Living positive: eHealth for people with HIV and depressive symptoms

Luenen, S. van

Chapter 8

Cost-utility of a guided Internet-based intervention in comparison with attention only for people with HIV and depressive symptoms: A randomized controlled trial.

Published as:

Van Luenen, S., Kraaij, V.*, Garnefski, N.*, Spinhoven, P., & Van den Akker, M. E. (2019). Cost-utility of a guided Internet-based intervention in comparison with attention only for people with HIV and depressive symptoms: A randomized controlled trial. *Journal of Psychosomatic Research, 118,* 34-40. Doi: 10.1016/j.jpsychores.2019.01.012. * Shared second authorship.

Abstract

Objective: The aim of this study was to evaluate the cost-utility of a guided Internet-based intervention for people living with HIV and depressive symptoms, compared to attention only (control condition). It was previously found that the intervention was effective in decreasing depressive symptoms, compared to the control group.

Methods: This economic evaluation was conducted alongside a randomized controlled trial. The control group received attention only and was put on a waiting list. Quality adjusted life years were calculated over six months. The study was conducted from a societal perspective and included intervention costs, healthcare costs, and non-healthcare costs. Participants completed a pretest, a post-test after two to three months, and a second post-test after six months. Cost-utility acceptability curves were constructed and two sensitivity analyses were conducted.

Results: No differences between the intervention and the control group were found in quality adjusted life years and total societal costs. The results indicate that the intervention is likely to be cost-effective, compared to attention only. The findings of the sensitivity analyses point in the same direction.

Conclusion: More research with larger samples is necessary to confirm the findings. The outcomes of this study may inform policy makers to decide which interventions will be included in policies. The guided Internet intervention may improve psychological care for people living with HIV and depressive symptoms, against low costs.

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

Keywords: HIV; depression; Internet intervention; cost utility; quality of life; economic evaluation.

Introduction

People living with HIV (PLWH) often suffer from depressive symptoms (1). Next to a negative influence of depressive symptoms on the quality of life of PLWH (2, 3), the symptoms are also associated with high healthcare costs (4-6). These healthcare costs, such as inpatient and outpatient services and use of medication, for PLWH with depression (or other psychiatric diseases) varied a lot between studies, from $17,911 to $33,037 per person per year in the USA between 1995 and 2010 (4-6). In addition to direct healthcare costs, more indirect costs related to losses in productivity from work due to illness may be present. As far as we know, no research is available regarding these indirect costs of PLWH with depressive symptoms. Though, it has been found that the reported annual indirect costs for PLWH, irrespective of depressive symptoms, range from €1,353 per person in 2010 in Italy (7), to €19,786 per person in 2002 in Switzerland (8). For people with depression, irrespective of HIV, the annual indirect costs have been investigated in 2010 in 30 European countries and were found to be €1,782 on average per person (9).

Because of the effect of depressive symptoms on quality of life and the high costs, it is important to treat PLWH. Several psychological interventions were found to be effective in reducing depressive symptoms in PLWH, such as cognitive behavioral therapy (CBT) and mindfulness (10-15). In addition to studying the effectiveness, it is also important to conduct economic evaluations of psychological interventions. Health insurance companies and policy makers are interested in the results of economic evaluations, to decide which interventions will be reimbursed and included in health care policies. Economic evaluations of psychological interventions for PLWH with depressive symptoms are scarce. One study found that collaborative care, including education, activation, and self-management, for depression in PLWH was likely to be cost-effective compared to usual care (16).

Internet-based interventions are used more and more often for people with depressive symptoms. Previous meta-analyses have found that Internet-based interventions are effective to treat depressive symptoms (17-19), also in people with a chronic somatic disease (20). Mixed results were found in previous studies regarding the cost-effectiveness of Internet-based interventions for depression, compared to different conditions. Two systematic reviews have found that guided Internet-based interventions for depression are likely to be cost-effective when compared to wait-list, treatment as usual, attention only, and unguided Internet-based CBT (21, 22). However, the results of an individual-participant data meta-analysis suggested that guided Internet interventions for depression were not cost-effective compared to care as usual, psychoeducation, or wait-list (23). Only a few studies were included in these reviews and meta-analysis, since many RCTs only investigated the effectiveness of Internet interventions, and not their cost-effectiveness. Therefore, more economic evaluations of Internet interventions on depression are needed.

In 2015, we have developed an Internet-based CBT intervention for PLWH with depressive symptoms: Living positive with HIV (24). In a randomized controlled trial (RCT), we have found that the intervention including telephone coaching was effective in reducing depressive symptoms, compared to a control condition that received attention only and was put on a waiting list (25). The aim of the current study was to evaluate the cost-utility of the intervention, compared to attention only. Therefore, an economic evaluation has been conducted alongside the RCT. We expected that effects would be larger in the intervention group compared to the control group. Costs were expected to be lower in the intervention group than in the control group, as intervention costs are low and PLWH in the intervention group will feel better over time, make less use of healthcare services and experience less decreases in productivity at work. The outcomes of this economic evaluation are important for policy makers; when it is found that the intervention is cost-effective compared to attention only, chances are higher that it will be included in health care policies.

Methods

Participants and procedure

This study was part of an RCT with an intervention and a control condition. The methods of this study are explained in detail elsewhere (24). Between February and December 2015, PLWH in 23 of the 26 HIV treatment centers in the Netherlands were screened on depressive symptoms with the Patient Health Questionnaire-2 (PHQ-2) (26) by their nursing consultants and doctors during regular consultations. The PHQ-2 contains the first two questions of the Patient Health Questionnaire-9 (PHQ-9) (27). When patients had a PHQ-2 score > 0 they were informed about the study and referred to the researchers after permission.

Subsequently, the researchers called the patients to inform and screen them on the inclusion criteria of the study: > 17 years old; HIV diagnosis > 6 months; good understanding of Dutch or English; available for eight weeks to work on the intervention; having Internet access and an e-mail address; no severe cognitive impairments; no current treatment from psychologist/psychiatrist; PHQ-9 (27) score > 4 and < 20 (mild to moderate depressive symptoms); PHQ-9 score question nine < 2 (none or few suicidal thoughts); and no use of antidepressants, or use for more than three months without a change in dosage or kind of antidepressants in the past three months. Patients with severe depressive symptoms and/or suicidal thoughts were referred to their general practitioner or nursing consultant/doctor at the HIV treatment center.

When patients were eligible and willing to participate they signed online informed consent. Thereafter, they completed the pretest and were randomly allocated to one of the two conditions. Randomization was stratified by treatment center and gender in blocks of six participants. An

independent researcher used random number tables to create the sequence, which was hidden from the main researcher. When participants were finished with the intervention (maximum ten weeks after the pretest) or after eight weeks in the control group, they received the first post-test. The second post-test was completed three months later. Participants that completed all questionnaires during the study received €25. The study was approved by the medical ethics committee of the Leiden University Medical Center (LUMC; nr. P14.091).

Study conditions

Guided Internet-based intervention

The intervention 'Living positive with HIV' was provided on a secured website. It contains CBT and consists of psychoeducation and exercises. The four main components are activation, relaxation, changing negative cognitions, and goal attainment. The intervention consists of eight lessons, which may be completed in eight weeks, one to two hours per week. In addition, participants received telephone support from a coach of about 15 minutes per week. Participants were asked how they were doing and how they progressed with the intervention. Furthermore, coaches motivated the participant to continue with the intervention by using motivational interviewing. Coaching was provided until participants completed the intervention, with a maximum of ten weeks. Coaches were Master students in clinical psychology or graduates with a Master's degree in psychology. They were trained to provide the coaching and they followed a manual with guidelines. In the beginning of the study, supervision sessions with coaches and the main researcher were arranged (later individual supervision via e-mail and phone).

Control condition

Participants in the control condition received attention only from a coach and were put on a waiting list. The coach called them for about five minutes per week during the first eight weeks of the waiting period. The well-being of participants was checked and they were motivated to continue with the study. When depressive symptoms worsened and became severe, participants were referred to their general practitioner or HIV treatment center. A couple of participants (see Table 1) started with psychological treatment before the first post-test was completed, e.g. treatment from a psychologist or psychiatrist. Participants were invited to start with the intervention after the second post-test. This control condition was different from standard care. PLWH with depressive symptoms in the Netherlands are often treated by a psychologist, psychiatrist, or general practitioner. In addition, mild to moderate depressive symptoms are not always recognized and treated in PLWH. Thus it could also be argued that standard care may be that they would not have received any treatment.

Assessments

All assessments were completed online.

Quality of life

The research question regarding the cost-utility analysis was added in a later stage of the study. Therefore, the PHQ-9 was used to indirectly measure quality of life as it was already included in the assessments to measure depressive symptoms. The PHQ-9 consists of nine items that are scored on a scale from zero to three, and higher scores indicate more depressive symptoms. Psychometric properties of the PHQ-9 are adequate (28). PHQ-9 scores were converted to Short-Form Six-Dimension (SF-6D) utilities (29), using a mapping algorithm. Mapping algorithms transform outcomes of disease specific measures into health-related quality of life utilities. Item specific weightings from the PHQ-9 mapping table of Brazier et al. (2014) (29), were used to convert PHQ-9 item scores to an SF-6D utility. The original PHQ-9 has nine questions and one extra question that is scored differently (If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?). This last question was not included in our assessment. However, to apply the item specific weighting from the PHQ-9 mapping table (29), also the individual score on question ten was needed. Therefore, the mean score of the nine PHQ-9 questions (per participant, per assessment) was used as the score on question ten. Thereafter, the SF-6D utilities were calculated; they range from zero (death) to one (perfect health). With the SF-6D utilities, Quality Adjusted Life Years (QALYs) were calculated over six months with the area-under-the-curve method. Higher QALYs point to more improvement in quality of life. The duration between completing the pretest and the post-tests varied between participants. The mean duration from pretest to post-test 2 was six months, therefore we adjusted all QALYs and costs to a duration of six months.

Costs

The economic evaluation was conducted from a societal perspective and included intervention costs, healthcare costs, and non-healthcare costs (e.g. productivity losses). All costs were adjusted to the year 2017 with the Consumer Price Index (30). The cost-effectiveness of the intervention compared to attention only was not a pre-specified outcome of the RCT. During the study we decided to include this outcome.

Intervention costs

The costs of the intervention consisted of costs for the website, coaching, training, and supervision of coaches. Website costs included costs related to updates, domain, and security. The fixed costs for the development of the website (€13,102) were not included in the analysis. These costs were not included

because they were one-off and they do not play a role when the intervention is further implemented. Coaches received a volunteer fee of €20.13 for the whole trajectory of coaching of one participant in the intervention group, and €12.58 for the whole trajectory of coaching of one participant in the control group. The costs related to training and supervision of coaches included the time investment of the main researcher multiplied by the hourly pay rate of the researcher (€21.00). The total costs for training and supervision were divided by the total number of participants to calculate the costs per participant.

Healthcare costs

Use of healthcare services during the study was measured with the Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness (TiC-P) (31) at post-test 2. This questionnaire measures the amount of visits to healthcare providers (e.g. general practitioner), day treatments, hospital admissions, and medication use since the start of the study (i.e. period of six months). The use of healthcare services was multiplied by the standard costs of these services, according to Dutch tariffs (32). The reference price for a consultation with the general practitioner was for example €33.41, for a session with a physiotherapist €33.41, and for a hospital outpatient doctor visit €92.14. Medication use (including dosage and amount) was multiplied with medications costs (33).

Non-healthcare costs

Non-healthcare costs are related to being absent from work due to illness (absenteeism), being less productive at work due to mental or physical problems (presenteeism), and the inability to perform unpaid work such as domestic tasks or voluntary work due to mental or physical problems. Absenteeism, presenteeism, and the inability to perform unpaid work since the start of the study (i.e. period of six months) were assessed with the TiC-P at post-test 2. The friction cost method was used to calculate costs associated with absenteeism. This method assumes that after a certain period of time (the friction period; 85 days) the productivity loss due to an absent employee should be resolved. The number of hours that one was absent within the friction period was multiplied by the standard productivity costs per hour, based on gender (€38.37 for males and 31.99 for females) (32). The Osterhaus method was used to calculate costs related to presenteeism (31). The productivity loss due to presenteeism (in hours) was calculated by: number of days with productivity losses * number of hours worked per day * one minus the efficiency on these days ranging from zero (could not do anything) to one (able to do as much as normal). The productivity loss due to presenteeism was multiplied by the standard productivity costs per hour, based on gender (32). To calculate costs related to the inability to perform unpaid work, the number of hours that would be spend by others to take

over the work were multiplied by the standard replacement costs for domestic help (€14.17 per hour) (32).

Statistical analysis

The analyses were based on the intention to treat sample. The pretest was completed by 188 PLWH, which were randomized to the intervention group (n= 97) or control group (n = 91). Seventy-five participants (77%) in the intervention group completed post-test 1 and 64 (66%) completed post-test 2. In the control group, 77 participants (85%) completed post-test 1 and 67 (74%) completed post-test 2. The number of participants that completed the TiC-P questionnaire is smaller (n = 38 in the intervention group and n = 41 in the control group), because this questionnaire was added to the assessment at a later stage. We investigated differences in baseline characteristics between the participants that completed the TiC-P and the participants that did not receive the TiC-P. No differences between the groups were found, except on age. Participants that completed the TiC-P had a mean age of 44.09 (*SD* = 9.73) and participants that did not receive the TiC-P had a mean age of 48.75 (*SD* = 10.21).

Missing data were imputed by conducting multiple imputation by chained equations (MICE) in Stata /IC 14.2. A total of 100 imputed datasets were generated, which were pooled according to Rubin's rules (34) for the analyses. Multiple imputation involves filling in the missing values multiple times, creating multiple "complete" datasets. Missing values are imputed based on the observed values for a given individual and the relations observed in the data for other participants, by including the observed variables in the imputation model. The following variables were used in the model: group (intervention or control), age, gender, time since HIV diagnosis, nationality, marital status, sexual orientation, education, AIDS diagnosis, time between pretest and post-test 1, time between pretest and post-test 2, scores on the Crandell Cognitions Inventory (CCI) (35), scores on generalized Anxiety Disorder-7 (GAD-7) (36) questionnaire, scores on relaxation questionnaire (self-designed), SF-6D utilities, and all cost variables. Questionnaire scores on the pretest, post-test 1 and post-test 2 were used as predictors. To assess values to impute, a series of regression models are run whereby each variable with missing data is modeled conditional upon the other variables in the data. This means that for the participants that did not complete the TiC-P, the relation between TiC-P outcomes and age observed in the data for other participants was taken into account by imputing missing values for the individuals without TiC-P data. In this way, MICE reduces bias due to selectively missing values, without ignoring the uncertainty of the imputation.

The cost-utility of the intervention group compared to the control group was evaluated with bootstrapping. A new intervention is cost-effective compared to an alternative when the extra cost of one extra QALY is less than the decision maker's willingness to pay (WTP) for it (37). In the current

cost-utility analysis the WTP was varied from €0 to €100,000. Using Microsoft Excel, 1000 bootstrap samples were created. The net benefit was calculated for different values of WTP for each sample: net benefit = WTP *Δ QALY – Δ total societal costs (37). When the net benefit is > 0, the intervention is cost-effective compared to the control condition for that sample. Thereafter, a cost-utility acceptability curve was constructed, which displays the probability of the intervention being cost-effective compared to attention only for a range of WTP values, i.e. the proportion of bootstrap samples for which the net benefit > 0. Cost-effectiveness is likely when the probability that the intervention is cost-effective is above 0.5 for a given WTP.

Two sensitivity analyses were conducted to investigate the robustness of the results. The first sensitivity analysis included only healthcare costs and no non-healthcare costs. This analysis was conducted to inform policy makers that are mainly interested in the healthcare perspective, instead of the societal perspective. The second sensitivity analysis included antiretroviral therapy (ART) costs on top of the costs of other medication. We expected no differences in use of ART between groups, as they should use ART during their whole life, but conducted this sensitivity analysis to be sure about this.

Results

Sample characteristics

In HIV treatments centers 3642 PLWH were screened, of which 445 were screened by the researchers. Thereafter, 188 PLWH completed the pretest and were randomized. Figure 1 presents a flow chart of participants during various stages in the study.

The majority of the sample was male (n = 166, 88%), and the mean age was 46.30 years (*SD* = 10.63). Ninety-five participants (51%) were employed and participants had HIV for 9.87 years on average (*SD* = 6.58). A minority of the participants had AIDS (n = 23, 12%), 184 (98%) participants used ART, and 22 (12%) used psychotropic medication. Participants suffered from moderate depressive symptoms at baseline (PHQ-9 score: *M* = 11.44, *SD* = 4.50). More information regarding baseline characteristics of the sample can be found elsewhere (25).

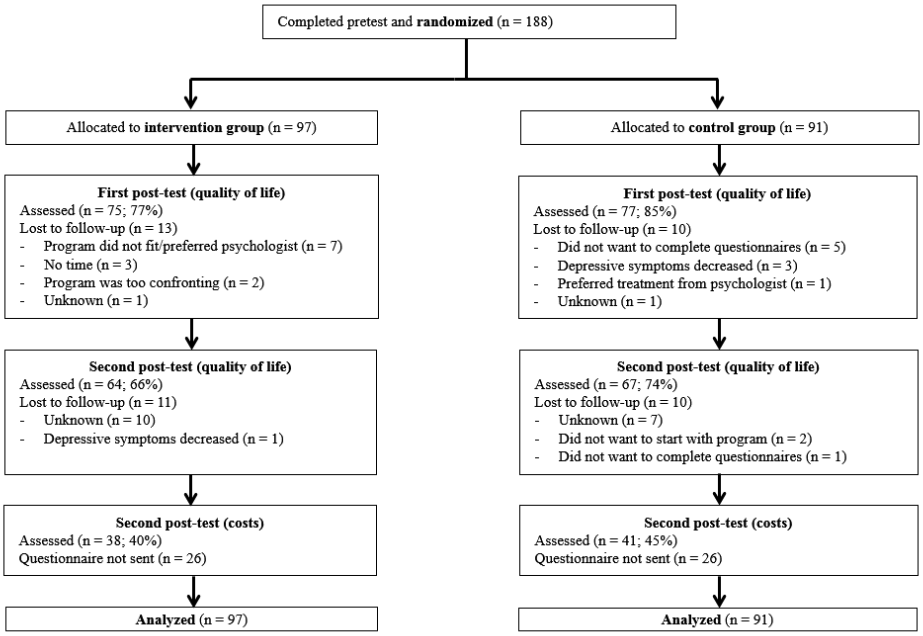

Figure 1. Flow chart of participants in the study.

Quality of life

Figure 2 presents the mean SF-6D utilities over the course of the study. The utilities of the intervention group were significantly higher than the utilities of the control group at post-test 1 (difference: 0.03; 95% CI [0.001, 0.05]). There were no significant differences between groups on the SF-6D utilities at post-test 2. Though, utilities increased from pretest to post-test 2 in both groups. In addition, mean QALYs over the course of the study were 0.34 (SEM = 0.003) in the intervention group and 0.33 (SEM = 0.003) in the control group, with no significant difference between groups (difference: 0.008; 95% CI [-0.0009, 0.018]).

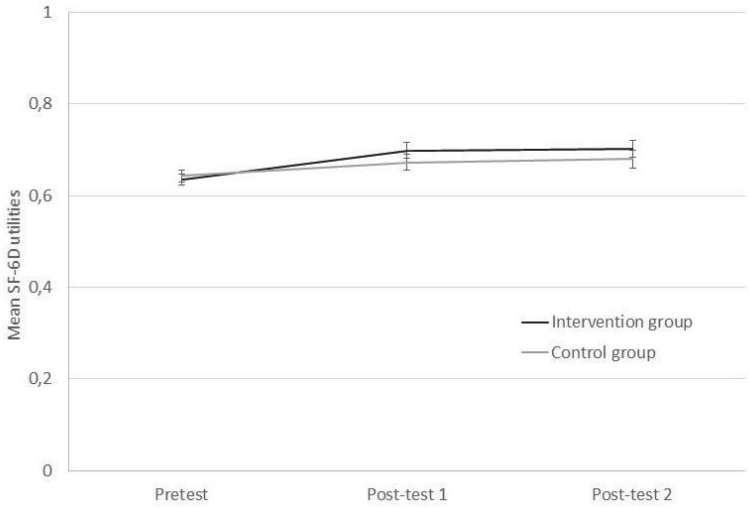

Figure 2. Mean SF-6D utilities over the course of the study in both groups. The data are based on the pooled results of 100 multiple imputed datasets. Error bars: 95% CI.

Costs

Table 1 shows the societal costs, divided into healthcare and non-healthcare costs in both groups. In addition, the number of participants that made use of each item was shown. Except for the costs for the website and the coaching, no significant differences in costs between groups were found.

Cost-utility

Figure 3 presents the cost-utility acceptability curves of the base case analysis and the two sensitivity analyses. The results of the base case analysis indicate that for all values of WTP, the intervention demonstrates a higher probability of being cost-effective, compared to attention only. The cost-utility acceptability curve of the sensitivity analysis with only healthcare costs included shows that for all values of WTP > €5,000, the intervention demonstrates a higher probability to be cost-effective, compared to attention only. Including ART costs in the medication costs, leads to mean additional costs of €2,802 (SEM = 391) in the intervention group and €3,657 (SEM = 442) in the control group, with no significant differences between groups (difference: -856; 95% CI [-2005, 294]). The results of the sensitivity analysis including ART costs indicate that the intervention has a higher probability of being cost-effective for all values of WTP, compared to attention only.

Table 1. Mean healthcare and non-healthcare costs per patient over six months (2017, in €) and the number of participants that made use of each item. The data are based on the pooled results of 100 multiple imputed datasets.

	Intervention group %[a]	Intervention group (n = 97) *M* (*SEM*)	Control group %[a]	Control group (n = 91) *M* (*SEM*)	Difference (95% CI)
Intervention					
Website	100%	3 (0)	-	-	3 (3, 3)[b]
Coaching	100%	20 (0)	100%	13 (0)	8 (8, 8)[b]
Training coaches	100%	3 (0)	100%	3 (0)	0 (0, 0)
Supervision coaches	100%	5 (0)	100%	5 (0)	0 (0, 0)
General practitioner	73%	87 (15)	70%	77 (15)	10 (-30, 49)
Social worker	8%	13 (7)	14%	20 (8)	-7 (-27, 12)
Physiotherapist	20%	62 (23)	18%	62 (24)	-1 (-63, 61)
Ergo therapist	0%	0 (1)	2%	1 (1)	-1 (-3, 2)
Dietitian	0%	0 (0)	2%	1 (1)	-1 (-2, 1)
Homeopath	7%	29 (15)	8%	34 (17)	-5 (-50, 39)
Ambulatory mental health service	6%	22 (13)	3%	6 (6)	17 (-12, 45)
Psychologist / psychiatrist / psychotherapist private practice	16%	78 (30)	13%	75 (37)	3 (-86, 93)
Psychologist / psychiatrist / psychotherapist hospital outpatient department	10%	15 (8)	14%	28 (10)	-13 (-37, 12)
Alcohol and drug rehab clinic	2%	0 (0)	0%	0 (0)	0 (-1, 1)
Self-help group	5%	12 (8)	5%	13 (8)	-2 (-24, 20)
Occupational health doctor	5%	6 (3)	4%	4 (3)	2 (-7, 11)
Domestic help	5%	75 (44)	3%	47 (37)	28 (-80, 135)
Medication[c]	45%	84 (25)	54%	107 (25)	-22 (-91, 46)
Hospital outpatient doctor visit	48%	123 (28)	50%	138 (32)	-15 (-98, 67)
Daycare treatment hospital	5%	29 (17)	5%	26 (17)	3 (-44, 50)

	Intervention group %[a]	Intervention group (n = 97) *M* (*SEM*)	Control group %[a]	Control group (n = 91) *M* (*SEM*)	Difference (95% CI)
Emergency room visit	14%	34 (13)	15%	63 (28)	-28 (-87, 31)
Hospital stay	7%	55 (30)	4%	24 (21)	32 (-37, 100)
Total healthcare costs	**100%**	**757 (103)**	**100%**	**747 (103)**	**11 (-271, 292)**
Absenteeism	15%	250 (123)	15%	362 (159)	-111 (-497, 275)
Presenteeism	23%	519 (264)	31%	907 (377)	-388 (-1229, 452)
Replacement unpaid work	28%	558 (248)	36%	800 (273)	-242 (-931, 446)
Total non-healthcare costs	**52%**	**1327 (394)**	**60%**	**2069 (494)**	**-742 (-1898, 415)**
Total societal costs[d]	**100%**	**2084 (426)**	**100%**	**2815 (517)**	**-731 (-1969, 507)**

[a] percentage of participants that made use of this item; [b] $p < .001$; [c] costs without ART; [d] total societal costs = total healthcare costs + total non-healthcare costs.

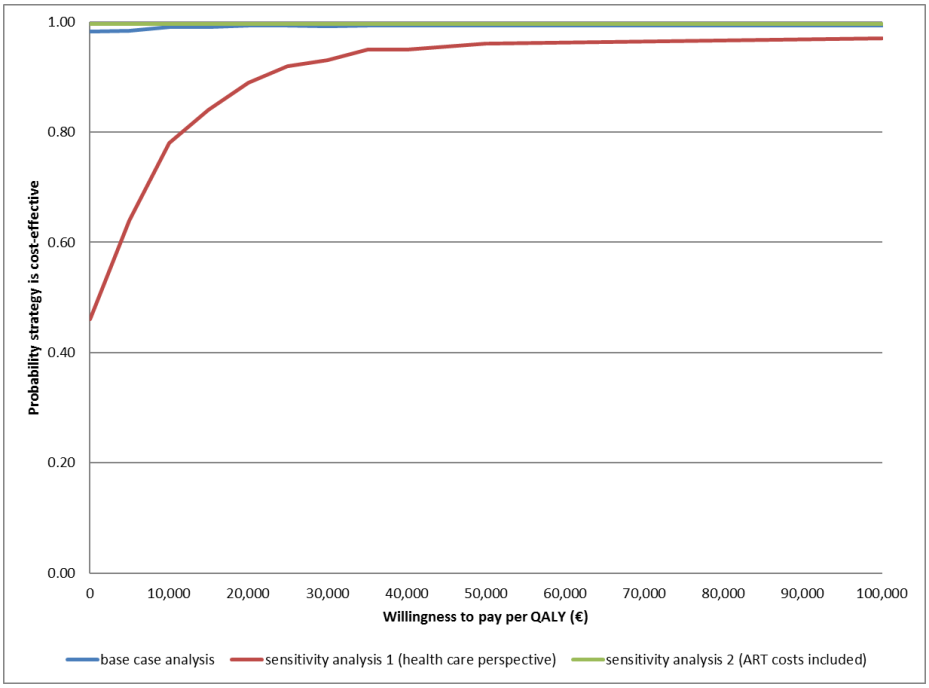

Figure 3. Cost-utility acceptability curves showing the probability that the guided online intervention is cost-effective compared to attention only for different values of willingness to pay.

Discussion

The current study aimed to investigate the cost-utility of a guided online intervention for PLWH with depressive symptoms, compared to attention only. We found no significant difference between groups in QALYs and total societal costs. The results indicate that for all values of WTP, the guided online intervention is likely to be cost-effective compared to attention only. In addition, the results of the two sensitivity analyses point in the same direction.

It has been found previously that collaborative care for PLWH with depressive symptoms was likely to be cost-effective compared to usual care (16). This is in line with our findings. Previous reviews (21, 22) and a meta-analysis (23) found mixed results regarding the cost-effectiveness of Internet interventions for depression, compared to different control conditions. The number of economic evaluations of Internet interventions for depression is small, especially in PLWH with depression. More of these economic evaluations are recommended.

In contrast to expectations, QALYs were not significantly different between groups. QALYs were calculated from the SF-6D utilities, and these were obtained by converting PHQ-9 scores. The SF-

6D is a general measure of quality of life, which also includes e.g. physical functioning. Hence, when PHQ-9 scores are converted into SF-6D utilities, differences between groups on mental health may have been weakened. A difference between groups on the SF-6D (and QALYs) is therefore more difficult to find in evaluating the effect of an intervention specifically targeting mental health. Though, it was previously found that the intervention was effective in decreasing depressive symptoms, compared to the control group (25).

We expected that costs would be higher in the control group than in the intervention group, but we have not found this. Healthcare and non-healthcare costs were not significantly different between groups. It is not clear what the costs would have been when participants would not have received any treatment (no coaching calls and waiting list), because we did not include a no-treatment control group. Furthermore, this study had not enough power to detect differences in costs between groups, because of the wide confidence intervals around the costs. This is the case in many economic evaluations that are conducted alongside clinical trials, because the sample size is too small; the power calculation is based on the clinical outcomes and not on the cost outcomes (38).

This study had some strengths and limitations. An important strength was that we performed an intention to treat analysis, with all participants that were randomized at baseline. Furthermore, the economic evaluation was conducted from a societal perspective and also included non-healthcare costs, in contrast to economic evaluations that only include healthcare costs. Lastly, two sensitivity analyses were conducted and these provided similar results as the main analysis. A first limitation is that there was a lot of missing data, especially on the costs, that needed to be imputed. This is related to the fact that cost-effectiveness was not a pre-specified outcome of the trial. Second, we did not administer the tenth question of the PHQ-9 and therefore the answer to this question was estimated by calculating the mean over the other nine items, before converting PHQ-9 scores into SF-6D utilities. Third, the costs were estimated retrospectively at the second post-test. Participants had to remember their healthcare use and productivity losses during the last six months, which is quite a long period and may have led to recall bias. Last, in the current study the comparison group was an attention only waiting list control condition, instead of usual care. When usual care would be used as comparison group, it may be investigated if the intervention is more cost-effective than usual care. Because of these limitations, the results should be interpreted with caution. Future studies with larger samples can investigate the cost-effectiveness of the intervention, compared to face-to-face interventions (usual care) for PLWH with depressive symptoms. In addition, longer follow-up measurements may be included to study the long term effects and cost-effectiveness of the intervention compared to a control condition.

In conclusion, this study investigated the cost-utility of a guided Internet intervention for PLWH with depressive symptoms, compared to attention only. It was previously found that the intervention

was effective in decreasing depressive symptoms compared to the control group (25). We found no differences between groups in QALYs and total societal costs. However, the results indicate that the intervention is likely to be cost-effective compared to attention only. When future studies find similar results, policy makers may use this information to include the intervention in health care policies. Furthermore, the intervention may be implemented in the healthcare for PLWH with depressive symptoms.

Funding

This study was supported by the Aidsfonds (file number 2013027).

References

1. Evans DL, Charney DS, Lewis L, Golden RN, Gorman JM, Krishnan KR, et al. Mood disorders in the medically ill: scientific review and recommendations. Biol Psychiatry. 2005;58(3):175-89.
2. Williams P, Narciso L, Browne G, Roberts J, Weir R, Gafni A. The prevalence, correlates, and costs of depression in people living with HIV/AIDS in Ontario: Implications for service directions. AIDS Educ Prev. 2005;17(2):119-30.
3. Reis RK, Haas VJ, Santos CBd, Teles SA, Galvão MTG, Gir E. Symptoms of depression and quality of life of people living with HIV/AIDS. Rev Lat Am Enfermagem. 2011;19(4):874-81.
4. Joyce GF, Chan KS, Orlando M, Burnam MA. Mental health status and use of general medical services for persons with human immunodeficiency virus. Med Care. 2005;43(8):834-9.
5. Rothbard AB, Miller K, Lee S, Blank M. Revised cost estimates of Medicaid recipients with serious mental illness and HIV-AIDS. Psychiatr Serv. 2009;60(7):974-7.
6. DeLorenze GN, Tsai A-L, Horberg MA, Quesenberry CP. Cost of care for HIV-infected patients with co-occurring substance use disorder or psychiatric disease: report from a large, integrated health plan. AIDS Res Treat. 2014;2014.
7. Trapero-Bertran M, Oliva-Moreno J. Economic impact of HIV/AIDS: a systematic review in five European countries. Health economics review. 2014;4(1):15.
8. Sendi P, Schellenberg F, Ungsedhapand C, Kaufmann GR, Bucher HC, Weber R, et al. Productivity costs and determinants of productivity in HIV-infected patients. Clin Ther. 2004;26(5):791-800.
9. Olesen J, Gustavsson A, Svensson M, Wittchen HU, Jönsson B. The economic cost of brain disorders in Europe. Eur J Neurol. 2012;19(1):155-62.
10. Crepaz N, Passin WF, Herbst JH, Rama SM, Malow RM, Purcell DW, et al. Meta-analysis of cognitive-behavioral interventions on HIV-positive persons' mental health and immune functioning. Health Psychol. 2008;27(1):4-14.
11. Brown JL, Vanable PA. Cognitive-behavioral stress management interventions for persons living with HIV: a review and critique of the literature. Ann Behav Med. 2008;35(1):26-40.
12. Himelhoch S, Medoff DR, Oyeniyi G. Efficacy of group psychotherapy to reduce depressive symptoms among HIV-infected individuals: a systematic review and meta-analysis. AIDS Patient Care STDS. 2007;21(10):732-9.
13. Sherr L, Clucas C, Harding R, Sibley E, Catalan J. HIV and depression--a systematic review of interventions. Psychol Health Med. 2011;16(5):493-527.
14. Spies G, Asmal L, Seedat S. Cognitive-behavioural interventions for mood and anxiety disorders in HIV: a systematic review. J Affect Disord. 2013;150(2):171-80.
15. van Luenen S, Garnefski N, Spinhoven P, Spaan P, Dusseldorp E, Kraaij V. The Benefits of Psychosocial Interventions for Mental Health in People Living with HIV: A Systematic Review and Meta-analysis. AIDS Behav. 2018;22(1):9-42.
16. Painter JT, Fortney JC, Gifford AL, Rimland D, Monson T, Rodriguez-Barradas MC, et al. Cost-Effectiveness of Collaborative Care for Depression in HIV Clinics. J Acquir Immune Defic Syndr. 2015;70(4):377-85.
17. Andersson G, Cuijpers P. Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. Cogn Behav Ther. 2009;38(4):196-205.
18. Richards D, Richardson T. Computer-based psychological treatments for depression: a systematic review and meta-analysis. Clin Psychol Rev. 2012;32(4):329-42.
19. Spek V, Cuijpers P, Nyklicek I, Riper H, Keyzer J, Pop V. Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. Psychol Med. 2007;37(3):319-28.
20. van Beugen S, Ferwerda M, Hoeve D, Rovers MM, Spillekom-van Koulil S, van Middendorp H, et al. Internet-Based Cognitive Behavioral Therapy for Patients With Chronic Somatic Conditions: A Meta-Analytic Review. J Med Internet Res. 2014;16(3):e88.
21. Donker T, Blankers M, Hedman E, Ljotsson B, Petrie K, Christensen H. Economic evaluations of Internet interventions for mental health: a systematic review. Psychol Med. 2015;45(16):3357-76.
22. Paganini S, Teigelkötter W, Buntrock C, Baumeister H. Economic evaluations of internet-and mobile-based interventions for the treatment and prevention of depression: A systematic review. J Affect Disord. 2018;225:733-55.
23. Kolovos S, Dongen JM, Riper H, Buntrock C, Cuijpers P, Ebert DD, et al. Cost effectiveness of guided Internet-based interventions for depression in comparison with control conditions: An individual–participant data meta-analysis. Depress Anxiety. 2018;35:209-19.
24. van Luenen S, Kraaij V, Spinhoven P, Garnefski N. An Internet-based self-help intervention for people with HIV and depressive symptoms: study protocol for a randomized controlled trial. Trials. 2016;17(1):1-12.

25. van Luenen S, Garnefski N, Spinhoven P, Kraaij V. Guided internet-based intervention for people with HIV and depressive symptoms: a randomised controlled trial in the Netherlands. The Lancet HIV. 2018;5(9):e488-e97.
26. Kroenke K, Spitzer RL, Williams JBW. The Patient Health Questionnaire-2 - Validity of a two-item depression screener. Med Care. 2003;41(11):1284-92.
27. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9 - Validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606-13.
28. Kroenke K, Spitzer RL, Williams JB, Lowe B. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. Gen Hosp Psychiatry. 2010;32(4):345-59.
29. Brazier J, Connell J, Papaioannou D, Mukuria C, Mulhern B, Peasgood T, et al. A systematic review, psychometric analysis and qualitative assessment of generic preference-based measures of health in mental health populations and the estimation of mapping functions from widely used specific measures. Health technology assessment (Winchester, England). 2014;18(34):vii.
30. Statistics Netherlands. Consumer Price Index: Retrieved from cbs.nl; 2017.
31. Hakkaart-van Roijen L, Straten Av, Tiemens B, Donker M. Manual Trimbos/iMTA questionnaire for Costs associated with Psychiatric illness (TiC-P). Erasmus University Rotterdam: Institute of Medical Technology Assessment (iMTA), 2002.
32. Hakkaart-van Roijen L, Van der Linden N, Bouwmans C, Kanters T, Tan SS. Kostenhandleiding [Cost manual]. Methodologie van kostenonderzoek en referentieprijzen voor economische evaluaties in de gezondheidszorg [Methodology of cost research and reference prices for economic evaluations in healthcare] In opdracht van Zorginstituut Nederland Geactualiseerde versie. 2015.
33. National Health Care Institute. Medicijnkosten [Medicine prices] 2017. Retrieved from medicijnkosten.nl.].
34. Rubin DB. Multiple imputation for nonresponse in surveys: John Wiley & Sons; 2004.
35. Crandell CJ, Chambless DL. The validation of an inventory for measuring depressive thoughts - The Crandell Cognitions Inventory. Behav Res Ther. 1986;24(4):403-11.
36. Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder - The GAD-7. Arch Intern Med. 2006;166(10):1092-7.
37. Hoch JS, Rockx MA, Krahn AD. Using the net benefit regression framework to construct cost-effectiveness acceptability curves: an example using data from a trial of external loop recorders versus Holter monitoring for ambulatory monitoring of" community acquired" syncope. BMC Health Serv Res. 2006;6(1):68.
38. Briggs A. Economic evaluation and clinical trials: size matters: The need for greater power in cost analyses poses an ethical dilemma. BMJ: British Medical Journal. 2000;321(7273):1362-3.