Effect of exercise on cardiovascular risk in sedentary postmenopausal women: a systematic review and meta-analysis

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Contributions: (I) Conception and design: Both authors; (II) Administrative support: Both authors; (III) Provision of study materials or patients: Both authors; (IV) Collection and assembly of data: Both authors; (V) Data analysis and interpretation: Both authors; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

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Background: Exercise training has cardiovascular benefits, but its effects on cardiovascular disease risk factors in sedentary postmenopausal women are uncertain. Therefore, we conducted a meta-analysis to explore the effects of exercise on cardiovascular disease (CVD) risk factors in sedentary postmenopausal women.

Methods: A literature search was conducted on the Web of Science, Cochrane, PubMed, Chinese National Knowledge Infrastructure (CNKI) and WanFang databases for studies published between January 2010 and January 2022. All publications relating to clinical randomized control trials on the effects of exercise on CVD risk factors in sedentary postmenopausal women were collected. A meta-analysis was performed using STATA 16.0. We assessed the quality of the included literature using the Cochrane risk bias assessment tool.

Results: Of the 623 articles initially retrieved, 14 were included in the meta-analysis (250 and 223 individuals in the exercise and non-exercise groups, respectively). The meta-analysis showed that oxygen consumption [standardized mean difference (SMD) =1.21; 95% confidence interval (CI): 0.38 to 2.05; P=0.004] and high-density lipoprotein (SMD =0.31; 95% CI: 0.08 to 0.54; P=0.008) were significantly higher in the exercise than non-exercise group; however, diastolic blood pressure (SMD =−0.81; 95% CI −1.38 to −0.24; P=0.005), systolic blood pressure (SMD =−0.98; 95% CI: −1.44 to −0.52; P=0.000), triglycerides (SMD =−0.48, 95% CI: −0.86 to −0.09; P=0.016), and body mass index (SMD =−0.94, 95% CI: −1.70 to −0.17; P=0.016) were markedly lower in the exercise group. There were no significant differences between the 2 groups in heart rate (SMD =−0.11; 95% CI: −0.92 to 0.70; P=0.796), cholesterol (SMD =−0.32; 95% CI: −0.79 to 0.15; P=0.186), or low-density lipoprotein (SMD =−0.23; 95% CI: −0.70 to 0.23; P=0.321).

Conclusions: Aerobic exercise not only increases oxygen consumption, but also reduces CVD-related factors, such as blood pressure, lipid profile, and body mass index, in sedentary menopausal women. Put simply, regular exercise is a beneficial lifestyle intervention that can reduce CVD risk.

Keywords: Blood pressure; cardiovascular disease risk; exercise; meta-analysis; sedentary

Introduction

Cardiovascular disease (CVD) is currently the leading cause of death in China (1). With age, metabolic abnormalities such as obesity, dyslipidemia, hypertension, and abnormal blood glucose become important risk factors for CVD (2) in both men and women (3). However, the risk of vascular dysfunction increases markedly in postmenopausal women because of estrogen deficiency, and so they face a higher risk

of CVD (4,5). For example, compared with premenopausal women, postmenopausal women have increased arterial stiffness, and a daily lack of physical exercise places them at increased risk of CVD (3,6). In the US, approximately 40% of adult women (25 million) are postmenopausal, so finding effective methods to reduce CVD risk in this population is of significance in terms of both lowering the healthcare burden and improving national health (7).

The American College of Sports Medicine has stated that the amount of physical exercise is related to the risk of developing various diseases, including CVD (8,9), and a lack of exercise is a well-known independent risk factor for CVD (10). Many studies have shown that moderate to low intensity aerobic exercise can help improve people's cardiovascular function, thereby reducing their risk of CVD (11,12). Such regular intervention can improve CVD-related metabolic syndrome presenting with abnormal blood pressure, lipid, and glucose levels (13). Due to estrogen depletion and metabolic alterations, postmenopausal women are at substantially increased risk for CVD; However, unfortunately, only 30% of postmenopausal women exercise regularly (9). In addition, a study confirmed that long-term aerobic exercise significantly decreased adiposity levels in previously sedentary postmenopausal women, which was significantly associated with the development of cardiovascular disease (14). At present, although a study has reported on the effects of physical activity on CVD-related risk factors in postmenopausal women, no systematic conclusion has been reached (15). Thus, in the present study we performed a meta-analysis to systematically analyze all related studies to come to an accurate conclusion. We present the following article in accordance with the PRISMA-P reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-1395/rc).

Methods

Search strategy

Literature searches were conducted on the Web of Science, Cochrane, PubMed, Chinese National Knowledge Infrastructure, and WanFang databases for articles published. The keywords used were "Exercise", "Sedentary", and "Cardiovascular risk".

Inclusion criteria

To be eligible for inclusion in the meta-analysis, articles had to meet the following criteria:

- ❖ Study subjects: all subjects had to postmenopausal (i.e., no menstrual period for at least 12 consecutive months), elderly (age >60 years), sedentary for long periods of time and without regular exercise for at least 1 year;
- ❖ Intervention measures: subjects were divided into an exercise group and a non-exercise group; the exercise group undertook routine aerobic physical exercise for at least 30 minutes per week according to the plan created by the investigators, whereas the non-exercise group did not participate in physical exercise;
- ❖ Study design: studies had to be randomized controlled trials (RCT) published in relevant medical journals in China and internationally;
- ❖ Outcome measures: studies had to report on at least 1 of the following measures: heart rate (HR), oxygen consumption (V_{O_2}), diastolic blood pressure (DBP), systolic blood pressure (SBP), triglycerides (TG), cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), body mass index (BMI), waist circumference, and glucose;
- ❖ Study subjects (or their family members) must have provided informed consent.

Exclusion criteria

Studies were excluded if they met the following criteria:
- ❖ Study subjects: current smokers, patients with

Highlight box

Key findings
- Physical exercise not only increases oxygen consumption, but also reduces CVD-related risk factors.

What is known and what is new?
- CVD is currently the leading cause of death in China. Postmenopausal women face a higher risk of CVD.
- In the present study we performed a meta-analysis to systematically analyze all related studies to come to an accurate conclusion.

What is the implication, and what should change now?
- The findings suggest that studies are needed into the effect of exercise on CVD risk factors in sedentary postmenopausal women and that postmenopausal women should undertake regular physical exercise.

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Figure 1 Risk of bias summary

CVD, renal disease, or thyroid disease, patients currently receiving hormone replacement therapy, patients who had undertaken a weight loss diet in the previous year, and patients with mental illness or cognitive impairment;

❖ Qualitative studies, secondary studies, systematic reviews, meta-analyses, animal experiments, and studies for which the full text was not available.

Literature screening and data extraction

The retrieved studies were imported into Endnote 7.0

(Stamford, Connecticut, USA), and duplicates were removed. Both authors independently screened the literature based on the inclusion and exclusion criteria, and extracted and organized the data (including title, author, study design, study subject, intervention measures, and outcome measures).

Literature quality assessment

The Cochrane Collaboration's tool for assessing risk of bias was used to assess the quality of the included studies, which mainly included six aspects: (I) selection bias, including whether the generation and allocation of random sequences were hidden; (II) implementation bias: whether the study patients and researchers were blinded; (III) measurement bias: whether the outcome was evaluated in a blinded manner; (IV) follow-up bias: whether the outcome data were missing; (V) reporting bias: whether there was selective reporting; (VI) other biases. The analysis results are shown in *Figure 1* and *Figure 2*.

Statistical analysis

The meta-analysis was performed using Stata16.0. (IBM Corp., Armonk, NY, USA) Continuous variable outcomes are presented as the standardized mean difference (SMD) with 95% confidence intervals (CIs), whereas categorical variable outcomes are presented as odds ratios (ORs) and 95% CIs. Heterogeneity was tested using a Chi-squared test and I^2 statistics, with the α level set to 0.05. If $I^2 < 50\%$ and P>0.05, there was no statistical heterogeneity across studies and a fixed-effects model was used to combine the effect size; otherwise, the random-effects model shall be adopted, and the sensitivity analysis shall be conducted for the possible causes of heterogeneity. Sensitivity analysis was performed to test the stability of the findings. Funnel plots and egger's test were used to assess publication bias. Differences were considered statistically significant at 2-sided P<0.05.

Results

Literature search results

From the 623 articles initially retrieved, 257 duplicates were excluded. A further 209 articles were excluded after screening the titles and abstracts and 143 articles were excluded after reading the full text and reported data.
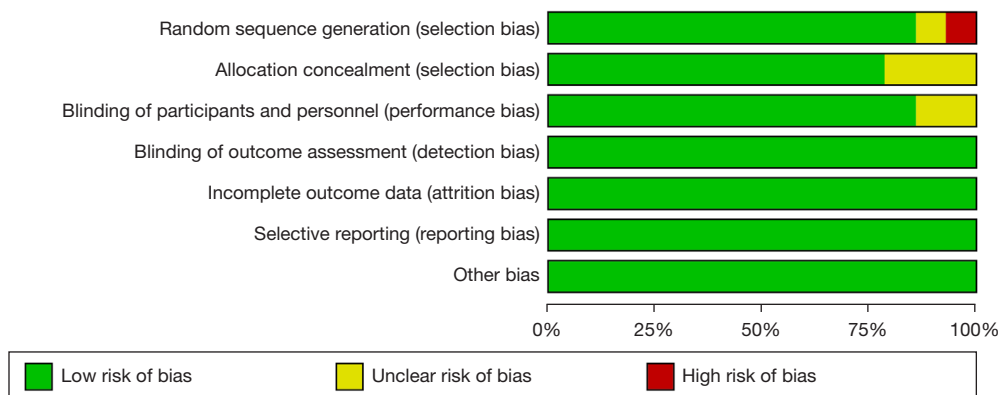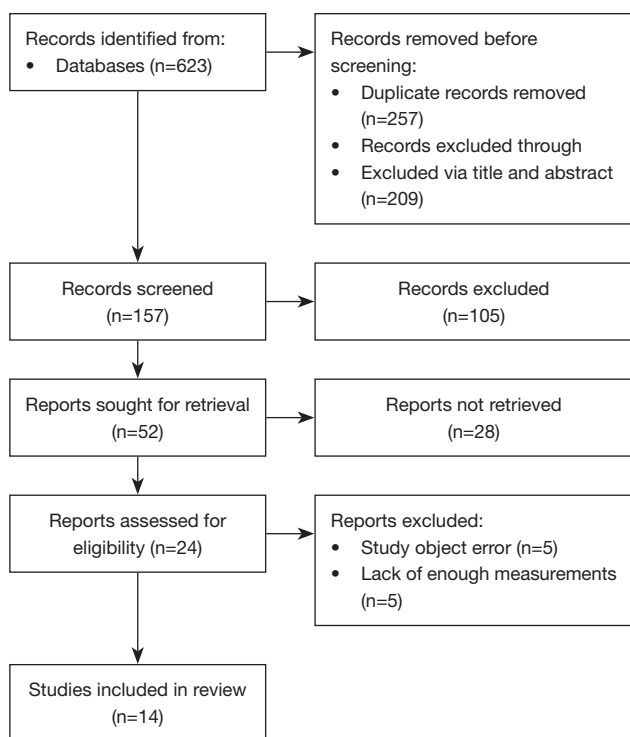
Figure 2 Risk of bias graph

Figure 3 Literature screening flowchart.

Finally, 14 studies were included in the meta-analysis (16-29). The literature screening process is shown in *Figure 3*. The 14 studies in the meta-analysis included 473 sedentary postmenopausal women, 250 in the exercise group and 223 in the non-exercise group. The characteristics of the included studies are presented in *Table 1*.

Meta-analysis results for cardiac indicators

Six studies (17,19,21,23,26,29) compared HR between the exercise and non-exercise groups, 4 (20,26-28) compared Vo_2 between the 2 groups, and 9 (20-26,28,29) compared DBP and SBP between the 2 groups. Random-effects models were used due to significant heterogeneity across studies (HR: I^2=79.8%, P<0.001; Vo_2: I^2=69.6%, P=0.020; SBP: I^2=77.1%, P<0.001; DBP: I^2=64.2%, P=0.004). There was no significant difference in HR between the 2 groups (SMD =–0.11; 95% CI: –0.92 to 0.70; P=0.796; *Figure 4A*). The results showed that Vo_2 was significantly higher in the exercise than non-exercise group (SMD =1.21; 95% CI: 0.38 to 2.05; P=0.004; *Figure 4B*), whereas DBP (SMD =–0.81; 95% CI –1.38 to –0.24; P=0.005; *Figure 4C*) and SBP (SMD =–0.98; 95% CI: –1.44 to –0.52; P=0.000; *Figure 4D*) were markedly lower in the exercise group.

Sensitivity analysis was performed on the study results. There was no significant change in results after removing each study, one by one, indicating that the results of the meta-analysis were robust and reliable (*Figure 5*). Publication bias was also analyzed for the included studies. Diffuse distribution was observed on scatter plots representing DBP, whereas symmetrical funnel plots of the other cardiac indicators were found, indicating no publication bias (*Figure 6*; Egger's test: HR: P=0.104; Vo_2: P=0.225; DBP: P=0.005; SBP: P=0.170).

Meta-analysis results for obesity-related indicators

TG comparisons were reported in 4 studies (18,20,23,24),

Table 1 Characteristics of the studies included in the meta-analysis

First author (reference)	Year	No. participants		Age (years)		Baseline BMI (kg/m^2)		Study design	Outcome measures
		Exercise	Non-exercise	Exercise	Non-exercise	Exercise	Non-exercise		
Rodrigo (16)	2008	37	22	54.3±2.5	53.1±1.9	–	–	RCT	(e) (j) (k)
Malandish (17)	2020	16	15	53.36±3.98	53.00±3.26	29.67±5.15	30.29±6.58	RCT	(b)
Gómez-Tomás (18)	2018	18	20	70.89±4.42	70.45±5.44	28.72±4.48	30.16±5.57	RCT	(f) (g) (h) (j) (k)
Wong (19)	2019	10	10	54±1	55±1	32.5±1.0	32.5±1.3	RCT	(a) (b)
Dalleck (20)	2009	8	10	55.4±3.2	57.4±4.6	28.1±4.5	30.0±8.7	RCT	(c) (d) (e) (f) (g) (h) (i) (j) (k)
Gerage (21)	2013	15	14	65.5±5.0	66.2±4.1	23.9±2.9	25.1±3.4	RCT	(a) (b)
Pekas (22)	2020	57	44	<75	<78	–	–	RCT	(c) (d) (j) (k)
Jeon (23)	2018	8	8	59±1	58±2	27.2±1.9	26.1±1.2	RCT	(a) (b) (d) (e) (f) (g)
Son (24)	2021	18	17	68.2±1.6	68.2±1.4	26.7±3.2	27.1±1.4	RCT	(a) (c) (c) (d) (e) (f) (h) (j) (k)
Lee (25)	2012	8	8	54.75±2.76	54.25±2.91	25.13±1.63	25.19±1.71	RCT	(a) (e) (j) (k)
Nishiwaki (26)	2011	8	8	56.4±1		24.14		RCT	(b) (c) (d) (i)
Shen (27)	2013	22	22	57.86±0.64	59.10±0.83	22.74±0.47	23.72±0.66	RCT	(a) (e) (i) (j) (k)
Son (28)	2017	10	10	76±5	74.7±2	22.77±0.7	24.05±0.2	RCT	(a) (c) (d) (i)
Zhang (29)	2019	15	15	53.2±3.5	53.0±3.1	28.2±3.9	26.9±0.9	RCT	(a) (b) (c) (d)

Age and BMI are presented as the mean ± SD. (a), BMI; (b), heart rate; (c), diastolic blood pressure; (d), systolic blood pressure; (e), glucose; (f), triglycerides; (g), cholesterol; (h), waist circumference; (i), oxygen consumption; (j), high-density lipoprotein; (k), low-density lipoprotein. BMI, body mass index; RCT, randomized controlled trial.
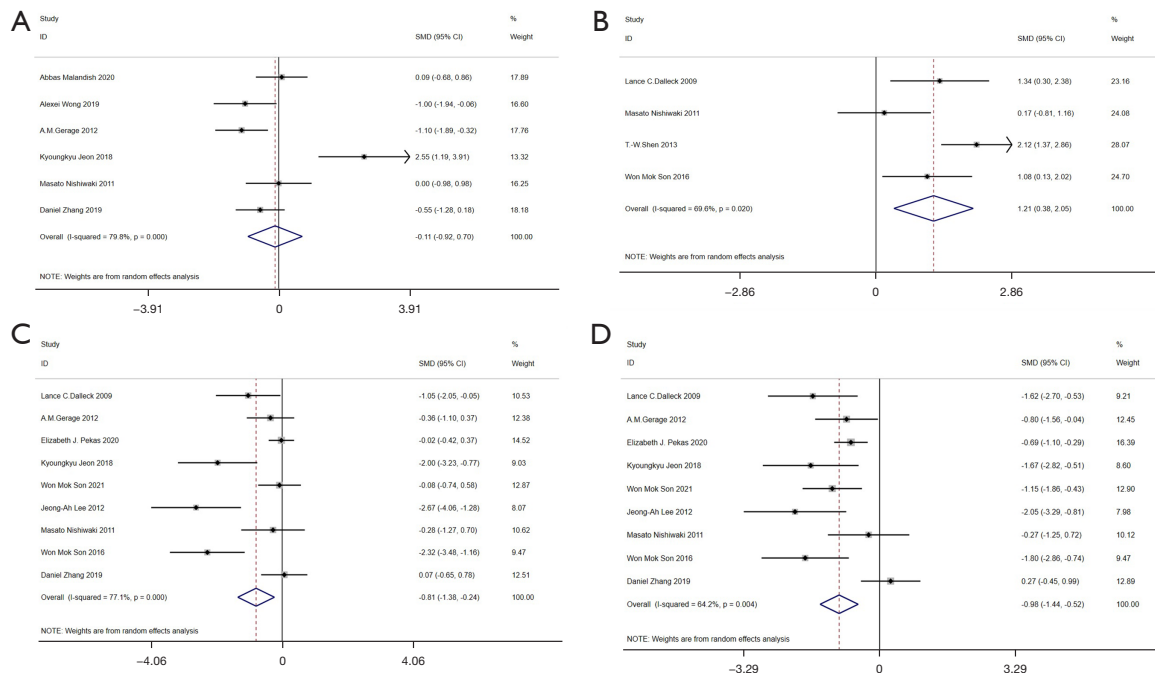

Figure 4 Forest plots comparing cardiac indicators, (A) heart rate, (B) oxygen consumption, (C) diastolic blood pressure, and (D) systolic blood pressure between the exercise and non-exercise groups of postmenopausal women. CI, confidence interval; SMD, standardized mean difference.
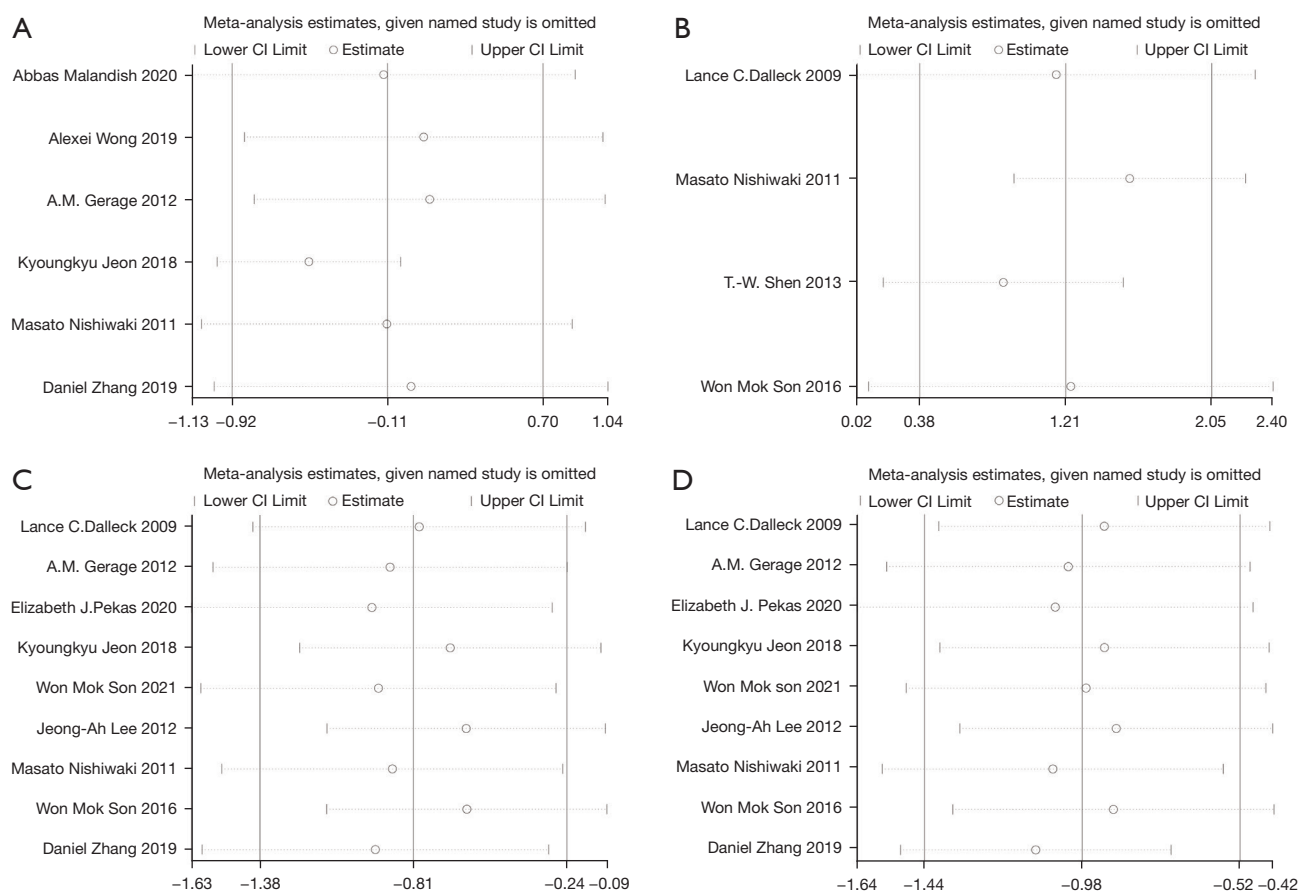
Figure 5 Sensitivity analysis of cardiac indicators, (A) heart rate, (B) oxygen consumption, (C) diastolic blood pressure, and (D) systolic blood pressure between the exercise and non-exercise groups of postmenopausal women. CI, confidence interval.

cholesterol comparisons were reported in 3 studies (18,20,23), HDL comparisons were reported in 7 studies (16,18,20,22,24,25,27), LDL comparisons were reported in 7 studies (16,18,20,22,24,25,27), BMI comparisons were reported in 9 studies (19-21,23-25,27-29), and waist circumference comparisons were reported in 3 studies (18,20,24). Fixed-effects models were used to analyze TG, cholesterol, HDL, and waist circumference (TG: $I^2=0.0\%$, P=0.791; cholesterol: $I^2=0.0\%$, P=0.388; HDL: $I^2=48.9\%$, P=0.068; waist circumference: $I^2=0.0\%$, P=0.619), whereas random-effects models were used to analyze LDL and BMI (LDL: $I^2=72.2\%$, P=0.001; BMI: $I^2=83.7\%$, P<0.001). Compared with the non-exercise group, the exercise group had significantly lower TG (SMD =–0.48; 95% CI: –0.86 to –0.09; P=0.016; *Figure 7A*). There were no marked differences in cholesterol (SMD =–0.32; 95% CI: –0.79 to 0.15; P=0.186; *Figure 7B*), significantly higher HDL (SMD =0.39; 95% CI: 0.04 to 0.73; P=0.027; *Figure 7C*), LDL

(SMD =–0.23; 95% CI: –0.70 to 0.23; P=0.321; *Figure 7D*) between the 2 groups, BMI (SMD =–0.94; 95% CI: –1.70 to –0.17; P=0.016; *Figure 7E*), and waist circumference (SMD =–0.64; 95% CI: –1.06 to –0.21; P=0.003; *Figure 7F*).

In sensitivity analysis, there was no significant change in results after removing each study, one by one, indicating good stability (*Figure 8*). Publication bias was also analyzed for the included studies. Diffuse distribution was observed on scatter plots representing BMI, whereas symmetrical funnel plots of the other cardiac indicators were found, indicating no publication bias. (*Figure 9*; Egger's test: TG: P=0.662; cholesterol: P=0.063; HDL: P=0.218; LDL: P=0.917; BMI: P=0.007; waist circumference: P=0.370).

Meta-analysis results for blood glucose

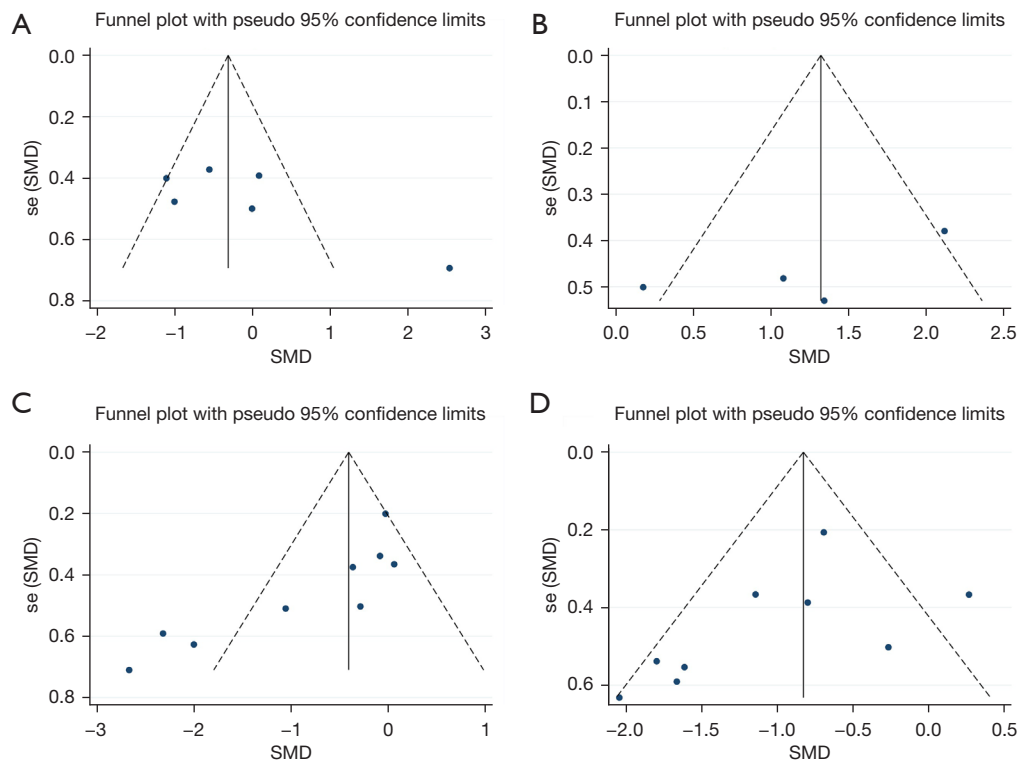Six studies (16,20,23-25,27) compared glucose between the exercise and non-exercise groups, and the random-

Figure 6 Funnel plots of cardiac indicators, (A) heart rate, (B) oxygen consumption, (C) diastolic blood pressure, (D) systolic blood pressure between the exercise and non-exercise groups of postmenopausal women. se (SMD), standard error of the standardized mean difference.

effects model was used to combine the effect sizes due to significant heterogeneity among the studies (glucose: I^2=77.6%, P<0.001). Glucose was found to be significantly lower in the exercise than non-exercise group (SMD =−1.03; 95% CI: −1.74 to −0.33; P=0.004; *Figure 10A*).

Further sensitivity analysis showed that there was no significant difference in the results after eliminating each study, one by one, indicating that the results of this study were stable (*Figure 10B*). Publication bias analysis was performed using a funnel plots, with the results showing basically symmetrically distribution on both sides of the funnel plot, indicating the absence of publication bias (*Figure 10C*; Egger's test: P=0.412).

Discussion

This study explored the effects of physical exercise on risk factors for CVD in menopausal women. Fourteen RCTs were included in the meta-analysis after applying strict and exclusion criteria, with CVD-related outcome measures such as blood pressure, blood glucose, HR, and

cholesterol. The data of various individual studies were combined through meta-analysis to enable a conclusion to be reached with high reliability. The combined results showed that postmenopausal women who undertook regular physical exercise had higher Vo_2, and that both DBP and SBP were lower than in postmenopausal women who did not undertake physical exercise. Hypertension is a major risk factor for the development of CVD (30). The increased blood pressure in postmenopausal elderly women is attributed to the reduction in estrogen, increased sympathetic nerve activity, and decreased endothelial function (31). In addition, this could explain why the prevalence of hypertension is lower among premenopausal women than men of the same age group, but higher among postmenopausal women than men of the same age group (31). Physical exercise has considerable benefits in enhancing muscle strength and cardiovascular health, and increased muscle mass and strength are inversely associated with the risk of hypertension and frailty in older women (6,32,33).

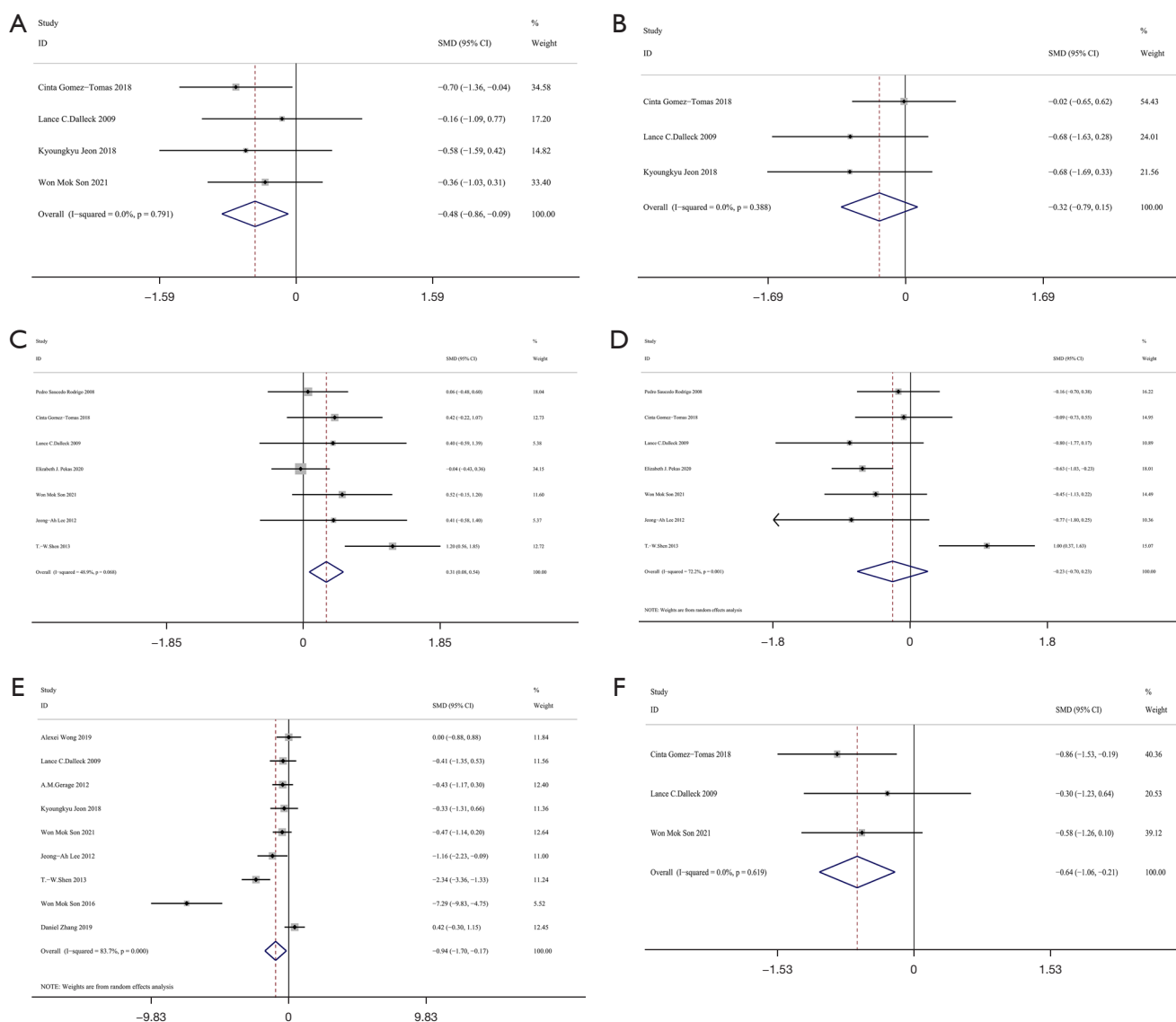Exercise has been proved to prevent age-related CVD

Figure 7 Forest plots comparing obesity-related indicators, (A) triglycerides, (B) cholesterol, (C) high-density lipoprotein, (D) low-density lipoprotein, (E) body mass index, (F) waist circumference between the exercise and non-exercise groups of postmenopausal women. CI, confidence interval; SMD, standardized mean difference.

risk factors (6,34). In the present meta-analysis, we found lower TG, BMI, and waist circumference and higher HDL in the exercise group, but no differences in cholesterol and LDL between the 2 groups. Optimal levels of LDL and HDL are <100 and >40 mg/dL, respectively (35). The lipid profile in menopausal women becomes abnormal due to changes in hormone levels, usually manifested as increased LDL and decreased HDL (36). This increase in LDL is thought to contribute to the increased risk of atherosclerosis

and CVD (37). Consistent with the findings of the present study, Wooten *et al.* (38) and Ammar (39) reported that physical exercise was effective in reducing LDL levels in postmenopausal women. Obesity is often accompanied by increases in both BMI and waist circumference, leading to increased stiffness of the central and peripheral arteries (40). Abdominal obesity is a strong predictor of insulin resistance in older people (41), and reducing abdominal obesity and total fat mass can improve glucose
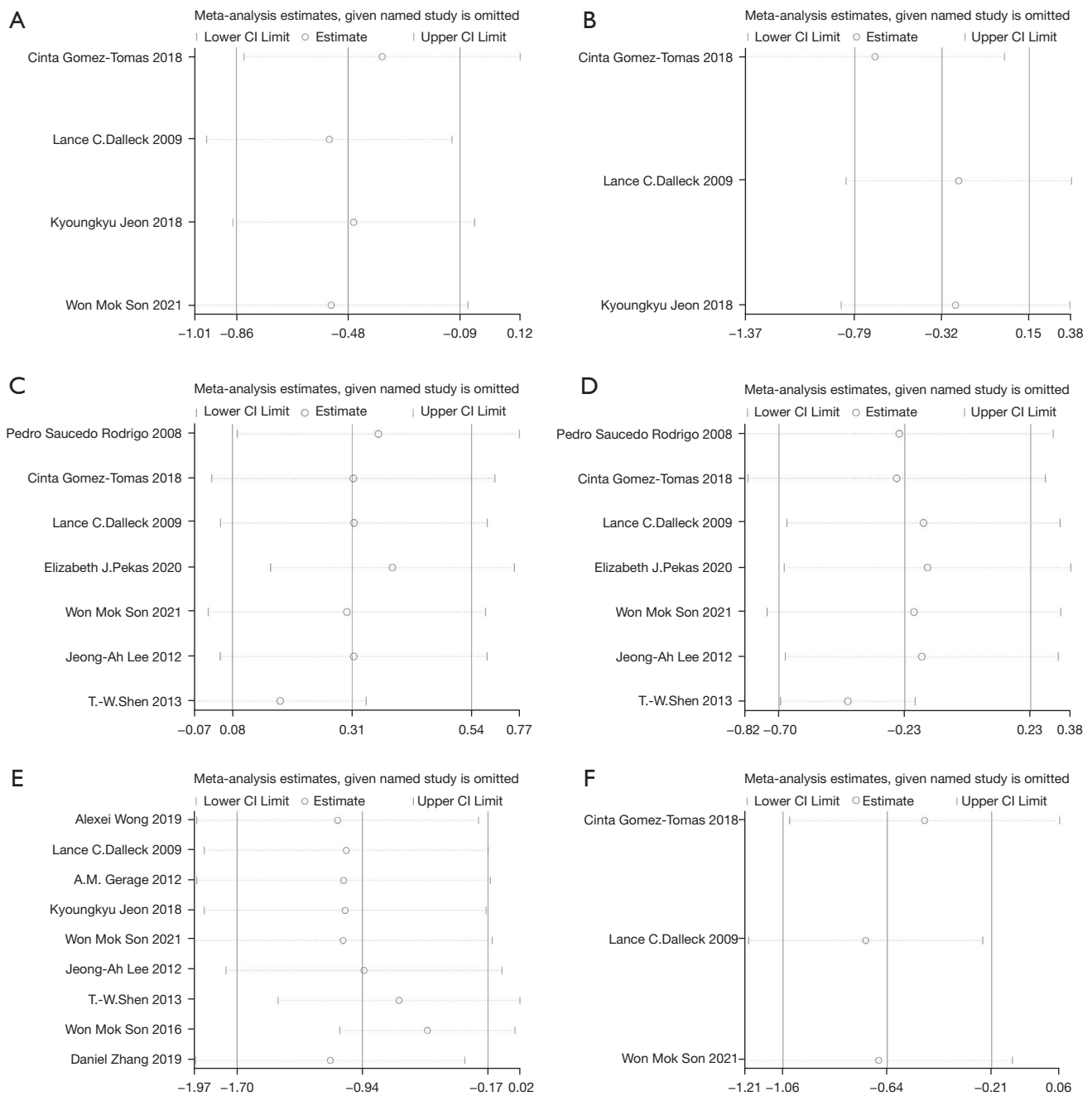
Figure 8 Sensitivity analysis of obesity-related indicators, (A) triglycerides, (B) cholesterol, (C) high-density lipoprotein, (D) low-density lipoprotein, (E) body mass index, (F) waist circumference between the exercise and non-exercise groups of postmenopausal women. CI, confidence interval.

levels in menopausal women (42). In the present study, glucose levels were lower in menopausal women who undertook physical exercise than in those who did not, which is similar to the findings of Conceição *et al.* (43). Collectively, physical exercise can comprehensively optimize

the metabolic level of menopausal women and reduce the risk of CVD.

However, the present study has some limitations, such as the relatively small number of studies included and the small sample size. Further large-sample and multicenter
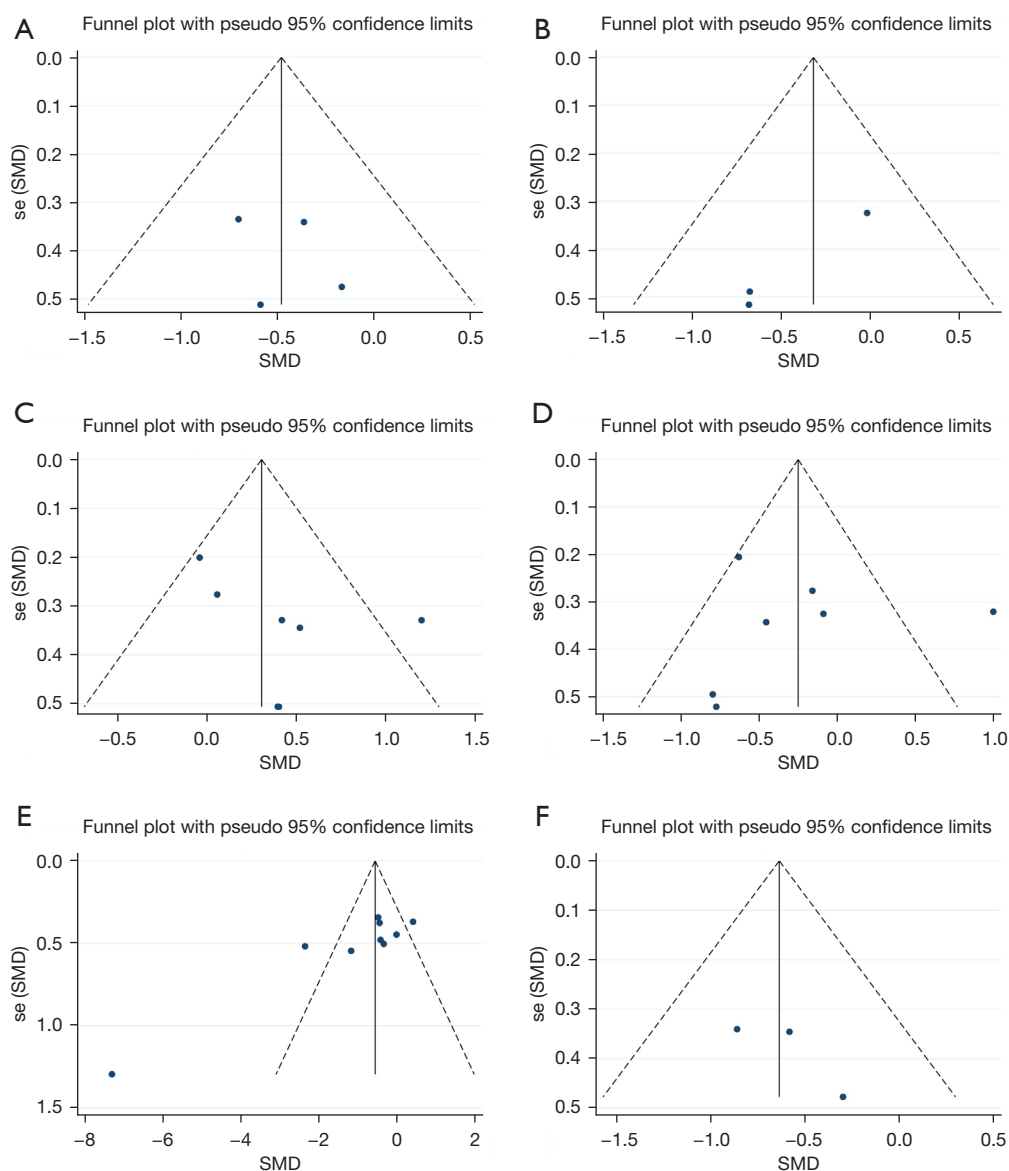
Figure 9 Funnel plots of obesity-related indicators, (A) triglycerides, (B) cholesterol, (C) high-density lipoprotein, (D) low-density lipoprotein, (E) body mass index, (F) waist circumference between the exercise and non-exercise groups of postmenopausal women. se (SMD), standard error of the standardized mean difference.

RCTs are required to enhance the accuracy and reliability of the study results in order to provide guidance for the prevention of CVD in postmenopausal women.

Conclusions

Physical exercise not only increases V_{O_2}, but also reduces CVD-related risk factors such as blood pressure, blood lipids, and BMI, in menopausal women. Thus, physical exercise is essential for reducing the risk of CVD and improving the quality of life in this population. Therefore, regular exercise, a beneficial lifestyle intervention, is recommended for postmenopausal elderly women to prevent CVD and promote physical performance.
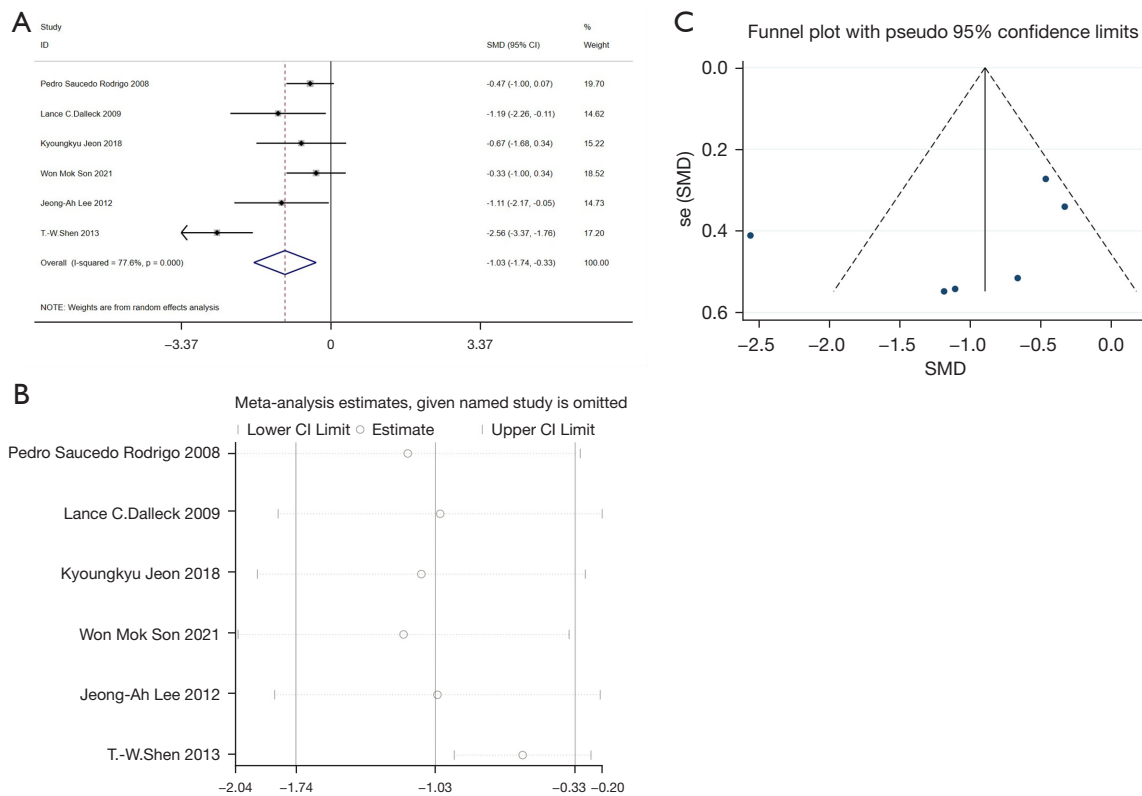
Figure 10 Meta-analysis results for blood glucose between the exercise and non-exercise groups of postmenopausal women. (A) Forest plot comparing blood glucose between the 2 groups; (B) sensitivity analysis of blood glucose between the 2 groups; (C) funnel plot of blood glucose between the 2 groups. CI, confidence interval; se (SMD), standard error of the standardized mean difference; SMD, standardized mean difference.

Acknowledgments

Footnote

Reporting Checklist: The authors have completed the PRISMA-P reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-1395/rc

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-1395/coif). The 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.

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