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# Effect of programmed exercise on perceived stress in middle-aged and old women: A meta-analysis of randomized trials



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#### ABSTRACT

*Objective*: To clarify the effect of programmed exercise (PE), performed for at least six weeks, on perceived stress (PS) in middle aged and old women.

Methods: A structured search was carried out in PubMed, Embase, Cochrane Library, Scielo, Web of Science and Scopus, from database inception through January 10, 2018, without language restriction. The US, UK, and Australian clinical trials databases were also searched. The search included a combination of the terms "programmed exercise", "perceived stress", "menopausal women" and "randomized controlled trial" (RCTs). PE was classified according to duration as "mid-term exercise intervention" (MTEI; mean duration 6 months), and "long-term exercise intervention" (LTEI; mean duration 12 months). Mean  $\pm$  standard deviations of changes in PS scores, as assessed with different questionnaires, were calculated as standardized mean differences (SMDs) and used as effect size for meta-analysis. SMDs of PS after intervention were pooled using a random-effects model. Study quality and bias risk were assessed with the Cochrane tool.

Results: Five RCTs that studied midlife and older women (mean age  $47.0 \pm 1.7$  years minimum to  $71.8 \pm 5.6$  maximum) were included in the meta-analysis. There was no significant effect of PE on PS score (SMD: -0.16; 95% CI: -0.43 to 0.11). In subgroup analyses, there was no significant effect of PE on PS with mid-term interventions (SMD: -0.17; 95% CI: -0.59 to 0.25) nor with long-term interventions (SMD: -0.02; 95% CI: -0.42 to 0.38) as compared with controls.

Conclusion: PE of low to moderate intensity does not improve PS in midlife and older women.

# 1. Introduction

Perceived stress (PS) is a defensive reaction against threatening environmental conditions, which is associated with activation of the sympathetic nervous system and other body systems responses. This status cannot be maintained for long periods, as the parasympathetic system restores equilibrium [1,2]. PS is experienced as a negative sensation and is associated with adverse health consequences, including increased cardiovascular risks, hypertension, cancer, social adversity, metabolic syndrome risk and insomnia [3–9].

Women experience higher PS levels than men, even after adjustment for demographic and psychosocial factors [10]. PS is highly prevalent among middle-aged and old women [11]. Lower education and financial difficulties are predictors [12]. Higher PS levels correlate negatively with female age, and positively with lower psychological and

uro-gynecological quality of life, insomnia and a partner's premature ejaculation [11]. Cumulative stress in women is associated with race/ethnicity, divorced or separated marital status, obesity, diabetes, smoking, depressive symptoms and anxiety [4].

Stress management is essential to prevent stress-related diseases. Different approaches have been recommended, including psychological techniques, relaxation, behavioral therapy and aerobic exercise. It is important to apply a specific physiological technique and not only a psychological approach. Physical activity and programmed exercise (PE) have been widely recommended to reduce PS, although some researchers have found that they have no effect [13,14]. Since there are controversial results concerning the effect of PE on PS in post-menopausal women [15,16], in the present study we aimed to systematically review randomized control trials (RCTs) investigating the effects of PE on PS in middle-aged and old women.

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#### 2. Methods

This systematic review followed the guidelines on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [17]. Formal institutional review board approval was not required, because this analysis consisted of pooling published studies.

#### 2.1. Systematic search strategy

The search included, but was not limited to, the following terms: "perceived stress", "programmed exercise", "menopausal women", and "randomized controlled trial". We searched PubMed-Medline, Embase, Cochrane Library, Scielo, Web of Science and Scopus, from database inception through January 10, 2018, without language restriction. We also conducted a manual search of systematic reviews and reports of RCTs to identify additional trials. In addition, the US Clinical Trials [18], the UK Clinical Trials Gateway [19] and the Australian clinical trials [20] databases were searched for related RCTs.

#### 2.2. Inclusion and exclusion criteria

Articles reviewed were restricted to original RCTs published in any language that involved: (i) women living independently and aged > 40 years without severe disease (cancer, heart disease), cognitive limitations, significant neuromuscular or skeletal diseases, or caring for other persons; (ii) PE for at least six weeks; (iii) an assessment of PS by validated questionnaires or similar tools that included a subscale for the quantitative evaluation of PS; (iv) control groups, defined as women who did not participate in PE.

Publications were excluded for the following reasons: (i) non-RCTs; (ii) lack of PE for at least 6 weeks; (iii) lack of PS assessment with a validated instrument; (iv) lack of a control group; (v) sample size < 20 women.

# 2.3. Outcomes

The primary outcome of interest was PS as assessed before and after PE with specific questionnaires, or tools with a subscale or subdomain for PS. Planned secondary outcomes of interest were hot flashes and other menopausal symptoms, quality of life, social support, self-efficacy, insomnia, muscle strength, body weight and body mass index (BMI).

#### 2.3.1. The Cohen Perceived Stress Scale (PSS)

The original Cohen Perceived Stress Scale (PSS) is a 14-item tool to measure non-specific stress that correlates with objective biologic markers of chronic stress [12,21]. Scores are calculated by reversing seven positive items that are summed along with another seven negative items for a final score. For the 10-item PSS (PSS-10), four positive items are reversed and then all items are summed.

#### 2.3.2. The Depression, Anxiety and Stress Scale (DASS)

The 42-item Depression, Anxiety and Stress Scale (DASS-42) are a screening tool to evaluate depressive, anxiety and stress symptoms in the general population [22]. The DASS-21 includes 21 items divided into three subscales: depression, anxiety and stress [23,24]. The stress subscale assesses nervous tension, difficulty relaxing, irritability and negative affect. The DASS-21 has a better factor structure than the DASS-42 [25].

# 2.4. Study selection and data extraction

After removing duplicates, papers were screened for eligibility by their title and abstract. Two authors independently screened the list of retrieved articles to choose potentially relevant papers, and then extracted relevant data (baseline characteristics and outcome variables) from each full-text included article to a previously designed (Microsoft Office Excel) data sheet. Disparities found within the extracted data were discussed by all the authors to reach a consensus.

Menopausal status was categorized as pre-, peri- and post-menopausal in accordance to the Stages of Reproductive Aging Workshop (STRAW + 10) criteria [26].

#### 2.5. Risk-of-bias assessment

The methodological quality of the selected RCTs was independently assessed by two authors (SJM-D, MPN) using the Cochrane Risk of Bias Tool [27,28]. This instrument evaluates seven aspects: "random sequence generation" (selection bias); "allocation concealment" (selection bias); "blinding of participants and research staff" (performance bias); "blinding of outcome assessment" (detection bias); "incomplete outcome data" (attrition bias); "selective reporting" (reporting bias); and "any other biases". Every assessed item was described for each RCT as having a "low", "high" or "unclear" risk of bias. RCTs presenting bias for "randomization" or "blinding" were considered as having an overall high risk of bias.

#### 2.6. Data synthesis and statistical analysis

Effect sizes with 95% confidence interval (CI) were calculated using Hedges' method. Standardized mean differences (SMDs) and 95% confidence intervals (95% CIs) for PS scores were calculated for each study by the baseline and follow-up PS scores for cases and controls. Individual SMDs were pooled using a random-effects model. The magnitude of SMDs was considered "small" (0.20), "moderate" (0.50) or "large" (0.80) [29].

We evaluated statistical heterogeneity using the Cochrane chisquare ( $X^2$ ), the  $I^2$  statistic, and the between-study variance using the tau-square ( $Tau^2$ ) [27,29].  $I^2$  values of 0–30% represented a low level of heterogeneity. A p-value < 0.1 for the chi-square defined the presence of heterogeneity; and a tau $^2 > 1$  defined the presence of substantial statistical heterogeneity. Depending on availability of data, subgroup analyses were planned according to the type of exercise and/or the duration of exposure.

For statistical analyses, we used the Review Manager software (RevMan 5.3; Cochrane Collaboration, Oxford, UK) [30].

# 3. Results

### 3.1. Eligible studies

A total of 1074 records with stress-related physiological parameters were initially retrieved. After removing duplicates, 859 abstracts were evaluated. Of these, 108 abstracts fulfilled the inclusion criteria and remained for full-text assessment. One hundred and two papers were excluded for various reasons (Fig. 1). Therefore, six articles reporting information from five RCTs were qualitative and quantitatively assessed for the current systematic review and meta-analysis [31–36]. There were no RCTs in the US, UK and Australian clinical trials registries concerning the effect of PS on peri- or post-menopausal women.

# 3.2. Characteristics of the included trials

The sample characteristics of women included in this systematic review and meta-analysis are outlined in Tables 1 and 2. Age ranged from  $47.0 \pm 1.7$  years [32,34] to  $71.8 \pm 5.6$  years [36]. One RCT studying pre-menopausal women reported outcomes in two publications [32,34] and the remaining four RCTs reported results for post-menopausal women [31,33,35,36].

The sample included young healthy women [32,34], overweight or obese early post-menopausal women (< 60 years) without co-morbidities [31,33], women in their sixth decade of life with chronic illness

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