VU VRIJE UNIVERSITEIT AMSTERDAM

VU Research Portal

Happy@Work

Geraedts, A.S.

2014

document version
Publisher's PDF, also known as Version of record

Link to publication in VU Research Portal

citation for published version (APA)
Geraedts, A. S. (2014). *Happy@Work: E-mental health in occupational health care*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Take down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:
vuresearchportal.ub@vu.nl

Download date: 04. Dec. 2024

Chapter 6

Economic evaluation of a Web-based guided self-help intervention for employees with depressive symptoms; results of a randomised controlled trial

Anna S. Geraedts, Johanna M. van Dongen, Annet M. Kleiboer, Noortje M. Wiezer, Willem van Mechelen, Pim Cuijpers, Judith E. Bosmans

Submitted for publication

Abstract

Objectives: To evaluate the cost-effectiveness and return on investment (ROI) of a worker-directed web-based guided self-help intervention compared to care-as-usual for employees with depressive symptoms.

Methods: A total of 231 employees with depressive symptoms were randomised to the intervention (n=116) or care-as-usual group (n=115). The intervention consisted of 6 weekly lessons and was guided by an online coach. Data on depressive symptoms and quality of life were collected at baseline, 8 weeks, 6 months, and 12 months. Data on healthcare utilisation, absenteeism, and presenteeism were collected with retrospective questionnaires over 12 months. Cost-effectiveness and cost-utility analyses were conducted from the societal and employer's perspective. A return-on-investment analysis was conducted from the employer's perspective. Statistical uncertainty was estimated using linear regression in combination with bootstrapping.

Results: At 12-month follow-up, a significant intervention effect on depressive symptoms was found (-2.3, 95% CI: -4.3 to -0.3). At a willingness-to-pay of 0 (€/unit of effect) the intervention's probabilities of cost-effectiveness were 0.62 (societal perspective) and 0.55 (employer's perspective), increasing to 0.95 with an increasing willingness-to-pay (societal perspective: €2,000; employer's perspective: €3,500). There was a 0.63 probability that the intervention resulted in a positive financial return for the employer.

Conclusions: The intervention's cost-effectiveness with regard to depressive symptoms and clinically significant change depends on the willingness-to-pay of societal and company decision-makers as well as the probability of cost-effectiveness that they consider acceptable. The intervention could not be considered cost-effective in terms of QALYs gained and was not cost-saving to the employer.

Introduction

Common mental disorders, such as depression, are highly prevalent in the working population[1] and a major problem in occupational medicine as they are the second most frequent cause of sickness absence in most West European countries [2-4] and in some countries, such as Finland and the UK, even the first [3, 5]. In Europe alone, the annual costs of absenteeism and lost productivity while at work (i.e. presenteeism) due to depression are estimated at €72 billion [6]. This problem is expected to become even more pronounced in the near future since the prevalence of mental disorders is increasing. Depressive disorders are expected to be the leading causes of lost DALYs (Disability Adjusted Life Year) in high-income countries by 2030 [7]. Furthermore, many West European countries are faced with an aging population, leading to a shrinking working population [5], which makes it even more important to keep the working population healthy and economically productive. Innovative and cost-effective solutions for this occupational health problem are, therefore, becoming increasingly important [5].

A possibly effective strategy to reduce sickness absence due to depression in European countries may be the implementation of preventive interventions (i.e. intervening before the employee reports sick from work). Such interventions may prevent worsening of depressive symptoms and may, thus, have the potential to reduce the costs of absenteeism and presenteeism [1, 5, 8]. Using the Internet in the prevention and treatment of health problems (also known as ''e-health'') has been suggested as a useful intervention strategy, since e-health has the potential to be cost-saving due to a more efficient use of resources. On top of that, e-health has many other advantages such as high reach and accessibility [8, 9]. In recent years, both effectiveness and cost-effectiveness studies have shown positive results of such web-based interventions for different (mental) health problems in community and primary care settings [10, 11]. We developed and evaluated a preventive worker-directed web-based guided self-help intervention, of which the effectiveness results have been published elsewhere [13].

Information on the effectiveness of occupational health interventions for mental health problems is of great importance to improve evidence-based medicine. However, since resources to implement such interventions are scarce, information is also needed about their efficiency in terms of their resource implications and benefits in comparison with usual care [14]. Cost-effectiveness analyses (CEAs) and/or cost-utility analyses (CUAs) provide this information [15]. Decision-makers, and particularly employers, may also be interested in the financial return of worker-directed interventions and this can be determined using return-on-investment analyses (ROI analyses). In ROI analyses, the costs of an intervention are compared to its financial benefits. Hereby ROI analyses provide an indication of an intervention's financial profitability [16].

The aim of the present paper was to evaluate the cost-effectiveness and financial return of a worker-directed web-based guided self-help intervention compared to care-as-usual for employees with depressive symptoms who were not on sick-leave. The CEA and CUA were performed from both the societal and employer's perspective. Additionally, a ROI analysis was performed from the employer's perspective only. To our knowledge, this is the first economic evaluation of a web-based intervention in an occupational health setting.

Methods

Study population and design

This economic evaluation was conducted alongside a 12-month randomised controlled trial [17], which took place between 2011 and 2013. The trial included two arms: a worker-directed web-based guided self-help intervention and a Care-As-Usual (CAU) group. The study was approved by the Medical Ethics Committee of the VU University Medical Centre (registration number 2011/2) and registered in the Dutch Trial Register (NTR2993). Participants were recruited at six companies in the Netherlands (two banking companies, two research institutes, one security company, and one university) through banners and digital pamphlets on the company's intranet and via posters. After participants had given informed consent, they received a link to an online questionnaire via e-mail to determine their eligibility. Employees with elevated depressive symptoms (i.e. scoring 16 or higher on the Center for Epidemiologic Studies Depression – scale [CES-D]) who were not on sick-leave were eligible for inclusion. Furthermore, access to the Internet and possession of an e-mail address were required. Participants were excluded if they were using medication for depressive symptoms for less than one month or if they had a legal labour dispute with their employer. Participants were randomised to the web-based intervention or CAU control group at the individual level, in blocks of 4, 6 or 8, and we used stratification at two levels: use of antidepressants (1) and receiving treatment from a psychologist or psychiatrist at study entry (2). An independent researcher created the allocation schedule with a computerised random number generator and participants were informed about their randomisation outcome via e-mail. Due to the nature of the intervention, blinding of participants and investigators was not possible.

Interventions

Happy@Work

The Happy@Work intervention [17] is a brief web-based intervention delivered with minimal guidance. It consists of two evidence-based treatments; Problem Solving Treatment (PST) [18], Cognitive Therapy (CT) [19], and a guideline for employees to help them prevent work-related stress [20, 21]. Happy@Work consists of 6 weekly lessons with an option of one

week extra time in case of delay (i.e. missed deadline for assignments). Each lesson has a different theme, but always follows the same structure: information about the theme, examples, and assignments. The themes were related to PST, CT or work-related problems and contained written material. Participants received feedback on their assignments from a coach. Coaches were trained Master-level students in clinical psychology. All coaches used a protocol-treatment manual and to ensure treatment fidelity, all feedback was reviewed by a supervisor (AG) before it was placed on the website. Happy@Work is a tunnelled intervention which means that participants can solely start with a new lesson after they have received feedback on their assignments from their coach.
At the start of the intervention, an account was generated on the website for each participant by the researchers and a coach was assigned on the website as well. Once the account was generated, an automatically generated e-mail was sent to the participant with a link to activate the account. Participants used their e-mail address and a self-created password to log in once the account was activated. After each lesson, participants received an automatic e-mail with the deadline for the next lesson. E-mail reminders were sent to participants when deadlines were not met.

Care-As-Usual (CAU)
Participants randomised to the CAU group only received an e-mail with the randomisation outcome and were advised to consult their (occupational) physician or a psychologist if they wanted treatment for their depressive symptoms.
Participants in both conditions were free to seek any additional (mental) health care.

Effect measures
Participants completed online questionnaires at baseline (t0), post-treatment (8 weeks, t1), 6 months (t2), and 12 months (t3). These assessments consisted of several questionnaires, assessing the participants' depressive symptoms and quality of life. Furthermore, data on demographic characteristics such as the participants' age, gender, educational level, marital status, nationality, number of weekly working hours, and working days were collected at baseline.

Depressive symptoms
The primary effect measure was the severity of depressive symptoms as measured by the Center for Epidemiological Studies Depression – scale (CES-D) [22]. Its validity has been tested in different populations [23, 24]. The CES-D consists of 20 items and the total score varies between 0 and 60. The Cronbach alpha in this study was .82 [13]. We also calculated clinical significant change (CSC) of depressive symptoms at one-year follow-up in accordance with the method of Jacobson and Truax [25]. This method uses a Reliable Change Index as

an index for improvement and its formula is: baseline score (t0) – 12 month follow-up score (t3) divided by the standard error of the difference between the two test scores. To calculate the standard error of the difference between the two test scores in the formula, the pre-test SD's of the outcome and the reliability of the original questionnaire (0.90) is used [22, 25]. If the outcome of the sum of the Reliable Change Index is above 1.96 this is considered as a significant improvement, because the amount of change is unlikely to have occurred by chance.

QALY

The EQ-5D (EuroQol) [26] was used to calculate quality-adjusted life-years (QALYs) [27]. The EQ-5D is a validated instrument to measure health-related quality of life that consists of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), all of which are rated as causing 'no problems', 'some problems' or 'extreme problems'. The EQ-5D health states were converted to utilities using the Dutch tariff [27]. Utilities represent the desirability of a particular health state on a scale from 0 (death) to 1 (perfect health). Subsequently, QALYs were calculated by multiplying the length of time spent in a particular health state by its utility value [28].

Outcome measures; costs

Intervention costs

Intervention costs consisted of website hosting and maintenance costs as well as labour costs of the coaches. Website hosting and maintenance costs were estimated using invoices of the website host during the trial. The intervention costs were based on completion of all six lessons of the intervention and an average time investment of the coaches of 25 minutes per lesson. The labour costs of the coaches were valued using the salary of a social worker [29]. Intervention costs included VAT (21%) from the employer's perspective, but not when the societal perspective was applied.

Medical costs

A slightly revised version of the Trimbos and iMTA Questionnaire on Costs Associated with Psychiatric Illness (TiC-P) [30] was used at every assessment to collect data on healthcare utilisation. The recall period of all questions covered the time period between two measurement points; i.e. 8 weeks, 4 months, and 6 months. The TiC-P was used to assess the participants' healthcare utilisation, including primary healthcare (health care without referral, e.g. general practitioner), secondary healthcare (health care for which referral is required, e.g. medical specialists, allied health professional, and hospitalisation, or which is paid by the participant, e.g. complementary healthcare), and the use of prescribed medications. Dutch standard costs were used to value healthcare utilisation [29]. If these

were not available, prices according to professional organisations were used. Medication use was valued using unit prices provided by the Dutch Society of Pharmacy [31].

Occupational health costs
Two questions were used to assess the participants' number of visits to an occupational physician and occupational social worker. Occupational health costs were valued using prices according to professional organisations.

Domestic tasks
As it is possible that depressed participants were too ill to perform domestic tasks, the numbers of hours of domestic tasks that they were unable to perform were assessed using the TiC-P. Domestic task costs were subsequently calculated in accordance with the Dutch manual of costing [29].

Absenteeism costs
Sickness absence was measured with the Short Form Health and Labour Questionnaire (SF-HLQ) [30]. Participants were asked to report their total number of sickness absence days between measurement points; i.e. during the past 8 weeks, 4 months, and 6 months. Absenteeism costs were estimated in accordance with the Friction Cost Approach (FCA) for the societal perspective and the Human Capital Approach (HCA) for the employer's perspective. In the FCA, absenteeism costs are truncated to the time-span organisations need to replace a sick worker (i.e. the friction period, which is assumed to be 23 weeks in the Netherlands). Also, when this method was applied, an elasticity factor of 0.8 was applied to account for the fact that a 100% loss of work time was assumed to correspond with an 80% reduction in productivity [32]. According to the HCA, lost productivity costs occur during the whole period that an employee is absent from work. For both methods gender- and age-specific price weights were used for estimating absenteeism costs [29].

Presenteeism costs
Presenteeism was assessed with one item of the WHO Health and Work Performance Questionnaire (WHO-HPQ) [33]. Participants were asked to rate their overall work performance during the previous 4 weeks on an 11-point scale, ranging from ''worst performance'' (0) to ''best performance'' (10). Subsequently, their average work performance during follow-up (*Wown*) was calculated. In the WHO-HPQ, presenteeism is conceptualised as a measure of actual work performance in relation to ''best performance'' (10), irrespective of the presence or absence of health complaints. Therefore, a participant's level of presenteeism (P_{HPQ}) was calculated using the following formula [33]:

$P_{HPQ} = (10\text{-}Wown/10)$

Presenteeism days were calculated by multiplying the participants' P_{HPQ} by their number of days worked during follow-up; i.e. working days minus sickness absence days. Presenteeism was valued using age-and gender-specific price weights [29].

All costs were converted to 2012 Euros using consumer price indices [34]. As the follow-up of the trial was one year, discounting of costs and effects was not necessary [28]. An overview of the price weights used for valuing resource use can be found in Supplemental Table 1.

Statistical analyses

Analyses were performed according to the intention-to-treat (ITT) principle. Baseline characteristics were compared between intervention and CAU group participants as well as participants with complete and incomplete data using Chi-square tests and independent-sample t-tests. Missing data were imputed using multiple imputation. Imputations were performed separately for the intervention and the CAU group. The imputation model included age, gender, number of working hours, and baseline and available follow-up cost and effect measure values. Using Fully Conditional Specification and Predictive Mean Matching, 15 complete data sets were created in SPSS (V20, Chicago IL) (Loss of Efficiency ≤5%). Pooled estimates were calculated according to Rubin's rules [35]. Unless otherwise stated, data were analysed using Stata (V12, Stata Corp, College Station, TX). Statistical significance was set at $p<0.05$.

Supplemental Table 1 Price weights used for the valuation of resource use in the study

Units	Price weight[a]
Intervention costs	235.54[b]
Medical costs	
Visits to a care provider [no. of visits; mean (SD)]	
General practitioner	
Office consultation	29.73
Double office consultation	59.46
Telephone consultation	14.87
House call	45.66
Occupational health	
Occupational physician	62.94[c]
Occupational social work or psychologist	76.99[d]
Allied health professional	
Social work	69.02
Physical therapist	38.23
Dietician	28.67
Primary care psychologist	84.95
Psychologist (private practice)	81.77
Psychologist (mental healthcare institute)	181.59
Other allied health professional	Variable
Medical specialist	
Other medical specialist	76.46
Psychiatrist (private practice)	109.38
Psychiatrist (mental healthcare institute)	183.71
Complementary medicine	48.07
Hospitalisation [no. of days; mean (SD)]	
Day-care hospital	266.54
Day-care rehabilitation centre	126.37
Ward	485.29
Homecare	
Domestic task care	25.49
Personal care	46.72
Medication [no. of participants using; number (%)]	Variable[e]
Productivity costs	
Absenteeism costs	
Sick leave [days; mean (SD)]	Variable[f]
Presenteeism costs	
Presenteeism [score; mean (SD)]	Variable[g]
Domestic task costs	
Domestic task [hour; mean (SD)]	13.27

Abbreviations: no: Number; SD: Standard Deviation
Note: costs are expressed in 2012 Euros
Price weight sources: [a] Prices are based on the Dutch manual of costing unless otherwise specified; [b] Intervention costs from societal perspective. From the employer's perspective costs are €285.00 (including VAT); [c] Based on professional organization prices; [d] Own cost calculation: based on mean costs from visit social work and primary care psychologist based on the Dutch manual of costing; [e] Based on Dutch Society of Pharmacy; [f] Based on friction cost and human capital approach from Dutch manual of costing; [g] Based on calculations with the WHO-HPQ and Dutch manual of costing

Cost-effectiveness analyses (CEA) and Cost-utility analyses (CUA)

Both the CEA and the CUA were performed from the societal perspective (i.e. all costs related to the intervention were taken into account irrespective of who pays or benefits) and the employer's perspective (i.e. only costs relevant to Dutch employers were considered, including intervention, absenteeism, presenteeism, and occupational health costs). Effectiveness at 12-month follow-up was determined using linear regression, adjusted for baseline values. Unadjusted mean cost differences between the intervention and CAU group during follow-up were calculated for total and disaggregated costs. The 95%CIs of these cost differences were estimated by means of Bias Corrected and Accelerated Bootstrap (BCA) intervals, with 5000 replications. In the CEAs and CUAs, seemingly unrelated regression (SUR) analyses were performed to correct for the possible correlation between costs and effects. Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the corrected cost differences by the differences in effects. Bootstrapped incremental cost-effect pairs (CE-pairs) were plotted on cost-effectiveness planes (CE planes) to graphically illustrate the uncertainty surrounding these ICERs [36]. A summary measure of the joint uncertainty of costs and effects was presented using cost-effectiveness acceptability curves (CEACs). These curves show the probability that the Happy@Work intervention is cost-effective in comparison with CAU at different values of willingness-to-pay (i.e. the maximum amount of money decision-makers are willing to pay for an additional unit of effect) [28, 37].

Return-on-investment (ROI) analysis

The ROI analysis was performed from the employer's perspective. Costs were defined as intervention costs and benefits as the difference in total monetised outcome measures between the intervention and CAU group during follow-up (i.e. absenteeism, presenteeism, and occupational health costs). Positive benefits indicate reduced spending. Three ROI-metrics were calculated; 1) Net Benefits (NB), 2) Benefit Cost Ratio (BCR), and 3) Return On Investment (ROI).

NB = Benefits – Costs
BCR = Benefits / Costs
*ROI = ((Benefits – Costs)/Costs)*100*

To quantify statistical uncertainty, 95% bootstrapped confidence intervals were estimated around these measures, using 5000 replications. Financial returns are considered positive if the following criteria are met: NB>0, BCR>1, and ROI>0% [15]. Moreover, the probability of financial return was estimated by determining the proportion of positive bootstrapped financial return estimates.

Sensitivity analyses

To test the robustness of the results, four sensitivity analyses (SA) were performed. First, analyses were performed using the complete cases only from both the societal and employer's perspective (SA1). Second, per-protocol analyses were performed using treatment completers only (i.e. participants who completed more than 50% of the intervention; i.e. 3 lessons) from both the societal and employer's perspective (SA2). Third, due to the lack of overall consensus regarding inclusion of presenteeism costs in economic evaluations [16], analyses from both the societal and employer's perspective were performed in which presenteeism costs were excluded (SA3). Finally, analyses from the societal perspective were performed in which absenteeism costs were estimated using the HCA instead of the FCA (SA4).

Results

Participants

A total of 231 participants were randomised to the intervention (n=116) or the CAU (n=115) group (Supplemental Figure 1). Baseline characteristics are described in Table 1. Participants in the intervention group were more often born outside the Netherlands (7.8%, n=9) than participants in the CAU group (1.7%, n=2; see table 2). Complete follow-up data were available from 54% of the study population on the effect measures (n=125; 60 intervention group, 65 CAU group) and from 46% on the cost measures (n=106; 51 intervention group, 55 CAU group). In the CAU group, participants with complete data had a significantly higher number of working days per week than those with incomplete data (see Table 1).

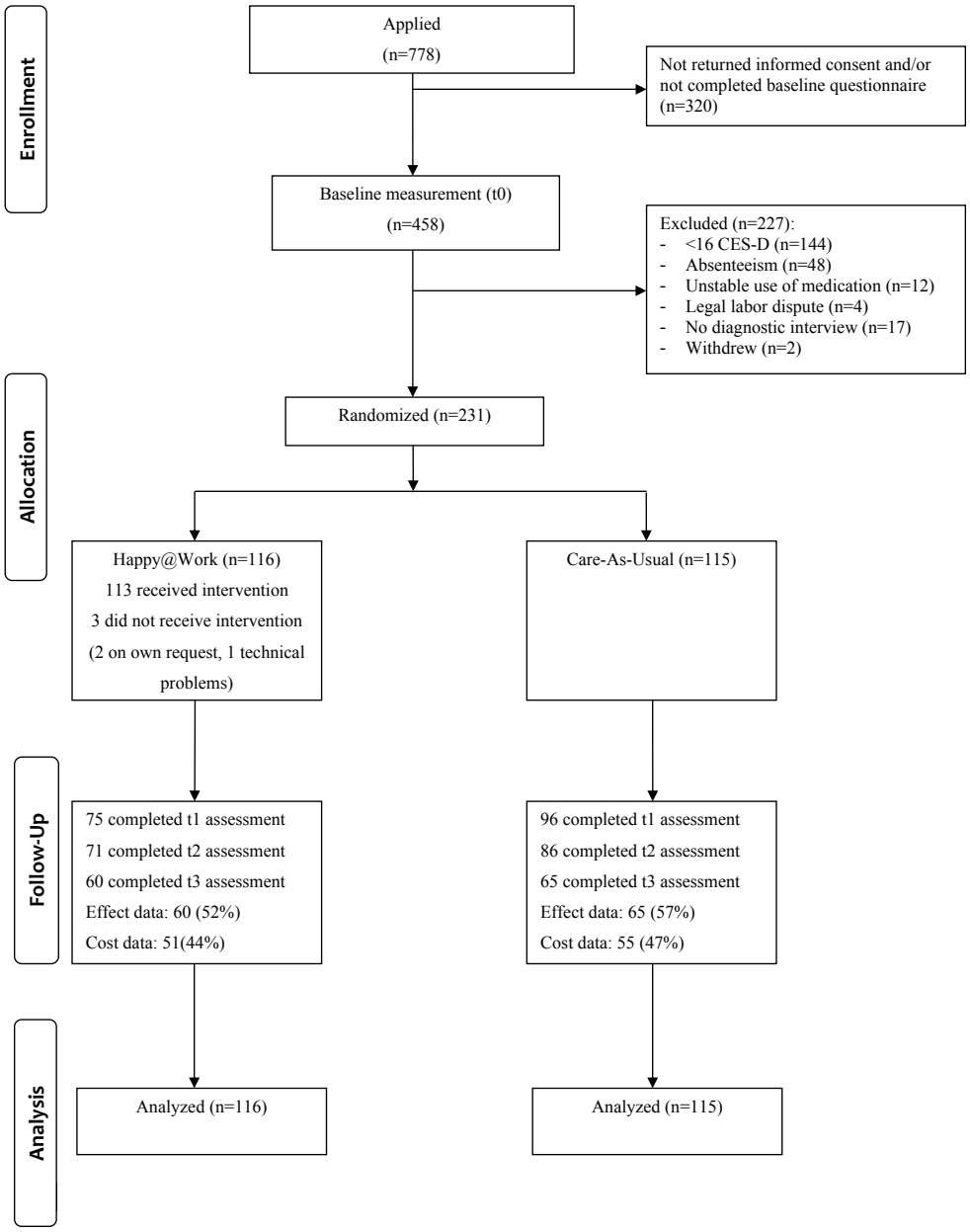

Figure 1 CONSORT flow diagram of participants.

Table 1 Baseline characteristics of the study population

Characteristic[a]	Intervention			Care As Usual		
	All (n=116)	Complete (n=51)	Incomplete (n=65)	All (n=115)	Complete (n=55)	Incomplete (n=60)
Age	43 (8.9)	43.1 (9.0)	43.0 (8.9)	43.8 (9.6)	45.0 (9.9)	42.7 (9.2)
Gender, n (%)						
Female	77 (66.4)	32 (62.8)	45 (69.2)	67 (58.3)	28 (50.9)	39 (65.0)
Male	39 (33.6)	19 (37.3)	20 (30.8)	48 (41.7)	27 (49.1)	21 (35.0)
Country of birth, n (%)*						
Netherlands	107 (92.2)	47 (92.2)	60 (92.3)	113 (98.3)	54 (98.2)	59 (98.3)
Other	9 (7.8)	4 (7.8)	5 (7.7)	2 (1.7)	1 (1.8)	1 (1.7)
Marital status, n (%)						
Relationship	86 (74.1)	41 (80.4)	45 (69.2)	90 (78.3)	44 (80.0)	46 (76.7)
No relationship	30 (25.9)	10 (19.6)	20 (30.8)	25 (21.7)	11 (20.0)	14 (23.3)
Education[b], n (%)						
Low	11 (9.5)	5 (9.8)	6 (9.2)	5 (4.3)	4 (7.3)	1 (1.7)
Middle	31 (26.7)	12 (23.5)	19 (29.2)	37 (32.2)	21 (38.2)	16 (26.7)
High	74 (63.8)	34 (66.7)	40 (61.5)	73 (63.5)	30 (54.6)	43 (71.7)
Working hours[c]	33.7 (4.8)	34.0 (4.5)	33.5 (5.0)	34.0 (5.3)	35.0 (4.5)	33.2 (5.8)
Working days	4.3 (0.6)	4.3 (0.6)	4.4 (0.7)	4.2 (0.7)	4.4 (0.6)	4.1 (0.7)*
Depressive symptoms (range 0-60)	25.7 (7.5)	25.0 (7.4)	26.3 (7.6)	26.1 (7.0)	26.0 (6.5)	26.2 (7.4)
Sickness absence[d]	1.8 (2.7)	1.6 (2.3)	1.9 (2.9)	2.0 (3.3)	1.8 (3.4)	2.1 (3.2)
Work performance (range 0-10)	6.8 (1.3)	6.7 (1.4)	6.8 (1.2)	6.4 (1.5)	6.2 (1.4)	6.5 (1.5)

* Significant at baseline; $p < 0.05$

[a] Characteristics are reported in mean (standard deviations) unless otherwise specified

[b] Low = primary education or lower general secondary education, middle = intermediate vocational education or high school, high = higher vocational education or university

[c] Mean working hours per week according to contract of the participant

[d] Number of sickness absence days during three months before baseline assessment

Effectiveness

At 12-month follow-up, the intervention was statistically significantly more effective than CAU in improving depressive symptoms (-2.3, 95% CI: -4.3 to -0.3). There were no statistically significant differences between the groups in clinically significant change (0.1, 95% CI: 0.0 to 0.2) or QALYs (0.00, 95% CI: -0.04 to 0.04).

Resource use

During the intervention period, 97% of the intervention participants started using the intervention. A total of 67 participants (58%) were considered as being treated per protocol since they completed three or more lessons of the intervention.

Costs

The intervention costs per participant were €236 from the societal perspective and €285 from the employer's perspective (including VAT). Medical and absenteeism costs were higher in the intervention group than in the CAU group, whereas occupational health and presenteeism costs were higher in the CAU group. None of these between-group differences were statistically significant (see Supplemental Table 2).

Supplemental Table 2 Mean costs per participant in the intervention and control group, and unadjusted mean cost differences between both groups during the 12-month follow-up

Cost category	Intervention group n=116; mean (SEM)	Control group n=115; mean (SEM)	Mean cost difference (95%CI)
Societal perspective			
Medical costs	847 (80)	721 (67)	126 (-60 to 354)
Domestic task costs	78 (9)	105 (15)	-27 (-64 to 2)
Occupational health costs	41 (5)	48 (8)	-7 (-30 to 9)
Absenteeism costs	7220 (1774)	6984 (1745)	236 (-4687 to 4932)
Presenteeism costs	13980 (1434)	15259 (1421)	-1278 (-5227 to 2274)
Intervention costs	236 (NA)	0 (NA)	236 (NA)
Total	22402 (1953)	23115 (1357)	-714 (-5018 to 3924)
Employer's perspective			
Occupational health costs	41 (5)	48 (8)	-7 (-30 to 9)
Absenteeism costs	8668 (3083)	8175 (2736)	492 (-7340 to 9187)
Presenteeism costs	13980 (1434)	15259 (1421)	-1278 (-5227 to 2274)
Intervention costs	285 (NA)	0 (NA)	285 (NA)
Total	22974 (3172)	23482 (2314)	-508 (-8080 to 7088)

Abbreviations: CI: Confidence Interval, n: number, NA: Not Applicable, SEM: Standard Error of the Mean
Note: Costs are expressed in 2012 Euros

Societal perspective: CEA and CUA

For depressive symptoms, an ICER of 314 was found (Table 2). This indicates that a 1-point decrease in depressive symptoms was associated with cost savings of €314. Bootstrapped incremental cost-effect pairs were distributed among all four quadrants of the CE plane indicating considerable uncertainty about the ICER (Figure 2). The majority of cost-effect pairs (62.1%), however, were located in the south-eastern quadrant of the CE plane indicating that the intervention was more effective and less costly than CAU. The CEAC in Figure 3 indicates that if societal decision-makers are not willing to pay anything for a 1-point improvement in depressive symptoms, the probability of the intervention being cost-effective in comparison with CAU is 0.62. However, a 0.95 probability of cost-effectiveness can be reached if they are willing to pay €2,000/point improvement. The analysis on clinically significant change resulted in an ICER of -6645, indicating that per extra participant with a clinically

significant improvement in depressive symptoms €6,645 was saved by society (Table 2). A 0.95 probability of cost-effectiveness was reached at a willingness-to-pay of €44,000/per participant with a clinical significant change in depressive symptoms.

The CUA showed that the ICER in terms of QALYs gained was 532,959, meaning that every QALY lost was associated with cost savings of €532,959. This monetary figure is extremely large, because the difference in effect was close to zero (-0.001, 95% CI: -0.04 to 0.04). The maximum probability of the intervention being cost-effective in terms of QALYs gained was 0.62, irrespective of the societal willingness-to-pay.

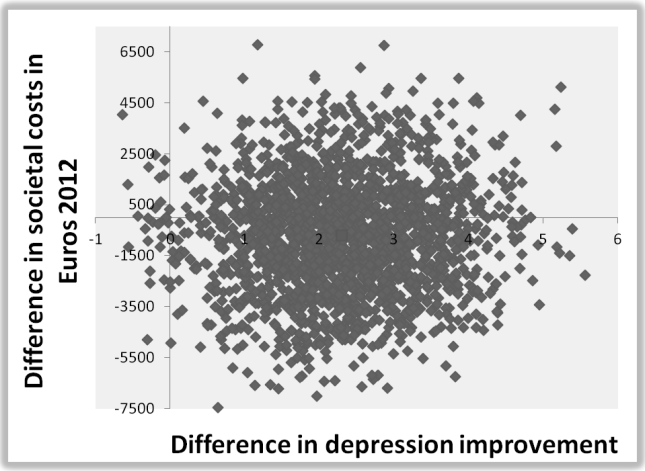

Figure 2 Cost-effectiveness plane for the difference in depressive symptoms at 12-months (societal perspective).

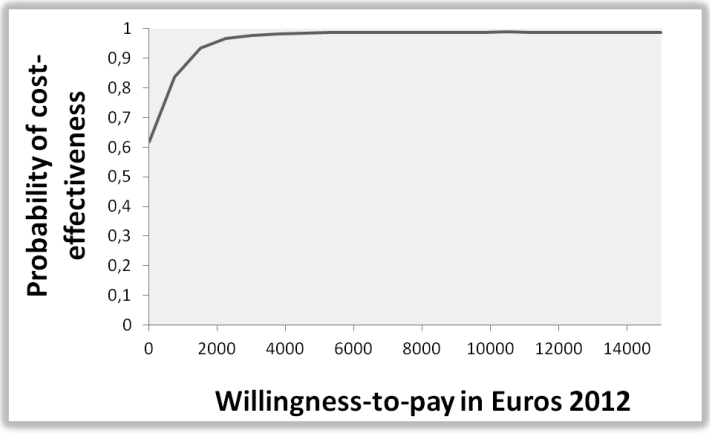

Figure 3 Cost-effectiveness acceptability curve for the difference in depressive symptoms at 12-months follow-up (societal perspective).

Table 2 Differences in pooled mean costs and effects (95% Confidence intervals), incremental cost-effectiveness ratios, and the distribution of incremental cost-effect pairs around the quadrants of the cost-effectiveness planes

Analysis		Sample size		Outcome	ΔC (95% CI)	ΔE (95% CI)	ICER	Distribution CE-plane (%)			
Societal perspective											
		Intervention	**CAU**		**€**	**Points**	**€/point**	**NE[1]**	**SE[2]**	**SW[3]**	**NW[4]**
Main analysis	- Imputed dataset	116	115	CES-D (range: 0-60)	-714 (-5018 to 3924)	-2.3 (-4.3 to -0.3)	314	36.7	62.1	7.4	0.5
		116	115	CSC (range: 0-1)	-714 (-5018 to 3924)	0.1 (0.0 to 0.2)	-6654	35.8	59.4	3.5	1.4
		116	115	QALYs (range: 0-1)	-714 (-5018 to 3924)	0.00 (-0.04 to 0.04)	532959	16.1	31.4	31.4	21.1
SA1	- Complete-cases	51	55	CES-D (range: 0-60)	-1919 (-5421 to 1832)	-2.1 (-1.5 to 5.6)	933	12.0	75.9	9.8	2.3
		51	55	CSC (range: 0-1)	-1919 (-5421 to 1832)	0.1 (-0.1 to 0.2)	-26518	11.1	67.9	16.7	4.3
		51	55	QALYs (range: 0-1)	-1919 (-5421 to 1832)	0.01 (-0.03 to 0.07)	-129808	7.8	62.9	23.2	6.3
SA2	- Per-protocol	67	115	CES-D (range: 0-60)	-3343 (-7040 to 582)	-2.3 (-4.8 to 0.2)	1466	4.2	91.9	3.6	0.3
		67	115	CSC (range: 0-1)	-3343 (-7040 to 582)	0.1 (0.0 to 0.3)	-25430	4.4	92.0	3.6	1.1
		67	115	QALYs (range: 0-1)	-3343 (-7040 to 582)	0.02 (-0.03 to 0.06)	-203896	3.1	74.4	21.2	1.4
SA3	- Excluding presenteeism costs	116	115	CES-D (range: 0-60)	565 (-4544 to 5061)	-2.3 (-4.3 to -0.3)	-249	58.2	40.6	0.5	0.8
		116	115	CSC (range: 0-1)	565 (-4544 to 5061)	0.1 (0.0 to 0.2)	5186	56.7	38.5	2.6	2.3
		116	115	QALYs (range: 0-1)	565 (-4544 to 5061)	0.00 (-0.04 to 0.04)	-419558	26.1	21.5	19.6	32.8
SA4	- HCA	116	115	CES-D (range: 0-60)	-458 (-8061 to 7046)	-2.3 (-4.3 to -0.3)	202	37.4	61.4	0.8	0.5
		116	115	CSC (range: 0-1)	-458 (-8061 to 7046)	0.1 (0.0 to 0.2)	-4203	36.5	58.7	3.5	1.4
		116	115	QALYs (range: 0-1)	-458 (-8061 to 7046)	0.00 (-0.04 to 0.04)	342788	15.6	31.9	30.2	22.2
Employer's perspective											
		Intervention	**CAU**		**€**	**Points/ proportions**	**€/point**	**NE[1]**	**SE[2]**	**SW[3]**	**NW[4]**
Main analysis	- Imputed dataset	116	115	CES-D (range: 0-60)	-508 (-8080 to 7088)	-2.3 (-4.3 to -0.3)	224	36.7	62.0	0.8	0.4
		116	115	CSC (range: 0-1)	-508 (-8080 to 7088)	0.1 (0.0 to 0.2)	-4664	35.9	59.3	3.5	1.3
		116	115	QALYs (range: 0-1)	-508 (-8080 to 7088)	0.00 (-0.04 to 0.04)	382354	15.3	21.2	30.6	21.8
SA1	- Complete-cases	51	55	CES-D (range: 0-60)	-1380 (-4894 to 3025)	-2.1 (-1.5 to 5.6)	673	20.2	66.7	9.3	3.8
		51	55	CSC (range: 0-1)	-1380 (-4894 to 3025)	0.1 (-0.1 to 0.2)	-19065	18.1	61.6	14.6	5.7
		51	55	QALYs (range: 0-1)	-1380 (-4894 to 3025)	0.01 (-0.03 to 0.07)	-93321	15.0	55.5	19.5	10.0
SA2	- Per-protocol	67	115	CES-D (range: 0-60)	-3697 (-9287 to 1921)	-2.3 (-4.8 to 0.2)	1621	8.4	87.7	3.5	0.4
		67	115	CSC (range: 0-1)	-3697 (-9287 to 1921)	0.1 (0.0 to 0.3)	-28119	8.6	87.7	3.5	0.2
		67	115	QALYs (range: 0-1)	-3697 (-9287 to 1921)	0.02 (-0.03 to 0.06)	-224587	6.5	71.1	20.1	2.3
SA3	- Excluding presenteeism costs	116	115	CES-D (range: 0-60)	770 (-6955 to 9573)	-2.3 (-4.3 to -0.3)	-340	57.2	41.6	0.6	0.7
		116	115	CSC (range: 0-1)	770 (-6955 to 9573)	0.1 (0.0 to 0.2)	7075	55.6	39.6	2.6	2.3
		116	115	QALYs (range: 0-1)	770 (-6955 to 9573)	0.00 (-0.04 to 0.04)	-578421	25.1	22.6	19.6	32.8

Abbreviations: C: Costs, CAU: Care As Usual, CE-plane: Cost-Effectiveness plane, CES-D: Center for Epidemiological Studies Depression – Scale, CI: Confidence Interval, CSC: Clinical Significant Change, E: Effects, HCA: Human Capital Approach, ICER: Incremental Cost-Effectiveness Ratio, SA: Sensitivity Analysis, QALY: Quality Adjusted Life Year
Note: Costs are expressed in 2012 Euros

[1] Refers to the northeast quadrant of the CE plane, indicating that the Happy@Work intervention is more effective and more costly than Care-As-Usual
[2] Refers to the southeast quadrant of the CE plane, indicating that the Happy@Work intervention is more effective and less costly than Care-As-Usual
[3] Refers to the northwest quadrant of the CE plane, indicating that the Happy@Work intervention is less effective and more costly than Care-As-Usual
[4] Refers to the southwest quadrant of the CE plane, indicating that the Happy@Work intervention is less effective and less costly than Care-As-Usual

Employer's perspective: CEA and CUA

For the depressive symptoms, an ICER of 224 was found, indicating that a 1-point decrease in depressive symptoms was associated with cost savings of €224. The majority of the incremental CE-pairs was located in the southeast quadrant of the CE-plane, indicating that the Happy@Work intervention is more effective and less costly to the employer than CAU (Table 2). The probability of cost-effectiveness was 0.55 at a willingness-to-pay of €0/point improvement, and gradually increased to 0.95 at a willingness-to-pay of €3,500. The analysis on clinical significant change resulted in an ICER of -4664, which indicates that per additional participant with a clinically significant improvement in depressive symptoms €4,664 was saved by the employer. Moreover, a 0.95 probability of cost-effectiveness was reached at a ceiling ratio of €115,000.

The CUA showed that the ICER for QALYs gained was 382,354. This indicates that every QALY lost was associated with cost savings to the employer of €382,354. Again, this monetary figure is extremely large, because the difference in effect is close to zero (-0.001 - 95% CI: -0.04 to 0.04). The maximum probability of cost-effectiveness in terms of this outcome was 0.55, irrespective of the employer's willingness-to-pay.

Employer's perspective: financial return

The total benefits in terms of occupational health, absenteeism, and presenteeism costs during follow-up were on overage €793 (95% CI: -7176 to 8039; see Table 3). The NB was on average €508 (95%CI: -7029 to 8160). The BCR was 2.8 (95% CI: -25.7 to 27.6), which means that for every Euro invested, the employer received €2.8 back. Finally, the ROI (i.e. the percentage of profit per Euro invested) was 178% (95% CI: -2466 to 2863). None of these estimates were statistically significant and the intervention's probability of financial return was 0.63.

Sensitivity analyses

Effect differences were similar in all sensitivity analyses, including the complete-case analyses (SA1) and the per-protocol analyses (SA2). Cost differences, on the other hand, were more in favour of the intervention group in SA1 (complete-cases), SA2 (per-protocol analyse), and SA4 (using the HCA when the societal perspective was applied), leading to more favourable cost-effectiveness and financial return outcomes. When presenteeism costs were excluded, however, cost-differences were in favour of the CAU group (tables 2 and 3). Moreover, in comparison with the main analyses, higher amounts of money had to be paid by society and employers to reach a 0.95 probability of cost-effectiveness in terms of depressive symptoms and clinical significant change (e.g. society has to pay €4,000/point improvement in depressive symptoms), and the maximum probabilities of cost-effectiveness in terms QALYs gained were lower than those of the main analyses at all ceiling ratios (i.e. ≤ 0.43).

Table 3 Intervention costs, benefits, Net Benefits (NB), Benefit Cost Ratio (BCR), and Return-On-Investment (ROI) per participant

Analysis		Sample size		Costs (€)	Benefits	Financial return			
		Intervention	CAU	Total (95% CI)	Total (95% CI)	NB[1] (95% CI)	BCR[2] (95% CI)	ROI (%)[3] (95% CI)	Probability
Main analysis	- Imputed dataset	116	115	285 (NA)	793 (-7176 to 8039)	508 (-7029 to 8160)	2.8 (-25.7 to 27.6)	178 (-2466 to 2863)	0.63
SA1	- Complete-cases	51	55	285 (NA)	1665 (-2212 to 5541)	1380 (-2541 to 5164)	5.8 (-7.9 to 19.2)	484 (-892 to 1812)	0.76
SA2	- Per-protocol	67	115	285 (NA)	3982 (-1152 to 10030)	3697 (-1733 to 9406)	14.0 (-5.1 to 34.0)	1297 (-608 to 3300)	0.92
SA3	- Excluding presenteeism costs	116	115	285 (NA)	-485 (-9687 to 6972)	-770 (-9711 to 6868)	-1.7 (-33.1 to 25.1)	-270 (-3407 to 2410)	0.42

Abbreviations: BCR: Benefit Cost Ratio, CAU: Care As Usual, CI: Confidence Interval, I: Intervention, NA: Not Applicable, NB: Net Benefit, ROI: Return-On-Investment,
Note: Costs are expressed in 2012 Euros
Note: Financial returns are positive if the following criteria are met: NB>0, BCR>1, and ROI>0
[1] Indicates the amount of money returned after intervention costs are recovered
[2] Indicates the amount of money returned per Euro invested in the intervention
[3] Indicates the percentage of profit per Euro invested in the intervention

Discussion

This study evaluated the cost-effectiveness and financial return of a worker-directed web-based guided self-help intervention aimed at reducing depressive symptoms versus care-as-usual. At 12 months follow-up, a significant effect on depressive symptoms was found in favour of the intervention group (-2.3, 95% CI: -4.3 to -0.3). If decision-makers are not willing to pay anything for an additional unit of effect in depressive symptoms and clinical significant change, the intervention's probabilities of cost-effectiveness were 0.62 (societal perspective) and 0.55 (employer's perspective), increasing to 0.95 with an increasing willingness-to-pay (societal perspective: €2,000; employer's perspective: €3,500). It is unknown, however, how much societal decision-makers, as well as decision-makers at the company level, are willing to pay per unit of effect gained in terms of these outcomes and what probability of cost-effectiveness they perceive to be acceptable. Therefore, strong conclusions about the intervention's cost-effectiveness with regard to depressive symptoms and clinically significant change cannot be made. For QALYs, the maximum probabilities of cost-effectiveness were low (≤0.62). As such, the intervention cannot be considered cost-effective in terms with regard to QALYs. Moreover, only a moderate probability of positive financial return to the employer was found (i.e. probability of financial return = 0.63). The sensitivity analyses indicated that these findings are robust since all sensitivity analyses did not lead to different conclusions.

Interpretation of the results

The results of this study are not in line with other studies on the cost-effectiveness of web-based interventions for depressive symptoms [38-41]. Previous studies generally found higher probabilities of cost-effectiveness for improvement in depressive symptoms or clinical significant change at lower willingness-to-pay values. For example, Warmerdam and colleagues [41] found that the probability of a problem solving web-based intervention for depressive symptoms being cost-effective in comparison with a waiting-list control group was 0.89 at a ceiling ratio of 10,000€/patient with a clinically significant improvement extra. Two studies [38, 41] also found more positive results of the web-based intervention on QALYs which is in contrast with our study. This difference may be explained by the mild symptoms experienced by participants in our study as previous research has shown that QALYs seem to lack sensitivity to mild conditions [16]. Other factors that might explain the difference in findings are the fact that all of the previous studies were performed in a community or primary care setting, three of the four studies followed participants less than 12 months, and that the participants in the previous studies had more severe depressive symptoms at baseline than our population.

Robustness of study results

Effect and cost differences were only slightly different in the sensitivity analyses and did not lead to different conclusions, indicating that the findings of this study are robust.

Strengths and limitations

There are several limitations to this study. First, only 54% of the participants had complete data on the effect measures, and 46% on the cost measures. Even though we used multiple imputation techniques to correct for missing data we cannot rule out the possibility of bias due to missing data. However, there were no indications for selective attrition. Another limitation of this study is the lack of power since the power calculation of this study was based on the expected difference in clinical outcomes [17] and not on economic outcomes. And finally, we only used self-report for all measures, whereas self-report may be vulnerable to recall bias [42].

This study also has some important strengths. First, this study used state-of-the-art statistical methods, such as SUR analyses and bootstrapping techniques in the ROI analyses, which are not frequently used in occupational health research. Secondly, we used a relatively long follow-up period of 12-months. Long periods of follow-up are not frequently studied in web-based interventions [12]. To illustrate, of the four aforementioned economic evaluations of web-based interventions for depressive symptoms [38-41] only one study [38] followed participants for a period of 12 months. And finally, to the best of our knowledge, we were the first to study the cost-effectiveness and financial return of a web-based intervention in occupational health care.

Implications and future research

The results of this study suggest that a worker-directed web-based intervention for employees with depressive symptoms will not be cost-saving to the employer and might not be judged cost-effective because high investments are needed to reach a 0.95 probability that the intervention is cost-effective in comparison with care-as-usual. Since we were the first to study the cost-effectiveness of a web-based intervention in occupational health care further research is necessary whether web-based interventions can reduce sickness absence due to depression in European countries. Based on the findings of this study we we do not recommend to implement Happy@Work into routine practice since both the effectiveness [13] and cost-effectiveness did not show positive results.

Conclusion

This study showed that a worker-directed web-based guided self-help intervention for employees with depressive symptoms was effective in reducing depressive symptoms compared to care-as-usual, but it might not be judged as cost-effective, because high

investments are needed to reach a 0.95 probability that the intervention is cost-effective in comparison with care-as-usual. The probability of financial return to employers was only moderate (i.e. probability= 0.63). The findings of this study should be interpreted with care as none of the results were statistically significant and uncertainty around the cost estimates was high.

References

1 Organisation for Economic Co-operation and Development. Sick on the job? Myths and realities about mental health and work. OECD Publishing 2012. doi:10.1787/9789264124523-en

2 Alexanderson K, Norlund A. Chapter 1. Aim, background, key concepts, regulations and current statistics. *Scand J Public Health* 2004;32(Suppl 63):12-30

3 Henderson M, Glozier N, Elliott KH. Long term sickness absence is caused by common conditions and needs managing. *BMJ* 2005;330:802-803.

4 Vaez M, Rylander G, Nygren A, et al. Sickness absence and disability pension in a cohort of employees initially on long-term sick leave due to psychiatric disorders in Sweden. *Soc Psychiatry Psychiatr Epidemiol* 2007;42:381-388.

5 Järvisalo J, Andersson B, Boedeker W, et al. (Eds.) Mental disorders as a major challenge in prevention of work disability: experiences in Finland, Germany, the Netherlands and Sweden. Helsinki: Edita Prima Ltd; 2005. ISBN:9516696589

6 Gustavsson A, Svensson M, Jacobi F, et al. Costs of disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol* 2011;21:718-779.

7 Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006;3:e442.

8 Szeto AC, Dobson KS. Mental disorders and their association with perceived work stress: an investigation of the 2010 Canadian Community Health Survey. *J Occup Health Psychol* 2013;18(2):191-197.

9 Cuijpers P, van Straten A, Andersson G. Internet-administered cognitive behavior therapy for health problems: a systematic review. *J Behav Med* 2008;31:169-177.

10 Griffiths F, Lindenmeyer A, Powell J, et al. Why are health care interventions delivered over the internet? A systematic review of the published literature. *J Med Internet Res* 2006;8:e11.

11 Andersson G, Titov N. Advantages and limitations of Internet-based intervention for common mental disorders. *World Psychiatry* 2014;13:4-11.

12 Richards D, Richardson T. Computer-based psychological treatments for depression: a systematic review and meta-analysis. *Clin Psychol Rev* 2012;32:329-342.

13 Geraedts AS, Kleiboer, AM, Wiezer NM, et al. Short-term effects of a web-based guided self-help intervention for employees with depressive symptoms: randomized controlled trial. *J Med Internet Res* 2014;16:e121. Published Online First: May 6 2014. doi:10.2196/jmir.3185

14 Giffin SC. Dealing with uncertainty in the economic evaluation of health care technologies. Thesis (PhD), University of York. 2010

15 Leigh JP. Expanding research on the economics of occupational health. *Scand J Work Environ Health* 2006;32:1-4.

16 van Dongen JM, van Wier MF, Tompa E, et al. Trial-based economic evaluations in occupational health: principles, methods, and recommendations. *J Occup Environ Med* 2014; in press.

17 Geraedts AS, Kleiboer AM, Wiezer NM, et al. Web-based guided self-help for employees with depressive symptoms (Happy@Work): design of a randomized controlled trial. *BMC Psychiatry* 2013;13:61.

18 Bowman D, Scogin F, Lyrene B. The efficacy of self-examination therapy and cognitive bibliotherapy in the treatment of mild to moderate depression. *Psychother Res* 1995;5(2):131-140.

19 Beck AT, Rush AJ, Shaw BF, et al. Cognitive therapy of depression. New York: Guilford Press; 1979. ISBN:0898620007

20 Franck E, Wiezer N. Handleiding Preventie Leidraad - Manual for Prevention Guideline. Hoofddorp: TNO; 2004.

21 Franck E, Wiezer N. Ervaringen met de Preventie Leidraad - Experiences with the Prevention Guideline. Hoofddorp: TNO; 2004.

22 Radloff L. The CES-D scale: a self report depression scale for research in the general population. *Appl Psychol Meas* 1977;1(3):385-401.

23 Haringsma R, Engels GI, Beekman AT, et al. The criterion validity of the Center for Epidemiological Studies Depression Scale (CES-D) in a sample of self-referred elders with depressive symptomatology. *Int J Geriatr Psychiatry* 2004;19:558-563.

24 Yang HJ, Soong WT, Kuo PH, et al. Using the CESD in a two-phase survey for depressive disorders among nonreferred adolescents in Taipei: a stratum-specific likelihood ratio analysis. *J Affect Disord* 2004;82(3):419-430.

25 Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. *J Consult Clin Psychol* 1991;59(1):12-19.

26 EuroQol Group: Euroqol – a new facility for the measurement of health related quality of life. *Health Policy* 1990, 16:199-208.

27 Lamers LM, Stalmeier PFM, McDonnell J, et al. Kwaliteit van leven meten in economische evaluaties: het Nederlands EQ-5D-tarief. *Nederlands Tijdschrift voor Geneeskunde* 2005, 149:1574-1578.

28 Drummond MF, Sculpher MJ, Torrance GW, et al. Methods for the economic evaluation of health care programmes. New York: Oxford University Press; 2005.

29 Hakkaart- van Roijen L, Tan SS, Bouwmans CAM. Handleiding voor kostenonderzoek. Methoden en standaardkostprijzen voor economische evaluaties in de gezondheidszorg. Diemen: College voor zorgverzekeringen; 2010.

30 Hakkaart-van Roijen L, van Straten A, Donker M, et al. Manual Trimbos/iMTA questionnaire for costs associated with psychiatric illness (TIC-P). Rotterdam: Institute for Medical Technology Assessment; 2002.

31 Z-index. G-standard. The Hague: Z-Index BV; 2009.

32 Koopmanschap MA, Rutten FFH, van Ineveld BM, et al. The friction cost method for measuring indirect costs of disease. *J Health Econ* 1995;14:171-189.

33 Kessler RC, Ames M, Hymel PA, et al. Using the World Health Organization Health and Work Performance Questionnaire (HPQ) to evaluate the indirect workplace costs of illness. *J Occup Environ Med* 2004;46(Suppl 6):S23-37.

34 Central Bureau of Statistics the Netherlands. 2012. http://cbs.nl

35 Rubin DB. Multiple imputation for nonresponse in Surveys. New York: Wiley; 1987. ISBN:9780471087052

36 Black WC. The CE plane: a graphic representation of cost-effectiveness. *Med Decis Making* 1990;10:212-214.

37 Fenwick E, O'Brien BJ, Briggs A. Cost-effectiveness acceptability curves – facts, fallacies and frequently asked questions. *Health Econ* 2004;15:405-415.

38 Gerhards SAH, de Graaf LE, Jacobs LE, et al. Economic evaluation of online computerised cognitive-behavioural therapy without support for depression in primary care: randomised trial. *Br J Psychiatry* 2010;196:310-318

39 Hollinghurst S, Peters TJ, Kaur S, et al. Cost-effectiveness of therapist-delivered online cognitive-behavioural therapy for depression; randomised controlled trial. *Br J Psychiatry* 2010:197:297-304.

40 McCrone P, Knapp M, Proudfoot J, et al. Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: randomised controlled trial. *Br J Psychiatry* 2004;185:55-62.

41 Warmerdam, Smit F, van Straten A, et al. Cost-utility and cost-effectiveness of internet-based treatment for adults with depressive symptoms: randomized trial. *J Med Internet Res* 2010;12:e53.

42 van den Brink M, van den Hout WB, Stiggelbout AM, et al. Cost measurement in economic evaluations of health care: whom to ask? *Med Care* 2004;42:740-746.