The efficacy of cognitive-behavioral therapy-based intervention on Type II diabetes patients with comorbid metabolic syndrome - a randomised controlled trial

Background

Diabetes mellitus [1] is a group of metabolic diseases characterized by hyperglycemia, caused by defective insulin secretion or impaired biological effects, or both [2]. Type 2 diabetes (T2DM) is the most common, and the proportion of T2DM patients accounts for more than 90% of all diabetes patients [3]. The global diabetes map released by the International Diabetes Federation (IDF) in 2019 showed that there were 463 million adults with diabetes globally. It is estimated that by 2030, the number of people with diabetes will reach 578.4 million [4]. At the same time, the number of people with diabetes in China ranks first in the world, up to 116.4 million [4]. Poor control of diabetes leads to a series of complications, such as dry mouth, fatigue, limb numbness, and other clinical symptoms, which seriously impair patients' quality of life.

Metabolic syndrome (MS) refers to the pathological state in which the body's protein, fat, carbohydrates, and other substances are metabolically disordered [5]. It is a complex set of metabolic disorder syndromes consisting of multiple metabolic abnormalities, including central obesity, glucose metabolism disorder, lipid metabolism disorder, and elevated blood pressure. MS is closely associated with the development of DM, cardiovascular disease, and mortality. Alarmingly, according to the US National Health and Nutrition Examination Survey, more than 1 in 3 adults have MS [6]. Furthermore, according to a meta-analysis with a total population of 226,653 Chinese subjects, results showed that among subjects aged 15 years and older, the pooled prevalence of MS was 24.5% [7]. Therefore, effectively intervening with MS will

significantly improve the body's abnormal metabolic level, delay the development of the disease, and achieve the goal of preventing diabetes and delaying the development of the disease.

DM is a preventable, chronic, and lifelong disease with many complications associated with cardiovascular disease. Because of the long-term nature and complexity of disease treatment, DM patients have experienced tremendous psychological pressure, often accompanied by anxiety, depression, and other negative emotions [8, 9], even developing into psychological disorders. DM patients with mood disorders such as anxiety and depression often show loss of interest and pleasure and a lack of concentration, accompanied by emotions such as anger and fear, which are not conducive to the control of diabetes and reduce the quality of life of patients. Therefore, effectively alleviating the negative emotions of DM patients is also essential for the relief of the disease.

Cognitive-behavioral therapy (CBT), which has sprung up in recent years, changes patients' non-adaptive cognition and behavior by developing therapeutic alliances, psychological education, cognitive reconstruction, and behavioral activation to improve self-management and achieve the goal of treatment. Some studies have applied it to the prevention and treatment of diabetes and found positive effects. Pan and colleagues [10] did research and found that CBT-based intervention significantly impacted patients with T2DM in reducing fasting blood glucose, glycated hemoglobin, and systolic and diastolic blood pressures compared to the control group. Clarke and colleagues [11] did a web-based CBT intervention and found that patients in the intervention group had better blood glucose monitoring behaviors and medication compliance when compared to the control group. Yang and colleagues [12] did a meta-analysis, and the findings indicated that CBT-based interventions were effective for improving glycaemic control and depression symptoms in adult patients with T1DM or T2DM with moderate to large effect size. Garcia-Silva and colleagues [13] applied CBT to a study to improve the compliance of the Mediterranean diet in patients with MS. They found that, compared with the control group, the intervention group had more improvements in compliance

with the Mediterranean diet and improved waist circumference and triglyceride levels.

The number of diabetic patients in China is increasing rapidly, and previous studies have shown that CBT has a positive impact on patients' health outcomes. However, there is no application of this method in DM patients with comorbid MS. Therefore, this study aims: to fill in this research gap by conducting a randomised controlled trial to evaluate the effectiveness of CBT on health outcomes in T2DM patients with comorbid MS; to guide patients to interpret disease events correctly, identify the controllable and uncontrollable aspects of the diseases, and stimulate patients' motivation for change; to help patients establish a good lifestyle and gradually improve their self-health management ability; to explore whether the intervention project guided by CBT can improve the physiological indexes, psychological indexes, and quality of life of T2DM patients with comorbid MS; to provide a scientific basis for CBT application in the rehabilitation of Chinese diabetes patients with comorbid MS; and to fill the gap in the research content and develop and enrich the mode and range of chronic disease management intervention of DM. Considering that some diabetic patients live far away from the hospital and cannot go to the endocrinology clinic to participate in all the sessions, this study will adopt the combination of online and face to face intervention modes.

Method

This study is a randomised controlled trial conducted in the Ningbo First Hospital, Ningbo City, Zhejiang Province, China. All participants will sign written informed consent before enrollment. The specific research plan is as follows.

Participants

1) Inclusion and exclusion criteria

The participants will be recruited from the Endocrinology Department of Ningbo First Hospital, Ningbo city, Zhejiang province, China. Recruited participants will be included in this research if they meet the following criteria: 1) Diagnosed T2DM with comorbid MS; 2) Age 18-75 years old; 3) Currently does not participate in similar intervention programs; 4) Sign informed consent form, willing to participate in this study, and good compliance. Participants will be excluded from the study if 1) T1DM; 2) they are pregnant; 3) taking medications unrelated to T2DM or MS; 4) had advanced diabetes complications; 5) had a severe mental illness, is not able to answer questions and participate in intervention activities; 6) cannot use the mobile phone.

The specific diagnostic criteria for diabetes refer to the report of the WHO Diabetes Expert Committee, 1999, which is as follows: typical symptoms of diabetes plus 1) random blood glucose≥11.1 mmol/L; 2) fasting blood glucose≥7.0 mmol/L; 3) oral glucose tolerance test 2 hours≥11.1 mmol/L; 4) When there is no definite hyperglycemia, it should be confirmed by repeated tests.

The specific diagnostic criteria for metabolic syndrome refers to the IDF standard (Alberti et al., 2005; Collaborators): central obesity, WC≥90cm (Chinese male) or >80cm (Chinese female) and those who have 2 or more of the following components, 1) TG≥1.70mmol/L or have received relevant treatment; 2) HDL-C<1.03mmol/L (male) or <1.30mmol/L (female), or have received relevant treatment; 3) SBP≥130 or DBP≥85mmHg, or have received relevant treatment; 4) FPG≥5.6mmol/L or have been diagnosed with T2DM.

2) Sample size

In this study, the HbA_{1c} value of diabetic patients was used as the calculation

sample index, and the intervention group and the control group have the same number of people. The formula for estimating the sample size required for the study is as follows [14]:

$$N = \frac{2S^2(Z\alpha/2 + Z\beta)^2}{\sigma^2}$$

In the formula, N represents the sample size per group; $Z_{\alpha/2}$ and Z_{β} represent the standard normal deviates for type I and type II errors, S represents the squared standard deviation, and σ^2 represents the squared difference between the treatment and control groups. By referring to the previous paper [12, 15], S=0.7%，σ=0.275%. Set the inspection level as α=0.05，$Z_{\alpha/2}$=1.96，Test efficiency 1-β=0.8，Z_{β}=0.842，Sample size for each group was calculated as 102. After considering the nonresponse (20%) and attrition (15%) conditions, we calculated the sample size as 140 per group. And the total number is estimated as 280, 140 in the intervention group and 140 in the control group.

3) Randomised grouping

Among the outpatients in the Department of Endocrinology in Ningbo First Hospital, those who meet the inclusion criteria and have signed the informed consent will participate in this intervention project. First, we will generate random integers through SPSS software. Then we will use the visual binning to randomise 280 random integers into intervention group or control group based on the ratio of 1:1. Due to the nature of the study, the researchers and participants cannot be blinded. But the data analysts will not know the grouping results and will be blinded.

4) Further into Small group

Eight to ten people will form one small group in the control or intervention groups. A Social Media group will be established for the small group. We will send the intervention schedule, intervention session materials, Q&A to the Social Media group. There will be about 28 groups, with 14 intervention groups and 14 control groups respectively.

Intervention method

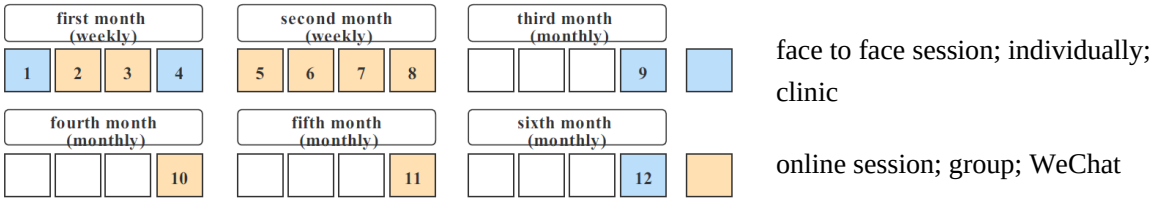
Patients in the control group will receive the usual care only. Patients in the

intervention group will receive the usual intervention + CBT-based intervention. The details of the intervention content are as follow.

1) Intervention content

Patients in the control group will receive the usual intervention only. Usual intervention includes individual health education at baseline in the endocrinology clinic, including guidance on routine medication, healthy eating, and scientific exercise according to the Guidelines for the Prevention and Treatment of Type 2 Diabetes in China (2020 Edition). We will remind patients in the Social Media group to go back to the hospital to review regularly and answer their questions. Patients will go back to hospital for regular review, take the medicine as prescribed by their doctors, receive their doctor's lifestyle guidance as usual.

Patients in the intervention group will receive usual intervention + CBT-based intervention. The CBT intervention consisted of twelve sessions. Each session lasts for about 45-60 mins. There will be 8 weekly sessions in the first two months. There will be 4 monthly sessions in the third, the fourth, the fifth month and sixth month. The first session, fourth session (at the end of the first month), ninth session (at the end of the third month), and the twelfth session (at the end of the sixth month) will be held in the endocrinology clinic individually. The face-to-face session will be recorded in the form of audio or video. At the same time, the rest of the sessions will be conducted through group video conference via Social Media and will be recorded by audio.



We will send the session schedule for the small group to the Social Media group in advance. We will send reminders to the Social Media group two days before the session. As for the session materials, we will send them to the Social Media group one day before the session. After-session quiz will be sent to the Social Media group after the session immediately. And we will remind them to upload the homework on time.

The main contents of the intervention applying CBT principles are as follows: develop an alliance between doctors and patients; confirm therapeutic targets together; psychological education, including the related basic knowledge of DM and MS; identify and correct distorted automatic thinking and intermediate beliefs about DM and MS; management of distress and anxiety; DM self-care behaviors; behavioral and lifestyle modification and so on.

CBT is a structured therapy that follows the same structure for each session. The time for each session is about 45-60 mins. The initial part includes mood examination, setting a plan, obtaining the latest information of patients, and reviewing. The middle part includes working on the specific problem, teaching cognitive behavioral skills in that context, conducting follow-up discussions, and setting homework together. The end part includes guiding patients to summarize, reviewing new homework assignments, and guiding patients to feedback. For example, the cognitive restructuring session will start with the Socratic Questioning method. First, to determine whether and how patients' automatic thoughts about DM or MS are biased, followed by the provision of healthier, more accurate ways of looking at DM. Then we will conduct a group activity to help patients learn and practice self-care and self-monitoring. Finally, we will assign homework such as making coping cards to remind them to replace the negative thoughts with new thoughts when similar thoughts occur again. The specific contents of the 12 intervention sessions are as follows.

TABLE 1 | Intervention session contents.

Session	Aim
1. Develop a treatment alliance and set treatment goals together	Build treatment alliances; identify group rules to be followed by members of the group; recognize group CBT; introducing therapy
2. Psychological education and normalization—develop a list of problems related to disease	Build treatment alliances, learn about DM and MS, and make a list of the problems caused by the disease
3. Use exposure therapy—common complications of diabetes	Understand the causes, primary symptoms, and preventive measures of common complications of DM
4. Use Socrates Questions—strengthen self-blood glucose monitoring	Understand the significance of self-blood glucose monitoring, master the methods of self-blood glucose monitoring, and develop a self-blood glucose monitoring program

5. Negative thinking substitution—maintain dietary nutrition and common diet-related distortions	Understand the relationship between diet and health; master the principles of diet for diabetes; calculate the amount of food a day that people with diabetes need; develop our diet plan; understand dietary-related cognitive distortions
6. Negative thinking substitution—maintain moderate exercise and common exercise-related distortions	Understand the relationship between exercise and health, choose the suitable activity, pay attention to the safety of the action, and understand common exercise-related distortions
7. Negative thinking substitution—adherence to drug use and common drug-related cognitive distortions	Understand the types, main mechanisms of action, side effects, and matters needing attention of commonly used drugs for diabetes; understand the characteristics of various types of insulin and insulin storage methods; master correct techniques of insulin injection; identify common misunderstandings in drug treatment
8. Use the cognitive triangle—identification and diagnosis of automatic thinking related to DM/MS	To understand automatic thinking; identify common thinking traps for DM/MS, and learning about the "cognitive triangle" for the first time
9. Use cognitive technology—identification, diagnosis, and replacement of distorted cognitive perceptions associated with DM/MS	Deepen understanding of the "cognitive triangle," identify common distortions of cognition in DM/MS, and attempt to substitute the distorted cognition
10. Use behavioral technology—identification, diagnosis, and replacement of distorted cognition associated with DM/MS	Review the "cognitive triangle" again to enhance the group's understanding of the interrelations between thoughts, emotions, behaviors, and physiological responses; Understand how to relieve negative emotions from the perspective of behavior, master the standard relaxation methods
11. Use exposure therapy—stop smoking and limit alcohol and develop good habits	Recognize the dangers of tobacco and excessive drinking, recognize the importance of good sleep, and develop good habits
12. Psychological education and normalization—level 3 prevention of diabetes	Understand the three levels of prevention of DM, review the core content of activities, and developing good lifestyle habits

2) Online intervention platform

The online sessions will be held through video conference at the Social Media. Session credits will be used to improve the patient's adherence to the intervention session. There are three ways for patients in the intervention group to accumulate their credits. Firstly, they can get 5 points if they attend the session online or face to face.

Secondly, they can get 5 points if they correctly answer six or more questions in the after-session tests. Thirdly, they can get 5 points if they upload homework on time. Meanwhile, the researchers in charge will provide guidance and answer questions in the Social Media group to help patients better understand the intervention content.

3) Intervention time

The CBT-based intervention includes twelve sessions. The intervention period is six months. The researchers who are in charge of the intervention is doctoral student in related majors. To ensure the quality of the intervention, before the intervention, all the researchers involved in the intervention will participate in a unified training and conduct the intervention in strict accordance with the intervention manual.

Measurement

The specific measurement for outcome variables is as follows:

1) The biochemical index values contained in the report of the participant's physical examination at Ningbo First Hospital at baseline, post-intervention will be used as the physiological variables' values, including the value of HbA_{1c}, FBG, 2PBG, LDL-C, HDL-C, TC, TG, blood pressure, BMI, WHR, and visceral fat.

2) The scores of the scale evaluation at baseline, post-intervention will be used to assess the secondary outcome variables. It takes about 30 mins to finish the assessment. The specific scales are as follow:

Patient Health Questionnaire-9 (PHQ-9) [16, 17] will be used to measure the depression state of the subjects. It is reported that [16] it has excellent internal reliability with a Cronbach's α of 0.89. It is a nine-item self-report instrument to evaluate the patient's condition of depression in the past two weeks. Each item has a score of 0-3. The total score ranges from 0-27. As the score increases, it shows that the severity of depression is increasing. Scores of 0-4, 5-9, 10-14, 15-19, 19-27 indicate no depression, mild depression, moderate depression, moderately severe depression, severe depression, respectively. It takes about three minutes to fill out the scale.

General Anxiety Disorder 7-Item (GAD-7) [18, 19] will be used to measure the anxiety state of the subjects. It is reported [20] that it has great internal reliability with a

Cronbach's α of 0.88. It is a seven-item self-report instrument to evaluate the patient's anxiety condition in the past two weeks. Each item has a score of 0-3. The total score ranges from 0-21. As the score increases, it shows that the severity of depression is increasing. Scores of 0-4, 5-9, 10-14, 15-21 indicate no anxiety, mild anxiety, moderate anxiety, severe anxiety, respectively. It takes about two minutes to fill out the scale.

The Summary of Diabetes Self-Care Activities (SDSCA) [21] is currently the most widely used diabetes self-management assessment tool. The SDSCA has an overall reliability coefficient (Cronbach's alpha) ranged from 0.69-0.99. The scale includes a total of 6 dimensions, namely, diet management, exercise management, self-blood glucose monitoring, medication, foot care, and smoking. There are four items in the diet management dimension, two items in the exercise management dimension, two items in the self-blood glucose monitoring dimension, two items in the medication dimension, two items in the foot care dimension, and one item in the smoking dimension. The questionnaire asks patients how many days they have been engaged in each of the above dimensions in the past seven days. And it takes this number of days as the score of the item (except for the smoking item) and takes the average score of all items in each dimension as the score of that dimension. The number of smokers and the number of cigarettes per day are counted in the smoking dimension, and the score is not calculated. Each item has a score of 0-7. The higher the score, the higher the level of DM self-management; if the higher the score of a dimension, the higher the level of DM self-management of patients in that dimension. The scores of each dimension of SDSCA are divided into three grades: <2 points indicating poor DM self-management behavior, 2-5 points indicating moderate DM self-management behavior, and >5 points indicating good DM self-management behavior. It takes about three minutes to fill out the scale.

The diabetes knowledge scale [10] used in the published research will be used to assess patients' diabetes awareness. It includes ten items, including the knowledge about the normal level of glucose, symptoms of diabetes, the measurement of diabetes, glucose control, exercise and a healthy diet. The score ranges from 0 to 10, with one correct answer per item. It takes about three minutes to fill out the scale.

The Evaluation for the Effectiveness of Cognitive Behavioral Therapy will be used the assess the cognition changes for patients after the intervention. It includes 20 items, including the conception of the CBT, the ability to use cognitive and behavioral techniques to regulate his or her emotions, the ability to cope with problems related to the disease. It is modified from a published questionnaire (Yan Liu et al., 2020) with a high level of reliability of 0.94. It takes about four minutes to fill out the scale.

The SF-12 scale [22] is a US 12-item concise health measurement scale, and it is a universal scale. The SF-12 has an overall test-retest reliability coefficient ranged from 0.81-0.88 [23]. It measures the quality of life of subjects in the past four weeks. It takes about four minutes to fill out the scale.

The Pittsburgh Sleep Quality Index (PSQI) [24] will be used to evaluate the sleep status of participants for nearly one month. The PSQI has an overall reliability coefficient (Cronbach's alpha) of 0.83 [25]. The scale is divided into seven dimensions: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medication, and daytime dysfunction. 0-3 points score each item, and the total score of each part is the total score of PSQI (0-21 points). Higher sleep scores show worse sleep quality. It takes about four minutes to fill out the scale.

3) The self-designed "The Intervention Project Satisfaction Questionnaire" will also be used to assess the participants' satisfaction with the project, and the self-designed "General Situation Questionnaire for T2DM Patients with comorbid MS" will be used to collect the demographic and clinical information.

The self-compiled "Intervention Project Satisfaction Questionnaire" will be used to collect the satisfaction degree of the intervention group patients with the intervention activities. The questionnaire includes four dimensions: intervention session (content setting, time progress arrangement); intervention personnel (professionalism, service attitude); intervention effect (self-improvement degree of health management skills); group support (group support among group members). It takes about two minutes to fill out the scale.

The self-designed "General Situation Questionnaire for T2DM Patients with

comorbid MS" will be used to collect the demographic and clinical variables. The main contents include demographic and sociological data: gender, age, marital status, education level, occupation, nationality, residence, household per capita monthly income, health insurance, lifestyle data: whether smoking, drinking, diet preference, drinking preference. It takes about two minutes to fill out the scale.

Data collection

The data will be collected at the baseline and the end of the intervention.

The biochemical index values contained in the report of the participant's physical examination at Ningbo First Hospital at baseline, post-intervention, will be used as the physiological variables' values. While the scale evaluation will be done at baseline, post-intervention, it takes about 30 mins to finish the questionnaires. Patients can choose to answer the paper questionnaire or online questionnaire. We will use Epidata to do the data entry for the paper questionnaire.

The specific data collection details are listed in the table below.

TABLE 2 | List of data collection details.

Staging	Screen	Enrollment	Intervention
Visiting	V0	V1	V2
	-2w±1w	-2w±0	24w + 2w
Informed consent	√		
Inclusion/exclusion criteria	√		
General Situation Questionnaire		√	
HbA_{1c}		√	√
FBG		√	√
2PBG		√	√
Blood lipids		√	√
Physical examination		√	√
Patient Health Questionnaire-9		√	√
General Anxiety Disorder 7-Item		√	√
The Summary of Diabetes Self-Care Activities		√	√
The Diabetes Knowledge Test		√	√
The Evaluation for the Effectiveness of Cognitive Behavioral Therapy		√	√
SF-12		√	√
The Pittsburgh Sleep Quality Index		√	√
Intervention Project Satisfaction Questionnaire			√

Data analysis

1) List of related variables

The outcome variables are physiological variables, including HbA_{1c}, FBG, 2PBG, TC, TG, LDL-C, HDL-C, blood pressure, BMI, WHR, visceral fat; psychological variables, depression, and anxiety symptoms; cognitive behavior-changing variables, including cognition changes, health-related behaviors changes, awareness of disease knowledge; quality of life and sleep quality.

The grouping and time variables: intervention group; control group; pre-post-follow up.

The confounding variables for the data analysis are age, sex, education, marital status, smoke, alcohol, and exercise.

The specific variable types are as follows:

TABLE 3 | List of demographic variables.

Demographic variables	Type of variable	
age	continuous variable	confounding
sex	categorical variable	confounding
education	categorical variable	confounding
marital status	categorical variable	confounding
smoke	categorical variable	confounding
alcohol	categorical variable	confounding
exercise	categorical variable	confounding

TABLE 4 | List of outcome variables.

Outcome variable	Measure	Type of variable	Analysis method
glycosylated hemoglobin	measured value	continuous variable	Mix linear model
fasting blood glucose	measured value	continuous variable	Mix linear model
2hour postprandial blood glucose	measured value	continuous variable	Mix linear model
total cholesterol	measured value	continuous variable	Mix linear model
triglyceride	measured value	continuous variable	Mix linear model
low density lipoprotein cholesterol	measured value	continuous variable	Mix linear model
high density lipoprotein cholesterol	measured value	continuous variable	Mix linear model
blood pressure	measured value	continuous variable	Mix linear model
body mass index	measured value	continuous variable	Mix linear model

waist-to-hip ratio	measured value	continuous variable	Mix linear model
visceral fat	measured value	continuous variable	Mix linear model
depression symptoms	scale score	continuous variable	Mix linear model
anxiety symptoms	scale score	continuous variable	Mix linear model
health-related behaviors changes	scale score	continuous variable	Mix linear model
cognition changes	scale score	continuous variable	Mix linear model
awareness of disease knowledge	scale score	continuous variable	Mix linear model
quality of life	scale score	continuous variable	Mix linear model
sleep quality	scale score	continuous variable	Mix linear model

2) Data analysis process

Stata 15 software will be used for analysis, in which the P-value is bilateral probability and the test level 0.05. The Shapiro-Wilk test will be used to check data normality.

For continuous variables, descriptive analyses will be presented as mean and standard deviation. Independent two-sample t-tests will be used to assess the between-group differences in constant demographic characteristics and clinical variables at baseline. For the categorical variables, the descriptive analysis will be presented as percentages. A chi-square test will be used to assess the between-group differences in categorical variables at baseline.

The independent variable is the groups (CBT-based intervention vs. usual intervention). In contrast, the dependent variables were physiological variables, including HbA_{1c}, FBG, 2PBG, TC, TG, LDL-C, HDL-C, blood pressure, BMI, WHR, visceral fat; psychological variables, depression and anxiety symptoms; cognitive behavior-changing indicators, including cognition changes, health-related behaviors changes, awareness of disease knowledge; quality of life and sleep quality. The intention to treat method will be used to assess the effectiveness of the intervention program, with patients retaining in their original group, regardless of program completion. The multiple-imputation will be used to estimate missing values.

Proposed timeline

A proposed timeline for this research project is presented in table 5.

TABLE 5 | Proposed timeline for the PhD research project.

Task-list	Year 1 (2020-2021)				Year 2 (2021-2022)				Year 3 (2022-2023)			
	7-9	10-12	1-3	4-6	7-9	10-12	1-3	4-6	7-9	10-12	1-3	4-6
Literature Research												
Paper 1: Effectiveness of cognitive-behavioral therapy-based interventions on health outcomes in patients with CHD: A meta-analysis												
Tentatively accepted with minor changes with two reviewers by World Journal of Psychiatry.												
Paper 2: The efficacy of cognitive-behavioral therapy-based interventions on patients with hypertension: a systematic review and meta-analysis												
Has been published online by the Preventive Medicine Reports on Jul 6.												
Paper 3: The efficacy of cognitive-behavioral therapy-based interventions on patients with diabetes: a systematic review and meta-analysis												
Undertake systematic review and submit it for publication												
RCT: The efficacy of cognitive-behavioral therapy-based intervention on type II diabetes patients with comorbid metabolic syndrome—a randomised controlled trial												
Data collection												
Paper 4: Differences of influencing factors for blood glucose among poorly controlled T2DM patients with comorbid MS and well-controlled T2DM patients with comorbid MS												
data analysis, write up, submit it for publication												
Paper 5: The efficacy of cognitive-behavioral therapy-based intervention on physiological and psychological health outcomes in T2DM patients with comorbid MS												
data analysis, write up, submit it for publication												
Paper 6: The efficacy of cognitive-behavioral therapy-based intervention on quality of life and sleep quality in T2DM patients with comorbid MS.												

data analysis, write up, submit it for publication												
Thesis Tasks												
Preparation for Confirmation												
Ethical Clearance												
Introduction												
Literature Review												
Methods												
Results												
Literature Review Update												
Discussion												
Conclusion												
Thesis Revisions												

Anticipated holidays	Year 1 (2020-2021)				Year 2 (2021-2022)				Year 3 (2022-202)			
	7-9	10-12	1-3	4-6	7-9	10-12	1-3	4-6	7-9	10-12	1-3	4-6
2 weeks (Chinese New Year: 11th -26th Feb)												
2 weeks (Chinese New Year: 31th Jan -7th Feb)												
2 weeks (Christmas Holiday: 25th Dec-8th Jan)												

References

1. Cohen BE, Edmondson D, Kronish IM. State of the Art Review: Depression, Stress, Anxiety, and Cardiovascular Disease. *Am J Hypertens* 2015;28(11):1295-1302. [PMID: 25911639 10.1093/ajh/hpv047]
2. Khan P, Qayyum N, Malik F, Khan T, Khan M, Tahir A. Incidence of Anxiety and Depression Among Patients with Type 2 Diabetes and the Predicting Factors. *Cureus* 2019;11(3):e4254. [PMID: 31131177 10.7759/cureus.4254]
3. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature reviews Endocrinology* 2018;14(2):88-98. [PMID: 29219149 10.1038/nrendo.2017.151]
4. Xie X. Development and application of diet health belief questionnaire for patients with type 2 diabetes [Master]: Bengbu Medical College; 2020.
5. Saklayen MG. The Global Epidemic of the Metabolic Syndrome. *Current hypertension reports* 2018;20(2):12. [PMID: 29480368 10.1007/s11906-018-0812-z]
6. Sherling DH, Perumareddi P, Hennekens CH. Metabolic Syndrome. *Journal of cardiovascular pharmacology and therapeutics* 2017;22(4):365-367. [PMID: 28587579 10.1177/1074248416686187]
7. Li R, Li W, Lun Z, Zhang H, Sun Z, Kanu JS, et al. Prevalence of metabolic syndrome in Mainland China: a meta-analysis of published studies. *BMC public health* 2016;16:296. [PMID: 27039079 10.1186/s12889-016-2870-y]
8. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes care* 2001;24(6):1069-1078. [PMID: 11375373 10.2337/diacare.24.6.1069]
9. Grigsby AB, Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. Prevalence of anxiety in adults with diabetes: a systematic review. *Journal of psychosomatic research* 2002;53(6):1053-1060. [PMID: 12479986 10.1016/s0022-3999(02)00417-8]
10. Pan X, Wang H, Hong X, Zheng C, Wan Y, Buys N, et al. A Group-Based Community Reinforcement Approach of Cognitive Behavioral Therapy Program to Improve Self-Care Behavior of Patients With Type 2 Diabetes. *Frontiers in psychiatry* 2020;11:719. [PMID: 32793007 10.3389/fpsyt.2020.00719]
11. Clarke J, Sanatkar S, Baldwin PA, Fletcher S, Gunn J, Wilhelm K, et al. A Web-Based Cognitive Behavior Therapy Intervention to Improve Social and Occupational Functioning in Adults With Type 2 Diabetes (The SpringboarD Trial): Randomized Controlled Trial. *Journal of medical Internet research* 2019;21(5):e12246. [PMID: 31115345 10.2196/12246]
12. Yang X, Li Z, Sun J. Effects of Cognitive Behavioral Therapy-Based Intervention on Improving Glycaemic, Psychological, and Physiological Outcomes in Adult Patients With Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trials. *Frontiers in psychiatry* 2020;11:711. [PMID: 32848906 10.3389/fpsyt.2020.00711]
13. Garcia-Silva J, N NN, Peralta-Ramírez MI, García-Sánchez A, Ferrer-González M, Caballo VE. Efficacy of Cognitive Behavioral Therapy in Adherence to the Mediterranean Diet in Metabolic Syndrome Patients: A Randomized Controlled Trial. *Journal of nutrition education and behavior* 2018;50(9):896-904. [PMID: 30100127 10.1016/j.jneb.2018.06.003]
14. Inouye J, Li D, Davis J, Arakaki R. Psychosocial and Clinical Outcomes of a Cognitive Behavioral Therapy for Asians and Pacific Islanders with Type 2 Diabetes: A Randomized Clinical Trial. *Hawai'i*

journal of medicine & public health : a journal of Asia Pacific Medicine & Public Health 2015;74(11):360-368. [PMID: 26568899]

15. Whitehead LC, Crowe MT, Carter JD, Maskill VR, Carlyle D, Bugge C, et al. A nurse-led education and cognitive behaviour therapy-based intervention among adults with uncontrolled type 2 diabetes: A randomised controlled trial. *Journal of evaluation in clinical practice* 2017;23(4):821-829. [PMID: 28397334 10.1111/jep.12725]

16. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine* 2001;16(9):606-613. [PMID: 11556941 10.1046/j.1525-1497.2001.016009606.x]

17. van Steenbergen-Weijenburg KM, de Vroege L, Ploeger RR, Brals JW, Vloedbeld MG, Veneman TF, et al. Validation of the PHQ-9 as a screening instrument for depression in diabetes patients in specialized outpatient clinics. *BMC health services research* 2010;10:235. [PMID: 20704720 10.1186/1472-6963-10-235]

18. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of internal medicine* 2006;166(10):1092-1097. [PMID: 16717171 10.1001/archinte.166.10.1092]

19. Xu C, Dong Z, Zhang P, Chang G, Xiang Q, Zhang M, et al. Effect of group cognitive behavioural therapy on psychological stress and blood glucose in people with type 2 diabetes mellitus: A community-based cluster randomized controlled trial in China. *Diabetic medicine : a journal of the British Diabetic Association* 2021;38(2):e14491. [PMID: 33296541 10.1111/dme.14491]

20. Tovote KA, Fleer J, Snippe E, Peeters AC, Emmelkamp PM, Sanderman R, et al. Individual mindfulness-based cognitive therapy and cognitive behavior therapy for treating depressive symptoms in patients with diabetes: results of a randomized controlled trial. *Diabetes care* 2014;37(9):2427-2434. [PMID: 24898301 10.2337/dc13-2918]

21. Wu Y. The study of intervention of Mindfulness-Based Stress Reduction in Type 2 Diabetes Patients in community [Master]: Nanjing University of Traditional Chinese Medicine; 2019.

22. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical care* 1996;34(3):220-233. [PMID: 8628042 10.1097/00005650-199603000-00003]

23. de Groot M, Shubrook JH, Hornsby WG, Jr., Pillay Y, Mather KJ, Fitzpatrick K, et al. Program ACTIVE II: Outcomes From a Randomized, Multistate Community-Based Depression Treatment for Rural and Urban Adults With Type 2 Diabetes. *Diabetes care* 2019;42(7):1185-1193. [PMID: 31221693 10.2337/dc18-2400]

24. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry research* 1989;28(2):193-213. [PMID: 2748771 10.1016/0165-1781(89)90047-4]

25. Alshehri MM, Alenazi AM, Alothman SA, Rucker JL, Phadnis MA, Miles JM, et al. Using Cognitive Behavioral Therapy for Insomnia in People with Type 2 Diabetes, Pilot RCT Part I: Sleep and Concomitant Symptom. *Behavioral sleep medicine* 2020:1-20. [PMID: 33108932 10.1080/15402002.2020.1831501]