

Psychotherapy for depression in college students

A protocol for systematic review and network meta-analysis

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Abstract

Background: Depression is a disease with a high incidence and easy to relapse. It not only affects the work and life of patients, but also brings a heavy economic burden. University is the peak of depression, and the prevalence of depression among college students is much higher than that of ordinary people. The purpose of this research is to evaluate depression symptoms, life satisfaction, self-confidence, substance use, social adjustment, and dropout rates of the use of psychological intervention for college students.

Methods: We will identify relevant trials from systematic searches in the following electronic databases: PubMed, Embase, Web of Science and The Cochrane Library. We will also search Clinical Trials.gov, the WHO International Clinical Trials Registry Platform for unpublished data. Additional relevant studies will be searched through search engines (such as Google), and references included in the literature will be tracked. All relevant randomized controlled trials (RCTs) will be included. There are no date restrictions. Use Cochrane Collaboration's Risk of bias tool to conduct risk of bias analysis. Use the Grades of Recommendation, Assessment, Development, and Evaluation to assess the quality of evidence. All statistical analysis will be performed using Stata (V.15.0.) and Review Manager (V.5.2.0).

Results: A total of 6238 records were obtained by searching the database and 27 records were obtained by other sources. After removing duplicate records, there are 4225 records remaining. We excluded 3945 records through abstract and title, leaving 280 full-text articles.

Conclusion: This will be the first study to compare the effects of different psychological treatments on depression in college students. We hope that this study will guide clinical decision-making of psychotherapy to better treat depression in college students.

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Abbreviations: ACT = acceptance and commitment therapy, BA = behavioral activation, BDI = beck depression inventory, CBT = cognitive-behavioral therapy, CESD-R = center for epidemiologic studies depression scale revised, CSCT = comprehensive self-control training, DSM = diagnostic and statistical manual of mental disorders, HRSD = Hamilton Rating Scale for depression, ICD = International Classification of Diseases, NMA = network meta-analysis, RCTs = randomized controlled trials, SASS = social adaptation self-evaluation scale, SMD = standard mean difference, SNRIs = serotonin norepinephrine reuptake inhibitors, SSRIs = selective serotonin reuptake inhibitors, SUCRA = surface under the cumulative ranking area, TAU = treatment as usual, TCAs = tricyclic antidepressants, WLC = waiting-list control.

Keywords: college students, depression, network meta-analysis, psychotherapy

XZ and M-MN contributed equally to this work.

This study is based on a network meta-analysis of published studies, so ethical approval and patient consent are not required. And this systematic review and network meta-analysis will be published in a peer-reviewed journal.

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There are no potential conflicts of interest to disclose.

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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1. Introduction

Depression is a common mental health disorder, which is mainly manifested by significant and lasting depression, slow thinking, sleep disturbance, loss of appetite, etc. In severe cases, suicide attempts or behaviors may occur.^[11] Each episode of depression lasts at least two weeks. In severe cases, it may last for several years. This has a serious impact on work and life, and has caused a heavy financial burden. According to the World Health Organization, more than 350 million people worldwide suffer from depression.^[12] The current incidence of depression in China is 6.1%.^[13] By 2020, depression may become the second largest disease after heart disease.^[14] And depression has become the main reason for people's loss of social function and ranks third in the global burden of disease.^[15] Studies have shown that in the United States alone, the annual cost exceeds \$43.7 billion.^[6,7] College students are faced with the pressure from interpersonal communication, arduous learning tasks and adaptation to the new environment and lifestyle, which makes them prone to produce strong psychological conflicts and lead to depression.^[18] Therefore, compared with their peers, college students have a higher risk of depression.^[19]

At present, the treatment of depression is mainly divided into medication and psychotherapy. Drug therapy mainly includes selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), serotonin norepinephrine reuptake inhibitors (SNRIs), etc.^[10] Psychotherapy is to establish a relationship with the patient through a structured and purposeful connection and use a series of specific techniques to improve the patient's mental state.^[11] It plays an important role in the treatment of depression. At present, the common psychotherapy in clinical treatment methods include cognitive behavior therapy, group psychotherapy, interpersonal behavior therapy, mindfulness therapy, etc. Previous studies showed that there are few systematic reviews and meta-analysis of depression in college students. However, the relevant evidence for the effectiveness of psychotherapy is still unclear, and there is no evidence to directly compare different psychological interventions. Therefore, this field urgently needs a Bayesian network meta-analysis (NMA) method that combines direct evidence with indirect evidence from multiple treatment comparisons to estimate the correlation between all treatments.^[12] In this study, we will conduct a systematic review and NMA to evaluate depression symptoms, life satisfaction, self-confidence, substance use, social adjustment, and dropout rates of the use of psychotherapy for college students.

2. Methods

2.1. Eligibility criteria

2.1.1. Type of study. We will include all relevant randomized controlled trials (RCTs) including crossover trials. There are no language restrictions.

2.1.2. Type of patient. The patients we will include are college students diagnosed with depression according to any diagnostic criteria, such as Diagnostic and Statistical Manual of Mental Disorders (DSM)-III,^[13] DSM-IV,^[14] and International Classification of Diseases, 10th Revision (ICD-10).^[15] Studies in which participants have a diagnosis of bipolar disorder, psychotic depression will be excluded. In addition, studies where participants are not clearly diagnosed with depression will also be excluded.

2.1.3. Type of interventions. We will include RCTs comparing one psychological intervention with another control conditions for depression in college students. For psychotherapy, mindfulness therapy, cognitive-behavioral therapy (CBT), meditation therapy, comprehensive self-control training (CSCT),^[16] acceptance and commitment therapy (ACT),^[17] and behavioral activation (BA) will be included. There will be no limit to the treatment session. In terms of control conditions, waiting-list control (WLC),^[18] non-treatment control, physical exercise, bibliotherapy,^[19] treatment as usual (TAU) will be included.

2.1.4. Type of outcomes. Primary outcome

Depression symptoms that mean the change in severity of depression from baseline to end point which is measured by the depression scale, such as Beck Depression Inventory (BDI),^[20] The Center for Epidemiologic Studies Depression Scale (CESD-R),^[21] Hamilton Rating Scale for Depression (HRSD).^[22]

Second outcomes

1. self-confidence, life satisfaction was assessed using visual rating scale
2. social adjustment was assessed using the Social Adaptation Self Evaluation Scale (SASS)^[23] and the Social Adjustment Scale-Self Report for Youth.^[24]
3. substance use was measured with 10 items to assess the use of eight substances, quantity per drinking and smoking day.^[25]
4. Dropout rates from the beginning of the study to the end of the intervention.

2.2. Data source

We will identify relevant trials from systematic searches in the following electronic databases: PubMed, Embase, Web of Science and The Cochrane Library. We will also search Clinical Trials.gov, the WHO International Clinical Trials Registry Platform for unpublished data. The search terms will include "depression", "depressive disorder", "students", "university student", "college student". Additional relevant studies will be searched through search engines (such as Google), and references included in the literature will be tracked. There is no date restriction. Detail of search strategy of PubMed is shown in Table 1 as well as detail of search strategy of Embase is shown in Table 2.

2.3. Study selection

All records identified in the databases will be collected in the reference management software EndNote X8 for data screening. Two (MMN and PFM) reviewers will use data extraction tables to extract data from the original report independently, including research characteristics (such author information, publication year, journal and country), patient characteristics, intervention and outcome. Any disagreements will be resolved by the third member of our review team.

2.4. Risk of bias analysis

According to Cochrane Collaboration's Risk of bias tool, we will assess risk of bias as 'low risk', 'unclear risk' or 'high risk'.^[26] The following items will be evaluated: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data and selective outcome reporting and other sources of bias.^[27] The evaluation

Table 1**Searching strategy in PubMed.**

- #1 "Depression"[Mesh] OR "Depressive Disorder"[Mesh] OR "Depressive Disorder, Treatment-Resistant"[Mesh] OR "Depressive Disorder, Major"[Mesh] OR "Affective Disorders, Psychotic"[Mesh] OR "Major Depressive Disorder 1" [Supplementary Concept] OR "Major Depressive Disorder 2" [Supplementary Concept] OR depressi*[Title/Abstract] OR melancholia[Title/Abstract] OR MDD[Title/Abstract]
- #2 "Students"[Mesh] OR "Students, Health Occupations"[Mesh] OR "Students, Public Health"[Mesh] OR "Students, Premedical"[Mesh] OR "Students, Pharmacy"[Mesh] OR "Students, Nursing"[Mesh] OR "Students, Medical"[Mesh] OR "Students, Dental"[Mesh] OR "Education, Medical, Undergraduate"[Mesh] OR "Education, Graduate"[Mesh] OR "Education, Pharmacy, Graduate"[Mesh] OR "Education, Nursing, Graduate"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Education, Dental, Graduate"[Mesh] OR "Universities"[MeSH Terms] OR "Faculty"[MeSH Terms] OR "Schools"[Mesh] OR "School Nursing"[Mesh] OR "School Dentistry"[Mesh] OR "Schools, Health Occupations"[Mesh] OR "Schools, Pharmacy"[Mesh] OR "Schools, Medical"[Mesh] OR "Schools, Dental"[Mesh] OR "Schools, Veterinary"[Mesh] OR "Schools, Public Health"[Mesh] OR "Schools, Nursing"[Mesh] OR college student*[Title/Abstract] OR university student*[Title/Abstract] OR graduate student*[Title/Abstract] OR freshman[Title/Abstract] OR sophomore[Title/Abstract] OR students[Title/Abstract] OR undergrad*[Title/Abstract] OR graduate[Title/Abstract]
- #3 "Clinical Trials, Phase II as Topic"[Mesh] OR "Clinical Trials, Phase III as Topic"[Mesh] OR "Clinical Trials, Phase IV as Topic"[Mesh] OR "Controlled Clinical Trials as Topic"[Mesh] OR "Randomized Controlled Trials as Topic"[Mesh] OR "Intention to Treat Analysis"[Mesh] OR "Pragmatic Clinical Trials as Topic"[Mesh] OR "Clinical Trials, Phase II"[Publication Type] OR "Clinical Trials, Phase III"[Publication Type] OR "Clinical Trials, Phase IV"[Publication Type] OR "Controlled Clinical Trials"[Publication Type] OR "Pragmatic Clinical Trials as Topic"[Publication Type] OR "Single-Blind Method"[Mesh] OR "Double-Blind Method"[Mesh] OR random*[Title/Abstract] OR blind*[Title/Abstract] OR singleblind*[Title/Abstract] OR doubleblind*[Title/Abstract] OR trebleblind*[Title/Abstract] OR tripleblind [Title/Abstract]
- #1 AND #2 AND #3

will be conducted by two independent raters (PFM and LD). Any disagreements will be resolved by a third review author.

2.5. Statistical analysis

2.5.1. Pairwise meta-analysis. We will use Review Manager (V.5.2.0) to perform traditional pairwise meta-analysis. Dichotomous data will be expressed as relative risk (RR) with 95% confidence interval (CI), and continuous outcomes will be expressed as standard mean difference (SMD) with 95% CI.^[28]

2.5.2. Network meta-analysis. To simultaneously assess the comparative effects of more than 2 psychotherapy, an NMA will be performed. An NMA synthesizes direct and indirect comparisons over an entire network of psychotherapy, allowing for all available evidence to be considered in one analysis. Based on the network development process as outlined above, the outcome variable for the NMA is the standardized mean change in the DSST (measured using Hedge's G) from baseline to end of study. The standardization is based on the pooled (across treatment arms within study) estimate of the SDs. The NMA will be carried out using a frequentist's approach, and a 2-way ANOVA model is used. As the residual variances between treatment groups are known, it is possible for random effect estimates to be produced, which account for the between-trial heterogeneity. The model is used to perform ordinary pairwise meta-analysis comparing the different psychotherapy based on direct evidence from the clinical studies. Ranking probabilities

will be calculated based on the joint distribution of the estimates of relative efficacy.^[29]

Consistency will be addressed through the principle of node splitting by using a network meta-regression model. The purpose of node-splitting is to investigate if the relative effect of 2 psychotherapy based on direct comparisons is comparable with the same effect based on indirect comparisons. Statistically, the model is an extension of the NMA, which allows for a different relative effect between the 2 psychotherapy that are being split in head-to-head trials compared with all other trials. NMA will be implemented by the mvmeta software package in Stata (15.0; Stata Corporation, College Station, TX, USA Stata),^[30] If P value $< .1$ and $I^2 > 50\%$, it is considered that there is heterogeneity in the study, and sensitivity analysis or subgroup analysis will be performed to detect the source of heterogeneity. Funnel plot and Egger linear regression analysis will be used to assess publication bias. Using Review Manager (V.5.2.0) to analyze the risk of bias in the included studies, where the green, yellow, and red in the image represent low, unclear, and high risks, respectively.^[31,32]

2.5.3. Subgroup analysis. If statistical heterogeneity is evident, we will analyze the causes of heterogeneity, if there is enough data (such as differences between sexes, comparison between different countries, studies sponsored versus not sponsored by companies).

2.5.4. Sensitivity analysis. We will use the exclusion method to conduct sensitivity analysis:

Table 2**Searching strategy in Embase.**

- #1 'depression'/exp OR 'major depression'/exp
- #2 depressi*:ab,ti OR mdd:ab,ti OR melancholia:ab,ti
- #3 #1 OR #2
- #4 'college student'/exp OR 'graduate student'/exp OR 'undergraduate student'/exp OR 'student'/exp
- #5 'college student':ab,ti OR 'university student':ab,ti OR 'graduate student':ab,ti OR freshman:ab,ti OR sophomore:ab,ti OR students:ab,ti OR undergrad*:ab,ti OR graduate:ab,ti
- #6 #4 OR #5
- #7 'randomized controlled trial (topic)'/exp OR 'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp
- #8 'random*':ti,ab OR 'blind*':ti,ab OR 'singleblind*':ti,ab OR 'doubleblind*':ti,ab OR 'trebleblind*':ti,ab OR 'tripleblind*':ti,ab
- #9 #7 OR #8
- #10 #3 AND #6 AND #9

Table 3
Summary of findings for the main comparison.

ACT compared with WLC for depression in college students
Patient or population: College students suffering from depression
Settings:
Intervention: ACT
Comparison:WLC

Outcome	Illustrative comparative risks* (95% CI)		Relatively effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk [†] WLC	Corresponding risk [†] ACT				

Overall mean change scores on BDI
 Overall mean change scores on SASS
 The score of visual rating scales

ACT= acceptance and commitment therapy, BDI=Beck Depression Inventory, CI=confidence interval, SASS=Social Adaptation Self Evaluation Scale, SE=standard error, SMD=standardized mean difference, WLC=waiting-list control.

GRADE Working Group grades of evidence.

High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

* The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

† The assumed and the corresponding risk was calculated from the SMD to SE.

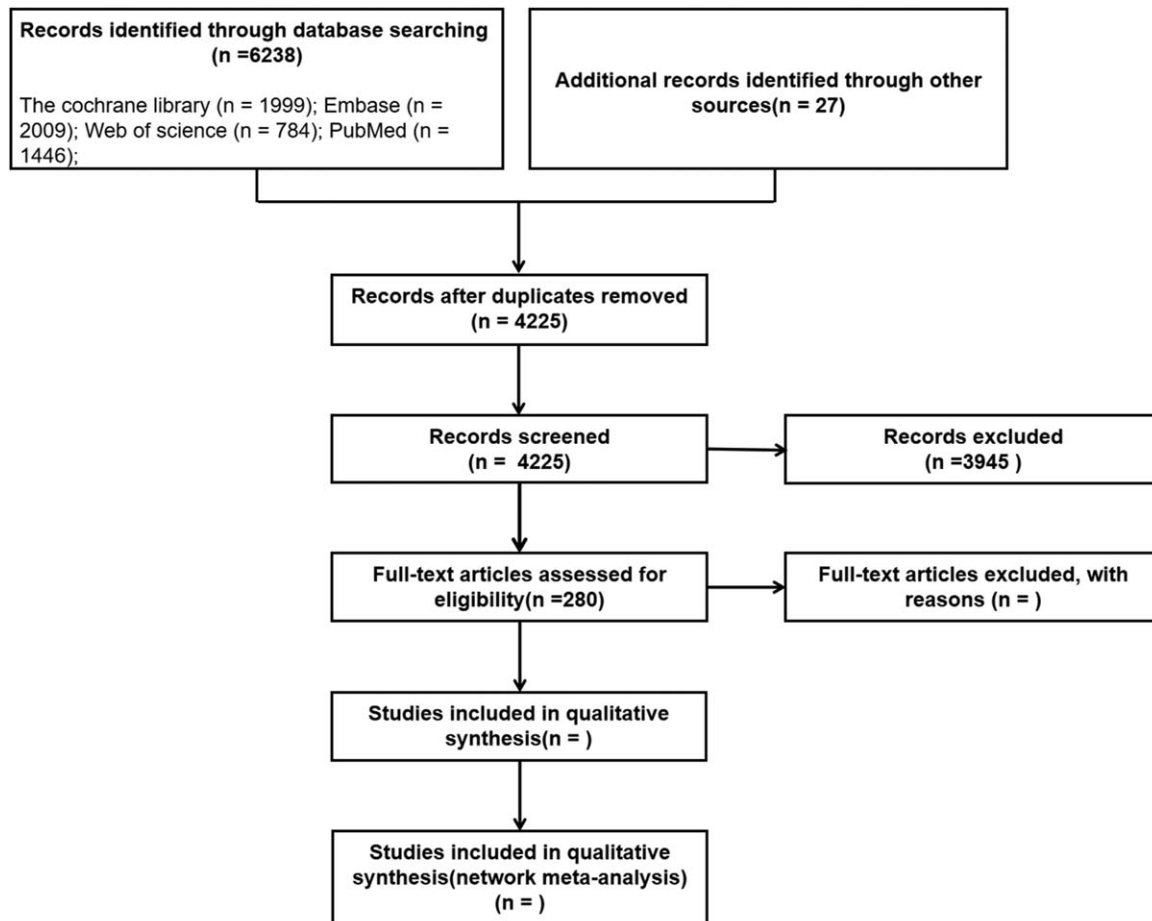


Figure 1. The flowchart of the screening process.

Table 4**Basic characteristics of some of the included studies.**

Author Year	Age	Gender (male /female)	Sample		Interventions		Outcomes	Duration
			Experimental Group	Controlled Group	Experimental Group	Controlled Group		
Falsafi, 2016 ^[6]	No report	No report	30/30	30	Mindfulness therapy /yoga	No treatment	Depression symptoms	2 semesters
Alsaraireh, 2017 ^[36]	22.00 ± 2.10	69/112	91	90	Meditation therapy	Physical exercise	Depression symptoms	3 months
Yang ^[16]	18.50 ± 1.00	30/44	37	37	CSCT	No treatment	Depression symptoms; dropout rates	6 months
Haddock, 2017 ^[7]	20.42 ± 2.58	0/32	17	15	Internal Family Systems therapy	TAU	Depression symptoms	16 weeks
McIndoo, 2016 ^[18]	No report	5/31	20/16	14	Mindfulness-based therapy/BA	WLC	Depression symptoms	1 month
Rohde, 2014 ^[19]	19.00 ± 0.90	25/57	27	22/33	CBT	Bibliotherapy; Educational brochure control	Depression symptoms; Substance use; Social adjustment	12 months
Kohtala, 2015 ^[17]	25.80 ± 5.40	12/45	28	29	ACT	WLC	Depression symptoms; Self-confidence; Life satisfaction; social functioning	6 months
Hamdan-Mansour, 2009 ^[37]	No report	46/38	44	40	CBT	no treatment	Depression symptoms	3 months

ACT = acceptance and commitment therapy, BA = behavioral activation, CBT = cognitive-behavioral therapy, CSCT = comprehensive self-control training, TAU = treatment as usual, WLC = waiting-list control.

- (1) exclude low-quality studies;
- (2) exclude studies with comorbid physical or mental illnesses;
- (3) exclude trials with missing data.

2.6. Quality of evidence

We will use Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework to assess the quality of evidence for the primary outcomes.^[33,34] The quality of evidence is assessed as ‘high’, ‘moderate’, ‘low’ or ‘very low’. The following item will be evaluated: limitations, inconsistency, imprecision, indirectness, and publication bias.^[35]

2.7. Summary of findings

A “summary of finding” table will be created for the major outcome. We will also add absolute and relative percentage changes to the “summary of finding”. For detailed information, see Table 3; we have listed partial summary of findings for the main comparison.

3. Result

3.1. Results of the search

A total of 6238 records were obtained by searching the database and 27 records were obtained by other means. After removing duplicate records, there are 4225 records remaining. We excluded 3945 records through abstract and title, leaving 280 full-text articles. The document screening flowchart is shown in Figure 1.

3.2. Characteristic of included studies

In a preliminary trial, we included 8 studies. The average age of patients was 18 to 26, with a maximum sample size of 181 and a

minimum sample size of 32. The research period ranges from one month to 12 months. For more detailed information, see Table 4.

4. Discussion

At present, although some studies have evaluated the intervention effects of psychotherapy, there is no NMA to compare the therapeutic effects of different psychological interventions for college students. Therefore, this systematic review and NMA will summarize the direct comparison and indirect comparison evidence to evaluate different psychological interventions. We hope that this study will help guide clinical decision-making for psychotherapy to better treat depression in college students.

Author contributions

Conceptualization: Xiu Zhang, Lin Wan.

Data curation: Xiu Zhang, Ming-Ming Niu, Pei-Fen Ma, Li Du, Lin Wan.

Methodology: Xiu Zhang, Lin Wan.

Software: Xiu Zhang, Ming-Ming Niu, Pei-Fen Ma, Li Du.

Writing – original draft: Xiu Zhang, Ming-Ming Niu, Lin Wan.

Writing – review & editing: Xiu Zhang, Lin Wan.

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