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## **Living positive: eHealth for people with HIV and depressive symptoms**

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## **Chapter 6**

# **For whom does online self-help work? Moderators of change in guided online self-help for people with HIV and depressive symptoms**

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Van Luenen, S., Kraaij, V., Spinhoven, P., Dusseldorp, E. & Garnefski, N. For whom does online self-help work? Moderators of change in guided online self-help for people with HIV and depressive symptoms.

## Abstract

**Objective:** The goal of the study was to investigate moderators of intervention effect of a guided Internet-based self-help intervention for people with HIV and depressive symptoms. This study was part of a randomized controlled trial where the intervention was found to be effective in reducing depressive symptoms compared to an attention-only control group.

**Methods:** The intervention consisted of guided online cognitive behavioral therapy. Demographic characteristics (e.g. age), HIV characteristics (e.g. duration of HIV), and psychological characteristics (e.g. coping self-efficacy) were investigated as potential moderators of intervention effect.

**Results:** In 2015, 188 people with HIV and depressive symptoms were included in the study: 97 were randomized to the intervention group and 91 to the control group. One moderator of intervention effect was found: coping self-efficacy. Participants with low coping self-efficacy improved more in the intervention group than in the control group, and participants with high coping self-efficacy improved in both groups.

**Conclusions:** The results indicate that the intervention may be provided to all people with HIV and depressive symptoms. It may be especially important for people with HIV and low coping self-efficacy to start with the intervention, since they do not improve in the control group with only minimal attention.

**Trial registration:** Nederlands Trialregister NTR5407, September 11, 2015.

**Keywords:** HIV; depression; Internet; cognitive behavioral therapy; moderator; randomized controlled trial.

## Introduction

Cognitive behavioral therapy (CBT) is frequently used to treat depressive symptoms in people living with HIV (PLWH). Numerous studies have found that it is an effective therapy for PLWH (1-5). Online treatments may be an alternative to face-to-face CBT, and may be more easily accessible, more cost-effective, and reach more people. A large body of research has found that Internet-based CBT was effective to treat depressive symptoms (6-9). In the last years, we have developed an Internet-based intervention for PLWH with depressive symptoms: Living positive with HIV (10). This CBT intervention was found to be effective in decreasing depressive symptoms in PLWH, compared to a control condition that received attention only (11).

However, we did not examine yet for whom the online intervention is especially effective. It is important to investigate this, as it may inform us which PLWH may benefit most from the treatment and for which PLWH it may be more beneficial to refer them to another treatment (12). Consequently, PLWH may be referred to a treatment that is more likely to decrease their symptoms and this may lead to lower costs, reduced therapy duration, and personalised care. For whom the intervention is most effective can be investigated by examining moderators: factors that influence the effectiveness of treatment (13). For example, it is possible that the intervention works better for men than for women, while in the control condition both men and women do not improve. In this case, sex is the moderator that affects outcome of treatment. Moderators have to be distinguished from general predictors: factors that have an effect on the outcome irrespective of treatment condition (12). A factor can be both moderator and general predictor.

As far as we know, no studies have been conducted in PLWH with depressive symptoms regarding moderators of effects of (online) CBT. Though, moderators of change in face-to-face CBT have been investigated in other patient groups with depression. Marriage, unemployment, and experience of more recent life events predicted superior response to cognitive therapy, compared to antidepressants (14). In a recent meta-analysis, gender was not found to be a moderator of CBT versus pharmacotherapy (15), just as baseline depression severity (16).

There are few studies into moderators of treatment outcome in online CBT for depressive symptoms. One study has found that baseline depression severity was a moderator: for participants with severe depressive symptoms online CBT resulted in a larger improvement than the waiting list control group and for participants with less severe depressive symptoms the differences in improvement between both groups were smaller (17). The same result was found for marital status, where widowed/divorced participants that received online CBT showed the largest improvement (17). Age was also found to be a moderator: for older participants online CBT was more effective, while online interpersonal psychotherapy was more effective for younger participants (18).

The current exploratory study investigated moderators of outcome of the online intervention Living positive with HIV. The first research question of the study was: which factors moderate the effectiveness of the intervention? Since moderators were not previously explored in CBT interventions for PLWH and depressive symptoms, a large selection of moderators was investigated: demographic characteristics (e.g. age), HIV characteristics (e.g. duration of HIV), and psychological characteristics (e.g. coping self-efficacy). The second research question of the study was: which subgroups of participants benefit most from the intervention? To answer this question, interactions between multiple moderators and the treatment variable were examined.

## Methods

### Participants and procedure

This study is based on a randomized controlled trial (RCT) on the effectiveness of the CBT-based online self-help intervention 'Living positive with HIV'. The methods of the RCT are explained in more detail elsewhere (10). In 2015, nursing consultants and doctors in 23 of 26 HIV treatment centers in the Netherlands screened PLWH during regular consultations on depressive symptoms with the Patient Health Questionnaire-2 (PHQ-2; (19)). When the PHQ-2 score was > zero, patients interested in the study were informed and their contact information was transferred to the researchers. The researchers called the patients and screened them on the inclusion criteria: being HIV positive for > six months, age > 17 years, mastery of Dutch or English language, available for eight weeks, having Internet and an e-mail address, no use of antidepressants or use for > three months and no change of type or dose in the past three months, absence of severe cognitive impairments, not currently treated by psychologist or psychiatrist, mild to moderate depressive symptoms (Patient Health Questionnaire-9 (PHQ-9 (20) score > 4 and < 20), and no severe suicide ideation (score < 2 on question 9 of PHQ-9).

When patients were eligible for the study and agreed to participate, online informed consent was signed. Thereafter, the pretest was completed and participants were randomly allocated to the intervention or control condition. Stratified randomization by treatment center and sex was conducted. Random number tables were used and the randomization sequence was generated by an independent researcher and concealed from the main researcher. There were multiple measurement moments; the pretest, first post-test (approximately eight weeks after pretest), and second post-test (approximately five months after pretest) were used in the current analyses. Participants received €25 when they completed all questionnaires. The study was approved by the medical ethics committee of Leiden University Medical Center (LUMC; nr. P14.091).

**Study conditions***Guided online self-help intervention*

The online self-help intervention was based on CBT. Four main components were included in the intervention: activation, relaxation, changing negative cognitions, and goal attainment. Participants worked approximately eight weeks on the intervention, one to two hours a week. In addition, they were supported by a personal coach, who called them each week for about 15 minutes until they had finished the intervention (maximum ten weeks). The coach motivated participants to continue with the intervention by using motivational interviewing. Well-being of participants was checked by the coach, as well as progress with the intervention. Coaches were Master students in clinical psychology or graduates with an MSc in psychology. They received a training concerning coaching procedures and they followed a coaching manual. Supervision sessions were arranged with coaches and the researcher in the beginning of the study (later via e-mail and phone).

*Control condition*

Participants in the control condition were put on a waiting list and received attention only. They were called by a personal coach for about five minutes per week during the first eight weeks of the waiting period. The coach asked how the participant was doing, enhanced motivation to stay in the study, and monitored depressive symptoms. Part of the protocol was to refer the participant to the HIV treatment center or general practitioner when symptoms deteriorated and became severe. Participants gained access to the intervention after post-test 2.

**Assessments**

All assessments were completed online. Potential moderating variables were measured at pretest and the outcome variable was measured at pretest, post-test 1 and post-test 2. For more information on the assessments, see (10).

*Outcome variable*

Depressive symptoms in the last two weeks, measured by the PHQ-9 (20), was the outcome variable. Higher scores indicate more depressive symptoms and total scores range from 0 to 27.

*Potential moderators***Demographic characteristics**

The following questions were asked regarding demographic characteristics: sex, age, education, marital status, and employment status.

### ***HIV characteristics***

Regarding HIV characteristics the following questions were asked: physical symptoms in last two weeks, diagnosis of AIDS, use of antiretroviral therapy (ART) known to have depression as side effect based on the *Farmacotherapeutisch Kompas* (Farmacotherapeutic Compass (21)). Data on the duration of HIV of participants was obtained from the Athena/SHM Cohort Study (22) after consent from the participant. The ATHENA Cohort Study is maintained by the Stichting HIV Monitoring, which is supported by the Dutch Ministry of Health via the National Institute for Public Health and Environment (RIVM).

### ***Psychological characteristics***

*Treatment for psychological symptoms.* Two questions were asked about treatment for psychological symptoms: use of psychotropic medication and treatment for psychological symptoms in last five years.

*Depressive symptoms at pretest.* The PHQ-9 score at pretest was included as potential moderating variable.

*Anxiety symptoms.* The Generalized Anxiety Disorder-7 (GAD-7) (23) was used to measure symptoms of anxiety in the last two weeks. Total scores range from 0 to 21 and higher scores represent more anxiety symptoms.

*Coping self-efficacy.* Self-efficacy to cope with having HIV was measured with an adapted version of the Generalized Self-Efficacy scale, which has good reliability and validity (24). The scale was adjusted for PLWH, Cronbach's  $\alpha$  at pretest for the adjusted scale was 0.92. Total scores range from 8 to 40 and higher scores indicate more self-efficacy to cope with having HIV.

*Use of alcohol, soft drugs, hard drugs, and sedatives.* The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (25) was used to measure psychoactive substance use (alcohol, soft drugs, hard drugs, and sedatives/sleeping pills) and related problems. Total scores for each substance range from 0 to 39. For alcohol, a total score of zero to ten indicates that no intervention is needed (i.e. no problematic alcohol use), and a score > ten indicates that an intervention is needed (i.e. problematic alcohol use). For soft drugs, hard drugs, and sedatives, a total score of zero to three indicates that no intervention is needed (i.e. no problematic drug use), and a score higher than three indicates that an intervention is needed (i.e. problematic drug use). The categorical variables with two categories (no intervention needed; intervention needed) were used in the moderator analyses.



*Depressive thoughts.* The hopelessness subscale of the Crandell Cognitions Inventory (CCI) (26) was used to measure depressive thoughts. Total scores range from 7 to 35 and higher scores reflect more black and white depressive thinking.

*Physical tension.* Physical tension was measured with a self-designed 10 item questionnaire. Questions were asked regarding difficulty to relax, ways to relax, and symptoms of physical tension. Total scores range from 10 to 30 and higher scores indicate less physical tension.

*Behavioral activation.* The subscale activation of the Behavioral Activation for Depression Scale (BADSD) (27) was used to measure behavioral activation during the past week. Total scores range from 0 to 42 and higher scores reflect higher levels of activation.

*Life events.* The number of life events that a participant had ever experienced was measured with the Life Events Scale (28). The scale consists of 17 negative life events and it was counted how many life events (e.g. divorce, dead of a loved one) a participant experienced during life.

### **Statistical analysis**

Analyses were conducted in SPSS version 23 and R version 3.2.2. SPSS was used to answer the first research question regarding moderators<sup>1</sup> of intervention effect. In SPSS, longitudinal multilevel moderated regression analyses (LMRA) (31) were conducted. Time, Group, moderators, and interactions were included as fixed effects and slopes for Time and the intercept were included as random effects. Two time contrasts were created: short term (pretest to post-test 1) and long term (pretest to post-test 2). Continuous moderator variables were grand mean centered and moderators were individually included in the model. All two-way and three-way interactions were included in the model. When the interaction Time x Group x Moderator was significant, this indicated a moderator effect. The moderator depressive symptoms at pretest was not included in the SPSS analysis, because it was part of the dependent variable. Maximum likelihood estimation was used to estimate the effects in the model. The variance components covariance structure provided the best fit and was chosen for the analyses. The analysis was intention-to-treat (ITT) and  $\alpha = 0.05$  was used for significance testing.

The second research question regarding subgroups of participants that benefit most from the intervention was answered with an analysis in R. It was conducted with the method Qualitative Interaction Trees (QUINT), using the corresponding R-package QUINT (32, 33). The aim of QUINT is to

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<sup>1</sup> Moderators are called predictive factors in medicine and general predictors are called prognostic factors (29, 30).

identify three subgroups of participants, based on different combinations of certain participant characteristics at baseline (i.e. moderators). For the first subgroup the intervention is more effective than the control condition, for the second subgroup the control condition is more effective than the intervention, and for the optional third subgroup both conditions are equally effective. The subgroups are to be found by splitting on values of moderators. QUINT has some advantages; multiple moderators can be included in the analysis at the same time, without a priori specifying which moderators interact and which type of interaction (as opposed to linear regression, where interactions are pre-specified and usually only first order interactions, also called two-way interactions, are included). In this way, higher order interactions can be detected, and QUINT may identify subgroups for which the direction of the intervention effect is different. The created subgroups are graphically represented in a binary tree with nodes and leaves that is easy to interpret. The QUINT algorithm starts with all participants in the root node. Then a moderator is searched that has the largest intervention-subgroup interaction. All moderators, possible split points on moderators, and possible assignments of leaves to the subgroups are considered. Then, the node splits into two child nodes (leaves) based on the best combination of moderator, split point, and assignment. Thereafter, the child nodes split again, etc. QUINT uses some criteria to stop the tree building process, e.g. the number of participants in a leaf should be large enough (for more information see (32)). The whole procedure may result in a large and complex tree which also models noise in the data, and may not fit future data. QUINT reduces this overfitting by pruning the tree back to an optimal subtree, using bias-corrected bootstrapping.

In QUINT analyses, type of partitioning criterion was set at effect size criterion, and the minimum absolute value of  $d$  (effect size) in each of two leaves after the first split ( $d_{min}$ ) was set at 0.40 (as suggested by (32)). Minimal sample size of a group in a leaf was 10, and number of bootstrap samples was 1000. Two analyses were conducted. First, PHQ-9 pretest minus PHQ-9 post-test 1 was used as outcome variable, and Group and all moderators were included in the formula. Second, PHQ-9 pretest minus PHQ-9 post-test 2 was used as outcome variable, and Group and all moderators were included. The analysis in QUINT was based on participants that completed questionnaires at post-test 1 or post-test 2.

## Results

### Participants

In HIV treatment centers 3642 PLWH were screened on depressive symptoms, of which 445 were referred to and screened by the researchers. One hundred and eighty eight PLWH participated in the study: 97 in the intervention group and 91 in the control group. The first post-test was completed by 75 participants (77%) in the intervention group and 77 (85%) in the control group and the second post-

test was completed by 64 participants (66%) in the intervention group and 67 (74%) in the control group. A flow chart of participants through the study including reasons for drop-out is available elsewhere (11).

The majority of participants was male, around 46 years, and had HIV for about ten years, see Table 1. The mean PHQ-9 score was 11.44 at pretest, which indicates moderate depressive symptoms.

**Table 1.** Baseline characteristics of the intervention and control group. Data are provided as M (SD) or n (%).

Characteristic	Intervention group (n = 97)	Control group (n = 91)	Total sample (n = 188)
Sex			
Male	85 (88%)	81 (89%)	166 (88%)
Female	12 (12%)	10 (11%)	22 (12%)
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%)
Employment status			
Employed	52 (54%)	43 (47%)	95 (51%)
Not employed	45 (46%)	48 (53%)	93 (49%)
Diagnosis of AIDS			
No	88 (91%)	77 (85%)	165 (88%)
Yes	9 (9%)	14 (15%)	23 (12%)
Use of ART <sup>a</sup> with side effect depression <sup>b</sup>			
Often	45 (48%)	40 (45%)	85 (46%)
Rarely	27 (29%)	29 (32%)	56 (30%)
Never	22 (23%)	21 (23%)	43 (24%)
Use of psychotropic medication			
No	85 (88%)	81 (89%)	166 (88%)
Yes	12 (12%)	10 (11%)	22 (12%)
Treatment of psychological symptoms last 5 years			
No	47 (48%)	41 (45%)	88 (47%)
Yes	50 (52%)	50 (55%)	100 (53%)
Age (years)	45.53 (10.32)	47.12 (10.94)	46.30 (10.63)

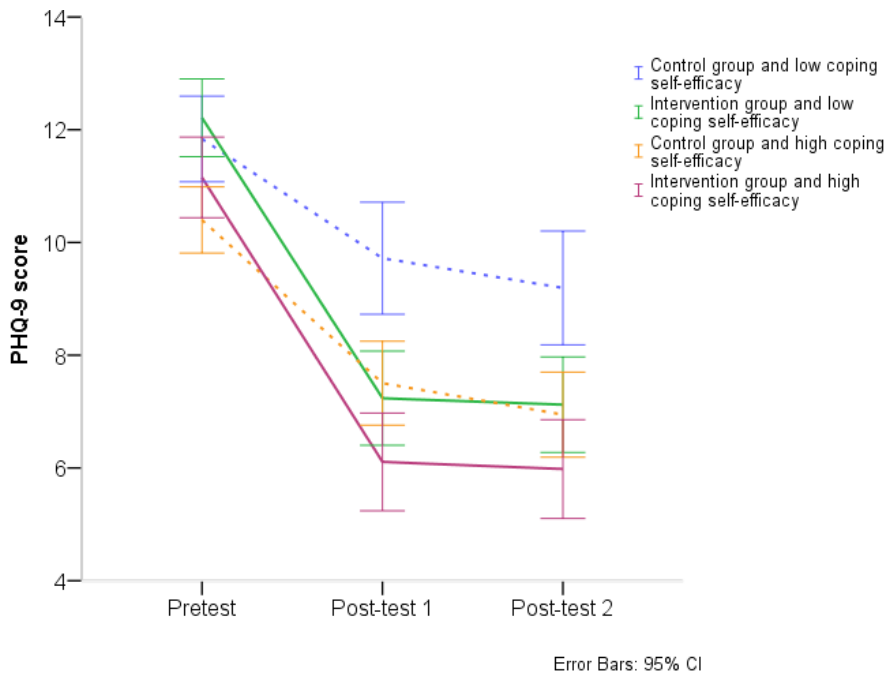
Characteristic	Intervention group (n = 97)	Control group (n = 91)	Total sample (n = 188)
Number of physical symptoms last 2 weeks	9.09 (3.57)	9.44 (3.66)	9.26 (3.61)
Time since HIV diagnosis (years) <sup>c</sup>	9.35 (6.46)	10.41 (6.70)	9.87 (6.58)
Depressive symptoms (PHQ-9 <sup>d</sup> )	11.74 (4.74)	11.11 (4.22)	11.44 (4.50)
Anxiety symptoms (GAD-7 <sup>e</sup> )	9.44 (4.72)	8.24 (4.41)	8.86 (4.60)
Coping self-efficacy	28.63 (6.38)	28.75 (6.02)	28.69 (6.20)
Alcohol use (ASSIST <sup>f</sup> ) <sup>g</sup>	10.29 (8.83)	7.11 (6.74)	8.75 (8.02)
Soft drugs use (ASSIST <sup>f</sup> ) <sup>h</sup>	7.73 (9.19)	6.27 (6.80)	7.00 (8.09)
Hard drugs use (ASSIST <sup>f</sup> ) <sup>i</sup>	8.06 (8.70)	7.96 (9.16)	8.01 (8.87)
Sedatives use (ASSIST <sup>f</sup> ) <sup>j</sup>	6.20 (6.75)	8.64 (9.21)	7.38 (8.09)
Depressive thoughts (CCI <sup>k</sup> )	15.27 (6.44)	15.09 (6.46)	15.18 (6.43)
Physical tension	21.14 (3.64)	21.58 (3.77)	21.36 (3.70)
Behavioral activation (BADs <sup>l</sup> )	18.88 (8.93)	17.90 (8.15)	18.40 (8.55)
Number of life events	5.66 (3.32)	5.18 (3.42)	5.43 (3.37)

<sup>a</sup> ART = antiretroviral therapy, <sup>b</sup> = based on 184 participants that use ART, <sup>c</sup> = available for 187 participants, <sup>d</sup> PHQ-9 = Patient Health Questionnaire-9, <sup>e</sup> GAD-7 = Generalized Anxiety Disorder-7, <sup>f</sup> ASSIST = Alcohol, Smoking and Substance Involvement Screening Test, <sup>g</sup> = based on 169 participants that ever used alcohol, <sup>h</sup> = based on 120 participants that ever used soft drugs; <sup>i</sup> = based on 98 participants that ever used hard drugs; <sup>j</sup> = based on 97 participants that ever used sedatives, <sup>k</sup> CCI = Crandell Cognitions Inventory, <sup>l</sup> BADs = Behavioral Activation for Depression Scale.

### Moderators of intervention effect: results of multilevel moderated regression analyses

Coping self-efficacy was found to be a significant moderator on the short term. Figure 1 displays the moderator effect, with coping self-efficacy based on a median split (i.e. value of 29) for illustrative purposes. The graph shows that participants in the intervention group improved, regardless of level of coping self-efficacy. However, in the control group, participants improved less when they have low coping self-efficacy, compared to high coping self-efficacy. In other words, participants with low coping self-efficacy seem to benefit more in the intervention group than in the control group. No other significant moderators were found, see Table 2.

In addition, to obtain more insight in the influence of coping self-efficacy on the development of depressive symptoms over time, we also inspected whether coping self-efficacy was a general predictor (Time x coping self-efficacy effect). It was not found to be a general predictor on the short term ( $b = -0.07$ ,  $t = -1.15$ ,  $p = 0.25$ ) and on the long term ( $b = -0.07$ ,  $t = -1.00$ ,  $p = 0.32$ ).



**Figure 1.** Coping self-efficacy as moderator of intervention effect.

#### Interactions between moderators: results of QUINT analyses

The results of the QUINT analyses show that no higher order interactions (e.g. three-way or four-way) between moderators and the treatment variable were present. The final pruned tree had two leaves and was split on the variable coping self-efficacy. The results indicate that participants with low/average coping self-efficacy ( $\leq 33.5$ ) showed larger reductions in PHQ-9 score from pretest to post-test 1 in the intervention group than in the control group ( $d = 0.68$ , 95% CI [0.31, 1.05]). Furthermore, for participants with high coping self-efficacy ( $> 33.5$ ), there were no differences between groups ( $d = -0.40$ , 95% CI [-1.28, 0.48]). The analysis with the change score from pretest to post-test 2 as outcome variable yielded the same results.

**Table 2.** Results of LMRA<sup>a</sup> investigating Time x Group x Moderator effects of an Internet-based intervention for PLWH<sup>b</sup> to improve depressive symptoms

Moderator	Short term effect				Long term effect			
	b	t	p	95% CI	b	t	p	95% CI
Sex	-2.43	-1.07	0.29	-6.90, 2.04	1.38	0.56	0.57	-3.44, 6.20
Education <sup>c</sup>	-2.67	-1.31	0.19	-6.68, 1.34	0.08	0.04	0.97	-4.29, 4.45
Marital status	-2.33	-1.52	0.13	-5.35, 0.68	-1.60	-0.98	0.33	-4.84, 1.63
Employment status	-0.17	-0.11	0.91	-3.18, 2.85	2.11	1.30	0.20	-1.09, 5.31
Diagnosis of AIDS	-0.95	-0.40	0.69	-5.64, 3.74	-1.63	-0.65	0.52	-6.61, 3.36
Use of ART <sup>d</sup> with side effect depression <sup>e</sup>	-1.21	-0.62	0.54	-5.07, 2.66	-3.10	-1.50	0.14	-7.18, 0.98
Use of psychotropic medication	-1.35	-0.57	0.57	-6.03, 3.33	-2.08	-0.81	0.42	-7.13, 2.98
Treatment psychological symptoms last 5 years	-2.41	-1.58	0.12	-5.41, 0.59	-2.35	-1.43	0.16	-5.59, 0.90
Age	-0.04	-0.54	0.59	-0.19, 0.11	-0.003	-0.04	0.97	-0.16, 0.16
Number of physical symptoms last 2 weeks	0.29	1.38	0.17	-0.13, 0.71	0.21	0.90	0.37	-0.25, 0.68
Time since HIV diagnosis	0.01	0.09	0.93	-0.23, 0.25	-0.23	-1.83	0.07	-0.47, 0.02
Anxiety symptoms (GAD-7 <sup>f</sup> )	-0.19	-1.14	0.26	-0.52, 0.14	-0.27	-1.48	0.14	-0.63, 0.09
Coping self-efficacy	0.28	2.26	0.03 <sup>g</sup>	0.04, 0.53	0.26	1.95	0.05	-0.004, 0.53
Alcohol use (ASSIST <sup>h</sup> )	-2.33	-1.30	0.20	-5.86, 1.20	-0.54	-0.28	0.78	-4.35, 3.27
Soft drugs use (ASSIST <sup>h</sup> )	0.08	0.05	0.96	-3.16, 3.32	0.68	0.38	0.70	-2.86, 4.23
Hard drugs use (ASSIST <sup>h</sup> )	-0.16	-0.09	0.93	-3.66, 3.34	0.08	0.04	0.97	-3.75, 3.92
Sedatives use (ASSIST <sup>h</sup> )	-1.84	-1.11	0.27	-5.12, 1.44	-0.75	-0.41	0.68	-4.33, 2.83
Depressive thoughts (CCI <sup>i</sup> )	-0.11	-0.93	0.35	-0.34, 0.12	-0.08	-0.64	0.52	-0.34, 0.17

Moderator	Short term effect			Long term effect		
	b	t	p	b	t	p
Physical tension	0.11	0.55	0.59	-0.07	-0.34	0.73
Behavioral activation (BADSI)	0.09	0.97	0.33	-0.10	-1.02	0.31
Number of life events	0.002	0.01	0.99	-0.10	-0.43	0.67

<sup>a</sup> LMRA = longitudinal multilevel regression analyses, <sup>b</sup> PLWH = people living with HIV, <sup>c</sup> Comparison between low and high education; comparison with medium education provided the same results, <sup>d</sup> ART = antiretroviral therapy, <sup>e</sup> comparison between often and never depression as a side effect of the ART that was used; comparison with sometimes depression as a side effect provided the same results, <sup>f</sup> GAD-7 = Generalized Anxiety Disorder-7, <sup>g</sup>  $p < 0.05$ , <sup>h</sup> ASSIST = Alcohol, Smoking and Substance Involvement Screening Test, <sup>i</sup> CCI = Crandell Cognitions Inventory, <sup>j</sup> BADS = Behavioral Activation for Depression Scale.

## Discussion

The first aim of this study was to investigate moderators of intervention effect of an online CBT intervention for PLWH with depressive symptoms. It has been found previously that this intervention may be effective in decreasing depressive symptoms among PLWH, compared to a control condition that received minimal attention (11). One moderator of intervention effect was found in the current study: coping self-efficacy. Participants with high coping self-efficacy improved on average in both groups, and participants with low coping self-efficacy improved more in the intervention group than in the control group. These results indicate that especially for PLWH with low coping self-efficacy it is important to start with this intervention to decrease their depressive symptoms. The second aim of this study was to investigate which subgroups of participants benefit most from the intervention by examining higher order interactions between moderators and treatment group, and none were found. As coping self-efficacy was found to be a moderator in this analysis, the two analyses yielded similar results.

This study shows that no moderators of intervention effect other than coping self-efficacy were found. The study was conducted to find factors that influence the effect of the intervention, to find out who benefits the most (12). Subgroups of participants that would not benefit from the intervention or would be harmed by the intervention, could be referred to other treatments in the future. Since we only found one moderator of intervention effect and based on the value of this moderator the treatment effect only differed in strength and not in sign, it can be concluded that the intervention could be beneficial for all participants, irrespective of certain demographic characteristics, HIV characteristics, or psychological characteristics. This knowledge is relevant for implementation; the intervention can be offered to all PLWH with mild to moderate depressive symptoms.

Previous studies did not investigate (coping) self-efficacy as moderator, but it has been investigated as general predictor of outcome of CBT for people with depression in three uncontrolled studies (34-36). Two studies have found that self-efficacy is not a general predictor of outcome (34, 35). However, another study has found that coping self-efficacy is a general predictor of outcome of face-to-face and telephone CBT for depression: participants with moderate or high coping self-efficacy were more likely to improve than participants with low coping self-efficacy (36). The current study investigated coping self-efficacy as moderator and general predictor and found that it was a moderator, but not a general predictor.

Some limitations of the study have to be mentioned. This was an exploratory post hoc analysis, so findings need to be interpreted with caution and replicated in future studies. Many possible moderators were investigated in SPSS, which is a strength, but the disadvantage is that some moderators may be found which may not all be 'real' moderators (type I error). However, the analysis



was exploratory and an additional analysis was conducted in QUINT where all moderators were included in one model. Furthermore, the analysis in SPSS was ITT, but the analysis in QUINT was with participants that completed questionnaires at the post-tests and there was some drop-out. Yet the results of both analyses support each other. In addition, there was no follow-up more than three months in the current study. It is possible that moderator effects will be evident on the long term, this needs to be investigated in future research.

To conclude, this study found one factor that influenced the effectiveness of the intervention: coping self-efficacy. PLWH with high coping self-efficacy improved in both groups, and PLWH with low coping self-efficacy improved more in the intervention group than in the control group. This indicates that it may be particularly important to provide the intervention to PLWH with low coping self-efficacy, as they do not improve with minimal attention only. When these findings are confirmed in future studies, it may be recommended to screen PLWH with depressive symptoms on coping self-efficacy before referral to an intervention. The results suggest that the intervention may be provided to all PLWH with mild to moderate depressive symptoms.

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