Living positive: eHealth for people with HIV and depressive symptoms

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Chapter 5

Guided Internet-based intervention for people with HIV and depressive symptoms: A randomised controlled trial in the Netherlands

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Abstract

Background Many people living with HIV have depressive symptoms, but some individuals do not receive adequate treatment. We developed an online self-help intervention for people with HIV with depressive symptoms on the basis of previous research. The aim of this study was to investigate the effectiveness of the intervention on depressive symptoms in individuals with HIV.

Methods In this randomized controlled trial, participants recruited from 23 HIV treatment centers in the Netherlands were eligible if they were aged 18 years and older, had been diagnosed with HIV at least 6 months before the study, and had mild to moderate depressive symptoms (Patient Health Questionnaire-9 [PHQ-9] score > 4 and < 20). Individuals also had to speak English or Dutch and have internet access and an email address. Participants were randomly assigned (1:1) to an internet-based intervention (Living positive with HIV) or an attention-only waiting-list control condition. Randomization was done using random number tables, with permuted blocks of 12, stratified by treatment center and sex. Participants, researchers, and coaches were not masked to group allocation. The primary outcome was depressive symptoms assessed with the PHQ-9 and the Center for Epidemiologic Studies Depression Scale (CES-D) at pretest, eight weeks after baseline, and three months after completion of the intervention or control condition (post-test 2). The primary analysis was done by intention to treat. Between group effect size was assessed with Cohen's *d*. This trial is registered with the Netherlands Trial Registry, number NTR5407.

Findings Between Feb 1, and Dec 31, 2015, we randomly assigned 188 participants to the intervention group (n = 97) or the control group (n = 91). Mean pretest PHQ-9 score was 11.74 (SD 2.49) in the intervention group and 11.11 (2.37) in the control group; at the post-test visits it was 6.73 (3.00) and 6.62 (3.03) in the intervention group and 8.60 (3.12) and 8.06 (3.17) in the control group. Mean pretest CES-D score was 24.91 (5.93) in the intervention group and 22.94 (6.48) in the control group; at the post-test visits it was 13.94 (6.39) and 15.71 (6.39) in the intervention group and 19.09 (7.05) and 18.43 (7.05) in the control group. The reduction in depressive symptoms was significantly larger in the intervention group than in the control group (*d* = –0.56 95% CI [–0.85, –0.27] for PHQ-9 and –0.72 [–1.02, –0.42] for CES-D at post-test 1; –0.46 [–0.75, –0.17] for PHQ-9 and –0.47 [–0.76, –0.18] for CES-D at post-test 2). No adverse events were reported.

Interpretation This guided internet-based intervention might be effective for the treatment of depressive symptoms. Future research should focus on the effectiveness of online psychological interventions for people with HIV who have mental health problems in low-income and middle-income countries.

Funding Aidsfonds.

Introduction

Depressive symptoms occur in around 33% of people with HIV (1). A possible consequence of depression in people with HIV is reduced adherence to antiretroviral therapy (2). Although several psychological interventions have been found to effectively reduce depressive symptoms (3, 4) and improve antiretroviral therapy adherence (5) and quality of life (4), many individuals with HIV do not seek treatment when they feel depressed because of factors such as perceived stigma (6). Internet-based interventions might increase the accessibility of treatment for people with HIV who have depression. Additionally, these interventions have the potential to reach a large number of people, can be followed anonymously at preferred times and places, and might be more cost-effective than face-to-face interventions. Previous studies found that internet-based treatments are effective for the treatment of depression in the general population (7), and in people with chronic somatic conditions (8). Furthermore, face-to-face and guided internet-based interventions for depression were found to be equally effective (9).

Only four studies (10-13) have assessed the effectiveness of computerised or internet treatments for depressive symptoms in people with HIV. Three of these interventions did not improve mood (10-12). An online support group intervention for individuals with HIV reduced depressive symptoms, but this study did not include a control condition (13). The other studies investigated a metacognitive therapy and positive psychology intervention (11), a cognitive behavioural intervention (12), and stress-management training (10). These interventions might have been ineffective because they did not meet the needs of people with HIV who have depressive symptoms (10, 12). For example, one of the interventions focused more on adherence than on depression (12). Therefore, the development of online interventions for people with HIV that effectively reduce depressive symptoms is needed.

We designed an internet-based treatment termed Living positive with HIV (14). The intervention is based on a booklet self-help programme for people with HIV who have depression (15). The booklet was designed specifically for individuals with HIV, to meet their needs and preferences (16). A randomized controlled trial (15) showed that the booklet was effective in decreasing depressive symptoms, compared with a waiting-list control condition. On the basis of these findings, we adapted the self-help booklet and converted it into the current internet-based self-help intervention. Thereafter, a focus group evaluated the intervention and we adjusted it accordingly. In a pilot study (14) in 2014, 20 individuals with HIV completed the intervention with telephone coaching. Depressive symptoms decreased after the intervention and user satisfaction was high (14).

The aim of this study was to investigate the effectiveness of the guided internet-based self-help intervention in decreasing depressive symptoms in people with HIV compared with an attention-

only waiting-list control condition. We also investigated the effect of the intervention on anxiety and user satisfaction with the intervention.

Research in context

Evidence before this study

In a previous study, we did a meta-analysis of 62 randomized controlled trials published up to Sept 29, 2014, to investigate the effectiveness of psychosocial interventions for people with HIV in improving mental health. The meta-analysis included one internet-based intervention for people with HIV that investigated effects on mood. On Augustus 30, 2017, our search was updated; we searched PubMed, PsycINFO, and Embase using terms related to "HIV", "Internet-based therapy", and "depression". One additional study was found. To date, only two studies have investigated the use of internet-based interventions for people with HIV who have depressive symptoms and both found that the interventions did not improve mood.

Added value of this study

Our results show that the guided internet-based intervention, Living positive with HIV, might be effective in improving depressive symptoms in people with HIV compared with an attention-only waiting-list control condition.

This improvement was sustained over time, and anxiety was significantly reduced in patients who followed the intervention compared with the control. Online interventions have advantages, such as large potential reach and accessibility. Additionally, this intervention is available in Dutch and English and could be adapted for use in other countries.

Implications of all the available evidence

People with HIV who have depressive symptoms should be referred to effective psychological treatments. eHealth interventions are emerging and have been shown to be as effective as face-to-face interventions. Therefore, treatment providers might refer people with HIV who have depressive symptoms to an online intervention, such as the intervention used in this study. More research on moderators, mediators, and the cost-effectiveness of internet-based interventions is needed.

Methods

Study design and participants

In this randomized controlled trial, participants were recruited from 23 HIV treatment centers in the Netherlands. Patients at these centers underwent a two-step screening for depressive symptoms.

Nursing consultants and doctors in HIV treatment centers initially screened patients with HIV for depressive symptoms during regular check-ups using the Patient Health Questionnaire-2 (PHQ-2) (17). Patients with PHQ-2 scores higher than zero who were interested in participating in the study were referred to the researchers for a second screening with the Patient Health Questionnaire-9 (PHQ-9), using established cutoff scores (18). One HIV treatment center screened patients with the Hospital Anxiety and Depression Scale (19), because this questionnaire was already in use. Patients with total scores higher than 2 and less than 16 on the Hospital Anxiety and Depression Scale were deemed eligible for referral to the researchers. The study was also advertised by the Dutch HIV Association. Researchers contacted all interested patients to provide more information and to screen for eligibility.

Eligible individuals were aged 18 years and older, had been diagnosed with HIV at least six months before the study, and had mild to moderate depressive symptoms (PHQ-9 score of > 4 and < 20). Eligible patients were also required to speak Dutch or English, have internet access and an email address, and to be available for eight weeks to work on the intervention. We excluded individuals with severe cognitive impairments, severe depressive symptoms (PHQ-9 score ≥ 20), or severe suicidal ideation (score > 1 on the suicide item of the PHQ-9), and those who were receiving treatment from a psychologist or psychiatrist, had been on antidepressants for less than three months, or had changed type or dose of antidepressants in the past three months. The study was approved by the medical ethics committee of Leiden University Medical Center. The study protocol has been published elsewhere (14). All participants provided online informed consent.

Randomization and masking

Participants were randomly assigned (1:1) to the internet-based intervention or the attention-only waiting-list control condition. Randomization was done using random number tables to generate the randomization sequence with block sizes of 12, stratified by treatment center and sex, and concealed from the main researcher. The main researcher allocated participants to conditions, but the characters in the randomization file were white until assignment of a participant was carried out (then the letters on one line in the file were made visible). Participants, researchers, and coaches were not masked to the participant's assigned treatment condition.

Procedures

Medical data (e.g., viral load) were obtained from the AIDS Therapy Evaluation in the Netherlands (ATHENA) cohort study after obtaining consent from the participant. The ATHENA cohort study is maintained by Stichting HIV Monitoring, which is supported by the Dutch Ministry of Health via the National Institute for Public Health and Environment. A self-designed questionnaire, included in the pretest, was used to obtain information about patient demographics.

All participants completed the pretest and were randomly assigned to one of two conditions. Participants in the intervention group did the first post-test after they had completed the intervention (duration six to ten weeks), followed by two further post-tests three and six months after completion of the intervention. Participants in the control group received two post-tests: the first post-test was sent eight weeks after the pretest and the second post-test was sent three months after the first post-test was completed (Appendix 1). Participants who completed all questionnaires received €25. The last post-test was completed on October 14, 2016. All assessments were completed online via a secured website, with the exception of screening with the PHQ-9, which was completed via telephone conversations.

The internet-based self-help intervention consisted of cognitive behavioural therapy. Psychoeducation was alternated with exercises and assignments. The intervention was based on a self-help booklet for people with HIV with depressive symptoms (15), which was extended to include an activation component and minimal coaching with motivational interviewing, and the programme was translated into English to reach more people with HIV. The intervention included four main components covered in eight lessons. The first component was activation, in which participants were encouraged to do pleasant activities. The second component contained relaxation exercises. The third component included assignments to identify and change negative thoughts. The fourth component included goal setting and increasing confidence to attain goals. Participants received login details for the secured website of the intervention. Participants did the intervention for one to two hours per week for a period of around eight weeks, and received telephone coaching.

Participants in the control condition were put on a waiting list and received attention only via telephone calls from a coach. After the second post-test, participants in the control condition were invited to start the intervention. Participants in the control group who started the intervention received one post-test, the results of which are not reported in this paper and will not be reported elsewhere.

All participants received minimal telephone coaching. Participants in the intervention group were called weekly for approximately 15 minutes by a personal coach, who asked the participants how they were doing and how they were progressing with the intervention. Furthermore, motivational interviewing was used to prevent attrition. Formal psychotherapy was not included in the coaching, but depressive symptoms and suicidal thoughts were monitored. Coaching was offered until participants completed the intervention (maximum duration ten weeks). After ten weeks, participants could complete the intervention independently and ask questions via email. Participants in the control group were called weekly for around five minutes by a personal coach, for a period of eight weeks. The coach asked participants how they were doing and motivated individuals to stay in the study. Coaches monitored depressive symptoms and suicidal thoughts in both the intervention and control groups and

patients with severe depressive symptoms or suicidal ideation were referred to their general practitioner or HIV treatment center.

All coaches were clinical psychology Masters students or graduates with an MSc in Psychology who had attended several clinical courses during their Masters, in which they learned communication skills and therapeutic strategies. Coaches were trained by the main researcher. During training, coaching procedures and motivational interviewing were explained and practiced. Coaches received a coaching manual with additional information about motivational interviewing, the study, the procedures, and content of coaching (e.g., what to do when depressive symptoms of a participant increase). At the beginning of the study, weekly supervision sessions were arranged with all coaches and the main researcher to discuss difficulties and questions. After a few months, these supervision sessions were phased out, but coaches and researchers could contact each other directly via telephone or email when needed.

Outcomes

The primary outcome was depressive symptoms, assessed with the PHQ-9 (18) and the Center for Epidemiologic Studies Depression Scale (CES-D; (20)) at pretest (baseline), immediately after the intervention (or eight weeks after baseline in the control group; post-test 1), and at three months after the first post-test. As a secondary outcome, in the intervention group only, we also assessed the PHQ-9 and CES-D scores six months after completion of the intervention. Total scores ranged between 0 and 27 for the PHQ-9 and 0 and 60 for the CES-D, with higher scores indicating increasing symptom severity. The secondary outcomes were anxiety symptoms, assessed with the Generalized Anxiety Disorder-7 (GAD-7) scale (21) (total score 0–21) at all assessment time points, with higher scores indicating increasing symptom severity, and user satisfaction, measured with a self-designed questionnaire at the first post-test. In the intervention group, participants were asked to grade the intervention (0–10; a higher score indicated higher user satisfaction) and whether they would recommend the intervention (yes, maybe, or no). In both groups, participants were also asked to grade the coach (0–10; a higher score indicated higher satisfaction with the coach).

Other secondary outcomes not reported in this paper were physical tension, activation (Behavioral Activation for Depression Scale; (22)), cognitive reappraisal (Emotion Regulation Questionnaire; (23)), cognitive coping (Cognitive Emotion Regulation Questionnaire; (24)), depressive thoughts (Crandell Cognitions Inventory; (25)), behavioral coping (Kraaij & Garnefski, Behavioral Emotion Regulation Questionnaire, unpublished questionnaire), coping self-efficacy (Kraaij & Garnefski, unpublished questionnaire), goal adjustment (Goal Disengagement and Reengagement Scale; (26)), personal growth (Garnefski & Kraaij, unpublished questionnaire), negative life events (Life Events Scale), motivation to start with the intervention, compliance, and dropout and reasons for

dropout. These outcomes were used in moderator and mediator analyses. The results of these outcomes will be reported elsewhere.

There was no data safety monitoring board. Participants were assessed multiple times during the intervention and the study, and the results regarding their symptoms were monitored by the researcher. Additionally, coaches monitored the participants.

Statistical analysis

A power analysis with the program Power Analysis and Sample Size Software (PASS) was performed. On the basis of the randomized controlled trial on the effectiveness of the self-help booklet (15), and an expected dropout of 15% at the first post-test, a sample size of 150 participants was required to detect an effect size of 0.50 with 0.80 power at the 5% significance level. We aimed to include 200 participants because attrition was expected during follow-up (14).

Statistical analysis was done with SPSS software (version 23.0), and a p value of less than 0.05 was considered to indicate statistical significance. Primary and secondary analyses were done by intention to treat.

χ^2 tests and ANOVA were used to investigate differences between participants who dropped out and those who completed the intervention. We did longitudinal multilevel regression analyses (27) using the maximum likelihood estimation method to investigate differences between the groups in changes in depressive and anxiety symptoms from the pretest to the post-tests. Time and group were included as fixed effects and slopes for time and the intercept as random effects. Pretest, post-test 1, and post-test 2 scores were included in the between-group analyses. Pretest and the three post-test scores for the intervention group were included in the within-group analyses to assess the long- term effects of the intervention. The variance components variance–covariance matrix was used for between-group analyses and the heterogeneous autoregressive matrix was used for within-group analyses. Additionally, all outcomes were analysed in the per-protocol sample, which included all randomly assigned participants who completed at least five lessons of the intervention (indicated by self-report); using this minimum ensured that at least three of the four main intervention components were completed. The effect of HIV treatment center on the random intercept was investigated in an exploratory analysis, by adding treatment center as an extra level in the analysis.

Cohen's *d* was calculated to assess effect size. For the between-group effect sizes, the mean difference scores for the control group were subtracted from the mean difference scores for the intervention group and divided by the pooled SD of the raw scores at pretest (28). For the effect size of time (i.e., long-term effect of the intervention), we used the formula unstandardized coefficient (b)/SD (28), using the SD of the raw scores of the intervention group at pretest. Effect sizes were calculated using the estimated values from the longitudinal multilevel regression analyses. The formula

used by de Zeeuw and colleagues (29) was used to calculate the SE of the between-group effect size and 95% CIs.

Clinically significant differences, deterioration, and number needed to treat from pretest to the first post-test were assessed for the PHQ-9 and the CES-D. A reliable change index was calculated for each individual to determine improvement and their pretest score was subtracted from their first post-test score and divided by the SE of difference between the two scores (30). To calculate the SE of difference, test–retest reliability (rxx) was used, where rxx was equal to 0.84 for both the PHQ-9 (18) and the CES-D. Reliable change index scores of less than –1.96 indicated symptom improvement. Recovery was calculated by examining whether a cutoff for depression (score 10 on the PHQ-9 (31) and 22 on the CES-D (32)) was reached at the first post-test. Recovery was only assessed in participants who scored above this cutoff at pretest (clinical cases), because participants who scored below this cutoff at pretest had already reached the criterion (30). For participants who scored above the cutoff at pretest, we assessed both improvement and recovery; in cases of both, the criteria for clinically significant change according to Jacobson and Truax (30) were met. Deterioration was also assessed, whereby a reliable change index score higher than 1.96 indicated deterioration. The number needed to treat was calculated using the percentage of participants who met the criteria for clinically significant change. Clinically significant change, deterioration, and number needed to treat were calculated in the per-protocol analysis sample that also completed the first post-test; the raw data were used.

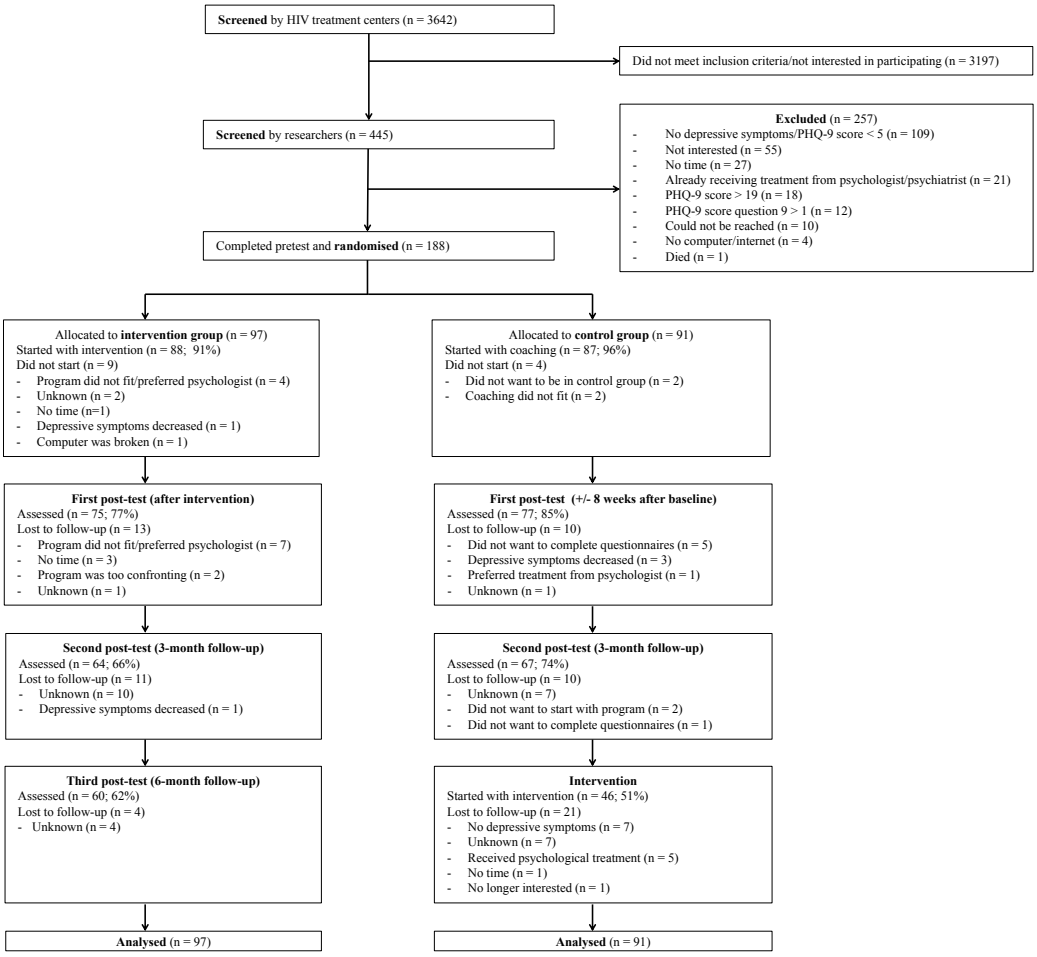

Figure 1. Trial profile

Results

Between February 1, and December 31, 2015, 3642 people with HIV were screened for depressive symptoms in HIV treatment centers, of whom 445 were screened for eligibility. One hundred eighty-eight participants were randomly assigned to the intervention group (n = 97) or the control group (n = 91; Figure 1). Of the 91 participants in the control group, 77 (85%) completed the first post-test and 67 (74%) completed the second post- test. Forty-six (51%) of 91 participants started the intervention after the second post-test. Of the 97 participants in the intervention group, 88 (91%) started the intervention, 75 (77%) completed the first post-test, 64 (66%) completed the second post-test, and 60 (62%) completed the third post-test. All participants in the intervention group who dropped out (i.e., did not complete the first post-test) stopped the intervention before completion of the fifth lesson.

Fourteen participants did not finish the intervention in ten weeks. We identified no significant differences in the proportion of participants who did not complete the first post-test between the two groups. Additionally, no significant differences in the baseline characteristics were identified between participants who completed the first post-test and those who did not.

Most participants were men, homosexual, and educated to a medium or high level, with a mean age of about 46 years (Table 1). Mean time since HIV diagnosis was about 10 years and most participants were on antiretroviral therapy. Participants in the intervention group received a mean of 6.38 telephone calls from the coach compared with a mean of 6.23 telephone calls in the control group, with no significant differences identified between groups ($p = 0.67$). The mean duration of phone calls per participant was significantly higher in the intervention group than the control group (90.74 minutes (*SD* = 60.32) vs 60.52 minutes (*SD* = 42.30); $p < 0.0001$).

Table 1. Baseline characteristics of the intervention and control group

Characteristic	Intervention group (n = 97)	Control group (n = 91)	Total sample (n = 188)
Age (years)	45.53 (10.32)	47.12 (10.94)	46.30 (10.63)
Sex			
Male	85 (88%)	81 (89%)	166 (88%)
Female	12 (12%)	10 (11%)	22 (12%)
Nationality			
Dutch	80 (83%)	78 (86%)	158 (84%)
Other	10 (10%)	8 (9%)	18 (10%)
Dutch and other	7 (7%)	5 (5%)	12 (6%)
Education			
Low	20 (21%)	22 (24%)	42 (22%)
Medium	44 (45%)	33 (36%)	77 (41%)
High	33 (34%)	36 (40%)	69 (37%)
Marital status			
Married or cohabiting	41 (42%)	44 (48%)	85 (45%)
Single or living without partner	56 (58%)	47 (52%)	103 (55%)
Sexual orientation			
Heterosexual	19 (20%)	13 (14%)	32 (17%)
Homosexual	73 (75%)	71 (78%)	144 (77%)
Bisexual	5 (5%)	7 (8%)	12 (6%)
Psychotropic medication			
No	85 (88%)	81 (89%)	166 (88%)
Yes	12 (12%)	10 (11%)	22 (12%)
Time since HIV diagnosis (years)[a]	9.35 (6.46)	10.41 (6.70)	9.87 (6.58)
Diagnosis of AIDS			

Characteristic	Intervention group (n = 97)	Control group (n = 91)	Total sample (n = 188)
No	88 (91%)	77 (85%)	165 (88%)
Yes	9 (9%)	14 (15%)	23 (12%)
CD4 count (cells per µl)[b]	726 (290)	647 (280)	690 (287)
Viral load[c]			
Undetectable (< 50 copies per mL)	59 (88%)	59 (86%)	118 (87%)
Detectable (≥ 50 copies per mL)	8 (12%)	10 (14%)	18 (13%)
Antiretroviral therapy			
Yes	94 (97%)	90 (99%)	184 (98%)
No	3 (3%)	1 (1%)	4 (2%)

Data are mean (SD), n (%), or n/N (%). Some percentages do not sum to 100% because of rounding.

[a] available for 187 participants, [b] available for 86 participants, [c] available for 136 participants.

Mean pretest PHQ-9 score was 11.74 (*SD* = 2.49) in the intervention group and 11.11 (2.37) in the control group; at the post-test visits it was 6.73 (3.00) and 6.62 (3.03) in the intervention group and 8.60 (3.12) and 8.06 (3.17) in the control group. Mean pretest CES-D score was 24.91 (5.93) in the intervention group and 22.94 (6.48) in the control group; at the post-test visits it was 13.94 (6.39) and 15.71 (6.39) in the intervention group and 19.09 (7.05) and 18.43 (7.05) in the control group (Appendix 2). A group-by-time interaction effect was identified for the PHQ-9 and CES-D: the reduction in depressive symptoms between pretest and post-test 1 was significantly larger in the intervention group than in the control group (Table 2 and Figure 2). The effect sizes for the differences in scores at post-test 1 (corrected for baseline) were *d* = –0.56, 95% CI [–0.85, –0.27] for the PHQ-9 and *d* = –0.72, 95% CI [–1.02, –0.42] for the CES-D. Furthermore, time had a significant effect on the PHQ-9 and CES-D: depressive symptoms decreased significantly between pretest and post-test 1 in both groups (Table 2). For the GAD-7, the time effect was not significant, but a significant group-by-time interaction effect was identified: the reduction in anxiety symptoms between pretest and post-test 1 was significantly larger in the intervention group than in the control group (*d* = –0.75, 95% CI [–1.05, –0.45]). No time effect or group-by-time interaction effect was identified between post-test 1 and post-test 2 for PHQ-9, CES-D, or GAD-7 (Table 2). The effect sizes for the differences in scores at post-test 2 (corrected for baseline) were smaller than those for the differences in scores at post-test 1 for the PHQ-9 (*d* = –0.46, 95% CI [–0.75, –0.17]), CES-D (–0.47, [–0.76, –0.18]) and the GAD-7 (–0.56, [–0.85, –0.27]).

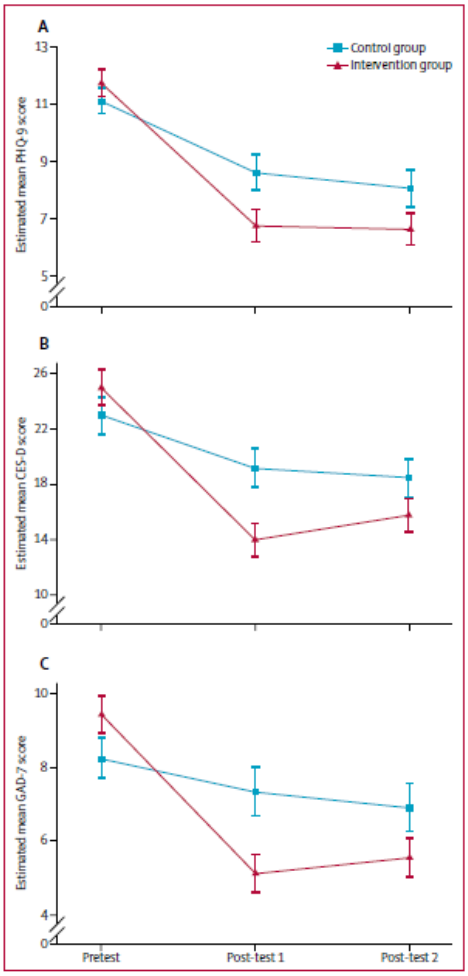

Figure 2. Estimated mean PHQ-9, CES-D, and GAD-7 scores over time in both groups. Error bars show 95% CI.

In the intervention group, time had a significant effect on all outcomes. Depressive and anxiety symptoms decreased from pretest to post-test 1 and remained low at post-tests 2 and 3 (Table 3). No significant time effect was identified from post-test 1 to post-test 2 or from post-test 2 to post-test 3 for PHQ-9, CES-D, and GAD-7. Within- group effect sizes were moderate between the pretest and post-test 1 and around zero between post-test 1 and post-test 2; and between post-test 2 and post-test 3.

In an exploratory analysis, we assessed the effect of HIV treatment center by use of an unconditional means model with three levels. The intraclass correlation was estimated to be

approximately zero in all models, indicating that treatment center had no effect; therefore we did not include it in the analyses. Furthermore, per-protocol analyses confirmed the findings of the intention-to-treat analyses (data not shown).

Table 2. Mixed model analyses comparing the differences in depressive and anxiety symptom scores over time in the intervention and control groups

	Time effect			**Time-by-group effect**		
	b[a] (SE)	**t[b]**	***P***	**b[a] (SE)**	**t[b]**	***p***
Primary outcome measures						
PHQ-9[c]						
Pretest to post-test 1	-2.51 (0.56)	-4.48	<0.0001	-2.50 (0.80)	-3.14	0.002
Post-test 1 to post-test 2	-0.54 (0.55)	-0.98	0.33	0.42 (0.79)	0.53	0.59
CES-D[d]						
Pretest to post-test 1	-4.21 (1.11)	-3.81	0.0002	-6.76 (1.57)	-4.31	<0.0001
Post-test 1 to post-test 2	-0.66 (1.11)	-0.59	0.55	2.44 (1.59)	1.53	0.13
Secondary outcome measure						
GAD-7[e]						
Pretest to post-test 1	-0.90 (0.51)	-1.77	0.08	-3.42 (0.72)	-4.75	<0.0001
Post-test 1 to post-test 2	-0.43 (0.52)	-0.83	0.41	0.86 (0.73)	1.17	0.24

[a] *b* = unstandardized coefficient [b] t-test statistic, [c] *PHQ-9* = Patient Health Questionnaire 9, [d] *CES-D* = Center for Epidemiologic Studies Depression Scale, [e] *GAD-7* = Generalized Anxiety Disorder 7.

In the intervention group, significantly more participants improved (reliable change index score less than –1.96) than in the control group ($p = 0.003$ for PHQ-9; $p = 0.001$ for the CES-D; Appendix 3). Sixty-two percent of participants scored above the cutoff on the PHQ-9 at pretest and were considered to be clinically depressed and 55% of participants scored above the cutoff on the CES-D. The proportion of participants who scored above the cutoff at pretest and recovered was significantly higher in the intervention group than in the control group ($p = 0.005$ for PHQ-9; $p = 0.001$ for the CES-D). A higher proportion of participants reached the criteria for clinically significant change (both recovery and improvement) in the intervention group than in the control group on PHQ-9 ($p = 0.005$) and CES-D ($p < 0.0001$; Appendix 3). Deterioration was rare and no significant differences were identified between the groups for the PHQ-9 (χ^2 1.35, $p = 0.25$) or CES-D (χ^2 3.42, $p = 0.06$). The number needed to treat was 3.30 for the PHQ-9 and 2.20 for the CES-D (Appendix 3).

Most participants were satisfied with the intervention (mean overall score 7.34 (*SD* = 1.62); n = 74). Of the 74 patients who graded the intervention at post-test 1, 55 participants (74%) would definitely recommend the intervention to others, 18 (24%) would maybe recommend it, and one (2%)

would not recommend the intervention. The mean score for the coach was 7.62 (*SD* = 1.52; n = 146): 7.92 (*SD* = 1.31) in the intervention group compared with 7.32 (1.66) in the control group (*p* = 0.02). No adverse events were reported.

Table 3. Mixed model analyses investigating the effects of the intervention on short-term and long-term depressive and anxiety symptoms in the intervention group

	b[a] (SE)	t[b]	*P*	Cohen's d (95%CI)
Primary outcome measures				
PHQ-9[c]				
Pretest to post-test 1	-3.75 (0.41)	-9.17	<0.0001	-0.79 (-1.02, -0.56)
Post-test 1 to post-test 2	-0.30 (0.37)	-0.80	0.43	-0.06 (-0.26, 0.14)
Post-test 2 to post-test 3	0.20 (0.46)	0.44	0.66	0.04 (-0.16, 0.24)
CES-D[d]				
Pretest to post-test 1	-7.56 (0.84)	-9.03	<0.0001	-0.72 (-0.94, -0.50)
Post-test 1 to post-test 2	0.60 (0.74)	0.81	0.42	0.06 (-0.14, 0.26)
Post-test 2 to post-test 3	0.02 (0.91)	0.02	0.99	0.002 (-0.20, 0.20)
Secondary outcome measure				
GAD-7[e]				
Pretest to post-test 1	-2.63 (0.38)	-6.91	<0.0001	-0.56 (-0.77, -0.34)
Post-test 1 to post-test 2	0.04 (0.34)	0.12	0.91	0.01 (-0.19, 0.21)
Post-test 2 to post-test 3	-0.22 (0.42)	-0.53	0.60	-0.05 (-0.25, 0.15)

[a] *b* = unstandardized coefficient [b] t-test statistic, [c] *PHQ-9* = Patient Health Questionnaire 9, [d] *CES-D* = Center for Epidemiologic Studies Depression Scale, [e] *GAD-7* = Generalized Anxiety Disorder 7.

Discussion

We found that a guided internet-based self-help intervention was effective for decreasing depressive symptoms in people with HIV compared with an attention-only control condition. Significantly more participants in the intervention group than in the control group had a clinically significant reduction in depressive symptoms. Additionally, anxiety symptoms decreased in the intervention group compared with the control group and user satisfaction was high. The results of this study are important, since only four previous studies have investigated the effectiveness of computerised or internet-based interventions for people with HIV, and three (10-12) of those studies found that the intervention had no effect on mood. This is the first randomized controlled trial to show that an internet-based intervention for people with HIV can significantly reduce depressive symptoms. Our results add to previous findings that online interventions for depression could be effective for the general population (7) and for people with a chronic somatic disease (8). In this study, the between-group effect sizes for depressive symptoms on the first post-test were larger than reported in previous research (7, 8).

Furthermore, the long term effect of the intervention on mental health was found to be enduring. The follow-up period in the present study was six months in the intervention group and three months in the control group; thus longer follow-up measurements are necessary.

Depressive symptoms were also reduced in the control group, and participants appreciated the coaching and graded the coaches highly. The weekly telephone contact with coaches might lead to a decrease in depressive symptoms, as reported previously (33). Furthermore, the coach also seemed important in the intervention group. Participants were satisfied with the coaching and this component of the intervention was made feasible because the coaches were Masters students and graduates in clinical psychology. Thus, this method of coaching could be used when implementing the intervention. Additionally, nurses in HIV treatment centers could also be trained to provide the coaching to increase scalability of the intervention.

The current study has important strengths and limitations. This randomized controlled trial was well designed and included a large sample of people with HIV treated at 23 of 26 HIV treatment centers in the Netherlands. Additionally, the intervention was designed specifically for individuals with HIV and was done online, which has advantages compared with face-to-face treatment, such as more people can be reached and stigma might be lessened. Furthermore, the intervention is available in Dutch and English and could be translated into other languages for use in other countries. Both the PHQ-9 and CES-D questionnaires were used to increase the strength of the findings and because they were recommended for people with HIV (34). The results of the PHQ-9 and CES-D questionnaires were comparable, which increases confidence in our results. The primary outcome was analysed in the intention-to-treat population. The number of patients who had not started or had dropped out at the first post-test was high (22 individuals in the intervention group and 14 individuals in the control group), which is a limitation of the study. However, internet-based interventions often have high dropout rates (7, 8). In the current study, no differences in baseline characteristics were identified between participants who dropped out and those who completed the intervention, which indicates that none of the characteristics assessed in this study were associated with dropout and that the results might be generalised. Only self-report measures were used, instead of other measures such as interviews, which can be used for diagnostic purposes. However, a diagnosis of depression was not an inclusion criterion in the current study and interviews would have been time consuming. Additionally, participants in the intervention group might have met participants in the control group and shared their experiences. However, since participants lived in various locations across the Netherlands we expect that this would be unlikely. Waiting-list control conditions might inflate the effects of interventions in studies and it is possible that this occurred in the current study. We used an attention-only waiting-list control condition, which is more active than a waiting-list only control and might have reduced the inflation. An additional limitation is that the intervention was developed by the

researchers. Every effort was made to avoid contact with participants after allocation to conditions. We recommend independent replication of this study. Our findings might not be generalizable to all people with HIV in the Netherlands. However, given that almost all HIV treatment centers in the Netherlands participated and there were no baseline differences between patients who dropped out and those who completed the study, the HIV population in our study is representative of the HIV population in the Netherlands (regarding characteristics such as sex, sexual orientation, and education). Study generalizability to non-western, low-income countries deserves further study.

For future research, it is important to investigate moderators and mediators of treatment effect to identify the subgroups for whom this intervention is the most optimal and the mechanisms that make this intervention effective. It would be valuable to investigate the cost-effectiveness of the intervention. Furthermore, the intervention could be implemented and the long-term effectiveness should be studied. HIV is highly prevalent in other parts of the world, such as Africa, and the intervention could be adapted to the local culture of these countries and its effectiveness could be investigated there.

In conclusion, this randomized controlled trial found that the guided internet-based intervention Living positive with HIV might be effective in decreasing depressive symptoms in the short-term and the long-term up to six months. Anxiety was reduced after the intervention, and the intervention and the coach were mostly positively evaluated. This new, online intervention might represent a clinically meaningful enhancement to psychological care for individuals with HIV who have depressive symptoms. Our findings suggest that implementation of the intervention including coaching might be justified in the Netherlands.

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Appendix

Appendix 1. Overview of assessments during the study

Assessment	Screening HIV treatment centers	Screening researchers	Pretest	Post-test 1	Post-test 2	Post-test 3[a]
PHQ-2[b] or HADS[c]	X					
PHQ-9[d]		X	X	X	X	X
CES-D[e]			X	X	X	X
GAD-7[f]			X	X	X	X
Demographics and HIV questionnaire			X			
User satisfaction				X		

[a] Not sent to participants in the control group, [b] *PHQ-2* = Patient Health Questionnaire-2, [c] *HADS* = Hospital Anxiety and Depression Scale, [d] *PHQ-9* = Patient Health questionnaire-9, [e] *CES-D* = Center of Epidemiologic Studies Depression Scale, [f] *GAD-7* = Generalized Anxiety Disorder-7.

Appendix 2. Estimated means and standard deviations on the PHQ-9, CES-D and GAD-7 over time in the intervention and control group

Measure and time point		Intervention group (n = 97)		Control group (n = 91)	
		M	***SD***	***M***	***SD***
PHQ-9[a]					
	Pretest	11.74	2.49	11.11	2.37
	Post-test 1	6.73	3.00	8.60	3.12
	Post-test 2	6.62	3.03	8.06	3.17
	Post-test 3[b]	7.18	3.45		
CES-D[c]					
	Pretest	24.91	5.93	22.94	6.48
	Post-test 1	13.94	6.39	19.09	7.05
	Post-test 2	15.71	6.39	18.43	7.05
	Post-test 3[b]	16.26	7.22		
GAD-7[d]					
	Pretest	9.44	2.59	8.24	2.90
	Post-test 1	5.12	2.77	7.34	3.27
	Post-test 2	5.55	2.77	6.91	3.27
	Post-test 3[b]	5.69	3.18		

[a] = *PHQ-9* = Patient Health Questionnaire 9, [b] Intervention group only, [c] *CES-D* = Center for Epidemiologic Studies Depression Scale, [d] *GAD-7* = Generalized Anxiety Disorder 7.

Appendix 3. Improvement, recovery, clinically significant change, deterioration, and NNT on the PHQ-9 and the CES-D on the first post-test in both groups

Condition	Improvement, n (%)		Baseline clinical case, n (%)		Recovery, n (%)		Clinically significant change, n (%)		Deterioration, n (%)		NNT[a]	
	PHQ-9[b]	CES-D[c]	PHQ-9	CES-D	PHQ-9	CES-D	PHQ-9	CES-D	PHQ-9	CES-D	PHQ-9	CES-D
Intervention	33/64 (52%)	30/64 (47%)	40/65 (62%)	37/65 (57%)	29/39 (74%)	27/36 (75%)	25/39 (64%)	24/36 (67%)	1/64 (2%)	0/64 (0%)	3.30	2.20
Control	21/77 (27%)	15/77 (19%)	56/91 (62%)	49/91 (54%)	21/47 (45%)	15/41 (37%)	16/47 (34%)	9/41 (22%)	4/77 (5%)	4/77 (5%)		

Clinically significant change, deterioration, and number needed to treat were calculated in the per-protocol analysis sample that also completed the first post-test.

[a] *NNT* = number needed to treat, [b] *PHQ-9* = Patient Health Questionnaire-9, [c] *CES-D* = Center for Epidemiologic Studies Depression Scale.

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