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Effect of metacognitive therapy on depression in patients with chronic disease: a protocol for a systematic review and meta-analysis

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ABSTRACT

Background Chronic diseases have a high prevalence worldwide, and patients with chronic diseases often suffer from depression, leading to a poor prognosis and a low quality of life. Metacognitive therapy is a transdiagnostic psychotherapy intervention focused on thinking patterns, with the advantages of reliable implementation effect, short intervention period and low cost. It can help patients change negative metacognition, alleviate depression symptoms, and has a higher implementation value compared with other cognitive interventions. Therefore, metacognitive therapy may be an effective way to improve the mental health of patients with chronic diseases.

Methods and analysis CNKI, Wanfang Database, VIP Database for Chinese Technical Periodicals, Sinomed, PubMed, SCOPUS, Embase, The Cochrane Library, Web of Science and PsycINFO will be used to select the eligible studies. As a supplement, websites (eg, the Chinese Clinical Registry, ClinicalTrials.gov) will be searched and grey literature will be included. The heterogeneity and methodological quality of the eligible studies will be independently screened and extracted by two experienced reviewers. All the data synthesis and analysis (drawing forest plots, subgroup analysis and sensitive analysis) will be conducted using RevMan 5.4.1.

Ethics and dissemination This article is a literature review that does not include patients' identifiable information. Therefore, ethical approval is not required in this protocol. The findings of this systematic review and meta-analysis will be published in a peer-reviewed journal as well as presentations at relevant conferences.

PROSPERO registration number CRD42023411105.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review and meta-analysis will evaluate the feasibility and effectiveness of metacognitive therapy (MCT) in reducing depression in patients with chronic diseases by collecting comprehensive evidence.
⇒ If heterogeneity is detected, differences in the effectiveness and durability of different types of MCTs will be determined in subgroup analysis.
⇒ Grey literature and clinical registration information will be searched manually to enrich evidence sources.
⇒ There may be a limited number of studies on the application of MCT to patients with chronic diseases, so the number of included studies may be small.
⇒ Only English and Chinese literature will be included.

INTRODUCTION

Chronic diseases, also called noncommunicable diseases (NCDs), refer to diseases that do not result from infection but rather from damage by long-term accumulation.[1] Data show that billions of people suffer from chronic diseases, which has become an important public health issue.[2 3] Also, the United Nations prioritised the management of chronic diseases in the sustainable development goals.[4]

Depression is one of the most common comorbidities among many chronic diseases. People with one chronic disease may have an increased risk of developing depressive symptoms by at least 20%.[5 6] Meanwhile, depression is associated with poor prognosis and increased medical costs in individuals with chronic diseases.[7 8] A literature review focused on patients with heart failure (HF) found that depression doubled the all-cause mortality in patients with HF, suggesting a possible association between depression and all-cause mortality.[9] The Lancet reported that data from 1990 to 2019 showed a high disability rate due to depression, and depression is considered one of the leading cause of burden worldwide.[10] Therefore, alleviating depression is crucial for maintaining the mental health of patients with chronic diseases. However, a systematic review comparing psychological and pharmacological interventions in patients with coronary artery disease found that neither strategy achieved the effect of alleviating depressive symptoms at the end of treatment.[11]

Metacognitive therapy (MCT) was initially developed by Wells[12] and is an emerging theoretical based transdiagnostic psychotherapy that has been proven effective in alleviating depression.[13] According to Self-Regulation Executive Function model (S-REF),[14] depression will occur, persist and reoccur due to the development of unmanageable, repeated negative thinking pattern.[15] This thinking strategy called cognitive attentional syndrome (CAS), which focuses on the inner (attention, thinking and physical sensations), reflects on the past and worries about the future, accompanied by avoidance and maladaptation behaviours. The S-REF model assumes that CAS is influenced by positive or negative metacognitive beliefs. Negative metacognitive beliefs manifest as uncontrollable beliefs about contemplation and worry. Patients may express 'My contemplation is uncontrollable'. While positive metacognitive beliefs manifest as useful beliefs about contemplation and worry, such as 'My contemplation will help me find a solution'.[16] To alleviate depression symptoms, MCT helps patients in reducing CAS and developing healthy metacognitive beliefs. This enables patients to understand the negative effects and adverse consequences of CAS without denying the negative thinking content.[17] It includes several specific skills such as attention training technique (ATT), spatial attention control exercise, situational attention refocusing, detached mindfulness, etc. In the treatment of MCT, the ruminative thinking mode is blocked in the early stage. Patients are required to pay attention to external sounds or recognise different sound sources, helping them realise the independence of attention control from any internal and external events.[18] MCT establishes adaptive conditioned emotional response by mobilising the positive mental state of the patients, blocking the connection between conditional stimuli and negative emotions.[19]

A systematic review and meta-analysis have indicated that MCT is an effective method for treating a range of psychological complaints.[13] Several clinical trials have examined the efficacy of MCT in patients with depression and chronic diseases. However, there are currently no meta-analysis related to MCT. Therefore, this protocol aims to conduct a systematic review and meta-analysis to assess the effectiveness of MCT in treating depression in patients with chronic disease.

METHODS AND ANALYSIS

Study registration

This protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database on 4 April 2023. This protocol was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses Statement.[20]

Inclusion criteria

Types of studies

Randomised controlled trials (RCTs) using MCT for treatment of patients with chronic disease will be included in the study. However, if <3 RCT studies will be included, we will also consider including quasi-experimental studies.

Types of participants

This study will include patients aged ≥18 years with any type of chronic disease. The NCDs considered in this study include, but are not limited to, cancer, stroke, coronary heart disease, HF, hypertension, diabetes and chronic obstructive pulmonary disease. The NCDs were diagnosed by 11th edition of the International Classification of Diseases (ICD-11).[21] There are no restrictions on gender, economic background, nationality, educational status or disease period.

Experimental and control interventions

Studies will be included if they assessed the effect of MCT or specific MCT techniques (eg, ATT) with appropriate qualified professionals are responsible for intervention delivery. According to Wells' educational programme,[14] interventions can be lectures, self-help manuals, telephone support calls, group discussions, role plays and homework. Sessions should focus on deriving a case formulation and socialisation, practicing techniques to regulate worry and rumination, challenging metacognitive beliefs that maintain maladaptive patterns of thinking and developing a 'helpful behaviours' plan. The form of intervention can be adjusted according to the research objective. There is no limitation on the intervention period or intervention time. Interventions will be excluded if studies combine MCT with other psychotherapies (eg, mindfulness therapy).

In the included studies, the control group was defined as other interventions without MCT such as cognitive behavioural therapy, pharmacological treatment, waitlist control, usual care, clinical management and no interventions.

Outcome measures

The primary outcome was symptom of depression, which was evaluated using standardised and validated depressive symptom scale scores, such as The Hospital Anxiety and Depression Scale (HADS), the Beck Depression Inventory I or II, the Hamilton Depression Rating Scale and so on. We will include studies where depression is assessed as a primary or secondary outcome. If the reliability and validity of the scale used in the study are relatively low, the decision on include this study will be made through group discussion.

To comprehensively assess the effect of MCT on patients with chronic disease, our study also included anxiety, metacognitive beliefs, adverse events and traumatic stress symptoms as the secondary outcomes.

Exclusion criteria

- RCTs with <10 participants.
- Studies published in non-English and non-Chinese languages.

Table 1 Search strategies in PubMed

Number	Searching items
#1	"metacognitive therap*" (Title/Abstract) OR "meta-cognitive therap*" (Title/Abstract) OR "metacognitive intervention*" (Title/Abstract) OR "metacognitive treatment*" (Title/Abstract)
#2	"Depression" [MeSH Terms] OR "Depressive Disorder" [MeSH Terms] OR "Depressive Disorder, Major" [MESH Terms]
#3	"depress*" (Title/Abstract) OR "depressive symptom*" (Title/Abstract) OR "emotional distress" (Title/Abstract) OR "emotional disorder*" (Title/Abstract) OR "mood disorder*" (Title/Abstract)
#4	#2 OR #3
#5	"Clinical Trials as Topic" [MeSH Terms]
#6	"therapy" (Title/Abstract) OR "trial" (Title/Abstract) OR "treatment" (Title/Abstract) OR "intervention" (Title/Abstract) OR "implement" (Title/Abstract) OR "investigation" (Title/Abstract) OR "test" (Title/Abstract)
#7	#5 OR #6
#8	((#1) AND (#4)) AND (#7)

- Studies that recruited ≥50% of patients with dementia or schizophrenia and it was not possible to distinguish between two groups of patients.
- Studies that combine MCT techniques with other types of treatment (eg, cognitive behavioural therapy).
- Studies that report similar results without further analysis or discussion.

Search methods

We will select literatures from the following four Chinese databases (CNKI, Wanfang Database, VIP Database for Chinese Technical Periodicals and Sinomed) and six English databases (PubMed, SCOPUS, Embase, The Cochrane Library, Web of Science and PsycINFO). The search time will be set from the beginning to January 2024, and the languages are limited to both Chinese and English. The Clinicaltrials.gov and Chinese Clinical Trial Registry will also be searched to obtain unpublished or ongoing trial data. The keywords of our study will be medical subject headings (MESH) terms and free-text terms corresponding to the subject heading for (1) MCT (eg, metacognitive therapy, metacognitive intervention); (2) depression (eg, depressive disorder, emotional distress, mood disorder) and (3) clinical trial. Specific searching strategy in PubMed is shown in table 1. Appropriate modifications will be made in actual searching according to the searching methods of those databases. In addition, reference lists of the included studies will be examined to identify potentially eligible studies.

Searching other sources

Other websites will be searched as a supplement including: the Chinese Clinical Registry, the WHO International Clinical Trials Registry Platform and ClinicalTrials.gov.

Data collection and analysis

Selection of studies

All search results will be imported into EndNote V.20 to select eligible studies, and duplicate studies will be deleted. The initial selection will be based on titles and abstracts, with two reviewers (ZZ and JG) working on separately. Those unrelated literature will be excluded. Next, full text of the remaining studies will be screened for further assessment according to the inclusion criteria. Any disagreements will be resolved through reviewers' discussion. If an agreement cannot be reached, a third reviewer (PPW) will be consulted. The study selection flow chart is shown in figure 1.

Data extraction and management

The data extraction will be completed by two researchers (ZZ and JG) independently with a predesigned Microsoft Excel. Discrepancies in the data extraction will be resolved by consensus. If consensus cannot be reached, a third reviewer (PPW) will be consulted. The predefined items for extraction are the following: publication details (title, the first author's name, publication year), characteristics of the research participants (sample size, gender, age, nationality, types of chronic disease, baseline data, diagnostic criteria for depression), interventions (type of MCT, number of sessions, duration of each lesson, intervention frequency), control condition (details of the treatment, including the name, dosage, frequency and course) and outcomes (outcome at each time point, adverse events in each group and numbers of dropouts). If the data are unclear or missing in our included studies, the corresponding author will be contacted through email to obtain complete data. If the data are still unattainable, only current data will be analysed, and the potential influence will be discussed.

Assessment of risk of bias

Cochrane Collaboration's tool will be used to assess the risk of bias of included RCT studies by two authors (ZZ and JG) independently. This tool identifies bias in the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias.[22] According to the criteria, the included RCTs will be classified as low, high or unclear risk of bias. Disagreement

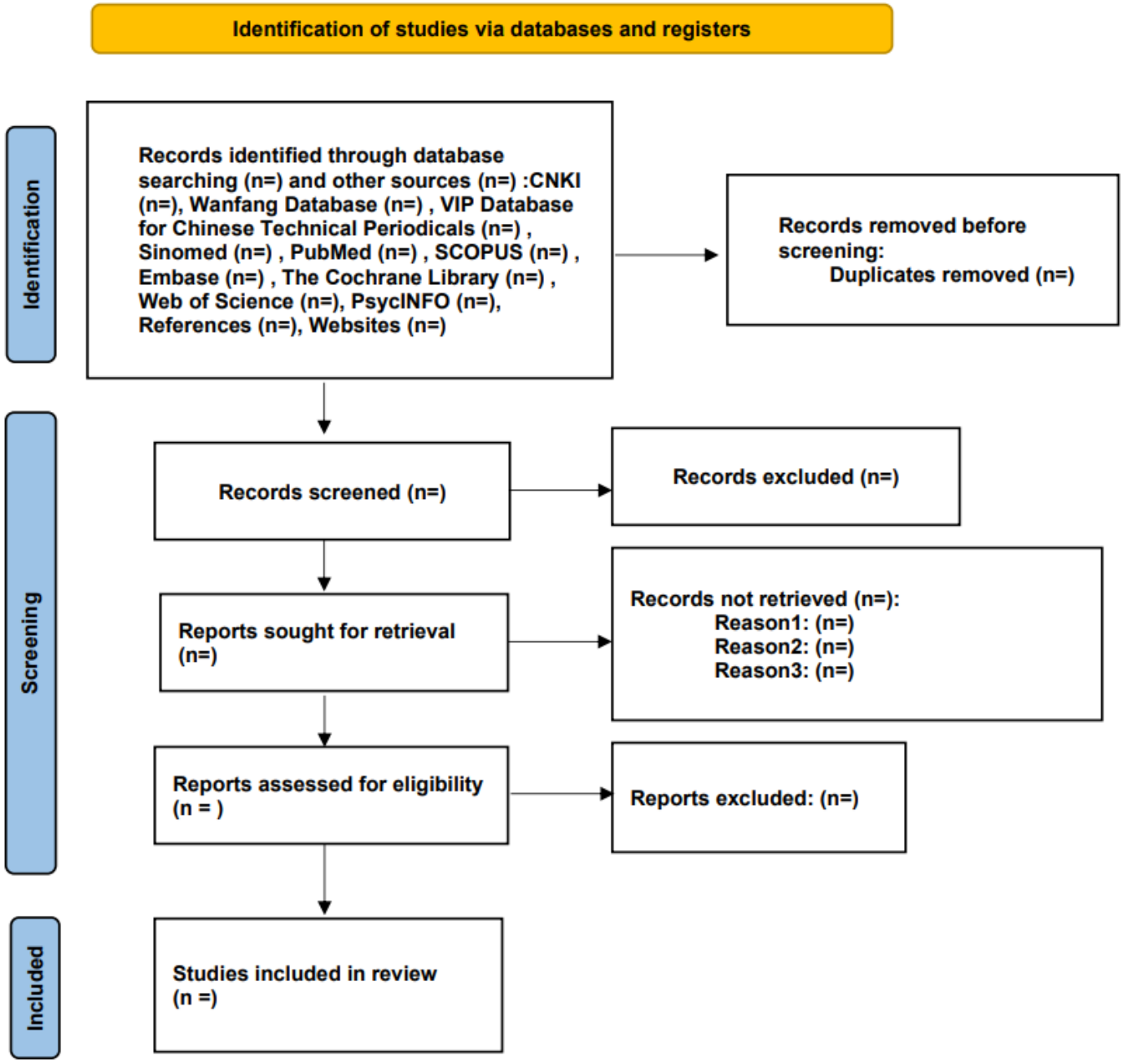

Figure 1 Flow chart of the literature screening process and results.

will be resolved by discussion and the third reviewer (PW) will be consulted when necessary. The quasi-experimental studies were evaluated by the JBI Critical Appraisal Checklist for Quasi-Experimental Studies.[23] If more than 10 trials are included, a funnel plot[24] will be used to detect publication bias, and the Egger test[25] will be carried out to analyse the asymmetry in the funnel plot.

Data synthesis

Quantitative data synthesis

RevMan V.5.4.1 will be used to conduct statistical analysis. For categorical variables, we will use risk ratio and 95% CIs as analysis indicators. For continuous variables, mean difference (MD) will be calculated. Data of same indicators measured by different scales will be converted to standardised MD and calculated as Hedges' g with 95% CI. When heterogeneity is not obvious ($p>0.1$ or $I^2<50\%$), the fixed effect model will be used for analysis, or we will choose the random effect model (when $p\leq0.1$ or $I^2\geq50\%$). If quantitative synthesis is not appropriate, we will explain the reasons and make a qualitative analysis of the research results in the Discussion section.

Assessment of heterogeneity

Following the guideline in the Cochrane Handbook, χ^2 and I^2 statistics will be chosen to evaluate the heterogeneity. High, moderate and low heterogeneity correspond to I^2 of 25%, 50% and 75%, respectively.[26] If $I^2>50\%$, subgroup analysis will be performed to detect the reasons of heterogeneity. If there is no reason be found, we will

provide a narrative summary without conducting data synthesis.

Subgroup analysis

If significant heterogeneity is detected, we will conduct subgroup analysis according to the characteristics of researches or participants including types of MCT, intervention time, frequency of intervention, age of participants, type of chronic diseases, nationality, etc.

Sensitivity analysis

Sensitive analysis will be performed to test the stability of the results. We will remove one study at a time to identify its effect on heterogeneity and effect size. Small change of heterogeneity and effect size after each removal shows reliable stability.

Strength of recommendations and the quality of evidence

To identify the quality of included studies, two researchers (ZZ and JG) will use the Grading of Recommendations Assessment, Development and Evaluation to evaluate the strength of evidence.[27] Disagreements will be solved by discussion or consultation with a third reviewer (PPW). Confidence in the results will be graded into high, moderate, low and very low. All eligible studies will be included in the final analysis irrespective of their quality score. Correspondingly, we will analyse the impact of different quality scores in our discussion and recommendations will be drawn cautiously.

Patient and public involvement

No patients or public will be involved in the design, conduct, reporting or dissemination of this research.

Study period

Our review had started in April 2023 and will be conducted until the end of April 2024.

DISCUSSION

Due to the high prevalence rates and the impact of depression on both physical and psychosocial outcomes, there is a need for effective depression interventions in chronic disease. However, the current depression treatment takes a long time and high costs, which brings a huge burden to patients with chronic diseases. Recent studies present that MCT is a theory-based, structured treatment and is suited to addressing the psychological needs of patients with chronic disease. Therefore, we intend to perform this systematic review and meta-analysis.

In our systematic review, we hold a keen interest in delving into the efficacy of MCT for patients with chronic diseases for several reasons: (1) specific intervention strategies of MCT will regulate repetitive negative thinking cycles and other unproductive behaviours that maintain depression, helping patients realise that worry and contemplation have no advantages and can be alleviated; (2) in MCT, patients will practice new reaction methods to enhance their attention control ability to get rid of worries and contemplation[28]; (3) contrast to other therapies, MCT does not require in-depth analysis and challenging the patients' concerns and (4) MCT has the advantages of short intervention period, convenient implementation methods, reliable implementation effects and low cost.[16]

Some studies have been published related to the application of MCT on patients with chronic diseases. Wells *et al* recruited 799 eligible cardiac rehabilitation patients for MCT treatment, but approximately 58% patients refused to participate.[29] Fisher *et al* conducted a short-term MCT treatment on cancer survivors and depression that was evaluated by the HADS.[30] The study showed an excellent effect of MCT intervention, but only 75% of patients completed the entire treatment process.[30] Zahedian *et al* conducted MCT intervention on 24 patients and found MCT can significantly improve depression, but the sample size was limited.[31] In summary, inconsistent measurement tools, intervention types and participant characteristics make it difficult to obtain effective clinical evidence.

To the best of our knowledge, this study is the first comprehensive evidence for the application of MCT in chronic disease patients, and plays a crucial role in clinical intervention of depression. The anticipated benefits of this research encompass: (1) exploring the clinical efficacy of MCT intervention on depression and anxiety; (2) fostering a deeper comprehension of the psychological mechanism of MCT by using metacognitive beliefs as a secondary outcome and (3) discerning if the efficacy varies in specific MCT and the reasons for the differences.

There were several limitations in this study. First, due to differences in outcome measurements, intervention intensities and types of scales, there may exist a high degree of clinical and statistical heterogeneity. If so, we will conduct subgroup analysis to identify heterogeneity sources. Second, although many clinical trials of MCT have been conducted, as an emerging psychological therapy, there may be many unpublished studies, and the lack of these data may have an impact on the research results. Therefore, we will also include clinical trial data to reduce this impact. Third, only English and Chinese literature was included in the analysis, which may have an impact on the results. We will discuss the impact in the discussion section.

ETHICS AND DISSEMINATION

Ethical approval is not required in this study because the patients' personal information is not involved. The findings of the systematic review and meta-analysis will be published in a peer-reviewed journal and presented at conferences. Any changes in this protocol will be updated in PROSPERO and explanations of these modifications will be stated in the paper of this review.

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Contributors PPW, CS and QZ were responsible for the formulation of the article framework. ZZ, JG and PPW were responsible for the data collection and meta-analysis process. QZ was responsible for the content supplement. PW, PPW and CS were responsible for the feasibility analysis and improvement of the article. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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