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RESEARCH ARTICLE

Effectiveness of online mindfulness-based interventions in improving mental health during the COVID-19 pandemic: A systematic review and meta-analysis of randomized controlled trials

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Abstract

Introduction

Psychotherapies, such as mindfulness-based interventions (MBIs), are currently needed to tackle mental health problems. Online MBIs have become promising since face-to-face interventions are limited during the COVID-19 pandemic due to lockdown and social distancing. This systematic review and meta-analysis aimed to investigate the effect of online MBIs in improving mental health, mainly depression, anxiety, and stress.

Materials and methods

A systematic literature search was conducted according to the PRISMA 2020 guidelines on several databases for eligible studies up to October 17, 2021. Study quality was assessed using the Cochrane's Risk of Bias 2 tool. Effect sizes were presented as standardized mean difference (Hedges' *g*) between the online MBIs and control groups at post-test and follow-up using a random-effects model.

Results

Eight randomized controlled trials involving 868 participants were included in this meta-analysis. The pooled adherence rate to online MBIs was 94% (95% CI = 91% to 98%). The findings revealed that online MBIs had a statistically significant small to moderate effect in reducing depression (g = -0.32; 95% CI = -0.49 to -0.14; f^2 = 0%), a small effect on anxiety (g = -0.25; 95% CI = -0.43 to -0.06; f^2 = 27%), and a moderate effect on stress (g = -0.62; 95% CI = -1.09 to -0.16; f^2 = 83%). In addition, significant small effects at follow-up were observed for depression (g = -0.26; 95% CI = -0.48 to -0.04; $f^2 = 0$ %) and anxiety (g = -0.28; 95% CI = -0.48 to -0.08; $f^2 = 0$ %), but not for stress.

Conclusion

Online MBIs have beneficial effects on mental health, particularly depression, anxiety, and stress, during the COVID-19 pandemic. Given the limitations of the current study, future trials that specifically consider potential effect influencing factors, longer follow-up evaluation, and methodological quality are warranted.

Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic has globally affected the community's mental health and heightened its prevalence, particularly for depression, anxiety, and stress [1–3]. This influence on mental health may be caused by the social restrictions, lockdowns, limitations in economic and educational activities, loss of livelihood, and shifting priorities of governments in order to control COVID-19 outbreaks. Additionally, social life has shifted into the online world as a part of adaptation during the pandemic [4]. Social media and online collaboration tools have become crucial for maintaining interaction and activities [5]. Unfortunately, the problematic use of these digital tools may further cause a negative impact on mental health and emotional well-being [6]. A recent worldwide meta-analysis showed that 27.6%, 32.6%, and 30.3% of the population suffered from depression, anxiety, and stress-related insomnia, respectively, during the COVID-19 pandemic [7]. The prevalence of depression and anxiety was higher in Asia than in Europe (35.3% vs. 32.4% and 32.9% vs. 23.8%, respectively), while the prevalence of stress in Europe was higher than in Asia (31.9% vs. 27.9%) [8]. Concerns regarding these mental health issues have grown since the start of the crisis. Hence, mental health interventions are urgently needed to tackle these problems [2].

A previous review has demonstrated evidence on the effectiveness of mindfulness-based intervention (MBI) programs in reducing some psychological symptoms, including depression, anxiety, stress, insomnia, addiction, psychosis, and post-traumatic stress disorder [9]. The MBI is known as one of several psychological intervention methods specifically designed for mental health. It works by improving the participants' ability to observe their inner thoughts or feelings oriented to their acceptance of life experiences [10]. Furthermore, MBI was also beneficial to teach the participants to address their thoughts and emotions in a nonjudgmental way [11]. Mindfulness practice was first incorporated into Western medicine for chronic pain treatment in 1982 by Jon Kabat-Zinn and was derived from Buddhist meditation traditions [12]. Since then, MBI practices in mental health management, specifically in alleviating one's emotional states, have been introduced in several modified methods, i.e., Mindfulness-Based Stress Reduction (MBSR), Mindfulness-Based Cognitive Therapy (MBCT), Dialectical Behaviour Therapy (DBT), and Acceptance and Commitment Therapy (ACT) [10]. Of those, the two most commonly adopted MBI programs are the MBSR and MBCT, which consist of eight weekly mindfulness sessions and a one-day retreat [9]. Both MBSR and MBCT have demonstrated an effective reduction in the three most common mental health problems, which are depression, stress, anxiety, and some physical health outcomes related to chronic diseases [10, 13].

During the COVID-19 pandemic, the face-to-face intervention method becomes limited due to quarantine, lockdown, and social distancing [13]. Many online platforms have been

used to deliver health interventions, including programs in the field of mental health [10, 13]. Several advantages of online mental health interventions as compared to offline or traditional face-to-face methods have been addressed: (1) easily accessible; (2) more suitable for people in any environment without significantly interfering with their work pace; (3) some may not necessarily require the direct involvement of a knowledgeable therapist; and (4) participants may access the treatment program information at any time outside the schedule and further facilitate more retention [14]. Moreover, online MBIs may be considered even more cost-effective than face-to-face MBIs [9, 14]. Many smartphone applications additionally offer some mindfulness-based practices [12]. Thus, these features allow further access to online MBI programs. Online delivery methods in mental health interventions are also helpful for clinicians and psychologists to reach better mental health care for the general population, since nowadays people tend to be more comfortable with internet-based interventions [15]. Various studies have been published on the effectiveness of online MBIs; however, no meta-analyses have evaluated it, particularly in the setting of the COVID-19 pandemic. Therefore, in this exploratory metaanalysis, we aim to estimate the effect of online MBIs in improving mental health outcomes, mainly depression, anxiety, and stress. This review focuses on the two most used MBI methods (i.e., MBCT and MBSR) in randomized clinical trials (RCTs) conducted amid the COVID-19 pandemic.

Materials and methods

This systematic review and meta-analysis were conducted in conformity with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [16]. The detailed protocol of the current study has been previously registered and published on the International Prospective Register of Systematic Reviews (PROSPERO) (https://www.crd. york.ac.uk/prospero/) with the registration number CRD42021287616 [17].

Search strategy

A computerized systematic literature data searching of relevant studies was conducted in PubMed, Scopus, Web of Science, ProQuest, Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCO, the Cochrane Central Register of Controlled Trials (CEN-TRAL), and the World Health Organization (WHO) COVID-19 Research Databases for studies published up to October 17, 2021. We additionally searched for grey literatures, specifically preprints, using MedRxiv and BioRxiv as the source databases. In systematic reviews and meta-analyses, grey literatures may help reduce the impact of publication bias, increase the comprehensiveness of the search, and provide a balanced view of the available evidence and more accurate effect sizes [18, 19]. It is also recognized that research sharing on the study of COVID-19 using preprints has increased rapidly during the pandemic [20]. At the same time, we performed a manual hand-search on Google Scholar and the reference lists of the included studies to maximize the search results. The following main keywords were initially established: "mindfulness", "online", "COVID-19", and "randomized controlled trial". We subsequently added several Medical Subject Headings (MeSH), thesaurus, and other free-text terms to construct database-specific search terms. The full search strings for each database are provided in SI Table in S1 File. No language and publication date restrictions were set in all searches.

Selection of studies

All search results were pooled and managed collectively using Google Sheets (https://docs. google.com/spreadsheets/) (Google LLC, Mountain View, CA, USA). After removing the duplicates, the articles were filtered by reviewing their title. Potentially relevant articles were then screened based on the abstract. All articles included in the next screening step were sought for retrieval. Afterwards, studies with available and published full-texts were retrieved and thoroughly assessed according to the pre-specified eligibility criteria. The reasonings of exclusion for all articles on each screening step were declared as appropriate in the spreadsheet. The initial literature searches and overall study selection process were performed independently by two investigators (BS and VV). Any disagreements were resolved in a consensus involving a third independent investigator (AP).

Eligibility criteria

We adopted the Population, Intervention, Comparison, Outcome, and Study Design (PICOS) framework [21] (**S2 Table in** <u>S1 File</u>) as a guide in formulating and establishing the eligibility criteria of the current study. To be included in the systematic review and meta-analysis, studies had to meet the following criteria: (1) the study population consisted of subjects aged 18 years or older; (2) employed MBIs (MBSR or MBCT); (3) delivered the intervention entirely using online method via internet-based platforms or applications; (4) used either an active (received other type of intervention) or inactive (no intervention) control group; (5) used validated instruments to assess mental health outcome measures of depression, anxiety, and stress; (6) used a randomized controlled design; and (7) the study course (from recruitment phase to the end of intervention) was fully conducted during the period of the COVID-19 pandemic (the start of the COVID-19 pandemic was defined according to the WHO announcement on March 11, 2020 [22]). We accepted studies published in any language.

Studies were excluded if: (1) the full-text was irretrievable; (2) the intervention also involved other forms of psychotherapy unrelated to mindfulness practice, making it difficult to judge the absolute effect of MBI; or (3) the study did not report mean and standard deviation values to calculate the meta-analytic effect size and the authors did not respond after they were contacted for data request or were not willing to provide the data.

Data extraction and quality assessment

Two investigators (BS and VV) independently performed data extraction from each study, using a pre-specified form tabulated within the spreadsheet. These were checked by the third investigator (AP). Disagreements were resolved through a discussion. The following relevant data were extracted: the first author, year of publication, study location (country and region), type of study population, sample size per study arm, gender (% of females), age, adherence rate to MBI, type of MBI (MBSR or MBCT), type of control group (active or inactive), delivery method (e.g., videoconferencing, website, or mobile application), guidance (with or without), number of sessions, length of intervention, time of measurements (post-intervention or follow-up), type of analysis (intention to treat [ITT] or per-protocol [PP]), and type of instruments used to assess outcome measures (depression, anxiety, or stress) along with the mean and standard deviation values per time of measurements. We defined adherence rate as the percentage of participants that completed all online MBI sessions compared to the baseline allocated participants in the intervention group. Studies that were not reported in the English language were translated using available online translators prior to data extraction. In case specific data were unavailable for extraction or not clearly reported in the paper, we contacted the author of the corresponding study. Finally, three authors were contacted, two of whom successfully responded and provided the data on request.

Two reviewers (BS and VV) then independently conducted a methodological quality assessment to evaluate the risk of bias of each eligible study using the Cochrane Collaboration's Risk of Bias 2 (RoB 2) tool [23]. Discordance of judgments were resolved simultaneously through a group discussion involving a third reviewer (AP). The RoB 2 is a revised tool consisting of five bias domains explicitly designed to consider the risk of bias of randomized trials arising from: (1) the randomization process; (2) deviations from intended interventions; (3) missing outcome data; (4) the measurement of the outcome; and (5) the selection of the reported result. The risk of bias on each domain was rated as low risk, high risk, or some concerns (unclear) according to the algorithms that incorporated several domain-specific signalling questions. The levels of judgments from all domains were later deduced into an overall risk of bias for each study. Studies were judged with a low overall risk of bias if all domains presented with low risk. If at least one domain was rated as unclear, studies were judged as having some concerns. Studies were judged to be at high risk of bias if at least one domain showed a high risk or there were some concerns in multiple domains that could considerably lower the confidence of the study's result.

Statistical analysis

Main analysis. All analyses were conducted using Review Manager version 5.4 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark) and STATA version 16.0 (Stata Corporation, College Station, TX, USA). We performed separate quantitative analyses to determine the effect of MBIs on three different mental health outcomes: depression, anxiety, and stress. In the case where a study used more than one instrument to measure depression, anxiety, and stress, we used the most valid instrument so that each study outcome had a single effect size. Comparison of means and standard deviations (SDs) between intervention and control groups measurements at post-test were analyzed as the primary outcomes of this study. We additionally performed secondary analyses for outcomes comparing between-groups means and SDs of depression, anxiety, and stress at follow-up measurements. The ITT analyses were preferred over PP if studies reported both types of analysis. Furthermore, to understand the overall adherence rate of participants to online MBIs, we conducted a meta-analysis of proportions using the double arcsine transformation method [24]. For all outcomes, we performed meta-analyses with and without outliers. A study was considered an outlier if its 95% confidence interval (CI) was located outside of the 95% CI of the pooled effect by visually examining it on the forest plot [25]. Forest plots were constructed only for the meta-analyses with outliers.

In this study, we did not perform analyses using change-from-baseline (pre-to-post and pre-to-follow-up differences) between-groups scores since this practice is not recommended by Cochrane [26]. Although this method could remove the component of between-subject variability from the analysis, it involves an additional calculation, in which it is considered more inefficient. Furthermore, due to the nature of randomized trials, as the type of studies included in this meta-analysis, we could assume in theory that comparison of final measurement (at post-test and follow-up) has approximately the same effect as the comparison of changes from baseline [27].

We applied the standardized mean difference (SMD) as the summary statistics of the primary and secondary outcomes since the included studies used different psychometric instruments to assess depression, anxiety, and stress. The SMD represents the difference in means between the intervention and control groups divided by the combined SD. We used Hedges' *g* as the standard metric of the effect size in all analyses. The Hedges' *g* is a type of effect size for SMD, which includes an additional adjustment for small sample studies. The pooled effect of intervention using Hedges' *g* is interpreted as similar to Cohen's *d*, where 0.2 represents small, 0.5 represents moderate, and 0.8 represents large effect sizes [28].

Heterogeneity between studies was examined with the Cochran's Q statistic and quantified using the Higgins' I^2 statistic, where I^2 values of 0%, 25%, 50%, and 75% indicated negligible,

low, moderate, and high heterogeneity, respectively [29]. Given that there was a considerable variability and diversity between studies interventions and characteristics of the study population, we primarily applied the random-effects model for all analyses. A *p*-value of < 0.05 was used to indicate statistical significance in all analyses.

Analysis of publication bias. Publication bias was assessed visually using the inverted funnel plot and quantitatively using the Egger's regression test [30] to detect small study effects and other potential reporting biases. Small-study effects are described as the tendency of smaller studies to result in a more significant intervention effect than the large ones. Consequently, these studies would be more likely to be published. In addition, publication bias could exist due to the tendency of authors and journals to publish studies with significant results [31]. These phenomena will result in the asymmetrical distribution in the funnel plot analysis and a significant Egger's test result.

Sensitivity, subgroup, and meta-regression analyses. We prioritized performing sensitivity, subgroup, and meta-regression analyses only for meta-analyses that evaluated the primary outcomes (including outliers). Sensitivity analyses were carried out by excluding each study from the analysis one at a time (leave-one-out method). Subgroup and meta-regression analyses were performed to evaluate the differences in effect sizes between subgroups and the effect of certain covariates on the pooled outcome. We conducted subgroup analyses based on: (1) study location (Asia vs. non-Asia); (2) characteristics of the study population (general vs. non-general population); (3) type of MBI (MBSR vs. MBCT); (4) type of control group (active vs. inactive); (5) delivery method (videoconferencing vs. non-videoconferencing); and (6) guidance (with vs. without). Subgroup analyses were performed only if each subgroup in the analyses contained at least two studies. Restricted maximum likelihood random-effects metaregression were carried out for: (1) mean of age; (2) % of females; (3) number of sessions; and (4) length of intervention in weeks. Meta-regression analyses that presented significant results were visualized through bubble plots.

Results

Overview of study selection

A PRISMA flow diagram of the overall study selection process is illustrated in **Fig 1**. The initial electronic database searches yielded 946 hits. A total of 252 duplicates were then removed. After reviewing 694 records, 554 and 31 were excluded based on the titles and abstracts, respectively. A total of 60 reports identified as study registers, conference abstracts, or with no access to full-texts were not retrieved. Afterwards, we thoroughly assessed the remaining 49 full-texts for eligibility and 42 were further excluded due to the irrelevancy of their population characteristics, type and method of interventions, reported and evaluated outcomes, study design, or samples recruitment period. In addition to database searching, we identified 11 extra records from websites and reference lists searching. Of those, two reports were not retrieved. After judging the eligibility of the remaining reports, eight were excluded. Accordingly, the overall screening process led to the inclusion of 8 RCTs [32–39] in this systematic review and meta-analysis.

Characteristics and outcomes of included studies

The characteristics of the included studies are summarized in Table 1. The 8 RCTs yielded a total of 868 adult participants (mean age: 22 to 36 years), from which 451 received the MBIs, and 417 were control samples. The study sample sizes were variable ranging from 51 to 183. All studies were conducted during the COVID-19 pandemic. Females accounted for more than half of the study population in all studies. Half of the studies (n = 4) were located in Asia,



Fig 1. PRISMA flow diagram of the study selection process. CENTRAL, Cochrane Central Register of Controlled Trials; CINAHL, Cumulative Index to Nursing and Allied Health Literature; COVID-19, Coronavirus Disease 2019; WHO, World Health Organization.

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and the rest were in America (n = 3) and Europe (n = 1). The studies included diverse type of population: general (unspecified) population (n = 2), university students (n = 3), healthcare workers (n = 1), social workers (n = 1), and obstetrics and gynecology outpatients (n = 1). Two studies examined MBSR, five MBCT, and one employed a combination of MBSR and MBCT intervention. In three studies, the duration of MBSR and MBCT interventions were conducted according to the original protocol in eight weekly sessions, while the other studies used a modified protocol. The MBIs were varied from 1 to 10 sessions, with the length of intervention ranging from 1 to 8 weeks. The interventions were most commonly delivered through a videoconference (n = 4). Other methods included a website (n = 1) and a mobile application (n = 3). The interventions in four studies were guided by either a specialist in MBIs or a trained therapist. An inactive control condition was used in five RCTs, all of which were waitlist groups. The three remaining RCTs used an active control, in which participants received access to mental health education (n = 1), social support-based condition (n = 1), or were asked to answer manipulated questions (n = 1).

Among the 8 RCTs, half reported outcomes using ITT analyses. The follow-up times after intervention in four studies were varied, ranging from 2 weeks to 2 months. All studies used

Table 1. Châ	nracteristic	cs of included st	udies.														
First Author, Year	Study Location	Characteristics of Population	Baseline Siz	: Sample ze	% Female ^a	Age ^b	Type of MBI	Type of Control Group	Delivery Method	Guidance	Number of	Length of Intervention	Measurements	Type of Analysis	Instrument o	of Outcome M	easures
			Online MBIs	Control							Sessions				Depression	Anxiety	Stress
Alvarado- García et al., 2021 [32]	Peru, America	General population	30	30	N/A	N/A	MBSR	Inactive (Waitlist)	Videoconferencing	With	8 sessions	8 weeks	Post	ITI	N/A	N/A	PSS-10
Hosseinzadeh Asl, 2021 [33]	Turkey, Asia	Social workers	30	21	55.1	33.06 ± 6.02	MBCT	Inactive (Waitlist)	Videoconferencing	With	4 sessions	4 weeks	Post, 1-month follow-up	ЬЬ	DASS- 21-D	DASS- 21-A	DASS- 21-S
Huang et al., 2021 [34]	China, Asia	Healthcare workers in COVID-19 isolation wards	58	60	77.1	32.27 ± 6.42	MBSR	Active (Mental health education)	Videoconferencing	With	8 sessions	8 weeks	Post	I'II	N/A	N/A	SRQ
Kam et al., 2021 [35]	Canada, America	University students	34	30	83.9	29.9 ± 8.8	MBCT	Inactive (Waitlist)	Mobile application	Without	10 sessions	2 weeks	Post	ЪР	PROMIS-D	PROMIS-A	N/A
Pheh et al, 2020 [36]	Malaysia, Asia	General population	104	79	73.9	28.75 ± 9.01	MBCT	Active (Answering manipulated questions)	Website	Without	1 session	1 week	Post, 2-week follow-up	Ър	N/A	GAD-7	SUDS
Simonsson et al., 2021 [37]	England, Europe	University students	88	89	64.4	23.27 ± 5.60	MBCT	Inactive (Waitlist)	Videoconferencing	With	8 sessions	8 weeks	Post, 1-month follow-up	ЪР	PROMIS-D	PROMIS-A	N/A
Smith et al., 2021 [38]	United States, America	Obstetrics and gynecology outpatients	50	51	100	36.21 ± 11.30	MBCT	Inactive (Waitlist)	Mobile application	Without	4 sessions	4 weeks	Post	ITT	HADS-D	HADS-A	PSS-10
Sun et al., 2021 [39]	China, Asia	University students	57	57	73.7	22.21 ± 2.67	MBSR and MBCT	Active (Social support)	Mobile application	With	4 sessions	4 weeks	Post, 2-month follow-up	ITT	рнд-9	GAD-7	N/A
^a % female of ^b Mean and st	the total st andard de	udy population viation of the stu	at baseli ıdy popı	ne. ulation a	ge at bas	eline.											
COVID-19, 4 21-S, Depres	Coronavin sion, Anxie	us Disease 2019; ety, and Stress So	DASS-2 cale-21-5	21-A , D¢ Stress Su	pression bscale; C	ı, Anxiety, a 3AD- 7, Ger	und Stree ieralized	ss Scale-21 An l Anxiety Disc	<pre>txiety Subscale; I structure transform tr</pre>	A, Hospitz	D , Deprea	sion, Anxiet and Depres	y, and Stress So sion Scale-Anx	cale-21-I iety Subs)epression { scale; HAD	Subscale; I S-D, Hosp	DASS- ital
Anxiety and Reduction; N	Depression /A, not ave	1 Scale-Depressi ailable; PHQ-9,	on Subs ¹ Patient l	cale; IT'] Health C	l, intenti Juestioni	ion-to-treat; naire-9; PP ,	mBCT	, Mindfulness tocol; PROM	-Based Cognitiv IS-A, Patient-Re	e Therapy sported O	; MBI, m utcomes l	indfulness-ba Measuremen	sed interventi t Information	on; MBS System-A	R, Mindful. Anxiety Sub	ness-Based scale;	Stress

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SUDS, Subjective Unit of Distress Scale.

PROMIS-D, Patient-Reported Outcomes Measurement Information System-Depression Subscale; PSS-10, Perceived Stress Scale-10; SD, standard deviation; SRQ, Stress Response Questionnaire;



Fig 2. Results of quality assessment of included studies using the Risk of Bias 2 tool. (A) Domain-specific quality assessment graph. (B) Detailed quality assessment summary.

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validated instruments to measure depression, anxiety, and stress. Outcome measures of depression were available in 5 studies, anxiety in 6, and stress in 5 studies. **S3 Table in <u>S1 File</u>** provides the outcome values reported in each included study.



Fig 3. Forest plot of meta-analysis of proportions for adherence rate to online MBIs.

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Study quality assessment

The result of the domain-specific quality assessment is provided in **Fig 2A**, while the detailed risk of bias evaluation of each study is summarized in **Fig 2B**. According to the Cochrane's RoB 2 tool, two studies were rated as low risk in all domains, thus having a low overall risk of bias. Five RCTs were rated as having some concerns, from which one study had unclear risk in 1 domain, while two studies in 2, and two studies in 3 domains. One RCT, i.e., Alvarado-García et al. [32], was rated as high risk since it was judged to have some concerns for multiple domains that might lower confidence of the study's result. If viewed from each domain individually, two studies reported incomplete information regarding the randomization process, and thus were rated as unclear risk of bias. There were some concerns of deviations from the intended interventions in three studies due to the lack of information on blinding procedures. All RCTs were rated as low of risk in the domain of bias due to missing outcome data. Some concerns were observed during the measurement of outcome in five studies since there was a potential influence by the knowledge of intervention status. Four studies had an unclear risk of bias in the selective reporting domain due to the unavailability of the pre-published trial protocol, and hence we could not judge the reliability of the reported results.

Adherence rate

When adherence was defined as the completion of all sessions, the rates from 8 RCTs were varied, ranging from 86% to 100%. The overall adherence rate to online MBIs obtained from

Α									
	Onli	ine ME	Bls	С	ontrol		1	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Hosseinzadeh Asl 2021	9.5	8.03	28	12.1	8.89	21	9.8%	-0.30 [-0.87, 0.26]	
Kam 2021	15.84	7.04	32	16.57	6.89	30	12.8%	-0.10 [-0.60, 0.39]	
Simonsson 2021	8.81	3.75	79	10.23	4.06	86	33.6%	-0.36 [-0.67, -0.05]	
Smith 2021	4	2.9	50	5.4	3.4	51	20.4%	-0.44 [-0.83, -0.04]	_
Sun 2021	6.42	3.76	57	7.63	5.24	57	23.4%	-0.26 [-0.63, 0.11]	
Total (95% CI)	D: Chi² -	- 1 23	246 df = 4	(P - 0 8	7).12 -	245	100.0%	-0.32 [-0.49, -0.14]	
Test for overall effect: Z =	3.47 (P	= 0.00	005)	(F – 0.8	, r), r –	0 /0			-1 -0.5 0 0.5 1 Favours [Online MBIs] Favours [Control]

		c

	Onli	ine ME	Bls	С	ontrol		5	Std. Mean Difference		Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	1	IV, Random, 95% Cl	
Hosseinzadeh Asl 2021	4.79	4.05	28	6	4.35	21	9.0%	-0.28 [-0.85, 0.28]			
Kam 2021	17.84	7.66	32	19.07	8.33	30	11.3%	-0.15 [-0.65, 0.35]			
Pheh 2020	12.59	4.94	82	12.92	4.8	79	22.8%	-0.07 [-0.38, 0.24]			
Simonsson 2021	9.81	3.54	79	11.7	3.72	86	22.6%	-0.52 [-0.83, -0.21]		_	
Smith 2021	5	3.9	50	6.9	4.7	51	16.2%	-0.44 [-0.83, -0.04]			
Sun 2021	6.08	3.99	57	6.13	4.26	57	18.1%	-0.01 [-0.38, 0.36]			
Total (95% CI)			328			324	100.0%	-0.25 [-0.43, -0.06]		•	
Heterogeneity: Tau ² = 0.0 Test for overall effect: Z =	1; Chi² = 2.64 (P	= 6.82, = 0.00	df = 5 08)	(P = 0.2	3); l² =	27%			- -1	-0.5 0 0.5 Favours [Online MBIs] Favours [Control]	├ ─ 1

С

	Onl	ine MB	ls	C	ontrol		;	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Alvarado-García 2021	37.83	6.07	30	50.58	8.12	30	17.5%	-1.76 [-2.36, -1.15]	
Hosseinzadeh Asl 2021	9.93	6.7	28	12.48	7.59	21	18.0%	-0.35 [-0.92, 0.22]	
Huang 2021	50.25	30.12	58	59.17	11.24	60	21.4%	-0.39 [-0.76, -0.03]	
Pheh 2020	4.02	1.58	82	4.22	1.86	79	22.2%	-0.12 [-0.42, 0.19]	
Smith 2021	12.7	5.6	50	17	6.7	51	20.8%	-0.69 [-1.09, -0.29]	
Total (95% CI)			248			241	100.0%	-0.62 [-1.09, -0.16]	•
Heterogeneity: Tau ² = 0.23	3; Chi² =	24.08,	df = 4 ((P < 0.0	001); l²	= 83%		-	
Test for overall effect: Z =	2.62 (P	= 0.009	9)						Favours [Online MBIs] Favours [Control]

Fig 4. Forest plots of meta-analyses of online MBIs effect on mental health outcomes at post-intervention. (A) Depression. (B) Anxiety. (C) Stress.

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meta-analysis was 94% (95% CI = 91% to 98%) with high heterogeneity ($I^2 = 70.6\%$). No study outliers were detected. The forest plot of pooled adherence rate analysis is presented in Fig 3.

Primary outcomes (effects at post-intervention)

Effects on depression. A total of 246 online MBIs and 245 control participants from 5 studies were included in the meta-analysis for depression outcome (**Fig 4A**). Online MBIs during the COVID-19 pandemic showed a significant, small to moderate effect in reducing depression at post-intervention (g = -0.32; 95% CI = -0.49 to -0.14; p < 0.001). The level of heterogeneity was negligible ($I^2 = 0$ %). No outliers were detected based on the forest plot. Sensitivity analysis using the leave-one-out method revealed that no study had a substantial influence on the significance of the overall effect size.

Effects on anxiety. Six RCTs with a total of 328 participants receiving online MBIs and 324 controls were analyzed to determine the pooled effect on anxiety (**Fig 4B**). A significant, small reduction in anxiety was observed at post-intervention (g = -0.25; 95% CI = -0.43 to -0.06; p = 0.008). The level of heterogeneity was low ($I^2 = 27\%$). Examination of the forest plot

Outcome	Covariate	Subgroup	Number of Studies		Effect Siz	æ		Heter	rogeneity	<i>p</i> -value of Difference between Subgroups
Measure				Hedges' g	95% CI	Z	<i>p</i> -value	I^2	<i>p</i> -value	
Depression	Study region	Asia	2	-0.28	-0.59, 0.03	1.75	0.08	0%	0.91	0.76
		Non-Asia	3	-0.34	-0.55, -0.12	3.01	0.003	0%	0.57	
	Delivery method	Videoconferencing	2	-0.35	-0.62, -0.08	2.52	0.01	0%	0.86	0.75
		Non-videoconferencing	3	-0.29	-0.53, -0.05	2.40	0.02	0%	0.57	
	Guidance	With	3	-0.32	-0.54, 0.10	2.86	0.004	0%	0.92	0.95
		Without	2	-0.31	-0.63, 0.01	1.87	0.06	7%	0.30	
Anxiety	Study region	Asia	3	-0.08	-0.30, 0.14	0.72	0.47	0%	0.73	0.03 ^a
		Non-Asia	3	-0.42	-0.64, -0.20	3.77	< 0.001	0%	0.47	
	Control type	Active	2	-0.04	-0.28, 0.19	0.37	0.71	0%	0.82	0.02 ^a
		Inactive	4	-0.40	-0.61, -0.20	3.87	< 0.001	0%	0.64	-
	Delivery method	Videoconferencing	2	-0.46	-0.74, -0.19	3.34	< 0.001	0%	0.48	0.06
		Non-videoconferencing	4	-0.15	-0.34, 0.04	1.55	0.12	0%	0.42	
	Guidance	With	3	-0.28	-0.62, 0.05	1.64	0.10	53%	0.12	0.69
		Without	3	-0.20	-0.43, 0.03	1.72	0.09	5%	0.35	
Stress	Study region	Asia	3	-0.25	-0.47, -0.03	2.24	0.02	0%	0.49	0.08
	Population type	Non-Asia	2	-1.20	-2.24, -0.16	2.25	0.02	88%	0.00	
		General population	2	-0.91	-2.52, 0.69	1.12	0.26	96%	< 0.001	0.61
		Non-general population	3	-0.50	-0.74, -0.25	3.98	< 0.001	0%	0.48	
	MBI type	MBSR	2	-1.05	-2.39, 0.28	1.54	0.12	93%	< 0.001	0.34
		MBCT	3	-0.37	-0.75, 0.00	1.94	0.05	60%	0.08	
	Control type	Active	2	-0.24	-0.51, 0.03	1.72	0.09	22%	0.26	0.09
		Inactive	3	-0.92	-1.66, -0.18	2.43	0.02	84%	0.002	
	Delivery method	Videoconferencing	3	-0.81	-1.64, 0.01	1.93	0.05	87%	< 0.001	0.40
		Non-videoconferencing	2	-0.39	-0.95, 0.17	1.35	0.18	80%	0.03	
	Guidance	With	3	-0.81	-1.64, 0.01	1.93	0.05	87%	< 0.001	0.40
		Without	2	-0.39	-0.95, 0.17	1.35	0.18	80%	0.03	1

Table 2. Summary of subgroup analyses of online MBIs effect on mental health outcomes at post-intervention (including outliers).

 $^{a} p < 0.05$

CI, confidence interval; MBCT, Mindfulness-Based Cognitive Therapy; MBI, mindfulness-based intervention; MBSR, Mindfulness-Based Stress Reduction.

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showed no potential study outliers. After removing one study by Simonsson et al. [37] in sensitivity analysis, the pooled effect was reduced to insignificance.

Effects on stress. For stress outcome, we successfully included five studies involving 248 online MBIs and 241 control subjects (**Fig 4C**). The overall effect on stress after online MBIs was significant with g = -0.62 (95% CI = -1.09 to -0.16; p = 0.009). This effect was considered moderate. A high level of heterogeneity was observed ($I^2 = 83\%$). After examining the forest plot, we identified one potential outlier (Alvarado-García et al. [32]). Removal of the outlier resulted in a reduction of the pooled effect to g = -0.37 (95% CI = -0.62 to -0.11), but this effect remained significant (p = 0.005). Additionally, the heterogeneity shifted to a moderate level (I^2

Outcome Measure	Covariate	Number of Studies	Z	<i>p</i> -value
Depression	Mean age	5	-0.29	0.77
	% female	5	-0.20	0.84
	Number of sessions	5	0.49	0.63
	Length of intervention	5	-0.59	0.55
Anxiety	Mean age	6	-0.37	0.71
	% female	6	-0.06	0.95
	Number of sessions	6	-1.21	0.23
	Length of intervention	6	-2.09	0.04 ^a
Stress	Mean age	4	-2.23	0.03 ^a
	% female	4	-1.36	0.17
	Number of sessions	5	-1.38	0.17
	Length of intervention	5	-1.38	0.17

Table 3. Summary of meta-regression analyses of online MBIs effect on mental health outcomes at post-intervention (including outliers).

^a p < 0.05

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= 40%). A subsequent leave-one-out sensitivity analysis suggested that the significance of the overall effect was robust and not affected by any single study.

Subgroup analysis. Subgroup analyses for all post-intervention outcomes (including outliers) are presented in Table 2. For anxiety outcome, we found significantly larger effect sizes for studies conducted outside of Asia than in Asia (p = 0.03) and studies that used an inactive control than an active control condition (p = 0.02). No significant differences between subgroups were found for depression and stress. Subgroup analyses for depression, anxiety, and stress outcomes based on several covariates were not conducted due to the lack of studies included in each subgroup.

Meta-regression analysis. Meta-regression analysis showed that length of intervention (**S1A Fig in S1 File**) had a significant positive moderating effect on anxiety (Z = -2.09; p = 0.04), meaning that online MBIs with longer intervention would result in greater anxiety reduction. Furthermore, a significant positive influence of mean age on stress outcome was observed (Z = -2.23; p = 0.03), by which we found that online MBIs were more effective in reducing stress in older populations (**S1B Fig in S1 File**). All other covariates did not have a significant influence on each outcome. The results of meta-regression analyses (including outliers) are summarized in Table 3.

Publication bias. For depression (**S2A Fig in S1 File**) and anxiety (**S2B Fig in S1 File**), funnel plots showed a rather symmetrical distribution of studies, indicating no potential of publication bias. These findings were confirmed by insignificant Egger's test results for depression (Z = 0.53; p = 0.59) and anxiety (Z = 0.10; p = 0.92). However, a skewed distribution towards a higher effect size was observed in the funnel plot for stress (**S2C Fig in S1 File**). The result of Egger's test for stress also revealed the potential of publication bias (Z = -2.06; p = 0.04). Surprisingly, the removal of outlier resulted in a more symmetrical distribution of the funnel plot (**S2D Fig in S1 File**) and an insignificant Egger's test (Z = -0.57; p = 0.57), suggesting that small study effects might arise from one study (Alvarado-García et al. [32]).

Secondary outcomes (effects at follow-up)

At follow-up (Fig 5A), pooled effect of online MBIs in reducing depression was maintained with a small significant result (n = 3; g = -0.26; 95% CI = -0.48 to -0.04; p = 0.02). Analysis on

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A									
	Onli	ine ME	ls	С	ontrol			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Hosseinzadeh Asl 2021	11.21	8.01	28	13.14	8.04	21	14.9%	-0.24 [-0.80, 0.33]	
Simonsson 2021	8.94	3.83	77	9.56	4.12	85	50.3%	-0.15 [-0.46, 0.15]	
Sun 2021	5.98	3.64	57	7.77	4.91	57	34.8%	-0.41 [-0.78, -0.04]	_
Total (95% CI)			162			163	100.0%	-0.26 [-0.48, -0.04]	
Heterogeneity: Tau ² = 0.00); Chi² =	= 1.09,	df = 2	(P = 0.5	58); l² =	= 0%			
Test for overall effect: Z =	2.29 (P	= 0.02)						Favours [Online MBIs] Favours [Control]
B									
B	Onli	ino MB	le	C	ontrol			Std. Moan Difforence	Std. Mean Difference
Study on Subanava	Maan		Tatal	Maan	0111101	Tatal	Mainht	N Dandom 05% Cl	N Dendem 05% Cl
Study or Subgroup	wean	<u>2D</u>	Total	wean	20	Total	weight	IV, Random, 95% CI	IV, Random, 95% CI
Hosseinzadeh Asl 2021	5.5	3.34	28	6.67	4.31	21	12.5%	-0.30 [-0.87, 0.26]	
Pheh 2020	13.91	5.53	33	13.31	5.59	28	16.0%	0.11 [-0.40, 0.61]	
Simonsson 2021	9.57	3.76	77	10.87	3.45	85	41.9%	-0.36 [-0.67, -0.05]	
Sun 2021	5.54	3.48	57	7.04	4.75	57	29.6%	-0.36 [-0.73, 0.01]	
									-
Total (95% CI)			195			191	100.0%	-0.28 [-0.48, -0.08]	\bullet
Heterogeneity: Tau ² = 0.00); Chi² =	= 2.69,	df = 3	(P = 0.4	4); l² =	= 0%			
Test for overall effect: Z =	2.70 (P	= 0.00	7)						- I -U.5 U U.5 I Favours [Online MBIs] Favours [Control]
C									
U I	0	ine ME		~	ontrol			Std. Moon Difference	Std Maan Difference

	Onli	ine ME	3ls	C	ontrol		:	Std. Mean Difference		Std. M	ean Differen	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Ra	ndom, 95%	CI	
Hosseinzadeh Asl 2021	10.86	6.15	28	13.24	7.2	21	48.0%	-0.35 [-0.92, 0.22]					
Pheh 2020	4.52	2.11	33	3.86	1.98	28	52.0%	0.32 [-0.19, 0.82]					
Total (95% CI)			61			49	100.0%	-0.00 [-0.66, 0.65]					
Heterogeneity: Tau ² = 0.15 Test for overall effect: Z =	5; Chi² = 0.01 (P	= 2.97, = 0.99	df = 1 9)	(P = 0.0	8); l² =	66%		-	-2 Favou	-1 rs [Online MI	0 3ls] Favours	1 s [Control]	2

Fig 5. Forest plots of meta-analyses of online MBIs effect on mental health outcomes at follow-up. (A) Depression. (B) Anxiety. (C) Stress.

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anxiety outcome at follow-up (Fig 5B) also showed a maintained significant, small reduction effect (n = 4; g = -0.28; 95% CI = -0.48 to -0.08; p = 0.007). The level of heterogeneity for depression and anxiety analyses was negligible ($I^2 = 0$ %). For stress (Fig 5C), no significant effect at follow-up was found (n = 2; g = -0.00; 95% CI = -0.66 to 0.65; p = 0.99). The heterogeneity was at a high level ($I^2 = 66$ %). The forest plots revealed no study outliers in all outcomes. No potential publication bias was observed in depression and stress outcomes as indicated by the funnel plots (S3A and S3C Fig in S1 File) and the results of the Egger's tests (depression: Z = -0.26, p = 0.80; stress: Z = -0.86, p = 0.39). The funnel plot for anxiety outcome was somewhat asymmetric (S3B Fig in S1 File). Nonetheless, the Egger's test result showed no potential publication bias (Z = 1.00; p = 0.32).

Discussion

Main findings

The results of our meta-analysis showed that online MBIs were effective in reducing depression, anxiety, and stress during the COVID-19 pandemic. We found small to moderate reductions in post-intervention depression, anxiety, and stress. Our results are comparable to the previous MBIs studies for clinical and general healthy populations [40, 41]. We also reported significant effects of online MBIs on depression and anxiety at follow-up, suggesting the medium-term effects of online MBIs in improving mental health problems. These findings may be caused by the fact that mindfulness is associated with acceptance skills, which facilitated further mental health resilience [42]. A previous review article by Guendelman et al. [43] also suggested that there were structural and functional changes in the neurons after 8-week mindfulness-based therapies. Evidence has shown an increase in the functional activity of the prefrontal cortex, cingulate cortex, insula, and hippocampus in either healthy or nonhealthy participants after receiving MBIs. In addition, the amygdala showed decreased functional activity and an improvement of its connectivity with the prefrontal cortex, leading to better one's emotional regulation [44]. These changes may be responsible for the strength resilience in patients after MBIs, making these interventions beneficial during the COVID-19 pandemic.

Our study did not exhibit a significant reduction effect on stress at follow-up. This insignificant finding was possibly due to the small number of studies included in the analysis. Moreover, there was a difference in the length of the intervention between the two included studies [33, 36]. The study by Hosseinzadeh Asl et al. [33] used a 4-week online MBI, while Pheh and his colleagues [36] used an ultra-brief online MBI protocol consisting of only one session. The effectiveness of ultra-brief MBIs is still debatable. A preceding study showed a long-lasting positive effect of ultra-brief MBIs [45], while another showed the opposite [46]. Pheh et al. [36] themselves argued that online ultra-brief mindfulness intervention might not be substantial enough to provide long-term changes. Additionally, as described by Mansell et al. [47], ultrabrief mindfulness practices can only dilute stress. The discovery of new perspectives from longer practices is needed to restore better and develop maintained well-being [47, 48].

Subgroup analysis showed that the type of control conditions used to compare the online MBIs potentially affected the pooled effect size for anxiety outcome. We found that studies with inactive controls tended to have larger effect sizes than studies with active controls. The given active interventions, including mental health education, answering manipulated questions, and social support, have been proven to reduce anxiety [49-53]. Therefore, the observed effect sizes seemed to be lower than using inactive controls.

Subgroup analysis for anxiety outcome showed a greater reduction effect for studies conducted outside of Asia than in Asia. This finding may be caused by the difference in racial ethnicities of the study participants between the subgroups [54]. A prior study showed that racial ethnicity affects the use of mindfulness in a weight loss program [55]. Masuda et al. [56] reported that mindfulness interventions could moderate the association between eating disorder cognition and behavior in the White American group, but not in the Asian American or the Black American groups. However, our finding must be carefully interpreted since it contradicted the result from Kahn et al. [57], which revealed that mindfulness is more relevant to Asian populations for regulating emotion. Future online MBIs studies incorporating inter-ethnic analyses are needed to confirm our finding.

According to the meta-regression analyses, we observed a greater anxiety reduction following a longer duration of mindfulness interventions. This finding was confirmed by the sensitivity analysis result after removing Simonsson et al. [37], where this study had the longest MBI duration (8 weeks) of the 6 RCTs included in the analysis. The longer length of psychological interventions will cultivate positive feelings, behaviors, and cognition, leading to an improvement in well-being and other mental health components [48]. Also, repeated mental health interventions in a longer duration will further improve participants' life satisfaction [58]. We additionally found that age was associated with the effect of online MBIs on stress. As argued by Geiger et al. [59], the MBI is a more well-suited type of mental health intervention for older adults due to its similar concept to their coping and emotional control mechanisms towards mental health problems. Older people as well tend to demonstrate a better acceptance towards mindfulness-based practices [60]. Hence, online MBIs may serve as a promising strategy to face age-related mental health problems in the COVID-19 pandemic era.

Feasibility of online MBIs during the COVID-19 pandemic

The practice of social distancing and staying home is needed to reduce the transmission of COVID-19 [61, 62]. Hence, online delivered medical interventions have become an essential strategy during the COVID-19 pandemic while still providing the best care for patients [63, 64]. Prior to the pandemic, online MBIs had been in fact considered as promising mental health treatment practices based on a previous meta-analysis by Spijkerman et al. [10]. Never-theless, our study was more focused on evaluating the role of online MBIs during the COVID-19 pandemic. When compared to the previous meta-analysis [10], our results showed a similar reduction effect for depression, anxiety, and stress, indicating that the implementation of online MBIs is still relevant during the pandemic.

We found that the adherence rates of participants were varied between 86% and 100%, with a pooled rate of 94%. This number was comparable with the previous study's finding, which revealed an 85% adherence to the multisession online intervention [65]. Despite the lack of studies that reported adherence in online mental health practices, this intervention method has been shown to be helpful and convenient for some participants [66]. The usage of telehealth sessions has also considerably decreased the frequency of missed appointments and dropouts and thus increased the efficiency of mental health care [67]. Although online intervention may not be suitable for some patients with complex and severe mental illnesses, this method is still helpful in fulfilling the need for psychological therapy in the general population.

Additionally, treatment costs may affect the patients' decisions to seek mental health treatment [68]. A study reported that approximately 57% of obsessive-compulsive disorders patients were unable to afford their treatment costs [69]. Marques and his colleagues [69] also reported complaints of inconvenience from more than a quarter of patients due to spending much time seeking treatment. Moreover, logistic factors such as transportation and treatment schedules also play a role in the patients' treatment-seeking actions [70]. Ultimately, onlinebased therapy will help in overcoming economic and adherence-related barriers because of its feasibility and high acceptability, leading to a more convenient method of intervention amidst the COVID-19 crisis [71, 72].

Strengths and limitations

To the best of our knowledge, this is the first comprehensive systematic review and meta-analysis that examined the effectiveness of online MBIs on depression, anxiety, and stress during the COVID-19 pandemic. We synthesized evidence from available RCTs, where these study designs are regarded as the most suitable and recommended way to evaluate the efficacy of interventions [73]. Furthermore, the total numbers of samples included in most analyses were relatively sufficient, supported by the wide range of areas covered in Asia, America, and Europe, which may strengthen the generalizability of the study's conclusion. In addition to the short-term effects, we were able to reveal the medium-term effects of online MBIs. Subgroup and meta-regression analyses were also conducted to search for potential variables that could affect the pooled results. Moreover, we identified an ongoing RCT (NCT04720404) [74] with a topic similar to the current study, suggesting the growing interest in implementing online MBIs during a crisis situation like the COVID-19 outbreak.

Although we have made every effort to provide the best possible quality of the study, we also acknowledged that there are still some limitations. First, there was considerable diversity in between-studies characteristics, such as population, instruments used to measure the outcomes, and notably the protocol and method for delivering the MBIs, including the length of follow-up. Although the random-effects model and the SMD of Hedges' *g* have been employed to minimize the possible variability-related effects, our results should be interpreted with

caution. Second, we were not able to determine the long-term effect of online MBIs, given that the length of follow-up reported at most was two months. Third, a publication bias was observed in the post-intervention effect of online MBIs on stress. Nevertheless, through an adequate analysis, we successfully identified that the bias most likely arose from one study by Alvarado-García et al. [32]. Also, the subsequent removal of this study showed no substantial effect on the significance of the pooled result. Fourth, given the small number of studies included in each subgroup, it was not possible to conduct analyses for several covariates. Lastly, the quality of the included studies was yet rather low.

Conclusion and recommendations

The online MBIs showed promising effects in improving mental health problems, notably depression, anxiety, and stress, during a restricted situation like the COVID-19 pandemic. Although the results were small to moderate, the low cost and ease of access of online MBIs supported with adequate adherence may facilitate them as feasible alternatives to promote mental health in a wide range of communities. In addition, the online MBIs provided maintained improvement on depression and anxiety after follow-up, suggesting their middle-term utility.

Given the growing interest and potential utility of online MBIs in clinical practice, particularly during the COVID-19 pandemic, we encourage more research to investigate further evidence regarding the maximum benefits of online MBIs and the potential influencing factors on the treatment effectiveness with several additional considerations. Future explorations and researchers could look into: (1) determining whether the observed beneficial effects are sustained after longer follow-up periods; (2) evaluating the effects of online MBIs in different patients' characteristics; (3) identifying subgroups of several factors which could not be analyzed in the current study; and (4) considering biases and quality criteria when conducting studies and publishing results, since the quality of the current included studies were yet unsatisfactory. Finally, we suggest that online MBIs may be incorporated in other forms of online psychotherapies to enhance their utility in improving various mental health issues.

Supporting information

S1 File. Supplementary materials. (PDF)

S2 File. PRISMA 2020 checklist. (PDF)

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