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Are web-based stress management interventions effective as an indirect treatment for depression? An individual participant data meta-analysis of six randomised trials

Mathias Harrer [1,2], Patricia Nixon [3], Antonia A Sprenger [4], Elena Heber [5], Leif Boß [3], Hanna Heckendorf [3], Claudia Buntrock [4], David Daniel Ebert [1], Dirk Lehr [3]

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[1]Technical University of Munich, Munich, Germany
[2]Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Germany
[3]Health Psychology and Applied Biological Psychology, Leuphana Universitat Luneburg, Luneburg, Germany
[4]Otto-von-Guericke-Universitat Magdeburg, Magdeburg, Germany
[5]GetOn Institut für Gesundheitstrainings GmbH/HelloBetter, Hamburg, Germany

Correspondence to
Professor Dirk Lehr, Health Psychology and Applied Biological Psychology, Leuphana University, Lüneburg, Germany; lehr@leuphana.de

MH and PN contributed equally.

MH and PN are joint first authors.

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ABSTRACT

Question Depression is highly prevalent and associated with numerous adverse consequences for both individuals and society. Due to low uptake of direct treatment, interventions that target related, but less stigmatising problems, such as perceived stress, have emerged as a new research paradigm. This individual participant data (IPD) meta-analysis examines if a web-based stress management intervention can be used as an 'indirect' treatment of depression.

Study selection and analysis Bayesian one-stage models were used to estimate pooled effects on depressive symptom severity, minimally important improvement and reliable deterioration. The dose–response relationship was examined using multilevel additive models, and IPD network meta-analysis was employed to estimate the effect of guidance.

Findings In total, N=1235 patients suffering from clinical-level depression from K=6 randomised trials were included. Moderate-to-large effects were found on depressive symptom severity at 7 weeks post-intervention (d=−0.65; 95% credibility interval (CrI): −0.84 to −0.48) as measured with the Center for Epidemiological Studies' Depression Scale. Effects were sustained at 3-month follow-up (d=−0.74; 95% CrI: −1.01 to −0.48). Post-intervention symptom severity was linearly related to the number of completed sessions. The incremental impact of guidance was estimated at d=−0.25 (95% CrI: −1.30 to 0.82), with a 35% posterior probability that guided and unguided formats produce equivalent effects.

Conclusions Our results indicate that web-based stress management can serve as an indirect treatment, yielding effects comparable with direct interventions for depression. Further research is needed to determine if such formats can indeed increase the utilisation of evidence-based treatment, and to corroborate the favourable effects for human guidance.

Study registration Open material repository: osf.io/dbjc8, osf.io/3qtbe.

Trial registration number German Clinical Trial Registration (DRKS): DRKS00004749, DRKS00005112, DRKS00005384, DRKS00005687, DRKS00005699, DRKS00005990.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Web-based interventions have been shown to be effective in treating depression, but uptake rates remain low. This individual participant data meta-analysis explores the potential of a novel paradigm, in which web-based stress management is used as a low-threshold, 'indirect' treatment for depression.

WHAT THIS STUDY ADDS

⇒ In this first systematic examination of web-based stress management as an indirect intervention for depression, we collected data from K=6 randomised trials with N=1235 patients suffering from clinically relevant symptoms of depression (Center for Epidemiological Studies' Depression Scale ≥20; M=28.57). We found clinically relevant and sustained reductions in depressive symptom severity. Completing more sessions and providing guidance enhanced the anti-depressive effect.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Large-scale provision of web-based stress management interventions might be an innovative, low-threshold approach to reduce the burden of depression in the general population.

BACKGROUND

Depression is highly prevalent, a leading cause of years lived with disability and poses a challenge for healthcare services worldwide.[1] Only a fraction of affected individuals receive any help at all, and mostly not even minimally adequate treatment.[2] Besides structural barriers, attitudinal factors play a major role in explaining this treatment gap for depression.[3] Fear of stigmatisation has repeatedly been suggested as a major barrier to help-seeking,[4] and suffering from depression appears to further increase the magnitude of this barrier.[5]

Delivering mental health interventions over the internet has been argued to have numerous advantages.[6] Web-based interventions allow for an easy

and low-threshold dissemination of evidence-based interventions on a large scale and at low costs. They can be used regardless of time and location[6] and may overcome barriers associated with fear of stigmatisation due to the perceived anonymity of the internet.[7] Further research has been called for to examine the effectiveness of such interventions aimed at the physical and mental health of patients with mental illness, and to promote their real-world implementation.[8 9]

Meta-analyses demonstrate the efficacy of web-based interventions targeting depression,[10] but the uptake of such interventions is often low.[11 12] Preliminary evidence suggests that fear of stigmatisation might also be a major barrier to depression treatment for web-based formats.[13]

A novel paradigm was introduced by Cuijpers to address this problem, proposing an 'indirect' prevention and treatment of depression.[14] Indirect interventions do not focus on depression itself, but on related risk or aggravating factors that might be better aligned with patients' perceived needs or preferences.

Stress management was suggested as a promising method for the indirect treatment of depression.[14] Compared with direct or transdiagnostic treatments, stress management interventions (SMIs) do not specifically focus on characteristic symptoms of clinical diagnoses. Instead, they target perceived stressors that a person feels exposed to, with the goal to minimise them or their negative emotional impact.[15] Although the exact implementation differs, many web-based SMIs implement problem-solving, as well as reappraisal and relaxation techniques for stressors that cannot be directly removed.[16] Stress and depression are closely interlinked,[17] and engaging in web-based stress management might be easier for some patients with depression, avoiding potential stigma associated with the label 'depression'. Previous studies suggest that the 'framing' of therapeutic contents is a crucial and under-rated factor in the dissemination of digital interventions.[18 19]

There is evidence that web-based SMIs may also alleviate depressive symptoms when evaluated as a secondary outcome. First, several meta-analyses demonstrated the efficacy of web-based SMIs on depressive symptoms in general[20] and working[21] populations. Second, stress reduction was identified as a mechanism of change in the prevention of depressive symptoms using web-based SMIs.[22] Third, a moderator study of a web-based SMI found that participants with high stress and depression at baseline showed greater reductions in depressive symptoms over time than those with lower symptoms.[23] Lastly, since the majority of participants were first-time help seekers, this suggests SMIs might be appealing to those who otherwise might not seek help.[24]

OBJECTIVE

While positive evidence is accumulating, no meta-analysis has yet systematically examined the potential of web-based SMIs as an indirect treatment for depression. This individual participant data (IPD) meta-analysis allows for more sophisticated types of analyses, based on randomised controlled trials (RCTs) evaluating the web-based SMI 'GET.ON Fit im Stress'.[25] We test if (1) participants with clinically relevant depressive symptoms show lower levels of depressive symptom severity at post-intervention and 6-month follow-up, compared with control; (2) if rates of patients with minimal clinically important improvement of depressive symptoms are higher, and rates of reliable symptom deterioration are lower; and (3) if a dose–response relationship can be found between the completed SMI modules and effects on depressive symptoms. IPD network meta-analysis is used to explore the effect of human guidance. Additionally, we examine the overall satisfaction with the intervention.

METHODS

The present study has been preregistered (osf.io/wa4h5). The code used for the analyses is openly available (osf.io/p3q6t). All analyses were implemented using R V.4.2.0. Where applicable, we resort to elements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses-IPD statement.[26]

Eligibility criteria

We included (1) RCTs in which (2) the effect of the web-based SMI 'GET.ON Fit im Stress'[25] was compared with (3) an inactive control group (waitlist, care as usual or combinations thereof) at (4) post-test (7 weeks) and 6-month follow-up. A detailed description of the eligible programme is provided in the online supplemental file 2. Since we aimed to analyse effects of the web-based SMI as an indirect treatment for depression, (5) analyses were restricted to patients with a Center for Epidemiological Studies' Depression Scale (CES-D) score ≥20 at baseline, indicating clinically relevant symptoms of depression.[27] We focused on one specific programme because contents of web-based SMIs vary between interventions.[16] Standardised treatments across all trials were assumed to enhance the internal validity of our analyses, especially those concerning the dose–response relationship and effect of guidance.

Identification and selection of studies

Three authors (DL, EH, DDE) contributed to the development of the web-based SMI examined in this IPD meta-analysis. The intervention is not openly accessible, and it cannot be employed for research or commercial purposes without explicit permission by the copyright holder Leuphana University (represented by DL). Instead of a systematic search, the number of trials was therefore assumed to be known, and the involved researchers were consulted to identify eligible studies. Once permission was granted to create an adapted intervention for college students ('StudiCare Stress'), whereby substantial changes were made to the contents and presentation (see online supplemental file 2). Evaluations of this new intervention were therefore not considered. Principal investigators of eligible trials were then contacted to obtain the IPD.

Data harmonisation and variable selection

Data of the included studies were harmonised to allow for joint analyses. Depressive symptom severity measures were extracted at baseline (T1), 7 weeks post-test (T2) and 3-month follow-up (T3) from each study, as well as sociodemographic information and putative prognostic variables. In all trials, the CES-D was used to measure depressive symptom severity. Following our protocol, for all assessment points, these scores were transformed into a common metric using the generalised partial credit model by Wahl *et al*.[28] This common metric is standardised to have a population mean of $\theta=50$, as well as a population SD of $\sigma=10$. All studies employed the same intervention, but with various degrees of human guidance. We coded a study's guidance concept as 'full guidance' if human assistance was provided after each module, as 'adherence-focused guidance'[21] if human feedback was available on demand and as 'unguided' otherwise.

Risk of bias assessment

Risk of bias assessment was conducted using the revised Cochrane Risk of Bias tool.[29] To minimise allegiance biases, the assessment

was conducted by trained personnel not otherwise involved in this study or any of the included trials (see the Acknowledgements section). Disagreements were resolved through discussion.

Missing data handling

All analyses were conducted according to the intention-to-treat principle. Two missing data handling approaches were used. For the main one-stage IPD meta-analysis, we used a Bayesian model-based imputation approach. This method jointly imputes missing values and estimates model parameters, thus ensuring compatibility with the substantive analysis model.[30] Potentially prognostic baseline variables were added as covariates, as well as an interaction between initial depressive symptom severity and treatment effects.

For the two-stage, dose–response relationship and network IPD model, missing values were imputed using the multivariate imputation by chained equations algorithm (m=100 sets; groupwise multilevel imputation model with individual and cluster-level effects). Due to the relatively small number of trials, a maximum penalised likelihood-based approach was used to estimate the heterogeneity variances τ^2.[31] Parameters were pooled by combining the posterior draws of all models fitted in the multiply imputed data. The imputation matrix and trace line plots are depicted in the online supplemental files 3 and 4.

Outcome measures

The primary outcome was depressive symptom severity at 7 weeks post-test (T2), based on the common metric scores derived from the CES-D values in each trial. Additionally, we examined meta-analytical effects on (1) depressive symptom severity at 3-month follow-up (T3; common metric), (2) minimally important improvement of depressive symptoms (post-test and follow-up) and (3) reliable deterioration of depressive symptoms (post-test and follow-up). Minimally important improvement was defined as a decrease of ≥10.1 points on the CES-D, compared with baseline. This threshold was derived from the cut-off value established in Ohno *et al*,[32] who used an anchor-based approach based on the Patient Global Impression of Change. Reliable deterioration was determined using the reliable change index,[33] corresponding with an increase of >8.99 points on the CES-D.

Statistical analyses

Average treatment effect (IPD meta-analysis). The pooled effect of the intervention was calculated using one-stage IPD meta-analysis. Meta-analytical models were implemented in a Bayesian framework using Gibbs sampling (JAGS V.4.3.0). The model included putative prognostic factors of post-test depression as predictors (baseline depressive symptom severity, perceived stress, age and sex) and terms to capture varying treatment effects conditional on the depressive symptom severity at baseline. The treatment effect size (ie, Cohen's d) was calculated by dividing the estimated between-group mean difference at the analysed endpoint by the pooled SD of the outcome. Dichotomous outcomes (minimally important improvement, reliable deterioration) were modelled using a binomial logit-link. Priors for model parameters had been determined beforehand (see 'statistical models' in the preregistration); a weakly informative Half-Cauchy $HC(0,5)$ prior was selected to estimate the heterogeneity variance τ^2. A more detailed model specification is provided in online supplemental file 5 (equations 1 and 2). As a sensitivity analysis, we (1) also estimated effects using Bayesian two-stage models, (2) reran all analyses using a less heavy-tailed $HC(0,3)$ prior and (3) estimated effects on minimally important change when defined as a one-third reduction in CES-D scores. The one-third reduction criterion was used as approximation of a 9-point decrease on the 15-item CES-D, a reference value recently put forward by German national guidelines to define minimal clinically important differences.[34]

Dose–response relationship. To explore the (potentially non-linear) relationship between post-test depression and the number of completed sessions, Bayesian generalised additive mixed models (GAMMs) were employed in the intervention groups. First, we fitted one overall GAMM using all participants, followed by a separate model for respondents (ie, patients showing minimally important improvement at post-test) and non-respondents. Online supplemental file 5 presents a detailed model specification (equation 3).

Effect of guidance (IPD network meta-analysis). To estimate differences in effects between the three guidance formats, an IPD network meta-analysis was conducted. In this model, the guided, adherence-focused and unguided intervention formats were treated as distinct treatments. We also estimated the posterior probability $P\left(\left|\delta_{ung,gui}\right| < MID \mid X\right)$ that the effect of (full) guidance does not exceed a minimally important difference (MID) of d=0.24 (ie, the probability that effects of both formats are practically equivalent from a patient perspective[35]). The same posterior probability $P\left(\left|\delta_{ung,afg}\right| < MID \mid X\right)$ was also calculated for adherence-focused guidance. The model specification is described in online supplemental file 5 (equations 4 and 5).

User satisfaction. A pooled analysis of intervention group participants' satisfaction with the intervention was conducted. We analysed individuals' agreement with items of the Client Satisfaction Questionnaire-8, which was administered in all trials at post-test. Descriptive statistics were calculated separately for the unguided versus guided intervention format and for both formats combined.

Findings

The harmonised dataset contained records of N=1852 individuals, 617 (33.3%) of which reported CES-D scores <20. After excluding these individuals, data of N=1235 patients (intervention: n=661; control: n=574) examined in K=6 trials remained for further analyses. In all trials, the same version of the intervention was used, and control conditions were all waitlists with full access to treatment as usual. Table 1 presents descriptive information about each included trial. The risk of bias ratings for each study can be found in online supplemental file 6. Baseline sample characteristics across all trials are displayed in table 2. Means and SDs of the primary outcome at all assessment points, expressed as the common metric and CES-D scores, are provided in online supplemental file 8.

Treatment effect

Table 3 shows results of the one-stage IPD meta-analysis. The pooled effect on depressive symptom severity at post-test was d=−0.65 (95% credibility interval (CrI): −0.84 to −0.48; number needed to treat (NNT)=7.19). The between-study heterogeneity was moderate (τ=0.11; 95% CrI: 0 to 0.33). The 95% prediction interval (PI) did not include zero (95% PI: −1.06 to −0.30), pointing to the robustness of the effect in future studies. A forest plot of the analysis is depicted in figure 1. Similar findings emerged in sensitivity analyses using a two-stage pooling model (see online supplemental file 9), and when using

Table 1 Descriptive summary of the included primary studies

Study	Inclusion (cut-off)	Conditions	$n_{condition}$	Primary outcome measure	Guidance	Intervention adherence*	Study dropout		Assessments (weeks)
							Post-test	FU	
Ebert, 2016a	PSS-10 ≥22	GET.ON Fit im Stress	132	Perceived stress, 7 weeks (PSS-10)	Guided (AFG)	79.2%	15.2%	26.5%	7, 24
		Waitlist+TAU	131		–	–	3.0%	7.6%	
Ebert, 2016b	PSS-10 ≥22	GET.ON Fit im Stress	131	Perceived stress, 7 weeks (PSS-10)	Unguided	63.4%	9.8%	1.52%	7, 24
		Waitlist+TAU	132		–	–	17.4%	2.27%	
Ebert, 2021	None	GET.ON Fit im Stress	198	Perceived stress, 7 weeks (PSS-10)	Unguided	70.3%	11.1%	5.6%	7, 24
		Waitlist+TAU	198		–	–	32.3%	9.6%	
Heber, 2016	PSS-10 ≥22	GET.ON Fit im Stress	132	Perceived stress, 7 weeks (PSS-10)	Guided (FG)	81.6%	12.1%	3.8%	7, 24, 52 (intervention only)
		Waitlist+TAU	132		–	–	12.9%	8.3%	
Nixon, 2021	PSS-10 ≥22	GET.ON Fit im Stress	135	Perceived stress, 7 weeks (PSS-10)	Guided (AFG)	80.6%	8.9%	21.5%	7, 24
		GET.ON Fit im Stress	134		Unguided	77.3%	5.2%	16.4%	
		Waitlist+TAU	135		–	–	2.2%	11.1%	
Nixon, 2022	ERI >0.715, PSS-10 ≥22	GET.ON Fit im Stress	130	Perceived stress, 7 weeks (PSS-10)	Guided (AFG)	74.4%	9.0%	22.0%	7, 24
		Waitlist+TAU	132		–	–	2.3%	12.6%	

References of the included studies are provided in online supplemental file 7.
*Defined as number of completed sessions/total number of sessions.
AFG, adherence-focused guidance; ERI, Effort-Reward Imbalance Questionnaire; FG, full guidance; FU, follow-up; PSS-10, Perceived Stress Scale; TAU, treatment as usual.

a less heavy-tailed $HC(0, 3)$ prior for τ (see online supplemental tables 10 and 11).

We also detected a pooled effect on minimally important improvement in depressive symptom severity, with an OR of 4.85 (95% CrI: 2.89 to 7.45). This equals an NNT of 2.82 and means that approximately 3 patients need to receive the intervention to achieve an additional case of minimally important improvement. Similar results were obtained when minimally important change was defined as a one-third symptom reduction on the CES-D (see online supplemental 12). In the one-stage model, the intervention was also found to reduce the number of participants experiencing reliable symptom deterioration (OR=0.19; 95% CrI: 0 to 0.75), with an NNT of 18.07. However, no effect on reliable deterioration was found using the two-stage approach (OR=0.43; 95% CrI: 0 to 1.52). Raw count data and non-adjusted (marginal) ORs are presented in online supplemental tables 13 and 14. Overall, n=19 (2.87%) participants in the intervention group experienced reliable symptom deterioration (follow-up: n=14; 2.12%), compared with n=38 (6.62%) in the control group (follow-up: n=48; 8.36%).

Table 2 Participant characteristics at baseline

Characteristic	Overall (N=1235)	Control (N=574)	Intervention (N=661)
Sociodemographics			
Age, M (SD)	42.46 (9.82)	42.43 (10.04)	42.49 (9.63)
Gender, female, n (%)	936 (75.79)	431 (73.34)	505 (76.40)
Gender, other, n (%)	3 (0.24)	2 (0.35)	1 (0.15)
Income, low, n (%)	705 (57.09)	333 (58.01)	372 (56.28)
Ethnicity, non-white, n (%)	216 (17.49)	94 (16.38)	122 (18.46)
Children, yes, n (%)	636 (51.50)	301 (52.44)	335 (50.68)
Working years, M (SD)	17.95 (10.57)	18.15 (10.89)	17.78 (10.29)
Training experience, yes, n (%)	171 (13.85)	89 (15.51)	82 (12.41)
Psychotherapy experience, yes, n (%)	568 (45.99)	269 (46.86)	299 (45.23)
Marital status			
Single, n (%)	376 (30.45)	179 (31.18)	196 (29.65)
Relationship/married, n (%)	702 (56.84)	311 (54.18)	391 (59.15)
Divorced/separated/widowed, n (%)	157 (12.71)	84 (14.63)	73 (11.04)
Educational level			
Up to high school (7–9 years), n (%)	166 (13.44)	87 (15.16)	79 (11.95)
High school education (12–13 years), n (%)	360 (29.15)	163 (28.57)	197 (29.80)
After high school, n (%)	708 (57.33)	323 (56.27)	385 (58.25)

Table 3 Pooled intervention effects on depressive symptom severity, minimally important improvement and reliable deterioration

	Effect size (95% CrI)	NNT (95% CrI)	τ (95% CrI)
Depressive symptom severity			
Post-test (d)	−0.65 (−0.84; −0.48)	7.19 (6.18; 8.93)	0.11 (0.00; 0.33)
Follow-up (d)	−0.74 (−1.01; −0.48)	5.61 (4.71; 7.67)	0.21 (0.00; 0.52)
Minimally important improvement			
Post-test (OR)	4.85 (2.89; 7.45)	2.82 (2.20; 4.43)	0.21 (0.00; 0.82)
Follow-up (OR)	4.94 (2.23; 8.50)	2.67 (2.04; 5.55)	0.42 (0.00; 1.28)
Reliable deterioration			
Post-test (OR)	0.19 (0.00; 0.75)	18.07 (14.52; 62.39)	1.67 (0.00; 4.64)
Follow-up (OR)	0.09 (0.00; 0.33)	13.14 (11.91; 18.19)	1.28 (0.00; 5.39)

CrI, credibility interval; NNT, number needed to treat.

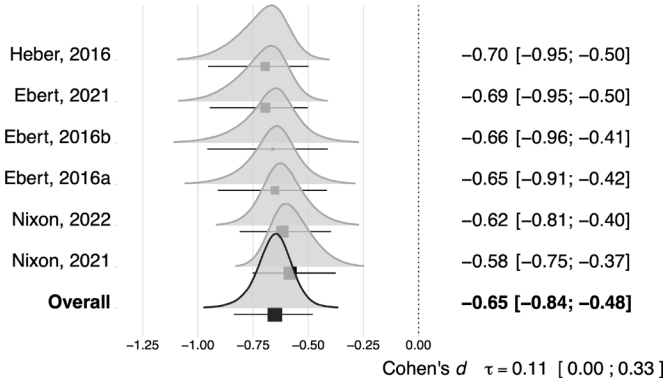

Figure 1 Forest plot (effects on depressive symptom severity at post-test). Study densities represent the estimated model-based effect, not empirical values of d found in the original studies.

For all analysed outcomes, similar findings emerged at 3-month follow-up. However, effects on depressive symptom severity were slightly higher (d=−0.74; 95% CrI: −1.01 to −0.48; NNT=5.61).

DOSE–RESPONSE RELATIONSHIP

Estimated smoothing parameters λ of the fitted GAMMs can be found in online supplemental file 15. Inspection of the dose–response relationship revealed a roughly linear association between the number of completed sessions and post-test depression scores (see figure 2). A non-linear trend was found in the subset of intervention non-respondents, where no additional benefits were visible after session 4. For the overall model, we compared the fit of our regression spline with a simpler model assuming a linear dose–response relationship. This model proved to be more parsimonious (Deviance Information Criterion=4679 vs 4731). Based on the linear model, each additional completed session was associated with a 0.63-point decrease on the 20-item CES-D at post-test (β=−0.631; 95% CrI: −0.93 to −0.329; τ_0=0.29).

Effect of guidance

A network graph of the included treatment comparisons is provided in figure 3. Using network IPD meta-analysis, the effect $\delta_{ung,gui}$ between the fully guided and unguided intervention format was estimated at d=−0.25, with a wide 95% CrI that included 0

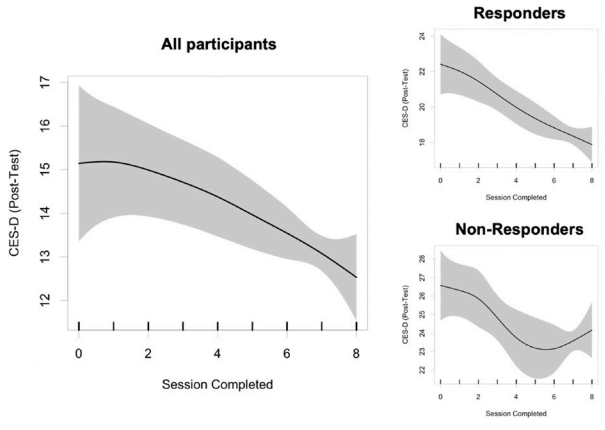

Figure 2 Dose–response relationship estimated by additive mixed models. CES-D, Center for Epidemiological Studies' Depression Scale.

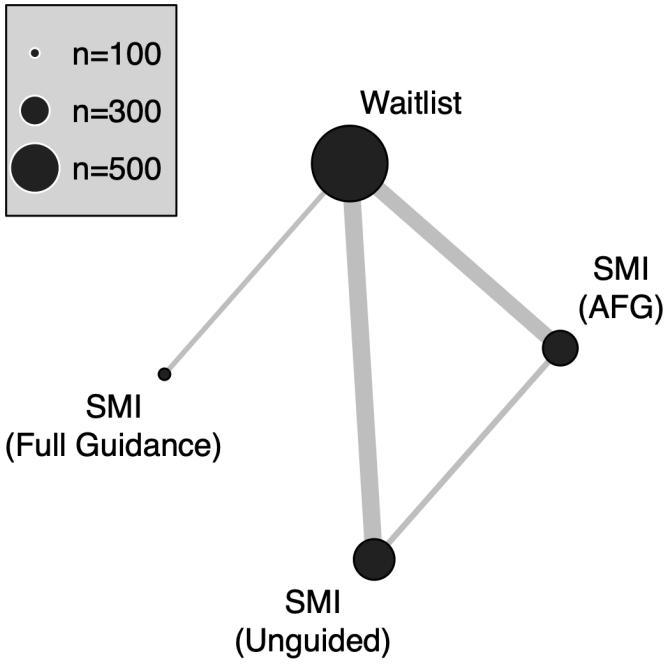

Figure 3 Network graph. Edge sizes represent the number of available data for the specific comparison. AFG, adherence-focused guidance; SMI, stress management intervention.

(−1.30 to 0.82). The impact of adherence-focused guidance was estimated at d=0.09 (95% CrI: −0.57 to 0.73). Online supplemental table 16 provides effect estimates for all comparisons implicated by the treatment network. The model's estimate of $P\left(\left|\delta_{ung,gui}\right| < MID \mid X\right)$ and $P\left(\left|\delta_{ung,afg}\right| < MID \mid X\right)$ was 0.35 and 0.60, respectively. This represents a 60% posterior probability that adherence-focused guidance provides no clinically relevant added benefits, while, for full guidance, this probability is considerably lower (only 35%).

User satisfaction

Complete results of the user satisfaction analysis are presented in online supplemental file 17. Overall user satisfaction was high (91.5% 'very' or 'mostly' satisfied; n=529), with 94.6% (n=547) rating the intervention quality as 'excellent' or 'good', and 89.5% (n=517) indicating that they would recommend the intervention to a friend. There were minor differences between guidance formats, with guided intervention participants reporting slightly higher satisfaction.

DISCUSSION

This IPD meta-analysis examined the effects of a web-based SMI as indirect treatment for depression, including 1235 patients with clinically relevant depressive symptoms. Results revealed moderate-to-large effects at 7 weeks post-test (d=−0.65) and 3-month follow-up (d=−0.74) which were corroborated with sensitivity analyses.

To the best of our knowledge, this is the first meta-analysis demonstrating that a specific web-based SMI can reduce depressive symptoms in clinical samples, with stronger effects compared to an earlier meta-analysis examining a variety of web-based SMIs (d=−0.34[20]). One explanation for these favourable effects might be that the present intervention employed problem-solving and behavioural activation techniques, methods that are also found in direct treatments for depression. Furthermore,

prior studies included participants with lower levels of distress,[20] while the current study focuses on participants with clinical levels of depression.

IPD meta-analyses with comparable inclusion criteria found that the effect of direct web-based interventions for depression, compared with waitlists, was d=−0.33 to −0.60 for self-guided and d=−0.80 for guided interventions.[10 36] The effect of psychotherapy for depression compared with waitlists, regardless of the delivery mode, is d=−0.62 to −0.92.[37] Thus, our effects compare with those of direct treatments. Use of co-interventions during the study period was low (8.3%) and equally distributed between groups, suggesting that the web-based SMI primarily accounted for the observed benefits. An anchor-based approach was employed to calculate response rates, following recent recommendations.[38 39] The effect on minimally important improvement was OR=4.85, NNT=2.82. Prior meta-analyses, using non-anchor-based methods, found similar effects for direct web-based depression interventions (OR=3.49[40] compared with inactive control), and for depression psychotherapy in general (NNT=3.9[41] vs waitlists). These results further corroborate that benefits of the intervention are comparable with a direct depression treatment.

User safety is important when web-based SMIs are used 'off-label' in the treatment of depression. Notably, the deterioration rate was low (2.87%) and comparable with direct web-based interventions for depression (3.57%).[42] Overall, there were no indications that the indirect treatment approach might be more harmful than direct treatment.

User satisfaction was slightly higher when personal support was available, and identical or higher than direct web-based interventions targeting depression prevention,[43] diabetes[44] and formally diagnosed depression.[45]

IPD network meta-analysis estimated benefits of the 'fully' guided intervention at d=−0.82, with lower effects for adherence-focused guidance (d=−0.48) and for unguided treatment (d=−0.57). However, CrIs of estimates were wide and included zero. Nevertheless, our findings imply a low (35%) posterior probability that the fully guided and unguided formats produce equivalent effects, and the majority preferred the guided format.[22] In contrast, adherence-focused guidance might not provide relevant benefits, and very few patients in this condition made use of this opportunity.[22 46 47]

The dose–response relationship indicated that post-treatment depression scores were linearly associated with the number of completed sessions, emphasising the importance of adherence. Importantly, while plausible, this analysis alone cannot show if some intervention components have 'specific' effects on depression. It is also possible that the intervention primarily reduces perceived stress, which ameliorates depressive symptoms; or that even more complex working factors are at play. Component network meta-analyses or fractional factorial designs could allow to illuminate this in the future.

Several limitations should be considered. First, the specific SMI we examined in this study might not be representative of other SMIs that include different techniques. Second, included patients were not diagnosed using a diagnostic interview. Third, adverse events other than reliable symptom deterioration were not considered. Fourth, while we found effect sizes comparable with direct interventions for depression, clinical trials with head-to-head comparisons are needed to confirm the non-inferiority of indirect treatment. This is important because all included trials used waitlist comparators, which could have inflated effect estimates.[24] It could also allow to examine between-group effects for patients with similar adherence levels, which was not possible in the current dose–response analysis. Lastly, the user satisfaction found in this study does not imply a generally higher intention to engage in indirect interventions compared with those explicitly targeting depression.

The goal of the indirect treatment paradigm is to increase the uptake of anti-depressive interventions in the population, and the present study suggests web-based SMIs should be considered in this novel strategy. The next step is to generate empirical evidence if offering web-based SMIs will lead to a higher uptake of evidence-based depression treatment, as indicated by the high rate of first-time help-seekers in the present sample (54%).

Indirect treatment is based on the conjecture that factors such as stress, insomnia, perfectionism or low self-esteem are related to depression. In contrast to the clinical label 'depression', these factors are assumed to better reflect some individuals' concept of their own mental health, thus increasing the willingness to engage in targeted psychological interventions. Indirect interventions probably share many 'specific' working factors with conventional depression treatments, but they are distinct in their therapeutic rationale, and in how they approach patients' perceived needs. More research is needed to test this paradigm, particularly how patients with depression cognitively represent their own symptomatology, and how this relates to (differential) help-seeking attitudes. It is possible that some patients will not even be willing to partake in an intervention that aligns better with their perceived mental health problem. Research on indirect interventions could allow to elucidate the scale of this problem.

We conclude that the web-based SMI evaluated in this meta-analysis can be an effective indirect treatment of depression. User satisfaction with the intervention was high. No increased harmful effects were found. Preliminary evidence suggests that professional guidance leads to better effects.

Twitter Mathias Harrer @MathiasHarrer

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Patient consent for publication Not required.

Ethics approval This study involves human participants. This is an individual participant data meta-analysis of multiple independently conducted studies, which themselves have been approved by the respective Ethics Committees. Participants gave informed consent to participate in the study before taking part.

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ORCID iDs
Mathias Harrer http://orcid.org/0000-0001-7016-2687
Patricia Nixon http://orcid.org/0000-0002-9747-3845
Antonia A Sprenger http://orcid.org/0000-0002-1180-7702
Elena Heber http://orcid.org/0000-0002-3438-0756
Leif Boß http://orcid.org/0000-0001-9012-0839
Hanna Heckendorf http://orcid.org/0000-0002-8665-0439
Claudia Buntrock http://orcid.org/0000-0002-4974-5455
David Daniel Ebert http://orcid.org/0000-0001-6820-0146
Dirk Lehr http://orcid.org/0000-0002-5560-3605

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