

Effects of nonpharmacological interventions on depressive symptoms and depression among nursing students: A systematic review and meta-analysis

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ABSTRACT

Objectives: We aim to examine whether nonpharmacological interventions could effectively improve depressive symptoms and depression to provide more treatment options for nursing students.

Methods: PubMed, the Cochrane Library, EMBase, Web of Science, PsycINFO, and three Chinese electronic databases were comprehensively searched for papers that were published from January 1990 through March 2018. Quality assessment, sensitivity analysis and heterogeneity were performed.

Results: In our review, 13 controlled trials met the inclusion criteria. The meta-analysis indicated that the depressive symptoms and depression of nursing students in the intervention groups showed significantly moderate improvements compared with the control groups. Three subgroup analyses showed that mindfulness interventions and stress management programs were common and effective, short-term interventions were beneficial to depression, nonpharmacological interventions had great improvements for Asian nursing students and more rigorous researches on methodological quality are recommended.

Conclusion: Nonpharmacological interventions can serve as promising complementary and alternative approaches in reducing the depressive symptoms and depression of nursing students.

1. Introduction

Depressive symptoms and depression are common mental disorders. The worldwide point, one-year and lifetime prevalence of depression are 12.9%, 7.2% and 10.8% respectively [1]. As a mood disorder, depression is linked with higher rates of morbidity, mortality, and suicide [2]. The depression is twice as prevalent in women as it is in men [3]. The people aged between 15 and 29 years and female gender with depression were more vulnerable to suicide [4,5]. Moreover, the World Health Organization (WHO) assesses depression to be the leading cause of disability worldwide [6], and it is predicted to increase to be the second most prevalent cause of disease burden by 2020 [7]. The average total cost of managing depression is around USD 7638 per patient-year and indirect costs such as loss of productivity dominated the total costs [8]. Many studies have confirmed that nursing students have high risk of depressive symptoms and depression in Asia and Europe [5,9–11]. And depression may persist for a long time among nursing students [12]. The available evidence indicated that approximately 34.0% of nursing students had experienced depression

worldwide [13]. In particular, Asian nursing students experienced the highest prevalence of depression (43.0%), compared to other areas in the world, Europe (38.0%), Arab states (28.0%), North America (26.0%), Latin America and the Caribbean (21.0%) [13]. Furthermore, nursing students aged 16–20 (41%) and 21–25 (39%) years had higher prevalence of depression than nursing students of above 25 (18%) years; therefore, the prevalence of depression declines among nursing students as the mean age increases [13].

Many factors caused or contributed to depression, such as disinterest in the nurse course, a low grade point average, worry about future placement, workload, study assignments in Asian nursing students [14–16], fear of unknown conditions, handling technical equipment and mistakes with patients in clinical practices in European nursing students [17]. Depression may also simultaneously affect their academic performance and clinical practice in Canada [18]. Furthermore, 25% of patients with major depressive disorder had suicidal behaviors, and 10–15% eventually died of suicide [19]. Therefore, it is necessary to identify valid and protracted approaches that aim to help nursing students deal with depressive symptoms and depression.

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Given the strong link between depressive symptoms and depression and physical and mental disorders in nursing students, studies have focused on interventions to relieve depressive symptoms and depression. Numerous studies have examined pharmacological approaches to improve depressive symptoms and depression. Antidepressants can improve cognitive function [20] and enhance occupational function [21]. Antidepressants, as the first-line treatments for moderate or severe depression [22], are often used to treat depressive symptoms and depression [23]. One study presented that the antidepressant pharmacotherapy and mindfulness-based cognitive therapy (MBCT) offered equal level protection against depression relapse [24]. Furthermore, Thase et al. [25] showed that participants who continued an antidepressant augmentation exhibited significantly more rapid remission than augmentation with cognitive therapy; however, individuals treated with antidepressants reported significantly more side effects than those who were assigned to cognitive therapy alone. Recently, some researchers and media proposed to use novel drugs with addiction potential (e.g. ketamine) to treat depression [26]. Ketamine can lead to serious side effects including urinary incontinence [27], cognitive impairment [28] and ethical concerns [29]. Such novel treatment has limited applicability [30] and its safety remains controversial [31]. Reports have suggested that antidepressants had adverse medical effects [32,33], and some patients reported worsening symptoms [34] and increased risks of mortality and morbidity [35]. Additionally, surveys indicated a strong tendency for depressed patients to prefer psychotherapy without adverse side-effects than pharmacotherapy [36]. Although antidepressants have positive therapeutic effects in depression, patients often discontinue pharmacotherapy due to side-effects and high cost [37].

Considering the extent of the problem, in recent years, numerous studies have focused on the effects of nonpharmacological interventions on the management of depressive symptoms and depression, such as mindfulness therapy, stress management interventions, music therapy and yoga interventions, to provide complementary and alternative therapies in the treatment of depression. However, we found that the results from nonpharmacological interventions for depressive symptoms and depression among nursing students did not reach a consistent conclusion. Moreover, an integrated literature review [38] showed that mindfulness meditation had positive impacts on nursing students' depression, stress, anxiety and other psychological outcomes. However, this review only included mindfulness meditation interventions and did not conduct meta-analysis for psychological results. Furthermore, a recent systematic review and meta-analysis indicated that psychotherapy should be recommended to reduce depression in nursing students; however, it only mainly conducted a comparative analysis of psychotherapy and non-psychotherapy interventions for nursing students' depression without further meta-analysis of the follow-up outcome, intervention methods, intervention duration, different population types and methodological qualities [39].

As far as we know, no systematic review and meta-analysis based on randomized controlled trials (RCTs) and controlled clinical trials (CCTs) have been conducted to explore the effects of nonpharmacological interventions on depressive symptoms and depression in nursing students. Therefore, the objective of this review was to employ subgroup analyses and sensitivity analysis to determine whether nonpharmacological interventions are effective at improving depressive symptoms and depression among nursing students and explore the effects of different intervention methods, intervention lengths, methodological qualities and in different population types for providing nursing students with more appropriate nonpharmacological intervention methods and intervention durations.

2. Methods

The review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines [40].

2.1. Literature search

PubMed, the Cochrane Library, EMBASE, Web of Science, PsycINFO, the Chinese National Knowledge Infrastructure (CNKI), the Wanfang and Weipu database were systematically searched for papers that were published from January 1990 through March 2018. Search terms were combined from conjunctions of the following terms: Depression [mh] OR Emotional Depressions OR Depressions, Emotional OR Depression, Emotional OR Emotional Depression OR Symptoms, Depressive OR Symptom, Depressive OR Depressive Symptom OR Depressive Symptoms OR Depressions AND Students, Nursing [mh] OR Pupil Nurses; Student, Nursing; Nurses, Pupil; Nurse, Pupil; Pupil Nurse; Nursing Student; Nursing Students AND Study OR Intervention OR Experiment OR Research. In addition, manual searches were conducted for cited references in relevant papers if appropriate. Missing relevant articles were obtained by contacting authors. Grey literature was also retrieved.

2.2. Study selection

Studies were eligible for inclusion if they met the following criteria: (1) Participants: nursing students or allied health care students (including nursing students); (2) Interventions: nursing students received nonpharmacological interventions; (3) Comparisons: The participants in the control group received usual care or waiting-list condition; (4) Outcomes: depressive symptoms or depression were assessed; and (5) Study designs: RCTs and CCTs. The exclusion criteria for the review were as follows: (1) studies were reviews of the literature; (2) participants were not nursing students; (3) the intervention methods in the studies were pharmacological interventions; (4) studies did not report depressive symptoms and depression; or (5) reports were qualitative studies.

Papers from the electronic databases were downloaded into Endnote X8.2. After eliminating duplicate studies, two reviewers independently screened the titles and abstracts of all potentially relevant studies. We ultimately identified the papers that met the previously described eligibility criteria and obtained the full text of these articles for this systematic review and meta-analysis. Discussion was used to resolve differences in selection.

2.3. Data extraction

The data were independently extracted using a standardized extraction form. It included sample characteristics, first author's name, year of publication, geographical location, study design, number of experimental and control groups, intervention methods, intervention length, follow-ups, control, measurement tools, and outcomes (Table 1). Two reviewers independently abstracted the data from every included study, and inconsistencies were discussed with a third reviewer. The corresponding author of an included study was contacted if additional information was required.

2.4. Quality assessment and methodological assessment

The methodological quality of all studies was measured using the Quality Assessment Tool for Quantitative Studies (Table 2), developed by the Effective Public Health Practice Project, Canada. This tool can be used for RCTs, quasi-experimental studies and uncontrolled studies. The content and construct validity have been established [41]. Two reviewers independently assessed the quality of all included studies. Studies were assessed via six criteria: selection bias, study design, confounders, blinding, data collection methods, and withdrawals and drop-out. And the quality rating for included studies was "strong", "moderate" or "weak". If two reviewers had disagreements, a third author was available for assessment.

Table 1
Study characteristics of the included studies.

Author, year	Country	Study Design	Sample Size	Age	Gender	Year of Study	Intervention Methods	Intervention length	Follow-ups	Control	Measurement of Outcomes	Outcomes
C. J. Chen, (2015)	China	RCT	E = 31 C = 40	E = 18.5 C = 18.6	Female = 69 Male = 2	NR	Chinese five-element music therapy	10-week	Baseline, right after intervention	Usual care	DMSRIA	Depression(+)
Chen, Yang, (2013)	China	RCT	E = 30 C = 30	19.5 ± 0.87	Female = 52 Male = 8	NR	Brief mindfulness meditation	1-week	Baseline, right after intervention	Usual care	CV-SDS	Depression(-)
Godbey, K. L (1994)	America	CCT	E = 7 C = 12	E = 29.9 C = 23.1	Female = 19 Male = 0	Junior and senior years	Stress-management program	6-week	Baseline, right after intervention, graduation	Usual care	GCS	Depression(-)
Guo et al. (2016)	China	RCT	E = 34 C = 42	20.39 ± 1.20	Female = 72 Male = 4	1st = 22 2nd = 27 3rd = 20 4th = 7	Positive psychotherapy	8-week	Baseline, right after intervention, 3 month, 6 month	Usual care	BDI-II	Depression(+)
Hughe (2003)	Australia	RCT	E = 43 C = 38	24 ± 6.31	NR	Junior students	Informal peer group experience	One semester	Baseline, one semester, two semesters	Usual care	CESDS	Depression(-)
Johansson (1991a)	America	RCT	E = 21 C = 21	22	Female = 42 Male = 0	2nd = 42	A stress management program	3-week	Baseline, right after intervention	Waiting-list condition	IPATDS	Depression(+)
Johansson (1991b)	America	RCT	E = 17 C = 17	22	Female = 34 Male = 0	> 2nd = 34	A stress management program	3-week	Baseline, right after intervention	Waiting-list condition	IPATDS	Depression(+)
Kang, Choi (2009)	Korea	RCT	E = 16 C = 16	E = 22.69 ± 1.49 C = 22.25 ± 0.86	Female = 32 Male = 0	NR	Stress coping program based on mindfulness	2-month	Baseline, right after intervention	Usual care	BDI	Depression(-)
Qiu, M Eng (2017)	China	RCT	E = 244 C = 244	E = 21.78 ± 0.82 C = 21.66 ± 0.87	NR	3rd = 488	Mindfulness intervention	5-week	Baseline, right after intervention	Usual care	SCL-90	Depression(+)
Ratanasiripong, Paul (2015)	Thailand	RCT	E = 30 C = 30	34.05 ± 7.61	Female = 58 Male = 2	1st = 27 2nd = 13 3rd = 10 4th = 6 5th = 4	Biofeedback intervention	4-week	Baseline, right after intervention	Usual care	CESDS	Depression(-)
Song & Lindquist (2015)	Korean	RCT	E = 21 C = 23	E = 19.6 ± 1.7 C = 19.5 ± 2.0	Female = 36 Male = 8	NR	MBSR	8-week	Baseline, right after intervention	Waiting-list condition	DASS-21	Depression(+)
Yazdani, Mohsen (2014)	Isfahan	CCT	E = 19 C = 19	NR	Female = 0 Male = 38	NR	laughter Yoga	4-week	Baseline, right after intervention, one month	Usual care	GHQ	Depression(+)
Yazdani, Mohsen (2010)	Isfahan	CCT	E = 38 C = 38	20.9 ± 1.3	Female = 43 Male = 33	NR	Stress management training program	4-week	Baseline, right after intervention, one month	Usual care	DASS-42	Depression(+)
Yoon, H. S (2011)	Korea	CCT	E = 31 C = 33	19–29	NR	NR	Interpersonal relationship program	10-week	Baseline, right after intervention	Waiting-list condition	KV-CESDS	Depression(-)

Abbreviations: BDI-II: Beck Depression Inventory-II; BDI: Beck depression inventory; C: control group; CVSDS: Chinese Version of the Self-Rating Depression Scale; CESDS: Chinese Version of the Self-Rating Depression Scale; CESDS: Center for Epidemiological Study-Depression Scale; DASS-21: Depression, Anxiety and Stress Scale-21; DASS-42: Depression, Anxiety and Stress Scale-42; DMSRIA: Depression Mood Self-Report Inventory for Adolescence; GCS: Generalized Contentment Scale; GHQ: General Health Questionnaire; IPATDS: Institute for Personality and Ability Testing Depression Scale; KV-CESDS: Korean Version of the Center for Epidemiological Study Depression Scale; MBSR: Mindfulness-based stress reduction; NR: not reported; SCL-90: Symptom Checklist 90.

Table 2
Assessment for the methodological quality of the included studies.

Author, Year	Selection Bias	Study Design	Confounders	Blinding	Data Collection	Withdrawals	Global Rating
C. J. Chen, (2015)	Strong	Strong	Strong	Weak	Strong	Moderate	Moderate
Chen, Yang, (2013)	Strong	Strong	Strong	Weak	Strong	Strong	Moderate
Godbey, K. L (1994)	Moderate	Strong	Weak	Moderate	Strong	Moderate	Moderate
Guo et al. (2016)	Strong	Strong	Strong	Weak	Strong	Strong	Moderate
Hughe (2003)	Strong	Strong	Strong	Weak	Strong	Moderate	Moderate
Johansson (1991a)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Johansson (1991b)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Kang, Choi (2009)	Strong	Strong	Weak	Moderate	Strong	Moderate	Moderate
Qiu, M Eng (2017)	Strong	Strong	Strong	Weak	Strong	Strong	Moderate
Ratanasiripong, Paul (2015)	Strong	Strong	Strong	Weak	Strong	Strong	Moderate
Song & Lindquist (2015)	Strong	Strong	Strong	Weak	Strong	Strong	Moderate
Yazdani, Mohsen (2014)	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
Yazdani, Mohsen (2010)	Moderate	Strong	Strong	Moderate	Weak	Strong	Moderate
Yoon, H. S (2011)	Strong	Strong	Strong	Weak	Strong	Strong	Moderate

2.5. Statistical analysis

The outcome scores of the preintervention and postintervention were extracted from the included studies. Rev Man 5.3 software (The Nordic Cochrane Center, The Cochrane Collaboration) was used to quantify the outcomes of the nonpharmacological interventions. The reported means, sample sizes, and standard deviations of the mean were inputted in Rev Man 5.3. Significance was defined as $p < 0.05$. Given that the outcomes of interest were assessed with different scales and units, standardized mean differences (SMD) were used for the effect size calculation. SMD were interpreted per Cohen's definitions: 0.2 to 0.5 is defined as a small effect, 0.5 to 0.8 is a moderate effect, and > 0.8 is a large effect [42].

Tests of heterogeneity were used to decide which method would be used to obtain the pooled results. The I^2 values indicate low (25%), moderate (50%) or high (75%) heterogeneity [43]. Most results of the meta-analysis had high heterogeneity ($> 50\%$) in this review; thus, the random-effects model was considered. Random-effect model attempted to generalize findings beyond the included studies by assuming that the selected studies are random samples from a larger population [44].

Publication bias was examined using Egger's test. Furthermore, given that different intervention methods and different intervention lengths have different effects on depression [39,45], and different population types experienced different prevalence of depression [13], we should quantify the relative effectiveness of the intervention methods, intervention lengths and interventions among different population types to provide more specific evidence and guidance for healthcare professionals. In order to also explore the impacts of methodological qualities on depression, therefore, we performed subgroup analyses of the intervention methods, intervention lengths, population types and methodological qualities. To test the stability of our primary meta-analysis, we conducted sensitivity analyses to determine whether choosing later follow-up time points would generate different results. And we performed a sensitivity analysis to parse out the origins of this heterogeneity.

3. Results

3.1. Study characteristics and characteristics

The selection process is summarized in Fig. 1. First, 837 articles were retrieved from English and Chinese databases. Excluding 230 duplicate documents, 607 articles were included and screened for further assessment. As shown in Figs. 1 and 13 studies met the inclusion criteria and were included for systematic review and meta-analysis [15,46–57].

Thirteen articles were included in this review. Table 1 summarizes the characteristics of the included studies. In particular, Johansson

study [49] included two different experimental subjects and they were sophomore and senior nursing students respectively; thus, we entered the information into Table 1 twice. A total of 1185 nursing students were included in this study. In the 13 studies, the types of interventions included mindfulness interventions ($n = 4$) [46,50,51,53], stress management programs ($n = 3$) [47,49,55], a biofeedback intervention ($n = 1$) [52], an informal peer group experience ($n = 1$) [57], a laughter yoga ($n = 1$) [54], a Chinese five-element music therapy ($n = 1$) [15], a positive psychotherapy ($n = 1$) [48] and an interpersonal relationship program ($n = 1$) [56]. Among these studies, mindfulness interventions and stress management programs were the most common.

Nine studies were RCTs, and the remaining four studies were CCTs. Most of nursing students were female and aged between 18 and 24. And the included studies covered all grades. All interventions were structured and time-limited. The lengths of the interventions were divided into short-term (1–8 weeks) and long-term (> 8 weeks) according to the study by Kral et al. [58]. Ten studies used short-term interventions, and the other studies used long-term interventions. However, only five studies had more than one follow-up time point [47,48,54,55,57]. Moreover, of the 13 included studies, 4 studies were conducted in China, 3 studies were conducted in Korea, 2 studies were conducted in the USA, 2 studies were conducted in Isfahan, 1 study was conducted in Thailand, and 1 study was conducted in Australia. Depressive symptoms and depression scores were measured using standardized questionnaires. These measurement tools included Beck Depression Inventory-II (BDI-II), Beck depression inventory (BDI), Chinese Version of the Self-Rating Depression Scale (CVSDS), Center for Epidemiological Study-Depression Scale (CESDS), Depression, Anxiety and Stress Scale-21 (DASS-21), Depression, Anxiety and Stress Scale-42 (DASS-42), Depression Mood Self-Report Inventory for Adolescence (DMSRIA), Generalized Contentment Scale (GCS), General Health Questionnaire (GHQ), Institute for Personality and Ability Testing Depression Scale (IPATDS), Symptom Checklist 90(SCL-90)and Korean Version of the Center for Epidemiological Study Depression Scale (KV-CESDS).

3.2. Quality appraisal

Of the thirteen studies, only three studies were assessed to have a high methodological quality (Table 2). The absent of bindings lowered the level of the methodological quality in most studies. However, most interventions were conducted by psychologists, and the studies could not be blind to the participants or assessors, which reduced the quality of the included studies. Overall, most of the studies had a medium methodological quality.

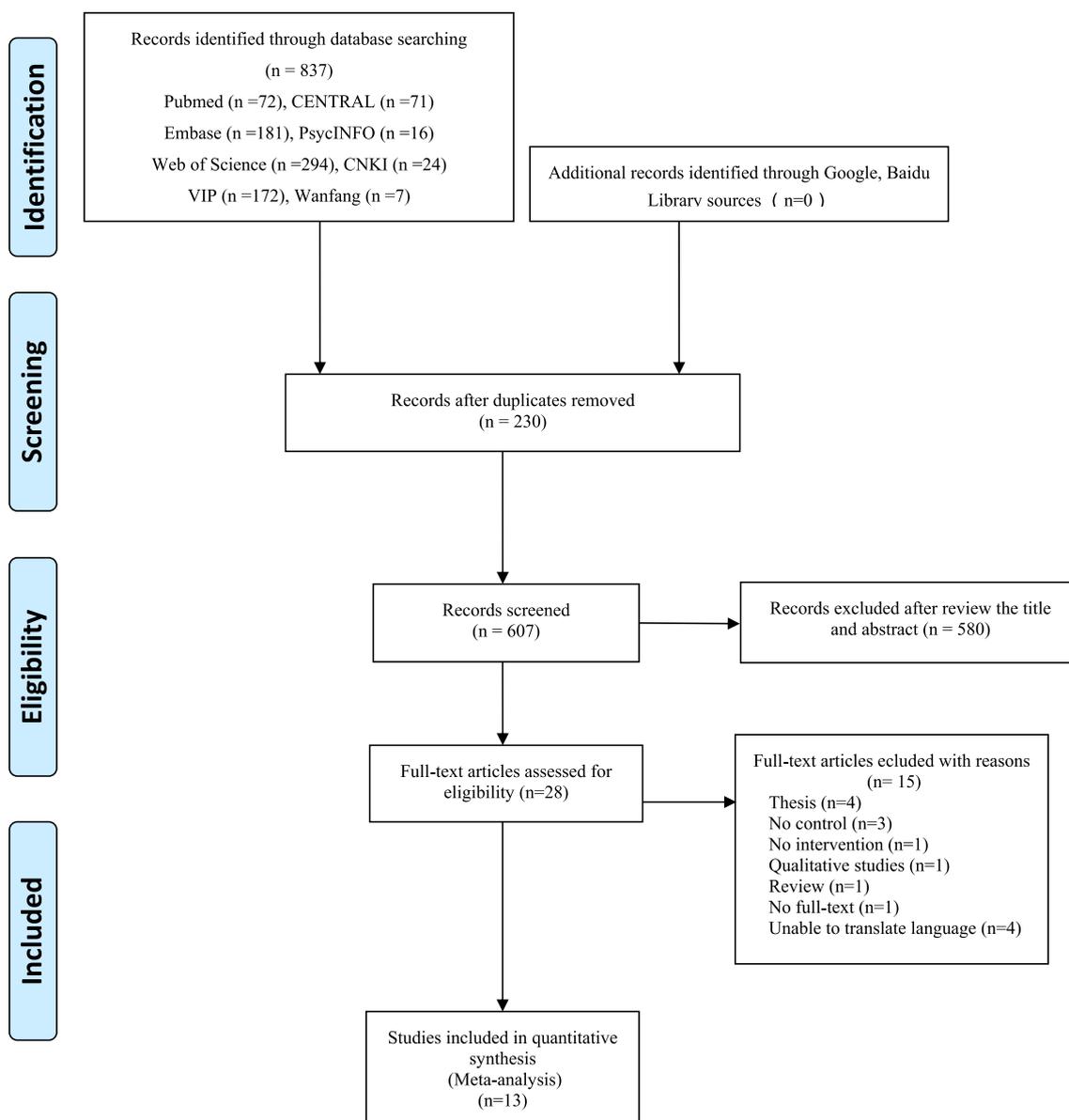


Fig. 1. Flow chart of article selection process.

4. Effectiveness of nonpharmacological interventions on depressive symptoms and depression in nursing students

4.1. Baseline comparison and publication bias

Across the 13 trials, there were no significant differences in the depressive symptoms and depression between the experimental and control groups prior to the nonpharmacological interventions (SMD = 0.08, 95% CI (−0.04 to 0.19), $p = 0.17$; Fig. 2). To assess for publication bias, Egger's test was conducted, which showed that publication bias did not exist ($p > 0.05$).

4.2. Primary outcome - depressive symptoms and depression

All 13 included studies chose depressive symptoms and depression as outcomes. The postintervention depressive symptoms and depression scores were lower in the experiment group than in the control group (SMD = −0.67, 95% CI (−1.00 to −0.33), $p < 0.01$; Fig. 3), with a moderate effect size across studies.

4.3. Subgroup of depressive symptoms and depression

4.3.1. Influence of intervention methods

Among these nonpharmacological interventions, four studies reported that mindfulness interventions had small positive effects on depressive symptoms and depression postintervention compared with the control group (SMD = −0.39, 95% CI (−0.68 to 0.09), $p < 0.01$; Fig. 4). Moreover, four studies presented that stress management programs also had small positive effects on depressive symptoms and depression postintervention compared with the control group (SMD = −0.48, 95% CI (−0.85 to 0.11), $p = 0.01$; Fig. 4). Positive psychotherapy (SMD = −2.45, 95% CI (−3.06 to −1.85), $p < 0.01$) and Chinese five-element music therapy (SMD = −1.89, 95% CI (−2.45 to −1.32), $p < 0.01$) had larger effect size than other intervention methods.

4.3.2. Influence of intervention lengths

Short-term (1–8 weeks) and long-term (> 8 weeks) interventions were compared. Significant improvements in depressive symptoms and depression scores were observed in short-term (1–8 weeks)

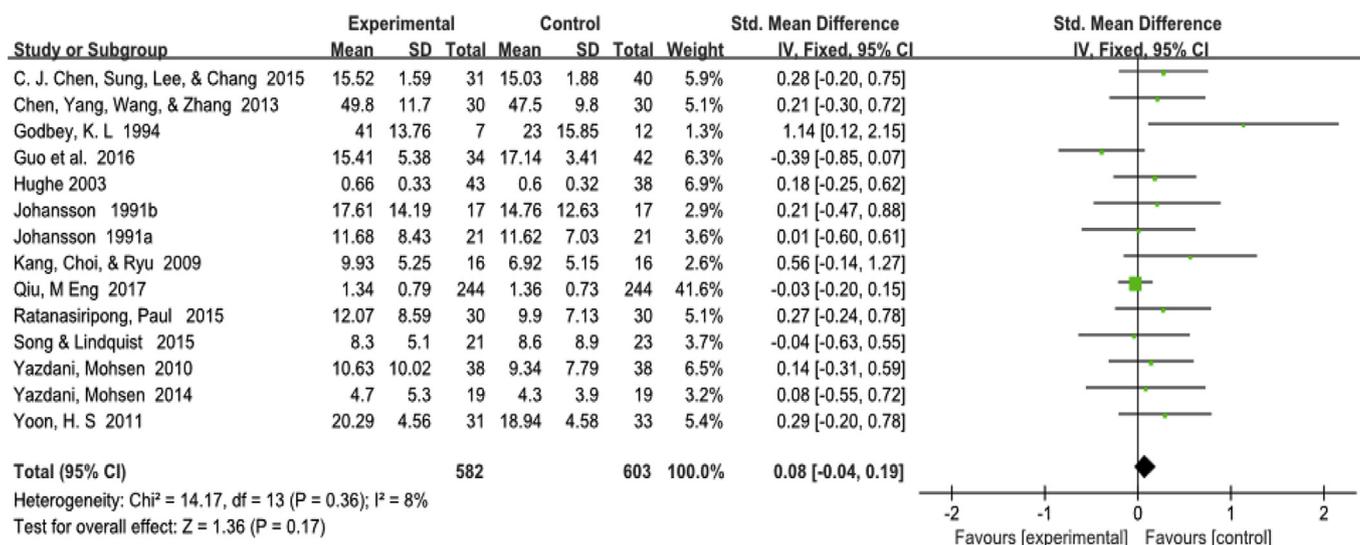


Fig. 2. Forest plot for pre-intervention differences between experimental and control groups.

interventions and not in long-term (> 8 weeks) interventions. The subgroup analysis showed that short-term nonpharmacological interventions (SMD = -0.63, 95% CI (-1.00 to 0.27), $p < 0.01$) had moderate effect size and long-term interventions had no significant differences in depression (SMD = -0.77, 95% CI (-1.55 to 0.01), $p = 0.05$) (Fig. 5).

4.3.3. Influence of population types

In the 13 included studies, 4 studies were conducted in China, 3 studies were conducted in Korea, 2 studies were conducted in the USA, 2 studies were conducted in Isfahan, 1 study was conducted in Thailand, and 1 study was conducted in Australia. Therefore, we aimed to determine whether the intervention effects on depressive symptoms and depression differed among nursing students from different countries. Significant improvements in depressive symptoms and depression scores were identified (Fig. 6). The subgroup analysis showed that nonpharmacological interventions had a large effect size for Chinese nursing students (SMD = -1.14, 95% CI (-2.17 to 0.12), $p = 0.03$), moderate effects size for Korean (SMD = -0.57, 95% CI (-0.91 to

0.23), $p < 0.01$) and Isfahan nursing students (SMD = -0.72, 95% CI (-1.26 to 0.19), $p < 0.01$); however, no significant improvements were seen for interventions in North American (SMD = -0.43, 95% CI (-1.04 to 0.17), $p = 0.16$), Australian (SMD = -0.11, 95% CI (-0.55 to 0.33), $p = 0.62$) and Thai (SMD = -0.15, 95% CI (-0.66 to 0.35), $p = 0.55$) nursing students.

4.3.4. Influence of methodological quality

In our review, 3 studies had high methodological qualities, and the remaining studies presented moderate qualities. Significant improvements in depressive symptoms and depression scores were observed in high methodological quality studies and moderate quality studies. The subgroup analysis showed that high quality researches has greater effects on depression (SMD = -0.82, 95% CI (-1.20 to 0.43), $p < 0.01$) than moderate quality studies (SMD = -0.63, 95% CI (-1.03 to 0.23), $p < 0.01$); however, we found that depression outcome did not differ significantly among studies with different methodological qualities ($p = 0.50$) (Fig. 7).

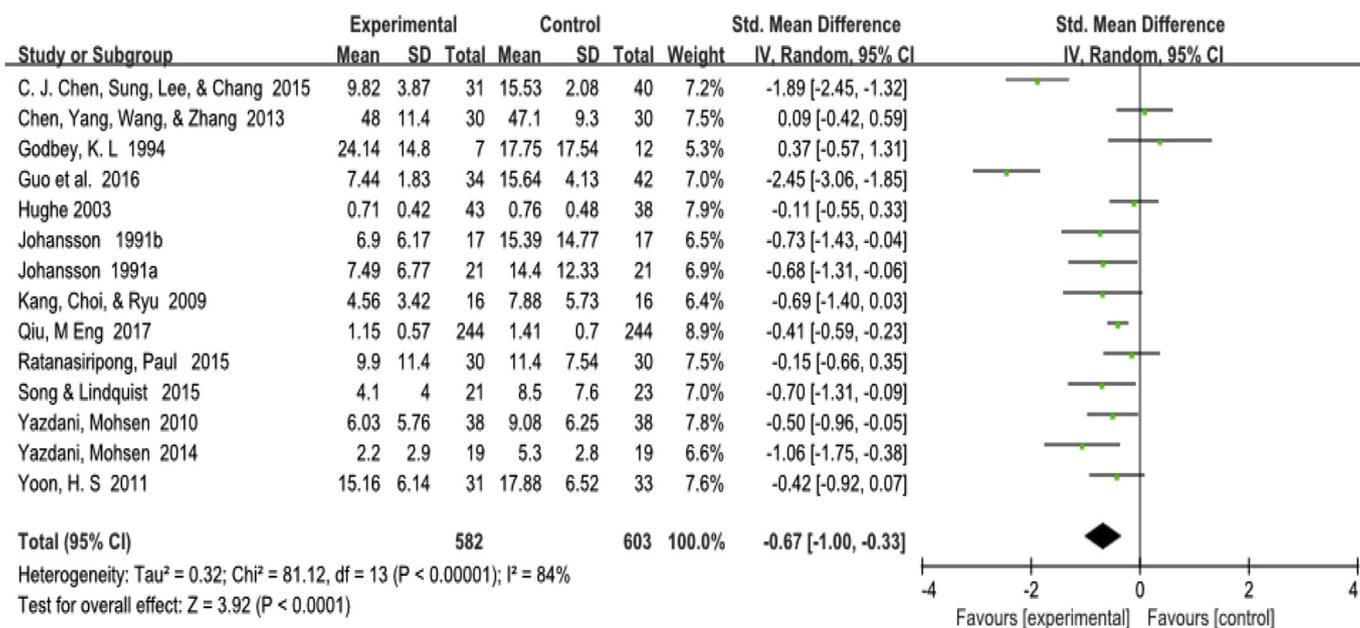


Fig. 3. Forest plot for effect of interventions on depression, post-intervention. Abbreviations: 95% CI: 95% confidence interval; SD: standard deviation.

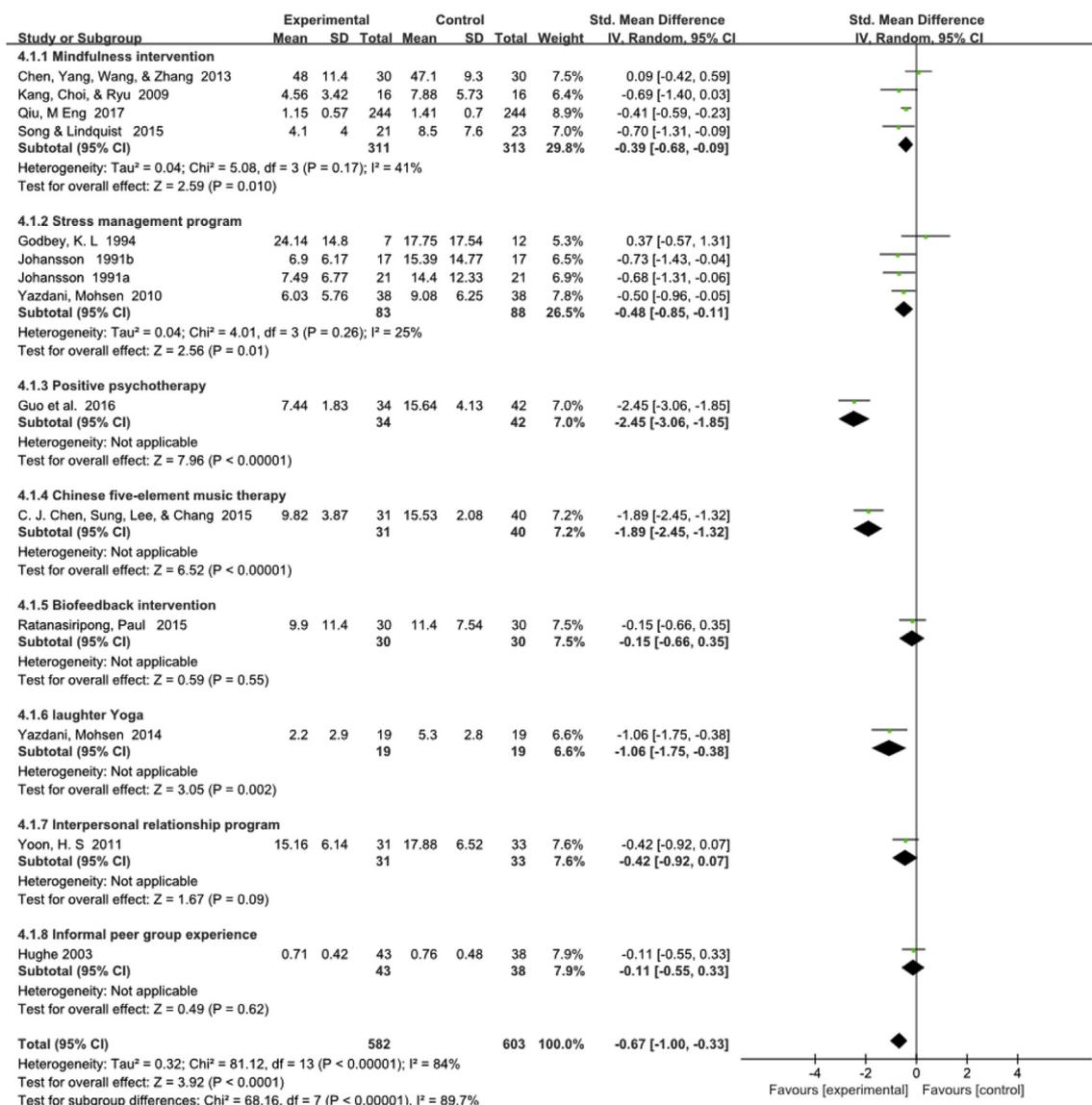


Fig. 4. Forest plot for effect of intervention types on depression, post-intervention. Abbreviations: 95%CI: 95% confidence interval; SD: standard deviation.

4.4. Sensitivity analysis

Five studies [47,48,54,55,57] had more than one follow-up time point. We conducted a sensitivity analysis to determine whether the selection of later follow-up time points of outcome would generate different findings. Our study showed that the selection of different follow-up time points had no impact on the results, which indicates the meta-analysis results are stable (SMD = -0.83, 95% CI = (-1.28 to -0.38), p < 0.01; Fig. 8). In addition, another sensitivity analysis was conducted to explore the origin of heterogeneity (I² = 84%; Fig. 3). Because of higher levels of depression at baseline among nursing students [15,48], two articles were removed. The findings showed the heterogeneity of the studies clearly decreased (SMD = -0.40, 95% CI = (-0.52 to -0.27), I² = 30%, p < 0.01; Fig. 9), which suggests the two studies may be the origins of the heterogeneity.

5. Discussion

Compared with previous reviews [38,39], our study conducted a more rigorous methodological investigation and more detailed discussion on depression to provide more specific information for health professionals. First, 13 studies with 1185 nursing students met the

inclusion criteria, including RCTs and CCTs, which are good standards for evidence-based clinical research. Second, we performed subgroup analyses to carefully investigate the effects of intervention types and intervention lengths, and compare the effects of interventions among different population types. Moreover, we conducted baseline comparison, publication bias and sensitivity analyses to ensure the accuracy and stability of the intervention results.

This systematic review and meta-analysis demonstrated that non-pharmacological interventions had moderate beneficial effects on depressive symptoms and depression compared with standard care in nursing students. Moreover, mindfulness interventions and stress management programs were common and had small positive effects on depressive symptoms and depression. Furthermore, short-term (1–8 weeks) nonpharmacological interventions moderately relieved depressive symptoms and depression, and nonpharmacological interventions had positive effects for Chinese, Korean, and Isfahan’ nursing students.

The present review suggested that nonpharmacological interventions investigated to date may be valid approaches to relieve depressive symptoms and depression in nursing students, which supported Li et al.’s study [39]. In addition, among different nonpharmacological therapies, we found that mindfulness interventions were common and focused on teaching nursing students the cognitive exercises of

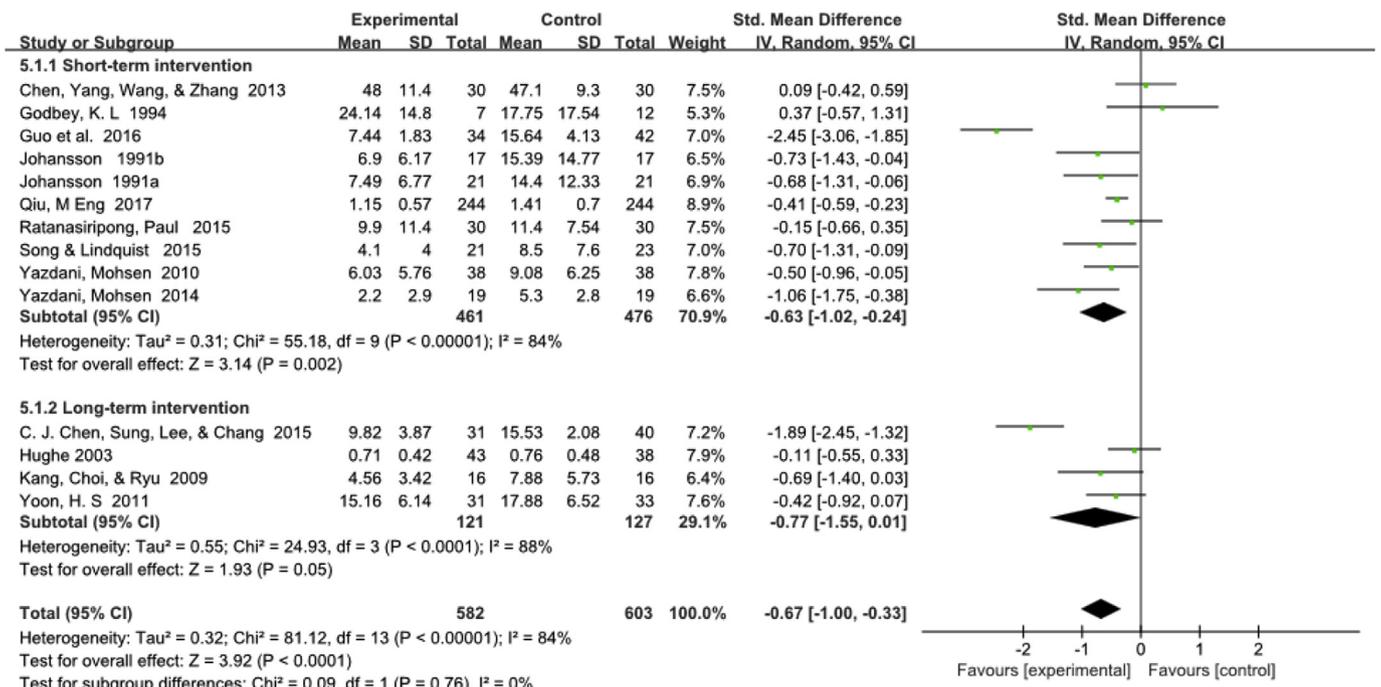


Fig. 5. Forest plot for effect of intervention lengths on depression, post-intervention. Abbreviations: 95%CI: 95% confidence interval; SD: standard deviation.

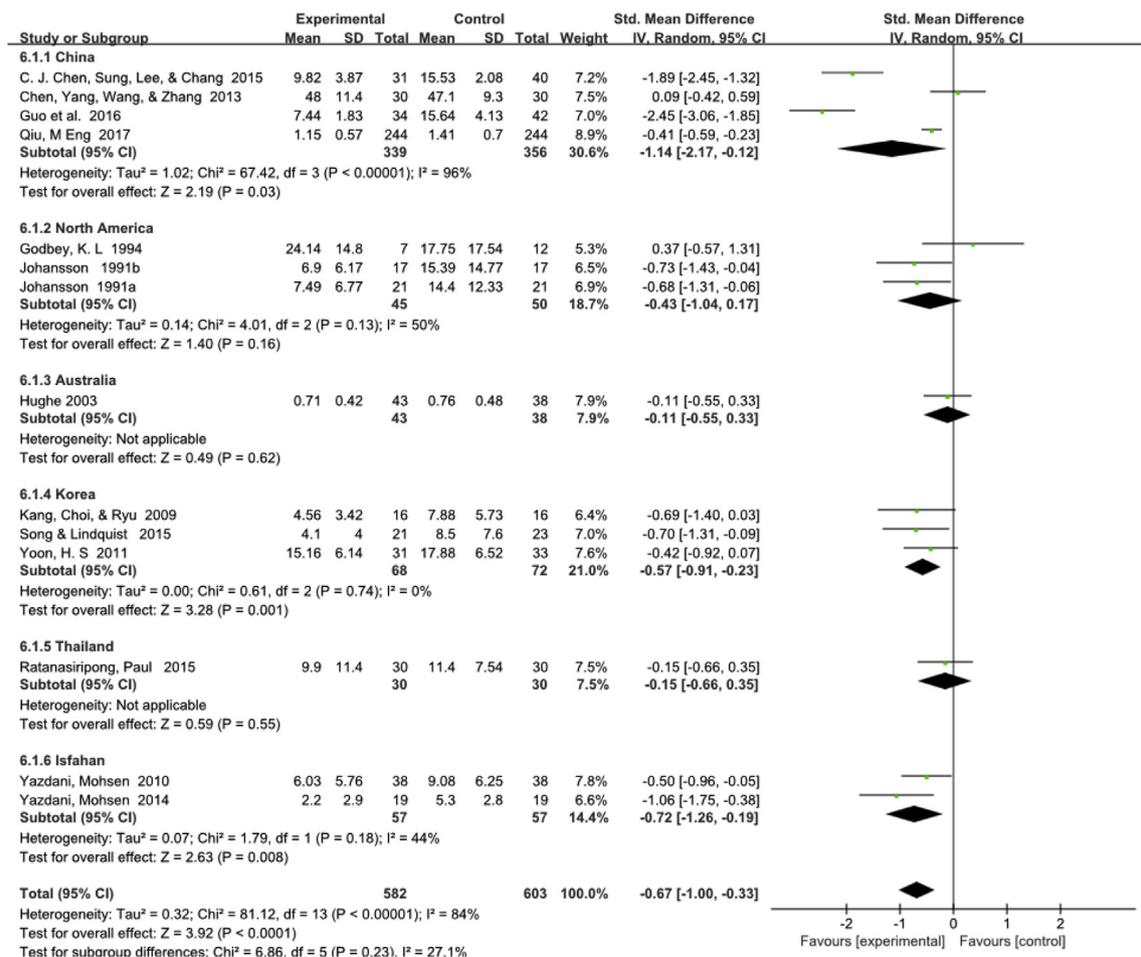


Fig. 6. Forest plot for effect of interventions on depression in different population types, post-intervention. Abbreviations: 95%CI: 95% confidence interval; SD: standard deviation.

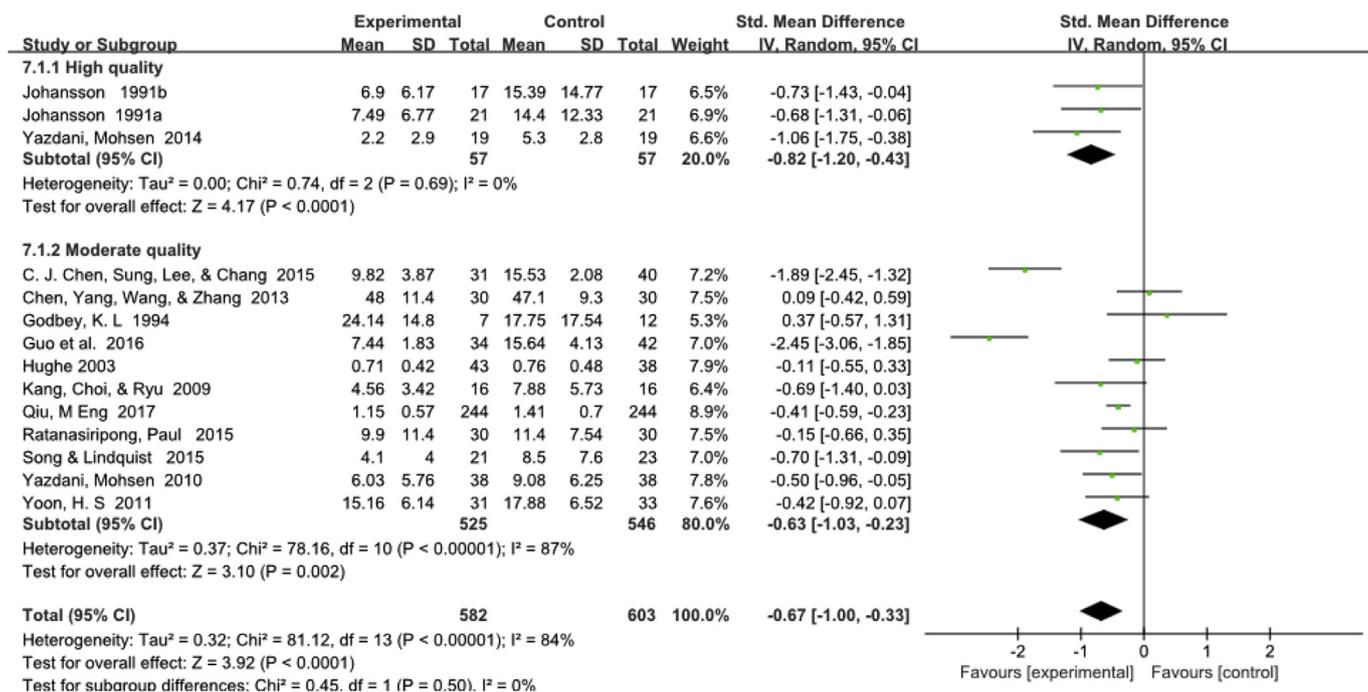


Fig. 7. Forest plot for effect of interventions on depression in different methodological quality, post-intervention. Abbreviations: 95%CI: 95% confidence interval; SD: standard deviation.

mindfulness meditation [46]; moreover, nursing students were typically given a body scan, sitting meditation and Hatha yoga practice [46,51,53]. After receiving mindfulness trainings, the depressive symptoms and depression of nursing students were alleviated. Our finding was consistent with another study [38], which indicated that mindfulness interventions had beneficial impacts on nursing students' depression. In addition, one study suggested that mindfulness interventions were effective to prevent depression relapse [36]. Furthermore, mindfulness meditation was more efficacious than physical exercise in the management of depression in nursing students [12]. Therefore, mindfulness interventions could be regarded as protective therapeutics in the reduction of depression [59,60]. Considering other benefits of mindfulness interventions for anxiety and stress among nursing students [53], health professionals could adopt mindfulness interventions to relieve their depressive symptoms and depression or other psychological outcomes. Moreover, one study recommended that mindfulness programs should be introduced early in the first year of a Bachelor of Nursing curriculum program [38]. As a result, nursing

students could adjust their mental health status by learning mindfulness skills.

As previously demonstrated, stress easily leads to depression [61]. Stress management programs were often used as strategies to improve depressive symptoms and depression [47,49,55]. Stress management practices included breathing exercises, yoga relaxation, progressive muscle relaxation, meditation and mental images [62]. Our study also suggested that stress management programs serve as effective and convenient complementary therapies for depressive symptoms and depression in nursing students, which was in line with the suggested benefits of stress management programs in depression in another trial [63]. Therefore, stress management programs are worth being recommended for nursing students.

These nonpharmacological interventions may provide benefits in reducing depressive symptoms and depression. Positive psychotherapy and Chinese five-element music therapy were the most effective interventions for improving depressive symptoms and depression; however, there is a relative lack of literature regarding Chinese five-element

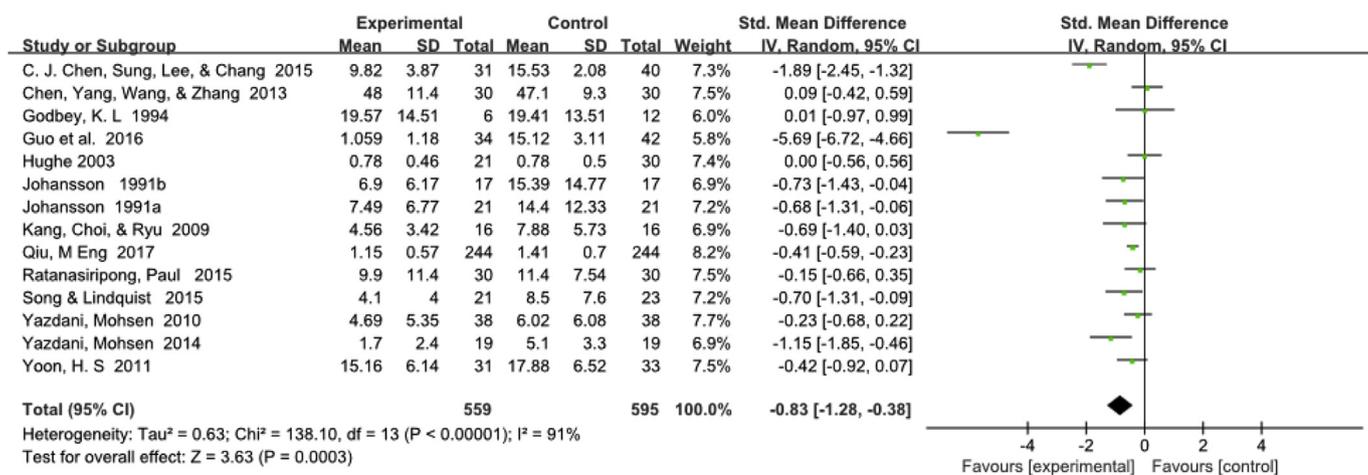


Fig. 8. Forest plot for effect of choosing later post-assessment time points on depression. Abbreviations: 95%CI: 95% confidence interval; SD: standard deviation.

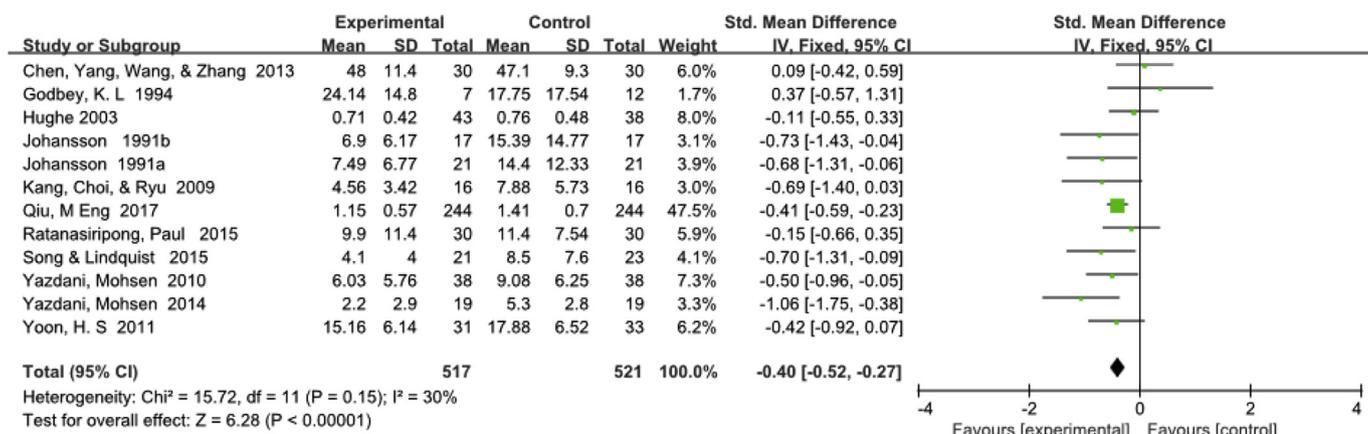


Fig. 9. Forest plot for effect of interventions except from positive psychotherapy and Chinese five-element music therapy on depression. Abbreviations: 95% CI: 95% confidence interval; SD: standard deviation.

music therapy, positive psychotherapy, biofeedback interventions, laughter Yoga, interpersonal relationship programs, and informal peer group experience. Thus, a meta-analysis of the effectiveness of different intervention types on outcomes of depressive symptoms and depression should be taken with caution, and their actual implementation results require additional trials for further verification. Furthermore, Cognitive behavioral therapy (CBT) has been confirmed as a promising approach for depression [25] because it can reduce maladaptive rumination which perpetuates depression [64]. The National Institute for Health and Clinical Excellence [65] proposes that individuals with depression should receive a combination of antidepressants and CBT, and future studies could consider applying antidepressants and CBT to regulate the depression of nursing students.

However, our subgroup analyses indicated that depression benefits from short-term (1–8 weeks) interventions, which was consistent with D et al. [45]. A possible explanation behind this phenomenon is that depression tends to relapse [66]. Inconsistent with previous studies [45], improvement was not observed from long-term (> 8 weeks) interventions. This may be because long-term (> 8 weeks) interventions may prevent patient compliance. However, due to limited data, our finding should be considered with caution. Our review also suggested that nonpharmacological interventions had larger effect sizes for Chinese nursing students, Korean nursing students and Isfahan's nursing students than for nursing students in North America and Australia. Although the reasons are multi-factorial, cultural backgrounds could not be ignored. Due to the values of hard work and filial piety inculcated by Confucian Heritage Culture (CHC) in Asian countries, such as China and Korea, education is highly emphasized. Academic achievement is seen as a way to earn money, enter famous schools and ultimately establish an excellent career [67]. In addition, for China, students had a greater sense of responsibility for their parents compared to their counterparts from Western cultures, and attributed their stronger achievement motivation to their parents' reaction to failure [68], which made them study harder. One study showed the students in China worked harder and experienced more exam anxiety than students in the West who had less academic stress [69], which easily lead to depression [61]. This phenomenon also applies to Asian medical students in which 12.9% suffered from depression [70]. Academic stress predicted medical lethality of suicide attempts in young Asians with depression [71]. Moreover, students tend to be expected by parents and teachers to achieve excellent academic performances and obtain and maintain good academic performances [72]. These meanings of hard work, sense of obligation and high expectation put tremendous anxiety and pressure on students, which easily lead to depression [61]. In contrast, western countries focus on the developments of students' personalities and capacities, and do not emphasize academic

achievements as much as in Asia. Therefore, the level of depression may be higher in Asian nursing students than in North American and Australian nursing students, and the effects of the intervention can be more easily observed. For this reason, nonpharmacological interventions may have greater improvements effects among Asian nursing students. However, due to the limited number of included studies in North American and Australian nursing students, future research is required to confirm this finding. In addition, considering that high quality researches had greater impacts on depression, we recommended more rigorous methodological studies in this field.

Our study indicated a variety of promising nonpharmacological intervention methods, and future studies should pay particular attention to performing a direct comparison of different nonpharmacological intervention approaches on depressive symptoms and depression among students by more relevant researches. Moreover, there is limited knowledge regarding the mechanism of how nonpharmacological interventions work, and further studies are strongly encouraged to carry out in this field. To provide evidence-based information, future studies should consider prospective study designs to assess the same individuals over time.

5.1. Strengths and limitations of this review

To our knowledge, our study is the first investigation that is based on all RCTs and CCTs regarding the effects of nonpharmacological interventions on depressive symptoms and depression among nursing students. Second, assessing depressive symptoms and depression before the start of interventions ensures the precise understanding of the intervention's effectiveness because we know that depressive symptoms and depression outcomes are due to the intervention rather than baseline variations. Moreover, we use formal statistical tests (e.g., Egger's test) to assess for publication bias. Third, three subgroup analyses are conducted to parse out the effects of intervention methods, intervention lengths and interventions in different population types. Finally, sensitivity analyses are performed to test the stability of the results and explore the origins of the heterogeneity.

Due to the methodological limitations of the included studies, we were unable to identify which intervention method is more preferable. The review only included studies published in English and Chinese; thus, relevant studies might have been missed. Additional high-quality studies should be included in the future. In addition, of the 13 studies, only five studies had outcome assessment time points beyond the immediate postintervention termination [47,48,54,55,57], which limit the ability of patients and health professionals to fully understand the long-term effects of these nonpharmacological interventions. Further studies are needed to examine the long-term effects of nonpharmacological

interventions on depressive symptoms and depression. This study did not explore other factors which could be potential confounders including year of study [73], the relationship between ethnicity, gender and suicide [74,75] and other outcome measures including quality of life [76]. Further study is required to explore the effect of other forms of psychotherapy such as schema therapy on nursing students [77]. Finally, the majority of the studies were conducted in the Asia, and the generalization of the study results should be considered with caution. Therefore, additional studies must be conducted on larger sample sizes in more areas.

5.2. Implications for practice

Nursing students were reserve force of nursing profession development. Their mental health statuses were not only related to their academic performance, retention and graduation, but also have important significances for patient safety, patient care, and professionalism after entering the workforce. In addition, the goal of higher education also requires nursing undergraduates to have good psychological qualities. In order to alleviate depressive symptoms and depression of nursing students, our study has provided evidence that nonpharmacological interventions are beneficial to the reduction of depression among nursing students. To obtain a high rate of improvements, mindfulness interventions, stress management programs and short-term (1–8 weeks) interventions are recommended. For health professionals, these non-pharmacological interventions should also be considered as alternative approaches with moderate positive effects and low costs to improve depressive symptoms and depression of nursing students. In view of the high incidence of depression among nursing students, for college counselors, educators, and family members who have close contact with the students, they should pay attention to mental health status of nursing students. Understanding the symptom performances of depression in nursing students is essential. When students experience depressive symptoms and depression, we should encourage students to actively treat depression. In addition to pharmacological interventions, nonpharmacological interventions could be also considered to relieve depression without side effects. As university students have positive perception of educational smartphone applications [78], smartphone applications can provide health information including depression [79] and delivers cognitive behavior therapy [80].

6. Conclusion

The present study suggested that nonpharmacological interventions had moderate positive effects on depressive symptoms and depression. Our studies indicated that mindfulness interventions and stress management programs were common and effective at improving depressive symptoms and depression. Moreover, a short-term (1–8 weeks) intervention length and researches with high methodological quality are recommended, and nonpharmacological interventions have greater improvement for nursing students in Asia. In the future, we should pay particular attention to determining which intervention types are most effective with more rigorous methodological studies. Overall, non-pharmacological interventions can be acceptable and promising adjunctive therapies for relieving depressive symptoms and depression.

Authorship statement

The authors contributed equally to the development of this paper. Wei Zhang and Dandan Chen were contributed to concepts, data collection, data extraction, and writing manuscript. Weijia Sun, Na Liu, and Jie Wang were contributed to data extraction, data analysis, and manuscript development. All authors have reviewed and are in agreement with the final version of this manuscript.

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References

- [1] T. WW, et al., Prevalence of depression in the community from 30 countries between 1994 and 2014. *Lim GY, Sci. Rep.* 8 (1) (2018) 2861–2810.
- [2] K. Peltzer, S. Yi, S. Pengpid, Suicidal behaviors and associated factors among university students in six countries in the Association of Southeast Asian Nations (ASEAN), *Asian Journal of Psychiatry* 26 (2017) 32–38.
- [3] M. Piccinelli, W. G. Gender differences in depression: critical review, *Br. J. Psychiatry* 177 (6) (2000) 486–492.
- [4] W.H. Organization, *Health in 2015: from MDGs to SDGs*, (2015).
- [5] S.V.D. Velde, P. Bracke, K. Levecque, Gender differences in depression in 23 European countries. Cross-national variation in the gender gap in depression, *Soc. Sci. Med.* 71 (2) (2010) 305–313.
- [6] W.H. Organization, *Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks*, (2009), pp. 1–63.
- [7] C.J. Murray, A.D. Lopez, Alternative projections of mortality and disability by cause 1990–2020: global burden of disease study, *Lancet* 349 (9064) (1997) 1498–1504.
- [8] R.C.M. Ho, et al., The effect of severity of depressive disorder on economic burden in a university hospital in Singapore, *Expert Rev. Pharmacoecon. Outcomes Res.* 13 (4) (2013) 549–559.
- [9] A. Aradilla-Herrero, J. Tomás-Sábado, J. Gómez-Benito, Associations between emotional intelligence, depression and suicide risk in nursing students, *Nurse Educ. Today* 34 (4) (2014) 520–525.
- [10] A.P. Fan, et al., Suicidal ideation in medical students: who is at risk? *Ann. Acad. Med. Singapore* 41 (9) (2012) 377–382.
- [11] C. Melissa-Halikiopoulou, et al., Suicidality and depressive symptoms among nursing students in northern Greece, *Health Sci. J.* 5 (2) (2014) 90–97.
- [12] F.A. Alsarairh, S.M. Aloush, Mindfulness meditation versus physical exercise in the management of depression among nursing students, *J. Nurs. Educ.* 56 (10) (2017) 599–604.
- [13] Y.J. Tung, et al., Prevalence of depression among nursing students: a systematic review and meta-analysis, *Nurse Educ. Today* 63 (2018) 119–129.
- [14] S. Chatterjee, et al., Depression among nursing students in an Indian government college, *Br. J. Nurs.* 23 (23) (2014) 316–320.
- [15] C.J. Chen, et al., The effects of Chinese five-element music therapy on nursing students with depressed mood, *Int. J. Nurs. Pract.* 21 (2) (2015) 192–199.
- [16] F.F. Zhao, et al., The study of perceived stress, coping strategy and self-efficacy of Chinese undergraduate nursing students in clinical practice, *Int. J. Nurs. Pract.* 21 (4) (2014) 401–409.
- [17] M. Pulido-Martos, J.M. Augusto-Landa, E. Lopez-Zafra, Sources of stress in nursing students: a systematic review of quantitative studies, *Int. Nurs. Rev.* 59 (1) (2012) 15–25.
- [18] W.M. Chernomas, C. Shapiro, Stress, depression, and anxiety among undergraduate nursing students, *Int. J. Nurs. Educ. Scholarsh.* 10 (1) (2013) 255–266.
- [19] T. Vos, C. Allen, M. Arora, Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015, *Lancet* 388 (10053) (2016) 1545–1602.
- [20] H. CS, et al., Effects of vortioxetine and fluoxetine on the level of Brain Derived Neurotrophic Factors (BDNF) in the hippocampus of chronic unpredictable mild stress-induced depressive rats. *Lu Y, Brain Res. Bull.* 142 (undefined) (2018) 1–7.
- [21] R. JD, et al., Efficacy of antidepressants on measures of workplace functioning in major depressive disorder: a systematic review. *Lee Y, J. Affect. Disord.* 227 (undefined) (2018) 406–415.
- [22] B. T, et al., World federation of societies of biological psychiatry (WFSBP) guidelines for biological treatment of unipolar depressive disorders in primary care. *Bauer M, World J. Biol. Psychiatr.: Off. J. World Fed. of Soc. Biol. Psych.* 8 (2) (2007) 67–104.
- [23] K.G.G. Vedana, D.F. Magrini, A.I. Miasso, A.C.G. Zanetti, T.L. Borges, Attitudes to pharmacological treatments for depression, *British Journal of Mental Health Nursing* 6 (1) (2017) 44–49.

- [24] Z.V. Segal, et al., Antidepressant monotherapy vs sequential pharmacotherapy and mindfulness-based cognitive therapy, or placebo, for relapse prophylaxis in recurrent depression, *Arch. Gen. Psychiatr.* 67 (12) (2010) 1256–1264.
- [25] M.E. Thase, et al., Cognitive therapy versus medication in augmentation and switch strategies as second-step treatments: a STAR*D report, *Am. J. Psychiatry* 164 (5) (2007) 739–752.
- [26] H. YX, et al., Analysis of print news media framing of ketamine treatment in the United States and Canada from 2000 to 2015.%A Zhang MW, *PLoS One* 12 (3) (2017) 1–13.
- [27] W.B. Zhang Melvyn, C.M. Ho Roger, Ketamine's potential as a rapid antidepressant was overplayed, *BMJ* 351 (2015) 1–2.
- [28] M.W. Zhang, R.C. Ho, Controversies of the effect of ketamine on cognition, *Front. Psychiatr.* 7 (4) (2016) 47.
- [29] M.W. Zhang, K.M. Harris, R.C. Ho, Is Off-label repeat prescription of ketamine as a rapid antidepressant safe? Controversies, ethical concerns, and legal implications, *BMC Med. Ethics* 17 (1) (2016) 1–8.
- [30] M.W. Zhang, R. Ho, Critical appraisal of existing ketamine trials: existing limitations and limited applicability for treatment, *Am. J. Psychiatry* 173 (4) (2016) 431.
- [31] M.W. Zhang, R.C. Ho, The paroxetine controversy: lessons for ketamine trials, *Lancet Psychiatry* 2 (12) (2015) 1057–1058.
- [32] Y. Finkelstein, et al., Second-generation anti-depressants and risk of new-onset seizures in the elderly, *Clin. Toxicol.* (2018) 1–6.
- [33] M.A.M. Rogers, et al., Depression, antidepressant medications, and risk of *Clostridium difficile* infection, 11,1(2013-05-07), *BMC Med.* 11 (6) (2013) 121–121.
- [34] S.A. Shankman, et al., Side effects to antidepressant treatment in patients with depression and comorbid panic disorder, *J. Clin. Psychiatr.* 78 (4) (2017) 433–440.
- [35] J.C. Nelson, D.A. Spyker, Morbidity and mortality associated with medications used in the treatment of depression: an analysis of cases reported to U.S. Poison control centers, 2000–2014, *Am. J. Psychiatry* 174 (5) (2017) 438–450.
- [36] J. Piet, E. Hougaard, The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: a systematic review and meta-analysis, *Clin. Psychol. Rev.* 31 (6) (2011) 1032–1040.
- [37] K.L. Capoccia, et al., Randomized trial of pharmacist interventions to improve depression care and outcomes in primary care, *Am. J. Health Syst. Pharm.: AJHP: Off. J. Am. Soc. Health-System Pharm.* 61 (4) (2004) 364–372.
- [38] d.R.P. Van, T. Levett-Jones, C. Aquino-Russell, The effectiveness of mindfulness meditation for nurses and nursing students: an integrated literature review, *Nurse Educ. Today* 65 (2018) 201–211.
- [39] C. Li, et al., Interventions to promote mental health in nursing students: a systematic review and meta-analysis of randomized controlled trials, *J. Adv. Nurs.* (2018) 1–15.
- [40] D. Moher, et al., Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, *Rev. Española Nutr. Humana Dietética* 18 (3) (2009) e123.
- [41] N. Jackson, E. Waters, Criteria for the systematic review of health promotion and public health interventions, *Health Promot. Int.* 20 (4) (2005) 367–374.
- [42] J. Cohen, The statistical power of abnormal-social psychological research: a review, *J. Abnorm. Soc. Psychol.* 65 (3) (1962) 145–153.
- [43] J.P.T. Higgins, et al., Measuring inconsistency in meta-analyses, *Br. Med. J.* 327 (7414) (2003) 557–560.
- [44] M.W. Cheung, et al., Conducting a meta-analysis: basics and good practices, *International Journal of Rheumatic Diseases* 15 (2) (2012) 129–135.
- [45] X. D, et al., A systematic review and meta-analysis of randomized controlled trials of cognitive behavior therapy for patients with diabetes and depression.%A Li C, *J. Psychosom. Res.* 95 (undefined) (2017) 44–54.
- [46] Y. Chen, et al., A randomized controlled trial of the effects of brief mindfulness meditation on anxiety symptoms and systolic blood pressure in Chinese nursing students, *Nurse Educ. Today* 33 (10) (2013) 1166–1172.
- [47] K.L. Godbey, M.M. Courage, Stress-management program: intervention in nursing student performance anxiety, *Arch. Psychiatr. Nurs.* 8 (3) (1994) 190–199.
- [48] Y.F. Guo, et al., Positive psychotherapy for depression and self-efficacy in undergraduate nursing students: a randomized, controlled trial, *Int. J. Ment. Health Nurs.* 26 (4) (2016) 375–383.
- [49] N. Johansson, Effectiveness of a stress management program in reducing anxiety and depression in nursing students, *J. Am. Coll. Health* 40 (3) (1991) 125–129.
- [50] Y.S. Kang, S.Y. Choi, E. Ryu, The effectiveness of a stress coping program based on mindfulness meditation on the stress, anxiety, and depression experienced by nursing students in Korea, *Nurse Educ. Today* 29 (5) (2009) 538–543.
- [51] M.E. Qiu, B.Q. Ping, M. Jin, Effect of mindfulness intervention on negative emotion and interpersonal acceptance ability among nurse trainees with left-behind experience, *Chin. J. Public Health* 33 (10) (2017) 1503–1506.
- [52] P. Ratanasiripong, et al., Biofeedback intervention for stress, anxiety, and depression among graduate students in public health nursing, *Nurs Res Pract* 2015 (2) (2015) 1–5.
- [53] Y. Song, R. Lindquist, Effects of mindfulness-based stress reduction on depression, anxiety, stress and mindfulness in Korean nursing students, *Nurse Educ. Today* 35 (1) (2015) 86–90.
- [54] M. Yazdani, et al., The effect of laughter Yoga on general health among nursing students, *Iran. J. Nurs. Midwifery Res.* 19 (1) (2014) 36–40.
- [55] M. Yazdani, S. Rezaei, S. Pahlavanzadeh, The effectiveness of stress management training program on depression, anxiety and stress of the nursing students, *Iran. J. Nurs. Midwifery Res.* 15 (4) (2010) 208–215.
- [56] H.S. Yoon, G.H. Kim, J. Kim, Effectiveness of an interpersonal relationship program on interpersonal relationships, self-esteem, and depression in nursing students, *Journal of Korean Academy of Nursing* 41 (6) (2011) 805–813.
- [57] L.C. Hughes, et al., Evaluation of an informal peer group experience on baccalaureate nursing students' emotional well-being and professional socialization, *J. Prof. Nurs.* 19 (1) (2003) 38–48.
- [58] T. Kral, et al., Impact of short- and long-term mindfulness meditation training on amygdala reactivity to emotional stimuli, *Neuroimage* 181 (2018) 301–313.
- [59] E.A. Hoge, et al., The effect of mindfulness meditation training on biological acute stress responses in generalized anxiety disorder, *Psychiatr. Res.* 262 (2017) 328–332.
- [60] N.E. Morone, C.G. Moore, C.M. Greco, Characteristics of adults who used mindfulness meditation: United States, 2012, *J. Alternative Compl. Med.* 23 (7) (2017) 545–550.
- [61] Y.S. Song, Depression, stress, anxiety and mindfulness in nursing students, *Korean Journal of Adult Nursing* 23 (4) (2011) 31–31.
- [62] J.J. Daubenmier, et al., The contribution of changes in diet, exercise, and stress management to changes in coronary risk in women and men in the multisite cardiac lifestyle intervention program, *Ann. Behav. Med.* 33 (1) (2007) 57–68.
- [63] R.K. Hersch, et al., Reducing nurses' stress: a randomized controlled trial of a web-based stress management program for nurses, *Appl. Nurs. Res.* 32 (2016) 18–25.
- [64] Y. Lu, et al., A regression analysis of maladaptive rumination, illness perception and negative emotional outcomes in Asian patients suffering from depressive disorder, *Asian Journal of Psychiatry* 12 (1) (2014) 69–76.
- [65] National Institute for Health and Clinical Excellence, *Depression: Management of Depression in Primary and Secondary Care*, (2004).
- [66] K. Clarke, et al., Can non-pharmacological interventions prevent relapse in adults who have recovered from depression? A systematic review and meta-analysis of randomised controlled trials, *Clin. Psychol. Rev.* 39 (2015) 58–70.
- [67] S. Lau, et al., Chinese and American adolescents' perceptions of the purposes of education and beliefs about the world of work, *Social Behavior & Personality An International Journal* 28 (1) (2000) 73–89.
- [68] C.Y. Chung, F.H. Walkey, Educational and achievement aspirations of New Zealand Chinese and European secondary school students, *Youth Soc.* 21 (2) (1989) 139–152.
- [69] F. Salili, C. Chiu, S. Lai, The Influence of Culture and Context on Students' Motivational Orientation and Performance, (2001), pp. 221–247.
- [70] A.N. Cutilan, A.A. Sayampanathan, R.C. Ho, Mental health issues amongst medical students in Asia: a systematic review [2000–2015], *Ann. Transl. Med.* 4 (4) (2016) 72.
- [71] C.C. Choo, et al., What predicts medical lethality of suicide attempts in Asian youths? *Asian Journal of Psychiatry* 29 (2017) 136–141.
- [72] J.B. Tan, S. Yates, Academic expectations as sources of stress in Asian students, *Soc. Psychol. Educ.* 14 (3) (2011) 389–407.
- [73] R. Puthran, et al., Prevalence of depression amongst medical students: a meta-analysis, *Med. Educ.* 50 (4) (2016) 456–468.
- [74] C.C. Choo, K.M. Harris, R.C. Ho, Prediction of lethality in suicide attempts: gender matters, *Omega* (5) (2017) 30222817725182.
- [75] C.C. Choo, et al., Does ethnicity matter in risk and protective factors for suicide attempts and suicide lethality? *PLoS One* 12 (4) (2017) e0175752.
- [76] S.H. Tan, et al., Determining the quality of life of depressed patients in Singapore through a multiple mediation framework, *Asian Journal of Psychiatry* 18 (2015) 22–30.
- [77] C.R. Lim, J. Barlas, R. Ho, The effects of temperament on depression according to the schema model: a scoping review, *Int. J. Environ. Res. Publ. Health* 15 (6) (2018).
- [78] M.W.B. Zhang, C.S.H. Ho, R.C.M. Ho, Methodology of development and students' perceptions of a psychiatry educational smartphone application, *Technol. Health Care* 22 (6) (2014) 847–855.
- [79] M.W. Zhang, et al., Current status of postnatal depression smartphone applications available on application stores: an information quality analysis, *Bmj Open* 7 (11) (2017) e015655.
- [80] M.W. Zhang, R.C. Ho, Moodle: the cost effective solution for internet cognitive behavioral therapy (I-CBT) interventions, *Tech. & Health Care Off. J. Eur. Soc. Eng. Med.* 25 (1) (2017) 163.