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Efficacy of oats for dyslipidaemia: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Dyslipidaemia is a critical factor in the development of atherosclerotic cardiovascular disease. Concerning dyslipidaemia regulation, we advocate for lifestyle interventions such as diet to complement drug treatment. Numerous studies have confirmed that oat β-glucan, a critical component of oats, can help lower cholesterol. However, there is no conclusive evidence for the efficacy of oats and their products in the treatment of dyslipidaemia. As a result, we have developed this protocol to serve as a guide for future research on oat intervention for dyslipidaemias.

Methods and analysis We will conduct a search of eight databases or websites (PubMed, Web of Science, Cochrane Library, EMBASE, CNKI, SinoMed, VIP and Wanfang) to identify studies on oats' ability to regulate blood lipid levels. Two authors will screen articles independently, extract data based on inclusion and exclusion criteria, and assess the quality and bias of included studies. To assess and quantify heterogeneity, Q and I^2 statistics will be used. If there is significant heterogeneity between studies, the source of the heterogeneity will be investigated using subgroup analysis and sensitivity analysis. We will analyse potential publication bias using the Begg funnel plot and Egger's weighted regression statistics. To assess the quality of evidence for the primary outcomes, the Grades of Recommendations, Assessment, Development and Evaluation method will be used.

Ethics and dissemination This study is based on the existing literature and data in the databases. It is not subject to ethical review. The findings, on the other hand, will be published in a peer-reviewed journal. These findings may aid in the management of dyslipidaemia on a daily basis.

PROSPERO registration number CRD42021226751.

Strengths and limitations of this study

- The intervention and possible control measures regarding oats will be considered fully and grouped.
- Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols guidelines will be strictly followed to ensure reproducibility of the study.
- The term 'oats' introduces the possibility of heterogeneity.
- Dosage is not standardised; hence, the relationship between dose and efficacy will not be explored.

INTRODUCTION

Dyslipidaemia is a term that refers to abnormalities in the metabolism of lipoproteins, such as excessive or deficient lipoproteins, which plays a critical role in atherosclerotic cardiovascular disease (ASCVD).[1 2] According to a cross-sectional study published in 2016, the overall prevalence of dyslipidaemia in Chinese adults is 34%. A recent studyshowed that as many as 43% of people over the age of 40 suffer from dyslipidemia in China.[3 4] More importantly, this graph demonstrates an upward trend.[5] In addition, ASCVD has become the leading cause of death and disability-adjusted life years in China, also poses a threat to global health.[6 7]

Over the last few decades, guidelines have emphasised statins as the cornerstone of lipid-lowering therapy and have widely publicised statin availability.[8 9] However, there are contraindications and side effects to statins. For instance, the use of statins can be limited by factors like liver function, drug allergies. Moreover, their clinically significant adverse reactions may include musculoskeletal disorders, endocrine disorders, liver function impairment, etc.[1 10] This significantly impairs effective atherosclerosis prevention in high-risk patients.[11] Additionally, relying solely on statins does not always result in adequate lipid reduction.[1] Lifestyle modification is critical for the primary prevention of ASCVD in patients with dyslipidaemia. It is the best treatment in terms of cost/benefit and risk/benefit ratios.[12] Dietary control of lipid metabolism is critical for lowering the risk of cardiovascular disease.[13] For patients unable to receive statin therapy or are currently receiving statin therapy while their blood lipid levels have not yet reached target levels, certain nutraceuticals may be beneficial.[14–16] It is worth noting that dietary and lifestyle improvements should be made regardless of whether medication is used.[12 17]

Oats have been cultivated on a global scale for over 2000 years and are a staple food in several countries.[18] Nowadays, oat is one of the most widely used auxiliary therapies for lowering cholesterol. The soluble fibre β-glucan has long been recognised as a critical active ingredient in cholesterol-lowering medications.[19] From North America to Europe and Asia, food agency standards indicate that oat β-glucan (OBG) lower cholesterol.[20–22] Previous meta-analyses have also demonstrated that β-glucan derived from oats has a cholesterol-lowering effect, but these studies focused primarily on the individual ingredient OBG.[23–25] Several reviews compared several whole grains rather than focusing exclusively on oat, overlooking some relevant oat-related research.[26 27] Others concentrated on oats. They did, however, examine the effects of oat on inflammatory factors or cardiovascular disease risk factors, rather than meta-analyses that specifically examined dyslipidaemias. Additionally, the target population is distinct, which may entail disparate results.[28 29] Numerous oat products, such as oatmeal, rolled oats, and oat bread, are readily available in real-world practical dietary plans. Thus, in this protocol, we propose to focus on various oat preparations and oat components and to conduct a systematic review and meta-analysis to compare the oat diet to other diets in patients with dyslipidaemia. Specific aspects include the effect on blood lipid indicators (triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL) and high-density lipoprotein (HDL)); whether the intervention effect of oats on blood lipids is affected by oat components, gender, region, oat dosage and other parameters; and whether oats affect blood lipid-related items such as body weight, body mass index (BMI) and inflammatory factors. The research conducted under the auspices of this protocol aims to develop more nutritious and healthy dietary recommendations for patients with dyslipidaemias.

METHOD

This protocol adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) 2015 Statement .[30] The final result will be reported in accordance with this statement.

Inclusion and exclusion criteria

Types of studies

Randomised controlled trials (RCTs).

We will exclude studies that are not RCTs or animal experiments, duplicate studies, reviews, meta-analyses, conferences and case reports.

Types of participants

In comparison to previous meta-analyses of the effect of oat interventions on risk factors for cardiovascular disease, we will include patients with abnormal lipid levels. The diagnostic criteria for dyslipidaemias are based on several international guidelines.[17 31–33] In this case, patients should meet one or more of the following criteria:

- TC ≥5.18 mmol/L (200 mg/dL).
- LDL cholesterol (LDL-C) ≥3.37 mmol/L (130 mg/dL).
- HDL cholesterol (HDL-C) <1.04 mmol/L (40 mg/dL).
- Non-HDL-C (non-HDL-C)≥4.1 mmol/L (160 mg/dL).
- TG ≥1.7 mmol/L (150 mg/dL).

At the literature screening stage, clinical classifications of dyslipidaemias will not be differentiated. Patients must, however, be adults over the age of 18, regardless of gender or region. The onset of dyslipidaemia is relatively insidious. There may be no aura symptoms, so the disease duration will not be limited.

Trials will be excluded if they are conducted on patients with LDL-C ≥190 mg/dL or diagnosed with familial hypercholesterolaemia or severe hypertriglyceridaemia (TG ≥500 mg/dL).

Type of interventions

In light of the study's purpose, the term 'oat' refers not only to foods made from wholegrain oats or diets high in oats, such as oatmeal, oat powder and oat bread, but also to the major components of oats, such as bran, endosperm and germ. If we could establish that certain cereal fibres (eg, OBG) were dependent on oats or oat products, they would be included in the study as well. According to a previous Cochrane review,[26] the effect of wholegrain oats on cholesterol levels was often observed after 4 weeks, indicating that the treatment duration should be ≥4 weeks. There will be no restrictions on dosage, frequency or preparation method to include as many relevant studies as possible. Oats can be used in conjunction with other therapies or as a stand-alone intervention. But if the study includes interventions other than oats and the effect of oats cannot be disentangled from the effect of the other interventions, it will be excluded.

Comparators/control

Placebo, no dietary intervention or a specific type of dietary intervention without oat (eg, low-calorie diet, rice, wheat).

Since 'oat' is a dietary intervention and this study's objective is to compare the effectiveness of oat to that of other dietary interventions, we will exclude studies that use complementary medicine, such as Chinese herbal medicine, as a controlled intervention.

All included RCTs will be divided into three sets according to their respective dietary backgrounds (table 1):

Outcomes

The primary outcome measures will be serum lipid profiles, specifically TC, TG, LDL-C and HDL-C.

Secondary outcomes will include body weight, BMI, inflammatory markers, adverse events and other indicators associated with dyslipdaemias.

Table 1 Intervention group versus control group

#	Intervention group	versus	Control group
1	Oats		Placebo OR no dietary intervention
2	Oats in combination with some kind of dietary restriction (eg, a low-calorie diet,etc.)		The same dietary restriction
3	Oats		Heterogeneous control arms (eg, rice, wheat, etc.)

We will exclude studies which use the term 'effectiveness rate' exclusively to quantify primary outcomes, and those do not report clinical data.

Publication date

From the database's inception to 1 October 2021, all databases will be searched.

Language

There will be no language restrictions in our review.

Search strategy

We will conduct a literature search in the following eight databases: PubMed, Web of Science, Cochrane Library, EMBASE, CNKI, SinoMed, VIP and Wanfang. Additionally, we will search the Chinese Clinical Trial Registry (http://www.chictr.org.cn) and the International Clinical Trial Registry (https://clinicaltrials.gov/) to mitigate selection bias. 'Dyslipidaemia,' 'oats' and 'randomised controlled trials' are among the search topics or subject words. The following are the precise search terms for PubMed (https://www.pubmed.ncbi.nlm.nih.gov) (search strategies for other databases are in the online supplemental file):

1. Dyslipidemias [MESH]
2. Dyslipidemia (ti/ab)
3. Dyslipoproteinemia* (ti/ab)
4. Hyperlipidemias [MESH]
5. Hyperlipidemia (ti/ab)
6. Hyperlipemia* (ti/ab)
7. Triglyceride* (ti/ab)
8. Hypertriglyceridemia* (ti/ab)
9. Cholesterol (ti/ab)
10. Hypercholesterolemia* (ti/ab)
11. Lipoprotein* (ti/ab)
12. Hyperlipoproteinemia* (ti/ab)
13. Lipid* (ti/ab)
14. Metabolic syndrome (ti/ab)
15. TG (ti/ab)
16. TC (ti/ab)
17. HDL (ti/ab)
18. LDL (ti/ab)
19. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18
20. Avena [MESH]
21. Avena* (ti/ab)
22. Oat (ti/ab)
23. Oats (ti/ab)
24. Oatmeal (ti/ab)
25. 20 OR 21 OR 22 OR 23 OR 24
26. randomized controlled trial (pt)
27. controlled clinical trial (pt)
28. randomized [ti/ab]
29. clinical trials as topic
30. randomly [ab]
31. trial [ti])
32. 26 OR 27 OR 28 OR 29 OR 30 OR 31
33. 19 AND 25 AND 32

Selection and data collection process

We will prescreen the articles in accordance with the search strategy. Then, import these articles into a literature management system (eg, Endnote or NoteExpress), eliminate duplicates and conduct additional screening by reading the title, abstract, and full text. Two independent researchers will choose studies based on inclusion and exclusion criteria. The PRISMA flow chart (figure 1) will be used to document the process of selecting articles for inclusion in this systematic review and meta-analysis. Standardised data extraction tables shall be used for data extraction. If we have any questions about the original data or results, we will contact the corresponding author via email and telephone. Two authors will independently

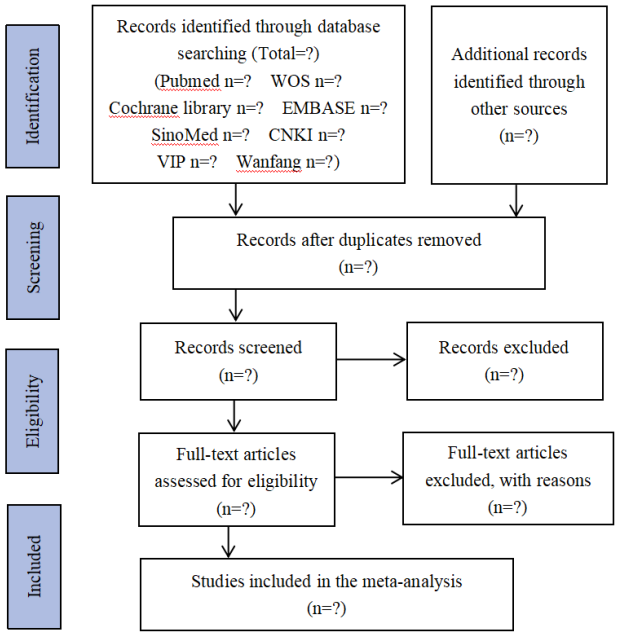

Figure 1 The flow chart illustrates the process of screening articles on oats intervention for dyslipidaemia.

select and extract data from the literature. If a disagreement arises, the article will be re-evaluated by a third reviewer. The reasons for excluding certain articles will be sufficiently documented. Finally, for research that has been published in multiple articles, we choose the most recent, largest sample size and most comprehensive article.

The following data will be extracted:

1. Study-related information (eg, title, authors, publication year, location of the study).
2. Information about the study population (eg, sample size, age, gender, groups, diagnostic criteria for dyslipidaemia).
3. Interventions and controls (eg, specific intervention measures, control measures, duration of trial).
4. Outcomes and adverse reactions.
5. Design of the study (eg, description for randomisation, allocation concealment, blinding, dropout, incomplete outcome data, selective reporting and other potential risks of bias).

Quality and risk of bias assessment

The Jadad scale,[34] which is effective at evaluating the quality of RCT evidence, will be used to assess the methodological quality of the included studies. The Jadad scale assigns a score of 0–5 to studies based on their randomisation, blinding, withdrawals, and dropouts. A score ≥3 indicates a high-quality study, while a score <3 indicates a low-quality one. The internal validity and risk of bias of trials will be assessed using Version 2 of the Cochrane risk of bias tool[35] on six dimensions: bias arising from the randomizsation process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported result and overall biases. The risk of bias of each domain will be assessed according to three criteria: 'low risk', 'high risk' or 'some concerns'. Two authors will independently evaluate the quality and risk of bias in these studies, with a third reviewer resolving any disagreements. None of the trials included will be excluded due to their quality or risk of bias, but the potential impact of their inclusion will be evaluated in a subsequent sensitivity analysis.

Data synthesis and statistical analysis

Blood lipids may be expressed in two distinct units (mmol/L and mg/dL) according to different studies. In this case, we must convert them to a more consistent unit—mmol/L—and collect the resulting data. Because the outcomes in this study are continuous, the mean difference (MD) with 95% CI will be used to assess the magnitude of change in various indicators and to estimate the combined effect. Cochran's Q statistic will be used to test the heterogeneity, while I^2 statistic[36] will quantify the heterogeneity. For Q statistic, p<0.10 indicates significant heterogeneity; for I^2 statistic, I^2 ≥50% indicates considerable heterogeneity. If the included studies are homogeneous (p≥0.10 and I^2 <50%), we will use the inverse variance fixed-effects model to estimate MD. If the included studies have considerable clinical heterogeneity (p<0.10 or I^2 ≥50%), the data cannot be directly combined. Rather than that, we will employ the random-effects model. By examining the characteristics of individual studies (eg, different oat components, gender, region, daily dosage and duration of intervention), we can identify potential sources of heterogeneity and conduct subgroup analysis. Additionally, a sensitivity analysis will be conducted by deleting a study at a time and reanalyzing the included literature to identify sources of bias and assess the meta-analysis results' stability and reliability. If p<0.05, the difference between the two groups is statistically significant. The Begg funnel plot[37] and Egger's weighted regression statistics[38] will be used to assess publication bias. The above analysis will be carried out in RevMan V.5.4 software. Additional meta-analyses will be conducted if there are sufficient data on cardiovascular events or on parameters such as BMI index, body weight and inflammatory factors.

Quality of evidence

We will assess the quality of evidence for the primary outcomes using the Grading of Recommendationsm, Assessment, Development and Evaluation approach.[39] To determine the evidence's certainty, it will be downgraded or upgraded based on factors such as imprecision or a large effect size. Finally, recommendations will be made for interpreting the evidence's quality.[40]

Patient and public involvement

This protocol is being developed without the involvement of patients or the general public.

DISCUSSION

This research will examine the therapeutic effect of oats on dyslipidaemia using data from previous clinical trials using oat products and oat components to regulate blood lipids. It will be the most comprehensive study to date and will provide the best evidence to date regarding oats' ability to regulate blood lipids. We will also assess the quality of the evidence supporting the primary outcomes to facilitate their application. Additionally, we hope to provide daily dietary advice and adjunctive lipid control strategies to patients with dyslipidaemia.

During the implementation of the study, there may be some limitations:

1. To ensure that as many relevant studies as possible are included, we will not restrict the dosage, frequency or method of preparation of oats.
2. To further refine the research and reduce heterogeneity, we will group studies according to their dietary backgrounds and conduct sensitivity analyses or subgroup studies on various oat components. However, the variety, quality control and manufacturing processes of oats are unique, making them difficult to consider and potentially introducing heterogeneity.

The protocol was completed in 2021, and we plan to complete the study in 2022. The final manuscript will detail any adjustments and modifications made to this protocol.

Contributors AL, ML and QH conceived the research. AL and ML completed the manuscript. ML and QH completed the PROSPERO registration. AL and JG designed the search strategy. JG, WY and QH strictly reviewed the protocol and provided comments. AL and ML are cofirst authors of the protocol. All authors approved the final protocol.

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Competing interests None declared.

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

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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