



A Systematic Review and Meta-Analysis of Applicability of Web-Based Interventions for Individuals with Depression and Quality of Life Impairment

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Objective The purpose of this meta-analysis was to determine the applicability of web-based treatment programs for individuals with depression and quality of life impairments.

Methods We conducted database and manual searches using imprecise search-term strategy and inclusion criteria. Research published from 2005 to December 2015 was included in this study. Upon review, a total of 12 published papers on web-based intervention for individuals with depression were assessed eligible for this meta-analysis. Effect sizes were estimated for depression and quality of life.

Results The mean effect size of web-based treatment on depressive symptoms was 0.72. However, unlike the result showing medium to large effect size, the analysis on the quality of life did not yield adequate effects of web-based interventions.

Conclusion Our results suggest robust benefits of employing web-based treatments for depressive symptoms. However, the adequacy of these relatively new intervention tools for individuals who suffer severe impairments of quality of life was found insufficient. The current study demonstrates the need to further develop web-based intervention techniques to improve overall functioning, as well as the clinical symptoms of patients with mental disorders.

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Key Words Web-based intervention, Internet-based intervention, Depression, Quality of life, Meta-analysis.

INTRODUCTION

Individuals with depression exhibit markedly decreased interest or pleasure in all daily activities, weight gain or loss, sleep problems, cognitive impairments, fatigue or loss of energy, and suicidal ideation.¹ That these symptoms can easily intensify or recur and reduce the daily function² render timely and steady interventions critical for patients with mood disorders.³

Cognitive behavioral therapy (CBT), a form of psychother-

apy, is a representative evidence-based therapy that has proved its therapeutic effect on mood disorder patients.⁴ The effectiveness of psychotherapy in depression treatment was found comparable to those of psychiatric medication, which is one of the primary treatments.^{5,6} Adequate and judicious interventions, however, remain inaccessible to a significant portion of psychiatric population, where in low income, geographical distance, and stigmatization pose major challenges.^{7,8}

Since the 2000s, the advent of easily accessible personal computers and smartphones fostered the emergence of web-based therapy as a new form of treatment for patients who cannot afford treatment due to economic or geographical reasons.^{9,10} Currently available web-based intervention efforts take various approaches, such as Cognitive Behavior Therapy, Psychoeducation, and Mindfulness.^{10,11} The ways to access these programs are also various, extending beyond the web sites to email correspondence, chat rooms, video chats, and mobile applications. These facets confer major advantages upon web-based interventions, allowing individuals to customize both the soft and hard contents according to his or her

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needs and to seek help without worrying the social stigma.¹²⁻¹⁴ In addition, most web-based therapies yield significant symptoms improvements in patients and demonstrate effectiveness.^{15,16} For instance, delivery of psychoeducation by web-based program was found to significantly decrease depression and anxiety symptoms in depressed patients.¹⁰

However, findings on the effectiveness of web-based intervention are difficult to generalize. For example, a study compared the effects of web-based psychotherapy and face-to-face treatment program in depressed outpatients and found the former to demonstrate less effect on symptom alleviation than the latter.¹⁷ The authors explained the superior treatment efficacy of face-to-face intervention with possibly enhanced rapport, motivations, and treatment compliance managed by the interpersonal, direct contact. In addition, meta-studies of the effectiveness of web-based therapy focusing only on symptom changes do not meaningfully address whether the decrease in symptom reflects changes in life quality. Poor quality of life is one of the most disabling aspects of depression.¹⁸ A multi-center study on quality-of-life dysfunction reported severely impaired quality of life in the majority of depressed patients.¹⁹ Fortunately, depression-related decrease in quality of life seems to be reversible, in that a significant improvement after appropriate treatment has been demonstrated even in patients with chronic depression.²⁰ The necessity and importance of incorporating “quality of life” in mental-health treatment settings are well represented in the World Health Organization (WHO)’s definition of health as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.”²¹ In web-based therapy, too, effectiveness needs to be demonstrated beyond the limited scope of solely focusing on symptomatic relief and extend to the accompanied changes in quality of life.

Therefore, the present meta-analysis examined the effectiveness of web-based intervention. The scope of this meta-analysis covered studies conducted between the years 2005 and 2015 that implemented depression scale scores and quality of life as outcome measures. Our study objectives were first, to provide meta-analytic evidence for the effectiveness of web-based psychotherapy on improving symptom and quality of life for depressed individuals. Second, to systematically review the clinical implications and limitations of web-based intervention demonstrated in the extant literature and to suggest practical directions for future developments of this new generation method of intervention.

METHODS

Database and search strategies

A systematic search was conducted using the following

electronic databases: MEDLINE, PUBMED, PsyARTICLES, PsycINFO. Extraction and assessment processes were independently conducted by three trained investigators (DY, YB, JL). The investigators first independently reviewed titles and abstracts, and the ensuing second independent review was conducted based on the full-text article. Discrepancies regarding study eligibility were resolved by discussion with a third reviewer (SC or JH). We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement in reporting this review.²² In order to identify studies examining the relevant issue, following keywords were used in combination: Depression, Depressive, Depressed, Treatment, Therapy, Intervention, Randomized Controlled Trial (RCT), Web, Internet, Online, Smartphone, Android or SMS. Lastly, we conducted a comprehensive grey literature search and manual searches in the reference lists from included articles and relevant review articles to identify papers missed in the database searches.

Inclusion and exclusion criteria

Inclusion criteria were determined following Participants, Interventions, Comparator and Outcomes (PICOS).²³ Inclusion criteria for the present study were as follow: 1) study population of adults who were at least 18 years old, 2) diagnoses conferred with diagnostic criteria or clinical scales, 3) psychological interventions protocol utilized computer or smart phone based delivery, 4) presence of control group with TAU (Treatment As Usual) or Wait List Control (WLC) status, 5) randomized controlled trial, 6) comparative analysis, 7) outcome variables included depression symptoms and quality of life, and 8) a peer review paper written in English.

The exclusion criteria employed were as follow: 1) the use of CD-ROM programs that did not use the web, 2) the use of a group that appealed to subjective depression without objective measures, and 3) research that may lead to bias in results by conducting research only on specific gender.

Data extraction

One investigator extracted data from candidate articles independently, and the other investigators crosschecked the extracted data. Data, including research design, diagnostic criteria for subjects, the characteristics of the sample, intervention format, and research results, were extracted from the selected articles for the meta-analysis. If necessary, authors were contacted to request of any missing data.

Data analysis

The statistical procedure in the meta-analysis follows the general statistical analysis methods. In our analysis, effect sizes were estimated from each research to determine the effec-

tiveness of web-based intervention on the clinical symptoms and the quality of life of individuals with depression. Then, assessments of heterogeneity and publication bias were performed in order to define the identity of summarized data. The number of sessions was excluded from the analysis because there was no correlation ($p=0.192$) between the variable and the decrease in depression scale scores [(baseline minus follow-up scores)/baseline scores].

First, the individual effect sizes were calculated for each of the study included in the analysis, and the mean effect size (Hedges' g) across studies were pooled using the extracted effect sizes. We calculated overall effect sizes both with the random effects model and the fixed effects model. Here, we presented only the results of the analyses based on either fixed or random effects model according to heterogeneity (the fixed effects for low heterogeneous studies vs. the random effects for high heterogeneous). Heterogeneity between studies was assessed using I^2 , the percentage of the total variation. To interpret the effect size results, we adopted the Cohen's "rules-of-thumb" as following: small, 0.20 to 0.49; medium, 0.50 to 0.79; and large, 0.80 or greater.²⁴ Because the meta-analyses based on the published-significant findings may overestimate the pooled effect size.

Funnel plots visualizing the possibility of publication bias were also created to prevent over-interpretation.²⁵ In this plot, which is most commonly used to examine the existence of publication bias in a meta-analysis, large size studies appear toward the top and smaller studies toward the bottom of the plot. When bias exists, the bottom of the plot shows a higher concentration of studies on one side of the mean than the other. Therefore, visual inspection of a funnel plot can give an indication of publication bias when the studies are non-symmetrically distributed across the pooled effect size. We performed

the analysis of publication bias only for the research related to the depression not for the quality of life, because the number of studies does not suffice the requirement for performing the analysis of publication bias.²⁶ The overall calculations were conducted using Microsoft Excel 2011 (Microsoft Corp., Redmond, MA, USA) for mac and Comprehensive Meta-Analysis 3.0 version (CMA 3.0; Biostat Inc., Englewood, NJ, USA) for windows 10.

RESULTS

Description of included trials

We screened 547 original bibliographic references. The flow chart illustrates the included trials, including the reasons for exclusion (Figure 1). Of the 547 papers, 300 were discarded because they were duplicated. Of the remaining 247 papers, 143 full texts were available and 12 articles on symptoms and 4 articles on quality of life met inclusion criteria and were included in the final review (Table 1).

Effects of interventions on depressive symptoms

The meta-analysis of web-based intervention revealed a significantly different mean effect of Hedges' $g=0.72$ (95% CI: 0.479–0.962) compared with controls. The results were based on random-effect model since the I^2 statistic, the indication of the heterogeneity revealed remarkable heterogeneity among studies ($I^2=73.3\%$) (Table 2 and 3, Figure 2).

Effects of interventions on quality of life

According to the fixed-effect model based-meta analysis, there was no difference in quality of life in favor of the web-based intervention (Hedges' $g=0.25$, 95% CI: 0.064–0.457). The difference in the treatment effect on quality of life was

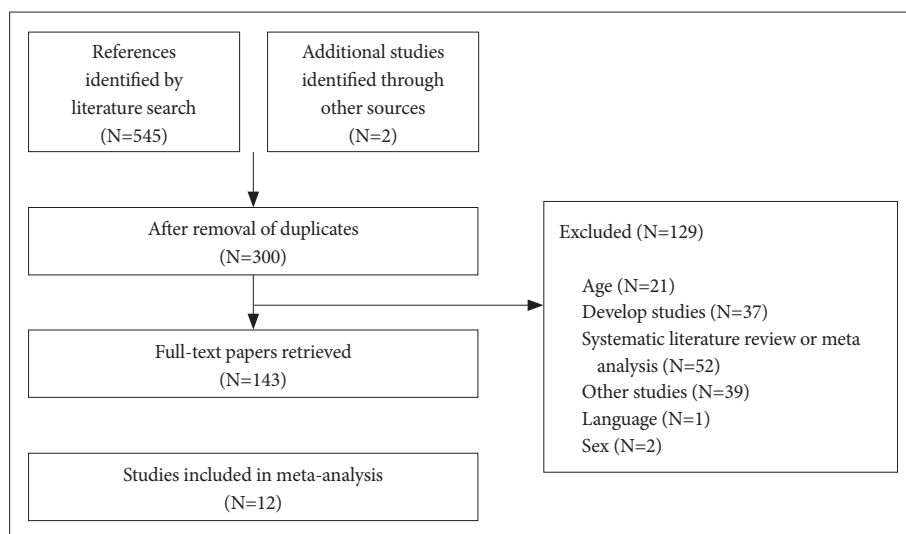


Figure 1. Details of the literature search.

Table 1. Program session information of thesis used for final screening

Authors (year)	Country	Diagnostic tool	Sample size (female %)		Mean ages (SD)		Web-based-program vs. control condition	Number of sessions	Intervention period
			Web-based intervention group	Control group	Web-based intervention group	Control group			
Bolter et al. (2013) ⁴¹	Finland	CES-D	143 (79.7)	141 (79.4)	43.5 (11.7)	42.8 (11.9)	Mental fitness (psyfit) vs. WLC	6	6 wks
Carlborg et al. (2013) ³⁵	Sweden	SCID	40 (77.5)	40 (87.5)	43.6 (13.7)	45.3 (13.4)	ACT vs. TAU	7	7 wks
Johansson et al. (2013) ³²	Sweden	MINI	50 (84)	50 (80)	43 (13.9)	46.6 (12.1)	CBT vs. TAU	8	10 wks
Kivi et al. (2014) ⁴²	Sweden	MINI	47 (N/A)	45 (N/A)	36.6 (11.3) for all participants		CBT vs. TAU	8	8 wks
Lappalainen et al. (2015) ⁴³	Sweden	SCID	13 (68.4)	15 (75)	50.3 (12.5)	53.4 (13.4)	ACT vs. WLC	9	9 wks
Moritz et al. (2012) ³⁴	German	Medical certificate	105 (77)	105 (80)	38 (10.8)	39.1 (15.8)	CBT vs. TAU	10	10 wks
Nobis et al. (2015) ⁴⁴	Netherlands	SCID	82 (64)	80 (63)	50 (12)	51 (12)	CBT vs. WLC	6	6 wks
Perini et al. (2009) ⁴⁵	Australia	MINI	27 (85.19)	18 (66.67)	49.3 (9.4)	49.3 (15.6)	CBT vs. WLC	6	8 wks
Ström et al. (2013) ³⁷	Sweden	SCID	24 (83.3)	24 (83.3)	48.8 (12.7)	49.6 (8.7)	Physical activity vs. TAU	7	7-8 wks
Titov et al. (2015) ³¹	Australia	MINI	27 (81.5)	25 (64)	64.5 (2.58)	66.2 (3.80)	CBT vs. TAU	5	8 wks
Vermmark et al. (2010) ³⁶	German	SCID	30 (70)	29 (55.2)	40.5 (13.9)	32.7 (10.6)	E-mail therapy vs. TAU	6	6 wks
Williams et al. (2013) ⁴⁶	Australia	MINI	35 (77)	28 (75)	44.3 (11.8)	45.4 (12.4)	CBT vs. WLC	6	10 wks

CES-D: a score of 10-24 on the Center for Epidemiologic Studies Depression Scale, MINI: Mini International Neuropsychiatric Interview, CBT: cognitive behavior therapy SCID: Structured Clinical Interview for DSM-IV, TAU: Treat As Usual, WLC: Wait List Control, Mental fitness (Psyfit): an online self-help intervention, Physical activity: Internet-administered treatment based on guided physical exercise

calculated using fixed-effect model when considering that there was found low heterogeneity ($I^2=12.7%$) (Table 2 and 4, Figure 3).²⁶

Publication bias

The funnel plot for depression is presented in Figure 4, and shows asymmetrically distributed studies in the bottom of the graph. As visually assessed, the slightly asymmetry funnel plot of the studies on depression suggested to consider the potential ‘file draw’ problem with unpublished papers due to the non-significant results.

DISCUSSION

The present meta-analysis examined the therapeutic effects of web-based intervention in relation to the changes in clinical symptoms and quality of life. Our meta-analysis of peer-reviewed papers published between 2005 and 2015, demonstrated the remarkable effects of web-based intervention on reducing depressive symptoms compared to control treatments or no treatment. However, web-based intervention was found to exert no significant effect on life quality changes. Our results suggest that although the internet setting, as a new environment for psychotherapy, can offer a compelling alternative for depression treatment, its impact on daily life, as well as on life satisfaction, remains obscure.

The application of web-based therapies are being studied for a wide variety of mental disorders, including anxiety disorders, post-traumatic stress disorder, schizophrenia as well as depressive disorder.^{9,27-29} Effectiveness of these applications have been demonstrated, such as in relieving symptoms and reducing stress. With further technological advances, the availability of these new platformed interventions are expected to become even more extensive. Extant literature offers limited information on comparisons between web-based psychotherapy and pharmacotherapy. However, the advantages of web-based psychotherapy was also advocated in a previous meta-analysis conducted by Hofmann and his colleagues, who compared the effectiveness of conventional psychotherapy with antipsychotics in subjects diagnosed with major depressive disorder receiving either offline CBT treatment or selective serotonin reuptake inhibitors (SSRIs).³⁰ Though the authors found symptoms alleviation in all subjects, side effects, such as anxiety or stress, were also reported in the medication groups. Together, these results suggest the potential strength of web-based intervention as a promising therapeutic alternative, especially when considering possible costs associated with drug treatments, such as spatial- and temporal constraints, adherence and adverse drug effects.

Furthermore, our systematic review indicated that 7 out of

Table 2. Summary of meta-analysis results

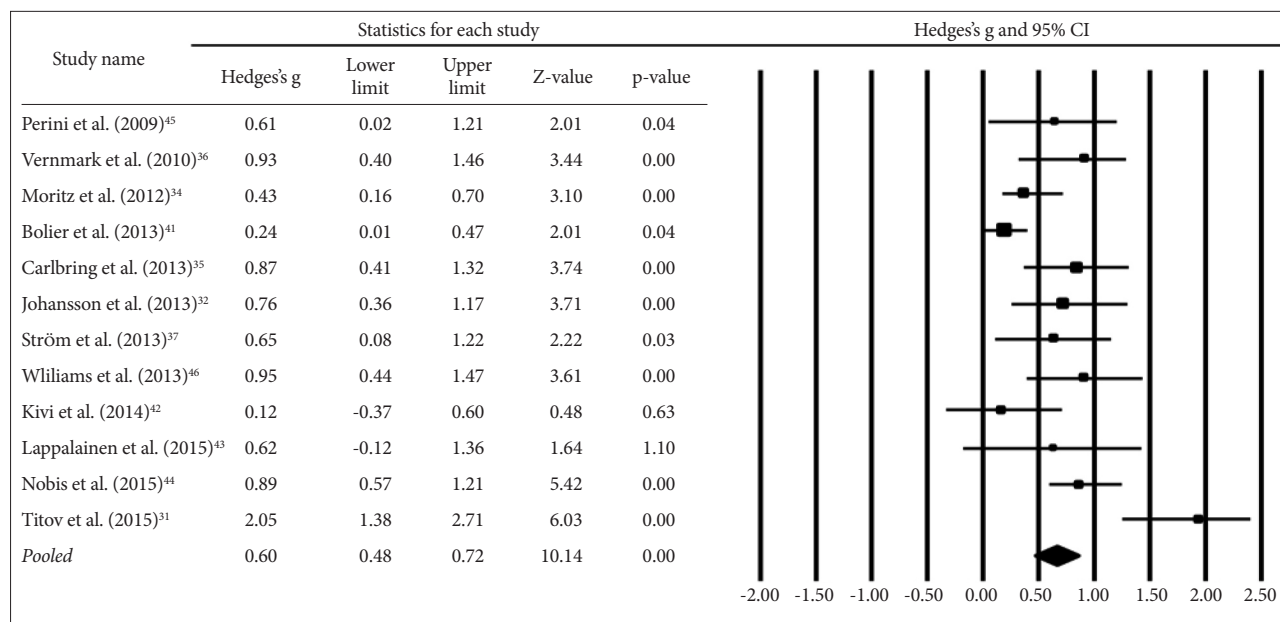
	N comp	Overall Hedges' g	95% CI	I ²
Depression	12	0.721	0.479–0.962	73.284
Quality in life	4	0.248	0.064–0.457	12.736

N comp: number of comparison, CI: confidence interval, I²: Heterogeneity index (%)

Table 3. Depressive symptoms at post-intervention

Authors (year)	Depression measures	Web-based intervention group, mean (SD)	Control group, mean (SD)
Bolier et al. (2013) ⁴¹	CES-D	21.08 (8.84)	28.9 (8.65)
Carlbring et al. (2013) ³⁵	BDI-II	16.65 (8.04)	23.43 (7.67)
Johansson et al. (2013) ³²	PHQ-9	6.32 (4.2)	10.26 (5.9)
Kivi et al. (2014) ⁴²	BDI-II	13.23 (10.94)	14.46 (9.88)
Lappalainen et al. (2015) ⁴³	BDI-II	13.34 (6.75)	17.85 (7.34)
Moritz et al. (2012) ³⁴	BDI-I	20.51 (12.22)	25.67 (11.65)
Nobis et al. (2015) ⁴⁴	CES-D	13.67 (6.69)	15.39 (7.64)
Perini et al. (2009) ⁴⁵	BDI-II	17.30 (9.86)	23.33 (9.29)
Ström et al. (2013) ³⁷	BDI-II	17.88 (11.30)	24.04 (6.86)
Titov et al. (2015) ³¹	PHQ-9	3.96 (2.48)	12.68 (5.48)
Vernmark. et al. (2010) ³⁶	BDI-I	10.3 (5.2)	16.6 (7.9)
Williams et al. (2013) ⁴⁶	BDI-II	10.40 (9.77)	20.54 (11.36)

CES-D: Center for Epidemiologic Studies-Depression Scale, BDI: Beck Depression Inventory, PHQ: Patient Health Questionnaire

**Figure 2.** Effect sizes for web-based treatments versus waiting list controls and forest plot on depression.**Table 4.** Quality of life measures at post-intervention

Authors (year)	Quality in life measures	Web-based intervention group, mean (SD)	Control group, mean (SD)
Carlbring et al. (2013) ³⁵	QOLI	0.78 (1.57)	0.75 (1.77)
Vernmark et al. (2010) ³⁶	QOLI	0.99 (1.85)	0.26 (1.82)
Moritz et al. (2012) ³⁴	WHOQOL-BREF	73.42 (14.27)	68.26 (12.04)
Ström et al. (2013) ³⁷	QOLI	0.16 (1.99)	0.23 (1.47)

QOLI: Quality in Life Inventory, WHOQOL-BREF: The World Health Organization Quality of Life assessment tool brief version

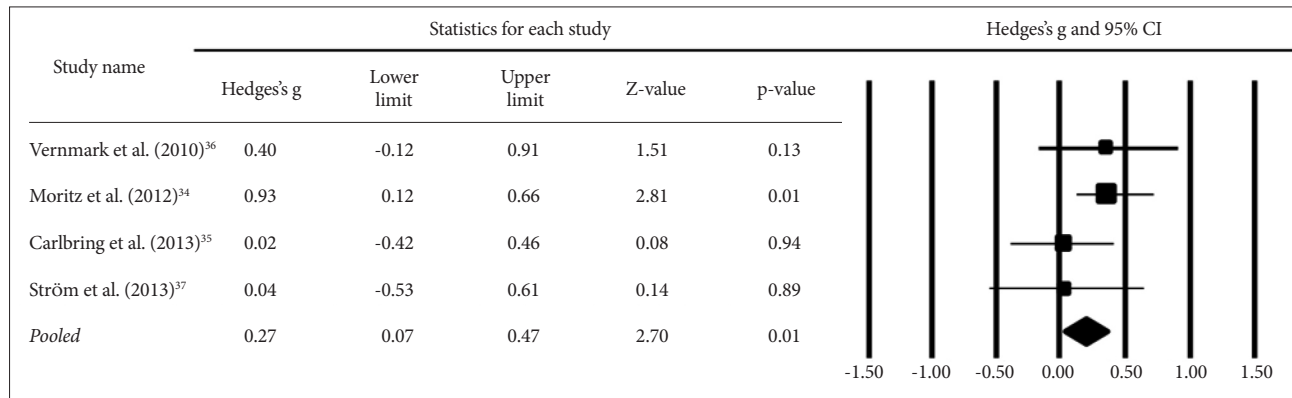


Figure 3. Effect sizes for web-based treatments versus waiting list controls and forest plot on quality of life.

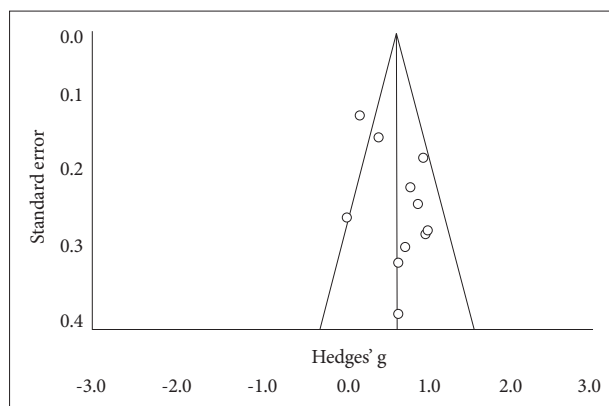


Figure 4. Funnel plot for depression.

9 researches employed internet-based CBT treatment and also suggested relatively better effect in web-based CBT compared to other interventions. The most prominent effect size (Hedges' $g=2.05$; 95% CI: 1.38–2.72) was reported for Titov et al.³¹ web-based CBT program. In this program, the depressed participants were asked to watch online lectures for 8 weeks on 5 topics: assertiveness communication skills, problem solving, managing worry, challenging beliefs, and sleep hygiene. In addition, all participants received 10-minutes calls or emails every week from professionals. As interpersonal contact can improve the effectiveness of web-based CBT,³² the notable impact this particular intervention had on depression may, at least partly, be due to the phone calls and emails by professionals.

The effects of a web-based treatment program demonstrated in the present study, however, were rather limited to the domain of symptom relief, and effects on improvements in facets of life quality were found inadequate. This negative result is inconsistent with the well-known positive impact that conventional CBT has on quality of life.³³ In a study comparing the proportion of patients with clinically severe impairment in quality of life, the records of depression (56–85%) were found remarkably higher compared to those of other mental disor-

ders such as panic disorder (20%), obsessive compulsive disorder (26%), or social phobia (21%). The role of web-based CBT in the quality of life, thus, should be further elaborated by future studies and developers in relevant fields.¹⁹

The lack of evidence found for the effectiveness in quality of life may be explained by the differences in content compositions of each web-based program. The web-based treatment devised by Moritz et al.³⁴ targeted a variety of psychological factors related to quality of life, such as cognitive modification, mindfulness, positive psychology and emotion-focus interventions. Intervention designed by Carlbring et al.,³⁵ on the other hand, focused on behavioral activation (BA) and employed, acceptance commitment therapy (ACT), while Vernmark et al.³⁶ implemented a psychoeducational program that included therapy theory and depressive symptoms from a CBT-perspective, and Ström et al.³⁷ applied therapist-guided physical exercise. Though the aforementioned studies all reported no significant effect on life quality changes in depressed populations, the broad range of differences in objectives and methods evident across studies should not be overlooked. Clinical symptoms constitute only a part of the multifaceted factors that affect the quality of life of patients.³⁸ As such, web-based interventions heavily focusing on symptom relief may be too narrow and miss important mental health indicators. On the other hand, there is also possibility that statistically insignificant results may be derived due to the quite complex and extensive nature of the variable, quality of life. Therefore, further research is required, focusing on the details of the quality of life.

Our present results reiterate the necessity of therapeutic techniques that monitor and intervene the general adaptation level and daily functions in individuals with psychiatric symptoms. Given that the ultimate goal of all psychotherapies is to enhance life satisfaction and adaptation levels,^{39,40} issues related to the coverage of web-based intervention deserves much attention. The currently available web-based pro-

grams that have been in use for more than a decade may now be on the crossroads of mainstream treatment and adjunctive therapy and heading to a new era on the crossroads.

Significance of this meta-study lies in its analysis of the effects that web-based treatment program has on symptom relief and quality of life of individuals with depression, the most common mood disorder. However, several limitations of the present study also need to be considered. Our inclusion of studies limited to those reporting outcome variables both for depressive symptom relief and quality of life led to the exclusion of other various contents of the web-based treatment program. A more encompassing meta-analysis will be avail with much research on web-based psychotherapy ongoing (ClinicalTrials.gov; a service of the U.S. National Institutes of Health, <https://clinicaltrials.gov/>). Likewise, further research examining the details of the clinical conditions associated with successful web-based psychotherapy, such of as self-esteem or personality traits, would be of great interest. The heterogeneity across programs should also be noted. Varying numbers of sessions, durations of a single session, and participant demography across studies may impact the extent of therapeutic effect. In the present study, however, we did not make a detailed distinction based on such differences, as doing so would lead to insufficient number of studies and impact the power of analysis. With further accumulation of relevant research, the necessary subcategorization and comparison of the effects based on differential study parameters and subject characteristics would be possible.

Despite limitations, our current meta-analysis provided compelling evidence for the effectiveness of web-based intervention in relation to depressive symptom alleviation. Web-based intervention availed a new platform for psychotherapy that may complement the present depression treatment regimes by widening the scope of treatment, or may serve as a good alternative to the existing options. The tool's promising prospects, however, yet remains in short of reaching the quality of life domains. Findings from the present meta-analysis advocate the necessity of expanding the scope of web-based intervention approaches by developing various intervention modules. In order to give practical assistance to users, future developments in the field should carry methodological rigor, while, at the same time remain close to the everyday life.

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REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual

- of Mental Disorders (DSM-5®). Washington DC: American Psychiatric Pub; 2013.
2. Paykel E. Partial remission, residual symptoms, and relapse in depression. *Dialogues Clin Neurosci* 2008;10:431-437.
3. Otto MW, Smits JA, Reese HE. Combined psychotherapy and pharmacotherapy for mood and anxiety disorders in adults: review and analysis. *Clin Psychol Sci Pract* 2005;12:72-86.
4. DeRubeis RJ, Gelfand LA, Tang TZ, Simons AD. Medications versus cognitive behavior therapy for severely depressed outpatients: mega-analysis of four randomized comparisons. *Am J Psychiatry* 1999;156:1007-1013.
5. Andersson G, Strömgen T, Ström L, Lyttkens L. Randomized controlled trial of internet-based cognitive behavior therapy for distress associated with tinnitus. *Psychosom Med* 2002;64:810-816.
6. Montgomery SA, Baldwin DS, Blier P, Fineberg NA, Kasper S, Lader M, et al. Which antidepressants have demonstrated superior efficacy? A review of the evidence. *Int Clin Psychopharmacol* 2007;22:323-329.
7. Sharp ML, Fear NT, Rona RJ, Wessely S, Greenberg N, Jones N, et al. Stigma as a barrier to seeking health care among military personnel with mental health problems. *Epidemiol Rev* 2015;37:144-162.
8. Fazel S, Geddes JR, Kushel M. The health of homeless people in high-income countries: descriptive epidemiology, health consequences, and clinical and policy recommendations. *The Lancet* 2014;384:1529-1540.
9. Allen AR, Newby JM, Smith J, Andrews G. Internet-based cognitive behavioural therapy (iCBT) for posttraumatic stress disorder versus waitlist control: study protocol for a randomised controlled trial. *Trials* 2015;16:544.
10. Christensen H, Griffiths KM, Korten A. Web-based cognitive behavior therapy: analysis of site usage and changes in depression and anxiety scores. *J Med Internet Res* 2002;4:e3.
11. Kuyken W, Warren FC, Taylor RS, Whalley B, Crane C, Bondolfi G, et al. Efficacy of mindfulness-based cognitive therapy in prevention of depressive relapse: an individual patient data meta-analysis from randomized trials. *JAMA Psychiatry* 2016;73:565-574.
12. Litz BT, Schorr Y, Delaney E, Au T, Papa A, Fox AB, et al. A randomized controlled trial of an internet-based therapist-assisted indicated preventive intervention for prolonged grief disorder. *Behav Res Ther* 2014;61:23-34.
13. Andersson G, Cuijpers P, Carlbring P, Riper H, Hedman E. Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. *World Psychiatry* 2014;13:288-295.
14. Tuerk PW, Yoder M, Ruggiero KJ, Gros DF, Acierno R. A pilot study of prolonged exposure therapy for posttraumatic stress disorder delivered via telehealth technology. *J Trauma Stress* 2010;23:116-123.
15. Buntrock C, Ebert DD, Lehr D, Smit F, Riper H, Berking M, et al. Effect of a web-based guided self-help intervention for prevention of major depression in adults with subthreshold depression: a randomized clinical trial. *JAMA* 2016;315:1854-1863.
16. Castonguay LG, Schut AJ, Aikens DE, Constantino MJ, Laurenceau JP, Bologh L, et al. Integrative cognitive therapy for depression: a preliminary investigation. *J Psychother Integr* 2004;14:4-20.
17. Kenter RM, Cuijpers P, Beekman A, van Straten A. Effectiveness of a web-based guided self-help intervention for outpatients with a depressive disorder: short-term results from a randomized controlled trial. *J Med Internet Res* 2016;18:e80.
18. Papakostas GI, Petersen T, Mahal Y, Mischoulon D, Nierenberg AA, Fava M. Quality of life assessments in major depressive disorder: a review of the literature. *Gen Hosp Psychiatry* 2004;26:13-17.
19. Rapaport MH, Clary C, Fayyad R, Endicott J. Quality-of-life impairment in depressive and anxiety disorders. *Am J Psychiatry* 2005;162:1171-1178.
20. Eaton WW, Regier DA, Locke BZ, Taube CA. The Epidemiologic Catchment Area Program of the National Institute of Mental Health. *Public Health Rep* 1981;96:319-325.

21. WHO. Constitution of the World Health Organization. WHO: Basic Documents. World Health Organization Constitution. WHO: Geneva; 1948.
22. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine* 2009;6:e1000097.
23. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: a key to evidence-based decisions. *ACP J Club* 1995; 123:A12-A13.
24. Cohen J. *Statistical power analysis for the behavioral sciences*. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988.
25. Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000;56:455-463.
26. Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343:d4002.
27. Blom K, Jernelöv S, Kraepelien M, Bergdahl MO, Jungmarker K, Ankartjärn L, et al. Internet treatment addressing either insomnia or depression, for patients with both diagnoses: a randomized trial. *Sleep* 2015;38:267-277.
28. Brunette MF, Ferron JC, Gottlieb J, Devitt T, Rotondi A. Development and usability testing of a web-based smoking cessation treatment for smokers with schizophrenia. *Internet Interv* 2016;4:113-119.
29. Rotondi AJ, Anderson CM, Haas GL, Eack SM, Spring MB, Ganguli R, et al. Web-based psychoeducational intervention for persons with schizophrenia and their supporters: one-year outcomes. *Psychiatr Serv* 2010;61:1099-1105.
30. Hofmann SG, Curtiss J, Carpenter JK, Kind S. Effect of treatments for depression on quality of life: a meta-analysis. *Cogn Behav Ther* 2017;46: 265-286.
31. Titov N, Dear BF, Ali S, Zou JB, Lorian CN, Johnston L, et al. Clinical and cost-effectiveness of therapist-guided internet-delivered cognitive behavior therapy for older adults with symptoms of depression: a randomized controlled trial. *Behav Ther* 2015;46:193-205.
32. Johansson R, Björklund M, Hornborg C, Karlsson S, Hesser H, Ljótsson B, et al. Affect-focused psychodynamic psychotherapy for depression and anxiety through the Internet: a randomized controlled trial. *Peer J* 2013;1:e102.
33. Hofmann SG, Asnaani A, Vonk IJ, Sawyer AT, Fang A. The efficacy of cognitive behavioral therapy: a review of meta-analyses. *Cognit Ther Res* 2012;36:427-440.
34. Moritz S, Schilling L, Hauschildt M, Schröder J, Tressl A. A randomized controlled trial of internet-based therapy in depression. *Behav Res Ther* 2012;50:513-521.
35. Carlbring P, Hagglund M, Luthstrom A, Dahlin M, Kadowaki Å, Vernmark K, et al. Internet-based behavioral activation and acceptance-based treatment for depression: a randomized controlled trial. *J Affect Disord* 2013;148:331-337.
36. Vernmark K, Lenndin J, Bjärehed J, Carlsson M, Karlsson J, Öberg J, et al. Internet administered guided self-help versus individualized e-mail therapy: a randomized trial of two versions of CBT for major depression. *Behav Res Ther* 2010;48:368-376.
37. Ström M, Uckelstam CJ, Andersson G, Hassmén P, Umefjord G, Carlbring P. Internet-delivered therapist-guided physical activity for mild to moderate depression: a randomized controlled trial. *Peer J* 2013;1:e178.
38. Fayers PM, Machin D. *Quality of Life: The Assessment, Analysis and Interpretation of Patient-Reported Outcomes*. West Sussex: John Wiley & Sons; 2013.
39. Frisch MB, Cornell J, Villanueva M, Retzlaff PJ. Clinical validation of the Quality of Life Inventory: a measure of life satisfaction for use in treatment planning and outcome assessment. *Psychol Assess* 1992;4: 92-101.
40. Zilcha-Mano S, Dinger U, McCarthy KS, Barrett MS, Barber JP. Changes in well-being and quality of life in a randomized trial comparing dynamic psychotherapy and pharmacotherapy for major depressive disorder. *J Affect Disord* 2014;152:538-542.
41. Bolier L, Haverman M, Kramer J, Westerhof GJ, Riper H, Walburg JA, et al. An Internet-based intervention to promote mental fitness for mildly depressed adults: randomized controlled trial. *J Med Internet Res* 2013;15:e200.
42. Kivi M, Eriksson MC, Hange D, Petersson EL, Vernmark K, Johansson B, et al. Internet-based therapy for mild to moderate depression in Swedish primary care: short term results from the PRIM-NET randomized controlled trial. *Cogn Behav Ther* 2014;43:289-298.
43. Lappalainen P, Langrial S, Oinas-Kukkonen H, Tolvanen A, Lappalainen R. Web-based acceptance and commitment therapy for depressive symptoms with minimal support: a randomized controlled trial. *Behav Modif* 2015;39:805-834.
44. Nobis S, Lehr D, Ebert DD, Baumeister H, Snoek F, Riper H, et al. Efficacy of a web-based intervention with mobile phone support in treating depressive symptoms in adults with type 1 and type 2 diabetes: a randomized controlled trial. *Diabetes Care* 2015;38:776-783.
45. Perini S, Titov N, Andrews G. Clinician-assisted Internet-based treatment is effective for depression: randomized controlled trial. *Aust N Z J Psychiatry* 2009;43:571-578.
46. Williams AD, Blackwell SE, Mackenzie A, Holmes EA, Andrews G. Combining imagination and reason in the treatment of depression: a randomized controlled trial of internet-based cognitive-bias modification and internet-CBT for depression. *J Consult Clin Psychol* 2013;81: 793-799.