Original Article

Efficacy of Online Mindfulness Program 'Mindful Senses' for Depression and Anxiety Reduction in Community Samples: A Randomized Controlled Trial

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Objective: To investigate the efficacy of the minimal therapist-guided four-week online audio-based mindfulness program titled 'Mindful Senses' (MS) for depression and anxiety reduction in community samples.

Materials and Methods: This open-label randomized controlled trial enrolled 80 participants from across Thailand. The authors randomly allocated 40 subjects each to the intervention and control groups. The authors included people aged 18 years or older with a Patient Health Questionnaire-9 (PHQ-9) score of 9 or more or Generalized Anxiety Disorder-7 (GAD-7) score of 10 or more. Both groups received four psychological self-help articles online. Only the intervention group attended the MS program. The outcomes were PHQ-9, GAD-7, Perceived Stress Scale (PSS), and Philadelphia Mindfulness Scale (PHLMS) scores measured at baseline (T_0), post-intervention (T_1), and one-month follow-up (T_2). Repeated measures ANOVA were used to analyze the outcomes.

Results: The intervention group showed significantly improved PHQ-9, GAD-7, PSS, and PHLMS scores compared to the controls at T_1 [intention-to-treat mean difference (95% CI): −6.97 (−9.23 to −4.72), p<0.001, d=1.38; −5.27 (−7.32 to −3.23), p<0.001, d=1.14; −5.85 (−8.10 to −3.60), p<0.001, d=1.16; 9.15 (5.47 to 12.83), p<0.001, d=1.11, respectively], and T_2 [intention-to-treat mean difference (95% CI): −5.27 (−7.55 to −3.00), p<0.001, d=1.03; −5.20 (−7.29 to −3.11), p<0.001, d=1.11; −5.43 (−8.21 to −2.64), p<0.001, d=0.87; 8.68 (4.90 to 12.45), p<0.001, d=1.02, respectively].

Conclusion: The MS program improved depression, anxiety, stress, and mindfulness in community samples, and those effects were preserved for one-month post-intervention. It has the potential to be another highly effective treatment option for people suffering from depression or anxiety who face barriers to accessing mental health facilities.

Keywords: Mindfulness; Online; Depression; Anxiety; Community samples

Received 2 May 2022 | Revised 5 September 2022 | Accepted 4 October 2022

J Med Assoc Thai 2022;105(11):1108-19

Website: http://www.jmatonline.com

Depression and anxiety are the major mental health concerns. The global prevalence of major depressive disorder (MDD) ranges from 3.7% to 8.6%[1], and 3.8% to 25.0%[2] for anxiety disorders. MDD and anxiety disorders are common comorbidities. Fifty-nine-point-two percent of MDD patients have comorbid anxiety disorders[3] and 63% of patients with anxiety disorders have comorbid depressive disorders[4]. Depression and anxiety lead to lower quality of life and a greater risk of disability[5]. Furthermore, they contribute to significant economic burden. In the year 2018, incremental direct cost per case of individuals with MDD in the United States was as high as $6,524[6]. The total medical costs for an individual with anxiety disorders was $6,475 per person[7].

One effective psychological intervention for depression and anxiety is the mindfulness-based intervention (MBI). Mindfulness-based stress reduction (MBSR), an eight-week group mindfulness intervention[8], and other mindfulness programs have proven their efficacy in reducing depression[9], anxiety[10,11], and stress[12]. Mindfulness-based cognitive therapy (MBCT) is also a proven treatment for GAD[11] and prevention of depression relapse[13]. The effects of these programs were mediated by increased mindfulness[14], decentering[15], and decreased rumination[16], worry[17], and emotional reactivity[18].

Despite the positive effects of MBIs, many

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How to cite this article:

Viravan N, Atsariyasing W, Srifuengfung M, Lortrakul J. Efficacy of Online Mindfulness Program 'Mindful Senses' for Depression and Anxiety Reduction in Community Samples: A Randomized Controlled Trial. J Med Assoc Thai 2022;105:1108-19.

DOI: 10.35755/jmedassocthai.2022.11.13700

patients were unable to attend the program. Only 51.6% of MDD patients received treatment or medication, and merely 21.6% received adequate treatment[3]. Moreover, only 10.8% of anxiety disorder patients received appropriate counseling, and just 17.5% received proper medications[19]. The barriers preventing access to mental health services were unaffordability, confidentiality concerns[20], lack of service or transportation, lack of time, and social stigma[21].

Online psychological interventions using multimedia can help overcome the aforementioned obstacles to mental healthcare[22]. Online interventions provide people with reduced mobility or those who live in remote areas access to healthcare[23]. Online care also costs less because it requires fewer economic and medical resources compared to traditional face-to-face intervention[24]. Additionally, internet-based psychological self-help interventions help reduce social stigma and maintains confidentiality, and their efficacy is comparable to face-to-face psychotherapies[25,26].

Previous meta-analyses have reported that online mindfulness-based interventions and mindfulness applications could significantly improve depression, anxiety, and stress[27,28]. However, the effect is minor, both for depression and anxiety. Moreover, another major limitation of online or application-based mindfulness interventions is the high dropout rates with a mean of 31.56% and a range of 0% to 73%[28].

The authors believe that highly effective online interventions can reform the mental health care system and help more people with mental health problems faster. Hence, the authors developed a mindfulness program by designing an online intervention that could yield better results and a lower dropout rate than the previous online mindfulness program. The authors maintained the present study online program as mostly self-help to ensure confidentiality and prevent social stigma. However, the authors included therapists' guidance and feedback to improve the outcomes[29] and retention rate[30]. The present study program length was four weeks, the shortest duration possible needed to ensure results[31-33], increase the program attendance rate for people with limited time, and reduce the dropout rate. Moreover, the authors asked participants in the program to listen to guided-mindfulness audio at least three times per day to improve outcomes.

The present study aimed to investigate 1) the efficacy of minimal therapist-guided four-week online audio-based mindfulness program titled "Mindful Senses" (MS) to reduce depression, anxiety, and stress and to increase mindfulness in community samples, and 2) program satisfaction, usefulness, and user-friendliness to learn the feasibility of the program in real practice. The authors hypothesized that MS would yield better outcomes than the previous studies and had a lower dropout rate.

Materials and Methods

Trial design

The present study was an open-label, parallel-group, randomized controlled trial, conducted at the Department of Psychiatry, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. The authors recruited participants, performed the intervention, and collected data between September and December 2020. The present study protocol was approved by the Siriraj International Review Board (SIRB) (COA no. 659/2020), and all participants gave their informed consents before study commencement.

Participants

VN advertised the present study on Facebook using the 'Boost Post' function to reach Thais across the country. Anyone interested in participating in the present study could scan a QR code provided in the post to access and complete the online application form. The applications of those interested were then checked for eligibility.

The present study included people who 1) were 18 or older, 2) could use the LINE application, and 3) had a Generalized Anxiety Disorder-7 (GAD-7) score of 10 or more or a Patient Health Questionnaire-9 (PHQ-9) score of 9 or more. Participants having one or more of the following were excluded, 1) practiced mindfulness daily for one year, 2) were already receiving psychotherapy, 3) had already began psychiatric disorder treatment within the last three months, or 4) had already started taking psychotropic medications or had their dose adjusted within the last three months. Participants were withdrawn from the study if, during the study, they 1) attended another mindfulness program, 2) started psychotherapy, 3) began treatment for a new psychiatric disorder, or 4) started a new psychotropic medication or had a dose adjustment of an existing psychotropic medication. Participants were informed prior to the start of the study that they could withdraw at their will anytime.

Eligible participants completed a baseline characteristics online questionnaire. AW generated a randomization list by using stratified randomization, dividing strata based on baseline PHQ-9, GAD-7, and

the Philadelphia Mindfulness Scale (PHLMS) scores, following by simple randomization within each stratum. Allocation sequence was saved in a computer with passcode and concealed to SM. She received allocation sequence after she had the full list of 80 eligible participants in order of research application. Then, she applied the allocation sequence to the list. Participants were assigned to the intervention or control group equally. After that, the authors allowed participants to join the intervention or control group rooms corresponding to the group they were allocated through the LINE Official Account (LOA), an online platform used to communicate with subjects in both groups. Neither participants, nor the therapist were blinded to group assignment.

Platform

The authors used LOA as a platform to deliver the present study online mindfulness program "Mindful Senses". LOA is a mobile application that allows users to chat by sending messages in a chat room. The authors created rooms for "Group A" and "Group B" for participants in the intervention and the control group, respectively, to join. Each participant did not know the other participants, both in the same group and the other group, and were to maintain confidentiality. The authors did not allow open chats, so participants could not discuss with each other. Each participant was able to chat only to the therapist. However, the therapist could chat with each participant by sending messages to each participant one-by-one or to all participants at once. Each participant did not know what the therapist communicated with other participants. The therapist also sent audio files, articles, and questionnaires to participants via LOA.

Therapist

VN was the designated therapist for the MS program. He had five years of experience in mindfulness practice. He completed a mindfulness course named "Human Work Course", teaching the meditation technique known as "Dynamic Meditation" created by Luangpor Teean Jittasubho, a famous Thai Buddhist monk. Dynamic Meditation is a unique vipassana practice involving rhythmic hands and arms movement, and requires practitioners be in the present moment by paying attention to the movements of their body. VN also completed an online mindfulness course for professionals using core skills of MBCT via www.mindfulnoggin.com. In addition, he had experience in facilitating mindfulness workshops for hospital personnel at Siriraj Hospital. He developed the MS program used in the present study based on his experience in mindfulness practices and insight from daily mindfulness training.

Intervention

Participants of the intervention group attended the MS program. The program duration was 28 days. Prior to the first day of the program, participants were briefly informed via LOA to listen to mindfulness audio at least three times per day and practice mindfulness as guided. They could freely select any time to listen to the audio. They could also make any inquiry regarding mindfulness practice to the therapist at any time during the program. The therapist would send a short message regarding essential points in mindfulness practice to participants daily throughout the course of the program so that participants could better understand mindfulness and indirectly remind them to practice. The therapist would not send any messages other than daily essential points in mindfulness practice to participants, except research-related announcements or responses to participants' inquiries.

The content of the four audio files were written and recorded by VN. The main themes of the four audio files are summarized in Table 1. The English versions of the audio file scripts were in the supplementary data, which was translated from the original Thai version. Each audio file is about 9 to 14 minutes in length. The links to first, second, third, and fourth files were sent to participants via LOA on day 1, 6, 11, and 16 of the programs, respectively. Participants were instructed to listen to the first, second, third, and fourth files on days 1 to 5, 6 to 10, 11 to 15, and 16 to 20 of the programs, respectively. Between days 21 to 28, participants could listen to any audio file of their preference.

In MS, the authors used body sensations, surrounding sounds, and front images as objects of attention. Participants practiced being in the present moment by paying attention to their body sensations, listening to the sounds surrounding them, and looking at things in front of them in each moment. In the present study program, the authors emphasized using these three sensory modalities as the focus of attention, which was partially adapted from other MBIs, to improve the chance of matching practice styles with participant preferences[34]. This method might increase adherence, and lead to incorporation of mindfulness practice into daily life more easily. The authors hypothesized that the present study adapted

Table 1. The content in mindfulness audio files and psychological self-help articles

Mindfulness audio files	
Files (minute)	Content
1 (9:20)	The instructor in the audio file slowly directed listeners' attention to each body part sensation, periodically helped them notice when thoughts were wandering, then gently brought their attention back to body sensations. The instructor let them experience the wandering nature of minds and know the space to rest their mind.
2 (9:35)	The instructor in the audio file helped listeners become aware of thoughts more often by letting them experience the differences between surrounding sounds and inner voices (thoughts). They were told to keep paying attention to surrounding sounds. The instructor would periodically help them notice when their attention moved to inner voices and gently bring their attention back to surrounding sounds. The instructor let them experience the present moment and a pause from stressful thoughts through paying attention to surrounding sounds.
3 (12:09)	The instructor in the audio file assisted listeners more often aware of thoughts by letting them experience the differences between front images and mental images (thoughts). They were instructed to keep paying attention to front images. The instructor would periodically help them notice when their attention wandered to mental images and gently return their attention to front images. The instructor let them experience the short-lived nature of emotions that gradually subsided when attention was pulled away from mental images to the front images.
4 (13:59)	The instructor in the audio file gently directed listeners' attention to each body part sensation, surrounding sounds, and front images, back and forth. The instructor let them become familiar with paying attention to the present moment experience through these three sensory modalities without fixing attention at any particular sensory modality. The instructors helped them notice when thoughts wandered and redirect their attention to the present moment experience. They were suggested to allow every thought and feeling to come and go even though they did not like them. They were encouraged to keep paying attention to the present moment experience in each moment of everyday activities.
Psychological self-help articles	
Articles	Content
1	How to cope with hopelessness during the COVID-19 pandemic? - Find your strength, good things in life, or reason to live. Use distractions, ventilate, or consult an expert.
2	How to relieve overwhelming stress during the COVID-19 pandemic? - Write down your thoughts and feelings, cooking, exercise, reading books, listening to music, watching TV, drawing, playing musical instruments, talking with family members or friends, chatting with the chatbot developed by the department of mental health and Mahidol University, consulting psychiatrists or psychologists, mental health hotline, helping other people.
3	How to deal with family conflicts during the COVID-19 pandemic? - Reframing your thoughts, communication skills, setting a routine schedule, respecting personal space, listening and understanding, seeking help from relatives or organizations.
4	How to promote mental health during the COVID-19 pandemic? - Regular bedtime, avoid daytime napping, regular exercise, outside activities, regular mealtime, avoid using smartphone or laptop before sleep, regular video call or phone call with friends or relatives.

mindfulness program could improve the outcome and retention of participants.

Control

Both groups received four psychological self-help articles (PSA). All the PSA were written by psychiatrists at the Department of Psychiatry, Faculty of Medicine Siriraj Hospital, Mahidol University and were published online via the department's website and application during the coronavirus sars-cov-2 (COVID-19) pandemic. The articles aimed to educate people on how to deal with negative emotions, relationship problems, and promote mental health (Table 1). The content in the articles did not include mindfulness practice. The authors received permission from all authors to use their articles in the present study as a control condition. All four articles were sent via LOA to participants in both groups on the first day of the MS program to decrease the chance of unequal mental health knowledge received from other resources during the program. It is notable that there was an abundance of mental health information online during the time the present study was being conducted (COVID-19 pandemic).

Outcomes

Primary outcomes: The Thai version[35] of the PHQ-9 is a self-rated nine-item questionnaire used for depressive disorder screening and severity grading. Each question is scored from 0 to 3 with 0 for not at all and 3 for nearly every day. A PHQ-9 cut-off score of 9 or more had a sensitivity of 0.84, a specificity of 0.77, and a positive and negative predictive value of 0.21 and 0.99, respectively, for identifying depression.

The GAD-7[36] is a self-rated seven-item questionnaire used to screen for and measure GAD severity. The Thai version of GAD-7 is available on Pfizer's website. No permission was required to use it. Each question is scored from 0 to 3 with 0 for not at all and 3 for nearly every day. A GAD-7 cut-off score of 10 or more had a sensitivity of 0.89, a specificity of 0.82, and a positive and negative predictive value of 0.29 and 0.99, respectively, for identifying GAD. Psychometric properties of the Thai version of GAD-7 are not available.

Secondary outcomes: The Thai version[37] of

PSS is a 10-item self-rated questionnaire. Each question is scored from 0 to 4 with 0 for never and 4 for very often. It has good internal consistency (Cronbach's alpha 0.85), and the intraclass correlation coefficient (ICC) was 0.82 (95% CI 0.72 to 0.88) for four-week retest reliability.

The Thai version[38] of PHLMS is a 20-item self-rated questionnaire with 10 items measuring for awareness, and the other 10 measuring acceptance. Each question is scored from 1 to 5 with 1 for never and 5 for very often. It has good internal consistency for the awareness subscale (Cronbach's alpha 0.87) and the acceptance subscale (Cronbach's alpha 0.88).

Feasibility and acceptability of the program were measured by having participants from the intervention group rate program satisfaction, program usefulness, and program user-friendliness as 0 for the lowest and 10 for the highest, as well as provide feedback with open-ended responses regarding obstacles to protocol adherence and suggestions for program improvement.

Time of assessment and incentive: The PHQ-9, GAD-7, PSS, and PHLMS were sent to participants in both groups via LOA immediately post-intervention (T_1) and at one-month follow-up (T_2). Since the participants had finished baseline (T_0) PHQ-9, GAD-7, PSS, and PHLMS scores before stratified randomization, the authors did not have them complete it again. Each participant received 300 baht for completion of each questionnaire, which was three times in total for the present study.

Participants in the intervention group had to rate program satisfaction, usefulness, and user-friendliness, as well as provide feedback about the program at T_1 in the questionnaires sent to them via LOA.

Adherence: The asked participants in the intervention group were asked to self-record how often they listened to the audio each day in LOA over 28 days of the MS program to measure adherence to the study protocol. The messages were sent every seven days to remind participants to record their audio listening statistics.

Withdrawal criteria assessment: The authors assessed if participants met any withdrawal criteria over the four weeks by having them report in the questionnaire sent to them via LOA at T_1 and T_2.

Statistical analyses

The sample size was calculated by using equations for comparing the means of two normally distributed samples of equal size using a two-sided test with significance level α (0.05) and power $1 - \beta$ (0.2)[39]. The optimal sample size was 70, plus 30% to compensate for withdrawals. Baseline characteristics of each group was compared using the Pearson's chi-square test, Fisher's exact test, or likelihood ratio for categorical variables, and t-test for normally distributed continuous variables. The general linear model (GLM) repeated measures ANOVA was used to compare PHQ-9, GAD-7, PSS, and PHLMS scores within a group and between groups. The authors performed both the intention-to-treat (ITT) and per-protocol (PP) analyses. The effect size was calculated using Cohen's d statistic. Cohen's d values of 0.2 or greater, 0.5, and 0.8 were interpreted as small, medium, and large, respectively[40]. The authors did not analyze audio listening statistics of participants who recorded less than 80% of total days[41]. The authors imputed the missing data of participants who recorded at least 80% using the last observation carried forward (LOCF) method. There was no missing data for other variables, and primary and secondary outcomes. The authors analyzed the correlation between protocol adherence and outcomes by Pearson's correlation and Spearman's correlation for normal and non-normal distributed data, respectively. A p-value of less than 0.05 was accepted as statistical significance. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA).

Results

One hundred thirty-nine people were assessed for eligibility (Figure 1), of these, 80 people met the inclusion criteria, gave consent to participate, and completed the baseline questionnaires. These 80 subjects were then randomly assigned with 40 subjects to the intervention group and 40 subjects to the control group. The authors controlled the participants for gender, age, race, education, employment, marital status, having children, perceived financial distress, the use of psychotropic medications, diagnosis of psychiatric disorders, frequency of mobile application use, and baseline depression, anxiety, stress, and mindfulness level. There were no statistically significant differences in baseline characteristics between the groups (Table 2).

Primary outcomes

The intervention group showed significant improvements in depression and anxiety from T_0 at T_1 and T_2 ($p<0.001$) (Table 3). There was no significant difference in depression or anxiety scores between T_1 and T_2. On the other hand, there was no significant

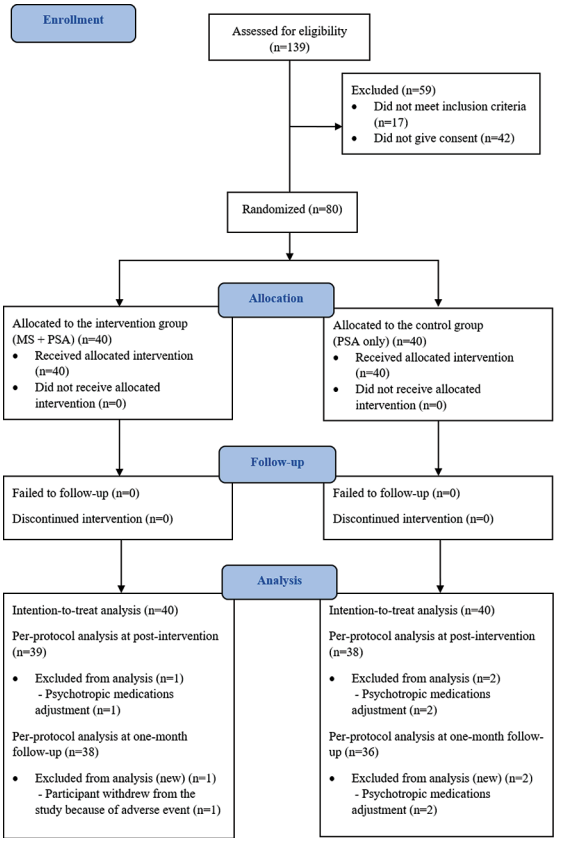

Figure 1. CONSORT flow diagram.

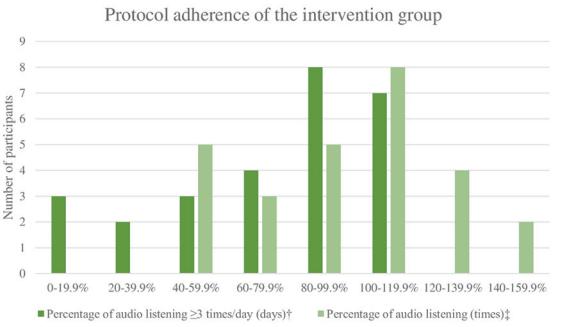

Figure 2. Protocol adherence of the intervention group.

† Calculated by [number of day participants listen to mindfulness audio file ≥3 times per day/28 days (total days of the program)] × 100%

‡ Calculated by [total number of audio file listening (times)/84 (total number of audio file listening assigned to participants during MS program (3 times/day for 4 weeks)] × 100%

difference in the depression or anxiety scores at each time point in the control group. These results applied to both the ITT and PP analysis.

The intervention group saw significant improvement in depression compared to the control group, with large effect sizes at T_1 (ITT $p<0.001$, $d=1.38$, PP $p<0.001$, $d=1.34$), and large effect sizes at T_2 (ITT $p<0.001$, $d=1.03$, PP $p<0.001$, $d=1.17$) (Table 4). The intervention group also showed significant improvement in anxiety compared to the control group, with a large effect size at T_1 and T_2 in an ITT analysis (T_1 $p<0.001$, $d=1.14$, T_2 $p<0.001$, $d=1.11$) and with very large effect sizes at T_1 and T_2 (T_1 $p<0.001$, $d=1.23$, T_2 $p<0.001$, $d=1.35$) in a PP analysis.

Secondary outcomes

For the intervention group, there was significant improvements in stress and mindfulness from T_0 to T_1 and T_2 ($p<0.001$) (Table 3). However, there was no significant difference in stress or mindfulness scores between T_1 and T_2. On the other hand, for the control group, there was no significant difference in stress or mindfulness scores among each timepoint for both the ITT and PP analysis, except difference in stress scores between T_0 and T_2 in the ITT analysis ($p=0.039$).

The intervention group showed a significant improvement in stress compared to the control group, with very large effect sizes at T_1 in a PP analysis ($p<0.001$ $d=1.24$) and large effect sizes at T_1 in the ITT analysis and T_2 for both analyses (ITT, T_1 $p<0.001$, $d=1.16$, T_2 $p<0.001$, $d=0.87$; PP, T_2 $p<0.001$, $d=0.99$) (Table 4). The intervention group saw significant improvement in mindfulness compared to the control group, with large effect sizes at T_1 and T_2 in the ITT and PP analysis (ITT, T_1 $p<0.001$, $d=1.11$, T_2 $p<0.001$, $d=1.02$; PP, T_1 $p<0.001$, $d=1.15$, T_2 $p<0.001$, $d=1.13$).

The median (interquartile range, IQR) score was 9 (8, 10) regarding program satisfaction, 10 (8, 10) for program usefulness, and 9 (8, 10) for program user-friendliness. Six participants or 15.0% rated program satisfaction, usefulness, and user-friendliness as medium with a score of 4 to 7, while the remaining 34 participants or 85.0% rated the parameters as high with a score of 8 to 10.

Participants also reported obstacles in listening to mindfulness audio three times per day, with the reasons including 1) tight schedule and family duties, and 2) working or staying where internet connection was absent or unstable, preventing them from downloading audio files. They suggested that 1) the authors improve the notification system for practice recording to make it more effective and provide feedback about participants' practice statistics intermittently to help them monitor their progress, and 2) have periodic phone calls or chats to maintain engagement. They commented that the MS program helped them relax and calm down. It was easy to

Table 2. Participant baseline characteristics compared between the intervention (MS + PSA) and control (PSA only) groups

Baseline characteristics	Intervention (MS+PSA) (n=40)	Control (PSA) (n=40)	p-value
Female; n (%)	32 (80.0)	32 (80.0)	1.000†
Age (year); mean±SD	33.55±10.88	34.15±10.00	0.798‡
Range	(18 to 64)	(18 to 63)	
Race; n (%)			1.000†
Asian	40 (100.0)	40 (100.0)	
Education; n (%)			0.675§
High school	4 (10.0)	2 (5.0)	
Bachelor degree or more	36 (90.0)	38 (95.0)	
Employment; n (%)			0.122¶
Full-time	36 (90.0)	28 (70.0)	
Part-time	1 (2.5)	3 (7.5)	
Unemployed	3 (7.5)	8 (20.0)	
Retired	0 (0.0)	1 (2.5)	
Marital status; n (%)			0.422¶
Married	6 (15.0)	2 (5.0)	
Single	31 (77.5)	36 (90.0)	
Widow	2 (5.0)	1 (2.5)	
Divorced	1 (2.5)	1 (2.5)	
Have at least one child; n (%)	9 (22.5)	7 (17.5)	0.576†
Perceived financial distress; n (%)			0.472†
No distress	8 (20.0)	9 (22.5)	
Some distress	25 (62.5)	20 (50.0)	
High level of distress	7 (17.5)	11 (27.5)	
Use at least one antidepressant medication; n (%)	3 (7.5)	6 (15.0)	0.481§
Use at least one anxiolytic medication; n (%)	4 (10.0)	6 (15.0)	0.499†
Use another psychotropic medication; n (%)	1 (2.5)	4 (10.0)	0.359§
Diagnosis of depressive disorders; n (%)	3 (7.5)	6 (15.0)	0.481§
Diagnosis of anxiety disorders; n (%)	1 (2.5)	4 (10.0)	0.359§
Diagnosis of other psychiatric disorders; n (%)	0 (0.0)	3 (7.5)	0.241§
Use applications in mobile phone everyday; n (%)	38 (95.0)	40 (100.0)	0.494§
PHQ-9 score; mean±SD	15.05±3.97	15.15±4.12	0.912‡
GAD-7 score; mean±SD	10.33±4.91	11.88±4.55	0.147‡
PSS score; mean±SD	25.68±5.35	25.08±5.64	0.627‡
PHLMS score; mean±SD	55.60±6.71	56.23±6.33	0.670‡

MS=Mindful Senses; PSA=psychological self-help articles; PHQ-9=Patient Health Questionnaire-9; GAD-7=Generalized Anxiety Disorder-7; PSS=Perceived Stress Scale; PHLMS=Philadelphia Mindfulness Scale; SD=standard deviation

† Chi-square test, ‡ t-test, § Fisher's exact test, ¶ Likelihood ratio

understand and follow, and they wanted to keep the audio files to practice further. The therapist answered participant inquiries quickly and clearly, which helped them solve their problems and better understand the content. The application provided effective communication and proved to be user-friendly and handy. They also expressed appreciation for being able to participate in the study, and that it helped them better understand and manage their emotions.

The authors analyzed the audio listening statistics of only 27 of 40 participants or 67.5% who logged their sessions for at least 23 to 28 days or 80% or more often (Figure 2) because data imputation of more than 20% of total data makes overall data unreliable. Participants who did not record their audio statistics as assigned reported they listened to the audio files but forgot to record. Raw data of all 40 participants' listening statistics are shown in supplementary data. Among the 27 participants, 19 or 70.4% listened to the audio files at least three times per day for more than 60% of total days. Median (IQR) number of days that the participants listened to the audio files at least

Table 3. Repeated measure ANOVA for within-group comparison of mean outcome score at each time point and between-group (Group×Time) comparison of the outcomes

Outcomes	Intervention group (MS + PSA) [n=40 (ITT), n=38 (PP)]; mean±SD			Within group p-value	Significantly different pairs	Control group (PSA) [n=40 (ITT), n=36 (PP)]; mean±SD			Within group p-value	Significantly different pairs	Group×Time p-value
	0 week (T_0)	4 weeks (T_1)	8 weeks (T_2)			0 week (T_0)	4 weeks (T_1)	8 weeks (T_2)			
ITT analysis											
PHQ-9	15.05±3.97	8.10±4.75	8.15±5.09	<.001†	T_0 T_1*** T_0 T_2***	15.15±4.12	15.08±5.36	13.43±5.11	0.049†	N/A	<.001†
GAD-7	10.33±4.91	5.25±4.04	4.75±3.87	<.001†	T_0 T_1*** T_0 T_2***	11.88±4.55	10.53±5.10	9.95±5.39	0.053‡	N/A	0.001†
PSS	25.68±5.35	17.63±5.38	17.18±6.08	<.001‡	T_0 T_1*** T_0 T_2***	25.08±5.64	23.48±4.69	22.60±6.43	0.027†	T_0 T_2*	<0.001†
PHLMS	55.60±6.71	64.72±9.07	65.15±9.71	<.001‡	T_0 T_1*** T_0 T_2***	56.22±6.33	55.58±7.39	56.48±7.04	0.592†	N/A	<0.001‡
PP analysis											
PHQ-9	15.03±4.08	7.95±4.74	7.76±4.69	<.001†	T_0 T_1** *T_0 T_2***	15.25±4.31	14.83±5.56	13.58±5.23	0.118†	N/A	<0.001†
GAD-7	10.26±5.03	4.95±3.56	4.24±3.17	<.001‡	T_0 T_1*** T_0 T_2***	12.00±4.71	10.36±5.16	10.22±5.44	0.069†	N/A	<0.001‡
PSS	25.68±5.46	17.29±5.23	16.76±5.94	<.001‡	T_0 T_1*** T_0 T_2***	25.11±5.66	23.50±4.80	22.92±6.54	0.050†	N/A	<0.001†
PHLMS	55.61±6.77	65.13±9.12	65.55±9.68	<.001‡	T_0 T_1*** T_0T_2***	55.83±6.23	55.36±7.72	56.06±6.79	0.762†	N/A	<0.001‡

MS=Mindful Senses; PSA=psychological self-help articles; ITT=intention-to-treat analysis; PP=per-protocol analysis; PHQ-9=Patient Health Questionnaire-9; GAD-7=Generalized Anxiety Disorder-7; PSS=Perceived Stress Scale; PHLMS=Philadelphia Mindfulness Scale; SD=standard deviation

† Sphericity assumed, ‡ Greenhouse-Geisser, * p<0.05, ** p<0.01, *** p<0.001

Table 4. Mean differences of the outcome scores between groups at each time point

Outcomes	ITT analysis			PP analysis		
	Mean difference† (95% CI)	p-value	d	Mean difference† (95% CI)	p-value	d
PHQ-9						
0 week	−0.10 (−1.90 to 1.70)	0.912	0.02	−0.22 (−2.17 to 1.72)	0.819	0.05
4 weeks	−6.97 (−9.23 to −4.72)	<0.001	1.38	−6.89 (−9.28 to −4.50)	<0.001	1.34
8 weeks	−5.27 (−7.55 to −3.00)	<0.001	1.03	−5.82 (−8.12 to −3.52)	<0.001	1.17
GAD-7						
0 week	−1.55 (−3.66 to 0.56)	0.147	0.33	−1.74 (−4.00 to 0.53)	0.130	0.36
4 weeks	−5.27 (−7.32 to −3.23)	<0.001	1.14	−5.41 (−7.46 to −3.37)	<0.001	1.23
8 weeks	−5.20 (−7.29 to −3.11)	<0.001	1.11	−5.99 (−8.04 to −3.94)	<0.001	1.35
PSS						
0 week	0.60 (−1.85 to 3.05)	0.627	0.11	0.57 (−2.00 to 3.15)	0.659	0.10
4 weeks	−5.85 (−8.10 to −3.60)	<0.001	1.16	−6.21 (−8.54 to −3.88)	<0.001	1.24
8 weeks	−5.43 (−8.21 to −2.64)	<0.001	0.87	−6.15 (−9.05 to −3.26)	<0.001	0.99
PHLMS						
0 week	−0.62 (−3.53 to 2.28)	0.670	0.09	−0.23 (−3.25 to 2.79)	0.881	0.04
4 weeks	9.15 (5.47 to 12.83)	<0.001	1.11	9.77 (5.84 to 13.70)	<0.001	1.15
8 weeks	8.68 (4.90 to 12.45)	<0.001	1.02	9.50 (5.60 to 13.39)	<0.001	1.13

ITT=intention-to-treat analysis; PP=per-protocol analysis; PHQ-9=Patient Health Questionnaire-9; GAD-7=Generalized Anxiety Disorder-7; PSS=Perceived Stress Scale; PHLMS=Philadelphia Mindfulness Scale; CI=confidence interval

† Mean outcome score of intervention group – mean outcome score of control group

three times per day was 25 (14, 28). Mean number of audio file listening was 79.89±25.27 times. No participant listened to the audio files less than 40% of the expected 84 times or three times a day for four

weeks. Nineteen or 70.4% listened to the audio files for more than 80% of the expected number.

There was no correlation between protocol adherence for total number of audio files listened to or the number of days the files were listened to at least three times and score changes from baseline at immediate post-intervention (T_0 to T_1) of PHQ-9, GAD-7, PSS, and PHLMS.

Adverse effect

One participant in the intervention group reported mild involuntary jerking in both legs when meditating. She reported having this symptom each time she meditated for the previous ten years. During the MS program, she continued to experience these symptoms every time she practiced mindfulness, so she stopped listening to the mindfulness audio files and withdrew from the study after finishing the four-week MS program. The symptom never evolved in severity. The authors suggested she have a neurologist consultation. No other harm or adverse effects were voluntarily reported by other participants. However, the authors did not systematically measure the adverse effects that occurred during the study.

Discussion

Interpretation

The present study aimed to evaluate the efficacy of the minimal therapist-guided four-week online audio-based mindfulness program titled "Mindful Senses" to reduce depression, anxiety, stress, and increase mindfulness in the general population. The program significantly improved depression, anxiety, stress, and mindfulness in the community samples with large to very large effect sizes. Moreover, the effects of training were preserved at the one-month follow-up. The outcomes were in accordance with face-to-face MBSR[42] and the previous online mindfulness RCT studies[43-45]. However, the MS program yielded larger effect sizes with a shorter duration of training. The authors hypothesized that the MS program, which used three main sensory modalities as objects of attention was easy to understand and apply to daily activities. Therefore, the outcomes became larger than the previous MBIs[46]. Furthermore, the MS program included little therapist guidance and allowed for inquiries every day that promoted mindfulness practice integration in participants' daily lives, accelerated skills development, and improved outcomes[8,29,47]. The outcomes were not influenced by the group effect because discussion was not allowed among participants. Additionally, positive feedback from participants regarding program satisfaction, usefulness, and user-friendliness supported the feasibility of MS program implication in society.

No correlation between protocol adherence and outcomes were found. This may be due to the incomplete recording of practice data. Moreover, the authors did not measure participants' amount of informal practice, which influenced the degree of outcomes.

Attrition

Even though six or 7.5% of the participants dropped-out during the study, it was much lower than the previous application-based psychological intervention studies at 47.8% (95% CI 35.8 to 60.0)[30]. Additionally, participants who dropped-out were not excluded from PP analysis because of failure to follow-up. Five participants had a dose adjustment of psychotropic medication but continued taking part in the study. The present study had a low dropout rate possibly because the MS program provided regular human feedback[30] and used multiple sensory modalities as objects of attention which could increase probability of preference matching with the participants[34].

Adverse events

One participant reported periodic involuntary jerking of legs each time she meditated. Studies also reported a similar phenomenon, including multiple chronic muscle contractions[48], involuntary movements[49], and involuntary jerks[50]. However, there has been no study to investigate its mechanism, treatment, or prognosis. The prevalence of meditation adverse events in the present study was 2.5%, which agrees with the previous experimental studies at 3.7% (95% CI 0.02 to 0.05)[51].

Limitation

There were limitations in the present study. First, neither the participants nor the therapist was blinded to the group assignment, because blinding was impossible in the present study. Therefore, there might be potential biases of results due to the placebo effect. Second, the practice record notification system in which messages were sent to participants every seven days to remind them to record their audio listening statistics was not effective enough as some participants still forgot to record their listening frequency. Hence, results regarding protocol adherence of the present study should be cautiously interpreted because of incomplete data. Further development of an automatic

practice recording system in the application will assist with data completeness. Third, the therapist did not have a mindfulness therapy certificate to prove his competency as there is no MBSR or MBCT teacher training program available in Thailand. Fourth, there were no independent assessors to monitor the therapist's adherence to the mindfulness concept when sending messages to the participants or answering their questions to approve the internal validity of the program. Lastly, 80% of participants were women, and only four participants were over the age of 50. In addition, the present study program could reach only those who had internet access and were able to use LOA. Hence, the present study results may not be reproducible to all subsets of the general population.

Clinical implications

The MS program was highly effective, easy-to-access, short in duration, confidential, and required minimal resources. Therefore, it has the potential to reach and treat people who cannot access mental health facilities. It is another treatment option for people suffering from depression, anxiety, and stress who want more intensive mindfulness practice and require human feedback that mindfulness applications available on the market such as Calm and Headspace cannot provide. Further research in long-term outcomes, adverse effects and cost-effectiveness is needed. However, developing a MS program for older adults who are not familiar with the use of mobile phones remains a challenge.

Conclusion

The MS program reduced depression, anxiety, stress, and improved mindfulness in community samples and its effects remained at least until one-month follow-up. The program was feasible and acceptable for users and had the potential to be another highly effective treatment option for people with mental health problems who have difficulties to access mental health facilities for reasons ranging from unaffordability, confidentiality issues, social stigma concerns, lack of service or transportation, and lack of time. Further studies of the program's long-term effects, adverse effects, and cost-effectiveness might support its further implication in society.

What is already known on this topic?

Online MBIs significantly improve depression and anxiety. However, the effects are small, and they have high dropout rate.

What this study adds?

Redesigning components of online MBIs can improve the efficacy of programs and reduce dropout rate. The MS program included daily messages regarding essential points in mindfulness practice, therapist's response to participants' inquiries, short training duration as four weeks, using a popular mobile application as a platform, encouragement of mindfulness practice in daily life, and audio-guided mindfulness practice using three sensory modalities as objects of attention. As a result, it could reduce depression and anxiety in community samples with large effect size and had low dropout rate.

Acknowledgement

The authors gratefully acknowledge Assistant Professor Woraphat Ratta-apha, MD, PhD for research methodology-related advice, and Ms. Naratip Sanguanpanich for her assistance with statistical analysis.

Funding disclosure

The present study was supported by a grant from the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (grant no. R016332027). The funding source had no influence on the design of the study, data collection, data analysis, interpretation, manuscript writing, or decision to submit the article for publication.

Conflicts of interest

The authors declare no conflicts of interest.

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