Original Article

Efficacy and safety assessment of traditional Chinese patent medicine for dyslipidemia: a systematic review of randomized clinical trials with meta-analysis and trial sequential analysis

Yini Fang[1,2#], Haoran Wu[2#], Xue Liang[2#], Tianxing Li[2,3], Ruiting Jia[1], Yang Dong[4], Yanfei Zheng[2], Qi Wang[1,2], Lingru Li[2]^

[1]Basic Medical College, Zhejiang Chinese Medical University, Hangzhou, China; [2]National Institute of Traditional Chinese Medicine Constitution and Preventive Medicine, Beijing University of Chinese Medicine, Beijing, China; [3]Institute of Basic Theory for Chinese Medicine, China Academy of Chinese Medical Sciences, Beijing, China; [4]National Administration of Traditional Chinese Medicine Monitoring and Statistics Research Center, Beijing, China

Contributions: (I) Conception and design: L Li, Y Fang; (II) Administrative support: Q Wang, Y Zheng; (III) Provision of study materials or patients: R Jia, Y Dong; (IV) Collection and assembly of data: X Liang, T Li; (V) Data analysis and interpretation: Y Fang, H Wu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work as co-first authors.

Correspondence to: Yanfei Zheng, PhD; Lingru Li, PhD. National Institute of Traditional Chinese Medicine Constitution and Preventive Medicine, Beijing University of Chinese Medicine, No. 11 North Third Ring East Road, Chaoyang District, Beijing 100029, China. Email: yanfei_z@163.com; lilingru912@163.com; Qi Wang, PhD. Basic Medical College, Zhejiang Chinese Medical University, Hangzhou, China; National Institute of Traditional Chinese Medicine Constitution and Preventive Medicine, Beijing University of Chinese Medicine, No. 11 North Third Ring East Road, Chaoyang District, Beijing 100029, China. Email: wangqi710@126.com.

Background: The overall prevalence of dyslipidemia continues to increase, which poses a significant risk for coronary artery disease. Some patients with dyslipidemia do not respond to or benefit from conventional lipid-lowering therapy, which warrants the need for alternative and complementary therapies. Chinese patent medicine (CPM) has shown great potential in the treatment of dyslipidemia, but its clinical value needs to be further explored. This study aims to systematically evaluate the efficacy and safety of CPM in treating dyslipidemia.

Methods: This study was registered in INPLASY as INPLASY202330090. The randomized controlled trials included in this study were published in January 2013 to March 2023 and retrieved from the Web of Science, PubMed, Embase, Cochrane Library, SinoMed, China National Knowledge Internet, WanFang, and VIP. The bias risk in the study was independently evaluated by two reviewers using the Cochrane Randomized Trial Bias Risk Tool (RoB 2) Review Manager 5.4 software was used for the overall effect analysis and subgroup analysis of four blood lipids, and the trial sequential analysis (TSA) was conducted to check the results.

Results: A total of 69 studies were included, involving 6,993 participants. The methodological quality was in the middle level. Meta-analysis showed that CPM markedly improved the levels of total cholesterol (TC) [mean difference (MD) =−0.54 mmol/L; 95% confidence interval (CI): −0.71 to −0.37; P<0.001], triglyceride (TG) (MD =−0.43 mmol/L; 95% CI: −0.53 to −0.33; P<0.001), low-density lipoprotein cholesterol (LDL-C) (MD =−0.40 mmol/L; 95% CI: −0.50 to −0.30; P<0.001) and increased levels of high-density lipoprotein cholesterol (HDL-C) (MD =0.23 mmol/L; 95% CI: 0.18 to 0.27; P<0.001), in patients with dyslipidemia. Though CPM did not differ significantly from statins when used alone, it could improve lipid profile better in all cases when used in combination with statins and with drugs used for comorbidities or co-morbidities.

^ ORCID: 0000-0003-3716-9304.

Subgroup analysis found that the efficacy of pill formulations was superior to other formulations, and CPM showed better lipid-lowering response in the context of comorbidity. The TSA confirmed the robustness of the analysis of the LDL-C level. No significant difference was observed in the incidence of adverse events between the treatment group and the control group [relative risk (RR) =0.89; 95% CI: 0.69–1.16; P=0.40].

Conclusions: CPM can yield superior therapeutic effects in ameliorating dyslipidemia without exacerbating adverse effects as an alternative and complementary therapy. In addition, the therapeutic effect can be improved by emphasizing pill formulation and strengthening the standardization of syndromes.

Keywords: Dyslipidemia; meta-analysis; Chinese patent medicine (CPM); trial sequential analysis (TSA)

Submitted Apr 01, 2024. Accepted for publication Jun 21, 2024. Published online Jun 27, 2024.
doi: 10.21037/cdt-24-146
View this article at: https://dx.doi.org/10.21037/cdt-24-146

Introduction

Dyslipidemia is a metabolic disease primarily caused by an imbalance in the body's lipid metabolism, thereby resulting in increased levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) (1). As a common metabolic disorder, dyslipidemia can increase the risk of atherosclerosis (2), cerebral infarction (3), coronary heart disease (4), type 2 diabetes (5), obesity and fatty liver disease (6), and serves as an important material basis in the pathogenesis of atherosclerosis, which can significantly increase the risk of cardiovascular disease (7). In recent years, the global prevalence of dyslipidemia has been rapidly increasing (8-11). For instance, a survey conducted in 2018 showed that the overall prevalence of dyslipidemia in adults in China was as high as 35.6%, whereas the average level of various blood lipid components was significantly improved (12), reaching or exceeding the average level of some western countries (13). It is estimated that the number of cardiovascular events will increase by about 9.2 million between 2010 to 2030 (14), which suggests that dyslipidemia and related diseases in China might continue to increase both the social and family burden (15,16). Therefore, early prevention and treatment of dyslipidemia is crucial.

Interestingly, decreasing the level of atherogenic lipoprotein has been observed to be effective in reducing the risk of clinical atherosclerotic cardiovascular disease (ASCVD), so statin therapy remains the cornerstone of lipid-lowering therapy (17,18). However, from the pharmacokinetics standpoint, statins have relatively limited solubility and bioavailability, which limits their lipid-lowering effects (19). Some patients are intolerant to statins, especially when the drugs are given in high doses (20), and can suffer from mild liver injury (21) and skeletal muscle toxicity (22-25). Thus, for the long-term treatment of statins, more comprehensive strategies are needed to ensure the safety and compliance of patients in clinics (26). As the clinical manifestations of dyslipidemia are rather complex and can lead to many diseases, multi-targeted and personalized treatment approaches that conform to the principles, methods, prescriptions, and evidence-based treatment of the holistic view of traditional Chinese

Highlight box

Key findings

- Chinese patent medicine (CPM) can effectively improve levels of total cholesterol, triglyceride, low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol in patients with dyslipidemia. Combination therapy with CPM and statins or other drugs can improve lipid profile better than using statins alone.

What is known and what is new?

- It is known that dyslipidemia is a risk factor for atherosclerotic cardiovascular disease (ASCVD), and LDL-C reduction is beneficial in preventing ASCVD events.
- CPM has potential as an alternative and complementary therapy for dyslipidemia. Heterogeneity in outcomes was attributed to different preparations and associated comorbidities. Controlled-release pill preparations showed more favorable outcomes. Adverse events were mostly mild, concentrated in the gastrointestinal tract.

What is the implication, and what should change now?

- CPM can be considered as an alternative and complementary therapy for dyslipidemia. Attention should be paid to the formulation of CPM, and further study of syndrome standardization in traditional Chinese medicine is necessary. Standardized approaches for dialectical treatment should be established to enhance the therapeutic efficacy, credibility, and long-term safety of CPM treatment in dyslipidemia.

medicine (TCM) are required (27).

The utilization of herbal medicines and natural products in the treatment of dyslipidemia is widespread globally, owing to their various advantages such as minimal side effects, multi-target effects, personalized therapy, as well as affordability, and several of them have been validated for treatment and prevention (28,29). Similarly, TCM is quite popular among dyslipidemia patients in China (30,31). A commonly employed approach in the current Chinese medical practice for managing dyslipidemia involves the integration of on-demand statin administration with regular consumption of traditional herbal remedies (32). Traditional Chinese patent medicine (CPM) refers to standardized, pre-formulated, and ready-to-use herbal medicines that are manufactured based on the principles of TCM. These medicines come in various forms, including tablets, capsules, and granules, and are designed to be easily administered without the need for further preparation or modification. A prior meta-analysis has also substantiated the effectiveness and safety of combining CPM with statin therapy to effectively treat dyslipidemia (33). It was found that in comparison to TCM decoction, intake of CPM has higher patient compliance, easier follow-up of long-term curative effects, and wider research. Considering these, we collated and analyzed the research published over the past decade to conduct a meta-analysis on the potential therapeutic efficacy and safety of patent Chinese herbal medicines (CHMs) in treating dyslipidemia patients to evaluate whether TCM can be effectively used as a supplementary or alternative therapeutic modality. We present this article in accordance with the PRISMA reporting checklist (34) (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-146/rc).

Methods

Study registration

Before initiation, this systematic review protocol was registered on INPLASY (INPLASY202330090-amended to limit the scope).

Eligibility criteria

The following inclusion criteria were used: (I) randomized controlled trials comparing patent CPM with placebo, other intervention measures, or other pharmacological treatments for dyslipidemia; (II) trials involving the participants with a confirmed diagnosis of dyslipidemia; (III) trials with a sample size exceeding 48 individuals; (IV) trials with an intervention duration exceeding 6 weeks; (V) trials in which CPM was the only difference between the two groups; (VI) using blood lipid parameters as the primary outcome measures (TC, TG, LDL-C, HDL-C).

We standardized the inclusion of participants across studies by adhering to the diagnostic criteria for dyslipidemia as defined by the Chinese Guidelines for Lipid Management (35). Specifically, dyslipidemia was identified in participants exhibiting one or more of the following lipid abnormalities: TC levels ≥5.2 mmol/L, LDL-C levels ≥3.4 mmol/L or TG levels ≥1.7 mmol/L. Its latest recommendations for lipid prevention and control in China indicate that those who take lipid-regulating drugs for the first time should have their blood lipids reviewed within 6 weeks of drug administration, and if the lipids can reach the optimal value with no adverse drug reactions, the review should be gradually changed to once every 6–12 months. Given the variations in the treatment comparisons, we established a minimum intervention duration of 6 weeks. Thereafter, by using the reference formula for sample size calculation, with a power (1-β) of 80% and a significance level (α) of 0.05, it was determined that, for each group, a minimum of 24 individuals would be required to detect the smallest observable change in the various lipid metabolism indicators when the participants' TC levels normalize (TC <5.2 mmol/L). After taking into account all the treatment comparisons, we set the minimum sample size to 48.

Search strategy

A literature search was conducted by using Web of Science, PubMed, Embase, Cochrane Library, SinoMed (Chinese database, http://www.sinomed.ac.cn/), China National Knowledge Internet (CNKI; Chinese database, https://www.cnki.net/), WanFang (Chinese database, http://www.wanfangdata.com.cn/) and VIP (Chinese database, http://www.cqvip.com/) from January 2013 to March 2023, with no language restrictions. The following terms were included in the exercise: ("dyslipidemias", "hyperlipidemias", "hypertriglyceridemia", "hypercholesterolemias", "hypercholesteremia", "hyperlipoproteinemia", "cholesterol", "LDL", or "HDL") and ("randomized controlled trial", "controlled clinical trial", "randomly", "randomized", or "randomized") and ("TCM", "traditional Chinese medicine", "Chinese patent medicine", "Chinese patent drug", or "proprietary Chinese medicine"). The

literature search was conducted up to March 30, 2023. The Table S1 describes the search strategy for PubMed, which was adjusted for each database based on its specific characteristics.

A clinical research guideline on TCM and natural medicine treatment of angina pectoris of coronary heart disease was issued by the China Food and Drug Administration in 2011, and the technical requirements for the application of new natural medicines were released in 2013. Consequently, over the past decade, both the quality and quantity of research in TCM have exhibited substantial improvements. As a result, our primary focus has been on the publications from the past decade.

Study selection and data extraction

We utilized NoteExpress software (version 3.7) for literature management which involved filtration and elimination of duplicate records. Two reviewers independently conducted the title and abstract screenings to identify eligible studies, followed by detailed full-text assessments. The discrepancies were resolved through a consultation with a third reviewer. However, in cases of potential overlapping populations being reported, only the most recent study was selected.

Upon the completion of the screening process, two independent reviewers performed the data extraction. The data extracted encompassed general publication information (including first author's name and publication year), trial design and methodology (including the sample size and participant details), intervention overview (including the drug name, dosage, duration, and administration method) and outcome measurements (including serum lipid levels, adverse events, TCM clinical efficacy, comprehensive syndrome scores, mean apolipoprotein A levels, mean apolipoprotein B levels, mean hemorheology parameters, etc.).

Risk of bias assessment

The bias risk in the study was independently evaluated by two reviewers using the Cochrane Randomized Trial Bias Risk Tool (RoB 2) (36). If there was any difference between the two reviewers, a third reviewer was consulted to reach a final decision. We used the Review Manager software (37) to display the results of the stool bias assessment. In addition, if the current meta-analysis included more than 10 articles, a funnel chart was used to evaluate the publication bias. Begg test and Egger test were mainly used to quantitatively evaluate publication bias.

Statistical methods

The comparable data were subjected to meta-analysis using RevMan 5.4 software. However, given the diverse application of different herbal compounds in the trials, data had to be pooled to explore the overall efficacy of the herbal medicine. Therefore, a random effects model (REM) was employed for the aggregated data to account for the potential variability. Mean differences (MDs) were calculated for the continuous data and relative risks (RR) were calculated for the binary data, both with 95% confidence interval (CI).

If data were available, subgroup analyses were performed to identify possible sources of heterogeneity, including the different intervention combinations and co-morbidities. In evaluating the statistical heterogeneity among the included studies, we calculated the I^2 statistic, which quantifies the proportion of total variation across studies due to heterogeneity rather than by chance. An I^2 value greater than 50% was considered indicative of substantial heterogeneity. Additionally, we used Tau^2 to estimate the between-study variance. We employed a random-effects model for meta-analytic pooling when substantial heterogeneity was present (I^2>50%), while a fixed-effect model was used in the absence of significant heterogeneity (I^2≤50%). If possible, the R meta package (v6.1-0) was used for regression analyses to identify sources of heterogeneity. Sensitivity analyses were performed to examine the influence of individual studies on the relevant results and the observed differences between the REM as well as fixed effects model (FEM) were observed to test result robustness. Specifically, the sensitivity analysis involved sequentially excluding individual studies and applying the differential-effect model to assess the variations in overall outcomes.

TSA

The primary outcome was assessed by conducting a TSA on the accumulated data. TSA was performed by utilizing the TSA software (38) to estimate the required information size (RIS), which possessed an adjusted threshold for statistical significance, considering an overall 80% power and 5% type I error risk. The sample size was taken as the RIS and calculated using the means and variances according to the results of the meta-analysis.

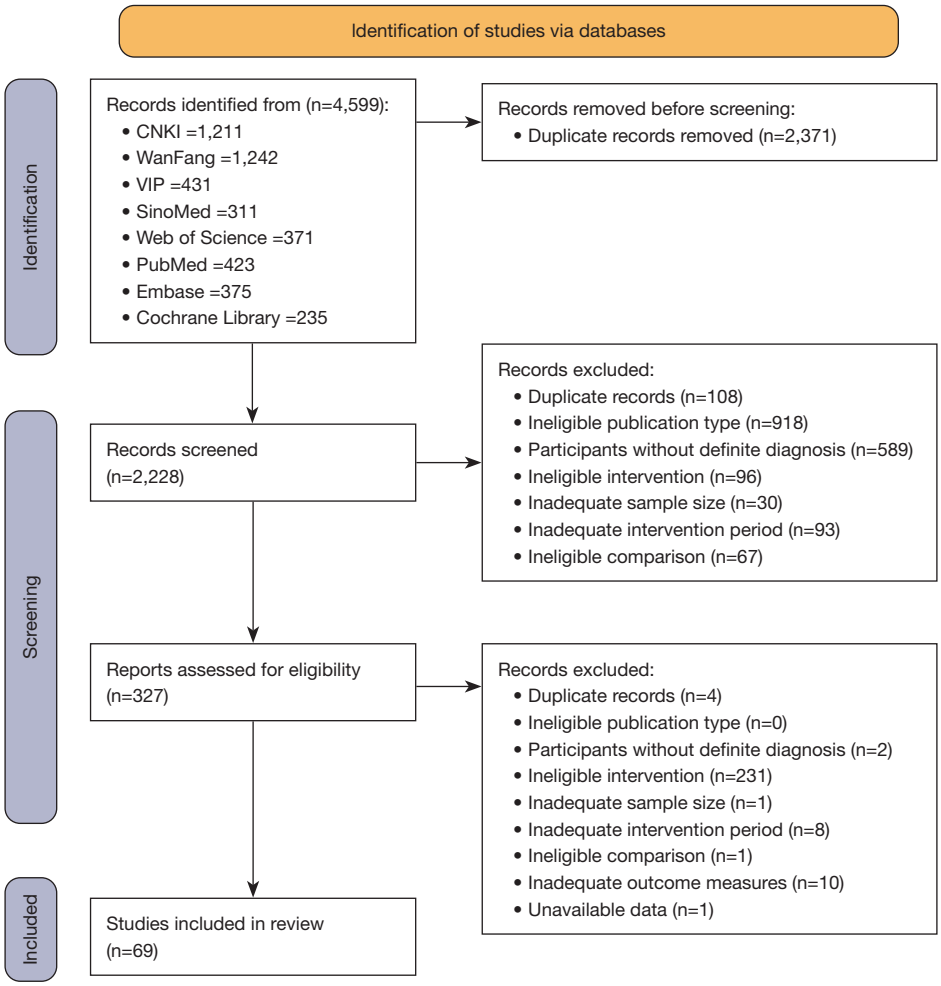

Figure 1 Flow diagram of the study selection process. CNKI, China National Knowledge Infrastructure; SinoMed, Chinese Medical Literature Database.

Identification of high-frequency CHMs

To explore the common CHMs for treating dyslipidemia, we summarized the various CHMs involved in the studies and classified them based on the frequency of occurrence.

Results

Description of included studies

Following the search strategy as described above, a total of 4,599 potential records were identified from eight different databases. After screening and evaluation, 69 eligible studies were included, which involved a total of 6,993 participants (*Figure 1*). One trial (39) was conducted in China and the United States at the same time and the rest were all conducted in China. Generally, the methodological quality of the included studies was in the middle level. The quality assessment has been shown in *Figure 2*. Methodological defects such as the lack of information about the generation and distribution of the random sequences, negligence in using the blind method or oversight in describing the implementation of the blind method were observed. For example, in one study, an increased risk was noted due to the use of a simple randomization method based on visit sequence numbers. Moreover, only five studies employed placebos, and fewer studies reported whether bias could have been introduced due to the trial background, potentially leading to bias. As for outcome measurements, deviations were relatively rare due to the relatively objective nature of blood lipid.

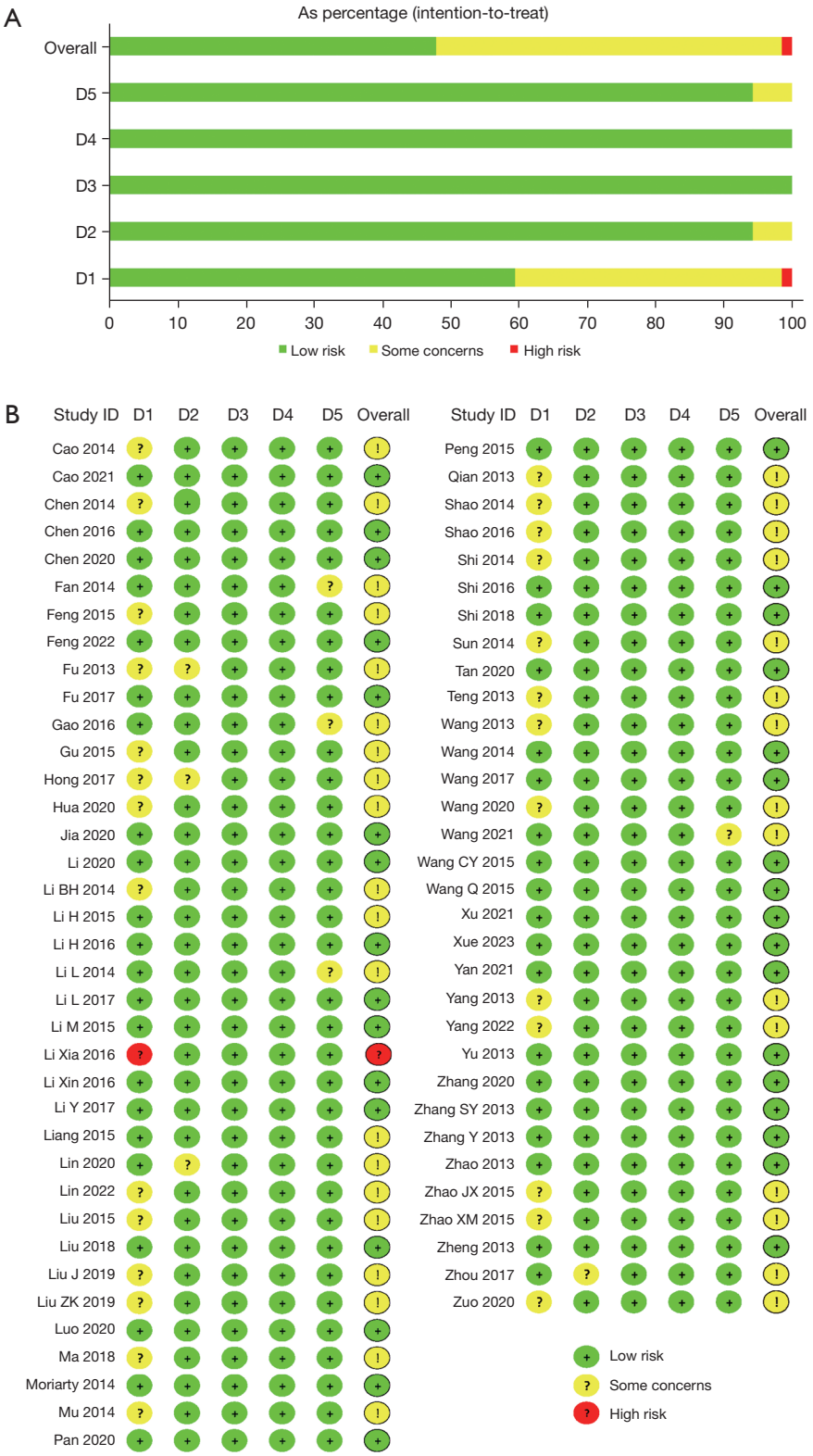

Figure 2 Risk of bias assessment in included studies: (A) risk of bias graph; (B) risk of bias summary. D1: bias due to randomization; D2: bias due to deviations from intended intervention; D3: bias due to missing data; D4: bias due to outcome measurement; D5: bias due to the selection of the reported results.

Table 1 and *Figure 3* outline the characteristics of the included trials. The total sample size of each study is more concentrated between ≥50–75 (30.26%) and ≥75–100 (34.21%) (*Figure 3A*). Only 14 studies stipulated TCM syndromes in the inclusion criteria (*Figure 3B*). The duration of the intervention was 6–48 weeks (*Figure 3C*). Among the selected studies, five studies compared CPM with the placebo, six studies compared CPM with statins, 45 studies focused on the additional effects of CPM as a supplement to statins, five studies emphasized the effect of CPM as a supplement to pharmaceuticals other than statins, whereas three studies compared CPM with a blank control (*Figure 3D*). Notably, five studies reported comparisons involving both CPM and statins, as well as comparisons involving CPM with statins, and only statins. Of the CPM used in the study, 49 (71.01%) were capsules, 11 (15.94%) were tablets, 7 (10.14%) were pills, and 2 (2.89%) were granules (*Figure 3E*), with the most frequently used being Xuezhikang capsules (20.29%), Zhibitai capsules (15.94%), and Pushen capsule (14.49%) (*Figure 3F*).

Efficacy assessment of the various lipid parameters

TC

A total of 76 trials, comprising 7,438 patients (including different comparisons of the same study), reported changes in TC levels. Although there was a high degree of heterogeneity, TC levels decreased significantly after CPM treatment as compared with the control group (P<0.001). Through subgroup analysis, it was found that the different intervention combinations might be part of the source of heterogeneity (*Figure 4*). The meta-analysis indicated that CPM was more effective than placebo in lowering TC levels (P=0.002). However, when compared to statins, the effect size was smaller, with statins showing a slight advantage (MD =0.3; 95% CI: 0.05 to 0.56). This suggests that statins may be more effective than CPM in reducing TC levels, although the difference is modest. The difference between CPM and blank was also observed (P=0.03), and the superior curative effect of CPM was observed after excluding a highly heterogeneous study (59) (P<0.001).

Sensitivity analysis revealed that studies by Li (64) and Shi (81) lead the heterogeneity in the second comparison (CPM *vs.* statins), whereas report by Li *et al.* (59) played a dominant role in the fifth comparison (CPM *vs.* blank). Li (64) and Shi (81) introduced TCM syndrome criteria into their inclusion criteria in the second comparison, which could impact efficacy when compared to the other trials. In the fifth comparison, Li *et al.* (59) reported that dyslipidemia patients with elevated baseline TC levels could be a major source of heterogeneity. Other comparisons demonstrated similar magnitudes of the combined effects, thus indicating relatively stable outcomes.

We conducted a meta-regression on the treatment duration, average age, preparation strategies and co-morbidities to determine the potential sources of heterogeneity. The results revealed that the average age (P=0.23), treatment duration (P=0.65) and the co-morbidities (P=0.62) did not serve as possible sources of TC heterogeneity, but preparation (P=0.03) might have contributed to TC heterogeneity. Further subgroup analysis of preparations indicated that CPM might be more efficacious via pills (MD =−1.07 mmol/L; 95% CI: −1.63 to −0.51; P<0.001) than capsules (MD =−0.48 mmol/L; 95% CI: −0.69 to −0.27; P<0.001) and tablets (MD =−0.43 mmol/L; 95% CI: −0.81 to −0.06; P=0.02) (Figure S1).

TG

A total of 76 trials involving 7,421 different patients (including different comparisons within the same study) reported changes in TG levels. The summarized results showed statistical significance (MD =−0.43 mmol/L; 95% CI: −0.53 to −0.33; P<0.001), suggesting that CPM treatment could significantly reduce TG levels in patients with dyslipidemia. The subgroup analysis revealed that the different intervention combinations contributed partially to the clinical heterogeneity (*Figure 5*). The results demonstrated that CPM in combination with statins or other interventions could significantly lower the TG levels (P<0.001). However, no significant difference was observed between CPM and statins (P=0.38) or even compared to placebo (P=0.05). Nonetheless, in the subgroup analysis of CPM and placebo, when two studies (60,103) with higher heterogeneity were excluded, the superior efficacy of CPM appeared (MD =−0.48 mmol/L; 95% CI: −0.64 to −0.31; P<0.001).

In addition, sensitivity analysis revealed that, in the first comparison (CPM *vs.* placebo), studies by Li (60) and Zhao (103) lead the heterogeneity, while reports by Pan *et al.* (75) and Xue (94) played a dominant role in the fourth comparison [CPM add-on study with other drugs (not statins)]. Li (60) introduced TCM syndrome criteria into their inclusion criteria in the first comparison, whereas Zhao (103) included dyslipidemia and diabetes patients, which might adversely impact efficacy. In the fourth comparison, Xue (94) excluded diabetes patients compared

Table 1 A summary of the included studies

Study	Sample size (E/C)	Duration (weeks)	Diagnosis	Age (years), (E/C)	TCM syndrome differentiation	Experimental	Control	Outcome measurement
Cao 2014a (40)	40/42	8	Dyslipidemia	57/59	N/A	Pushen capsule (0.25 g), 1 g, PO, tid	Atorvastatin, 20 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Cao 2014b (40)	42/42	8	Dyslipidemia	58/59	N/A	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) atorvastatin, 20 mg, PO, qn	Atorvastatin, 20 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Cao 2021 (41)	32/32	12	Dyslipidemia and coronary heart disease	60.09±5.61/59.25±5.53	N/A	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) rosuvastatin calcium tablets, 10 mg, PO, qn	Rosuvastatin calcium tablets, 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Chen 2014 (42)	42/42	8	Dyslipidemia	70.2±8.4/69.7±8.1	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, bid; (II) fenofibrate capsule, 200 mg, PO, qn (patients with predominantly elevated TG); (III) atorvastatin calcium tablets, 20 mg, PO, qn (patients with predominantly non-TG elevations)	(I) Fenofibrate capsule, 200 mg, PO, qn (patients with predominantly elevated TG); (II) atorvastatin calcium tablets, 20 mg, PO, qn (patients with predominantly non-TG elevations)	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Chen 2016 (43)	42/42	8	Dyslipidemia	62.5±5.6/63.5±6.2	N/A	(I) Zhibitai capsule (0.24 g), 240 mg, PO, bid; (II) atorvastatin calcium tablet (10 mg),10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	TG, TC, HDL-C, LDL-C
Chen 2020 (44)	63/63	12	Dyslipidemia	70.1±7.6/71.2±8.1	Phlegm turbidity and blood stasis	(I) Zhibitai capsule (0.24 g), 240 mg, PO, bid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Fan 2014 (45)	35/35	8	Dyslipidemia	42.1±9.7/43.5±8.1	Phlegm and blood stasis	(I) Hedan tablet (0.73 g), 3.65 g, PO, tid; (II) atorvastatin calcium tablets (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablets (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Feng 2015 (46)	60/60	12	Dyslipidemia	67.3±5.8/66.8±5.6	N/A	(I) Zhibituo tablets (0.35 g), 105 mg, PO, bid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	TG, TC, HDL-C, LDL-C
Feng 2022 (47)	43/44	8	Dyslipidemia and early menopause	50.9±3.8/50.6±3.5	N/A	Xuezhikang capsule (0.3 g), 0.6 g, PO, bid	Atorvastatin tablets (20 mg), 10 mg PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Fu 2013 (48)	61/56	8	Dyslipidemia	55.31±13.13/52.58±11.53	N/A	(I) Hedan tablet (0.73 g), 1.46 g, PO, tid; (II) rosuvastatin calcium tablets, 10 mg, PO, qd	Rosuvastatin calcium tablets, 10 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Fu 2017 (49)	75/75	12	Dyslipidemia	63.2±9.3/61.8±9.3	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, bid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Gao 2016 (50)	37/37	8	Dyslipidemia	29–72	N/A	(I) Hedan tablet (0.73 g), 1.46 g, PO, tid; (II) simvastatin, PO, 10 mg/d for the first 4 weeks and 20 mg/d for the following 4 weeks	Simvastatin, PO, 10 mg/d for the first 4 weeks and 20 mg/d for the following 4 weeks	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Gu 2015 (51)	30/30	8	Dyslipidemia	85	N/A	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) simvastatin tablets, 5 mg, PO, qd	Simvastatin tablets, 5 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Hong 2017 (52)	38/36	12	Dyslipidemia and unstable angina pectoris of coronary heart disease	56±5.8/54±7.3	N/A	(I) Shanzha Xiaozhi capsule (0.35 g), 0.7 g, PO, tid; (II) isosorbide dinitrate, 25 mg, PO, tid; (III) metoprolol, 10 mg, PO, bid; (IV) atorvastatin, 20 mg, PO, qn	(I) Isosorbide dinitrate, 25 mg, PO, tid; (II) metoprolol, 10 mg, PO, bid; (III) atorvastatin, 20 mg, PO, qn	TG, TC, HDL-C, LDL-C
Hua 2020 (53)	40/40	8	Dyslipidemia	51–72	N/A	Zhibitai capsule (0.24 g), 240 mg, PO, bid	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Jia 2020a (54)	141/71	12	Dyslipidemia	51.33 (12.58)/50.56 (11.72)	N/A	(I) Xuezhitong capsule, 2,450 mg, PO, tid; (II) Xuezhikang placebo, 2,300 mg, PO, bid	(I) Xuezhitong placebo, 2,450 mg, PO, tid; (II) Xuezhikang placebo, 2,300 mg, PO, bid	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Jia 2020b (54)	138/71	12	Dyslipidemia	52.54 (12.06)/50.56 (11.72)	N/A	(I) Xuezhikang capsule, 2,300 mg, PO, bid; (II) Xuezhitong placebo, 2,450 mg, PO, tid	(I) Xuezhitong placebo, 2,450 mg, PO, tid; (II) Xuezhikang placebo, 2,300 mg, PO, bid	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Li 2020 (55)	41/41	8	Dyslipidemia	51.12±7.45/51.20±5.32	Stagnation of phlegm and blood stasis	Zhibitai capsule (0.24 g), 480 mg, PO, bid	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Li 2014 (56)	60/60	8	Dyslipidemia	52.8	N/A	(I) Hedan tablet (0.73 g), 1.46 g, PO, tid; (II) atorvastatin calcium tablets (10 mg), 10 mg, PO, qd	Atorvastatin calcium tablets (10 mg), 10 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Li 2015 (57)	50/50	12	Dyslipidemia	53.0±11.7/57.0±10.2	N/A	(I) Zhikang granule, 8 g, PO, bid; (II) rosuvastatin calcium tablets, 10 mg, PO, qn; (III) aspirin enteric-coated tablets, 100 mg, PO, qn	(I) Rosuvastatin calcium tablets, 10 mg, PO, qn; (II) aspirin enteric-coated tablets, 100 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events

Table 1 (*continued*)

Table 1 (*continued*)

Study	Sample size (E/C)	Duration (weeks)	Diagnosis	Age (years), (E/C)	TCM syndrome differentiation	Experimental	Control	Outcome measurement
Li 2016 (58)	30/30	8	Dyslipidemia	53.4±3.7/52.4±3.1	Qi stagnation and blood stasis or phlegm and blood stasis repression	(I) Tiandan Tongluo capsule (0.4 g), 2 g, PO, tid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Li 2014 (59)	55/55	12	Dyslipidemia	53.5±0.50/54.5±0.45	Stagnation of phlegm or yin deficiency of liver and kidney	Huazhi pill, 9 g, PO, bid	Therapeutic life-style change	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Li 2017 (60)	43/44	12	Dyslipidemia	42.65±11.52/45.20±11.76	Spleen deficiency and phlegm turbidity	(I) Huazhi pill, 9 g, PO, bid; (II) therapeutic life-style change	(I) Placebo, 9 g, PO, bid; (II) therapeutic life-style change	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Li 2015 (61)	65/63	12	Dyslipidemia	54.3±7.9/54.1±8.4	Phlegm stagnation, spleen and kidney yang deficiency, liver and kidney yin deficiency, yin deficiency and yang hyperactivity, qi stagnation and blood stasis	Gaodijiangzhi capsule, 320 mg, PO, bid	Placebo, 320 mg, PO, bid	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Li 2016 (62)	30/30	8	Dyslipidemia	47.50±10.46/46.36±10.38	N/A	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Li 2016 (63)	60/60	8	Dyslipidemia and coronary artery atherosclerosis sclerosing heart disease	67.5±2.4/67.1±2.3	N/A	(I) Zhibitai capsule (0.24 g), 240 mg, PO, tid; (II) rosuvastatin calcium tablets, 10 mg, PO, qn	Rosuvastatin calcium tablets, 10 mg, PO, qn	TG, TC, HDL-C, LDL-C
Li 2017a (64)	39/40	8	Dyslipidemia	48.21±9.31/49.45±10.12	Blood stasis	Pushen capsule (0.25 g), 1 g, PO, tid	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Li 2017b (64)	39/40	8	Dyslipidemia	51.51±8.92/49.45±10.12	Blood stasis	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Liang 2015 (65)	56/56	8	Dyslipidemia	68.4±4.1/69.3±5.2	N/A	(I) Dantian Jiangzhi pills, 1 g, PO, bid; (II) simvastatin, 10 mg, PO, qn	Simvastatin, 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Lin 2020 (66)	52/56	16	Dyslipidemia	68±5.3/67.3±5.8	N/A	(I) Hedan tablet (0.73 g), 2.92 g, PO, tid; (II) atorvastatin calcium tablet (10 mg), 120 mg, PO, qd	Atorvastatin calcium tablet (10 mg), 120 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Lin 2022 (67)	40/40	48	Dyslipidemia and PMOP	≥65	N/A	(I) Alendronate sodium tablet (70 mg), 70 mg, PO, qw; (II) atorvastatin, pravastatin, simvastatin, or fluvastatin, 10–40 mg, PO, qn; (III) Qianggu capsule, 0.25 g, PO, tid	(I) Alendronate sodium tablet (70 mg), 70 mg, PO, qw; (II) atorvastatin, pravastatin, simvastatin, or fluvastatin, 10–40 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Liu 2015 (68)	40/40	8	Dyslipidemia	54.8±11.6/53.8±9.4	N/A	(I) Compound Danshen dripping pill (27 mg), 270 mg, PO, tid; (II) simvastatin, 20 mg, PO, qn	Simvastatin, 20 mg, PO, qn	TG, TC, HDL-C, LDL-C
Liu 2018 (69)	52/52	8	Dyslipidemia	58.7±3.8/58.5±4.1	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, bid; (II) atorvastatin calcium tablet, 20 mg, PO, qd	Atorvastatin calcium table, 20 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Liu 2019 (70)	45/45	24	Dyslipidemia and coronary heart disease	73.9±8.2/72.7±8.5	N/A	(I) Zhibitai capsule (0.24 g), 480 mg, PO, bid; (II) rosuvastatin calcium tablets (10 mg), 10 mg, PO, qn	Rosuvastatin calcium tablets (10 mg), 10 mg, PO, qn	TG, TC, HDL-C, LDL-C
Liu 2019a (71)	57/50	8	Dyslipidemia and type 2 diabetes	65.6±5.8	N/A	Zhibitai capsule (0.24 g), 240 mg, PO, bid	Rosuvastatin calcium tablets (10 mg), 10 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Liu 2019b (71)	43/50	8	Dyslipidemia and type 2 diabetes	65.6±5.8	N/A	(I) Zhibitai capsule (0.24 g), 240 mg, PO, bid; (II) rosuvastatin calcium tablets, 10 mg, PO, qd	Rosuvastatin calcium tablets, 10 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Luo 2020 (72)	45/45	8	Dyslipidemia	51±6/48±9	N/A	(I) Hedan tablet (0.73 g), 1.46 g, PO, tid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qd	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qd	TG, TC, HDL-C, LDL-C
Ma 2018 (73)	29/28	8	Dyslipidemia	18–75	Stagnation of phlegm and blood stasis	(I) Zhibitai capsule (0.24 g), 240 mg, PO, bid; (II) rosuvastatin calcium tablets (5 mg), 15 mg, PO, qn	Rosuvastatin calcium tablets (5 mg), 15 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events

Table 1 (*continued*)

Table 1 (*continued*)

Study	Sample size (E/C)	Duration (weeks)	Diagnosis	Age (years), (E/C)	TCM syndrome differentiation	Experimental	Control	Outcome measurement
Moriarty 2014a (39)	28/32	12	Dyslipidemia	57.8 (9.0)/56.0 (12.5)	N/A	(I) Xuezhikang capsule (300 mg), 600 mg, PO, bid; (II) placebo (300 mg), 600 mg, PO, bid	Placebo (300 mg), 1,200 mg, PO, bid	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Moriarty 2014b (39)	37/32	12	Dyslipidemia	56.3 (10.8)/56.0 (12.5)	N/A	Xuezhikang capsule (300 mg), 1,200 mg, PO, bid	Placebo (300 mg), 1,200 mg, PO, bid	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Mu 2014 (74)	43/43	8	Dyslipidemia	61/55	N/A	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) rosuvastatin calcium tablets, 10 mg, PO, qn	Rosuvastatin calcium tablets, 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Pan 2020 (75)	60/60	12	Dyslipidemia and type 2 diabetes	62.55±2.37/62.70±2.40	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, bid; (II) metformin, 0.5 g, PO, tid	Metformin, 0.5 g, PO, tid	(I) TG, TC, HDL-C, LDL-C (II) adverse events
Peng 2015 (76)	155/155	8	Dyslipidemia and type 2 diabetes	55.2±9.8/54.8±9.3	N/A	(I) Yindanxinnaotong soft capsule (0.4 g), 1.6 g, PO, tid; (II) melbine, 500 mg, PO, tid; (III) the appropriate insulin is selected according to individual condition	(I) Melbine, 500 mg, PO, tid; (II) the appropriate insulin is selected according to individual condition	TG, TC, HDL-C, LDL-C
Qian 2013 (77)	43/43	12	Dyslipidemia and type 2 diabetes	69.13±10.25/68.47±11.63	N/A	(I) Liuwei Dihuang pill, 9 g, PO, bid; (II) routine treatment to control blood sugar and blood lipid	Routine treatment to control blood sugar and blood lipid	TG, TC, HDL-C, LDL-C
Shao 2014 (78)	30/30	10	Dyslipidemia and coronary heart disease	62.35±6.7/63.09±6.5	N/A	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) rosuvastatin calcium tablets (10 mg), 10 mg, PO, qn	Rosuvastatin calcium tablets (10 mg), 10 mg, PO, qn	TG, TC, HDL-C, LDL-C
Shao 2016 (79)	75/30	12	Dyslipidemia and coronary heart disease	63.91±7.95/61.49±9.42	N/A	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Shi 2014 (80)	102/104	24	Dyslipidemia	54.5±13.2/55.2±11.7	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, bid; (II) therapeutic life-style change	Therapeutic life-style change	TG, TC, HDL-C, LDL-C
Shi 2016 (81)	62/63	12	Dyslipidemia	52.72±9.41/54.94±8.67	Obstruction of dampness and turbidity	Gypenosides tablets (60 mg), 60 mg, PO, tid	Simvastatin (20 mg), 20 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Shi 2018 (82)	62/62	8	Dyslipidemia	62.13±7.27/63.03±7.52	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, bid; (II) fluvastatin sodium, 40 mg, PO, qd	Fluvastatin sodium, 40 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Sun 2014 (83)	30/30	8	Dyslipidemia	52.3±0.59/52.7±0.62	Stagnation of phlegm or yin deficiency of liver and kidney	(I) Xiaozhi capsule (0.5 g), 1.5 g, PO, tid; (II) fenofibrate tablets, 200 mg, PO, qd	Fenofibrate tablets, 200 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Tan 2020 (84)	30/30	8	Dyslipidemia and coronary heart disease	61.5±18.5/62.5±19.5	N/A	(I) Zhibitai capsule (0.24 g), 240 mg, PO, bid; (II) atorvastatin calcium tablet (10 mg),10 mg, PO, qd	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Teng 2013 (85)	40/41	12	Dyslipidemia	68/67	N/A	Jiangzhi Daozhi capsule, 3#, PO, bid	Fluvastatin sodium capsules, 40 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Wang 2013a (86)	90/90	24	Dyslipidemia and atherosclerosis	≥60	N/A	Hedan tablet (0.73 g), 1.46 g, PO, tid	Fluvastatin sodium capsules, 41 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Wang 2013b (86)	90/90	24	Dyslipidemia and atherosclerosis	≥60	N/A	(I) Hedan tablet (0.73 g), 1.46 g, PO, tid; (II) fluvastatin sodium capsules, 40 mg, PO, qd	Fluvastatin sodium capsules, 40 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Wang 2014 (87)	32/32	12	Dyslipidemia	68.7±6.1/68.9±5.4	N/A	Xuezhikang capsule (0.3 g), 0.6 g, PO, bid	Rosuvastatin (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Wang 2017 (88)	67/67	12	Dyslipidemia	59.66±8.24/59.66±8.24	Qi stagnation and blood stasis	(I) Xuefu Zhuyu capsule (0.4 g), 2.4 g, PO, bid; (II) simvastatin tablets, 20 mg, PO, qn	Simvastatin tablets, 20 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Wang 2020 (89)	35/35	12	Dyslipidemia and end stage renal failure	58.4±7.8/59.2±8.4	N/A	(I) Haikun Shenxi capsule (0.22 g), 0.44 g, PO, tid; (II) fluvastatin sodium capsule (40 mg), 80 mg, PO, qn; (III) maintenance hemodialysis treatment	(I) Fluvastatin sodium capsule (40 mg), 80 mg, PO, qn; (II) maintenance hemodialysis treatment	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Wang 2021 (90)	34/34	8	Dyslipidemia and slow coronary flow	64.5±6.3/65.8±5.7	N/A	(I) Compound Danshen dripping pill (27 mg), 270 mg, PO, tid; (II) rosuvastatin, 10–20 mg, PO, qd	Rosuvastatin,10–20 mg, PO, qd	TG, TC, HDL-C, LDL-C

Table 1 (*continued*)

Table 1 (*continued*)

Study	Sample size (E/C)	Duration (weeks)	Diagnosis	Age (years), (E/C)	TCM syndrome differentiation	Experimental	Control	Outcome measurement
Wang 2015 (91)	32/32	6	Dyslipidemia	66.5±5.2/67.2±4.5	N/A	(I) Zhibitai capsule (0.24 g), 240 mg, PO, bid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Wang 2015 (92)	50/50	12	Dyslipidemia and type 2 diabetes	45.9±2.3/46.0±2.4	N/A	(I) Hedan tablet (0.73 g), 1.46 g, PO, tid; (II) rosuvastatin calcium tablets (10 mg), 10 mg, PO, qd; (III) blood glucose maintenance therapy	(I) Rosuvastatin calcium tablets (10 mg), 10 mg, PO, qd; (II) blood glucose maintenance therapy	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Xu 2021 (93)	50/50	24	Dyslipidemia	56.54±3.25/55.21±3.65	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, qn; (II) rosuvastatin, 10 mg, PO, qd	Rosuvastatin, 10 mg, PO, qd	TG, TC, HDL-C, LDL-C
Xue 2023 (94)	40/40	8	Dyslipidemia	57.03±1.62/54.50±1.46	N/A	(I) Zhibitai capsules (0.24 g), 0.24 g, PO, bid; (II) probucol tablets (0.125 g), 0.5 g, PO, bid	Probucol tablets, 0.5 g, PO, bid	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Yan 2021 (95)	31/31	8	Dyslipidemia	56.2±8.5/56.8±8.1	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, bid; (II) simvastatin (20 mg), 20 mg, PO, qn; (III) basic treatment	(I) Simvastatin (20 mg), 20 mg, PO, qn; (II) basic treatment	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Yang 2013 (96)	42/42	8	Dyslipidemia	49±8.7/49±9.1	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, bid; (II) simvastatin tablets, 20 mg, PO, qn	Simvastatin tablets, 20 mg, PO, qn	TG, TC, HDL-C, LDL-C
Yang 2022 (97)	25/25	24	Dyslipidemia and carotid atherosclerotic plaque	66.2±9.8	N/A	(I) Naoxintong capsule (0.4 g), 1.6 g, PO, tid; (II) atorvastatin, 20 mg, PO, qd	Atorvastatin, 20 mg, PO, qd	TG, TC, HDL-C, LDL-C
Yu 2013a (98)	40/40	10	Dyslipidemia	58.80±9.60/55.40±8.89	N/A	Pushen capsule (0.25 g), 1 g, PO, tid	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Yu 2013b (98)	40/40	10	Dyslipidemia	56.43±9.92/55.40±8.89	N/A	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Zhang 2020 (99)	46/46	8	Dyslipidemia	51.0±7.9/51.9±8.4	N/A	(I) Dantian Jiangzhi pills, 1 g, PO, bid; (II) ezetimibe tablets (10 mg), 10 mg, PO, qd	Ezetimibe tablets (10 mg), 10 mg, PO, qd	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Zhang 2013 (100)	30/30	8	Dyslipidemia and coronary heart disease	61.8±10.3/61.0±9.4	N/A	(I) Pushen capsule (0.25 g), 1 g, PO, tid; (II) rosuvastatin calcium tablets, 10 mg, PO, qn	Rosuvastatin calcium tablets, 10 mg, PO, qn	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Zhang 2013 (101)	85/85	8	Dyslipidemia and type 2 diabetes	63.76±10.32/64.02±9.05	N/A	(I) Zhibituo tablets (0.35 g), 105 mg, PO, bid; (II) atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	Atorvastatin calcium tablet (10 mg), 10 mg, PO, qn	TG, TC, HDL-C, LDL-C
Zhao 2013 (102)	30/30	12	Dyslipidemia and type 2 diabetes	58±5/57±5	Deficiency of both qi and yin, deficiency of spleen and kidney	(I) Zhike Yangyin capsule (0.5 g), 1.5 g, PO, tid; (II) simvastatin capsule, 20 mg, PO, qn; (III) blood sugar maintenance therapy with hypoglycemic drugs or subcutaneous injection of insulin	(I) Simvastatin capsule, 20 mg, PO, qn; (II) blood sugar maintenance therapy with hypoglycemic drugs or subcutaneous injection of insulin	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Zhao 2015 (103)	32/33	8	Dyslipidemia and type 2 diabetes	59.6±4.7/57.6±5.3	N/A	(I) Xuezhikang capsule (0.3 g), 0.6 g, PO, tid; (II) routine treatment of oral medications or insulin to control blood glucose	(I) Placebo (0.3 g), 0.6 g, PO, tid; (II) routine treatment of oral medications or insulin to control blood glucose	TG, TC, HDL-C, LDL-C
Zhao 2015 (104)	40/40	8	Dyslipidemia	54.3±7.6/56.8±7.7	N/A	(I) Zhikang granule, 8 g, PO, bid; (II) atorvastatin calcium tablet (20 mg), 20 mg, PO, qd	Atorvastatin calcium tablet (20 mg), 20 mg, PO, qd	TG, TC, HDL-C, LDL-C
Zheng 2013 (105)	40/40	24	Dyslipidemia and carotid intima-media thickening and plaque	63.2±15.3/62.1±15.1	N/A	(I) Tongxinluo capsule (0.26 g), 1.04 g, PO, tid; (II) atorvastatin, 20 mg, PO, qn; (III) aspirin enteric-coated tablets, 200 mg, PO, qn; (IV) routine treatment of controlling blood sugar and blood pressure	(I) Atorvastatin, 20 mg, PO, qn; (II) aspirin enteric-coated tablets, 200 mg, PO, qn; (III) routine treatment of controlling blood sugar and blood pressure	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Zhou 2017 (106)	41/39	24	Dyslipidemia and carotid atherosclerosis	58.6±9.82/57.8±8.59	N/A	(I) Songling Xuemaikang capsule (0.5 g), 1.5 g, PO, tid; (II) atorvastatin calcium tablet, 20 mg, PO, qd; (III) low fat diet and routine therapy	(I) Atorvastatin calcium tablet, 20 mg, PO, qd; (II) low fat diet and routine therapy	(I) TG, TC, HDL-C, LDL-C; (II) adverse events
Zuo 2020 (107)	25/25	12	Dyslipidemia	55.2±1.1/54.2±1.3	N/A	(I) Tongxinluo capsule (0.26 g), 1.04 g, PO, tid; (II) simvastatin, 20 mg, PO, qd	Simvastatin, 20 mg, PO, qd	TG, TC, HDL-C, LDL-C

Age is presented as the mean, mean ± standard deviation, or range. E, experimental group; C, control group; PMOP, postmenopausal osteoporosis; TCM, traditional Chinese medicine; N/A, not applicable; PO, per oral administration; tid, three times a day; qn, once a day before sleep; qd, once a day; qw, once a week; bid, twice a day; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

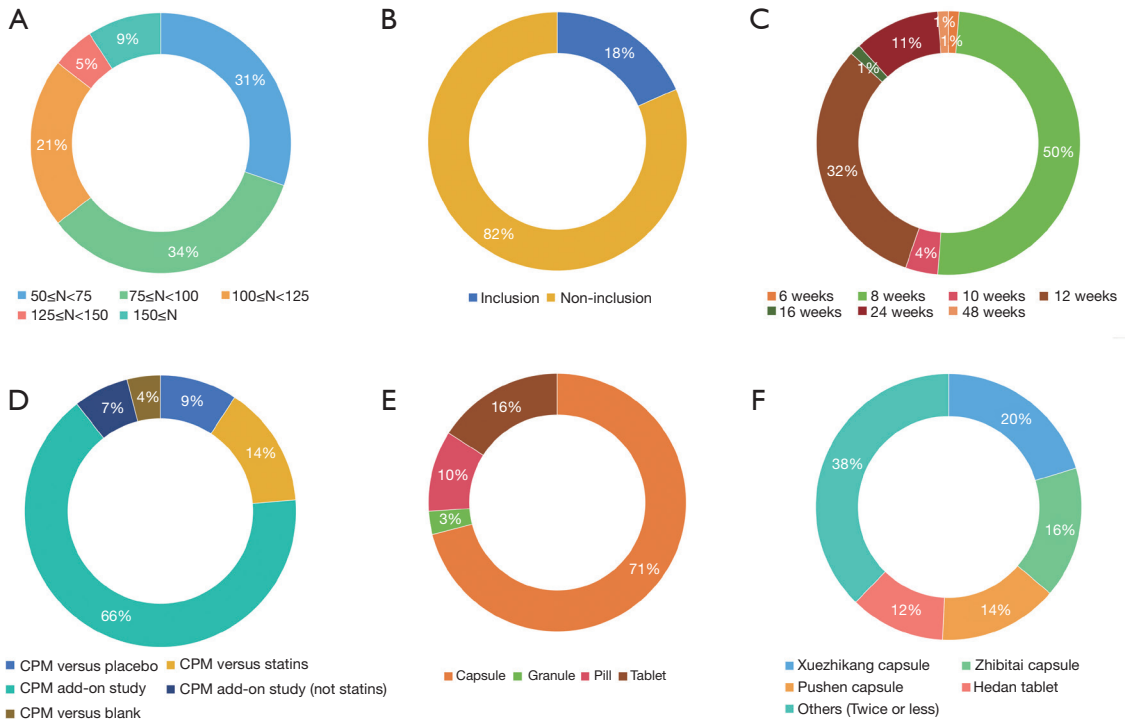

Figure 3 Characteristics of included study. Annotations: (A) sample size; (B) TCM syndromes; (C) duration; (D) interventions; (E) preparation; (F) mainly used CPM. TCM, traditional Chinese medicine; CPM, Chinese patent medicine.

to other trials included in the third comparison. Pan *et al.* (75) recruited patients with both dyslipidemia as well as diabetes and treated blood glucose with the same dose of metformin. However, the study did not describe blood glucose control, which could adversely affect efficacy. Moreover, other comparisons demonstrated similar magnitudes of combined effects, thus indicating relatively stable outcomes.

We conducted a meta-regression to determine the possible sources of heterogeneity. Overall, the treatment duration (P=0.71), the average age (P=0.13), the co-morbidities (P=0.57) and the preparation (P=0.73) were not identified as the sources of heterogeneity for TG.

LDL-C

A total of 76 trials involving 7,405 different patients (including different comparisons within the same study) reported changes in LDL-C levels. Despite high heterogeneity (P<0.001, I^2=95%), CPM treatment led to a significant reduction in LDL-C levels in comparison to the control groups (MD =−0.40 mmol/L; 95% CI: −0.50 to −0.30; P<0.001) (*Figure 6*). Subgroup analysis based on the different intervention combinations revealed that CPM was more effective in lowering LDL-C levels in comparison to both the placebo (P<0.001), blank control (P<0.01) and statins (P=0.03). Additionally, a combination of CPM and statin drug treatment (P<0.001) or other medications (P<0.001) also significantly reduced LDL-C levels.

Sensitivity analysis revealed that the study by Li (60) dominated the clinical heterogeneity of CPM compared with placebo, Shi (81) in the comparison of CPM and satins, Xue (94) in the fourth comparison, and Li *et al.* (59) in the fifth comparison (CPM *vs.* blank). The possible reasons for the heterogeneity observed in these studies have been analyzed in the previous sections. Other comparisons indicated similar magnitudes of the combined effects, thus suggesting relatively stable outcomes.

We conducted a meta-regression to determine the sources of heterogeneity. Overall, the treatment duration (P=0.35), average age (P=0.35), the co-morbidities (P=0.42) and preparation (P=0.41) were not identified as the potential sources of LDL-C heterogeneity. Sensitivity analysis indicated similar magnitudes of the combined effects, thereby suggesting relatively stable outcomes.

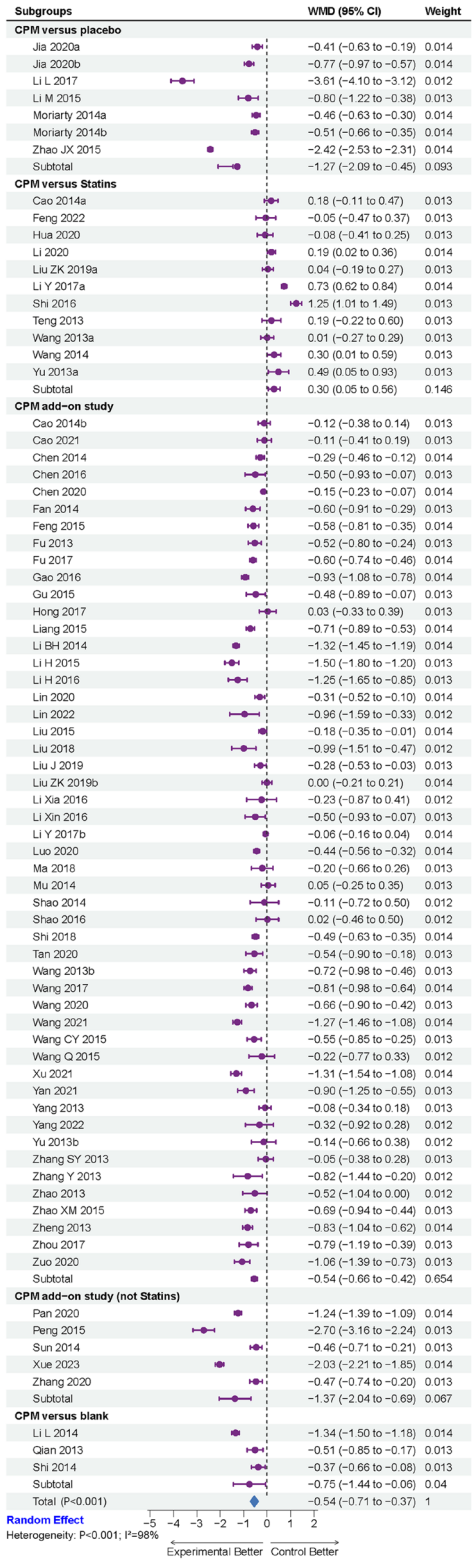

Figure 4 Subgroup analysis for TC based on the different interventions. WMD, weighted mean difference; CI, confidence interval; CPM, Chinese patent medicine; TC, total cholesterol.

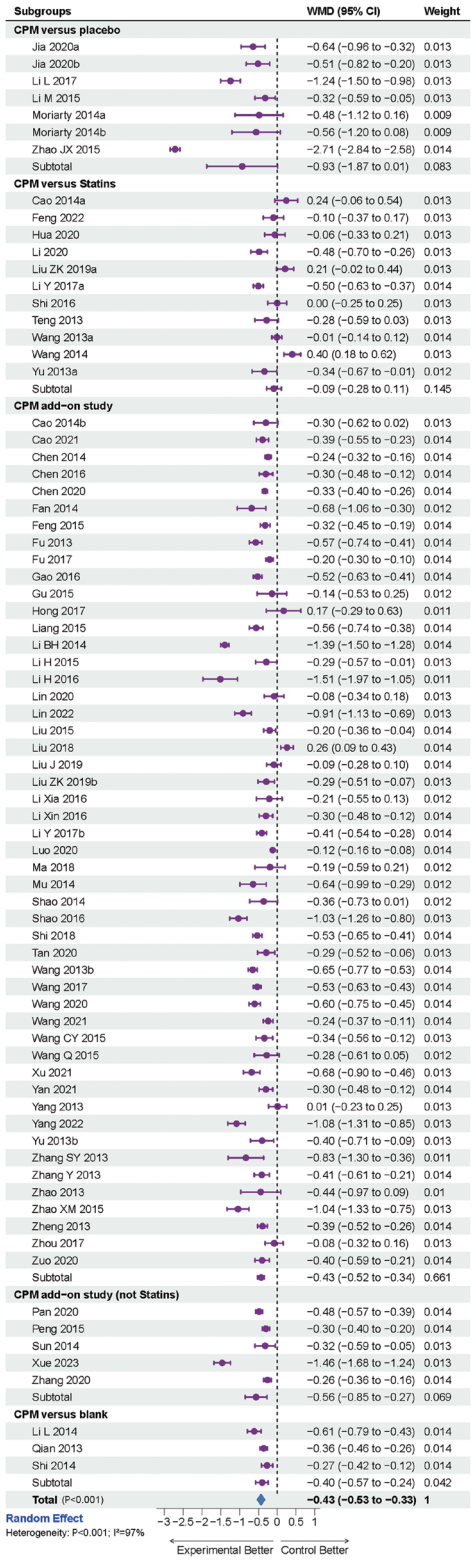

Figure 5 Subgroup analysis for TG based on the different interventions. WMD, weighted mean difference; CI, confidence interval; CPM, Chinese patent medicine; TG, triglyceride.

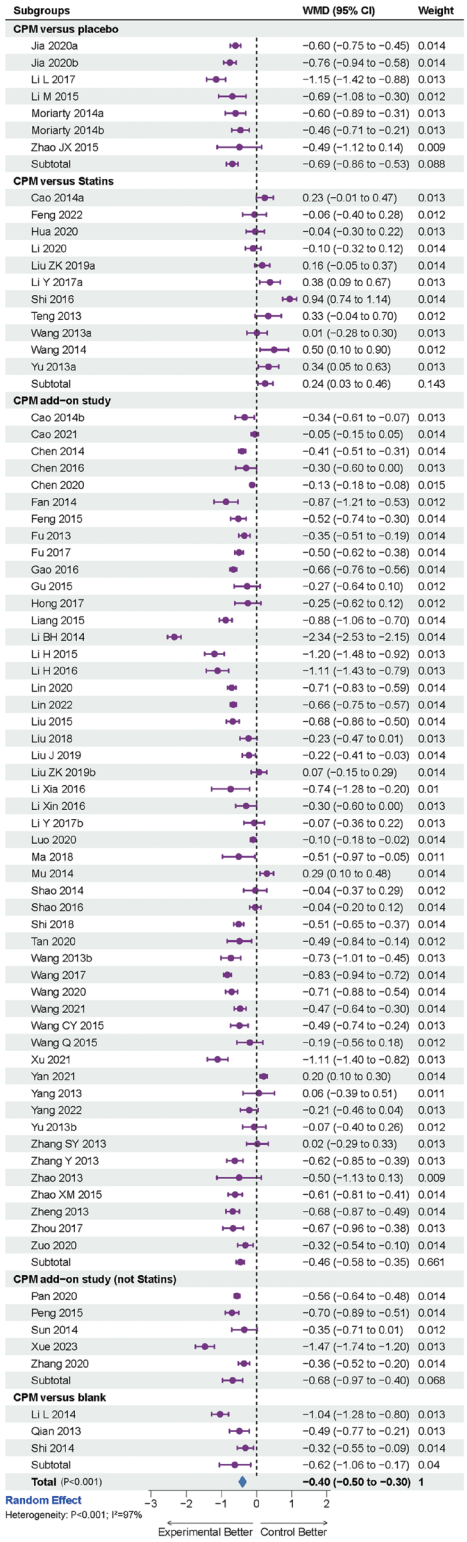

Figure 6 Subgroup analysis for LDL-C based on the different interventions. WMD, weighted mean difference; CI, confidence interval; CPM, Chinese patent medicine; LDL-C, low-density lipoprotein cholesterol.

HDL-C

There were 76 trials comprising 7,405 patients (including different comparisons of the same study) that reported changes in HDL-C levels. Despite a high degree of heterogeneity (P<0.001, I^2=94%), it was observed that in comparison with the control group, HDL-C levels increased significantly after CPM treatment (P<0.001). Through subgroup analysis, it was found that the different intervention combinations might be part of the source of the heterogeneity (*Figure 7*). The results showed that CPM was more effective than the placebo in improving HDL-C level (P<0.001). In addition, CPM combined with statins (P<0.001) or other drugs (P=0.004) also improved HDL-C levels significantly. However, no difference was found between CPM and statins (P=0.64), and CPM and statins may have similar effects on HDL-C.

In general, the treatment duration (P=0.40) and the average age (P=0.98) were not identified as possible sources of heterogeneity for the HDL-C. Through meta-regression analysis, we found that the preparation (P<0.001) and comorbidities (P=0.009) could be part of the sources of HDL-C heterogeneity. Subgroup analysis based on preparation indicated that CPM might be more effective in improving HDL-C levels when formulated as pills (MD =0.62 mmol/L; 95% CI: 0.32–0.92; P<0.001) compared to the capsules (MD =0.19 mmol/L; 95% CI: 0.15–0.24; P<0.001) and the tablets (MD =0.18 mmol/L; 95% CI: 0.09–0.27; P<0.001) (Figure S2). Interestingly, an important phenomenon was observed in the subgroup analysis. It was found that compared with simple dyslipidemia (MD =0.17 mmol/L; 95% CI: 0.13–0.21; P<0.001), patients with different disease backgrounds (MD =0.33 mmol/L; 95% CI: 0.22–0.44; P<0.001) exhibited a more significant lipid-regulating reaction to CPM (Figure S3).

Safety assessment

The percentage of the participants who reported adverse events was used for the safety assessment. Among the included trials, 40 trials reported different adverse events, 17 trials did not report any adverse events, and 19 trials did not mention adverse events (*Table 2*). Two adverse events leading to patient withdrawal were reported due to the controlled interventions (39,54). However, no significant differences were observed between the experimental and control groups in trials reporting adverse events (P=0.40, *Figure 8*). However, the trial by Tan (84) was particularly noteworthy in which about a quarter of the participants

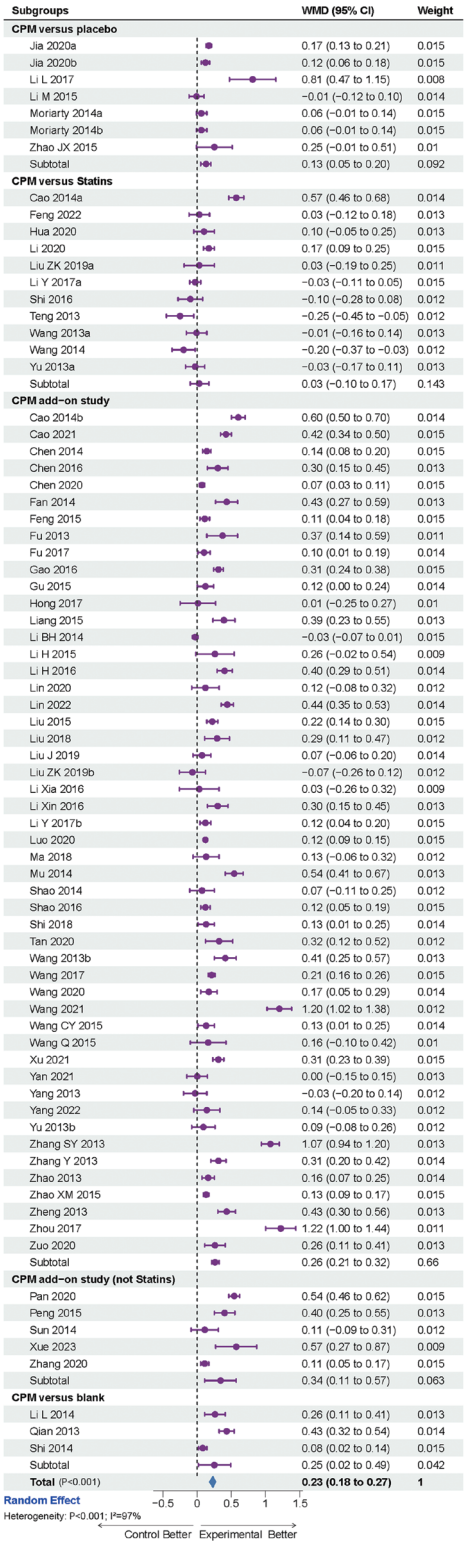

Figure 7 Subgroup analysis for HDL-C based on the different interventions. WMD, weighted mean difference; CI, confidence interval; CPM, Chinese patent medicine; HDL-C, high-density lipoprotein cholesterol.

Table 2 Summary of the different adverse events

Adverse event	Number and severity reported in the treatment group	Number and severity reported in the control group
Gastrointestinal discomfort	52 mild	42 mild
Abnormal liver function	19 mild	25 mild
Dizziness and headache	5 mild	7 mild
Cutaneous effects	4 mild	2 mild
Hypoglycemia reaction	3 mild	0
Dry mouth	3 mild	0
Abnormal renal function	2 mild	1 mild
Fatigue	2 mild	4 mild
Musculoskeletal and connective-tissue disorders	2 mild	3 mild
Anemia	1 mild	0
Increased uric acid	1 mild	0
Increased blood CK	1 mild	0
All adverse events reported in treatment or control group	95 mild	84 mild

CK, creatine kinase.

reported mild adverse events that did not need any treatment.

Publication bias

To effectively mitigate the risk of ASCVD in clinical settings, LDL-C is recommended as the primary target for lipid-lowering interventions in most countries or regions. Thus, regarding LDL-C, a funnel plot demonstrated an approximately symmetric distribution of the various study points with an inverse pattern (Figure S4). Based on Begg's test (P=0.17) and Egger's test (P=0.81), no significant publication bias was observed. These findings lend support to the efficacy of the reported interventions.

TSA

The robustness of LDL-C was evaluated by TSA and the RIS was calculated. The results for LDL-C indicated that the optimal sample size needed to draw reliable conclusions about the possible beneficial effects of CPM treatment on lipid abnormalities was 3,261 participants,

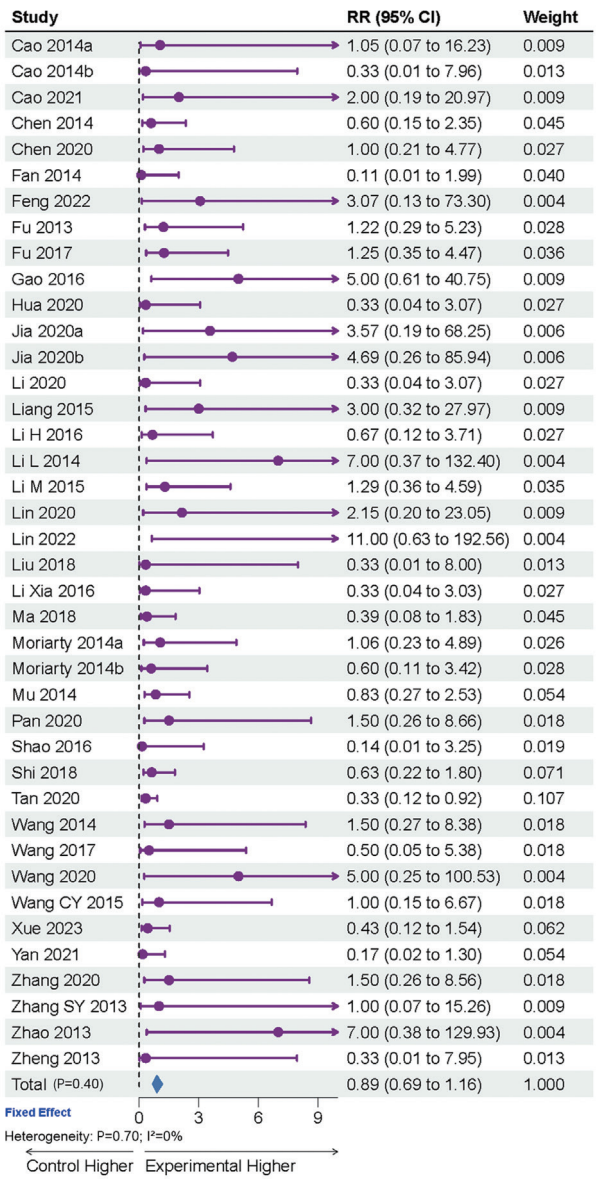

Figure 8 Forest plot of the various adverse events. RR, relative risk; CI, confidence interval.

thus surpassing the currently enrolled participants in the present study. The cumulative Z-curve was found to cross the TSA and traditional boundary value (*Figure 9A*). The subgroup analysis results of the different interventions also consistently supported the reliability and validity of cumulative evidence (*Figure 9B-9E*).

Frequency distribution analysis of Chinese herb medicines

A total of 77 different CHMs were used in the included studies. We summarized CHMs with a frequency of 5 times or more as depicted in *Table 3*. These identified CHMs could be potentially considered for prescription in cases of dyslipidemia. The top five were Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Shanzha (Crataegus pinnatifida), Hongqu (Red koji), Zexie (Alismatis Rhizoma) and Chuanxiong (Chuanxiong Rhizoma).

Discussion

Dyslipidemia is a major risk factor for the development of ASCVD. It has been established that early treatment could be of great significance in preventing cardiovascular and cerebrovascular events in dyslipidemia patients. TCM has consistently achieved superior results in the treatment of dyslipidemia with its forte in multi-target and multi-component coordinated regulation. Hence, we searched 4,599 articles from eight databases, and 69 studies (including 6,993 patients) were finally included in the analysis. The curative effect was analyzed from four parameters of blood lipid and the source of heterogeneity was explored through meta-regression and subgroup analysis. The occurrence of adverse events was also compared.

The overall risk assessment of ASCVD is the basis of blood lipid intervention decisions (108). A large number of observational studies and clinical trials have indicated that LDL-C is a risk factor for ASCVD, and for every 1 mmol/L reduction of LDL-C, ASCVD events will decrease by approximately 20–23% (109-111). Targeting LDL-C as the primary goal presents certain limitations, particularly in situations characterized by an increased ratio of triglyceride-rich lipoproteins, as seen in conditions like diabetes and obesity. Non-HDL-C, encapsulating the cholesterol within all atherogenic lipoprotein particles, more accurately predicts the risk of ASCVD (112). TGs also indicate the residual risk for ASCVD (113). Therefore, we evaluated the potential curative effect of CPM on dyslipidemia from four dimensions: TC, TG, LDL-C and HDL-C. The most significant clinical finding of this study was that CPM can markedly improve the levels of the TC, TG, LDL-C, and HDL-C in patients with dyslipidemia. Though there was high heterogeneity, in comparison with the control group, dyslipidemia was significantly improved after treatment with CPM. Surprisingly, though dyslipidemia after CPM treatment did not differ significantly from statins when used alone, it could improve lipid profile better in all cases when used in combination with statins and with drugs used for comorbidities or co-morbidities. Thus, it was concluded

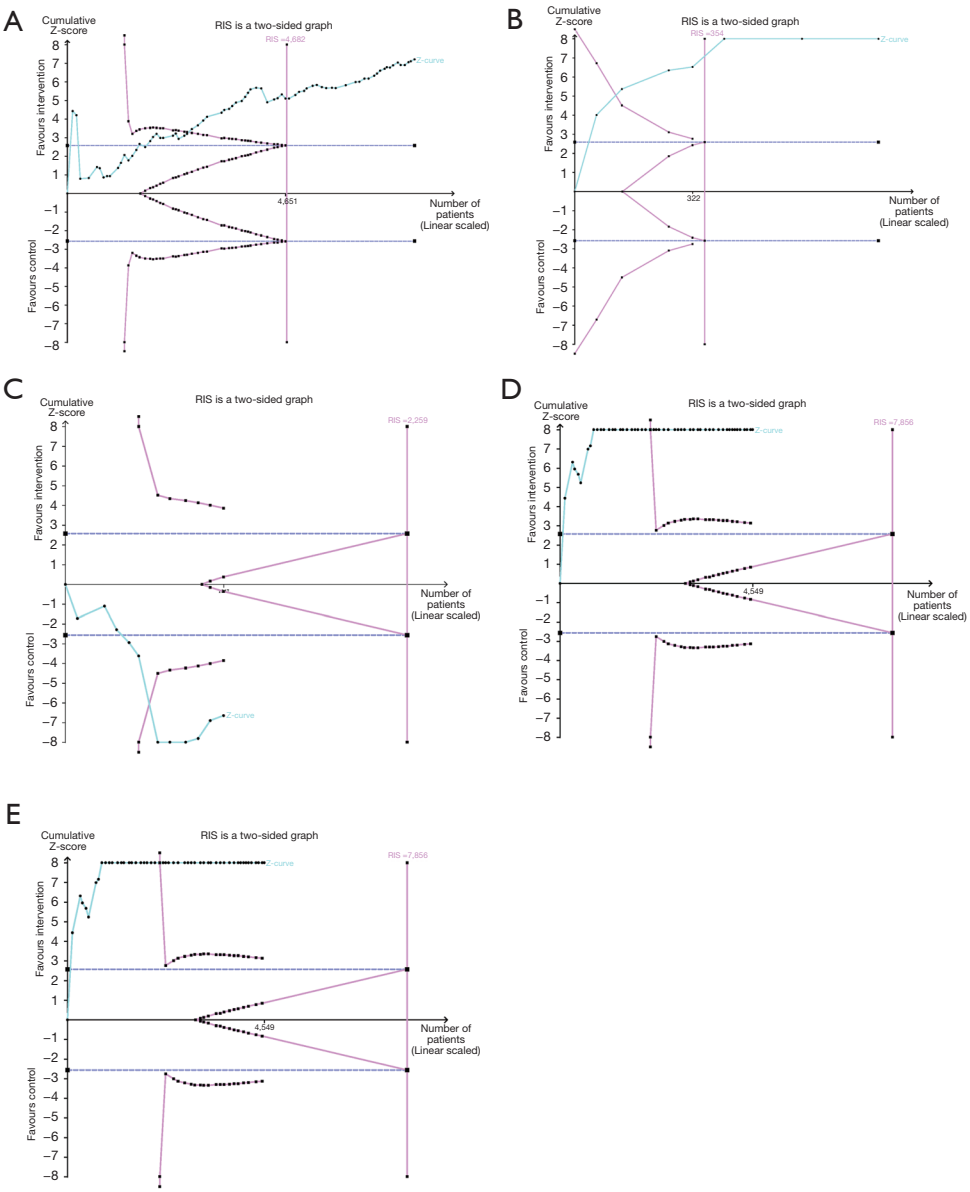

Figure 9 Trial sequential analysis of LDL-C. (A) Overall evaluation of improvement in LDL-C with CPM; (B) CPM versus placebo; (C) CPM versus statins; (D) add-on study; (E) CPM add-on study with other drugs (not statins). RIS, required information size; LDL-C, low-density lipoprotein cholesterol; CPM, Chinese patent medicine.

that CPM may achieve better efficacy in improving dyslipidemia as an alternative and complementary therapy. It remains unclear whether the efficacy of adjunctive therapy can originate from improved tolerance following long-term statin use, additional effects, or even synergistic effects.

TCM theories indicate that dyslipidemia primarily originates from liver qi stagnation, spleen and kidney qi deficiencies. These deficiencies could be induced by an uncontrolled diet and a non-ideal lifestyle, manifesting as inner phlegm and dampness, as well as blood stasis (114). The TCM prescriptions involved in the studies are shown in *Table 4*. The therapeutic efficacy and active ingredients mainly focused on: (I) strengthening the spleen and eliminating food (triterpenes and anthraquinone components); (II) removing phlegm, dampness, and blood

Table 3 Frequency of CHMs (5 times or more)

Components	Number of studies
Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	35
Shanzha (Crataegus pinnatifida)	35
Hongqu (Red koji)	27
Zexie (Alismatis Rhizoma)	25
Chuanxiong (Chuanxiong Rhizoma)	15
Chishao (Paeoniae Radix Rubra)	14
Heshouwu (Polygoni Multiflori Radix)	13
Baizhu (Atractylodis Macrocephalae Rhizoma)	11
Puhuang (Pollen Typhae)	10
Buguzhi (Psoraleae Fructus)	8
Fanxieye (Folium sennae)	8
Heye (Lotus leaf)	8
Dahuang (Rhubarb)	5
Danggui (Angelicae Sinensis Radix)	5
Renshen (Ginseng Radix et Rhizoma)	5
Sanqi (Notoginseng Radix Et Rhizoma)	5

CHMs, Chinese herbal medicines.

stasis (to improve the cardiovascular function consisting of flavonoids, phenols, saponins, etc.); and (III) benefiting qi and nourishing yin (polysaccharides) (*Figure 10*) (115). Just as the high-frequency CHMs summarized in *Table 3*, including Hongqu (Red koji), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma) and Chuanxiong (Chuanxiong Rhizoma), their efficacy was also found to be consistent with the currently recognized and commonly used CHMs, which are in line with the pathogenesis of dyslipidemia. The effective mechanism of the active components of these TCMs is similar to that of the commonly used lipid-lowering drugs at present, but they have more targets and comprehensive advantages than the single route. For example, hawthorn extract can increase the expression of Peroxisome proliferator-activated receptor alpha (PPARα) to promote the lipid degradation and blood lipid reduction of β-oxidation related enzymes in the liver (116), which is similar to that of fibrates, and also has the effect similar to that of statins, which can inhibit the activity of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase (117). Salvia miltiorrhiza extract can not only act as a farnesoid X receptor/liver x receptor α co-agonist (118) but also improve blood lipid disorder by reversing the flora imbalance and enhancing intestinal integrity (119). Salvianolic acid B, one of the active components of Danshen, can antagonize the CD 36 pathway, which can reduce the expression of the CD 36 gene and lipid uptake of macrophages (120), and can also alleviate the disorder of blood lipid by regulating downstream effect factors of Adenosine monophosphate-activated protein kinase (AMPK) such as Acetyl-CoA carboxylase (ACC) and PPARα (121). Tanshinone IIA, another active component of Salvia miltiorrhiza, has been proven to regulate the expression of *miR-33a* and SREBP-2/PCS 9 signaling pathway proteins, thus up-regulating HDL levels (122). However, when several herbs are combined into a formula, each of which has a different mechanism of action, there may be a better effect of lowering blood lipids than any herb used alone. Since the formula of TCM is composed of many herbs with different mechanisms of action, they act through multiple targets and the verification of these effects needs more preclinical and clinical evidence.

Furthermore, our study revealed significant heterogeneity in the outcomes of LDL-C, TG, TC and HDL-C, thereby prompting us to conduct a meta-regression analysis to identify the possible sources of this heterogeneity. Meta-regression analysis revealed two main reasons for heterogeneity, which were preparations form and the associated co-morbidities. Specifically, the heterogeneity in TC and HDL-C levels could be attributed, at least in part, to the different preparations used. The use of controlled-release pill preparations was found to yield more favorable outcomes compared to other forms of administration. This could be likely due to the slow dissolution and prolonged drug effect observed with the different pill preparations, which may be particularly beneficial for individuals with dyslipidemia. This finding implied that there could be potential for the development of CPM pills to enhance the treatment efficacy in the long term. Additionally, another source of heterogeneity was identified in HDL-C levels. Interestingly, patients with complications or comorbidities exhibited more pronounced lipid-regulating responses to CPM in comparison to those with simple dyslipidemia. We hypothesized that the observed heterogeneity could be attributed to both variations in the methodological quality among the included studies and the specific characteristics of TCM intervention. It has been reported that the syndrome differentiation and treatment represent a prominent feature within the realm of TCM. Thus, to

Table 4 The characteristics of CPM prescriptions

Study	TCM prescription	Components	Preparations	Therapeutic function
Cao 2014 (40)	Pushen capsule	Heshouwu (Polygoni Multiflori Radix), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Chuanxiong (Chuanxiong Rhizoma), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Cao 2021 (41)	Pushen capsule	Heshouwu (Polygoni Multiflori Radix), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Chuanxiong (Chuanxiong Rhizoma), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Chen 2014 (42)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Chen 2016 (43)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Chen 2020 (44)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu(Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Fan 2014 (45)	Hedan tablet	Heye (Lotus leaf), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Shanzha (Crataegus pinnatifida), Fanxieye (Folium sennae), Buguzhi (Psoraleae Fructus)	Tablet	Resolving phlegm and turbidity, promoting blood circulation and removing blood stasis
Feng 2015 (46)	Zhibituo tablets	Hongqu (Red koji)	Tablet	Spleen invigorating, digestion promoting, dampness removing, phlegm eliminating, blood circulation promoting and blood stasis removing
Feng 2022 (47)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Fu 2013 (48)	Hedan tablet	Heye (Lotus leaf), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Shanzha (Crataegus pinnatifida), Fanxieye (Folium sennae), Buguzhi (Psoraleae Fructus)	Tablet	Resolving phlegm and turbidity, promoting blood circulation and removing blood stasis
Fu 2017 (49)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Gao 2016 (50)	Hedan tablet	Heye (Lotus leaf), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Shanzha (Crataegus pinnatifida), Fanxieye (Folium sennae), Buguzhi (Psoraleae Fructus)	Tablet	Resolving phlegm and turbidity, promoting blood circulation and removing blood stasis
Gu 2015 (51)	Pushen capsule	Chuanxiong (Chuanxiong Rhizoma), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Heshouwu (Polygoni Multiflori Radix), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Hong 2017 (52)	Shanzha Xiaozhi capsule	Shanzha (Crataegus pinnatifida), Dahuang (Rhubarb), etc.	Capsule	Reduce fat, remove stagnation, clear heat and cool blood
Hua 2020 (53)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Jia 2020 (54)	Xuezhitong capsule	Xiebai (Bulbus Allii Macrostemon)	Capsule	Activating yang to disperse stagnation, activating qi to guide stagnation
Li 2015 (61)	GaodijiangZhi capsule	Shiliu (Pomegranate)	Capsule	Clearing phlegm and turbidity, invigorating spleen and eliminating dampness
Li 2020 (55)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Li 2014 (56)	Hedan tablet	Heye (Lotus leaf), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Shanzha (Crataegus pinnatifida), Fanxieye (Folium sennae), Buguzhi (Psoraleae Fructus)	Tablet	Resolving phlegm and turbidity, promoting blood circulation and removing blood stasis
Li 2015 (57)	Zhikang granule	Juemingzi (Cassiae Semen), Gouqizi (Lycii Fructus), Sangshen (Mori Fructus), Honghua (Carthami Flos), Shanzha (Crataegus pinnatifida)	Granule	Nourishing yin and clearing liver, promoting blood circulation and dredging collaterals
Li 2016 (58)	Tiandan Tongluo capsule	Chuanxiong (Chuanxiong Rhizoma), Shuizhi (Hirudo), Xixiancao (Siegesbeckiae Herba), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Tianma (Gastrodiae Rhizoma), Huaihua (Sophora japonica), Shichangpu (Acori T atarinowii Rhizoma), Rengongniuhuang (artificial bezoar), Huangqi (Astragali Radix), Niuxi (Achyranthis Bidentatae Radix)	Capsule	Promoting blood circulation and dredging collaterals, calming wind and resolving phlegm
Li 2014 (59)	Huazhi pill	Fuling (Poria), Shanzha (Crataegus pinnatifida), Jiaogulan (Gynostemma pentaphyllum), Dahuang (Rhubarb), Zhishi (Aurantii Fructus Immaturus), Juemingzi (Cassiae Semen)	Pill	Invigorating spleen and reinforcing the middle energizer, purging turbid urine and relaxing bowels
Li 2017 (60)	Huazhi pill	Fuling (Poria), Shanzha (Crataegus pinnatifida), Jiaogulan (Gynostemma pentaphyllum), Dahuang (Rhubarb), Zhishi (Aurantii Fructus Immaturus), Juemingzi (Cassiae Semen)	Pill	Invigorating spleen and reinforcing the middle energizer, purging turbid urine and relaxing bowels
Li 2016 (62)	Pushen capsule	Chuanxiong (Chuanxiong Rhizoma), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Heshouwu (Polygoni Multiflori Radix), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Li 2016 (63)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Li 2017 (64)	Pushen capsule	Chuanxiong (Chuanxiong Rhizoma), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Heshouwu (Polygoni Multiflori Radix), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Liang 2015 (65)	Dantian Jiangzhi pills	Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Sanqi (Notoginseng Radix Et Rhizoma), Renshen (Ginseng Radix et Rhizoma), Danggui (Angelicae Sinensis Radix), Huangjing (Rhizoma polygonati), Zexie (Alismatis Rhizoma), Rougui (Cinnamomi Cortex), Yinyanghuo (Epimedii Folium), Chuanxiong (Chuanxiong Rhizoma), Wujiapi (bark of the slender acanthopanax), Heshouwu (Polygoni Multiflori Radix)	Pill	Invigorating spleen and qi, warming and tonifying kidney yang, promoting blood circulation and removing blood stasis, and eliminating dampness and turbidity
Lin 2020 (66)	Hedan tablet	Heye (Lotus leaf), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Shanzha (Crataegus pinnatifida), Fanxieye (Folium sennae), Buguzhi (Psoraleae Fructus)	Tablet	Resolving phlegm and turbidity, promoting blood circulation and removing blood stasis

Table 4 (*continued*)

Table 4 (*continued*)

Study	TCM prescription	Components	Preparations	Therapeutic function
Lin 2022 (67)	Qianggu capsule	Drynaria fortunei	Capsule	Tonify kidney, strengthen bone and relieve pain
Liu 2015 (68)	Compound Danshen dripping pill	Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Sanqi (Notoginseng Radix Et Rhizoma), Bingpian (Borneolum)	Pill	Promoting blood circulation, removing blood stasis, relieving pain and regulating qi
Liu 2018 (69)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Liu 2019 (71)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Liu 2019 (70)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Luo 2020 (72)	Hedan tablet	Heye (Lotus leaf), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Shanzha (Crataegus pinnatifida), Fanxieye (Folium sennae), Buguzhi (Psoraleae Fructus)	Tablet	Resolving phlegm and turbidity, promoting blood circulation and removing blood stasis
Ma 2018 (73)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Moriarty 2014 (39)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Mu 2014 (74)	Pushen capsule	Chuanxiong (Chuanxiong Rhizoma), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Heshouwu (Polygoni Multiflori Radix), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Pan 2020 (75)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Peng 2015 (76)	Yindanxinnaotong soft capsule	Yinxinye (Folium ginkgo), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Dengzhanxixin (Epimedium brevicornum), Jiaogulan (Gynostemma pentaphyllum), Shanzha (Crataegus pinnatifida), Dasuan (Garlic), Sanqi (Notoginseng Radix Et Rhizoma), Aipian (Blumea balsamiborneolum)	Capsule	Promoting blood circulation, removing blood stasis, promoting qi circulation, relieving pain, promoting digestion and resolving stagnation
Qian 2013 (77)	Liuwei Dihuang pill	Shanzhuyu (Corni Fructus), Dihuang (Rehmanniae Radix), Shanyao (Dioscoreae Rhizoma), Mudanpi (Moutan Cortex), Zexie (Alismatis Rhizoma), Fuling (Poria)	Pill	Nourishing the yin of liver, spleen and kidney, preventing nourishing greasy and clearing pathogenic fire
Shao 2014 (78)	Pushen capsule	Chuanxiong (Chuanxiong Rhizoma), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Heshouwu (Polygoni Multiflori Radix), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Shao 2016 (79)	Pushen capsule	Chuanxiong (Chuanxiong Rhizoma), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Heshouwu (Polygoni Multiflori Radix), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Shi 2014 (80)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Shi 2016 (81)	Gypenosides tablets	Gypenosides	Tablet	Nourishing heart and spleen, benefiting qi and blood, removing phlegm and blood stasis, and reducing blood fat
Shi 2018 (82)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Sun 2014 (83)	Xiaozhi capsule	Heshouwu (Polygoni Multiflori Radix), Zexie (Alismatis Rhizoma), Huangqi (Astragali Radix), Danggui (Angelicae Sinensis Radix), Jianghuang (Rhizoma Curcumae Longae), Gualou (Trichosanthes kirilowii), Dahuang (Rhubarb), etc.	Capsule	Strengthening the body resistance and eliminating pathogenic factors, invigorating the liver and kidney, invigorating the spleen and qi, removing phlegm and removing blood stasis
Tan 2020 (84)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Teng 2013 (85)	Jiangzhi Daozhi capsule	Chaihu (Bupleuri Radix), Shaoyao (Paeonia), Yinchen (Artemisia capillaris Thunb), Zhishi (Aurantii Fructus Immaturus), Hongqu (Red koji), Laifuzi (Semen Raphani), Dahuang (Rhubarb)	Capsule	Soothing liver, benefiting gallbladder, promoting digestion and removing fat
Wang 2013 (86)	Hedan tablet	Heye (Lotus leaf), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Shanzha (Crataegus pinnatifida), Fanxieye (Folium sennae), Buguzhi (Psoraleae Fructus)	Tablet	Resolving phlegm and turbidity, promoting blood circulation and removing blood stasis
Wang 2014 (87)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Wang 2017 (88)	Xuefu Zhuyu capsule	Taoren (Semen Persicae), Honghua (Carthami Flos), Dihuang (Rehmanniae Radix), Chishao (Paeoniae Radix Rubra), Danggui (Angelicae Sinensis Radix), Chuanxiong (Chuanxiong Rhizoma), Niuxi (Achyranthis Bidentatae Radix), Chaihu (Bupleuri Radix), Jiegeng (Platycodonis Radix), Zhiqiao (Aurantii Fructus), Gancao (Glycyrrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, promoting qi circulation and relieving pain
Wang 2020 (89)	Haikun Shenxi capsule	Fucoidan	Capsule	Removing turbidity and expelling toxin
Wang 2021 (90)	Compound Danshen dripping pill	Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Sanqi (Notoginseng Radix Et Rhizoma), Bingpian (Borneolum)	Pill	Promoting blood circulation, removing blood stasis, relieving pain and regulating qi
Wang 2015 (91)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach

Table 4 (*continued*)

Table 4 (*continued*)

Study	TCM prescription	Components	Preparations	Therapeutic function
Wang 2015 (92)	Hedan tablet	Heye (Lotus leaf), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Shanzha (Crataegus pinnatifida), Fanxieye (Folium sennae), Buguzhi (Psoraleae Fructus)	Tablet	Resolving phlegm and turbidity, promoting blood circulation and removing blood stasis
Xu 2021 (93)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Xue 2023 (94)	Zhibitai capsule	Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Baizhu (Atractylodis Macrocephalae Rhizoma), Hongqu (Red koji)	Capsule	Eliminating phlegm and removing blood stasis, invigorating spleen and regulating stomach
Yan 2021 (95)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Yang 2013 (96)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Yang 2022 (97)	Naoxintong capsule	Huangqi (Astragali Radix), Chishao (Paeoniae Radix Rubra), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Danggui (Angelicae Sinensis Radix), Chuanxiong (Chuanxiong Rhizoma), Taoren (Semen Persicae), Honghua (Carthami Flos), Ruxiang (Olibanum), Moyao (Myrrha), Jixueteng (Caulis Spatholobi), Niuxi (Achyranthis Bidentatae Radix), Guizhi (Cinnamomi Ramulus), Sangzhi (Ramulus Mori), Dilong (Pheretima), Quanxie (Scorpio), Shuizhi (Hirudo)	Capsule	Invigorating qi and promoting blood circulation, removing blood stasis and dredging collaterals
Yu 2013 (98)	Pushen capsule	Heshouwu (Polygoni Multiflori Radix), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Chuanxiong (Chuanxiong Rhizoma), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Zhang 2013 (100)	Pushen capsule	Chuanxiong (Chuanxiong Rhizoma), Puhuang (Pollen Typhae), Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Heshouwu (Polygoni Multiflori Radix), Chishao (Paeoniae Radix Rubra), Shanzha (Crataegus pinnatifida), Zexie (Alismatis Rhizoma), Danshen (Salviae Miltiorrhizae Radix et Rhizoma)	Capsule	Promoting blood circulation and removing blood stasis, nourishing yin and resolving turbidity
Zhang 2020 (99)	Dantian Jiangzhi pills	Danshen (Salviae Miltiorrhizae Radix et Rhizoma), Yinyanghuo (Epimedii Folium), Danggui (Angelicae Sinensis Radix), Sanqi (Notoginseng Radix Et Rhizoma), Renshen (Ginseng Radix et Rhizoma), Huangjing (Rhizoma polygonati), Zexie (Alismatis Rhizoma), Rougui (Cinnamomi Cortex), Chuanxiong (Chuanxiong Rhizoma), Wujiapi (bark of the slender acanthopanax), Heshouwu (Polygoni Multiflori Radix)	Pill	Invigorating spleen and qi, warming and tonifying kidney yang, promoting blood circulation and removing blood stasis, and eliminating dampness and turbidity
Zhang 2013 (101)	Zhibituo tablets	Hongqu (Red koji)	Tablet	Spleen invigorating, digestion promoting, dampness removing, phlegm eliminating, blood circulation promoting and blood stasis removing
Zhao 2013 (102)	Zhike Yangyin capsule	Renshen (Ginseng Radix et Rhizoma), Huangqi (Astragali Radix), Shanyao (Dioscoreae Rhizoma), Dihuang (Rehmanniae Radix), Shanzhuyu (Corni Fructus), Zhuyizangfen (Pig pancreas powder), Tianhuafen (Trichosanthis Radix)	Capsule	Nourishing qi and yin, nourishing kidney and spleen
Zhao 2015 (103)	Xuezhikang capsule	Hongqu (Red koji)	Capsule	Eliminating dampness and phlegm, promoting blood circulation and removing blood stasis, invigorating spleen and promoting digestion
Zhao 2015 (104)	Zhikang granule	Juemingzi (Cassiae Semen), Gouqizi (Lycii Fructus), Sangshen (Mori Fructus), Honghua (Carthami Flos), Shanzha (Crataegus pinnatifida)	Granule	Nourishing yin and clearing liver, promoting blood circulation and dredging collaterals
Zheng 2013 (105)	Tongxinluo capsule	Renshen (Ginseng Radix et Rhizoma), Shuizhi (Hirudo), Quanxie (Scorpio), Chishao (Paeoniae Radix Rubra), Chantui (Cicadae Periostracum), Tubiechong (Eupolyphaga Steleophaga), Wugong (Scolopendra), Tanxiang (Santali Albi Lignum), Jiangxiang (Dalbergiae odoriferae lignum), Ruxiang (Olibanum), Suanzaoren (Ziziphi Spinosae Semen), Bingpian (Borneolum)	Capsule	Benefiting qi and promoting blood circulation, dredging collaterals and relieving pain
Zhou 2017 (106)	Songling Xuemaikang capsule	Xiansongye (Fresh pine leaves), Gegen (kudzuvine root), Zhenzhucengfen (Pearl layer powder)	Capsule	Calming the liver and suppressing yang, calming the heart and calming the nerves, promoting blood circulation and removing blood stasis
Zuo 2020 (107)	Tongxinluo capsule	Renshen (Ginseng Radix et Rhizoma), Tanxiang (Santali Albi Lignum), Shuizhi (Hirudo), Quanxie (Scorpio), Chishao (Paeoniae Radix Rubra), Chantui (Cicadae Periostracum), Wugong (Scolopendra), Jiangxiang (Dalbergiae odoriferae lignum), Ruxiang (Olibanum), Suanzaoren (Ziziphi Spinosae Semen), Tubiechong (Eupolyphaga Steleophaga), Bingpian (Borneolum)	Capsule	Benefiting qi and promoting blood circulation, dredging collaterals and relieving pain

CPM, Chinese patent medicine; TCM, traditional Chinese medicine.

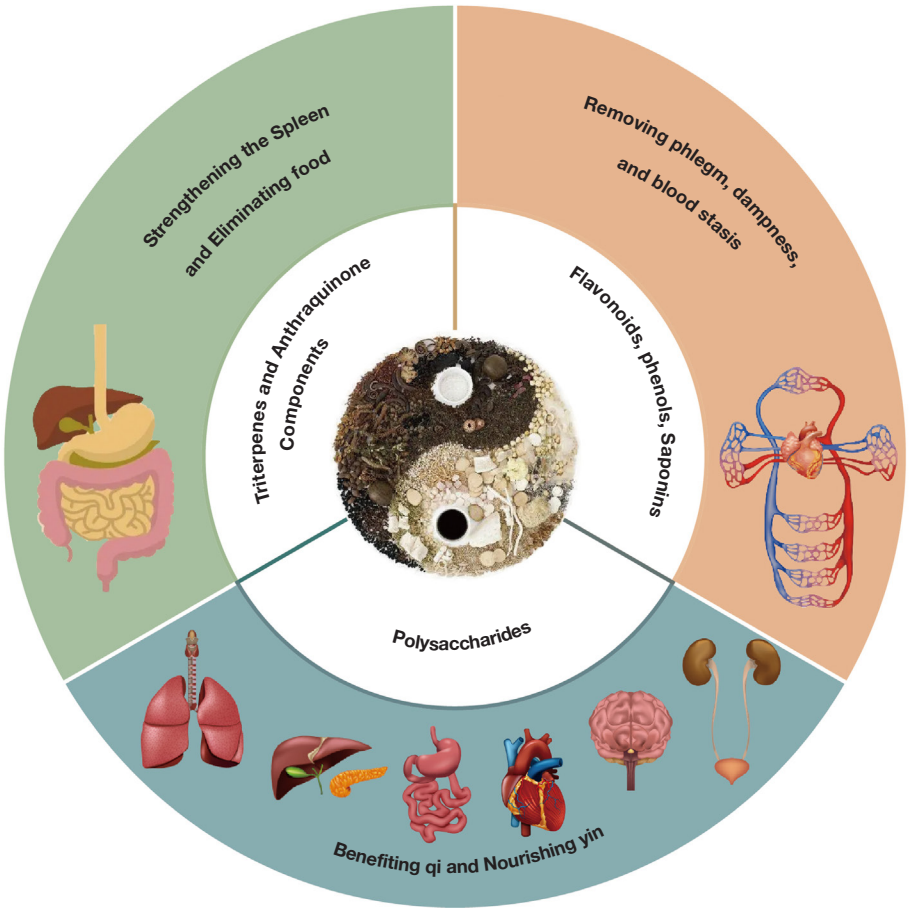

Figure 10 The main mechanism of the three kinds of traditional Chinese herbal medicines in treating dyslipidemia.

effectively address the unique conditions of patients with varying constitutions and pathogenesis, distinct CHMs were selected to specifically target their ailments, thereby yielding diverse herbal ingredients and dosages for each prescription. Furthermore, dissimilar grades of dyslipidemia could potentially elicit disparate responses to TCM interventions. However, the international general TCM syndrome differentiation standard for dyslipidemia has not been formed, hence it is necessary to strengthen the study of syndrome standard in the future.

Among the included 69 studies, 40 reported adverse events. Among them, 17 cases reported no adverse events occurred during the study, and the other 23 studies reported adverse events. The adverse events were mostly concentrated in the gastrointestinal tract, which might be related to the symptoms of diarrhea and vomiting in the digestive system that are easily observed by patients or their families, thus suggesting that attention should be paid to gastrointestinal protection when CPM is used in the clinic. In addition, other reported adverse events included dizziness, headache, abnormal liver function and hypoglycemia. These adverse reactions were relatively mild in nature and resolved on their own after symptomatic treatment. There were no reports of severe adverse events or deaths from these studies. The meta-analysis of adverse events did not display any significant difference between the treatment group and the control group (P=0.40), thus suggesting that combined CPM therapy was generally safe and tolerable.

These results might be limited by the duration of intervention, modern medicine, TCM and the subtypes of dyslipidemia, as well as the use of therapy combinations. According to the Chinese Guidelines for Lipid Management (35), we considered a minimum of 6 weeks as the optimal treatment duration. It remains unknown whether a longer invention duration can achieve better

curative effects without increasing the different adverse events. Additionally, the current studies encompass various complications or comorbidities, contributing to the heterogeneity. Still, we were able to address all the objectives of the current study and confirmed the potential role of CPM in treating dyslipidemia. In summary, these results need cautious interpretations and should be validated in future studies.

Conclusions

In general, CPM could effectively regulate the levels of the TC, TG, LDL-C, HDL-C, making it a potent adjunct to statins with a primary focus on reducing LDL-C level. The main function of CPM is targeted towards addressing the underlying causes of diseases, with liver qi stagnation, and spleen and kidney qi deficiencies being identified as the key pathogenic factors. The therapeutic effects of CPM could be potentially attributed to its ability to eliminate dampness and phlegm, promote blood circulation, remove blood stasis, invigorate the spleen, and enhance digestion, benefiting qi and nourishing yin. These effects have been substantiated through precious pharmacological research. Heterogeneity mainly originates from the particularity of preparation and syndrome differentiation and treatment, hence one should pay attention to pills and strengthen the study of syndrome standardization to improve the treatment outcome. These findings demonstrate that CPM, as an alternative and complementary therapy, can yield superior therapeutic effects in ameliorating dyslipidemia without exacerbating adverse effects. However, to further enhance the therapeutic efficacy, credibility, and long-term safety evaluation of CPM treatment in dyslipidemia, including both during treatment as well as after drug discontinuation, further clinical studies are needed to establish standardized approaches for dialectical treatment.

Acknowledgments

The authors would like to thank all the reviewers who participated in the review, as well as MJEditor (www.mjeditor.com) for providing English editing services during the preparation of this manuscript.
Funding: This work was supported by the Key Research and Development Program of the Ministry of Science and Technology (No. 2022YFC2010104 to Q.W.), Beijing Nova Program (No. Z201100006820027 to L.L.) and National Nonprofit Institute Research Grant for Institute of Basic Theory for Chinese Medicine, CACMS (No. YZ-202151 to T.L.).

Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-146/rc

Peer Review File: Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-146/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-146/coif). T.L. reports funding support from National Nonprofit Institute Research Grant for Institute of Basic Theory for Chinese Medicine, CACMS (No. YZ-202151); Q.W. reports funding support from the Key Research and Development Program of the Ministry of Science and Technology (No. 2022YFC2010104); L.L. reports funding support from Beijing Nova Program (No. Z201100006820027). The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Karr S. Epidemiology and management of hyperlipidemia. Am J Manag Care 2017;23:S139-48.
2. Xiang Q, Tian F, Xu J, et al. New insight into dyslipidemia-induced cellular senescence in atherosclerosis. Biol Rev Camb Philos Soc 2022;97:1844-67.
3. Park SK, Jung JY, Oh CM, et al. Components of metabolic syndrome and their relation to the risk of incident cerebral

infarction. Endocr J 2021;68:253-9.
4. Doi T, Langsted A, Nordestgaard BG. Elevated Remnant Cholesterol Reclassifies Risk of Ischemic Heart Disease and Myocardial Infarction. J Am Coll Cardiol 2022;79:2383-97.
5. Yousri NA, Suhre K, Yassin E, et al. Metabolic and Metabo-Clinical Signatures of Type 2 Diabetes, Obesity, Retinopathy, and Dyslipidemia. Diabetes 2022;71:184-205.
6. Pouwels S, Sakran N, Graham Y, et al. Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. BMC Endocr Disord 2022;22:63.
7. Chait A. Hypertriglyceridemia. Endocrinol Metab Clin North Am 2022;51:539-55.
8. Liu T, Zhao D, Qi Y. Global Trends in the Epidemiology and Management of Dyslipidemia. J Clin Med 2022;11:6377.
9. Nikparvar M, Khaladeh M, Yousefi H, et al. Dyslipidemia and its associated factors in southern Iranian women, Bandare-Kong Cohort study, a cross-sectional survey. Sci Rep 2021;11:9125.
10. Tripathy JP, Thakur JS, Jeet G, et al. Burden and risk factors of dyslipidemia-results from a STEPS survey in Punjab India. Diabetes Metab Syndr 2017;11 Suppl 1:S21-7.
11. Farzadfar F, Finucane MM, Danaei G, et al. National, regional, and global trends in serum total cholesterol since 1980: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3·0 million participants. Lancet 2011;377:578-86.
12. Bureau Of Disease Prevention And Control NHAW. Report on Nutrition and Chronic Diseases of Stratified People in China 2020. Beijing: People's Medical Publishing House; 2020.
13. Repositioning of the global epicentre of non-optimal cholesterol. Nature 2020;582:73-7.
14. Chu J, Gao R, Zhao S, et al. Guidelines for the prevention and treatment of adult dyslipidemia in China (revised edition in 2016). Chinese Circulation Journal 2016;31:937-53.
15. Report on Cardiovascular Health and Diseases in China 2021: An Updated Summary. Biomed Environ Sci 2022;35:573-603.
16. Lu Y, Zhang H, Lu J, et al. Prevalence of Dyslipidemia and Availability of Lipid-Lowering Medications Among Primary Health Care Settings in China. JAMA Netw Open 2021;4:e2127573.
17. Cheeley MK, Saseen JJ, Agarwala A, et al. NLA scientific statement on statin intolerance: a new definition and key considerations for ASCVD risk reduction in the statin intolerant patient. J Clin Lipidol 2022;16:361-75.
18. Oesterle A, Laufs U, Liao JK. Pleiotropic Effects of Statins on the Cardiovascular System. Circ Res 2017;120:229-43.
19. Etemad L, Salmasi Z, Moosavian Kalat SA, et al. An overview on nanoplatforms for statins delivery: Perspectives for safe and effective therapy. Environ Res 2023;234:116572.
20. Cheeley MK, Clegg K, Lockridge C, et al. Statin Intolerance: an Overview of US and International Guidance. Curr Atheroscler Rep 2023;25:517-26.
21. Russo MW, Hoofnagle JH, Gu J, et al. Spectrum of statin hepatotoxicity: experience of the drug-induced liver injury network. Hepatology 2014;60:679-86.
22. Martirossian AN, Goldberg AC. Management of patients with statin intolerance. Best Pract Res Clin Endocrinol Metab 2023;37:101714.
23. Jacobson TA, Cheeley MK, Jones PH, et al. The STatin Adverse Treatment Experience Survey: Experience of patients reporting side effects of statin therapy. J Clin Lipidol 2019;13:415-24.
24. Norata GD, Tibolla G, Catapano AL. Statins and skeletal muscles toxicity: from clinical trials to everyday practice. Pharmacol Res 2014;88:107-13.
25. Zhang H, Plutzky J, Skentzos S, et al. Discontinuation of statins in routine care settings: a cohort study. Ann Intern Med 2013;158:526-34.
26. Backes JM, Hilleman DE. Lipid lowering therapy: implications of recent clinical trials. Future Cardiol 2024;20:89-98.
27. Pang T, Mai L, Chen Y, et al. Research progress on changes of chemical components in compatibility of chinese medicine pairs. Journal of Chinese Medicinal Materials 2015;38:2429-34.
28. Rauf A, Akram M, Anwar H, et al. Therapeutic potential of herbal medicine for the management of hyperlipidemia: latest updates. Environ Sci Pollut Res Int 2022;29:40281-301.
29. Orekhov AN, Ivanova EA. Cellular models of atherosclerosis and their implication for testing natural substances with anti-atherosclerotic potential. Phytomedicine 2016;23:1190-7.
30. Li Y, Liu C, Zhang Y, et al. Pharmacokinetics of ferulic acid and potential interactions with Honghua and clopidogrel in rats. J Ethnopharmacol 2011;137:562-7.
31. Li SP, Zhao J, Yang B. Strategies for quality control of Chinese medicines. J Pharm Biomed Anal 2011;55:802-9.

32. An D, Wu Z, Liang C, et al. Expert consensus on diagnosis and treatment of dyslipidemia with integrated traditional Chinese and western medicine. Chinese General Practice 2017;20:262-9.
33. Meng TT, Xie XL, Li TT, et al. Oral Chinese patent medicine combined with statins in treatment of dyslipidemia:A network Meta-analysis. Chinese Traditional and Herbal Drugs 2021;52:1092-104.
34. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ 2021;372:n160.
35. Wang Z, Liu J, Li J, et al. Chinese Guidelines for Lipid Management (2023). Chinese Circulation Journal 2023;38:237-71.
36. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.
37. Review Manager (RevMan). 5.4 version: The Cochrane Collaboration; 2020.
38. Trial Sequential Analysis (TSA). 0.9.5.10 Beta version. Centre for Clinical Intervention Research, The Capital Region, Copenhagen University Hospital – Rigshospitalet: The Copenhagen Trial Unit; 2021.
39. Moriarty PM, Roth EM, Karns A, et al. Effects of Xuezhikang in patients with dyslipidemia: a multicenter, randomized, placebo-controlled study. J Clin Lipidol 2014;8:568-75.
40. Cao C, Zhu H. Clinical observation of Pushen capsule combined with atorvastatin in the treatment of hyperlipidemia. Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine 2014;14:25-6.
41. Cao XC, Zhao HZ, Kong DY, et al. Clinical observation of Pushen capsule combined with rosuvastatin calcium in the treatment of dyslipidemia in coronary slow flow. Chinese Journal of Integrative Medicine on Cardio/Cerebrovascular Disease 2021;19:1861-3.
42. Chen H. To clinical observation the 42 cases of elderly patients with hyperlipidemia for Integrative Medicine. Cardiovascular Disease Journal of Integrated Traditional Chinese and Western Medicine (Electronic) 2014;(4):27-8.
43. Chen B, Luo JC, Wang CY. Effect of zhibitai capsule on blood lipid and high-sensitivity C-reactive protein in patients with hyperlipidemia. Chinese Journal of Integrative Medicine on Cardio/Cerebrovascular Disease 2016;14(4):420-1,422.
44. Chen YY, Liu QS, Chen QL, et al. Clinical effect of Zhibitai capsule in the treatment of senile hyperlipidemia patients with phlegm and blood stasis syndrome. Chinese Journal of Primary Medicine and Pharmacy 2020;27:733-7.
45. Fan YL, Zhu Y, Yin DH. Treatment of 35 cases of dyslipidemia in middle-aged and young people with Hedan tablets combined with atorvastatin. Herald of Medicine 2014;(8):1029-31.
46. Feng D. Effect of zhibituo tablet on blood lipid and high-sensitivity C-reactive protein in elderly patients with dyslipidemia. China Practical Medicine 2015;(15):151-2.
47. Feng Y, Lu SL, Jin XG, et al. Effect of "Natural Polypill", Xuezhikang on Serum Cholesterol Metabolism Markers in Early Menopausal Women with Hypercholesterolemia. Chin J Integr Med 2022;28:202-7.
48. Fu X, Zhan Q, Meng F, et al. Effects of Hedan Tablets Combined with Rosuvastatin Calcium on Carotid Intima-Media Thickness and Vascular Endothelial Function in Patients with Hyperlipidemia. Journal of Anhui University of Chinese Medicine 2013;32:27-30.
49. Fu YJ. Observation on the effect of Xuezhikang capsule combined with atorvastatin calcium on hyperlipidemia. Chinese Journal of Rural Medicine and Pharmacy 2017;24:52-3.
50. Gao F. Clinical effect of Hedan tablets combined with simvastatin on hyperlipidemia. Tianjin Pharmacy 2016;28:41-2.
51. Gu SM, Sun Y. Observation on the therapeutic effect of routine plus Pushen capsule on hyperlipidemia in the elderly. People's Military Surgeon 2015;58:71-2.
52. Hong J, Hou X, Chen H, et al. Treatment of 38 cases of unstable angina pectoris complicated with hyperlipidemia with hawthorn Xiaozhi capsule. Hunan Journal of Traditional Chinese Medicine 2017;33:42-3.
53. Hua JP. Observation on therapeutic effect of Zhibitai capsule on hyperlipidemia. Cardiovascular Disease Electronic Journal of Integrated Traditional Chinese and Western Medicine 2020;8:67-8.
54. Jia W, Li Y, Wan J, et al. Effects of Xuezhitong in Patients with Hypertriglyceridemia: a Multicentre, Randomized, Double-Blind, Double Simulation, Positive Drug and Placebo Parallel Control Study. Cardiovasc Drugs Ther 2020;34:525-34.
55. Li P, Li Y. Clinical Efficacy of Zhibitai Capsule in Treating Patients of Dyslipidemia with Phlegm-stasis Binding Pattern. Chinese Journal of Experimental Traditional Medical Formulae 2020;26:137-41.
56. Li BH, Song Y. Observation on therapeutic effect of Hedan tablets combined with atorvastatin on hyperlipidemia. Chinese Journal of Integrative Medicine

on Cardio/Cerebrovascular Disease 2014;(7):806-7.
57. Li H, Wen L, Zhan QL, et al. Effect of Zhikang Granule Combined with Rosuvastatin on Intima-media Thickness and Inflammatory Factors of Carotid Artery in Patients with Hyperlipidemia. Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease 2015;23:111-3.
58. Li H. Clinical Research on Integrated Traditional Chinese and Western Medicine Treatment of Mixed Type Hyperlipidemia. China Journal of Chinese Medicine 2016;31:1175-7.
59. Li L, Yang S, Wu F, et al. Effects of HuaZhi Pill on Blood Lipid of the Patients with Hyperlipemia. Western Journal of Traditional Chinese Medicine 2014;27:31-3.
60. Li L. Summary of Li Yuxian's academic thought and clinical experience and clinical study of Huazhi Pill in treating dyslipidemia (spleen deficiency and phlegm turbidity syndrome). Beijing University of Chinese Medicine; 2017.
61. Li M. Clinical study on the efficacy and safety of Gaodi Jiangzhi capsule in the treatment of primary dyslipidemia IIC. China Academy of Chinese Medical Sciences; 2015.
62. Li X. The Randomized parallel controlled study of the PuShen capsule and Atorvastatin Calcium Tablets On Treatment of Hyperlipidemia. Journal of Practical Traditional Chinese Internal Medicine 2016;30:73-5.
63. Li X, Wang YX, Shao C. Clinical efficacy and safety of zhibitai combined with rosuvastatin in the treatment of elderly patients with coronary atherosclerotic heart disease complicated with dyslipidemia. China Journal of Pharmaceutical Economics 2016;11:67-8.
64. Li Y. Clinical observation of Pushen capsule combined with atorvastatin in the treatment of hyperlipidemia (blood stasis syndrome). Shanxi Medical University; 2017.
65. Liang ZM, Jiang LP. Clinical efficacy of Dantian Jiangzhi Pill in the treatment of senile hyperlipidemia. Chinese Journal of Gerontology 2015;35:2973-5.
66. Lin L. Clinical observation of Hedan capsule combined with atorvastatin in the treatment of blood lipid in patients with hyperlipidemia. Xinxueguanbing Fangzhi Zhishi 2020;10:18-20.
67. Lin L, Wang Z, Zhang H, et al. Drynaria fortunei improves lipid profiles of elderly patients with postmenopausal osteoporosis via regulation of Notch1-NLRP3 inflammasome-mediated inflammation. Gynecol Endocrinol 2022;38:176-80.
68. Liu J, Wang T, Kong L, et al. Clinical assessment on treatment of hyperlipidemia by compositie salviae dropping pill combined with Simvas-tatin. Hebei Journal of Traditional Chinese Medicine 2015;(1):93-4,158.
69. Liu C, Xu W, Wang J. Effect Research on the Hyperlipidemia Patients Treated by Hematopoeia and Atorvastatin Calcium Tablets. Chinese Medical Record 2018;19:92-4.
70. Liu J, Tao T, Wang N, et al. Effect of Zhibitai combined with rosuvastatin on patients with dyslipidemia of coronary heart disease. Clinical Research and Practice 2019;4:29-30,33.
71. Liu ZK. Clinical observation of rosuvastatin, zhibitai and their combination in the treatment of type 2 diabetes mellitus with hyperlipidemia. Guide of China Medicine 2019;17:122-3.
72. Luo H, Zhang T, Wang Z. Effects of Hedan tablet combined with atorvastatin on serum homocysteine, inflammatory factors and vascular endothelial dilation function in patients with dyslipidemia. China Medicine 2020;15:1518-22.
73. Ma WX, Feng XJ. Clinical observation on zhibitai in treating hyperlipidemia with phlegm and blood stasis. Chinese Journal of Integrative Medicine on Cardio/Cerebrovascular Disease 2018;16:3341-3.
74. Mu M. Pushen Capsule Combined with Rosuvastatin Tablet in Treating Senile Mixed Hyperlipidemia in 43 Cases. China Pharmaceuticals 2014;23:102-3.
75. Pan T, Lv S, Wang D, et al. Effect of Xuezhikang Capsule Combined with Metformin on Hyperlipidemia in type 2 Diabetes. Clinical Research 2020;28:33-4.
76. Peng J. Observation of the Therapeutic Effect of Yindanxinnaotong Capsule in the Treatment of Diabetes Mellitus with Hyperlipidemia. Diabetes New World 2015;35:68-70.
77. Qian Z. Clinical efficacy of the Liuwei Dihuang pill in the treatment of diabetes and hyperlipidemia. Clinical Journal of Chinese Medicine 2013;5:20-1.
78. Shao ZH. Observation on therapeutic effect of rosuvastatin calcium tablets combined with Pushen capsule on hyperlipidemia. Modern Journal of Integrated Traditional Chinese and Western Medicine 2014;(28):3143-4.
79. Shao Z, Gu N. Effects of Pushen Capsules and Atorvastatin on Blood Lipid Levels in Patients with Coronary Heart Disease Complicated with Hyperlipidemia. Chinese Journal of Integrative Medicine on Cardio/Cerebrovascular Disease 2016;14:282-4.
80. Shi Y. Clinical observation of Xuezhikang combined with lifestyle intervention on 102 cases of hyperlipidemia in community residents. Guiding Journal of Traditional Chinese Medicine and Pharmacy 2014;20:115-6.

81. Shi L. Clinical study on treatment of hyperlipidemia with Yunpi Tongxin recipe. China Academy of Chinese Medical Sciences; 2016.
82. Shi C, Wang X, Zhu H. Clinical therapeutic effect of the Xuezhikang capsule combined with fluvastatin sodium on hyperlipidemia. World Clinical Drugs 2018;39:43-6.
83. Sun H, Sun Y. Clinical observation of Xiaozhi capsule combined with fenofibrate in the treatment of hyperlipidemia. Drugs & Clinic 2014;29:766-9.
84. Tan B. Effect of atorvastatin combined with Zhibitai on coronary heart disease complicated with hyperlipidemia. Contemporary Medicine 2020;26:9-11.
85. Teng Z, Lu Y, Zhong X, et al. Clinical observation on 41 cases of hyperlipidemia treated with Jiangzhi Daozhi capsule. Journal of Gansu University of Chinese Medicine 2013;30:21-3.
86. Wang Q. Clinical observation on the treatment of senile hyperlipidemia with combination of traditional Chinese and western medicine. Chinese Journal of Urban and Rural Enterprise Hygiene 2013;28:22-3.
87. Wang Y. Clinical efficacy of Xuezhikang maintenance treatment for senile hyperlipidemia. Chinese Journal of Primary Medicine and Pharmacy 2014;(z2):7-9.
88. Wang X, Tang Y, Sun Y. Clinical Study on Xuefu Zhuyu Capsule in Treating Hyperlipidemia of Qi Stagnation and Blood Stasis Type. Pharmacology and Clinics of Chinese Materia Medica 2017;33:177-80.
89. Wang J, Liu M, Wei W, et al. Effect of integrated traditional Chinese and western medicine therapy on patients with end-stage renal failure complicated with dyslipidemia. Contemporary Medical Symposium 2020;18:214-5.
90. Wang L. Clinical effect of integrated traditional Chinese and western medicine (compound Danshen dripping pills combined with rosuvastatin) on patients with coronary heart disease complicated with hyperlipidemia. China Health Food 2021;(12):170-1.
91. Wang C, Chen H. Influence of Zhibitai Capsule Combined with Atorvastatin Calcium Tablet on Blood Lipid and Inflammatory Factors in Elder Patients with Dyslipidemia. Herald of Medicine 2015;(8):1047-9.
92. Wang Q. Clinical observation of Hedan Tablets combined with rosuvastatin in treatment of type 2 diabetes with hyperlipidemia. Drugs & Clinic 2015;(6):670-3.
93. Xu BT, Liu XH, Li YM, et al. Clinical observation of Xuezhikang capsule combined with rosuvastatin calcium tablets in the treatment of primary hyperlipidemia. OUR Health 2021;(24):290.
94. Xue J. Clinical study on Zhibitai Capsules combined with probucol in treatment of hyperlipidemia. Drugs & Clinic 2023;38:346-9.
95. Yan S. Lipid-regulating effect of Xuezhikang capsule combined with simvastatin and its influence on 24-hour urinary albumin and plasma endothelin-1 levels. Cardiovascular Disease Electronic Journal of Integrated Traditional Chinese and Western Medicine 2021;9:36-38,123.
96. Yang W. Clinical analysis of Xuezhikang in the treatment of hypercholesterolemia. Contemporary Medicine 2013;19:143-4.
97. Yang C, Liu J, Xiong Y. Clinical observation on Naoxintong capsule in the treatment of senile hyperlipidemia complicated with carotid atherosclerotic plaque. Chinese Medicine Modern Distance Education of China 2022;20:91-3.
98. Yu G, Yan H, Hu M, et al. Clinical Observation of Hyperlipemia Treated by Pushen Capsule. Journal of Nanjing University of Traditional Chinese Medicine 2013;29:594-5.
99. Zhang J, Meng J, Chen K, et al. Clinical study of Dantian Jiangzhi Pills combined with ezetimibe in treatment of hyperlipidemia. Drug Evaluation Research 2020;43:299-303.
100. Zhang S, Wu Z. Effect Observation of Pushen Capsules Combined with Rosuvastatin Calcium in the Treatment of Coronary Heart Disease in Patients with Combined Hyperlipidemia. Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease 2013;21:52-4.
101. Zhang Y, Zhang J, Yang H, et al. Efficacy of zhibituo combined with atorvastatin on type 2 diabetic patients with hyperlipidemia. Clinical Medicine of China 2013;29:942-5.
102. Zhao H. Effect of Zhike Yangyin Capsule on TG and HDL-C in Type 2 Diabetes Patients with Deficiency of both Qi and Yin. Heilongjiang Academy of Traditional Chinese Medicine; 2013.
103. Zhao J. Clinical Observation on Type 2 Diabetes With Dyslipidemia Xuezhikang. Continuing Medical Education 2015;(1):115-6.
104. Zhao XM. Efficacy and safety of Zhikang granule combined with atorvastatin in the treatment of hyperlipidemia. Clinical Focus 2015;30:268-72.
105. Zheng M. Clinical study on the effect of integrated traditional Chinese and western medicine on carotid intima-media thickness and plaque in patients with hyperlipidemia. Acta Chinese Medicine and Pharmacology 2013;41:112-4.

106. Zhou Y. Clinical Observation of Songling Xuemaikang Capsules Combined with Atorvastatin Calcium Tablets for Carotid Atherosclerosis in Patients with Lipid Abnormality. New Chinese Medicine 2017;49:15-7.
107. Zuo N. Clinical efficacy analysis of simvastatin combined with Tongxinluo capsule in lipid-lowering therapy. Medical Diet and Health 2020;18:76-7.
108. Writing Committee; Lloyd-Jones DM, Morris PB, et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2022;80:1366-418.
109. Navarese EP, Robinson JG, Kowalewski M, et al. Association Between Baseline LDL-C Level and Total and Cardiovascular Mortality After LDL-C Lowering: A Systematic Review and Meta-analysis. JAMA 2018;319:1566-79.
110. Silverman MG, Ference BA, Im K, et al. Association Between Lowering LDL-C and Cardiovascular Risk Reduction Among Different Therapeutic Interventions: A Systematic Review and Meta-analysis. JAMA 2016;316:1289-97.
111. Cholesterol Treatment Trialists' (CTT) Collaboration; Fulcher J, O'Connell R, et al. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. Lancet 2015;385:1397-405.
112. Thanassoulis G, Williams K, Ye K, et al. Relations of change in plasma levels of LDL-C, non-HDL-C and apoB with risk reduction from statin therapy: a meta-analysis of randomized trials. J Am Heart Assoc 2014;3:e000759.
113. Kopin L, Lowenstein C. Dyslipidemia. Ann Intern Med 2017;167:ITC81-96.
114. Ma G, Zhang Y. Research progress of treating hyperlipidemia with traditional Chinese medicine. Chinese Journal of Integrative Medicine on Cardio-Cerebrovascular Disease 2019;17:2116-9.
115. Raja V, Aguiar C, Alsayed N, et al. Non-HDL-cholesterol in dyslipidemia: Review of the state-of-the-art literature and outlook. Atherosclerosis 2023;383:117312.
116. Niu C, Chen C, Chen L, et al. Decrease of blood lipids induced by Shan-Zha (fruit of Crataegus pinnatifida) is mainly related to an increase of PPARα in liver of mice fed high-fat diet. Horm Metab Res 2011;43:625-30.
117. Hu HJ, Luo XG, Dong QQ, et al. Ethanol extract of Zhongtian hawthorn lowers serum cholesterol in mice by inhibiting transcription of 3-hydroxy-3-methylglutaryl-CoA reductase via nuclear factor-kappa B signal pathway. Exp Biol Med (Maywood) 2016;241:667-74.
118. Ji W, Gong BQ. Hypolipidemic activity and mechanism of purified herbal extract of Salvia miltiorrhiza in hyperlipidemic rats. J Ethnopharmacol 2008;119:291-8.
119. Ai ZL, Zhang X, Ge W, et al. Salvia miltiorrhiza extract may exert an anti-obesity effect in rats with high-fat diet-induced obesity by modulating gut microbiome and lipid metabolism. World J Gastroenterol 2022;28:6131-56.
120. Bao Y, Wang L, Xu Y, et al. Salvianolic acid B inhibits macrophage uptake of modified low density lipoprotein (mLDL) in a scavenger receptor CD36-dependent manner. Atherosclerosis 2012;223:152-9.
121. Huang MQ, Zhou CJ, Zhang YP, et al. Salvianolic Acid B Ameliorates Hyperglycemia and Dyslipidemia in db/db Mice through the AMPK Pathway. Cell Physiol Biochem 2016;40:933-43.
122. Jia L, Song N, Yang G, et al. Effects of Tanshinone IIA on the modulation of miR-33a and the SREBP-2/Pcsk9 signaling pathway in hyperlipidemic rats. Mol Med Rep 2016;13:4627-35.

Cite this article as: Fang Y, Wu H, Liang X, Li T, Jia R, Dong Y, Zheng Y, Wang Q, Li L. Efficacy and safety assessment of traditional Chinese patent medicine for dyslipidemia: a systematic review of randomized clinical trials with meta-analysis and trial sequential analysis. Cardiovasc Diagn Ther 2024;14(3):419-446. doi: 10.21037/cdt-24-146

