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Effects of Long-term Aerobic or Resistance Exercise on Chronic Inflammatory Markers in Overweight or Obese Postmenopausal Women: A Systematic Review of Controlled Clinical Trials

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Abstract

Background: *Chronic low-grade inflammation is a key contributor to cardiometabolic disease risk, marked by elevated C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α). Overweight and obese postmenopausal women are particularly vulnerable due to hormonal changes exacerbating inflammatory pathways. Exercise (aerobic and resistance) has been shown to have anti-inflammatory effects. However, prior reviews focused on short-term interventions or heterogeneous populations, leaving the long-term impact in this specific group unclear.*

Methods: *We searched PubMed, Web of Science, and Cochrane between April 18 and May 1, 2025, for literature published from inception through April 2025.*

Results: *Seven trials (n = 1,278 participants) were included. Five showed some concerns, and two were judged to have high risk of bias. Six trials assessed CRP, four IL-6, and three TNF-α. Between-group analyses showed no significant reductions in CRP or TNF-α. Only one study reported a significant reduction in IL-6. Significant within-group decreases were observed in two CRP trials and one IL-6 trial, but these occurred exclusively in interventions combining exercise with dietary modification. Exercise-only interventions generally did not produce significant reductions in inflammatory markers.*

Conclusions: *Exercise alone does not consistently reduce CRP, IL-6, or TNF-α in overweight and obese postmenopausal women. Observed effects may be confounded by dietary co-interventions, methodological limitations, and heterogeneity across trials. Further well-designed long-term studies isolating the independent effects of exercise are warranted.*

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Introduction

Chronic low-grade inflammation is a key mechanism connecting lifestyle, metabolism, and chronic disease, contributing to cardiovascular disease, type 2 diabetes, and metabolic syndrome, which are major causes of morbidity and mortality in aging populations (Winn et al., 2021). In women, menopause marks a critical transition, with declining estrogen levels promoting visceral fat accumulation and metabolic imbalance, triggering persistent inflammation characterized by elevated C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) (Carr, 2003). These biomarkers are well-established predictors of cardiometabolic risk and diminished quality of life (Chu et al., 2022; Franceschi & Campisi, 2014; Hotamisligil, 2006; Ridker et al., 2000)

Managing this chronic inflammatory state is an important clinical goal. Pharmacologic approaches exist but may be costly, less sustainable, or associated with side effects. In contrast, regular physical activity represents a safe and practical non-pharmacologic alternative, with growing evidence showing that exercise can attenuate inflammation by improving body composition, insulin sensitivity, and immune balance (Gleeson et al., 2011; Libardi et al., 2012; Winn et al., 2021).

Both aerobic and resistance training produce health benefits (Gleeson et al., 2011; Lee et al., 2024). Most prior studies have been short-term or involved heterogeneous populations, limiting conclusions about long-term effects in postmenopausal women (Khalafi et al., 2021; Tan et al., 2023). Because inflammation develops gradually, programs lasting 6 months or more may be needed to detect meaningful changes in inflammatory markers (Franceschi & Campisi, 2014; Imayama et al., 2012; Stewart et al., 2010).

Aerobic activities (e.g., walking, cycling, jogging) and resistance exercises (e.g., squats, push-ups, weightlifting) are accessible and complementary forms of physical activity. Aerobic training improves cardiovascular and metabolic function, while resistance exercise preserves muscle mass and strength—both factors that influence inflammatory processes (Petersen & Pedersen, 2005).

Materials and Methods

Search strategy

A comprehensive literature search in PubMed, Web of Science, and the Cochrane Library was conducted between April 18 and May 1, 2025, covering all records from each database's inception through April 2025. The search strategy utilized both Medical Subject Headings (MeSH) and relevant keywords, structured according to the Population, Intervention, Comparator, and Outcomes (PICO) framework. Terms within each concept were combined using 'OR', while the main concepts were combined using 'AND'. Search terms addressed the following concepts: "overweight" OR "obesity" AND "aerobic exercise" OR "resistance exercise" AND "inflammatory marker" OR "C-Reactive Protein" OR "Tumor Necrosis Factor-alpha" OR "Interleukin-6" AND "randomized controlled trial" OR "controlled clinical trial" OR "clinical trials as topic". The complete search strategy for each database is provided in Supplementary File 1.

Inclusion Criteria

Studies were eligible for inclusion in this systematic review if they met the following criteria: (1) study design: randomized controlled trials (RCTs) or controlled clinical trials; (2) language: published in English; (3) population: postmenopausal women with a body mass index (BMI) $\geq$25 kg/m^2, classified as overweight or obese; (4) intervention: aerobic exercise (e.g., treadmill walking, running, jogging, brisk walking), resistance exercise (e.g., weightlifting, push-ups, squats), or a combination of both, with a minimum intervention duration of six months; (5) outcomes: studies reporting at least one inflammatory biomarker, specifically CRP, IL-6, or TNF-α.

Additional eligibility criteria stipulated that non-exercise co-interventions likely to influence inflammation (e.g., dietary modification, supplements, weight-loss programs, pharmacotherapy) were delivered identically to both exercise and comparator arms, or if the chosen comparison held these co-interventions constant (e.g., diet + exercise vs diet-only), so that exercise was the only difference. Trials were excluded when such co-interventions were given to only one of the arms being compared, while trials with multiple intervention arms were included if $\geq$1 arm involved aerobic and/or resistance exercise and $\geq$1 comparator had no structured exercise. Arms were combined or split to avoid double-counting and to isolate the exercise effect needed here. A detailed list of eligible exercise types (with synonyms) is provided in Appendix E, Table S1.

Exclusion Criteria

Studies were excluded if they met any of the following criteria: (1) study design: uncontrolled

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trials, observational studies, narrative reviews, systematic reviews, meta-analyses, conference abstracts or proceedings, cell culture studies, or animal studies; (2) language: published in languages other than English; (3) population: studies involving men, individuals with autoimmune diseases, active cancer or malignancy, or infectious conditions known to influence inflammatory marker levels significantly.

Selection of studies and data extraction

Records were successfully imported into the Covidence platform, where duplicates were removed, resulting in 2,723 records. Two independent reviewers conducted the title and abstract screening, with a third reviewer available to resolve any disagreements. Subsequently, 448 records were selected for full-text screening according to predefined eligibility criteria. Any discrepancies identified during the full-text review were resolved by a third reviewer. A detailed PRISMA flow diagram of this process is presented in Figure 1.

Two reviewers independently extracted data from each study. The pre-piloted, standardized data extraction form in Covidence included the following information: study characteristics, methodology, population demographics, baseline characteristics, interventions, comparators, reported outcomes, and risk of bias. Disagreements were resolved through discussion, with a third reviewer involved as needed.

Data synthesis

The studies were categorized according to the specific inflammatory markers assessed: CRP, IL-6, and TNF-α. Summary tables were used to present key information, including study reference, type of exercise intervention. They also show the levels of inflammatory markers before and after the intervention for both the intervention and control groups. These tables provide details on whether the changes were statistically significant between the groups and within the intervention group over time. Additional information on study characteristics (e.g., study location, design, and sample size), participant baseline data (e.g., mean BMI, body fat percentage), intervention specifics (e.g., intensity and duration), and more comprehensive results are available in the supplementary files.

Risk of bias assessment

The risk of bias of the included RCTs was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool for RCTs and Risk of Bias in Non-randomized Studies – of Interventions (ROBINS-I) tool for the non-randomized controlled trials. Two independent reviewers conducted the risk-of-bias assessment, and any disagreements were resolved through discussion with a senior author until consensus was reached. Visual summaries of the assessments were generated using the robvis R package (Appendix C - Figures 2 and 3) (McGuinness & Higgins, 2021).

Results

A total of seven studies that met the defined criteria were included in the final analysis, with overall characteristics presented in Tables 1 and 2. This systematic review consisted of five RCTs and two non-randomized trials, with six studies conducted in the United States and one in Canada (Table 2). All the studies had a six-month intervention period, except Imayama et al. (2012), which had a 12-month intervention period.

Population

A total of 1,278 participants were included in this systematic review. All studies included sedentary, overweight, and obese postmenopausal women. The baseline characteristics are presented in Table 1. Five of the seven studies focused on generally healthy participants, excluding individuals with comorbid conditions such as diabetes, severe hypertension, hypertriglyceridemia, or cancer (Brochu et al., 2009; Imayama et al., 2012; Ryan et al., 2014; Silverman et al., 2009; You et al., 2004). One study included women with systolic blood pressure as high as 160 mmHg (Arsenault et al., 2009), and another study specifically enrolled women with elevated systolic blood pressure (Stewart et al., 2010).

Intervention characteristics and effects, Exposure and Control Conditions

Three studies implemented a combination of aerobic exercise and dietary modification for the intervention group, with the control group receiving dietary intervention only (Ryan et al., 2014; Silverman et al., 2009; You et al., 2004). Daily food records/logs were a standard tool for the dietary component. In another three studies, the intervention group participated solely in aerobic exercise, whereas the control group received no intervention (Arsenault et al., 2009; Imayama et al., 2012; Stewart et al., 2010). One study employed resistance exercise with caloric restriction as the intervention, with the control group receiving only caloric restriction (Brochu et al., 2009).

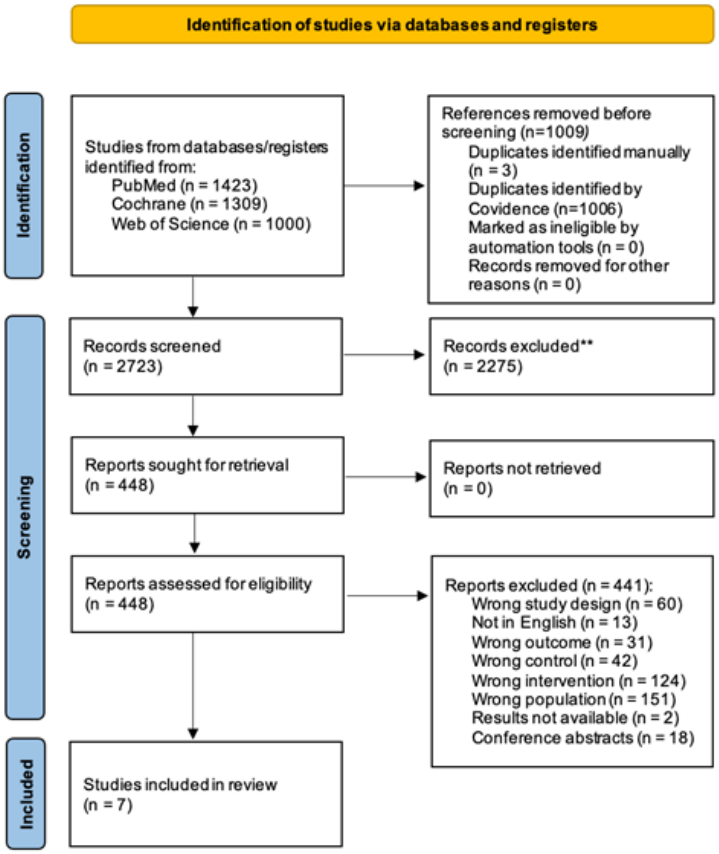

Figure 1: *PRISMA flow diagram of study selection.*

Study	Age (years) [mean (SD) or *(SEM)]	Sample size	Intervention and control groups	Intervening measure and intensity	Interventions duration	Outcomes
Arsenault 2009	59 (1)	349	INT: aerobic exercise (n= 267)	Aerobic exercises (alternated training sessions on semi-recumbent cycle ergometers and treadmills) heart rate corresponding to 50% of each woman's peak VO2	20-55 min session, 3 or 4 training sessions each week, for 6 months	CRP, IL-6, TNF-α
	57 (1)		CO: No intervention (n= 82)		No intervention	CRP, IL-6, TNF-α
Brochu 2009	60 (5)	107	INT: diet + resistance training (n= 36)	Hypocaloric diet + resistance training (treadmills, leg press, chest press, lateral pull downs, shoulder press, arm curls, and triceps extensions) 65% to 85% of maximal heart rate	Warm up 10 min + 3 to 4 sets per exercise / session, 3x/week, for 6 months	hsCRP*
	58 (5)		CO: diet (n= 71)	Hypocaloric diet (128-133 kcal/day deficit)	No intervention	hsCRP*
Imayama 2012	58.1 (5.0)	204	INT: aerobic exercise (n= 117)	aerobic exercise (treadmills, ellipticals, rowing machines, and stationary bikes, walking) 70% to 85% of maximal heart rate	45 min/ session, 225 min/ week, 5 sessions/ week, for 12 months	IL-6, hsCRP*
	57.4 (4.4)		CO: no intervention (n= 87)	-	No intervention	IL-6, hsCRP*
Ryan 2014	60 (1)*	77	INT: diet and aerobic exercise (n= 37)	Hypocaloric diet + aerobic exercise (treadmills, ellipticals) > 85% HRR	45 min/ session, 3x/week, for 6 months	CRP
	61 (1)*		CO: diet and instruction in Therapeutic Lifestyle Changes (TLC) (n= 40)	hypocaloric diet (300 to 500 kcal/d deficit)	No intervention	CRP
Silverman 2009	57.2 (5.0)	86	INT: diet + aerobic exercise (n= 46)	hypocaloric diet + aerobic exercise (walking) 50–75% HRR	45–60 min/session, 3x/week, for 6 months	IL-6, TNF-α
	58.0 (4.7)		CO: diet (n= 40)	hypocaloric diet (250–350 kcal/day deficit)	No intervention	IL-6, TNF-α
Stewart 2010	57.3 (6.6)	421	INT: three aerobic exercise groups: INT 1: 4 kcal/kg/week (n = 143) INT 2: 8 kcal/kg/week (n = 87) INT 3: 12 kcal/kg/week (n = 95)	Aerobic exercises (treadmill and cycling sessions) 50% of each participant's peak VO_2	INT 1: ~28 min/session, 2.6 sessions/week INT 2: ~49 min/session, 2.8 sessions/week INT 3: ~62 min/session, 3.1 sessions/week, 6 months	CRP
	57.2 (6.1)		CO: No intervention (n= 96)		No intervention	
You 2004	INT 1: 58.0 (6.5) INT 2: 56.8 (6.6) INT 3: 56.6 (6.5)	34	INT: diet + aerobic exercise (n= 17)	Hypocaloric diet + aerobic exercise (treadmill) 65–70% heart rate reserve (HRR)	Up to 60 min/session, 3x/week, for 24 weeks	CRP, IL-6, TNF-α
	57.3 (5.9)		CO: diet (n= 17)	hypocaloric diet (250–350 kcal/day deficit)	No intervention	CRP, IL-6, TNF-α

INT: intervention group, CO: control group *hsCRP: high-sensitivity C-reactive protein.

Table 1: *Baseline characteristics of included studies.*

Study	Country	Study design	BMI [mean (SD) or *(SEM)]	Fat% [mean (SD) or *(SEM)]
Arsenault 2009	USA	RCT	32.0 (5.7)	NA
			31.9 (3.8)	NA
Brochu 2009	Canada	RCT	32.6 (4.9)	46.5 (4.9)
			32.2 (4.6)	45.0 (4.3)
Imayama 2012	USA	RCT	30.7 (3.9)	NA
			30.7 (3.7)	NA
Ryan 2014	USA	Non-randomized controlled trial	32 (1)*	47.1 (0.9)*
			33 (1)*	47.8 (0.6)*
Silverman 2009	USA	Non-randomized controlled trial	32.1 (4.2)	NA
			32.6 (4.6)	NR
Stewart 2010	USA	RCT	INT 1: 31.5 (3.7) INT 2: 32.4 (4.0) INT 3: 31.2 (3.5)	NR
			32.2 (3.9)	NR
You 2004	USA	RCT	weight (kg)#: 85.8 (2.9)	42.4 (1.3)
			weight (kg)#: 90.0 (3.9)	45.7 (1.1)

No information about BMI in the study by You 2004. RCT: randomized controlled trial, NA: not available, NR: not reported.

Table 2: *Summary of included studies' overall characteristics.*

Treadmills, elliptical trainers, cycle ergometers, and walking were commonly used for aerobic exercise. Most exercise programs incorporated progression by gradually increasing repetitions, sets, or intensity (Brochu et al., 2009), heart rate reserve (HRR) targets (Ryan et al., 2014; Silverman et al., 2009; You et al., 2004), or energy-expenditure targets (Arsenault et al., 2009; Stewart et al., 2010). Heart-rate metrics (e.g., HRR, % peak VO_2, max HR) were widely used to prescribe and monitor aerobic-exercise intensity. Resistance training loads were set using the one-repetition maximum (1-RM).

Outcomes

C-Reactive Protein (CRP)

Six studies evaluated the effect of aerobic/resistance exercise on CRP levels in postmenopausal overweight and obese women. Four studies measured changes in CRP levels, and two measured changes in high-sensitivity CRP (hsCRP) levels (Table 3). No studies reported significant differences compared to controls at the end of the study. Additionally, CRP level changes were examined from the beginning to the end of the exercise intervention. Two studies showed a statistically significant reduction: You et al. (2004) showed a reduction in CRP level of $p<0.05$ (estimation 34% lower), with an effect size estimated in 1.86 mg/L by subtracting the given values of before and after in the study's Table 2. Ryan et al. (2014) showed $p<0.001$ (29/% lower), with estimated effect size of 1.5 mg/L when comparing aerobic exercise and weight loss before and after graphs in their Figure 1. The effect size was estimated in both studies since the values weren't mentioned in the text or tables. In contrast, Arsenault et al. (2009) and Imayama et al. (2012) reported that the difference was not statistically significant. Importantly, both studies demonstrating positive results (Ryan et al., 2014; You et al., 2004) implemented a combined exercise and dietary intervention, whereas studies evaluating exercise alone (Arsenault et al., 2009; Brochu et al., 2009; Imayama et al., 2012; Silverman et al., 2009; Stewart et al., 2010) showed inconsistent or nonsignificant effects.

Interleukin-6 (IL-6)

Four studies analyzed IL-6 level change (Table 4). You et al. (2004) found a statistically significant reduction compared with controls ($p<0.05$; 46% lower; estimated effect size of 1.14 pg/mL) and within-group changes ($p<0.001$; 27% lower; estimated effect size difference of 0.48). Conversely, (Arsenault et al. (2009, Imayama et al. (2012, and Silverman et al. (2009) reported differences that were not statistically significant. Changes in IL-6 levels were examined from the beginning to the end of the exercise intervention. Regarding within-group changes, You et al. (2004) also demonstrated a statistically significant reduction in IL-6 levels from baseline to post-intervention. The remaining three studies (Arsenault et al., 2009; Imayama et al., 2012;

Study	CRP / hsCRP	Intervention type	CRP/hsCRP in mg/L		Intervention vs. Control	End of study vs baseline in Intervention group
			Intervention group	Control group		
Arsenault (2009)	CRP	Intervention: aerobic exercise Control: no exercise for 6 months	Baseline: 5.36 (4.93) End of study: 5.46 (5.67) #	Baseline: 5.59 (5.62) End of study: 5.44 (4.90) #	Not statistically significant	Not statistically significant
Brochu (2009)	hsCRP	Intervention: caloric restriction + resistance exercise Control: caloric restriction for 6 months	Baseline: 2.97 (2.16) End of study: NR #	Baseline: 3.38 (2.99) End of study: NR #	Not statistically significant	NR
Imayama (2012)	hsCRP	Intervention: aerobic exercise Control: no exercise for 12 months	Baseline: 2.48 (2.00 - 3.06) End of study: 2.46 (2.23 - 2.72)*	Baseline 1.90 (1.50–2.40) End of study: 2.06 (1.84 - 2.30)*	Not statistically significant	Not statistically significant
Ryan (2014)	CRP	Intervention: diet + aerobic exercise Control: diet for 6 months	NR	NR	NR	29% lower Statistically significant reduction (p<0.05)
Stewart (2010)	CRP	Intervention: aerobic exercise Control: no exercise for 6 months	4kcal/kg/week exercise group Baseline: 5.3 (5.3) End of study: NR # 8kcal/kg/week exercise group Baseline: 6.4 (6.1) End of study: NR # 12kcal/kg/week exercise group Baseline: 5.0 (4.8) End of study: NR #	Baseline: 6.0 (SD = 5.8) End of study: NR #	Not statistically significant	NR
You (2004)	CRP	Intervention: diet + aerobic exercise Control: diet for 6 months	Baseline: 5.46 (0.8), End of study: 3.60 (0.58) $	Baseline: 8.57 (1.27), End of study: 9.54 (2.12) $	Not statistically significant	34% lower Statistically significant reduction (p<0.001)

* geometric mean (95% confidence interval (CI)), # arithmetic mean (standard deviation (SD)), $ unclear if arithmetic or geometric mean was reported in these studies, NR not reported.

Table 3: *CRP levels before and after intervention across included studies.*

Silverman et al., 2009) reported no statistically significant within-group changes.

Tumor Necrosis Factor-alpha (TNF-α)

Three studies analyzed changes in TNF-α levels (Table 5). None of these studies reported statistically significant differences in TNF-α levels between the intervention and control groups. Moreover, regarding within-group changes from baseline to the end of the intervention period, two studies reported differences that were not statistically significant (Arsenault et al., 2009; Silverman et al., 2009).

Assessment of risk of bias in individual studies

The risk of bias was evaluated using the RoB 2 tool for RCTs and the ROBINS-I tool for the two non-randomized controlled trials. Regarding the RCTs, Arsenault et al. (2009), Brochu et al. (2009), Imayama et al. (2012) and Stewart et al. (2010) were judged as "some concerns" about their overall risk of bias. Brochu et al. (2009) limited their analysis to participants who completed the intervention and applied a per-protocol approach, raising issues related to deviations from the intended interventions and missing outcome data; they also did not describe an imputation strategy for missing biomarkers. Stewart et al. (2010) showed strong adherence and clear reporting; however, they did not provide details on how missing CRP data were addressed, leading to concerns about the handling of missing outcome data. Arsenault et al. (2009) also raised some concerns due to combining intervention groups after randomization and using a per-protocol analysis with about 25% attrition, which increased the risk in deviation and missing data domains. Lastly, You et al. (2004) was considered to have a high risk of bias due to insufficient details regarding the randomization process and the exclusion of 32% of participants from the final analysis. These evaluations are summarized in the RoB2 table (Figure 2).

Ryan et al. (2014) was assessed as having an overall moderate risk of bias regarding bias due to confounding, as it was non-randomized and details on adjustment for potential confounders were limited. Additionally, there were moderate concerns regarding bias due to the selection of participants and missing outcome data, given the exclusion of 16 participants for comorbidities or low adherence, leaving data for only 77 of 174 enrolled participants.

Silverman et al. (2009) was considered high overall risk of bias primarily due to serious concerns in two domains, participant selection and missing

Study	Intervention type	IL-6 in pg/ml		Intervention vs. Control	Baseline vs. End of study in Intervention group
		Intervention group	Control group		
Arsenault (2009)	Intervention: aerobic exercise Control: no exercise for 6 months	Baseline: 0.00270 (0.00199) End of study: 0.00282 (0.00279) #	Baseline: 2.54 (1.33) End of study: 2.53 (1.30) #	Not statistically significant	Not statistically significant
Imayama (2012)	Intervention: aerobic exercise Control: no exercise for 12 months	Baseline: 1.47 (1.30–1.66) End of study: 1.57 (1.48–1.65)	Baseline:1.43 (1.25–1.64)* End of study: 1.60 (1.50–1.69)*	Not statistically significant	Not statistically significant
Silverman (2009)	Intervention: diet + aerobic exercise Control: diet for 6 months	Baseline: 2.42 (1.71), End of study: 2.40 (2.85) $	Baseline: 2.04 (0.9), End of study: 2.03 (1.24) $	Not statistically significant	Not statistically significant
You (2004)	Intervention: diet + aerobic exercise Control: diet for 6 months	Baseline: 1.77 (0.18), End of study: 1.29 (0.11) $	Baseline: 2.59 (0.36) End of study: 2.43 (0.40) $	Statistically significant reduction (p<0.05)	Statistically significant reduction (p<0.001)

* geometric mean (95% CI), # arithmetic mean (SD), $ unclear if arithmetic or geometric mean (SE) was reported in these studies.

Table 4: *IL-6 levels before and after intervention across included studies.*

Study	Intervention type	TNF-α in pg/ml		Intervention vs. Control	Baseline vs. End of study in Intervention group
		Intervention group	Control group		
Arsenault (2009)	Intervention: aerobic exercise Control: no exercise for 6 months	Baseline: 1.76 (0.76) End of study: 1.83 (0.95)#	Baseline: 1.63 (0.50) End of study: 1.58 (0.47) #	Not statistically significant	Not statistically significant
Silverman (2009)	Intervention: diet + aerobic exercise Control: diet for 6 months	Baseline: 1.74 (2.34), End of study: 1.64 2.51)$	Baseline: 2.12 (3.49), End of study: 3.02 (7.90)	Not statistically significant	Not statistically significant
You (2004)	Intervention: diet + aerobic exercise Control: diet for 6 months	Baseline: 1.88 (0.47), End of study: 1.76 (0.67 $	Baseline: 3.13 (1.03), End of study: 3.92 (1.11)$	Not statistically significant	Not statistically significant

* geometric mean (95% CI), # arithmetic mean (SD), $ unclear if arithmetic or geometric mean was reported in these studies.

Table 5: *TNF-α levels before and after intervention across included studies.*

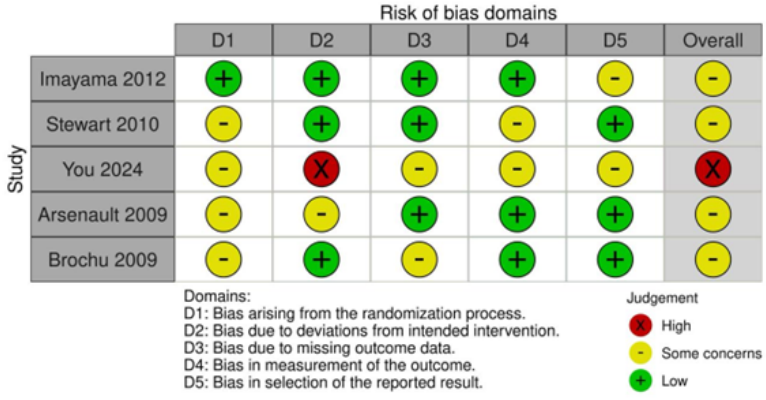

Figure 2: *RoB 2 summary table for included RCTs.*

outcome data. The lack of randomization and the fact that nearly half of the women were excluded before the final analysis raised significant concerns. Additionally, there were also moderate concerns regarding bias due to confounding. The judgments for these studies are summarized in the ROBINS-I table (Figure 3).

The overall risk of bias profile supports a cautious interpretation of the results, particularly emphasizing the need to reduce the weight given to studies assessed at high or serious risk in any quantitative synthesis. The most frequently flagged domains across both assessment tools included concerns related to missing outcome data, selection of participants/randomization process, and deviations from intended interventions.

Discussion

Contextualization of Findings

This systematic review evaluated the effects of aerobic and resistance exercise on inflammatory markers (CRP, IL-6, and TNF-α) in overweight and obese postmenopausal women. Among the included studies, only two (Ryan et al., 2014; You et al., 2004) demonstrated a statistically significant reduction in CRP levels, and one of these (You et al., 2004) also reported decreases in IL-6. These positive findings were observed exclusively in interventions combining exercise with dietary modification. However, CRP and IL-6 levels in that study were already lower at baseline in the diet-plus-exercise group, suggesting possible baseline imbalance and regression-to-the-mean effects that may overestimate the true exercise impact. The small sample size (n = 34) in You et al. (2004) further limits statistical power and generalizability.

Given our focus on trials lasting at least six months, lower adherence over time may have attenuated the observed effects. Nevertheless, this does not imply that exercise lacks benefit for postmenopausal women. Instead, the pattern across studies indicates that combining exercise with dietary modification may enhance anti-inflammatory outcomes through synergistic effects on metabolism and immune regulation.

Specific Differences Between Included Studies

While our systematic review adhered to precise inclusion criteria, a detailed examination of the seven included studies revealed several sources of heterogeneity among their designs and participant characteristics, which warrant discussion as they influence the interpretation and generalizability of our findings.

Studies varied considerably the stringency of exclusion criteria. While Arsenault et al. (2009) and Stewart et al. (2010) primarily excluded only severe conditions affecting safety or adherence, Brochu et al. (2009), Ryan et al. (2014), Silverman et al. (2009) and You et al. (2004) more stringently excluded participants with various comorbidities. This clinical diversity impacts the comparability of results and the generalizability to a broader population of postmenopausal women, who often present with age-related conditions. Even though one study (You et al., 2004) consistently found significant changes in CRP and IL-6 between the experimental groups and from baseline levels to the end of the study, it also had the highest risk of bias and the smallest sample size (34 participants), contrasting with the six larger, moderate-to-high bias studies that found no significant effects.

Sample sizes varied substantially. Smaller sample sizes, such as those in You et al. (2004), can reduce statistical power, leading to underestimations of effects or an inability to detect actual changes. Furthermore, the limited reporting of social factors, with only Imayama et al. (2012) providing comprehensive baseline social characteristics, represents a gap in the evidence base, hindering our understanding of potential socio-demographic influences on intervention outcomes.

The included studies defined sedentary lifestyle in different ways. Arsenault et al. (2009) defined women as sedentary if they did not engage in exercise lasting more than 20 minutes on three or more days per week and took fewer than 8,000 steps per day, as assessed over the course of one week. Brochu et al. (2009) classified women as sedentary if they performed less than two hours per week of structured exercise. Ryan et al. (2014) and Silverman et al. (2009) both defined sedentary women as those performing less than 20 minutes of aerobic exercise twice per week. Similarly, Stewart et al. (2010) defined sedentary women as exercising for less than 20 minutes on fewer than three days per week and taking fewer than 8,000 steps per day, assessed over one week. The variability in the operational definitions of "sedentary" across studies introduces heterogeneity that may affect the comparability of findings in this systematic review.

Crucially, the nature of the interventions themselves was a significant source of heterogeneity impacting our primary findings. Four studies (Brochu et al., 2009; Ryan et al., 2014; Silverman et al., 2009; You et al., 2004) utilized combined dietary and exercise interventions, making it challenging

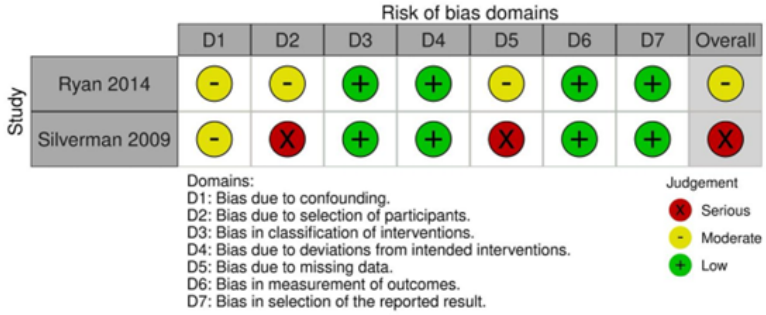

Figure 3: *ROBINS-I summary table for included non-randomized controlled trials.*

to isolate the independent effect of exercise on inflammatory markers. In contrast, the remaining studies focused solely on exercise interventions. Our analysis suggests that these combined approaches were more consistently associated with significant reductions in inflammatory markers. Importantly, both studies demonstrating positive results (Ryan et al., 2014; You et al., 2004) implemented a combined exercise and dietary intervention, whereas studies evaluating exercise alone (Arsenault et al., 2009; Brochu et al., 2009; Imayama et al., 2012; Silverman et al., 2009; Stewart et al., 2010) showed inconsistent or nonsignificant effects. This pattern suggests that the integration of dietary modification with exercise may be critical to achieving meaningful reductions in CRP levels.

Exercise setting and adherence varied widely across studies, influencing intervention quality and outcome validity. Studies implementing fully supervised or partially supervised programs, such as those by Arsenault et al. (2009), Imayama et al. (2012) and Stewart et al. (2010), reported higher adherence and lower dropout rates. In contrast, Brochu et al. (2009) reported low completion rates despite supervision, while studies incorporating home-based or self-directed components (Silverman et al., 2009; You et al., 2004) achieved moderate adherence through periodic supervision and monitoring tools. Poor adherence or irregular participation diminishes the training stimulus, increasing variability and reducing statistical power, ultimately increasing the likelihood that studies will report non-significant results even when a true effect exists. Dietary adherence was similar to exercise adherence in each study.

Strengths and Limitations

This systematic review possesses several methodological strengths that enhance its rigor. We meticulously selected seven distinct studies, including five RCTs involving 1,115 participants, from an initial pool of 2,723. This focus on RCTs strengthens the evidence foundation. Furthermore, our concentration on overweight and obese postmenopausal women addresses a clinically relevant population with often co-occurring health conditions, and the inclusion of studies accepting participants with well-controlled comorbidities (e.g., diabetes, hypertension) significantly enhances external validity. Critically, our consistent focus on interventions lasting at least six months addresses the scarcity of long-term data, offering valuable insights into sustained effects.

Despite these strengths, the review faces significant limitations, primarily concerning the quality and reliability of the included evidence. A comprehensive risk of bias assessment revealed substantial methodological concerns across most studies, compromising the validity of their results and reducing confidence in our overall findings. Inherent research challenges, such as the impracticality of blinding participants in exercise groups, introduced potential for performance and detection bias. Given this risk-of-bias profile, the results need to be interpreted with caution, and findings from studies assessed as high risk were given less weight in forming the overall conclusions. Additionally, limiting the review to English-language articles may have excluded relevant trials from non-English-speaking regions, potentially introducing publication bias and reducing the generalizability of the findings. A critical limitation was the significant methodological and clinical heterogeneity across primary studies, particularly in intervention designs and comorbidity criteria, which complicated direct comparisons. Moreover, the interpretation of exercise effects was challenged by inconsistently assessed or controlled confounding factors, such as broader lifestyle habits (e.g., diet, stress, sleep, alcohol), which could independently influence inflammation and make it difficult to isolate the true effect of exercise. Also, we included only studies that used aerobic

and/or resistance exercise. This may limit the generalizability of our findings, as other exercise modalities, such as yoga, tai chi, or Pilates, were excluded.

Implications for Practice and Future Research

Current evidence, often limited by significant methodological concerns and varying risks of bias, does not consistently support aerobic or resistance training as effective interventions for reducing chronic inflammatory markers (CRP, IL-6, TNF-α) in overweight and obese postmenopausal women. However, given the broader cardiometabolic and functional benefits of physical activity, regular exercise should still be encouraged as part of a comprehensive lifestyle approach. Healthcare providers should individualize recommendations, taking into account patient preferences, functional status, and other risk factors. Future research should prioritize well-designed, long-term trials with standardized exercise protocols, robust adherence tracking, and stratified analyses to clarify who may benefit most. Investigating the interplay between exercise type, intensity, baseline inflammation, and hormonal status will be key to advancing personalized recommendations in this high-risk group.

This review focused exclusively on aerobic and resistance training interventions. Mind–body exercises such as yoga, tai chi, and Pilates were excluded because their physiological mechanisms and intensity profiles differ substantially, primarily influencing inflammation through neuroendocrine or stress-related pathways. Future reviews could also compare mind–body interventions and traditional exercise modalities within a unified analytical framework to elucidate a more comprehensive understanding of exercise-induced anti-inflammatory mechanisms.

Conclusion

This systematic review found that exercise alone did not consistently reduce inflammatory markers (CRP, IL-6, TNF-α) in overweight, obese postmenopausal women. This limited evidence base, partly due to a low conversion rate from an initial broad search suggesting a scarcity of studies, combined with significant methodological concerns and high risk of bias in the included studies, contributed to the lack of clear impact. Confounding factors also contributed to the limitation of the findings. Notably, positive outcomes were typically associated with combined exercise and dietary interventions, suggesting a multi-faceted approach may be more effective. Future research must address these limitations, including controlling confounding lifestyle factors and employing rigorous study designs, to better understand exercise's anti-inflammatory potential.

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Supplementary Materials

Search strategies; included and excluded types of interventions, with synonymous terms and examples.

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Conflicts of Interest

The authors declare no conflict of interest.

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