A universal digital stress management intervention for employees: Health-economic evaluation alongside a randomized controlled trial

Johanna Freund, Filip Smit, Dirk Lehr, Anna-Carlotta Zarski, Matthias Berking, Heleen Riper, Burkhardt Funk, David Daniel Ebert, Claudia Buntrock

Submitted to: Journal of Medical Internet Research
on: April 25, 2023

Table of Contents

A universal digital stress management intervention for employees: Health-economic evaluation alongside a randomized controlled trial

Johanna Freund[1, 2] BSc, BA, MSc, PhD; Filip Smit[3, 4, 5] PhD; Dirk Lehr[6] PhD; Anna-Carlotta Zarski[1, 2, 7] PhD; Matthias Berking[1] PhD; Heleen Riper[5, 8, 9, 10] PhD; Burkhardt Funk[11] PhD; David Daniel Ebert[2] PhD; Claudia Buntrock[1, 12] PhD

[1]Department of Clinical Psychology and Psychotherapy Friedrich-Alexander-Universität Erlangen-Nürnberg Erlangen DE
[2]Professorship Psychology & Digital Mental Health Care Technical University of Munich Munich DE
[3]Trimbos Institute Utrecht NL
[4]Department of Epidemiology and Biostatistics Amsterdam University Medical Centers Amsterdam NL
[5]Department of Clinical, Neuro and Developmental Psychology VU University Amsterdam NL
[6]Department of Health Psychology and Applied Biological Psychology Leuphana University of Lueneburg Lueneburg DE
[7]eHealth in clinical psychology Philipps University Marburg Marburg DE
[8]Faculty of Behavioural and Movement Sciences VU University Amsterdam NL
[9]Amsterdam Public Health Research Institute VU University Amsterdam NL
[10]Medical Centre VUmc Amsterdam NL
[11]Institute of Information Systems Leuphana University of Lueneburg Lueneburg DE
[12]Institute of Social Medicine and Health Systems Research Otto von Guericke University Magdeburg Magdeburg DE

Corresponding Author:
Johanna Freund BSc, BA, MSc, PhD
Department of Clinical Psychology and Psychotherapy
Friedrich-Alexander-Universität Erlangen-Nürnberg
Nägelsbachstr. 25a
Erlangen
DE

Abstract

Background: Stress is highly prevalent and known to be a risk factor for a wide range of physical and mental disorders. The effectiveness of digital stress management interventions has been confirmed; however, research on its economic merits is still limited.

Objective: To assess the cost-effectiveness, cost–utility, and cost-benefit of a universal digital stress management intervention for employees compared to a waitlist control condition within a time horizon of 6 months.

Methods: Recruitment was directed at the German working population. A sample of 396 employees was randomly assigned to the intervention group (n = 198) or the waiting list control (WLC) group (n = 198). The digital stress management intervention included seven sessions plus one booster session and was offered without therapeutic guidance. Health service use, patient and family expenditures, and productivity losses were self-assessed and used for costing from a societal and an employer's perspective. Costs were related to symptom-free status (PSS-10 score 2 standard deviations below the study population baseline mean) and quality-adjusted life years (QALYs) gained. Sampling error was handled using nonparametric bootstrapping.

Results: From a societal perspective, the digital intervention had a 56% (55%) probability of being cost-effective at a willingness-to-pay of €0 per symptom-free person (QALY) gained, compared to WLC. This probability increased to 80% at a societal willingness-to-pay of €20,000 per QALY gained. Taking the employer's perspective, the digital intervention showed a probability for a positive return on investment of 78%.

Conclusions: Digital preventive stress management for employees appears to be cost-effective societally and provides a favorable return-on-investment for employers. Clinical Trial: German clinical trials register (DRKS00005699)

(JMIR Preprints 25/04/2023:48481)
DOI: https://doi.org/10.2196/preprints.48481

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Original Paper

A universal digital stress management intervention for employees: Health-economic evaluation alongside a randomized controlled trial

Abstract

Background: Stress is highly prevalent and known to be a risk factor for a wide range of physical and mental disorders. The effectiveness of digital stress management interventions has been confirmed; however, research on its economic merits is still limited.
Objective: To assess the cost-effectiveness, cost–utility, and cost-benefit of a universal digital stress management intervention for employees compared to a waitlist control condition within a time horizon of 6 months.
Methods: Recruitment was directed at the German working population. A sample of 396 employees was randomly assigned to the intervention group (n = 198) or the waiting list control (WLC) group (n = 198). The digital stress management intervention included seven sessions plus one booster session and was offered without therapeutic guidance. Health service use, patient and family expenditures, and productivity losses were self-assessed and used for costing from a societal and an employer's perspective. Costs were related to symptom-free status (PSS-10 score 2 standard deviations below the study population baseline mean) and quality-adjusted life years (QALYs) gained. Sampling error was handled using nonparametric bootstrapping.
Results: From a societal perspective, the digital intervention had a 56% (55%) probability of being cost-effective at a willingness-to-pay of €0 per symptom-free person (QALY) gained, compared to WLC. This probability increased to 80% at a societal willingness-to-pay of €20,000 per QALY gained. Taking the employer's perspective, the digital intervention showed a probability for a positive return on investment of 78%.
Conclusions: Digital preventive stress management for employees appears to be cost-effective societally and provides a favorable return-on-investment for employers.
Trial Registration: German clinical trials register (DRKS00005699)

Keywords: Economic evaluation; cost-utility; return-on-investment; employees; universal prevention; internet-based

Introduction

In Europe, up to 27% of the working population suffers from stress [1]. Stress is often caused by work-related factors, including high perceived work demands, little work control, and little support from co-workers and supervisors [2]. Stress is linked to numerous diseases including mental health problems and psychiatric diseases [3]. Besides the great burden of disease for the individual, stress is linked to formidable costs for employers as well as the society as a whole. Due to stress and stress-related disorders individuals suffer from impairment at work and lower productivity, are more days

absent from work and utilize health services at a higher rate [4]. Lazarus's transactional model of stress [5] delineates two distinct coping strategies. On the one hand, problem-focused coping involves actively influencing a stressful situation positively by employing cognitive or behavioral efforts. On the other hand, emotion-focused coping primarily serves the purpose of managing challenging emotions, such as anger, disappointment, and sadness, in response to the specific situation.

The efficacy of stress management interventions has been confirmed in numerous meta-analyses of randomized trials in the general population [6] and in occupational settings [7]. However, high levels of psychological stress among employees are omnipresent and remain largely untreated [8]. Easily accessible and highly scalable digital interventions independent of time and place represent a promising approach to lowering the threshold for use compared to face-to-face interventions [9]. A recent meta-analysis provides evidence that digital or internet-based stress management interventions (iSMIs) are effective in terms of stress reduction in adults with small-to-medium effect sizes at post-treatment (Cohen's *d*=0.43; 95% CI 0.31-0.51) [10]. In the workplace in particular, a universal prevention approach is especially desirable because more employees can be reached without prior screening that might be costly [11]. Compared to selective prevention with a focus on groups of people at increased risk or indicated prevention with a focus on individuals with elevated symptoms, universal prevention aims to reach the entire population regardless of any risk status [12]. A scalable digital intervention for universal prevention of stress in the working population has potential for a substantial reach. Furthermore, with a focus on the entire working population, individuals can also be reached who do not want to disclose symptoms due to fear of stigmatization [13]. Concerning the efficacy of a universal iSMI for employees, the findings from a pragmatic randomized controlled trial indicate significantly reduced perceived stress with medium-to-large effect sizes both at post-treatment (*d*=0.71, 95% CI 0.51-0.91) and at 6-month follow-up (*d*=0.61, 95% CI 0.41-0.81) in the iSMI group when compared to a waitlist control (WLC) condition [14].

Yet, although the effectiveness of iSMI has been demonstrated, research on its economic merits is still limited. Evidence suggests that an indicated iSMI to proactively prevent onset of stress in employees represents good value for money from both a societal and an employer's perspective [15,16]. However, no study has yet evaluated the cost-effectiveness of a universal iSMI in the working population. The present study thus aimed to evaluate the cost-effectiveness and cost-utility of a universal iSMI for stress in employees compared to a WLC from a societal perspective and the cost-benefit from the employer's perspective over a time horizon of six months. The clinical effectiveness of this iSMI has already been established [14].

Methods

Study design

We carried out the health-economic evaluation alongside a two-arm RCT comparing the effects of a self-guided iSMI for stress prevention with a WLC. Detailed information about the study design can be found elsewhere [14]. We carried out and reported the health economic evaluation in accordance with the guidelines of the International Society for Pharmacoeconomics and Outcomes Research [17] and the Consolidated Health Economic Evaluation Reporting Standards statement [18], see supplementary material.

Recruitment

Recruitment was carried out as part of the occupational health program of a large German health insurance company (BARMER) in a way similar to the intended implementation of the intervention

in routine practice in the future. The goal was to recruit from the general working population not limited to individuals insured by this health insurance company. This was done primarily through reports in the member magazine of the health insurance company and the insurance company's occupational health and safety management staff who informed the human resources departments of collaborating companies about their employees' possibility to participate in the study. Interested individuals who completed an online screening questionnaire and met eligibility criteria were asked to fill out the informed consent form. To best reflect the routine conditions, the inclusion and exclusion criteria were reduced to a minimum. Individuals were included who (a) were 18 years and older, (b) were currently employed, and (c) had internet access and a valid email address. Exclusion criteria only included a) a risk of suicide as indicated by a score of greater than 1 on the Beck Depression Inventory suicide item [14] or b) any diagnosis with psychosis or dissociative symptoms (self-reported). If participants were excluded from the study, they were provided with information about alternative treatment options available in routine care.

Overall, 396 participants were included for the study, with n = 198 randomized to either the iSMI or WLC condition. All participants completed the assessment at baseline, while 313 participants (79%) provided data at 6-month follow-up. Study drop-out was not statistically significantly associated with any sociodemographic characteristics or initial perceived stress level. The average participant was 41.76 years old (*SD*=10.09), female (302/396; 76%), highly educated (285/396; 72%), and employed full-time (296/396; 75%) with a working experience of 17.58 years (*SD*=10.36). Almost half of the participants worked in a management position (169/396; 43%).

Randomization and Masking

Study participants were randomly assigned to the invention or control group in a 1:1 ratio by an independent researcher not otherwise involved in the study. Randomization took place using a computer-based random numbers table (Randlist) to ensure equal sample sizes for both conditions. Detailed information about the randomization procedure can be found elsewhere [14]. During the randomization process, the assignment was hidden from the participants as well as the researchers involved in the recruitment and in the study administration. After randomization, participants were not blind to the study conditions due to the nature of the intervention.

Control condition

In both study conditions, the participants had full access to treatment as usual (TAU). We did not interfere in TAU. Rather, we tried to maintain a naturalistic TAU state in order to represent routine care as much as possible.

Intervention

Participants in the intervention group (IG) received the iSMI GET.ON Stress. This iSMI entails seven regular modules and one additional booster session for reviewing the most relevant content. Each module consists of psychoeducation, strategies for problem-solving, emotion regulation techniques and plans for the future. It was recommended to complete 1-2 modules per week. The iSMI is based on the transactional model of stress [14]. The training includes interactive education, exercises, testimonials, audio, and video files. The content of the intervention is tailored to the individual needs and interests of the participants, since several choices were made available through different answer options. In order to integrate the new knowledge sustainably into everyday life, homework, behavior planning, and an online diary are parts of the intervention. There was no therapeutic guidance provided. However, the participants had the opportunity to receive automatic text messages on their mobile phones. Participants could choose between light support with one text message every other day or intensive support with two or three text messages per day. Text messages contained very short exercises that should be carried out in everyday life to support the transfer from

training to real life. More details about the intervention can be found elsewhere [14]. In this study, IG participants completed on average 5.23 (*SD*=2.74) sessions. In total, 94 participants (48%) finished all seven modules, while 66 participants (33%) completed the additional booster session.

Outcome Measurements

Health-related outcome

The health outcome in the cost-effectiveness analysis (CEA) was symptom-free status based on the Perceived Stress Scale (PSS) and defined as a score at 6-month follow-up of 2 standard deviations (SDs) below the baseline mean of study population (22.65; *SD* = 5.63) [19].

Quality-adjusted life years

Quality-adjusted life years (QALYs) were used as a health outcome in the cost–utility analysis (CUA). QALYs were based on 35 items version of the Assessment of Quality of Life (AQoL-8D) assessed at baseline and 6-month follow-up, which is a reliable and validated instrument [20]. Eight dimensions of health-related quality of life were covered (i.e., independent living, relationships, mental health, coping, pain, senses, self-worth, and happiness) and preference-based valuations of health states (utilities) on a scale of 0 (death) to 1 (perfect health) were generated, using the time trade-off method [21]. Cumulative QALYs gains over the study's follow-up time of 6 months were estimated by calculating the area under the curve (AUC) of linearly interpolated AQoL-8D utilities between measurement points to cover the whole follow-up period.

Costs

Resource use and costing

We used the Trimbos and Institute for Medical Technology Assessment "Treatment Inventory of Costs in Patients with psychiatric disorders" questionnaire (TiC-P) to collect data on healthcare utilization, patient and family costs, and productivity losses [22]. The TiC-P is a retrospective questionnaire with a 3-month recall period and has been used in a similar study [15]. Costs were expressed in Euro and indexed from 2011 to 2013, the year the study was conducted, based on the German consumer price index (index factor 1.04) [23]. Costs were converted to pound sterling (£) using the purchasing power parities reported by the Organization for Economic Cooperation and Development [24]. For the reference year 2013, €1 was equated to £0.85.

Intervention costs

At the time of conducting the study, the market price of the digital intervention provided by the GET.ON Institute, a commercial health-care service provider, was €99 (£84) per participant, including costs for text messages, costs for website maintenance and hosting, technical support, and overheads.

Healthcare costs

We used two German guidelines for calculating health care costs [25,26]. Health-care costs on a per-participant level were based on available lists of unit costs[26]. Unit costs were as follows: €20.92 (£17.78) for a visit to the general practitioner, €46.55 (£39.57) for a session with a psychiatrist and €81.44 (£69.22) with a psychotherapist, respectively. Costs per contact for allied health services (e.g., physiotherapist) were valued at €17.08 (£14.52). Hospital stays were computed at €335.52 (£285.19) for an in-patient day in a psychiatric hospital and €306.41 (£260.45) for an in-patient day in a hospital for psychosomatic medicine and psychotherapy. Costs were estimated by multiplying the units of resource use with corresponding unit costs. The costs of prescribed medication were based on the LauerTaxe [27].

Patient and family costs

Out-of-pocket payments were directly obtained from participants. Costs for travelling were valued at

€0.30 (£0.27) per kilometre. Productivity losses from unpaid work (e.g. household chores, shopping, child care) and informal care were valued using the proxy good method (e.g., price of a close market substitute: domestic help). The average gross wage of domestic help per hour was estimated at €18.33 (£15.58) per hour.

Productivity costs

Costs due to absenteeism (i.e., days not worked) were valued according to the human capital method [28]. Lost working days due to absenteeism were valued at the gross average income of participants per day. Lost working days due to presenteeism (i.e., reduced efficiency while at work) were computed by taking into account the number of working days for which the participant reported a reduced work performance weighted by an inefficiency score for those days (Osterhaus method) [29].

Statistical analysis

Health-related outcome, quality-adjusted life years and costs

Analyses were conducted according to the intention-to-treat principle using Stata version 16 (StataCorp) [30]. Missing data were imputed using multiple imputations by chained equations (MICE) using predictive mean matching to account for the skewed distribution of cost and utility data. The imputation model was stratified by study arm and included demographic data (e.g., age, gender, marital status, education) alongside health-related outcome variables at baseline (e.g., utility values, perceived stress). The number of imputed datasets was at least equal to the percentage of incomplete cases (i.e., m = 30). Analyses as described below were performed on each dataset separately and results were pooled using Rubin's rules.

Economic evaluation: Societal perspective

Disaggregated and total costs from the employer's and societal perspectives as well as QALYs per study group were assessed with a set of ordinary last square regression equations, the latter adjusted for baseline utility values. Group differences in symptom-free status were tested using logistic regression.

From a societal perspective, the incremental cost-effectiveness ratio (ICER) was calculated as the extra costs per additional symptom-free participant or QALY gained, respectively. We bootstrapped seemingly unrelated regression equations (SURE) models to generate 2500 simulations of incremental cost and effect pairs while allowing for correlated residuals of the cost and effect equations and adjusting for potential confounders (e.g., initial utility values in the effect equation). Based on the bootstrapped SURE models, bias-corrected and accelerated 95% CIs were obtained for incremental costs and effects. Bootstrapped cost and effect pairs were plotted on cost-effectiveness planes to graphically represent the uncertainty surrounding the ICERs. Cost-effectiveness acceptability curves (CEACs) were created to depict the probability of the intervention being cost effective compared to the control condition for varying willingness-to-pay (WTP) thresholds.
To determine subgroups in which the intervention was particularly cost-effective net-benefit regression framework (NBRF) was used [31]. In the NBRF, the treatment dummy, prognostically relevant baseline characteristics, and their interactions are regressed on net-benefit. Net-benefit (NB) is defined as: $NB = (E*\lambda)–C$, where E are the effects per participant (e.g., QALYs), C are the costs per participant and λ is the willingness-to-pay for a unit of effect (i.e., €20,000 per QALY gained). Analyses were conducted using gender, age, education, marital status, work experience, previous health trainings / psychotherapy, level of perceived stress, resilience, agreeableness, psychological strain, and self-regulation competencies as independent variables.

Economic evaluation: Employer's perspective

From the employer's perspective, cost-benefit analyses were performed using two metrics: (1) net benefits (NB = benefits - costs; amount of money gained after costs are taken into account) and (2) return-on-investment (ROI = [(Benefits–Costs)/Costs]*100%; percentage of profit per Euro invested), where costs are defined as intervention costs and benefits as the difference in productivity costs between the iSMI group and the control condition. The metrics were estimated by bootstrapping linear regression models (N = 2500). The probability of a positive financial return was assessed by the proportion of positive estimates (e.g., NB > 0, ROI > 0%).

Sensitivity analyses

To test the robustness of the base case findings, we performed three sensitivity analyses. First, we applied Winsorizing, where extreme values of cost outliers (e.g. those above the 95 percentile) were replaced by the value at the 95th percentile. Second, we varied the costs of the intervention (i.e., €299) to reflect uncertainties about the actual market price. Third, we used another instrument, the EQ-5D-3L [32], to assess health-related quality of life instead of the AQoL-8D. While the first two sensitivity analyses were applied to both the societal and employer's perspective, the latter was only done in the societal perspective.

Ethical Considerations

The study was approved by the ethics committee of the University of Marburg (Germany) and registered in the German clinical trials register (DRKS00005699) on December 12, 2014.

Results

Health related outcomes and quality-adjusted life years

Participants in the iSMI condition had a statistically significantly higher probability for symptom-free status at 6-month follow-up with an Odds Ratio (OR) of 5.14 (95% CI 3.23 – 8.18) compared to WLC based on bootstrapped data. The mean of the cumulative QALYs were higher in the iSMI condition (0.321 QALYs: 95% CI 0.316 – 0.326) compared to the WLC (0.306 QALYs: 95% CI 0.302 – 0.310). Adjusted incremental differences in QALYs between the iSMI condition and the WLC were statistically significant (Δ(e) = 0.015 QALYs, 95% CI 0.009 – 0.022).

Costs

Baseline costs were slightly higher in the iSMI condition (€2283, 95% CI 1916-2650) but comparable to the WLC (€1936, 95% CI 1569-2303). The imputed mean 6-month cumulative per-participant costs (in €) separately for various cost categories by study condition are presented in Table 1. Direct medical costs as well as patient and family costs were similar in both groups. In the iSMI group, costs for absenteeism were higher than costs due to presenteeism. The opposite was seen in the WLC. Employer's costs were slightly higher in the WLC compared to the iSMI (incremental difference of €76, 95% CI -667−515). Average total costs were comparable in both groups with €3195 (95% CI 2661−3729) in the iSMI condition and €3233 (95% CI 2722−3744) in the WLC resulting in an incremental difference of €38 (95% CI -771−695) in favor of the iSMI group.

Table 1. Imputed mean cumulative per-participant costs (in €) by condition over a 6-month follow-up period.

	Intervention group (n = 198)		Control group (n = 198)		Incremental difference	
	Mean, €	95% CI	Mean, €	95% CI	Mean, €	95% CI

Direct medical costs						
Intervention costs						
	99	–	–	–	99	–
GP						
	52	42–62	50	41–58	2	-11–16
Mental health care						
	126	67–185	227	168–286	-101	-184–-18
Antidepressants						
	4	-5–14	15	5–25	-10	-24–4
Allied health services[a]						
	41	23–60	30	13–46	11	-13–36
Patient and family costs						
Over the counter drugs						
	20	13–28	26	19–34	-6	-16–5
Out of pocket expenses[b]						
	106	56–156	104	61–148	2	-63–66
Travel						
	11	6–16	15	10–20	-4	-11–4
Unpaid work						
	159	90–229	187	122–252	-28	-125–70
Informal care						
	330	195–466	194	92–297	136	-35–307
Domestic help						
	168	89–248	133	44–223	35	-88–159
Productivity costs						
Absenteeism						
	1217	897–1538	884	584–1184	334	-102–770
Presenteeism						
	859	616–1103	1368	1128–1609	-509	-852–-166
Employer's perspective						
Intervention costs + productivity costs						
	2176	1747–2605	2252	1841–2663	-76	-667–515
Societal perspective						
Total societal costs[c]						
	3195	2661–3729	3233	2722–3744	-38	-771–695

[a]For example, massage, physiotherapist, occupational therapist.

[b]For example, allied health services without prescription.

[c]Includes all cost categories based on a bootstrapped (n = 5000) linear regression model. Columns may not add up correctly due to rounding. CI = confidence interval.

Economic evaluation

Societal perspective

Cost-effectiveness

Table 2 shows the incremental costs, effects, mean ICERs and the distribution of cost and effect pairs on the cost-effectiveness plane based on 2500 bootstrap simulations. Cost-effectiveness analysis revealed that the iSMI generated more symptom-free individuals (Δ[E]=0.39; 95% CI 0.29-0.48) at lower costs (Δ[C]=–€38 [£953]; 95%CI –€-705 to €692) relative to the WLC. With regard to the cost-effectiveness plane, 56% of the bootstrapped ICERs fell in the southeast quadrant, indicating a 56% probability that the intervention dominates WLC (Figure 1). The remaining 44% of ICERs fell in the northeast quadrant, demonstrating a 44% probability that the intervention leads to greater health gains but at higher costs than WLC. At a willingness-to-pay of €1500 per additional symptom-free person, the iSMI showed a probability of 94% of being cost-effective compared to the WLC (Figure 2).

Cost-utility

Cost-utility analysis revealed similar results (Table 2). Again, the iSMI was likely to be dominant relative to the WLC with more QALY gains at lower costs resulting in a 55% probability that the iSMI is cost-effective at a societal willingness-to-pay threshold of €0 (Figure 3). This probability increased to 80% at a societal willingness-to-pay per QALY gained of €20,000 (Figure 4). Using NBRF, no subgroups were identified for which iSMI was significantly more (or less) cost-effective (all p-values ≥ .05 for both WTPs of 0€ and €20,000 per QALY gained, respectively).

Table 2. Results from the societal perspective (main and sensitivity analysis) based on 2500 bootstrap simulations.

Outcome	Incremental costs, € (95% CI)	Incremental effects, points (95% CI)	Incremental cost-effectiveness ratio, €/ points (95% CI)[a]	Distribution over the cost-effectiveness plane (%)			
				North-east quadrant[b]	South-east quadrant[c]	South-west quadrant[d]	North-west quadrant[e]
Main analysis							
Symptom-free status (0/1)							
	-38 (-705-692)	0.39 (0.29-0.48)	Dominant	44	56	0	0
QALYs[f] (range: 0-1)							
	-38 (-735-687)	0.015 (0.009-0.022)	Dominant	45	55	0	0
Sensitivity analysis 1[g]							
Symptom-free status (0/1)							
	-110 (-652-477)	0.39 (0.29-0.48)	Dominant	34	66	0	0
QALYs[f] (range: 0-1)							
	-110 (-652-477)	0.02 (0.01-0.01)	Dominant	34	66	0	0
Sensitivity analysis 2[h]							
Symptom-free status (0/1)							
	162 (-505-892)	0.39 (0.29-0.48)	€418	89	11	0	0
QALYs[f] (range: 0-1)							
	162 (-505-892)	0.025 (0.011-0.039)	€6,515	89	11	0	0
Sensitivity analysis 3[j]							
QALYs[f] (range: 0-1)							
	-38 (-735-687)	0.011 (0.003-0.019)	Dominant	45	55	0	0

[a]In accordance with ISPOR best practice guidelines on 'Model Parameter Estimation and Uncertainty', we do not report any negative incremental cost effectiveness Ratios (ICERs) since they are meaningless. Instead, we use the term 'dominant' which means that the intervention has a higher impact and comparatively lower cost with the WLC.

[b]The north-east quadrant of the CE plane, indicating that intervention is more effective and more costly.

[c]The south-east quadrant of the CE plane, indicating that intervention is more effective and less costly.

[d]The south-west quadrant of the CE plane, indicating that intervention is less effective and less costly.

[e]The north-west quadrant of the CE plane, indicating that intervention is less effective and more costly.
[f]QALYs: quality-adjusted life years.
[g]Sensitivity analysis 1 analyses for winzorizing cost outlier to 95% percentiles.
[h]Sensitivity analysis 2 analyses adding intervention costs of €299 (instead of 99€).
[j]Sensitivity analysis 3 analyses for EuroQol for quality-adjusted life years.

Employer's perspective

The iSMI condition showed a net benefit per participant of €76 (£65) (95% CI = €-498–665) and a benefit-to-cost ratio of 1.77 (95% CI = €-4.03-7.72). The ROI was 77% (95% CI = -503–672%), respectively. The probability of a positive return on investment was 78% for the iSMI condition (Table 3).

Table 3. Results from the employer's perspective (main and sensitivity analysis) of adjusted cost-benefit analyses based on 5000 bootstrapped linear regression models.

	Costs[a]		Benefits[b]		Financial Return				
	Total	95% CI	Total	95% CI	NB[c]	95% CI	ROI[d] (%)	95% CI	P[e] (%)
Main Analyses									
Unguided intervention									
	99	NA	175	-399 – 764	76	-498 – 665	77	-503–672	78
Sensitivity analysis 1[g]									
Unguided intervention									
	99	NA	217	-226 – 687	118	-325 – 588	120	-329–594	96
Sensitivity analysis 2[h]									
Unguided intervention									
	299	NA	175	-399 – 764	-124	-698 – 465	-41	-233–156	14
Sensitivity analysis 2[h]									
Unguided intervention									
	299	NA	175	-399 – 764	-124	-698 – 465	-41	-233–156	14

[a]Includes intervention costs.
[b]Benefits are the difference in productivity costs between the intervention group and the control condition.
[c]Net benefit (NB) linear regression models adjusted for baseline costs due to absenteeism and presenteeism.
[d]Return on investment (ROI) linear regression models adjusted for baseline costs due to absenteeism and presenteeism.
[e]Probability of positive return on investment.
[f]Intervention costs increased by 50%.
[g]Sensitivity analysis 1 analyses for winzorizing cost outlier to 95% percentiles.
[h]Sensitivity analysis 2 analyses adding intervention costs of €299 (instead of 99€).

Sensitivity analyses

Results of the sensitivity analyses are summarized in Table 2 and Table 3. Winsorizing cost outliers led to a slightly higher probability that the intervention produces higher health gains at lower costs

than WLC with regard to symptom-free status (66%) and QALYs (65%) at a societal WTP threshold of €0. The net benefit increased when cost outliers were winzorized and the probability of a positive return on investment was 96% for the iSMI. Increasing intervention costs up to 3 times (€299 instead of €99) this probability decreased to 33% regarding symptom-free status and QALYs gained at a WTP of €0. However, at a WTP of €20,000 per QALY gained, the probability of being cost-effective was comparable to the main analysis (e.g., 78%). Return on investment became negative when intervention costs were increased up to 3 times and the probability of a positive financial return decreased to 14% for the iSMI. Using the EQ-5D-3L resulted in a probability of 55 % regarding QALYs gained at a WTP of €0, identical to the main analysis.

Discussion

Principal Results

This study evaluated the cost-effectiveness and cost–utility of a universal unguided digital stress management intervention for employees from a societal perspective and the cost-benefit from the employer's perspective compared to a waitlist control condition over a 6 months' time horizon. From a societal perspective, the iSMI had a high probability of being cost-effective (e.g. 80% at a WTP of €20,000 per QALY gained). From an employer's perspective, the iSMI had a high probability of a positive return on investment with 78%.

Comparison with Prior Work

Evidence for economic evaluations of universal digital prevention of mental disorders is scarce. To our knowledge, this is the first economic evaluation of a universal iSMI to reduce stress in employees using a societal and an employer's perspective. The results of our study are in line with other economic evaluations of the same iSMI for stressed employees in the field of indicated prevention (PSS ≥ 22) in which e-coaches provided personalized feedback throughout the intervention [15]. Kählke et al. [15] demonstrated that more QALYs were generated for lower costs in the guided iSMI compared to a waitlist control condition indicating a similar probability of 76% compared to our study that the intervention was cost-effective compared to WLC at a societal WTP of €20,000 per QALY gained. A similar probability of 71% at a societal WTP of US $25,000 was also found by Lindsäter et al. [33] who evaluated therapist-guided iCBT for stress-related disorders compared to WLC.

Results from the employer's perspective are comparable to the study by Ebert et al. [16], who examined the cost-benefit of the same iSMI as Kählke et al. [15]. The analysis of Ebert et al. [16] yielded a similar benefit-to-cost ratio of 1.6 (95% CI = €-1.2-4.5) compared to a benefit-to-cost ratio of 1.77 (95% CI = €-4.0-7.7) in this study. Our results from the employer's perspective are also in line with findings from a recent systematic review indicating that addressing mental health in employees improves both their wellbeing and productivity [34]. Regarding the ROI analyses, our findings compare favorably to a systematic review of face-to-face health promotion interventions at the workplace (n = 12 RCTs) that showed on average a negative ROI (ROI = –0.22, 95% CI = 0.27–0.16; min = −4.3; max = 5) [35]. Van Dongen and colleagues (2017) also showed a negative return-on-investment of a combined social and physical environmental intervention in office employees [36].

Limitations

The following limitations have to be considered. First, contrary to the pharmaco-economic guidelines recommending treatment-as-usual as comparator [37], the iSMI was compared with a wait-listed

control condition, albeit with unrestricted access to usual care. Second, due to the limited time horizon of 6 months, longer term costs and effects caused by chronic stress (e.g., onset of a new health disorder or staff turnover) could not be analyzed. Future studies should examine whether treatment effects and costs are sustained over a longer period of time or decline. Third, preference-based utility values were only evaluated at baseline and after 6 months and thus, an immediate treatment effect has not been assessed. Fourth, costs due to presenteeism were only assessed with the Osterhaus method. However, this method tends to overestimate costs because it assumes a 1:1 relationship between workhours lost and productivity losses, but that relationship might be better described as an elastic relationship, e.g., 100% to 90%. Future studies should also include alternative methods (e.g., Health and Labor Questionnaire method) to calculate costs due to presenteeism. Fifth, self-report questionnaires were used which may have led to effects related to social desirability and response bias [38]. Future studies could consider claims data from health insurance companies. Sixth, the sample is characterized by a high proportion of female (302/396; 76.3%) as well as highly educated (285/396; 72.0%) participants, limiting the generalizability of the study findings. However, women with higher education are often the typical target group who take part in preventive internet-based interventions [39].

Clinical implications

Evidence-based recommendations on the cost-effectiveness of interventions can help inform decision-makers from the societal and employer's perspective when choosing preventive stress interventions. The findings of this study support the hypothesis that a universal prevention approach could be a cost-effective strategy to reduce the adverse consequences of work-related stress besides its shown effectiveness [14]. However, it must be taken into account that the participants in the study already had a rather high initial stress level on average. That is, we cannot say whether the cost-effectiveness results will hold up if increased numbers of participants with low levels of stress participate in the intervention. An unguided universal iSMI might be appropriate from an economic perspective, since there are no costs for screening compared to an iSMI for indicated prevention and additionally no costs for eCoach guidance, compared to guided interventions. Since health care professionals and available resources are often limited, unguided interventions have the potential to be implemented in routine occupational care on a large scale. Meta-analytic evidence shows that unguided interventions generate similar effects compared to guided interventions in individuals with low symptom severity [40]. However, the evidence on this is heterogeneous [41]. Therefore, future studies should directly compare cost-effectiveness of guided compared to unguided iSMIs. From a health economic point of view, no moderators were revealed in NBRF analyses. However, this could also have been due to a too small sample size and should be further researched in an individual participant data meta-analysis in the future.

Conclusions

A universal unguided digital stress management intervention appears to be cost-effective (i.e., the health effects achieved represent good value for the invested money) as well as offering a favorable benefit-to-cost ratio (i.e., the financial gains outweigh the intervention costs, so the return on investment is positive). Further research is needed to examine the long-term effects on cost-effectiveness and comparing a digital stress management intervention with standard care. Unguided digital stress prevention carries the promise to be scalable, which would leverage the cost-effectiveness and positive return-on-investment of this type of universal stress prevention in the working population.

Acknowledgements

Authors' contributions

BF and MB obtained funding for the study. DDE and DL designed the randomized controlled trial. DDE, DL, HR, and MB developed the intervention content. ACZ was responsible for recruitment of participants, data collection, and data curation, supervised by DL and DDE. CB developed the analysis plan for the health-economic evaluation, supported by FS. CB and JF accessed and verified the data. MB provided the analysis tool. CB conducted the analyses. CB, JF, and FS interpreted the data. JF drafted the manuscript, supervised by CB. All authors participated in the critical review of the manuscript and approved the final manuscript.

Role of the funding source

The funders did not have a role in study design, data collection, analysis and interpretation of results, or the decision to publish the study results.

Conflicts of Interest

BF and DDE are stakeholders of the GET.ON Institute/HelloBetter, which aims to implement scientific findings related to digital health interventions into routine care. MB is co-founder and stakeholder of mentalis GmbH, a provider of digital mental health care products and services. DDE has served as a consultant to/on the scientific advisory boards of Sanofi, Novartis, Minddistrict, Lantern, Schoen Kliniken, Ideamed and German health insurance companies (BARMER, Techniker Krankenkasse) and a number of federal chambers for psychotherapy.
JF, FS, AZ, HR, and CB report no conflicts of interest.

Data sharing

The health economic analysis plan will be made available on request by qualified scientific and medical researchers for legitimate research purposes. The data will be shared under a data sharing agreement once the results of the health-economic evaluation are published. Investigators are invited to submit study proposal requests detailing research questions and hypotheses to receive access to the data. Collected participant-level data will be deidentified. Requests should be sent to the last author.

Abbreviations

AQoL-8D: Assessment of Quality of Life
AUC: area under the curve
CEA: cost-effectiveness analysis
CEAC: cost-effectiveness acceptability curve
CI: confidence interval
CUA: cost–utility analysis
EQ-5D-3L: European Quality of Life 5 Dimensions 3 Level instrument
ICER: incremental cost-effectiveness ratio
IG: intervention group
iSMI: (digital or) internet-based stress management intervention
MICE: multiple imputations by chained equations
NB: net-benefit
NBRF: net-benefit regression framework
OR: Odds Ratio
QALY: Quality-adjusted life year
PSS: Perceived Stress Scale
RCT: randomized controlled trial

ROI: return-on-investment
SD: standard deviation
SURE: seemingly unrelated regression equations
TAU: treatment as usual
TiC-P: Treatment Inventory of Costs in Patients with psychiatric disorders questionnaire
WLC: waitlist control condition
WTP: willingness-to-pay

Multimedia Appendix 1: CHEERS 2022 Checklist

References

1. Eurofound. Developments in working life in Europe 2016: EurWORK annual review. Luxembourg: Publications Office of the European Union; 2017.
2. Nieuwenhuijsen K, Bruinvels D, Frings-Dresen M. Psychosocial work environment and stress-related disorders, a systematic review. Occup Med (Lond). 2010;60(4):277–86.
3. Duric V, Clayton S, Leong ML, Yuan LL. Comorbidity Factors and Brain Mechanisms Linking Chronic Stress and Systemic Illness. Neural Plast. 2016;2016:1–16.
4. Jensen I, Arapovic-Johansson Z, Aboagye E. The Cost-Effectiveness Analysis of the Productivity Measurement and Enhancement System Intervention to Reduce Employee Work-Related Stress and Enhance Work Performance. Int J Environ Res Public Health. 2022;19(4):2431.
5. Lazarus RS, Folkman S. Stress, appraisal, and coping. New York: Springer publishing company; 1984.
6. Khoury B, Sharma M, Rush SE, Fournier C. Mindfulness-based stress reduction for healthy individuals: A meta-analysis. J Psychosom Res. 2015;78(6):519–28.
7. Heckenberg RA, Eddy P, Kent S, Wright BJ. Do workplace-based mindfulness meditation programs improve physiological indices of stress? A systematic review and meta-analysis. J Psychosom Res. 2018;114:62–71.
8. Hilton MF, Whiteford HA, Sheridan JS, Cleary CM, Chant DC, Wang PS, et al. The prevalence of psychological distress in employees and associated occupational risk factors. J Occup Environ Med. 2008;50(7):746–57.
9. Carlbring P, Andersson G, Cuijpers P, Riper H, Hedman-Lagerlöf E. Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: an updated systematic review and meta-analysis. Cogn Behav Ther. 2018;47(1):1–18.
10. Heber E, Ebert DD, Lehr D, Cuijpers P, Berking M, Nobis S, et al. The benefit of web- and computer-based interventions for stress: A systematic review and meta-analysis. J Med Internet Res. 2017;19(2):e32.
11. McLaughlin KA. The public health impact of major depression: a call for interdisciplinary prevention efforts. Prev Sci. 2011;12(4):361–71.
12. Muñoz RF, Cuijpers P, Smit F, Barrera AZ, Leykin Y. Prevention of Major Depression. Annu Rev Clin Psychol. 2010;6:181–212.
13. Couser GP. Challenges and opportunities for preventing depression in the workplace: a review of the evidence supporting workplace factors and interventions. J Occup Environ Med. 2008;50(4):411–27.
14. Ebert DD, Franke M, Zarski AC, Berking M, Riper H, Cuijpers P, et al. Effectiveness and Moderators of an Internet-Based Mobile-Supported Stress Management Intervention as a

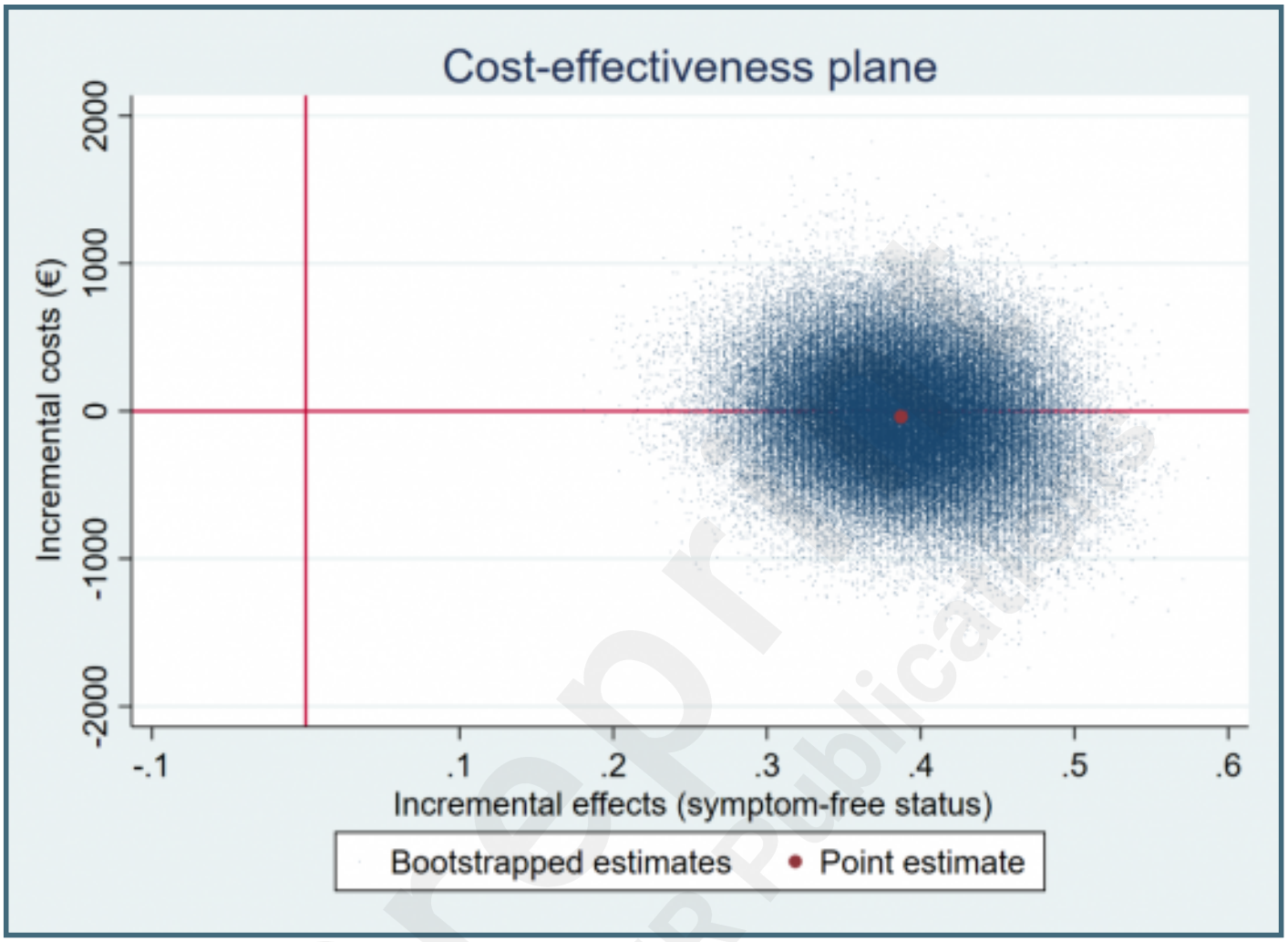
Universal Prevention Approach: Randomized Controlled Trial. JMIR. 2021;23(12):e22107.
15. Kählke F, Buntrock C, Smit F, Berking M, Lehr D, Heber E, et al. Economic evaluation of an internet-based stress management intervention alongside a randomized controlled trial. JMIR Ment Heal. 2019;6(5):e10866.
16. Ebert DD, Kählke F, Buntrock C, Berking M, Smit F, Heber E, et al. A health economic outcome evaluation of an internet-based mobile-supported stress management intervention for employees. Scand J Work Environ Heal. 2018;44(2):171–82.
17. Ramsey SD, Willke RJ, Glick H, Reed SD, Augustovski F, Jonsson B, et al. Cost-Effectiveness Analysis Alongside Clinical Trials II—An ISPOR Good Research Practices Task Force Report. Value Heal. 2015;18(2):161–72.
18. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. Value Heal. 2013;16(2):231–50.
19. Reis D, Lehr D, Heber E, Ebert DD. The German Version of the Perceived Stress Scale (PSS-10): Evaluation of Dimensionality, Validity, and Measurement Invariance With Exploratory and Confirmatory Bifactor Modeling. Assessment. 2017;26(7):1246–59.
20. Richardson J, Iezzi A, Khan MA, Maxwell A. Validity and Reliability of the Assessment of Quality of Life (AQoL)-8D Multi-Attribute Utility Instrument. Patient - Patient-Centered Outcomes Res. 2014;7(1):85–96.
21. Richardson J, Sinha K, Iezzi A, Khan MA. Modelling utility weights for the Assessment of Quality of Life (AQoL)-8D. Qual Life Res. 2014;23(8):2395–404.
22. Bouwmans C, De Jong K, Timman R, Zijlstra-Vlasveld M, Van der Feltz-Cornelis C, Tan SS, et al. Feasibility, reliability and validity of a questionnaire on healthcare consumption and productivity loss in patients with a psychiatric disorder (TiC-P). BMC Health Serv Res. 2013;13(1):217.
23. DESTATIS. German Consumer Price Index. [Internet]. [cited 2022 Mar 15]. Available from: https://www.destatis.de/EN/Themes/Economy/Prices/Consumer-Price-Index/_node.html;jsessionid=EFCA4B68C432A43E7B23742AC4640517.live712
24. Organization for Economic Cooperation and Development. Exchange rates (indicator). 2015.
25. Krauth C, Hessel F, Hansmeier T, Wasem J, Seitz R, Schweikert B. Empirical standard costs for health economic evaluation in Germany -- a proposal by the working group methods in health economic evaluation. Gesundheitswesen. 2005;67(10):736–46.
26. Bock JO, Brettschneider C, Seidl H, Bowles D, Holle R, Greiner W, et al. Calculation of standardised unit costs from a societal perspective for health economic evaluation. Gesundheitswesen. 2015;77(1):53–61.
27. WEBAPO Lauer Taxe (Accessed 24 June 2014 (over central pharmacy University Medical-Center Hamburg Eppendorf (call)). 2009.
28. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. 3rd ed. Oxford: Oxford university press; 2015.
29. Osterhaus JT, Gutterman DL, Plachetka JR. Healthcare resource and lost labour costs of migraine headache in the US. Pharmacoeconomics. 1992;2(1):67–76.
30. Stata version 16 (Stata Corp., College Station, TX).
31. Hoch JS, Briggs AH, Willan AR. Something old, something new, something borrowed, something blue: A framework for the marriage of health econometrics and cost-effectiveness analysis. Health Econ. 2002;11(5):415–30.

32. Group TE. EuroQol - a new facility for the measurement of health-related quality of life. Health Policy (New York). 1990;16(3):199–208.
33. Lindsäter E, Axelsson E, Salomonsson S, Santoft F, Ljótsson B, Åkerstedt T, et al. Cost-Effectiveness of Therapist-Guided Internet-Based Cognitive Behavioral Therapy for Stress-Related Disorders: Secondary Analysis of a Randomized Controlled Trial. J Med Internet Res. 2019;21(9):e14675.
34. de Oliveira C, Cho E, Kavelaars R, Jamieson M, Bao B, Rehm J. Economic analyses of mental health and substance use interventions in the workplace: a systematic literature review and narrative synthesis. The Lancet Psychiatry. 2020;7(10):893–910.
35. Baxter S, Sanderson K, Venn AJ, Blizzard CL, Palmer AJ. The Relationship between Return on Investment and Quality of Study Methodology in Workplace Health Promotion Programs. Am J Heal Promot. 2014;28(6):347–63.
36. Van Dongen JM, Coffeng JK, Van Wier MF, Boot CRL, Hendriksen IJM, Van Mechelen W, et al. The cost-effectiveness and return-on-investment of a combined social and physical environmental intervention in office employees. Health Educ Res. 2017;32(5):384–98.
37. Sacristán JA, Abellán-Perpiñán JM, Dilla T, Soto J, Oliva J. Some reflections on the use of inappropriate comparators in CEA. Cost Eff Resour Alloc. 2020;18(1):1–6.
38. van de Mortel TF. Faking It: Social Desirability Response Bias in Self-report Research. Aust J Adv Nurs. 2008;25(4):40–8.
39. Kelders SM, Bohlmeijer ET, Van Gemert-Pijnen JE. Participants, usage, and use patterns of a web-based intervention for the prevention of depression within a randomized controlled trial. J Med Internet Res. 2013;15(8):e172.
40. Karyotaki E, Efthimiou O, Miguel C, Bermpohl FM genannt, Furukawa TA, Cuijpers P, et al. Internet-Based Cognitive Behavioral Therapy for Depression: A Systematic Review and Individual Patient Data Network Meta-analysis. JAMA Psychiatry. 2021;78(4):361–71.
41. Domhardt M, Geßlein H, von Rezori RE, Baumeister H. Internet- and mobile-based interventions for anxiety disorders: A meta-analytic review of intervention components. Depress Anxiety. 2019;36(3):213–24.

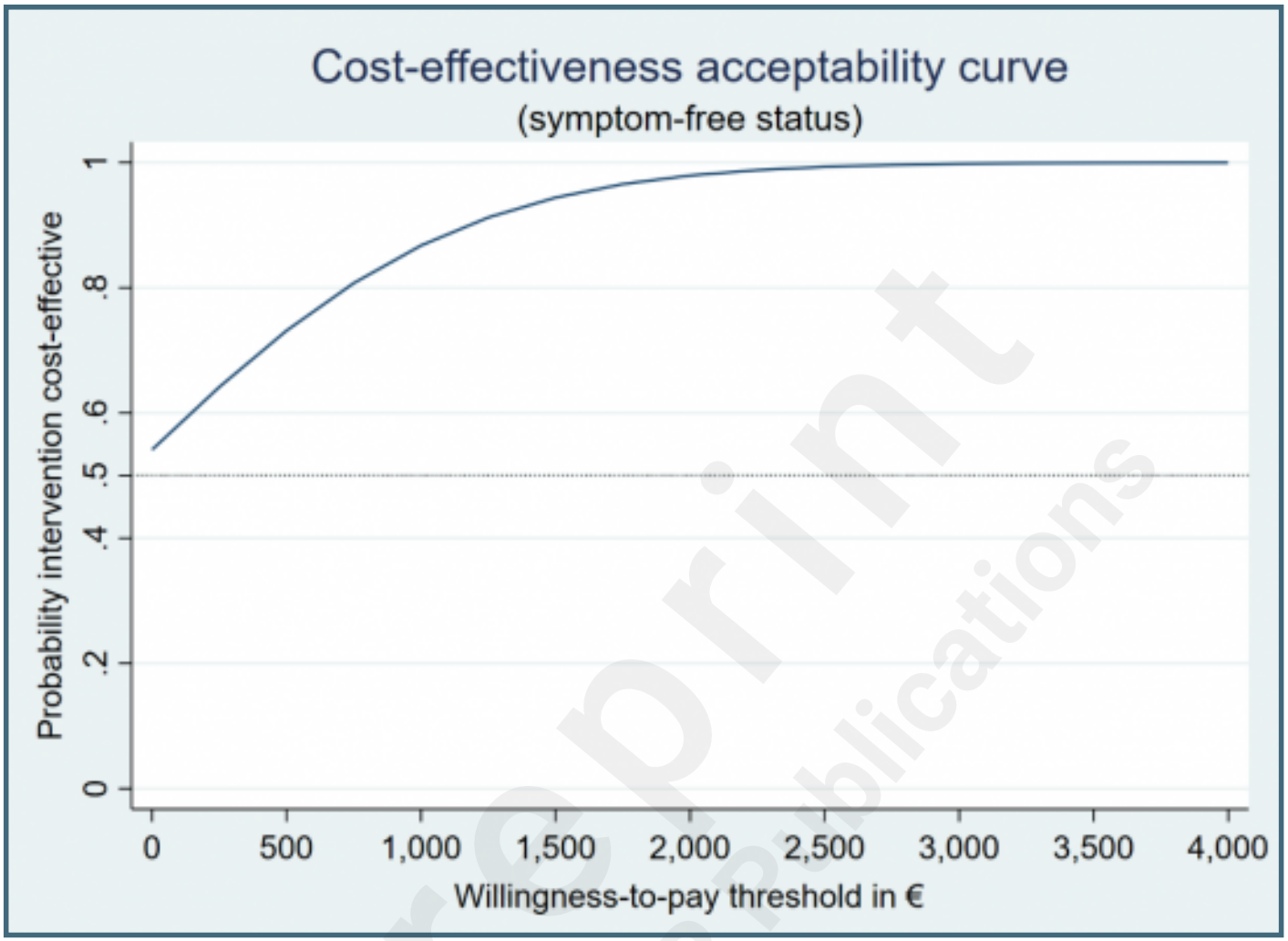
Supplementary Files

Figures

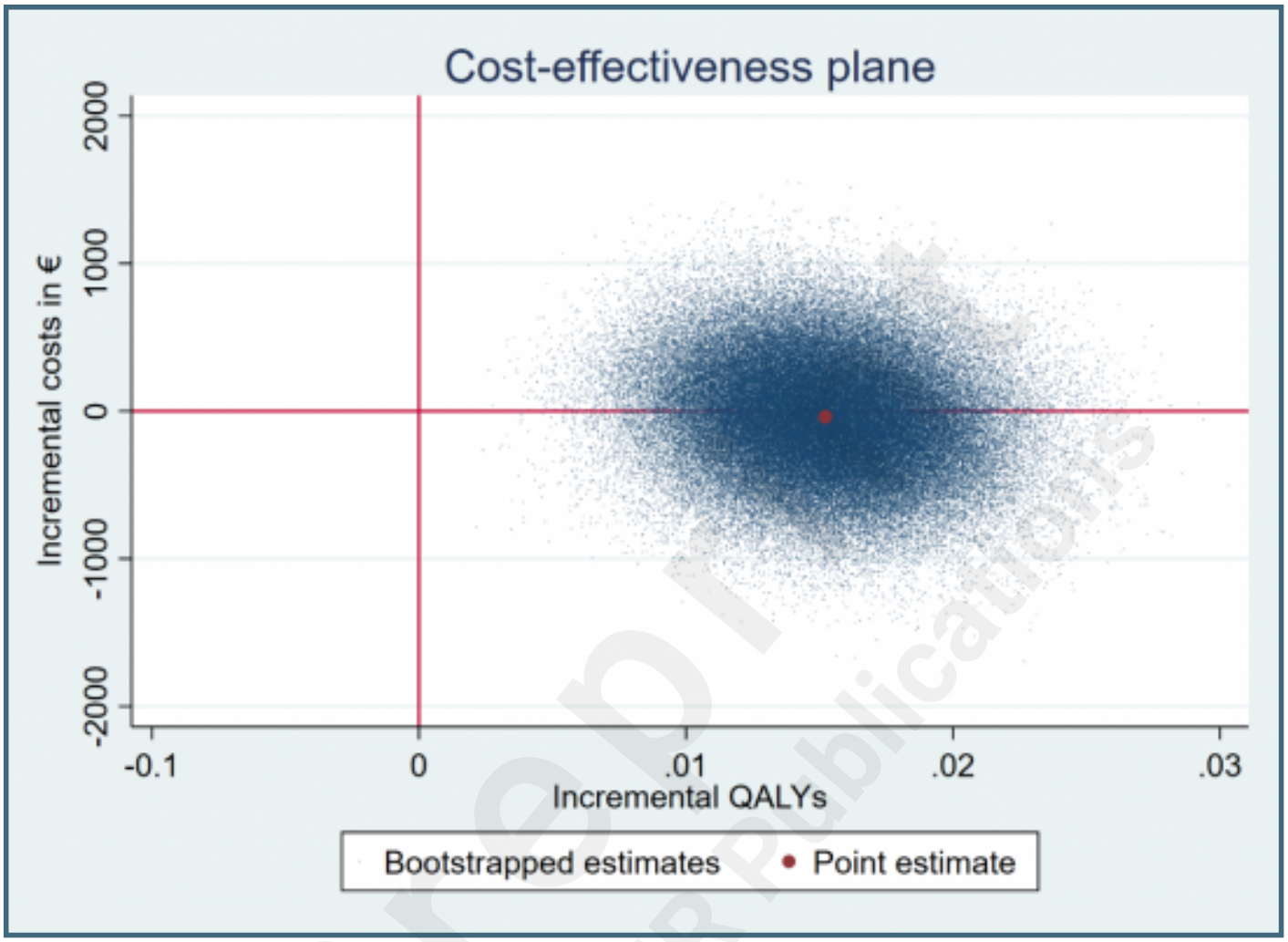
Scatterplot of 5000 replicates of the incremental cost-effectiveness ratio (mean differences in costs and symptom-free status) on the cost-effectiveness plane from the societal perspective: iSMI versus WLC.



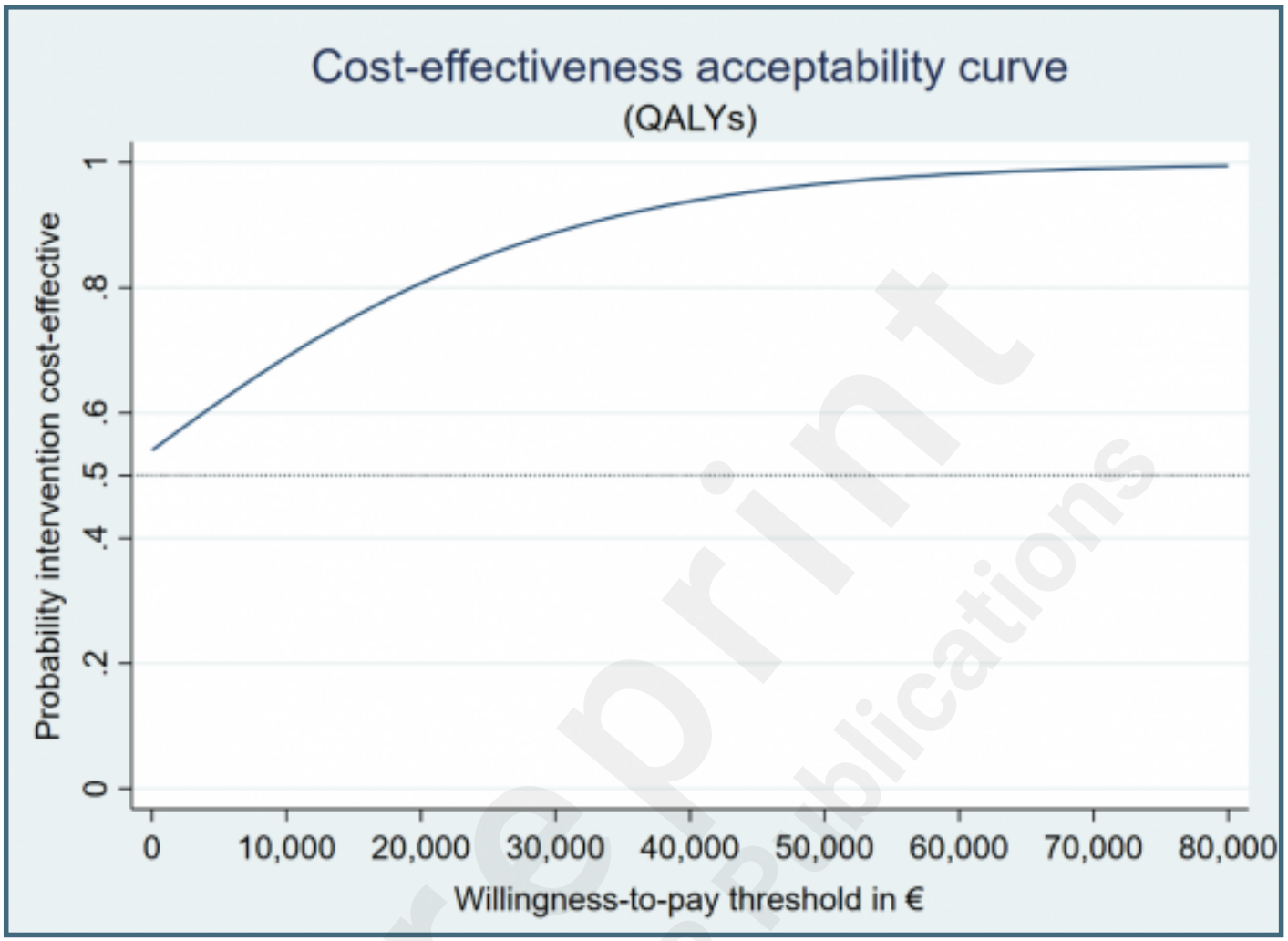
Cost-effectiveness acceptability curves (symptom-free status) from the societal perspective.



Scatterplot of 5000 replicates of the incremental cost-effectiveness ratio (mean differences in costs and QALYs) on the cost-effectiveness plane from the societal perspective: iSMI versus WLC.



Cost-effectiveness acceptability curves (QALYs) from the societal perspective.



Multimedia Appendixes

CHEERS Checklist.
URL: http://asset.jmir.pub/assets/a07a17e00594a807e4ab90e40626a8f4.docx

Related publication(s) - for reviewers eyes onlies

Reivsed manuscript with tracked changes.
URL: http://asset.jmir.pub/assets/45d2b73279c850307a4e7b3748c60a1f.pdf