Review Article

# Effects of Coenzyme Q10 Supplementation on Anthropometric Indices in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

**Abed Ghavami, Hamed Mohammadi[1], Amir Hadi[2], Rahele Ziaei[1], Elyas Nattagh-Eshtivani[3], Mohammad Veysi Sheykhrobat[4], Gholamreza Askari[1]**

*Student Research Committee, Department of Clinical Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran, [1]Department of Community Nutrition, Food Security Research Center, School of Nutrition and Food Sciences, Isfahan University of Medical Sciences, Isfahan, Iran, [2]Halal Research Center of IRI, FDA, Tehran, Iran, [3]Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran, [4]Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*

***Address for correspondence:***
*Dr. Gholamreza Askari, Department of Community Nutrition, Isfahan University of Medical Sciences, Isfahan 81745, Iran.*
*E-mail: askari@mui.ac.ir*
*Mr. Amir Hadi, Halal Research Center of IRI, FDA, Tehran 81745, Iran.*
*E-mail: amirhadi.vnt@gmail.com*

## Abstract

**Background:** Obesity is related to increase in the incidence of morbidity and mortality. Previous studies have led to conflicting results regarding the effect of coenzyme Q10 (CoQ10) supplementation on anthropometric indices. This study aimed to evaluate the efficacy of CoQ10 supplementation on body weight, body mass index (BMI), and waist circumference (WC) through a systematic review and meta-analysis of randomized controlled trials (RCTs). **Methods:** PubMed, Scopus, Web of Science, and Cochrane Library as well as the reference lists of the identified relevant RCTs were searched up to March 2019, and weighted mean differences (WMDs) were pooled by using the random-effects model. **Results:** Twenty RCTs (976 participants) were eligible to be included in the systematic review. The meta-analysis revealed that CoQ10 supplementation had no effect on body weight (WMD = −0.04 kg; 95% confidence interval [CI]: −1.96, 1.6; $I^2$ = 0.0%), BMI (WMD = −0.06 kg/m$^2$; 95% CI: −0.54, 0.42; $I^2$ = 0.0%), and WC (WMD = 0.79 cm; 95% CI: −2.83, 0.04; $I^2$ = 0.0%). **Conclusions:** CoQ10 supplementation might not improve anthropometric indices. Future well-designed trials are still needed to confirm these results.

**Keywords:** *Body mass index, body weight, CoQ10, meta-analysis, ubiquinone, waist circumference*

## Introduction

The increasing prevalence of obesity and overweight affects different population throughout the world.[1] Obesity can induce several noncommunicable diseases including type 2 diabetes mellitus (T2DM), cardiovascular diseases, stroke, and some types of cancer.[2-4] Furthermore, it implied a high economic burden to societies.[5] It results in reduced quality of life.[6] Therefore, it is important to find effective treatment strategies to decrease the risk of obesity-related complications.

Common intervention including restriction on energy intake and increase in energy expenditure by different ways such as exercise for managing body weight has been unsuccessful over a long time period.[7] In addition, use of different ways for beginning or accelerating process of weight loss has been popular among obese and overweight subjects. Antiobesity supplements can be considered as auxiliary treatment to increase compliance and adherence of obese subjects to common intervention for managing weight.[8] Pharmacists have attempted to produce effective weight loss supplement with minimum serious side effects to human health.[9] Because an antiobesity supplement has become increasingly popular among obese subjects, it is important to evaluate the efficacy of available antiobesity products.

Coenzyme Q10 (CoQ10) is fat-soluble and has a vital role in the electron transport chain where energy is obtained by a process called oxidative phosphorylation from dietary intakes. This common supplement has various good health effects such as it reduces blood pressure,[10-12] reduces inflammation factors,[13] reduces plasma lipoprotein like Lp(a) concentrations,[14] and plays crucial role in energy expenditure and adenosine triphosphate production.[15]

Animal studies showed that oral administration of CoQ10 led to significant weight loss.[16] Weight loss effects of CoQ10 are modulated by increasing lipid oxidation and energy consumption in adipose tissue and inhibiting adipogenesis through adenosine-monophosphate-activated protein kinase.[17]



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Literature review from clinical trials about effects of CoQ10 supplementation on weight and other anthropometric indices have been inconsistence. Izadi *et al*.[18] investigated the effect of CoQ10 supplementation on hormonal and metabolic indices in patients with polycystic ovary syndrome (PCOS). Intervention resulted in reducing weight and body mass index (BMI) in these patients. Conversely, Moazen *et al*.[19] observed a slight weight gain after 2 months of consuming CoQ10 supplementation. Thus, to clarify the inconsistences, and for accurate decision-making, a comprehensive systematic review and meta-analysis of all available randomized clinical trials was performed to determine the effect of CoQ10 intervention on anthropometric indices in adults.

## Methods

### Search strategy

This systematic and meta-analysis was performed based on the Preferred Reporting Item for Systematic Review and meta-analysis (PRISMA) guideline. A systematic research of studies published until March 2019 was conducted on PubMed, Scopus, Web of Science, and Cochrane Library. The search process used the following terms: ("Coenzyme Q10" OR "Co-enzyme Q10" OR CoQ10 OR ubiquinone OR ubiquinol) AND ("Intervention Studies" OR "intervention" OR "controlled trial" OR "randomized" OR "randomised" OR "random" OR "randomly" OR "placebo" OR "assignment"). A manual reference check was performed on pertinent studies to identify further relevant trials. Due to the fact that several studies examined the effect of CoQ10 supplementation on anthropometric indices as the secondary outcome, we did not use anthropometric keywords. The search was performed by two authors (H.M and A.G) without any restrictions. In addition, the reference lists of all eligible articles were checked at the final step to find relevant studies not found from computerized search.

### Eligibility criteria

Relevant articles were included if they (1) applied a clinical trial design; (2) examined the effects of CoQ10 on weight, BMI, and waist circumference (WC); (3) provided sufficient information on aforesaid indices in both treatment and control groups; (4) conducted on adults (over 18 years); and (5) administered CoQ10 for at least 4 weeks. Studies were excluded if they (1) were uncontrolled studies; (2) used a mixture of CoQ10 with other substance; (3) reported duplicate data; and (4) were reviews, letters, editorial articles, or case reports. Participants, interventions, comparisons, outcomes, and study design (PICOS) are shown in Table 1.

**Table 1: PICOS criteria used to perform the systematic review and meta-analyses**

| Parameter | Criteria |
|---|---|
| Population | Adults |
| Intervention | Q10 |
| Comparator | Matched control group |
| Outcome | Weight, BMI, WC |
| Setting or study design | Randomized controlled trials |

PICOS=Participants, interventions, comparisons, outcomes, and study design; BMI=Body mass index; WC=Waist circumference

### Quality assessment

Two authors (A.G and H.M) independently evaluated the quality of the selected articles using Cochrane Collaboration's tool[20] including six domains as follows: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, and (6) selective reporting. Each domain was classified into three categories: low risk of bias, high risk of bias, and unclear risk of bias. Each domain was classified into three categories: low risk of bias, high risk of bias, and unclear risk of bias. According to the mentioned domains, the overall quality of individual study was considered as good (low risk for more than two items), fair (low risk for two items), or weak (low risk for less than two items).

### Data extraction

Two independent investigators (H.M and A.H) extracted the relevant data. Any controversy among study selection was discussed and eventually resolved by a third reviewer (A.G). The relevant data were extracted including the following: first author, study location, year of publication, study design, target population, sex, number of participants, intervention duration, outcomes reported in study, and supplement dosage. In addition, we extracted the mean and standard deviation (SD) of anthropometric indices at baseline and end of intervention.

### Statistical analysis

The mean change and SD for each anthropometric indices were used to estimate the overall effect size of the intervention. The mean change was calculated as (measure at the end of follow-up in the treatment group − measure at baseline in the treatment group) − (measure at the end of follow-up in the control group − measure at baseline in the control group). The SD of the mean difference for studies that were not reported was calculated by the following formula: $SD^2 = [(SD\ baseline^2 + SD\ final^2) - (2 \times R \times SD\ baseline \times SD\ final)]$ where correlation coefficient (R) was considered as 0.5.[21] To make sure that our meta-analysis is not sensitive to the selected correlation coefficient (R = 0.5), all the analyses for body indices were repeated by the use of correlation coefficient of 0.2 and 0.8. The random-effects model was used to compute the weighted mean differences (WMDs) with 95% confidence intervals (CIs) for body weight, BMI, and WC. The between-study heterogeneity was evaluated using *I*-square ($I^2$) test. To elucidate the effects of CoQ10 on anthropometric indices, we carried out a preplanned subgroup analysis based on study duration

(≤8 weeks and >8 weeks) and CoQ10 dose (>100 mg/day and ≤100 mg/day). Meta-regression analyses were carried out to examine the effects of CoQ10 dose on anthropometric indices. The proportion of each study in the overall effect was assessed by sensitivity analysis. We used Begg's rank correlation test and Egger's regression asymmetry test to evaluate the publication bias. Statistical analysis was performed using STATA 11 software (Stata Corp., College Station, TX, USA).

## Results

### Literature search

Overall, 4223 studies were identified in a combined search of electronic databases. Of the 2729 unduplicated papers, 2694 studies were eliminated after primary evaluation of inclusion criteria. After reading full text of the 35 remaining articles, 15 studies were excluded due to inappropriate data ($n$ = 3) and duplicate publication ($n$ = 5), protocol ($n$ = 1), studies with follow-up less than 4 weeks ($n$ = 1), trials on children or adolescence ($n$ = 2), and studies that administrated CoQ10 with other components ($n$ = 3). Finally, 20 records[18,19,22-39] met the eligibility criteria and were included in the systematic review and meta-analysis. The PRISMA flow diagram for the study selection process is presented in Figure 1.

### Study characteristics

A total of 976 participants (490 intervention/486 control) were included in analysis and the mean age of participants ranged from 19 to 60 years. The publication date of articles ranged from 1999 to 2018. Selected studies were conducted in Iran,[18,19,22,25,26,28,30,32-38] China,[31] Denmark,[27] Hong Kong,[23] Finland,[24] and Australia.[29,39] All included studies used parallel design. The duration of intervention ranged from 4 to 24 weeks. The included trials enrolled participants with T2DM ($n$ = 5),[19,24,26,34,39] nonalcoholic fatty liver disease ($n$ = 2),[25,35] dyslipidemia ($n$ = 1),[31] rheumatoid arthritis ($n$ = 1),[22] type 1 diabetes ($n$ = 1),[27] PCOS ($n$ = 2),[18,30] chronic kidney disease ($n$ = 1),[29] hemodialysis ($n$ = 2),[32,38] ischemic left ventricular systolic dysfunction ($n$ = 1),[23] acute myocardial infarction ($n$ = 1),[28] men with idiopathic oligoasthenoteratozoospermia ($n$ = 1),[36] diabetic nephropathy ($n$ = 1),[33] and metabolic syndrome ($n$ = 1).[37] The dose of CoQ10 ranged from 100 to 300 mg/day. Sixteen trials included both genders,[19,22-25,27-29,31-35,37,38] three trials included woman,[18,26,30] and one trial included man.[36] The characteristics of eligible studies are summarized in Table 2.

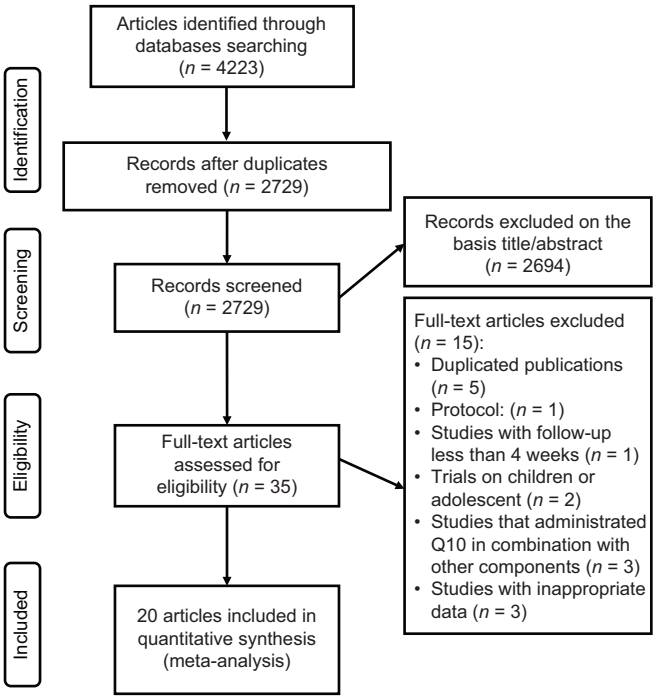


**Figure 1: PRISMA flow diagram of study selection process**

### Risk of bias assessment

Table 3 describes the risk of bias assessment based on different quality domains using Cochrane collaboration tool. From studies included in the systematic review, 11 achieved positive score in more than two main domains and were classified as high quality[18,19,22,23,28-33,37] and nine were classified as fair[24-27,34-36,38,39] because they were low risk in two key domains.

Of 20 included studies in the systematic review and meta-analysis, 13 trials used random allocation[18,19,22,23,27-29,31-34,37,38] and mentioned randomization techniques. Eleven studies had a blinded design[18,19,22,23,26,28,30-33,37] and eleven of them described methods of blinding.[18,19,22,23,26,28,30-33,37] Nineteen studies had no or few participant's withdrawal and did not describe the reason of excluded subjects.[18,19,22-25,27-39] Most of the studies showed low/unclear risk of bias based on incomplete outcome data and selective outcome reporting.

### Effects of CoQ10 supplementation on body weight

The effect of the CoQ10 supplementation on weight was examined in 15 clinical.[19,22,25-28,30-34,37] Pooled effect size indicated a nonsignificant effect of CoQ10 supplementation on body weight (WMD: −0.04 kg; 95% CI: −1.96, 1.60, $P$ = 0.959) [Figure 2]. The effect was homogeneous across the included trials ($I^2$ = 0.0%, $P$ = 1.000). Subgroup analysis based on CoQ10 dose and study duration suggested the nonsignificant effect of CoQ10 on weight [Table 4]. The meta-regression test based on the dosage of CoQ10 did not reveal any dose–response association for weight changes ($P$ = 0.466). In addition, findings from the sensitivity analysis revealed that the exclusion of Moazen (WMD: 0.01 kg; 95% CI: −1.73, 1.76) Attar (WMD: 0.11 kg; 95% CI: −1.69, 1.71), Zhang (WMD: 0.11 kg; 95% CI: −1.73, 1.75), and Izadi (WMD: 0.76 95% CI: −1.65, 1.80) studies from the analysis changed the overall effect.

**Table 2: Characteristics of eligible studies**

| First author (location; year) | RCT design (blinding) | Population | Sex | Sample size (Q10/placebo) | Duration (weeks) | Dose of Q10 (mg/day) | Outcomes |
|---|---|---|---|---|---|---|---|
| Abdollahzad (Iran; 2015) | Parallel (double) | Rheumatoid arthritis | Both | 22/23 | 8 | 100 | Weight, BMI |
| Rahmani (Iran; 2018) | Parallel (double) | Polycystic ovary syndrome | Woman | 20/20 | 12 | 100 | Weight, BMI |
| Fallah (Iran; 2018) | Parallel (double) | Hemodialysis patients | Both | 30/30 | 12 | 120 | Weight, BMI |
| Gholami (Iran; 2018) | Parallel (double) | Type 2 diabetes | Woman | 34/34 | 12 | 100 | Weight, BMI, WC |
| Attar (Iran; 2015) | Parallel (double) | Type 2 diabetes | Both | 31/33 | 12 | 200 | Weight, BMI, WC |
| Jafarvand (Iran; 2016) | Parallel (double) | Nonalcoholic fatty liver disease | Both | 20/21 | 4 | 100 | BMI, WC |
| Zhang (China; 2018) | Parallel (double) | Dyslipidemia | Both | 51/50 | 24 | 120 | WC, weight, BMI |
| Mori (Australia; 2009) | Parallel (double) | Chronic kidney disease | Both | 21/15 | 8 | 200 | Weight |
| Henriksen (Denmark; 1999) | Parallel (double) | Type 1 diabetes mellitus | Both | 17/17 | 12 | 100 | Weight |
| Moazen (Iran; 2015) | Parallel (single) | Type 2 diabetes | Both | 26/26 | 8 | 100 | Weight, BMI |
| Ericsson (Finland; 1999) | Parallel (double) | Type 2 diabetes | Both | 12/11 | 24 | 100 | BMI |
| Dai (Hong Kong; 2011) | Parallel (double) | Ischemic left ventricular systolic dysfunction | Both | 28/28 | 8 | 300 | BMI |
| Farsi (Iran; 2016) | Parallel (double) | Nonalcoholic fatty liver disease | Both | 20/21 | 12 | 100 | Weight, BMI, WC |
| Mohseni (Iran; 2015) | Parallel (double) | Acute myocardial infarction | Both | 26/26 | 12 | 200 | Weight, BMI |
| Gholnari (Iran; 2018) | Parallel (double) | Diabetic nephropathy | Both | 25/25 | 12 | 100 | Weight, BMI |
| Hodgson (Australia; 2002) | Parallel (double) | Type 2 diabetes | Both | 19/18 | 12 | 200 | Weight |
| Izadi (Iran; 2018) | Parallel (double) | Polycystic ovary syndrome | Woman | 22/21 | 8 | 200 | Weight, BMI |
| Shojaei (Iran; 2011) | Parallel (double) | Hemodialysis patients | Both | 13/13 | 12 | 100 | BMI |
| Nadjarzadeh (Iran; 2011) | Parallel (double) | Idiopathic oligoasthenoteratozoospermia | Man | 23/24 | 12 | 200 | BMI |
| Raygan (Iran; 2016) | Parallel (double) | Metabolic syndrome | Both | 30/30 | 8 | 100 | Weight, BMI |

RCT=Randomized controlled trial; BMI=Body mass index; WC=Waist circumference

### Effects of CoQ10 supplementation on BMI

The effect of the CoQ10 supplementation on BMI was examined in 17 clinical trials.[18,19,22-26,28,30-38] Overall, the meta-analysis showed that there was no significant effect of the CoQ10 supplementation on BMI (WMD: −0.06 kg/m$^2$; 95% CI: −0.54., 0.42, $P$ = 0.81) [Figure 3]. There was no evidence of heterogeneity between the effect sizes of included studies ($I^2$ = 0.0%, $P$ = 1.000). The subgroup analysis based on study duration and CoQ10 dose showed that the effect is not statistically significant in all subgroups [Table 4]. The meta-regression test based on the dosage of CoQ10 did not reveal any dose–response association for BMI changes ($P$ = 0.636). In addition, findings from the sensitivity analysis revealed that the exclusion of any single study from the analysis did not alter the overall effect.

### Effects of CoQ10 supplementation on WC

The pooled mean difference of five datasets[25,26,31,34,35] for the effects of CoQ10 on WC compared with the placebo group was (WMD: −0.79 cm; 95% CI: −2.83, 0.04, $P$ = 1.25) with no significant heterogeneity ($I^2$ = 0.0 0.873) [Figure 4]. Findings from the sensitivity analysis revealed that the exclusion of any single study from the analysis did not alter the overall effect.

### Publication bias

There was no evidence of publication bias for studies examining the effect of CoQ10 on weight ($P$ = 0.96, Begg's

**Table 3: Risk of bias assessment for included randomized controlled clinical trails**

| First author (publication year) | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting |
|---|---|---|---|---|---|---|
| Abdollahzad (2015) | + | + | + | + | + | ? |
| Rahmani (2018) | + | ? | + | ? | + | ? |
| Fallah (2018) | + | + | + | - | + | ? |
| Gholami (2018) | ? | ? | + | + | - | ? |
| Attar (2015) | + | ? | - | - | + | ? |
| Zhang (2018) | + | + | + | + | + | ? |
| Mori (2009) | + | + | - | - | + | ? |
| Henriksen (1999) | ? | + | - | - | + | ? |
| Moazen (2015) | + | + | + | - | + | ? |
| Ericsson (1999) | ? | ? | - | - | + | ? |
| Dai (2011) | + | + | + | + | + | ? |
| Farsi (2016) | ? | ? | - | - | + | ? |
| Mohseni (2015) | + | + | + | + | + | ? |
| Jafarvand (2016) | ? | ? | - | - | + | ? |
| Gholnari (2018) | + | + | + | - | + | ? |
| Hodgson (2002) | ? | ? | - | - | + | ? |
| Izadi (2018) | + | + | + | - | + | ? |
| Shojaei (2011) | + | ? | - | - | + | ? |
| Nadjarzadeh (2011) | ? | ? | - | - | + | ? |
| Raygan (2016) | + | + | + | - | + | ? |

**Table 4: Subgroup analysis to assess the effect of CoQ10 supplementation on anthropometric indices**

| Subgrouped by | No. of trials | Effect size[1] | 95% CI | $I^2$ (%) | *P* for heterogeneity |
|---|---|---|---|---|---|
| Weight | | | | | |
| Dose | | | | | |
| Under 100 mg/day | 8 | 0.64 | −1.83, 3.11 | 0.0 | 1.000 |
| Over 100 mg/day | 7 | −0.59 | −2.81, 1.62 | 0.0 | 1.000 |
| Duration | | | | | |
| Under 8 weeks | 4 | −0.04 | −1.69, 1.60 | 0.0 | 1.000 |
| Over 8 weeks | 11 | 0.1 | −1.75, 1.96 | 0.0 | 1.000 |
| BMI | | | | | |
| Dose | | | | | |
| Under 100 mg/day | 10 | 0.09 | −0.69, 0.87 | 0.0 | 1.000 |
| Over 100 mg/day | 7 | −0.15 | −0.76, 0.46 | 0.0 | 1.000 |
| Duration | | | | | |
| Under 8 weeks | 5 | −0.06 | −1.11, 0.99 | 0.0 | 1.000 |
| Over 8 weeks | 12 | −0.06 | −0.60, 0.48 | 0.0 | 1.000 |

[1]Calculated by Random-effects model. CI=Confidence interval; BMI=Body mass index

test and $P = 0.97$, Egger's test), BMI ($P = 0.36$, Begg's test and $P = 0.26$, Egger's test), and WC ($P = 0.99$, Begg's test and $P = 0.07$, Egger's test).

## Discussion

Obesity and overweight are one of the major health problems worldwide.[1] Genetic background and environmental factors, that is, excessive energy intake and inactivity, are the main causes of obesity and overweight.[40] The management of this condition is challenging. Nevertheless, common strategies for reducing and managing body weight such as restriction on energy intake and increase in energy expenditure by exercise and other ways have limited success over a long time period.[7] Therefore, antiobesity supplements are very popular among this population. Although there is a lack of conclusive information in their efficacy and possible side effects of these supplements. This issue made it one of the important problems faced by dictations. In this case, a comprehensive systematic review and meta-analysis of available clinical trials can represent the most reliable evidence of CoQ10 supplementation efficacy.

To the best of our knowledge, the current systematic review and meta-analysis examined the efficacy of CoQ10 supplementation on anthropometric indices including body weight, BMI, and WC for the first time. Our meta-analysis

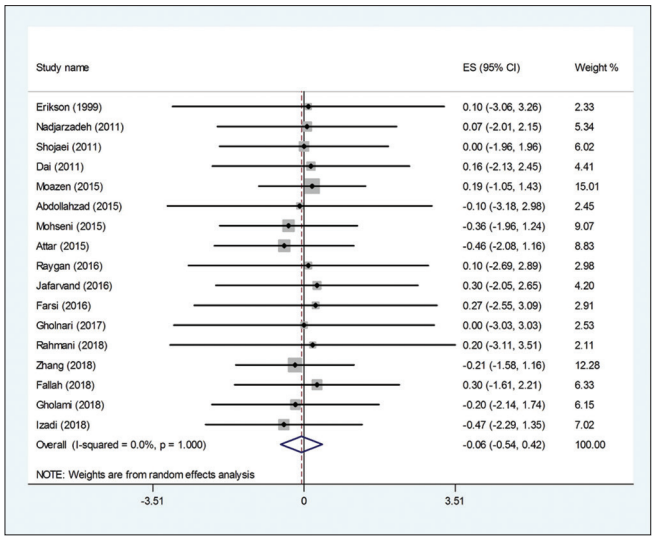


**Figure 2: Forest plot of the effect of Q10 supplementation on weight**

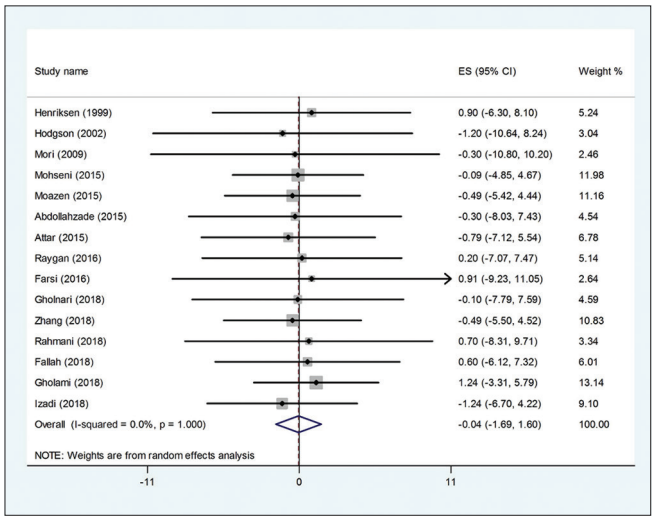


**Figure 3: Forest plot of the effect of Q10 supplementation on BMI**

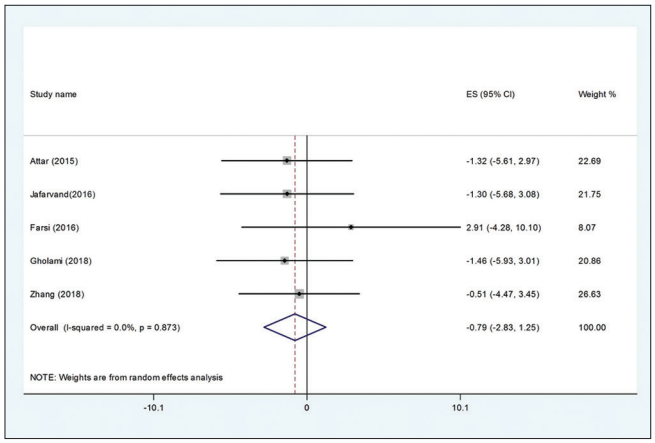


**Figure 4: Forest plot of the effect of Q10 supplementation on WC**

results showed that CoQ10 intake is not associated with significant changes in body weight, BMI, and WC. Also, the subgroup analysis based on dose and duration of CoQ10 supplementation had no significant effect on our meta-analysis results.

Recent meta-analyses suggest some beneficial health for CoQ10 supplementation such as reducing the plasma Lp(a) concentrations,[14] partly improving the process of inflammatory state,[41,42] reducing serum triglycerides levels, and helping improve the lipid profiles in patients with metabolic disorders.[43]

Although the exact mechanisms were not clarified yet, the following probable pathways may explain the influence effect of CoQ10 supplementation on body weight: (1) improving cellular bioenergetics because of the roles of CoQ10 in cellular energy processes;[44] (2) inhibition of CoQ10 synthesis strongly triggers adipocyte differentiation while increment of CoQ10 acts in inverse direction;[45] (3) CoQ10 treatment increases fat oxidation and energy consumption in adipose tissue;[46] and (4) CoQ10 inhibits adipogenesis through AMP-activated protein kinase (AMPK). AMPK is an important modulator of energy metabolism that could diminish the expression of important genes involved in adipogenesis such as peroxisome proliferator-activated receptor (PPAR)γ, CCAAT/enhancer binding protein (C/EBP)α, and fatty-acid-binding protein (FABP)[47-50]

The results showed that CoQ10 supplementation partly decreases the body weight, although these results were not significant. Also, the subgroup analysis based on the dose and duration of CoQ10 supplementation showed a small size and nonsignificant of loss weight. It should be considered that the characteristics of participants have important role in effectiveness of CoQ10. The overall results of this meta-analysis about BMI were not significant. Also, the subgroup analysis could not show any significant effects. It is to be considered that change in BMI is more complex than body weight and other anthropometric indices. Because BMI is depended on height which is fixed in participants. The results showed that CoQ10 supplementation had a nonsignificant effect on WC; the finding should be interpreted with caution because only five studies assessed the WC after CoQ10 supplementation.

Most included studies reported that CoQ10 was well-tolerated and had no adverse side effects. However, some clinical trials with CoQ10 administration found CoQ10 treatment to possibly produce nausea and heartburn. Evidence from well-designed randomized controlled human clinical trials indicates that the upper level for supplements for CoQ10 is 1200 mg/day.[51]

This is the first systematic review and meta-analysis of randomized controlled trials (RCTs) investigating the effect of CoQ10 supplementation on body weight, BMI, and WC. But there are some limitations that must be noted. First, the included trials were performed in subjects with different

health condition. So it was so hard find a conclusive result from these trials. Second, usual dietary intakes were not monitored in terms of meat and dairy products in included RCTs which might have an important effect on the results. Third, the results of most of the studies were not adjusted for confounding factors which can affect the weight reduction. There are several evidence regarding the association between anthropometric indices and physical activity,[52] diet,[53] and smoking.[54] Fourth, most of the trials included in this study assessed anthropometric indices as secondary outcomes and there were not much specific trial that designed for evaluation of the effect of CoQ10 on anthropometric indices. This can reduce the accuracy and paresis of data. As the last limitation for our meta-analysis, all trials that were included in the meta-analysis have ignored the measurement of the baseline levels of CoQ10 in participants. It is very important in the interpretation of the effect of CoQ10 on anthropometric indices. The nonsignificant effects of CoQ10 could be related to low level of CoQ10 in participants.

## Conclusions

In conclusion, the results of this study suggest that CoQ10 supplementation has no significant beneficial effects on anthropometric indices in adults. However, well-designed clinical trials, particularly in patients with obesity and overweight, are warranted to ultimately assess the effectiveness of this supplementation.

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### Conflicts of interest

There are no conflicts of interest.

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