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Research article

Efficacy and safety of combined Chinese and western medicine in the treatment of metabolic syndrome: A network meta-analysis of randomized controlled trials

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ABSTRACT

Objectives: To comprehensively analyze the randomized controlled clinical trials of integrated traditional Chinese medicine (TCM) and western medicine in the treatment of metabolic syndrome (MetS), and to explore the clinical efficacy and safety of different TCM combined with western medicine for MetS. The purpose of this study is to provide specific suggestions for clinical guidance in the treatment of MetS.

Methods: A comprehensive literature review was conducted across several databases, including China Knowledge Network, Wanfang Data, VIP Information, China Biomedical Literature Service System, Embase, PubMed, and Web of Science, up to October 2023. The scope of this review was confined to RCTs focusing on the treatment of metabolic syndrome through an integrated approach of TCM and Western medicine. The primary efficacy endpoints analyzed were clinical efficacy, fasting blood glucose (FBG), triglyceride (TG), and high-density lipoprotein (HDL). Data synthesis and analysis were performed using Stata 16 and RevMan 5.4 for both traditional and network meta-analyses.

Results: The findings from both traditional and network meta-analyses reveal that the combination of JiangZhiHuoXue pills (JZHX) + Conventional Western Medicine (CWM) significantly reduces FBG levels. Similarly, the AnShenNingXin capsules (ASNX) + CWM combination markedly lowers TG levels, while the FuFangQiMa capsules (FFQM) + CWM combination shows enhanced efficacy in elevating HDL levels. Notably, the combination of KangNing capsules (KNJN) + CWM demonstrates a more pronounced clinical effect compared to CWM/placebo alone.

Conclusions: The study concludes that the synergistic combination of TCM and Western medicine exhibits superior therapeutic benefits in treating MetS compared to CWM/Placebo treatments alone. The combinations of JZHX, AXNX, FFQM, and KNJN with CWM emerge as potentially effective treatments.

Abbreviations: MetS, Metabolic Syndrome; RCT, Randomized Controlled Trial; NMA, Net meta-analysis; SUCRA, Surface Under the Cumulative Ranking Curve; TCM, Traditional Chinese Medicine; CWM, Conventional Western Medicine.

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1. Introduction

Metabolic syndrome (Metabolic Syndrome, MetS) is a metabolic disorder syndrome, which involves the metabolic imbalance of proteins, fats and carbohydrates. It often has the following characteristics: the common disease basis is insulin resistance, related to obesity, accompanied by a series of diseases, such as hyperglycemia, hypertension, dyslipidemia and so on [1]. These factors interact to accelerate atherosclerosis and vascular damage, thus significantly increasing the risk of cardiovascular diseases such as heart disease and stroke [2]. At present, nearly 40 % of the world's population is facing health problems related to overweight and obesity, and this trend increases the global burden of MetS [3]. In addition, projections show that high blood pressure, high body mass index (BMI) and fasting blood glucose (FBG) will evolve into major global risk factors for loss of life by 2040, highlighting the severity of metabolic risk [4]. The universality and complexity of MetS have made it a major challenge in the field of global public health. Therefore, there is an urgent need for effective prevention and treatment strategies to meet this challenge.

At present, in the clinical treatment of MetS, weight management, anti-insulin resistance drugs and lipid-lowering therapy are the main treatment methods. As the basic treatment of MetS, weight management aims to adjust lifestyle through physical exercise and reasonable diet in order to reduce body weight and optimize metabolic parameters. Physical exercise has been shown to significantly improve the metabolic health of patients with MetS, which is essential for preventing complications and maintaining long-term health [5,6]. Specific diets, such as ketogenic diets, may bring additional benefits to patients with type 2 diabetes under medical supervision [7]. The high fruit and vegetable intake of the Mediterranean diet provides nutrition for MetS patients, and its anti-inflammatory and antioxidant properties may promote metabolic health, which also needs to be carried out under professional guidance [8,9]. Anti-insulin resistance drugs, such as metformin, effectively reduce blood glucose and body weight by improving liver insulin resistance and inhibiting endogenous glucose production, while having potential cardiovascular protection, are recommended as the first choice for the treatment of type 2 diabetes, although in some cases a combination of drugs is needed to more comprehensively control abnormal glucose metabolism and reduce side effects [10]. Beta and statins play a key role in the management of blood lipids. Fibrates significantly reduce the level of serum triglyceride by activating PPAR α receptor, but it is necessary to guard against the increase of liver enzyme and creatinine level [11]. Statins have become the first choice for the treatment of dyslipidemia because of their ability to reduce cholesterol and prevent coronary heart disease [12]. Despite the diversity of treatments available, the increase in the incidence of MetS highlights the urgent need to develop comprehensive treatments that are more effective and have fewer side effects.

The recognition of traditional Chinese medicine (TCM) in the world is gradually increasing, especially in the treatment of MetS combined with western medicine shows great potential. The core advantage of TCM lies in its unique overall concept and principle of treatment based on syndrome differentiation, which makes the treatment not only limited to the relief of symptoms, but also to comprehensively adjust and improve the overall health status of patients. The advantage of TCM in the treatment of MetS lies in its multi-target mechanism, which is realized by a variety of active components in TCM, which cooperate with multiple biological pathways and provide comprehensive intervention. Previous studies have shown that a single drug can optimize metabolic indexes pertinently [13–15]. TCM's personalized compound treatment scheme, tailored according to the patient's physique and specific condition, not only effectively regulates glucose and lipid metabolism, enhances the therapeutic effect, but also may reduce side effects [16–18]. TCM treatment of MetS is not limited to drug therapy, but also includes lifestyle adjustments such as diet, exercise and emotional management to promote overall health and disease prevention. In addition, emerging studies have emphasized the role of intestinal flora in the pathogenesis of MetS, while TCM intervention shows hope in regulating intestinal microecology [19]. The combination of TCM and western medicine can exert the synergistic effect of multi-mechanism and multi-pathway, effectively improve the symptoms of MetS, and reduce the risk of adverse reactions such as gastrointestinal reaction and muscular toxicity. This comprehensive treatment strategy is not only of great significance, but also a promising strategy for the treatment of MetS, which provides a new prospect for the management of MetS.

Proprietary Chinese medicine has been approved by the national or local drug regulatory authorities. In the face of MetS, a syndrome that includes multiple symptoms, western medical treatment often requires a combination of multiple drugs, but most of the included literature does not provide a detailed and specific description of the western medical treatment of the control group, which is usually generalized as conventional western medical treatment, which means that patients with hypertension, hyperlipidemia, hyperglycemia, etc., are treated with antihypertensive, lipid-regulating, hypoglycemic and other treatments in accordance with the principles of national or international guidelines on the use of medications, involving Insulin, Rosiglitazone, Atorvastatin, Fenofibrate, Acarbose, Valsartan, Metoprolol, Irbesartan and Hydrochlorothiazide, Enalapril. Glimepiride, Repaglinide and many other drugs. Therefore, in this study, the combined Western medicine drug treatment measures and placebo treatment measures were uniformly defined as conventional Western medicine/placebo (CWM/placebo). This study used network meta-analysis (NMA), an advanced technique that goes beyond the limitations of traditional meta-analysis by directly comparing and indirectly comparing multiple interventions. NMA was conducted to assess the clinical efficacy of different Chinese herbal medicines combined with Western medicines in the treatment of MetS by conducting randomized controlled trials (RCTs) of combined Chinese and Western medicines in the treatment of MetS. The goal of this study is to provide specific recommendations and clinical guidance for the treatment strategy of MetS, with the aim of optimizing treatment protocols and achieving personalized and precision medicine.

2. Methods

2.1. Inclusion criteria

The inclusion criteria include: (1) the type of study is RCT; (2) the subjects are patients who meet the diagnostic criteria of MetS. (3) in terms of intervention measures, the control group was treated with CWM/placebo (including healthy diet, general exercise and drug therapy, and patients with hypertension, hyperlipidemia and hyperglycemia were treated with antihypertensive, lipid-lowering and hypoglycemic therapy in accordance with national or international guidelines), while the treatment group used additional proprietary Chinese medicines approved by national or local drug regulatory authorities on this basis. (4) the clinical efficacy indicators concerned by this study should be reported in the included literature. (5) the literature data should be available from the public platform.

2.2. Exclusion criteria

The excluded research criteria are as follows: (1) Literature on the combination of two or more TCM intervention methods. (2) Include the literature that the patients are children, pregnant women and other special groups. (3) The literature that the outcome index is not consistent with the design of this study. (4) The literature in which the research data is incorrect or the information is incomplete and the data cannot be integrated; the literature with full text cannot be obtained; the literature published repeatedly or with similar content is included only the one with the most complete data, in order to reduce data duplication, avoid publication deviation and improve the reliability of the results.

2.3. Search strategy

China Knowledge Network, Wanfang Data, VIP Information, China Biomedical Literature Service System, Embase, PubMed, and Web of Science were searched by computer. The search time range is from the date of the establishment of each database to October 2023. 2 researchers developed search strategies based on the Cochrane Handbook of Systematic Evaluation. The Chinese search words include "MetS", "tablet", "pill", "powder", "ointment", "Dan", "capsule", "granule", "dropping pill", "oral liquid", "proprietary Chinese medicine", "traditional Chinese and western medicine", "random"control"group", and excluding "mice", "pig" and "rabbit". English search words include: "pill", "tablet", "powder", "ointment", "unguents", "salve", "unguent", "paste", "skin ointment", "capsule", "micro-capsule", "granule", "drop pills", "al liquid", "chinese medicine", "Metabolic Syndrome", "Randomized Controlled Trials", etc., and exclude "mice", "rabbit" and "pig". The retrieval strategy adopts the method of combining subject words with free words, and also includes a list of references tracking related literature. For specific retrieval strategies for each database, please see supplementary materials.

2.4. Literature screening and information extraction

The literature screening process was conducted independently by two researchers using EndNote and NoteExpress. First of all, independently review the title and abstract, and according to the preset criteria to exclude irrelevant literature, and then read the full text to finally determine the included literature. Four researchers were tasked with the detailed analysis of the selected literature. They independently read the full texts, extracted pertinent data, and managed this information using Excel. The extracted data encompassed a range of information, including publication details (title, first author, journal name, year of publication), subject characteristics (population characteristics, sample size, gender, age), intervention measures (drug name, dosage, treatment duration), and outcome indicators (both pre- and post-treatment), as well as information regarding the risk of bias. Upon completion of the literature screening and data extraction process, a cross-check was performed to ensure consistency and accuracy. Discrepancies were resolved through consultation with a third party, if necessary.

2.5. Risk of bias assessment

The two evaluators independently used the Cochrane evaluation method to evaluate the quality of the literature from seven aspects, one by one according to "low risk", "high risk" and "ambiguity". The assessment was facilitated by the use of RevMan 5.4 software for automated processing. The results of these evaluations were then cross-checked for consistency. In cases of disagreement, resolution was sought through discussion or, if necessary, by consulting a third party.

2.6. Statistical analysis

In this study, RevMan 5.4 was used to evaluate the methodological quality of the selected literature, and Stata 16 was used to conduct Bayesian network meta-analysis (NMA). For binary data, we calculate odds ratio (OR), and for continuous data, we calculate Standardized Mean Difference (SMD), both with 95 % credible interval (CI). The fixed effect or random effect model is selected based on the data characteristics. We use network diagrams to depict direct comparisons and correlations between interventions. X^2 test and I^2 statistics were used to quantify heterogeneity, and node splitting analysis was used to check the consistency of direct and indirect evidence. The effectiveness of the intervention was ranked according to surface under the cumulative ranking curve (SUCRA) [20]. Through the comprehensive analysis of a variety of outcome indicators, the overall effect of different intervention measures was

evaluated, and the stability of the results was ensured by sensitivity analysis. Finally, a funnel chart is drawn to check for possible publication bias.

The whole research process follows the PRISMA extension guide [21] and is registered on the PROSPERO platform (registration number: CRD42023492978).

3. Results

3.1. Literature search and screening

A total of 3100 articles were obtained (2497 in Chinese and 603 in English). After repetitive articles were excluded, the remaining 1988 articles were left. After continuing to read the title and abstract, 257 items that may be relevant are initially included. After reading the full text, 23 kinds of proprietary Chinese medicines and 25 items of [22–46] RCTs were included (Fig. 1). The duration of all interventions is relatively standardized and converted into a common unit, month. Basic information is provided in Table 1.

3.2. Basic characteristics of literature

In terms of random sequence generation methods, 23 studies used methods such as random number tables and dice rolls, which were considered to be low risk, while two other studies did not specify the specific way in which they were randomly grouped, so their bias risk is unknown. With regard to allocation concealment, only one study used sealed and opaque envelopes and was considered low-risk; other studies did not mention the implementation of allocation concealment, resulting in unknown bias risks. For blind use by patients and experimenters, one study used a double-blind design and was identified as low-risk; another study, a single-blind design, was identified as high-risk; and other studies did not mention whether blind methods were implemented. So the risk of bias is unknown. As for the blind approach of outcome evaluators, because the outcome indicators of all studies are objective, they are considered to be low risk. In terms of outcome data integrity, the data of all studies are complete, so they are also considered to be low-

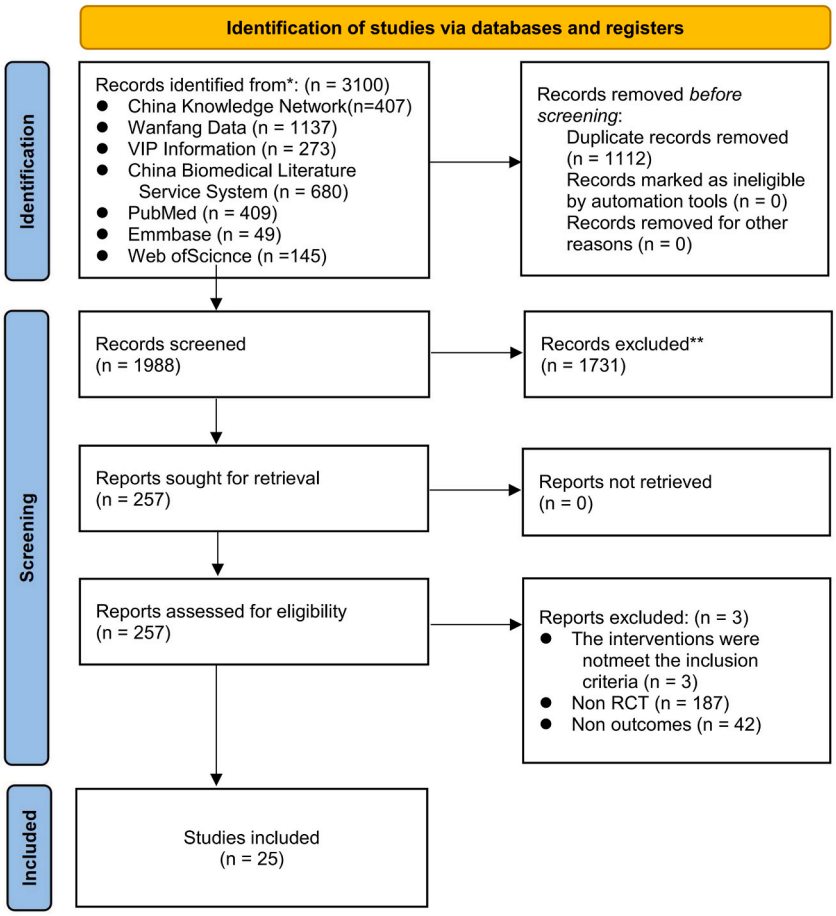


Fig. 1. Flow chart.

Table 1
Basic features of the study.

Study	Year	Age (EvsC)	Sample size	Duration of intervention	Interventions	Outcome
Ningna Bi [22]	2010	71.22 ± 1.87vs67.33 ± 2.36	60	1month	C:CWM/placebo; E:DJKL + CWM	①②③
Boqian Chen [23]	2015	64.87vs67.9	60	1month	C:CWM/placebo; E:FFSQ + CWM	①
Xiaowen Chen [24]	2010	60.7 ± 8.8vs59.3 ± 9.5	60	1month	C:CWM/placebo; E:FFJY + CWM	①②③④
Yunhu Chen [25]	2013	61.5 ± 8.45vs66.3 ± 6.78	60	3months	C:CWM/placebo; E:HYFY + CWM	①②③④
Zhanrong Feng [26]	2014	51.2 ± 9.3VS50.5 ± 9.5	60	1month	C:CWM/placebo; E:WSLSHZ + CWM	①②③④
Lianfen Hu [27]	2007	36~67	151	3months	C:CWM/placebo; E:SLXMK + CWM	①③④
Tianwei Ji [28]	2012	52.83 ± 9.73vs52.02 ± 9.81	167	3months	C:CWM/placebo; E:JTW + CWM	①②③④
Xuejian Lei [29]	2016	55.6vs54.28	102	2months	C:CWM/placebo; E:SXBX + CWM	①②③④
Yan Li [30]	2021	42~55vs44~55	140	1month	C:CWM/placebo; E:ASNX + CWM	①②③④
Shirong Liao [31]	2014	64.07 ± 7.76vs62.05 ± 7.70	61	3months	C:CWM/placebo; E:HYFY + CWM	①②③④
Yingyan Ou [32]	2006	22~67vs23~65	60	6months	C:CWM/placebo; E:KNJN + CWM	①③④
Yiwen She [33]	2014	45~79vs41~77	76	3months	C:CWM/placebo; E:YXTZ + CWM	①
Hong Tang [34]	2010	51.73 ± 10.13vs52.30 ± 14.29	60	3months	C:CWM/placebo; E:TZJT + CWM	①②③④
Li Tong [35]	2006	33~81vs32~79	60	3months	C:CWM/placebo; E:FFXQ + CWM	①②③
Weiqun Wang [36]	2009	50.24 ± 10.21vs49.03 ± 9.87	71	2months	C:CWM/placebo; E:TWK + CWM	①③④
Dong Yan [37]	2019	56.42 ± 10.74vs55.36 ± 9.52	228	2months	C:CWM/placebo; E:SDTL + CWM	①②③④
Yingqiao Yang [38]	2013	61.55 ± 8.38vs60.30 ± 6.67	60	3months	C:CWM/placebo; E:HYFY + CWM	①②③④
Jun Yao [39]	2013	30~75vs35~73	72	3months	C:CWM/placebo; E:JZHX + CWM	①②③④
Hui Zhang [40]	2006	75.82 ± 10.16vs79.184 ± 4.7	34	1month	C:CWM/placebo; E:YYHY + CWM	①
Yun Zhang [41]	2008	53 ± 9.84vs52.05 ± 8.86	50	3months	C:CWM/placebo; E:SZKL + CWM	①②③④
Shuying Zheng [42]	2015	60.7 ± 8.3vs61.5 ± 7.9	150	1month	C:CWM/placebo; E:JZJF + CWM	①②
Jiacheng Zhou [43]	2016	58.77 ± 9.73vs58.17 ± 9.51	60	2months	C:CWM/placebo; E:SQD + CWM	①②③④
Jiacheng Zhou [44]	2008	59.27 ± 6.43vs60.07 ± 6.36	60	2months	C:CWM/placebo; E:FFQM + CWM	①②③④
Xiaoming Zhuang [45]	2018	42.6 ± 6.3vs40.1 ± 7.2	60	1month	C:CWM/placebo; E:JPQS + CWM	①②③④
Cuifen Gong [46]	2020	43.2 ± 8.1vs45.1 ± 7.3	56	3months	C:CWM/placebo; E:JJSZQ + CWM	①②③④

Note: C: Control group; E: Treatment group. ①Clinical efficacy; ②FBG; ③TG; ④HDL. DJKL + CWM, DanJu g-ranules; FFSQ + CWM, FuFangSanQi granules; FFJY + CWM, FuFangJianYi granules; HYFY + CWM, HuaYuFuYua-n capsules; WSLSHZ + CWM, We-nShenLiShiHuaZhuo prescription; SLXMK + CWM, SongLingXueMaiKang capsul-es; JTW + CWM, Jia-ngTang pills; SXBX + CWM, SheXiangBaoXin pills; ASNX + CWM, AnShen-NingXin capsules; KNJN + CWM, KangNing capsules; YXTZ + CWM, YinXingTongZhi drops; TZJT + CWM, TiaoZhiJiangTang pil-ls; FFXQ + CWM, FuFangXiongQi capsules; TWK + CWM,TangWeiKang; SDTL + CWM, ShuangDanT-ongLuo granules; JZHX + CWM, JiangZhiHuoXue pills; YYHY + CWM, YangYinHeYu prescription; SZKL + CWM, ShuZheng granules; JZJF + CWM, JiangZhiJianFeicapsules; SQD + CWM, SanQi granule-s; FFQM + CWM, FuFangQiMa capsules; JPQS + CWM, JianPiQuShi prescription; JJSZQ + CWM, Ju-JuSuanZhiQing granules; CWM/Placebo, Conventional Weste-rn Medicine/Placebo.

risk. With regard to selective reporting, since the options of all studies are not available, the risk of bias is unknown. In addition, in terms of other possible biases, the included studies do not provide sufficient information to assess whether there are other biased risks, so the risks of this part are also unknown (Fig. 2).

3.3. Network evidence

The Stata16 software is used to generate the network evidence map of the intervention, the circle represents each intervention, the size of the circle indicates the number of patients taking such measures, and the thickness of each line indicates the number of studies to be compared directly. By constructing the network evidence map, we comprehensively evaluated the effects of 24 different interventions on the clinical efficacy of MetS patients (Fig. 3A); the effects of 18 different interventions on FBG levels of MetS patients (Fig. 3B); the effects of 20 different interventions on TG levels of MetS patients (Fig. 3C); and the effects of 18 different interventions on HDL levels of MetS patients (Fig. 3D). Because there is no closed loop in the network evidence diagram of the four outcome indicators, only the consistency model is used for statistical analysis.

3.4. Outcomes

3.4.1. Clinical efficacy

The NMA included 25 studies [22–46] showing that compared to CWM/Placebo, DJKL + CWM [OR = 15.16, 95%CI (4.09,56.24)]; FFSQ + CWM [OR = 6.00, 95%CI (1.48,24.30)]; FFJY + CWM [OR = 4.50, 95%CI (1.09,18.5)]; HYFY + CWM [OR = 6.39, 95%CI (2.77,14.75)]; ASNX + CWM [OR = 3.12, 95%CI (1.21,8.03)]; KNJN + CWM [OR = 40.69, 95%CI (9.15,180.99)]; TZJT + CWM [OR = 4.50, 95%CI (1.09,18.50)]; FFXQ + CWM [OR = 6.00, 95%CI (1.48,24.30)]; TWK + CWM [OR = 11.33, 95%CI (2.91,44.09)]; SDTL + CWM [OR = 4.45, 95%CI (2.18,9.09)]; JZHX + CWM [OR = 4.73, 95%CI (1.14,19.68)]; YYHY + CWM [OR = 22.86, 95%CI (2.44, 214.55)]; SZKL + CWM [OR = 6.00, 95%CI (1.07,33.65)]; JZJF + CWM [OR = 3.78, 95%CI (1.50,9.55)], were statistically different (Fig. 4A).

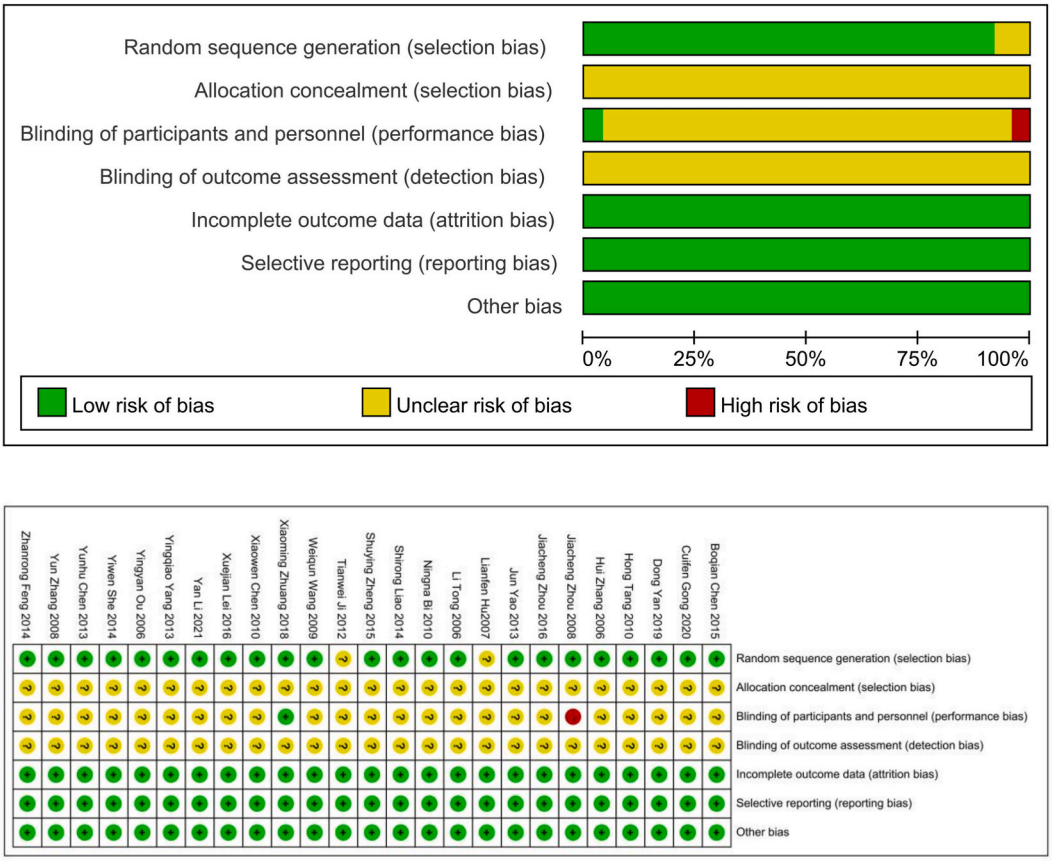


Fig. 2. Risk of bias.

According to SUCRA, KNJN + CWM is the most likely to be the best intervention in improving the total clinical effective rate. The following are the top three results of the probability ranking of the total effective rate of 24 interventions in the treatment of MetS: KNJN + CWM (95.8 %) > YYHY + CWM (86.1 %) > DJKL + CWM (84.2 %) (Fig. 5A). Additionally, the sensitivity analysis results were relatively stable (Fig. 6A).

3.4.2. FBG

The NMA included 19 studies [22,24–26,28–31,34,35,37–39,41–46] showing that compared to the control group, DJKL + CWM [SMD = 0.15, 95%CI (0.08,0.28)]; WSLSHZ + CWM [SMD = 0.24, 95%CI (0.13,0.42)]; ASNX + CWM [SMD = 0.61, 95%CI (0.43, 0.85)], etc. 8 items, with differences (Fig. 4B).

According to SUCRA, JZHX + CWM is the most probable best intervention for improving FBG levels. The following are the top three results of the probability ranking of 18 interventions for the treatment of high FBGs in MetS: JZHX + CWM (99.7 %) > DJKL + CWM (93.4 %) > WSLSHZ + CWM (88.6 %) (Fig. 5B). Additionally, the sensitivity analysis results were relatively stable (Fig. 6B).

3.4.3. TG

The NMA included 21 studies [22,24–32,34–39,41,43–46] showing that compared to controls, DJKL + CWM [SMD = 0.59, 95%CI (0.35,0.99)]; HYFY + CWM [SMD = 0.51, 95%CI (0.37,0.71)]; WSLSHZ + CWM [SMD = 0.07, 95%CI (0.03,0.14)], etc. 11 items, with differences (Fig. 4C).

According to SUCRA, ASNX + CWM is the most likely to be the best intervention in improving TG. The following are the top three results in the order of high TG probability of 20 interventions for MetS: ASNX + CWM (82.5 %) > FFJY + CWM (78.2 %) > CWM/placebo (70.7 %) (Fig. 5C). Additionally, the sensitivity analysis results were relatively stable (Fig. 6C).

3.4.4. HDL

The NMA included 21 studies [22,24–32,34–39,41,43–46] showing that compared to controls, DJKL + CWM [SMD = 0.59, 95%CI (0.35,0.99)]; HYFY + CWM [SMD = 0.51, 95%CI (0.37,0.71)]; WSLSHZ + CWM [SMD = 0.07, 95%CI (0.03,0.14)]; SLXMK + CWM [SMD = 0.29, 95%CI (0.20,0.41)], etc. 7 items, with differences (Fig. 4D).

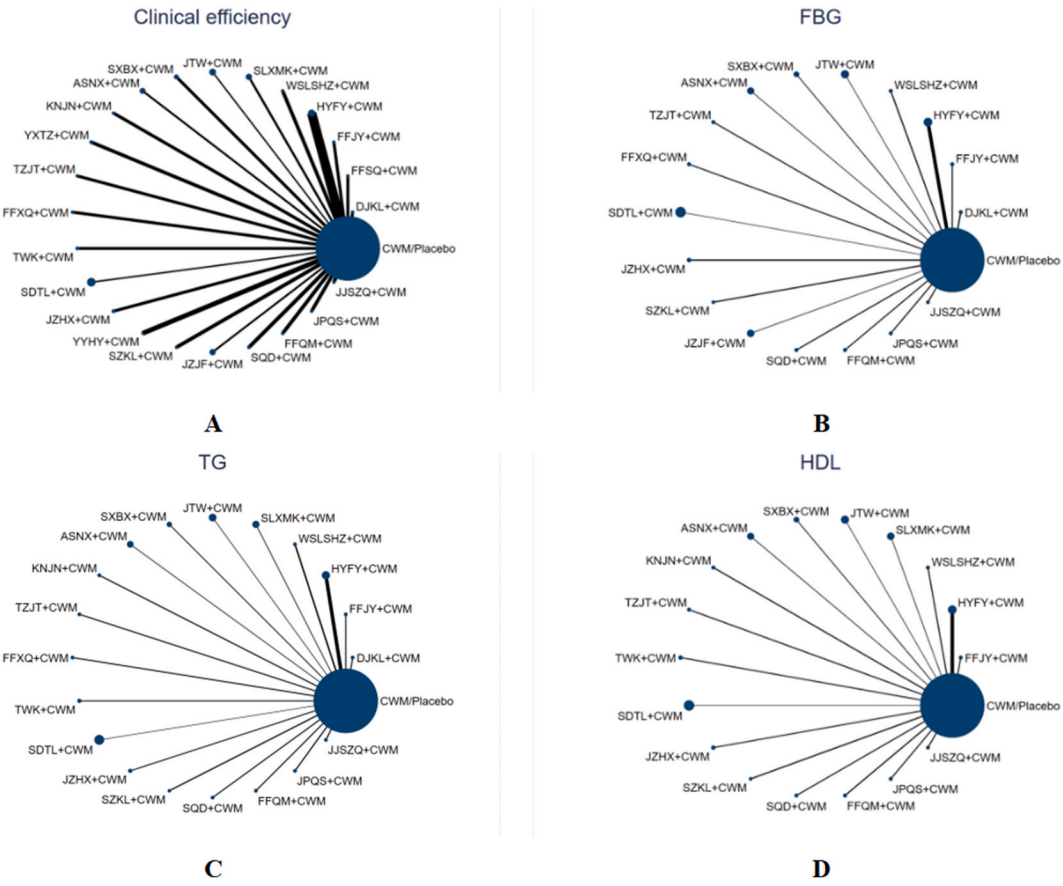


Fig. 3. Network evidence graph.

According to SUCRA, ASNX + CWM is the most likely to be the best intervention in improving TG. The following are the top three results in the order of high TG probability of 20 interventions for MetS: ASNX + CWM (82.5 %) > FFJY + CWM (78.2 %) > CWM/placebo (70.7 %) (Fig. 5D). Additionally, the sensitivity analysis results were relatively stable (Fig. 6D).

3.5. Safety analysis

12 items of RCTs described safety, of which 9 items of RCTs treatment group and control group had no obvious adverse reactions, only 3 items of RCTs showed adverse events such as abdominal pain, nausea, diarrhea, increased exhaust, anorexia and other gastrointestinal reactions and skin rash, these adverse events were acceptable.

3.6. Publication bias assessment

Publication bias was assessed for the study data of the main outcome indicators, and the funnel plot results showed that most of them were concentrated in the lower-middle position and roughly symmetrically distributed, and publication bias might exist (Fig. 7A, B, 7C and 7D).

4. Discussion

In this study, we used NMA to evaluate the efficacy of integrated traditional Chinese and western medicine in the treatment of MetS, focusing on the clinical effective rate, FBG, TG and HDL and other key indicators. Other related indicators, such as BMI, leptin, insulin, and adverse events, were not included in the analysis due to insufficient data. The consistency test for TC and LDL did not meet the standard, possibly due to variations in study design, patient characteristics, intervention details, and other factors. These were excluded to ensure the accuracy and reliability of the results.

The direct and indirect comparison results from 25 randomized controlled trials showed that the clinical effect of KNJN + CWM was more significant than that of CWM/Placebo alone, the effect of JZHX + CWM on reducing FBG was more significant, the effect of ASNX + CWM on reducing TG was more significant, and the effect of FFQM + CWM on HDL was more significant. This finding provides

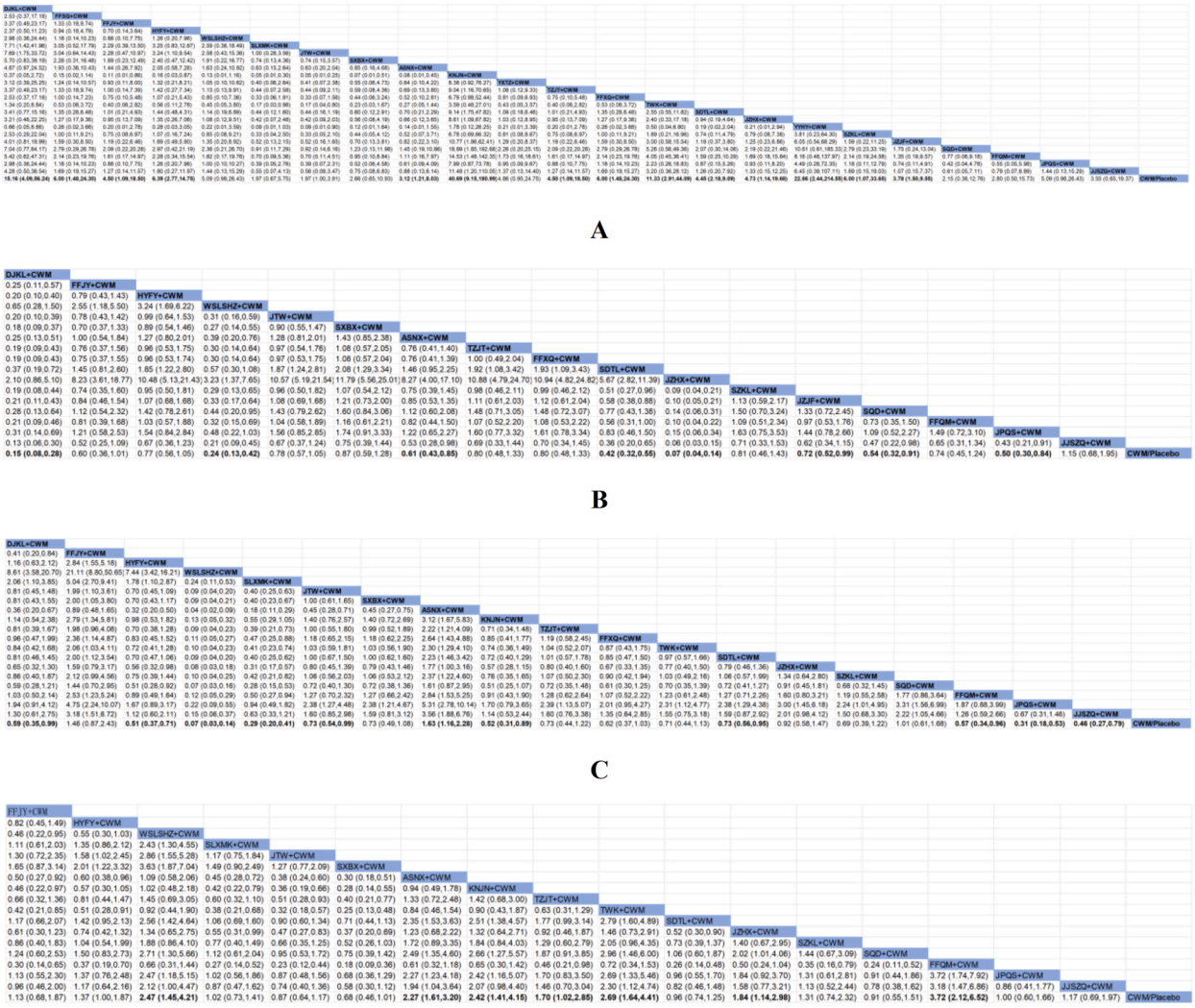
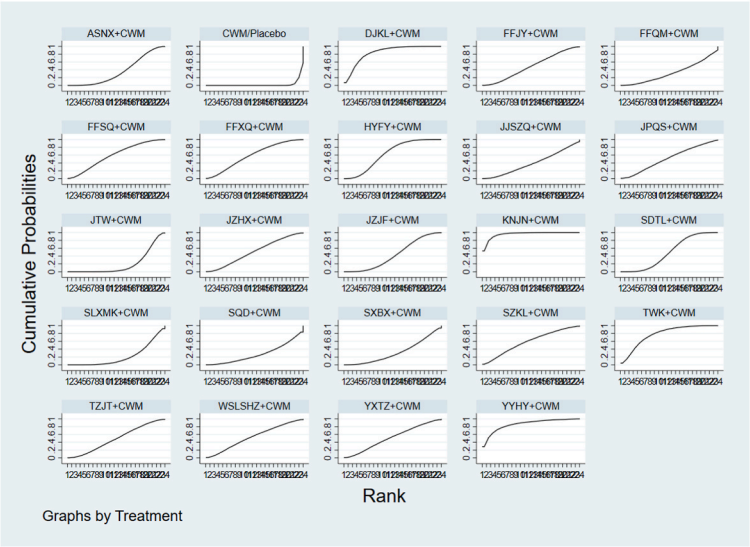


Fig. 4. Results from the NMA showing the effect of each of the interventions.

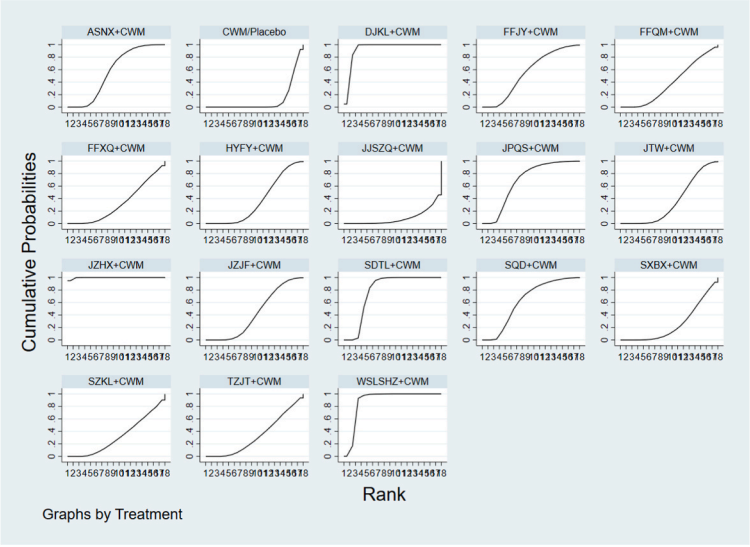
a new perspective and strategy for the clinical treatment of MetS. The specific ingredients of the four TCM that may be the best intervention measures can be found in Table 2.

Clinically, some CWMs have side effects due to intolerance in the treatment of MetS. For example, gastrointestinal side effects occurring in metformin intolerance; lactobacillosis may occur in patients with renal insufficiency taking metformin; and muscular toxicity may exist in long-term use of statins [47–49]. With the modern development of TCM, its application in treating MetS is steadily growing. As natural medicines, TCM exhibit strong pharmacological activity, including anti-inflammatory, antioxidant, and antidiabetic effects [50]. In this study, a variety of herbal medicines are included, who exert therapeutic effects by affecting core metabolic regulatory pathways through their unique bioactive components and may touch upon regulatory mechanisms at the epigenetic level. mTOR and PI3K signaling pathways not only regulate cell growth, metabolism, protein synthesis, and lipid homeostasis, but also are involved in insulin signaling, affecting the body's sensitivity to insulin, which is a key regulators in the pathogenesis of MetS. Astragalus in KNJN contains active ingredients such as astragaloside, which has anti-inflammatory and antioxidant effects, and can inhibit the activity of the PI3K/AKT/mTOR signaling pathway by up-regulating the expression of miR-155 and others, thus promoting the autophagy process, and can inhibit the expression of inflammatory factors, thus reducing insulin resistance and regulating lipid metabolism [51,52]. In addition, KNJN contains extracts of the root of Scutellaria baicalensis, such as baicalein can reduce the degradation of SIRT1 and increase its activity by inhibiting the JNK signaling pathway, which in turn inhibits the transcriptional activity of NF-κB by deacetylating p65 and reduces the expression of pro-inflammatory factors, such as IL-1β, TNF-α, and IL-6, which may help to ameliorate the pathology of obesity and related metabolic diseases [53]. Herbal components such as Pueraria Mirifica and Astragalus in JZHX have been found to enhance the efficiency of glucose absorption and utilization. The combination of Astragalus and



Treatment	SUCRA	PrBest	MeanRank
DJKL+CWM	84.2	7.2	4.6
FFSQ+CWM	59.1	0.6	10.4
FFJY+CWM	48.6	0.3	12.8
HYFY+CWM	62.9	0.0	9.5
WSLSHZ+CWM	53.7	0.9	11.6
SLXMK+CWM	21.4	0.0	19.1
JTW+CWM	20.0	0.0	19.4
SXBX+CWM	32.0	0.0	16.6
ASNX+CWM	36.2	0.0	15.7
KNJN+CWM	95.8	53.1	2.0
YXTZ+CWM	52.0	0.7	12.0
TZJT+CWM	49.1	0.2	12.7
FFXQ+CWM	58.9	0.6	10.5
TWK+CWM	77.7	4.2	6.1
SDTL+CWM	49.4	0.0	12.6
JZHX+CWM	50.7	0.3	12.3
YYHY+CWM	86.1	28.8	4.2
SZKL+CWM	58.5	1.6	10.5
JZJF+CWM	43.2	0.0	14.1
SQD+CWM	27.7	0.1	17.6
FFQM+CWM	34.4	0.2	16.1
JPQS+CWM	53.3	0.9	11.7
JJSZQ+CWM	41.5	0.2	14.5
CWM/Placebo	3.6	0.0	23.2

A

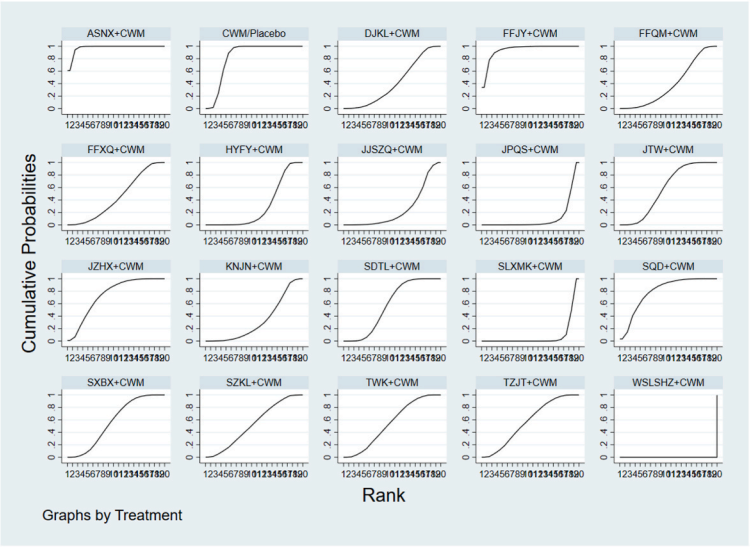


Treatment	SUCRA	PrBest	MeanRank
DJKL+CWM	93.4	5.0	2.1
FFJY+CWM	55.2	0.0	8.6
HYFY+CWM	36.3	0.0	11.8
WSLSHZ+CWM	88.6	0.3	2.9
JTW+CWM	35.3	0.0	12.0
SXBX+CWM	25.5	0.0	13.7
ASNX+CWM	57.4	0.0	8.2
TZJT+CWM	33.2	0.0	12.3
FFXQ+CWM	32.0	0.0	12.6
SDTL+CWM	78.4	0.0	4.7
JZHX+CWM	99.7	94.8	1.1
SZKL+CWM	32.3	0.0	12.5
JZJF+CWM	42.8	0.0	10.7
SQD+CWM	62.8	0.0	7.3
FFQM+CWM	38.7	0.0	11.4
JPQS+CWM	68.2	0.0	6.4
JJSZQ+CWM	8.9	0.0	16.5
CWM/Placebo	11.2	0.0	16.1

B

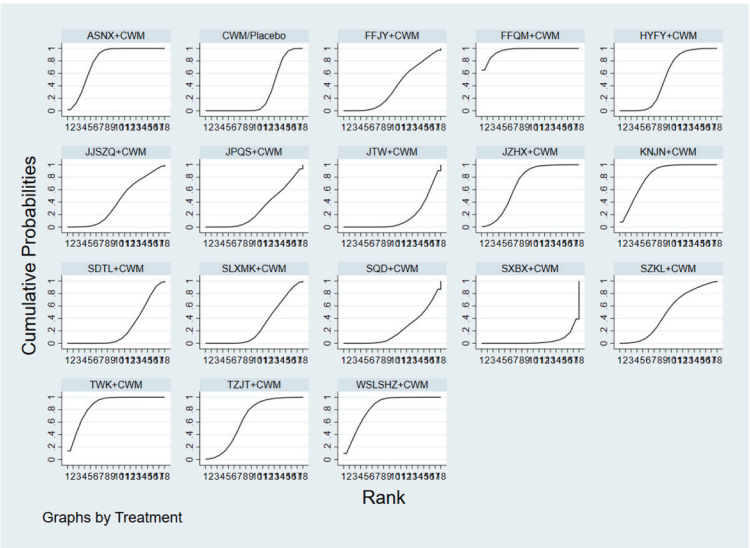
Fig. 5. Curve diagram of SUCRA of outcome indicators.

Pueraria Mirifica may regulate the AMPK signaling pathway by acting on key factors such as IL-6 and TNF-α, which in turn positively affects metabolic processes such as insulin resistance, glycogen synthesis and gluconeogenesis [54]. In addition, the anti-inflammatory properties of JZHX help to attenuate the negative effects of inflammatory mediators on the vascular endothelium, while its antioxidant capacity effectively counteracts the damage of oxidative stress on endothelial cells, thus reducing the risk of vascular complications of MetS [39]. Previous studies have shown that ASNX may be effective in alleviating disorders of glycolipid metabolism in patients with



Treatment	SUCRA	PrBest	MeanRank
DJKL+CWM	41.6	0.0	12.1
FFJY+CWM	94.0	34.0	2.1
HYFY+CWM	30.0	0.0	14.3
WSLSHZ+CWM	0.0	0.0	20.0
SLXMK+CWM	8.5	0.0	18.4
JTW+CWM	58.0	0.0	9.0
SXBX+CWM	57.5	0.0	9.1
ASNX+CWM	97.6	60.9	1.5
KNJN+CWM	33.0	0.0	13.7
TZJT+CWM	57.4	0.2	9.1
FFXQ+CWM	44.7	0.0	11.5
TWK+CWM	54.8	0.0	9.6
SDTL+CWM	57.7	0.0	9.0
JZHX+CWM	73.9	1.0	6.0
SZKL+CWM	53.1	0.3	9.9
SQD+CWM	79.3	3.5	4.9
FFQM+CWM	39.5	0.0	12.5
JPQS+CWM	10.8	0.0	18.0
JJSZQ+CWM	25.7	0.0	15.1
CWM/Placebo	82.9	0.0	4.2

C



Treatment	SUCRA	PrBest	MeanRank
FFJY+CWM	37.8	0.0	11.6
HYFY+CWM	53.0	0.0	9.0
WSLSHZ+CWM	83.6	9.7	3.8
SLXMK+CWM	30.0	0.0	12.9
JTW+CWM	16.5	0.0	15.2
SXBX+CWM	4.6	0.0	17.2
ASNX+CWM	80.3	1.6	4.4
KNJN+CWM	82.2	8.0	4.0
TZJT+CWM	65.1	0.7	6.9
TWK+CWM	87.1	13.9	3.2
SDTL+CWM	25.0	0.0	13.7
JZHX+CWM	69.5	0.9	6.2
SZKL+CWM	48.8	0.0	9.7
SQD+CWM	22.2	0.0	14.2
FFQM+CWM	96.3	65.2	1.6
JPQS+CWM	29.1	0.0	13.1
JJSZQ+CWM	40.6	0.0	11.1
CWM/Placebo	28.5	0.0	13.2

D

Fig. 5. (*continued*).

MetS by regulating estrogen levels [30]. Estrogen plays an important role in maintaining normal glucose-lipid metabolism, and proper regulation of its levels may help improve insulin resistance and dyslipidemia. ASNX contains Salvia miltiorrhiza and Yujin, whose components 15,16-Dihydrotanshinone I and curcumin have been shown to exert their multi-targeted effects in regulating lipid metabolism, enhancing insulin sensitivity, anti-inflammation, and antioxidant effects by modulating multiple key metabolic pathways, providing a potential integrative therapeutic strategy for MetS [55,56]. In addition, Salvianolic acid B in Salvia divinorum is involved in the regulation of obesity and metabolic disorders by regulating obesity-related lncRNA and circRNA expression and affecting energy metabolism and inflammatory responses [57]. Curcumin can alter chromatin structure and regulate gene expression by regulating histone acetylation, especially H3K9 and H3K18 [58]. MetS is closely associated with chronic low-grade inflammation, and previous studies have shown that FFQM reduced inflammatory markers such as VCAM-1, ICAM-1, PECAM-1, MMP-9, MCP-1, NLRP3, and TNF-α in New Zealand rabbits, which may help to improve insulin sensitivity and regulate lipid metabolism [59]. Low HDL-C levels are

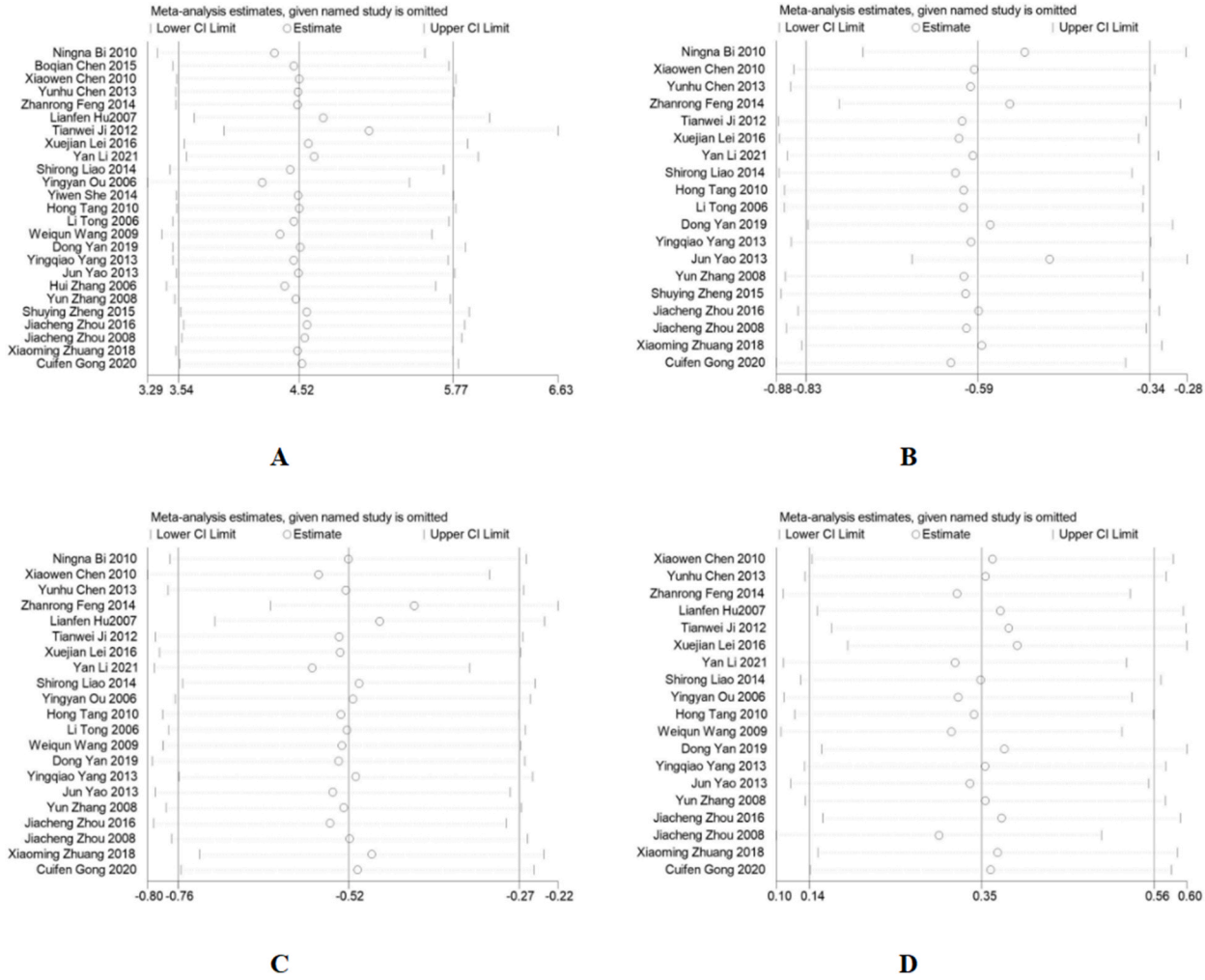


Fig. 6. Sensitivity analysis diagram.

one of the diagnostic criteria for MetS and are associated with an increased risk of cardiovascular disease. Previous studies have shown that FFQM can effectively alleviate the clinical symptoms of MetS patients, such as fatigue, dizziness, chest tightness, epigastric congestion, phlegm congestion, and body fatness, by improving insulin resistance and lipid metabolism, as well as reducing vascular damage caused by dyslipidemia, which is helpful for the prevention and treatment of cardiovascular and cerebrovascular complications [44]. Nevertheless, the specific mechanism of action of FFQM still needs further scientific studies to elucidate.

The prevalence and severity of MetS show significant differences in gender, age, physical activity and education level. The incidence of MetS is relatively low in women of childbearing age, however, after menopause, it may rise due to loss of estrogen protection [60]. Older individuals face a higher risk of MetS due to slowed metabolism. Individuals with higher levels of education are more likely to adopt a healthy lifestyle [61]. Inadequate physical activity, including low frequency of walking and strength training, as well as sedentary behavior, have been associated with an increased risk of MetS, especially in economically disadvantaged groups [62]. These findings highlight the need for personalized MetS prevention and treatment strategies. By comprehensively assessing the patient's constitution, etiology, symptoms, age and gender, and other information, TCM develops individualized treatment plans including herbs, acupuncture, and dietary therapy, aiming to restore the balance of yin and yang and promote health. This study focuses on pharmacological interventions combining Chinese and Western medicine, and more effective therapies will be further explored in the future. By integrating the holistic approach of TCM and the precision treatment of Western medicine, we aim to employ personalized treatment strategies that leverage the strengths of both medical systems to improve treatment outcomes, optimize patients' life experiences, and meet the specific health needs of patients in different socioeconomic contexts.

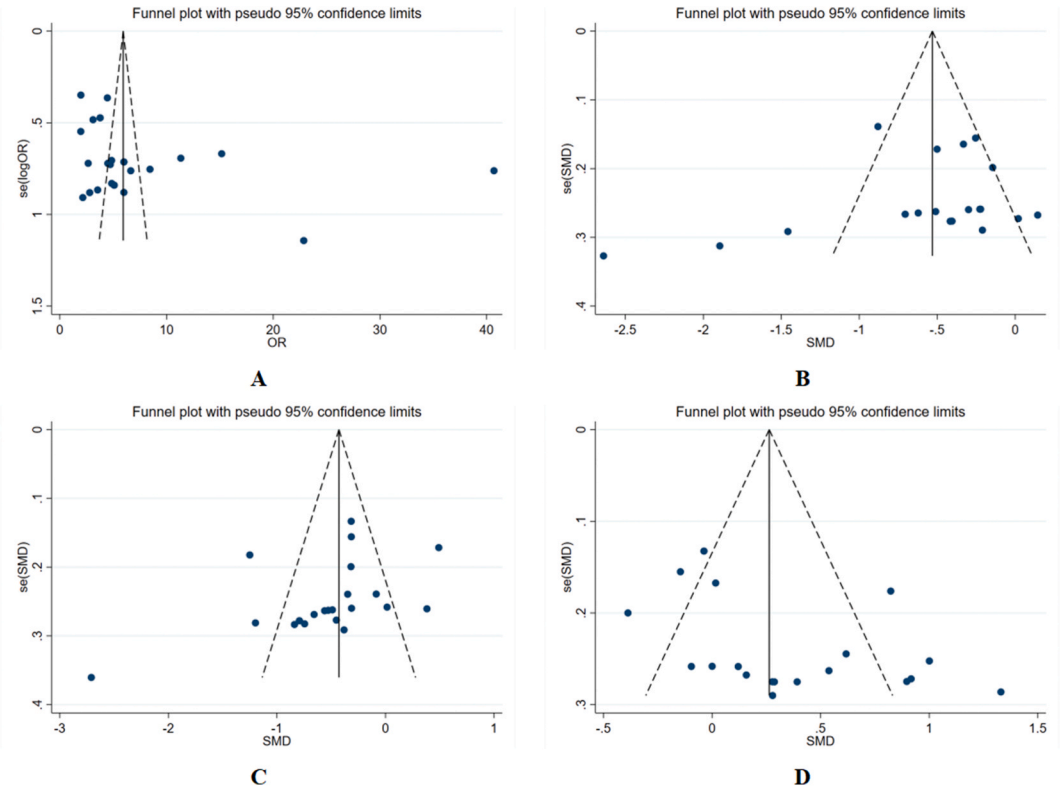


Fig. 7. Funnel plots.

Table 2
Ingredients of four kinds of TCM.

Name	Composition
KangNing capsules	Radix Astragali, Scutellaria baicalensis, Chrysanthemum, Salvia miltiorrhiza, Hawthorn, biphenyl diester.
AnShenNingXin capsules	Poria with hostwood, Lily, Polygni Multiflori Caulis, Suanzaoren, Platycladi Semen, Yuanzhi, Fructus Schisandrae Sphenantherae, Reishi, Salvia Miltiorrhiza, Yujin, Sichuan Kovase Rhizome, Zhishi, Rhizoma Anemarrhenae, Maidong, Codonopsis Pilosula.
FuFangQiMa capsules	Radix Astragali, Atractylodes, Rhizoma Pinelliae, Sichuan lovase rhizome, Eucommia, Rhizoma Gastrodiae, Poria cocos, Alisma orientalis, Tangerine Peel.
JiangZhiHuoXue pills	Radix Astragali, Cassia, Pueraria, Salvia miltiorrhiza, alisma, Polygonum multiflorum, Hawthorn, safflower.

5. Advantages and limitations

This study harnesses the analytical prowess of network meta-analysis to discern the comparative efficacy of various combinations of TCM with CWM. This methodological approach is instrumental in offering a clearer, more systematic comparison of treatment efficacies, thereby facilitating informed clinical decision-making. The insights gleaned from this analysis are poised to contribute significantly to clinical treatment strategies, offering valuable recommendations and support for practitioners in the realm of metabolic syndrome management.

Despite its methodological strengths, the study is not without its limitations, which warrant careful consideration: (1) Scope of Literature: The majority of the literature reviewed in this study is sourced from domestic Chinese research. The underrepresentation of international studies in the analysis could constrain the generalizability of the results. (2) In the included studies, there were a wide variety of drug treatments in the control group, most of which were not classified in detail and were only unified as conventional Western medicine treatment, which was not specific enough.

In response to these limitations, future research should pivot towards conducting comprehensive clinical trials characterized by larger sample sizes, multicenter collaborations, and double-blind designs. Such methodological enhancements are essential for bolstering the validity and reliability of the findings. Additionally, incorporating a more diverse array of international studies would enrich the research, ensuring a more universally relevant and nuanced understanding of TCM's efficacy in conjunction with Western medical practices for metabolic syndrome treatment.

6. Conclusion

In this study, using NMA, we found that compared with conventional western medicine alone, oral proprietary Chinese medicine combined with conventional western medicine showed advantages in improving FBG, TG and HDL. The study also determined the best order of interventions for different outcome indicators. Specifically, JZHX + CWM is effective in reducing FBG; ASNX + CWM is outstanding in reducing TG; FFQM + CWM is more effective in improving the level of HDL; and KNJN + CWM shows a better clinical effect than using CWM/placebo alone. However, it is essential to recognize the limitations inherent in this study. The conclusions drawn, while promising, call for further corroboration through additional high-quality research. Future studies are anticipated to validate and build upon these initial findings, thereby enriching the understanding and application of integrated TCM and CWM in the treatment of metabolic syndrome.

Ethical approval and to participate

Not applicable.

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Data availability statement

Data supporting the results of this study are available from the author [SZ] upon request.

CRediT authorship contribution statement

Shuang Zhao: Writing – original draft, Visualization, Methodology, Data curation, Conceptualization. **Rui Hao:** Writing – original draft, Supervision, Methodology, Data curation. **Jinyue Zhao:** Writing – review & editing, Supervision, Formal analysis, Data curation. **Kaile Ma:** Validation, Supervision, Investigation, Data curation. **Jiarui Li:** Resources, Investigation, Formal analysis. **Chuanxi Tian:** Supervision, Project administration, Investigation. **Huifang Guan:** Supervision, Resources, Investigation. **Min Li:** Writing – review & editing, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e35811.

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