

# Effect of Exercise Intervention on the Cardiovascular Health of Untrained Women: A Meta-analysis and Meta-regression

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## Abstract

**Objective:** Research on the untrained women's cardiovascular health is a hot topic in the world. It is important to systematically assess the effects of exercise duration on cardiovascular health in untrained women.

**Methods:** Published articles from 1988 to May 2015 were identified using electronic databases for randomized controlled trials. The weighted mean differences and 95% confidence intervals were calculated using fixed-effects and random-effects models. Meta-regression and subgroup analysis were performed to explore the possible heterogeneity.

**Results:** Data from 28 published studies with a total of 544 untrained women aged less than 60 years were identified. There were significant pooled effects of different exercise durations on VO<sub>2</sub>max (within 3 months 95% CI: -2.51 to -1.57; I<sup>2</sup>=0%; 4-6 months 95% CI: -4.63 to -2.44; I<sup>2</sup>=0%) and Systolic Blood Pressure (4-6 months 95% CI: 5.55 to 7.52; I<sup>2</sup>=35%). Additionally, Systolic Blood Pressure was significantly decreased in unhealthy women (95% CI: 5.78 to 8.73; I<sup>2</sup>=84.3%). The Heart Rate, Total Cholesterol, High Density Lipoprotein-Cholesterol and Low Density Lipoprotein-Cholesterol of untrained women were significantly improved with short-duration, mid-duration and long-duration exercise.

**Conclusion:** There are different effects of exercise duration on cardiovascular health in untrained women aged less than 60 years. The short-duration exercise can improve aerobic capacity in women, but the improvement becomes less with the increase of age. The short-duration, mid-duration and long-duration exercise can improve cholesterol metabolism and decrease Heart Rate in untrained women. The mid-duration exercise can significantly decrease Systolic Blood Pressure in unhealthy women but not in healthy women.

**Keywords:** Exercise intervention; Cardiovascular health; Untrained women; Exercise duration; Meta-regression

## Introduction

More attention has been paid to the cardiovascular health of women. The investigation on the effects of exercise intervention on the cardiovascular health of untrained women is valuable. It is well established that aerobic exercise can improve the cardiovascular health of untrained women and men [1-4] including aerobic capacity, cardiac functions and endothelial functions [5,6]. The meta-analysis between exercise intervention and the health of adult women was performed, including the effect of exercise intervention on VO<sub>2</sub>max, resting Heart Rate (HR), Systolic Blood Pressure (SBP) and Total Cholesterol (TC) [7,8]. Many studies have reported that exercise intervention improves aerobic fitness, decreases arterial blood pressure and reduces cardiovascular risk [9,10]. However, some studies demonstrated that there were no changes or relatively small effects on the women who were performed short-duration exercise intervention [11-13]. Therefore, it is controversial for the effect of aerobic exercise intervention on the cardiovascular parameters of untrained women at different durations.

Based on the studies between aerobic exercise and the health status of people, some researchers have reported that gender differences are associated with the different physiological and cardiovascular adaptations to exercise interventions [14,15]. On one hand, Kelley found that there were different responses to women and men in some parameters such as blood pressure and fat mass. For instance, there were no significant differences in blood pressure before and after exercise intervention in comparison with that of men, and fat mass had smaller change in women [9-10,16-18]. On the other hand, few

data were reviewed and analyzed comprehensively between exercise and the health of untrained women. In summary, the study of women's cardiovascular health is valuable as a result of women's special role in society and the differences of cardiovascular functions compared to men. Therefore, it is interesting and important to investigate and analyze the effect of aerobic exercise on the cardiovascular health of untrained women at different exercise durations.

The parameters such as VO<sub>2</sub>max, TC, High Density Lipoprotein-Cholesterol (HDL-C), Low Density Lipoprotein-Cholesterol (LDL-C), HR and SBP were used for evaluating the cardiovascular health in this meta-analysis. The aim of this study was to analyze and then assess quantitatively the effect of exercise intervention on aerobic capacity, cholesterol metabolism, HR, and SBP of untrained women at different durations. It will be a strong evidence of relations between exercise intervention and women for further studies, and it is useful for

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healthy women or unhealthy women to arrange exercise programs or prescriptions at different durations in hospital or at home.

## Methods

### Search strategy

A system review was made in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The following databases were searched, including PubMed, Cochrane library, Cochrane Central Register of Controlled Trials (CENTRAL), Google scholar, Embase and Web of Science. These databases were searched using the terms “women”, “untrained women”, “exercise”, “aerobic exercise”, “exercise therapy”, “sports”, “cardiovascular health”. Further searches were performed using “untrained women and exercise”, “untrained women and aerobic exercise and RCTs” and “untrained women and aerobic exercise and cardiovascular health and RCTs”.

### Inclusion criteria

(i) Only randomized controlled trials (RCTs) of effect of aerobic exercise on the cardiovascular health in untrained women were included in this study. No restrictions on language or publication date were set.

(ii) The adult women ( $\geq 18$  years) and untrained women who are healthy and unhealthy (obesity, mild hypertension or mild diabetics) were included, and the untrained women who are the patients with serious cardiovascular disease were excluded in this study.

(iii) Only RCTs that exercise groups practicing aerobic exercise at different durations and control groups had no exercise or medication interventions were included. And the included exercise groups who were practiced exercise intervention of less than 8 weeks were excluded.

(iv) The outcome measures included the  $VO_2$ max, HR and SBP. In addition, TC, High Density Lipoprotein-Cholesterol (HDL-C) and Low Density Lipoprotein-Cholesterol (LDL-C) were included in this study. The outcomes were analyzed as short-duration exercise (within 3 months), mid-duration exercise (4-6 months) and long-duration exercise (more than 6 months).

### Selection of studies

The pre-specified criteria were used by two reviewers to screen the titles, abstracts and full papers of relevant articles. An article was excluded if it did not meet the inclusion criteria and selection standard. Any uncertain problems in this study and any disagreements about the included studies were discussed and then resolved by a third author.

### Data extraction

The following data from included articles were extracted, including participants characteristic, author, years, study design, description of interventions between exercise groups and control groups, different exercise durations and outcome measures. A standard table was performed to comply with these data. Similarly, the two reviewers extracted these data and evaluated the risk of bias. An arbiter was contacted to solve any disagreements.

### Quality assessment

The Cochrane Collaboration recommendations were used to assess the risk of bias for all the included articles in this study [19]. The following information was extracted from these studies, including the design of study, participant characteristics, the selection of follow-up and outcome measures, detailed information of intervention group

(i.e., type of exercise, intensity and duration of exercise intervention) and nature of control group. Three reviewers were needed to evaluate the methodological quality of all articles in this study. A third author reconciled to the disagreements.

### Statistical analysis

The data in this study was analyzed according to the Cochrane Handbook for Systematic Reviews of Interventions [19]. Continuous outcomes were analyzed in this study, including the mean value and standard deviation in outcomes between baseline and follow-up for exercise group. The weighted mean differences (MD) and corresponding 95% CI were calculated by random-effects models and fixed-effects model [20]. Heterogeneity between studies was evaluated by analyzing the characteristics of studies and assessed quantitatively using the  $I^2$  statistic. A fixed-effects model in meta-analysis would be used when statistic heterogeneity was identified ( $I^2$  statistic $<50\%$ ). A weighted random-effect meta-regression was used to examine the possible sources of heterogeneity. The between-study characteristics which may attribute to the heterogeneity were examined in this study, including exercise durations, age and health (healthy or unhealthy). Univariate meta-regressions were performed and these factors were input into the meta-regression model respectively. Coefficient, Adj R-squared (Proportion of between-study variance explained) and p value were analyzed and evaluated in meta-regression. A subgroup analysis was analyzed by the categorical variables which were significant in the univariate meta-regressions model to identify the effects of aerobic exercise on the cardiovascular health of untrained women. Statistical analysis was performed using standard software packages (Review Manage 5.3 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014 and Stata MP. 13.0, College Station, Texas).

## Results

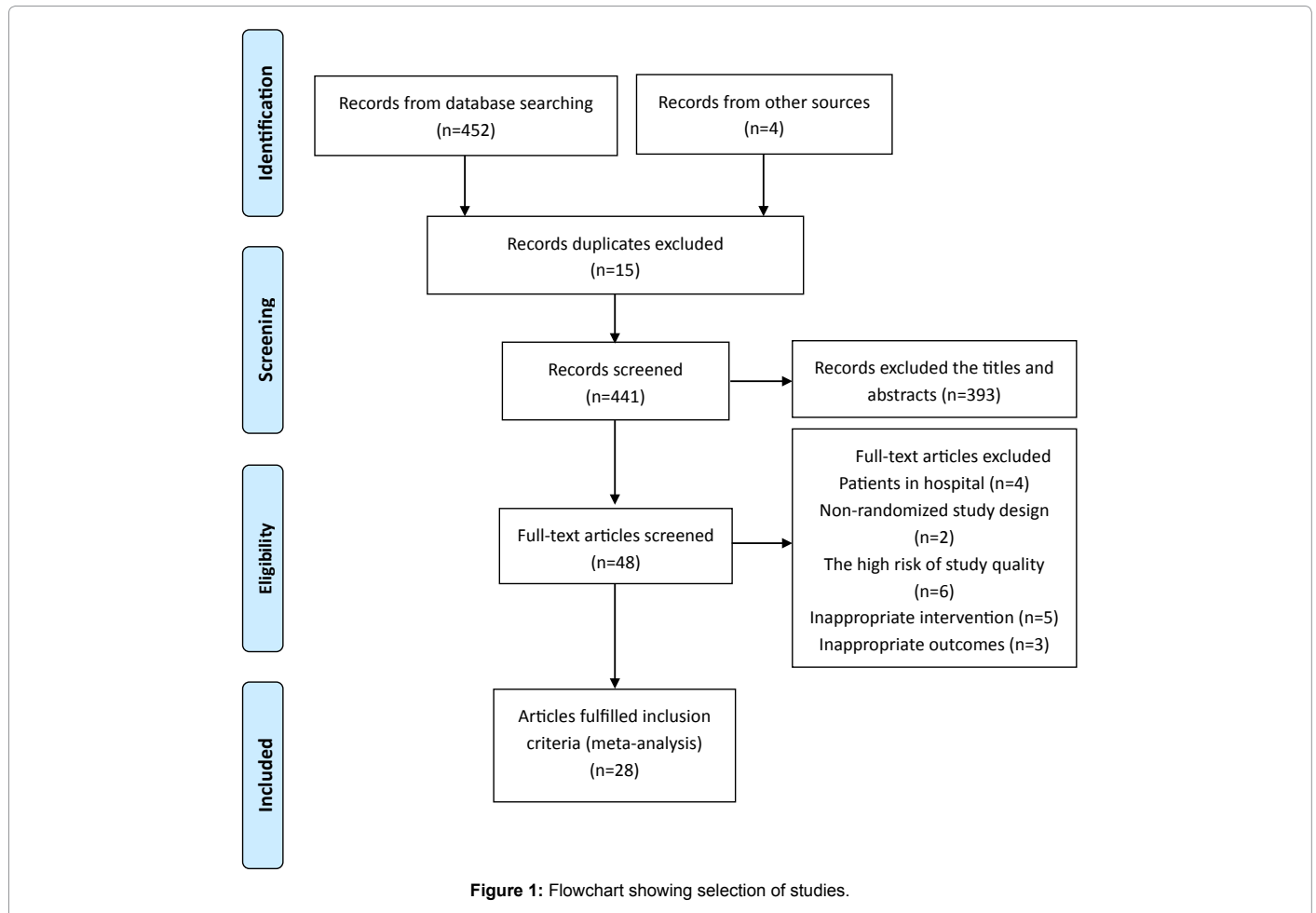
### Search results

A total of 456 records were identified through PubMed, Cochrane library, Embase, Web of Science and other sources. Among these identified records, 48 potentially eligible articles were screened based on the titles and abstracts. After a comprehensive review of these 48 studies, 28 published reports, which investigated and analyzed exercise intervention in 544 untrained women, met the criteria of included RCTs studies (Figure 1). 28 RCTs [21-38] with exercise durations for at least 8 weeks were enrolled. 20 articles were excluded due to the participants having serious cardiovascular diseases, non-RCTs and high risk of study quality. Other articles were removed because of inappropriate intervention and inappropriate outcome measures. In addition, subject characteristics of women enrolled in RCTs are listed in Table 1.

### Risk of bias of included studies

Every included study had a high risk according to the Cochrane Collaboration recommendations. Accordingly, the evidence in this meta-analysis had a high overall risk of bias. Quality assessment of included studies was performed by the risk of bias table of RevMan 5.3, including the selection bias, performance bias, detection bias and attrition bias. The detailed risk of bias was illustrated in Table 2. 28 articles had low risk in adequate sequence generation, blinding of outcome assessment, incomplete outcome data and selective reporting. In these included studies, three studies had high risk, and three studies had unclear risk in allocation concealment. Three studies had unclear risk in blinding of participants and personal. And six studies had high risk and twenty-two studies had unclear risk in other bias.

### Effect of aerobic exercise on aerobic capacity of untrained



Literature Reference	Characteristic and Sample Size	Exercise Group Intervention	Durations of trail period	Outcomes
Akazawa [21]	21 sedentary postmenopausal women(EG=11, CG=10); Age(M ± SD): EG=59 ± 5; CG=64 ± 6	Exercise group underwent aerobic exercise training more than 3 days per week (2-3 supervised sessions and additional home-based training)	8 weeks	TC, HDL-C, LDL-C, Triglyceride, Glucose, VO <sub>2</sub> max
Miyaki [22]	72 middle-aged and elderly Women(EG=33, CG=39); Age(M ± SD): EG=60 ± 6; CG=60 ± 7	2 months of regular aerobic exercise training (walking and cycling).	2 months	TC, HDL-C, LDL-C, Triglyceride, Fasting Blood Glucose, HR, SBP, VO <sub>2</sub> max, Carotid Arterial Compliance, β-stiffness, Diastolic Blood Pressure
Lee [23]	14 middle-aged Korean females(EG=7, CG=7); Age(M ± SD): EG=41.7 ± 4.3; CG=38.3 ± 4.9	High-intensity exercise training for 14 weeks at 50% maximal oxygen consumption.	14 weeks	Fat free mass, VO <sub>2</sub> max, TC, HDL-C, LDL-C, Triglyceride
Lee [23]	15 middle-aged Korean females(EG=8, CG=7); Age(M ± SD): EG=41.6 ± 4.5; CG=38.3 ± 4.9	High-intensity exercise training at 70% maximal oxygen consumption.	14 weeks	Fat free mass, VO <sub>2</sub> max, TC, HDL-C, LDL-C, Triglyceride
Hammer [24]	26 obese premenopausal women(EG=14, CG=12); Age(M ± SD): EG=32 ± 7; CG=35 ± 6	Training exercise (walking)	16 weeks	Body composition, VO <sub>2</sub> max
Hammer [24]	26 obese premenopausal women(EG=14, CG=12); Age(M ± SD): EG=32 ± 7; CG=35 ± 6	Training exercise (jogging)	12 weeks	Body composition, VO <sub>2</sub> max
Leidy [25]	12 normal-weight young women(EG=5, CG=7); Age(M ± SD): EG=20.2 ± 1.0; CG=21.3 ± 3.4	Aerobic exercise five times per week at 70–80% of maximum heart rate.	15 weeks	Fat free mass, Fat mass, VO <sub>2</sub> max, Body fat
Leidy [25]	17 normal-weight young women(EG=10, CG=7); Age(M ± SD): EG=20.3 ± 1.6; CG=21.3 ± 3.4	Aerobic exercise intervention	3 months	Fat free mass, Fat mass, VO <sub>2</sub> max, Body fat
Layman [26]	48 Adult women(EG=24, CG=24); Age(M ± SD): EG=47.9 ± 1.4; CG=45.2 ± 1.4	A supervised exercise program (EX: 5 d/wk walking and 2 d/wk resistance training)	16 weeks	Fat mass, Lean mass, TC, HDL-C, LDL-C, Triglyceride
Uusi-Rasi [27]	82 postmenopausal women(EG=41, CG=41); Age(M ± SD): EG=53 ± 2.8; CG=54.2 ± 2.4	Progressive jumping exercise	12 months	Skeletal Sites, VO <sub>2</sub> max, Grip strength

Uusi-Rasi [27]	82 postmenopausal women(EG=24, CG=24); Age(M ± SD): EG=53.3 ± 3.2; CG=53.2 ± 2.1	Progressive jumping exercise	12 months	Skeletal Sites, VO <sub>2</sub> max, Grip strength
Stefanick [28]	88 postmenopausal women(EG=43, CG=45); Age: EG=64; CG=64	Aerobic exercise program	1 year	Cholesterol intake, Total fat, VO <sub>2</sub> max, Calories from nutrients, TC, HDL-C, LDL-C, Triglyceride, Fasting Blood Glucose, HR, SBP
Stefanick [28]	89 postmenopausal women(EG=43, CG=46); Age: EG=64; CG=64	Aerobic exercise intervention	1 year	Cholesterol intake, Total fat, VO <sub>2</sub> max, Calories from nutrients, TC, HDL-C, LDL-C, Triglyceride, Fasting Blood Glucose, HR, SBP
Fahlman [29]	29 healthy elderly women(EG=15, CG=14); Age(M ± SD): EG=76 ± 5; CG=77 ± 6	10-week endurance training	10 weeks	Body fat, HR,VO <sub>2</sub> max
Kraemer [30]	17 healthy premenopausal women(EG=9, CG=8); Age(M ± SD): EG=35.4 ± 8.5; CG=35.4 ± 8.5	Aerobic endurance exercise and strength exercise 3 days/week	12 weeks	Fat free mass, Fat mass, Body mass, Repetition maximum strength, metabolic rate determinations, VO <sub>2</sub> max
Kraemer [30]	16 healthy premenopausal women(EG=8, CG=8); Age(M ± SD): EG=35.4 ± 8.5; CG=35.4 ± 8.5	Aerobic endurance exercise training program 3 days/week	12 weeks	Fat free mass, Fat mass, Body mass, Repetition Maximum Strength, Metabolic rate determinations, VO <sub>2</sub> max
Krustrup [31]	40 untrained premenopausal women CDR(EG=25, CG=15); Age(M ± SD): EG=37 ± 2; CG=33 ± 2	Football exercise for 1 h twice a week after 16 weeks.	16 weeks	TC, HDL-C, LDL-C, Triglyceride, HR, SBP, VO <sub>2</sub> max, Mean arterial pressure, Diastolic blood pressure, Lean body mass
Krustrup [31]	40 untrained premenopausal women CDR(EG=25, CG=15); Age(M ± SD): EG=37 ± 2; CG=33 ± 2	Running for 1 h twice a week after 16 weeks (training frequency <1.2 times per week)	16 weeks	TC, HDL-C, LDL-C, Triglyceride, HR, SBP, VO <sub>2</sub> max, Mean arterial pressure, Diastolic blood pressure, Lean body mass
Nualnim [32]	43 women with prehypertension(EG=24, CG=19); Age(M ± SD): EG=61 ± 2; CG=58 ± 2	12 weeks of swimming exercise	12 weeks	TC, HDL-C, LDL-C, Triglyceride, HR, SBP, VO <sub>2</sub> max, Carbohydrate intake, Pulse pressure, Mean blood pressure, Diastolic blood pressure, SBP
Figuerola [33]	28 obese postmenopausal women(EG=14, CG=14); Age(M ± SD): EG=57 ± 1; CG=56 ± 1	Stretching exercises 3 d/wk for 8 weeks	8 weeks	Augmentation Index, Augmented Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Pulse Wave Velocity, Tension Time Index, SBP, Diastolic blood pressure
Figuerola [34]	28 obese postmenopausal women(EG=14, CG=14); Age(M ± SD): EG=54 ± 1; CG=55 ± 1	Low-intensity resistance exercise for 12 weeks	12 weeks	Augmentation Index, Augmented Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Pulse Wave Velocity, Tension Time Index, SBP, Diastolic blood pressure
Mohr [35]	41 sedentary premenopausal women with mild to moderate arterial hypertension(EG=21, CG=20); Age(M ± SD): EG=46 ± 2; CG=45 ± 2	High-intensity swimming training with 3 training sessions per week for 15 wks	15 weeks	TC, HDL-C, LDL-C,
Mohr [35]	41 sedentary premenopausal women with mild to moderate arterial hypertension(EG=21, CG=20); Age(M ± SD): EG=44 ± 2; CG=45 ± 2	Moderate-intensity continuous front crawl swimming	15 weeks	TC, HDL-C, LDL-C,
Brandenburg [36]	18 women with type 2 diabetes(EG=8, CG=10); Age(M ± SD): EG=37 ± 6; CG=43 ± 7	3 months of moderate intensity exercise training	3 months	Fasting glucose, Fasting insulin, HR, VO <sub>2</sub> max
Brandenburg [36]	17 women with type 2 diabetes(EG=8, CG=10); Age(M ± SD): EG=37 ± 6; CG=43 ± 7	Aerobic exercise training in a 3-month program of supervised exercise, three times per week	3 months	Fasting glucose, Fasting insulin, HR, VO <sub>2</sub> max
Izquierdo [37]	25 obese women(EG=13, CG=12); Age(M ± SD): EG=51.4 ± 5.5; CG=48.6 ± 6.4	Modest resistance training for 16 weeks	16 weeks	Energy intake, Muscle strength, TC, HDL-C, LDL-C, TC/HDL
Mohr [38]	21 premenopausal hypertensive women(EG=21, CG=20); Age(M ± SD): EG=45 ± 3; CG=43 ± 3	Football training 1-h sessions 3 times per week.	15 weeks	SBP, Diastolic Blood Pressure, Mean Arterial Pressure, HR, TC, HDL-C, LDL-C, Triglyceride

Note: EG: exercise group; CG: control group; Age (M ± SD): Age=Means ± Standard Deviation; TC/HDL: The ratio of TC and HDL

**Table 1:** Baseline characteristics in untrained women and Intervention of included literature.

## women

Sixteen studies (comprising of 322 untrained women) measuring VO<sub>2</sub>max, which is the most common aerobic capacity variable, were pooled for meta-analysis using random effect model. The VO<sub>2</sub>max at different exercise durations was assessed by subgroup analysis. The VO<sub>2</sub>max of the untrained women who exercised at duration of less than 3 months (6 RCTs, random-effect WMD -2.04, 95% CI: -2.51 to -1.57; I<sup>2</sup>=0%, Figure 2A(1)), and 4-6 months (6 RCTs, random-effect WMD -6.70, 95% CI: -8.23 to -5.18; I<sup>2</sup>=0%, Figure 2A(2)) was increased respectively. However, no significant change occurred for the exercise

group with aerobic exercise of more than 6 months (5 RCTs, random-effect WMD -2.65, 95% CI: -5.33 to 0.03; I<sup>2</sup>=88.7%, Figure 2A(3)). And there appears high heterogeneity in VO<sub>2</sub>max at exercise duration of more than 6 months. In the analysis of univariate meta-regression, the Adj R-squared of age has high percentage, and p value shows a significant difference (p=0.000) in meta-regression (Table 3), so that age has influence on the VO<sub>2</sub>max of untrained women. According to the subgroup analysis, there was a significant difference before and after aerobic exercise in untrained women at 41-60 years old (7 RCTs, random-effect WMD -1.80, 95% CI: -2.47 to -1.13; I<sup>2</sup>=33.3%). The VO<sub>2</sub>max was significantly increased in untrained women under 40



Author	Adequate sequence generation	Allocation concealment	Blinding of participants and personal	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Akazawa [21]	✓	✓	✓	✓	✓	✓	?
Miyaki [23]	✓	✓	✓	✓	✓	✓	?
Lee [23]	✓	✓	✓	✓	✓	✓	?
Lee [23]	✓	✓	✓	✓	✓	✓	?
Hammer [24]	✓	✓	✓	✓	✓	✓	?
Hammer [24]	✓	?	✓	✓	✓	✓	?
Leidy [25]	✓	✓	✓	✓	✓	✓	?
Leidy [25]	✓	✓	✓	✓	✓	✓	?
Layman [26]	✓	✓	?	✓	✓	✓	?
Layman [26]	✓	✓	?	✓	✓	✓	?
Uusi-Rasi [27]	✓	x	✓	✓	✓	✓	x
Uusi-Rasi [27]	✓	x	✓	✓	✓	✓	x
Stefanick [28]	✓	✓	✓	✓	✓	✓	?
Stefanick [28]	✓	✓	✓	✓	✓	✓	?
Fahlman [29]	✓	x	✓	✓	✓	✓	x
Figuroa [34]	✓	✓	✓	✓	✓	✓	?
Figuroa [34]	✓	✓	✓	✓	✓	✓	?
Krustrup [31]	✓	✓	✓	✓	✓	✓	?
Krustrup [31]	✓	✓	✓	✓	✓	✓	?
Nualnim [32]	✓	✓	✓	✓	✓	✓	?
Mohr [35]	✓	✓	✓	✓	✓	✓	?
Mohr [35]	✓	✓	✓	✓	✓	✓	?
Brandenburg [36]	✓	?	✓	✓	✓	v	x
Brandenburg [36]	✓	✓	✓	✓	✓	✓	x
Izquierdo [37]	✓	✓	?	✓	✓	✓	?
Mohr [38]	✓	✓	✓	✓	✓	✓	?
Kraemer [30]	✓	✓	✓	✓	✓	✓	x
Kraemer [30]	✓	✓	✓	✓	✓	✓	?

Note: High risk "x", Low risk "✓", unclear risk "?"; let : low-intensity exercise training; het: high-intensity exercise training; enx: exercise nonexercise; ex: exercise; wse: weight-stable exercisers; wle: weight-loss exercisers; pro: protein; cho: carbohydrates; alex: alendronate +exercise training; ex: exercise training; et: exercise training; det: diet+ exercise training; fg: football group; rg: running group; hit: high-intensity exercise; mod: moderate-intensity exercise; lean: lean participants; des: diet+aerobic endurance exercise+strength training; de: diet+aerobic endurance exercise

Table 2: Risk of bias assessment of included studies.

years old (9 RCTs, random-effect WMD -4.77, 95% CI: -6.40 to -3.15; I<sup>2</sup>=34.6%,) Figure 2B (1,2). There appears homogeneity in the VO<sub>2</sub>max of both untrained women aged 41-60 and younger than 40 years old.

### Effect of aerobic exercise on cholesterol metabolism

All studies reported significant improvement in cholesterol metabolism with aerobic exercise. Meta-analysis results of pooled data from 12 studies were performed using the fixed effects model. The TC, HDL-C and LDL-C were the most important parameters to evaluate cholesterol metabolism. The TC, reported in 254 untrained women enrolled in 12 RCTs, was significantly decreased after aerobic exercise intervention (n=254, 95% CI: 0.07 to 0.16, p<0.00001; I<sup>2</sup>=5%, Figure 3A). And the HDL-C, reported in 254 untrained women enrolled in 12 RCTs, was significantly increased after aerobic exercise (n=254, 95% CI: -0.10 to -0.06, p<0.00001; I<sup>2</sup>=23%, Figure 3B). The LDL-C, reported in 250 untrained women enrolled in 12 RCTs, was significantly decreased after aerobic exercise (n=250, 95% CI: 0.07 to 0.16, p<0.00001; I<sup>2</sup>=33%, Figure 3C). There is no heterogeneity in parameters such as TC, HDL-C and LDL-C in untrained women at different exercise durations.

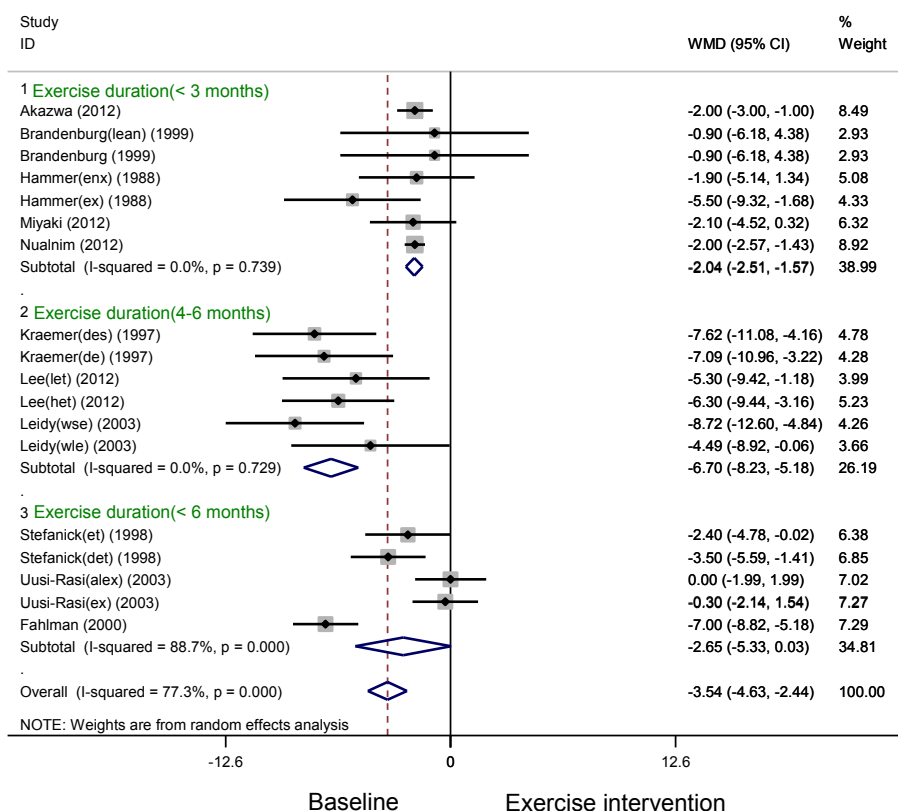
### Effect of aerobic exercise on HR

Similarly, the meta-analysis results of pooled data from 11 studies using the random effects model comprising of 223 untrained women. The HR was assessed by meta-regression and subgroup analysis at different exercise durations. The HR of untrained women increased

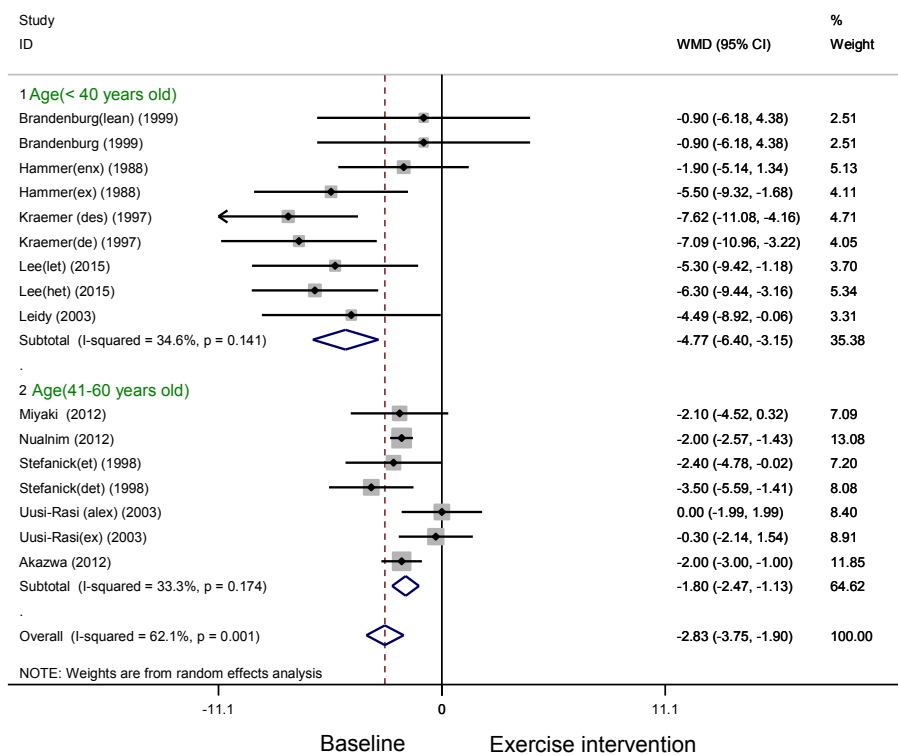
significantly with aerobic exercise 3 months or less (7 RCTs, random-effect WMD 2.68, 95% CI: 1.52 to 3.85; I<sup>2</sup>=44.7%, Figure 4A(1)), 4-6 months (3 RCTs, random-effect WMD 5.16, 95% CI: 4.72 to 5.60; I<sup>2</sup>=0%, Figure 4A(2)) and more than 6 months (4 RCTs, random-effect WMD 6.06, 95% CI: 0.84 to 11.27; I<sup>2</sup>=91.3%, Figure 4A(3)). The HR of untrained women has some heterogeneity at exercise duration of more than 6 months and within 3 months. According to the results of univariate meta-regression, the Adj R-squared of age has high percentage, and p value shows significant difference (p=0.016) by meta-regression (Table 3), so that age is associated with HR of untrained women. A subgroup analysis demonstrated that there was a significant difference in HR before and after aerobic exercise for both untrained women aged 41-60 (5 RCTs, random-effect WMD 1.97, 95% CI: 0.96 to 2.99; I<sup>2</sup>=16.6%,) and younger than 40 years old (6 RCTs, random-effect WMD 5.15, 95% CI: 4.71 to 5.59; I<sup>2</sup>=0%,) (Figure 4B(1,2)). There appears homogeneity for the subgroup analysis both untrained women aged 41-60 and younger than 40 years old.

### Effect of aerobic exercise on SBP

The SBP of these 12 studies (comprising of 295 untrained healthy women and unhealthy women) were pooled using the random effects model. The SBP, was significantly increased at the exercise duration of 4-6 months (4 RCTs, random-effect WMD 6.54, 95% CI: 5.55 to 7.52; I<sup>2</sup>=35%,). However, there were no significant changes in the group whose exercise duration is within 3 months (3 RCTs, random-effect



**Figure 2A:** Forest plot showing the effect of aerobic exercise on VO<sub>2</sub>max in subgroup analysis. (1) Exercise duration < 3 months; (2) Exercise duration 4-6 months; (3) Exercise duration > 6 months.



**Figure 2B:** Forest plot showing the effect of aerobic exercise on VO<sub>2</sub>max in subgroup analysis. (1) Untrained women at < 40 years old; (2) Untrained women at 41-60 years old.

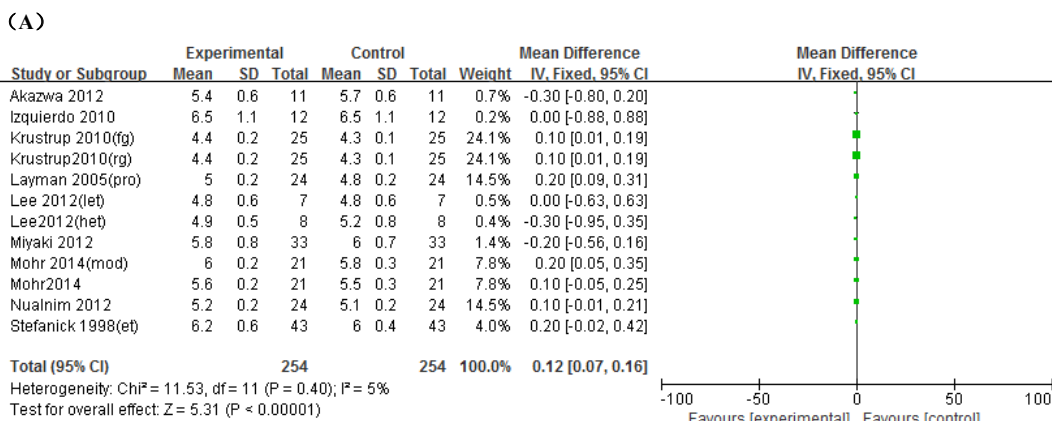


Figure 3A: Forest plot showing the effect of aerobic exercise on TC from baseline to exercise intervention at different durations.

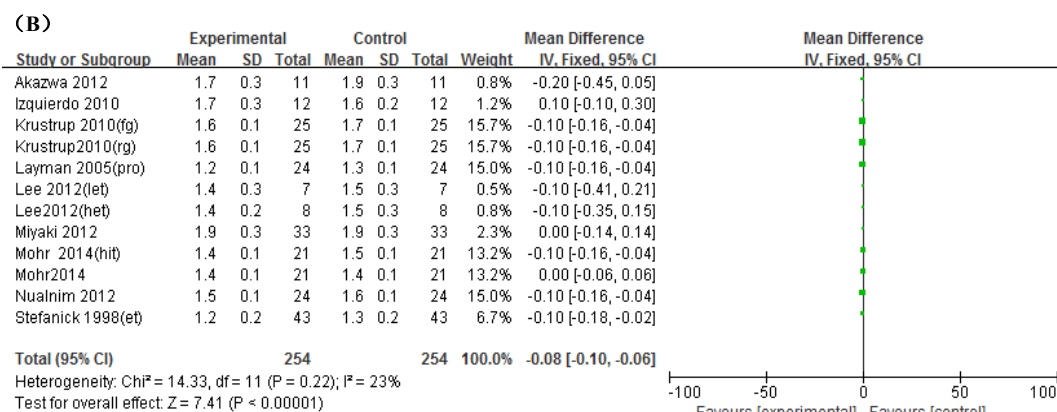


Figure 3B: Forest plot showing the effect of aerobic exercise on HDL-C from baseline to exercise intervention at different durations.

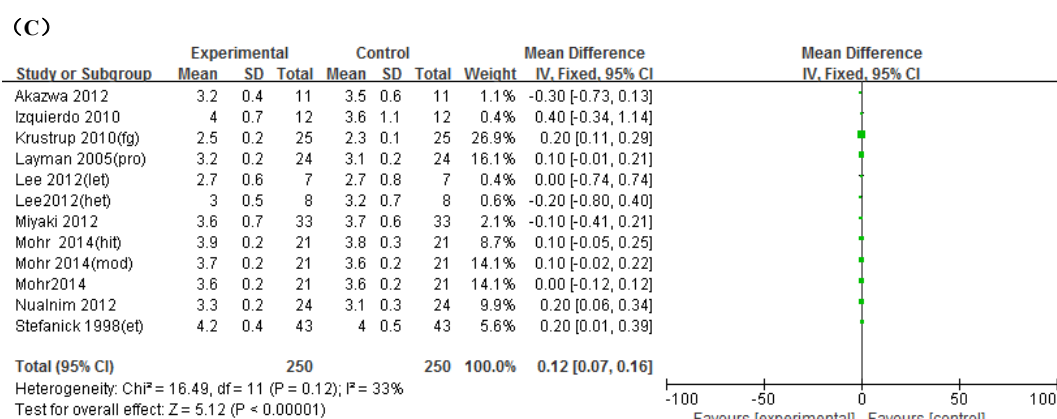


Figure 3C: Forest plot showing the effect of aerobic exercise on LDL-C from baseline to exercise intervention at different durations.

WMD 2.71, 95% CI: -2.39 to 7.81; I<sup>2</sup>=61.3%), and more than 6 months (2 RCTs, random-effect WMD 2.08, 95% CI: 3.94 to 6.65; I<sup>2</sup>=0%) (Figure 5A (1-3)). There appears heterogeneity in SBP at the exercise duration of within 3 months. A univariate meta-regression analysis indicated that the Adj R-squared of health has high percentage, and p value shows significant difference (p=0.019) by meta-regression

(Table 3), so that the SBP of untrained women is effected by health. A subgroup analysis was determined that there was no significant change in SBP of healthy women (4 RCTs, random-effect WMD 1.34, 95% CI: -1.77 to 4.45; I<sup>2</sup>=0%, Figure 5B(1)). However, SBP was significantly decreased in unhealthy women after exercise intervention (8 RCTs, random-effect WMD 7.26, 95% CI: 5.78 to 8.73; I<sup>2</sup>=84.3%, Figure

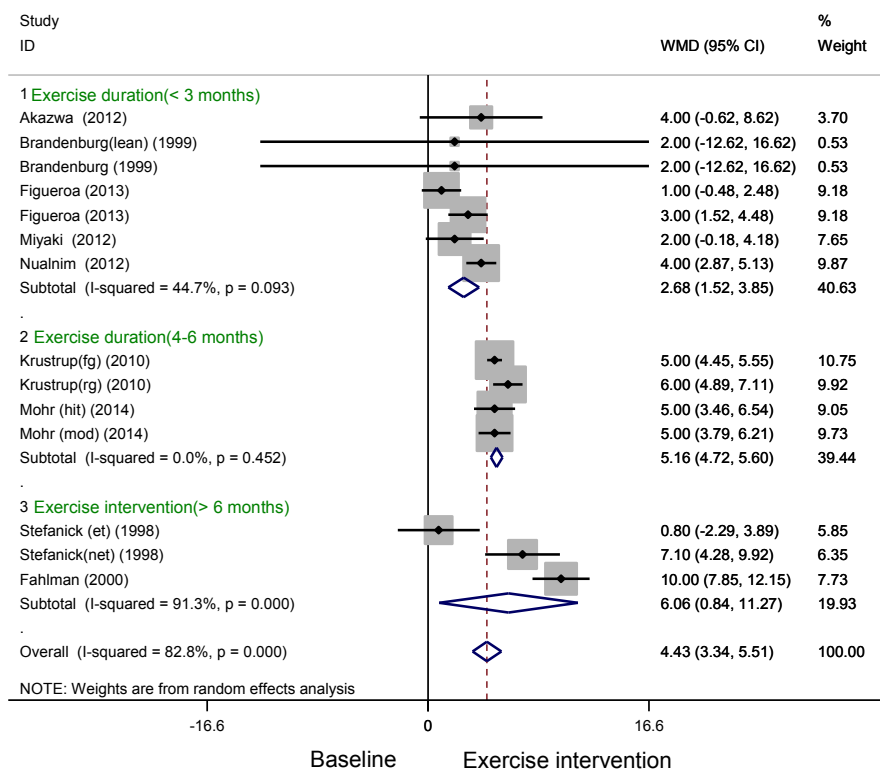


Figure 4A: Forest plot showing the effect of aerobic exercise on HR in subgroup analysis; (1) Exercise duration < 3 months; (2) Exercise duration 4-6 months; (3) Exercise duration > 6 months.

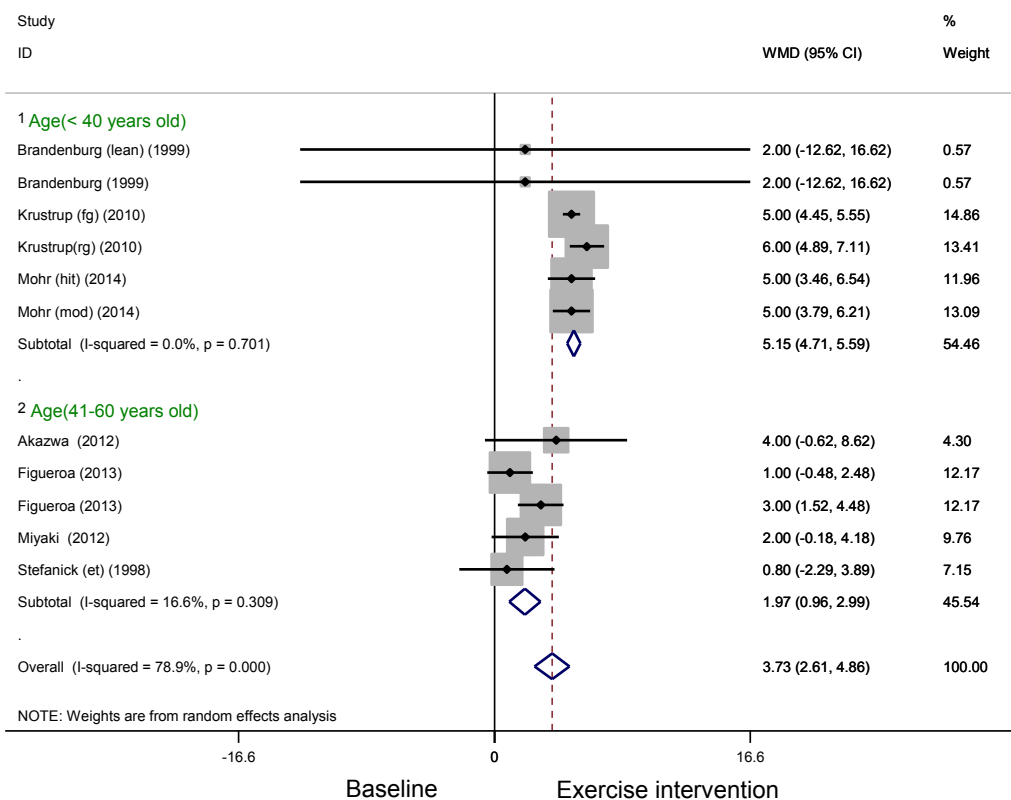


Figure 4B: Forest plot showing the effect of aerobic exercise on HR in subgroup analysis. (1) Untrained women at < 40 years old; (2) Untrained women at 41-60 years old.



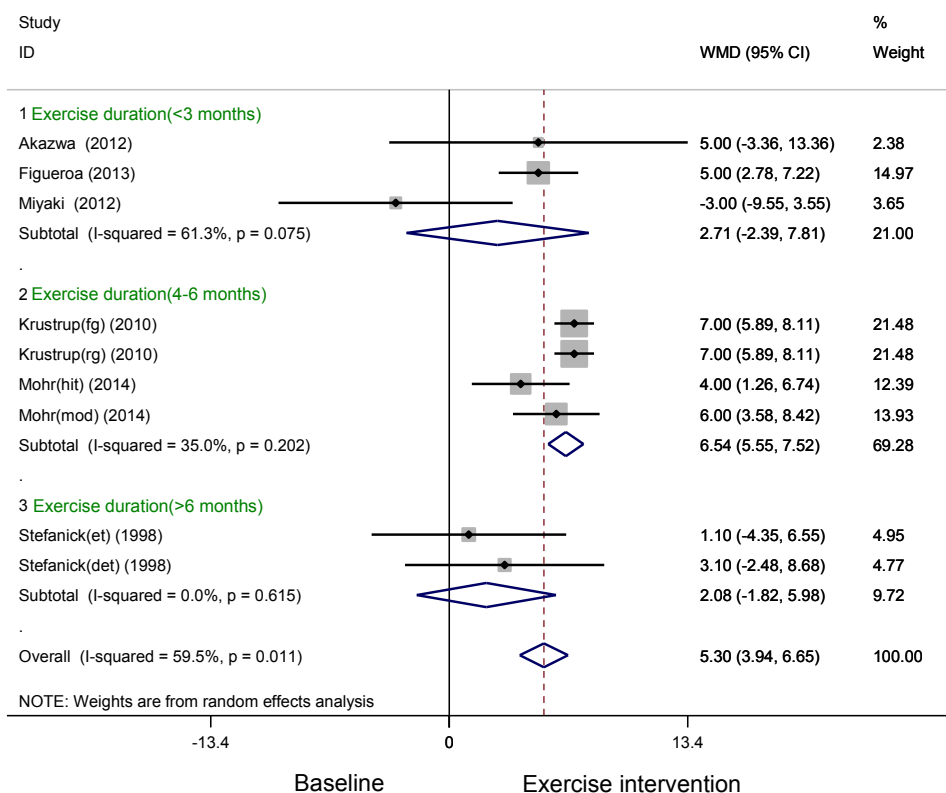


Figure 5A: Forest plot showing the effect of aerobic exercise on SBP in subgroup analysis. (1) Exercise duration < 3 months; (2) Exercise duration 4-6 months; (3) Exercise duration > 6 months.

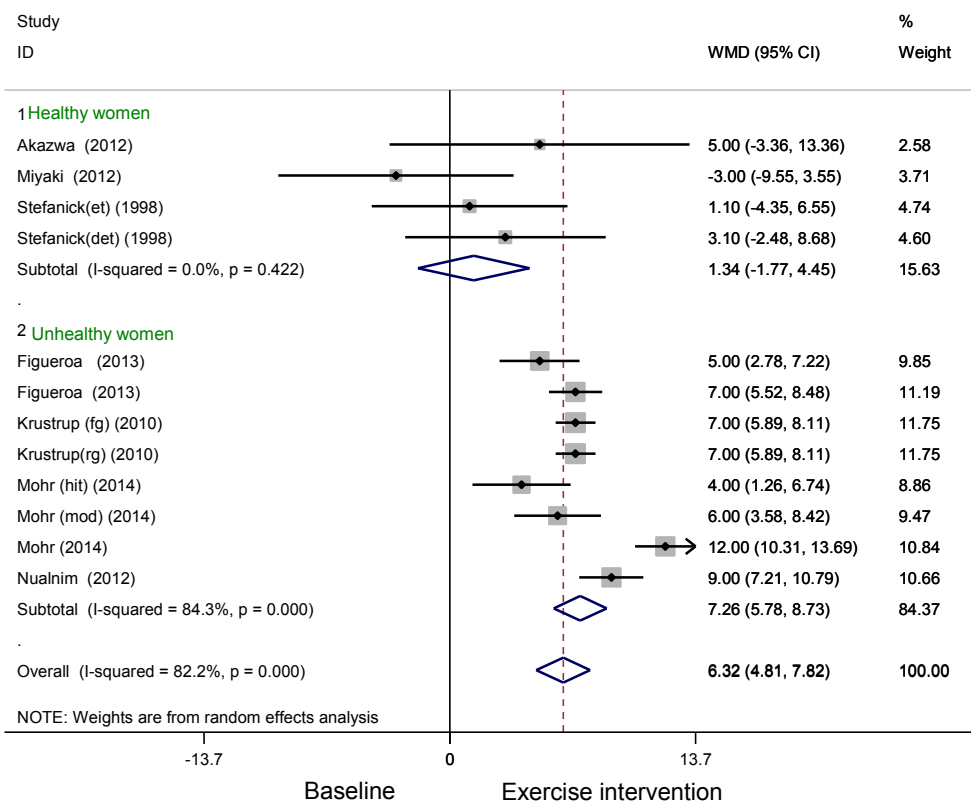


Figure 5B: Forest plot showing the effect of aerobic exercise on SBP in subgroup analysis. (1) The healthy women; (2) The unhealthy women.

5B(2)). It has some heterogeneity for unhealthy women.

## Discussion

In contrast to the research on exercise intervention and cardiovascular health of men, there are few data to comprehensively evaluate the effect of exercise intervention on the cardiovascular health of women. Even though there is some literature including the effects of physical activities on endothelial function, [39-42] heart disease [43] and metabolic health [44]. Meanwhile, it is controversial for the effect of exercise on cardiovascular parameters of untrained women [12] and for the different responses of cardiovascular functions of untrained women and men after exercise intervention [17]. Therefore, it is valuable to comprehensively assess the effects of exercise intervention on the cardiovascular health of untrained women at different durations. In this meta-analysis and meta-regression, the data of 28 published studies are provided on the aerobic capacity, cholesterol metabolism, HR and SBP of 544 untrained women. The risk of bias was evaluated by using the Cochrane Collaboration recommendations. According to the results of meta-regression and subgroup analysis, aerobic exercise can play different roles in the cardiovascular health of untrained women at different durations.

There are different effects of aerobic exercise on the aerobic capacity, cholesterol metabolism, HR and SBP of untrained women at different durations. The parameters such as  $VO_2$ max, HR and SBP were analyzed in a univariate meta-regression model, and the covariates such as age and health attributed to the heterogeneity in this study.  $VO_2$ max, which is the most important parameter to evaluate the aerobic capacity, was significantly decreased at the exercise durations of 4-6 months and within 3 months, while it had no significant difference at exercise duration of more than 6 months. On one hand, there appears high heterogeneity, and the data of untrained women at exercise duration more than 6 month can be not merged to explain effectively the effect of long-duration exercise on the  $VO_2$ max. On the other hand, the possible reason may be that  $VO_2$ max is affected by many other factors, including exercise intensity, sex, age, cardiac output [45]. In addition, the  $VO_2$ max of untrained women increased less with age. Our results support previous reviews which many kinds of aerobic sports can improve the aerobic capacity of people [46-48]. The TC and LDL were significantly decreased in untrained women and HDL-C was significantly increased at different aerobic exercise durations. TC, HDL-C and LDL-C characterize the level of cholesterol metabolism. A decreased TC and LDL-C, or increased HDL-C will reduce risk of cardiovascular diseases [49] and the study indicated that aerobic exercise intervention can improve the cholesterol metabolism in middle-age or the elderly after a period of exercise [50-52].

There were significant differences in HR when comparing before and after aerobic exercise at the durations of less than 3 months, 4-6 months and more than 6 months for both untrained women aged 41-60 and younger than 40 years old. However, the HR has some heterogeneity at the exercise duration more than 6 months and less than 3 months. Previous studies have demonstrated that HR decreased and the capacity of myocardial ejection improved after long-duration exercise [53]. There was a significant difference in SBP before and after exercise at the exercise duration of 4-6 months. However, SBP had no significant change at exercise duration of within 3 months and at exercise duration of more than 6 months. There appears heterogeneity in SBP at exercise duration less than 3 months and more than 6 months. Furthermore, SBP was significantly decreased for unhealthy women, but not for healthy women. It has heterogeneity in SBP of unhealthy women. The effect of exercise intervention on SBP is contradictory. The SBP reduced in premenopausal women with mild hypertension

for short-duration recreational football training. The reduced SBP was related with a reduction in sympathetic tone and an increase in parasympathetic activity [29]. Tanaka et al. [54] found that SBP decreased and Nualnim et al. [32] demonstrated that a 12-week regular swimming training lowered SBP. However, SBP had no significant difference after a short-duration exercise training [55].

In summary, the improvements of  $VO_2$ max, cholesterol metabolism, HR and SBP may be related to the exercise frequency, exercise intensity, types of exercise and rest HR or blood pressure of untrained women but not just to exercise durations or cardiovascular diseases [56].

## Study Limitation

This study was characterized by some limitations that need to be noticed. The articles still have some risk of bias according to the Cochrane Collaboration recommendations, and some methods of literature quality evaluation had a high subjectivity. Therefore, methodologically rigorous articles were still limited. In addition, the subgroup analysis and meta-regression was used for identifying potential sources of heterogeneity. However, the types of exercises, exercise frequency, publication years and study design were not analyzed to explore the heterogeneity due to a limited number of articles. Furthermore, the primary and secondary outcomes have no distinction due to the non-uniform outcomes, so that the results may be at higher risk of chance findings because of the multiple testing and selective reporting. Finally, the further studies for the influence of aerobic exercise at different exercise durations, exercise frequencies and types of exercise on aerobic capacity, cholesterol metabolism, HR and SBP need to be performed.

## Conclusions

The different durations of aerobic exercise (such as walking, jogging, swimming football, dance, Taichi, yoga and stretch exercise) can improve the different cardiovascular parameters in untrained women aged less than 60 years.

There are different effects of aerobic exercise on the aerobic capacity, cholesterol metabolism, HR and SBP in untrained women aged less than 60 years at different durations. The short-duration exercise can improve aerobic capacity in women under 40 years and 41-60 years, but it can be improved less with the increase of age. The short-duration, mid-duration and long-duration exercise can improve the cholesterol metabolism and decrease HR in untrained women under 40 years and 41-60 years. The mid-duration exercises can significantly decrease SBP in unhealthy women under 40 years and 41-60 years but not in healthy women after aerobic exercise.

## Conflict of Interest

The authors declare that there is no conflict of interest.

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