycho-educational intervention in pregnancy to prevent PPD: a randomized control trial. *J Affect Disord.* 2010; 122(1-2): 109-17.
27. Urizar GG, Jr., Munoz RF. Impact of a prenatal cognitive-behavioral stress management intervention on salivary cortisol levels in low-income mothers and their infants. *Psychoneuroendocrinology.* 2011; 36(10): 1480-94.
28. Vazquez FL, Torres A, Blanco V, Diaz O, Otero P, Hermida E. Comparison of relaxation training with a cognitive-behavioural intervention for indicated prevention of depression in university students: a randomized controlled trial. *Journal of psychiatric research.* 2012; 46(11): 1456-63.
29. van't Veer-Tazelaar PJ, van Marwijk HW, van Oppen P, van Hout HP, van der Horst HE, Cuijpers P, et al. Stepped-care prevention of anxiety and depression in late life: a randomized controlled trial. *Arch Gen Psychiatry.* 2009; 66(3): 297-304.
30. Hautzinger M, Bailer M, Hofmeister D, Keller F. Allgemeine Depressionskala. Hogrefe, 2012.
31. Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, et al. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. *International Quality of Life Assessment. J Clin Epidemiol.* 1998; 51(11): 1171-8.

32. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1983; 67(6): 361-70.
33. Hermann-Lingen C, Buss U, Snaith RP. Hospital Anxiety and Depression Scale - Deutsche Version (HADS-D). Verlag Hans Huber, 2011.
34. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res.* 2002; 52(2): 69-77.
35. D'Zurilla TJ, Nezu AM, Maydeu-Olivares A. Social Problem-Solving Inventory-Revised (SPSI-R). MHS, 2002.
36. Manos RC, Kanter JW, Luo W. The behavioral activation for depression scale-short form: development and validation. *Behav Ther.* 2011; 42(4): 726-39.
37. Pearlin LI, Schooler C. The structure of coping. *J Health Soc Behav.* 1978; 19(1): 2-21.
38. Berle D, Starcevic V, Moses K, Hannan A, Milicevic D, Sammut P. Preliminary validation of an ultra-brief version of the Penn State Worry Questionnaire. *Clin Psychol Psychother.* 2011; 18(4): 339-46.
39. Bastien CH, Vallieres A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Med.* 2001; 2(4): 297-307.
40. Morin CM, Belleville G, Belanger L, Ivers H. The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep.* 2011; 34(5): 601-8.
41. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry.* 2000; 31(2): 73-86.
42. Schmidt J, Lamprecht F, Wittmann W. Satisfaction with inpatient management. Development of a questionnaire and initial validity studies. [Article in German]. *Psychotherapy, Psychosomatic and Medical Psychology.* 1989; 39: 248-55.
43. Nguyen TD, Attkisson CC, Stegner BL. Assessment of patient satisfaction: development and refinement of a service evaluation questionnaire. *Eval Program Plann.* 1983; 6(3-4): 299-313.
44. Attkisson CC, Zwick R. The client satisfaction questionnaire. Psychometric properties and correlations with service utilization and psychotherapy outcome. *Eval Program Plann.* 1982; 5(3): 233-7.
45. Lipsey MW, Wilson DB. The efficacy of psychological, educational, and behavioral treatment. Confirmation from meta-analysis. *The American psychologist.* 1993; 48(12): 1181-209.
46. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *J Pharmacol Pharmacother.* 2010; 1(2): 100-7.
47. Hedges L, Olkin I. *Statistical methods for meta-analysis.* Academic Press, 1985.
48. Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. *J Consult Clin Psychol.* 1991; 59(1): 12-9.
49. Kraemer HC, Kupfer DJ. Size of treatment effects and their importance to clinical research and practice. *Biological psychiatry.* 2006; 59(11): 990-6.
50. Le HN, Perry DF, Stuart EA. Randomized controlled trial of a preventive intervention for perinatal depression in high-risk Latinas. *J Consult Clin Psychol.* 2011; 79(2): 135-41.
51. Haringsma R, Engels GI, Cuijpers P, Spinhoven P. Effectiveness of the Coping With Depression (CWD) course for older adults provided by the community-based mental

- health care system in the Netherlands: a randomized controlled field trial. *Int Psychogeriatr*. 2006; 18(2): 307-25.
52. Allart-van Dam E, Hosman CM, Hoogduin CA, Schaap CP. Prevention of depression in subclinically depressed adults: follow-up effects on the 'Coping with Depression' course. *Journal of affective disorders*. 2007; 97(1-3): 219-28.
  53. Furukawa TA, Horikoshi M, Kawakami N, Kadota M, Sasaki M, Sekiya Y, et al. Telephone cognitive-behavioral therapy for subthreshold depression and presenteeism in workplace: a randomized controlled trial. *PLoS One*. 2012; 7(4): e35330.
  54. Posternak MA, Miller I. Untreated short-term course of major depression: a meta-analysis of outcomes from studies using wait-list control groups. *J Affect Disord*. 2001; 66(2-3): 139-46.
  55. Cuijpers P, Berking M, Andersson G, Quigley L, Kleiboer A, Dobson KS. A meta-analysis of cognitive-behavioural therapy for adult depression, alone and in comparison with other treatments. *Can J Psychiatry*. 2013; 58(7): 376-85.
  56. NICE. NICE Clinical Guidelines, No. 90. Depression: The Treatment and Management of Depression in Adults (Updated Edition). British Psychological Society, 2010.
  57. Association AP. Practice guideline for the treatment of patients with major depressive disorder. American Psychiatric Association, 2010.
  58. Konnert C, Dobson K, Stelmach L. The prevention of depression in nursing home residents: a randomized clinical trial of cognitive-behavioral therapy. *Aging Ment Health*. 2009; 13(2): 288-99.
  59. Mack S, Jacobi F, Gerschler A, Strehle J, Hofler M, Busch MA, et al. Self-reported utilization of mental health services in the adult German population--evidence for unmet needs? Results of the DEGS1-Mental Health Module (DEGS1-MH). *Int J Methods Psychiatr Res*. 2014; 23(3): 289-303.
  60. van Zoonen K, Buntrock C, Ebert DD, Smit F, Reynolds CF, 3rd, Beekman AT, et al. Preventing the onset of major depressive disorder: a meta-analytic review of psychological interventions. *Int J Epidemiol*. 2014; 43(2): 318-29.
  61. Warmerdam L, van Straten A, Twisk J, Riper H, Cuijpers P. Internet-based treatment for adults with depressive symptoms: randomized controlled trial. *J Med Internet Res*. 2008; 10(4): e44.
  62. Cuijpers P, Karyotaki E, Weitz E, Andersson G, Hollon SD, van Straten A. The effects of psychotherapies for major depression in adults on remission, recovery and improvement: a meta-analysis. *J Affect Disord*. 2014; 159: 118-26.
  63. Rozental A, Andersson G, Boettcher J, Ebert DD, Cuijpers P, Knaevelsrud C, et al. Consensus statement on defining and measuring negative effects of Internet interventions. *Internet Interventions*. 2014; 1(1): 12-9.
  64. Breslau N. Depressive symptoms, major depression, and generalized anxiety: a comparison of self-reports on CES-D and results from diagnostic interviews. *Psychiatry Res*. 1985; 15(3): 219-29.
  65. de Figueiredo JM. Demoralization and Psychotherapy: A Tribute to Jerome D. Frank, MD, PhD (1909-2005). *Psychother Psychosom*. 2007; 76(3): 129-33.
  66. Tecuta L, Tomba E, Grandi S, Fava GA. Demoralization: a systematic review on its clinical characterization. *Psychol Med*. 2015; 45(4): 673-91.

67. Andersson G, Titov N. Advantages and limitations of Internet-based interventions for common mental disorders. *World psychiatry : official journal of the World Psychiatric Association (WPA)*. 2014; 13(1): 4-11.
68. Ebert DD, Berking M, Cuijpers P, Lehr D, Portner M, Baumeister H. Increasing the acceptance of internet-based mental health interventions in primary care patients with depressive symptoms. A randomized controlled trial. *J Affect Disord*. 2015; 176: 9-17.

