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# Relação dose-resposta do treinamento resistido de membros inferiores para o tratamento de mulheres com dor patelofemoral: uma revisão sistemática e meta-regressão

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Dissertação submetida ao Programa de Pós-Graduação em Ciências da Reabilitação da Universidade Federal de Ciências da Saúde de Porto Alegre como requisito para a obtenção do grau de Mestre.

Orientador: Prof. Dr. Bruno Manfredini Baroni

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**Relação dose-resposta do treinamento resistido de membros inferiores para o tratamento de mulheres com dor patelofemoral: uma revisão sistemática e meta-regressão**

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## RESUMO

A dor patelofemoral (DPF) é uma condição clínica muito prevalente, especialmente em mulheres entre 18-40 anos. É caracterizada por dor na região da patela, principalmente durante atividades diárias como caminhar, agachar, subir e descer degraus, ajoelhar-se. O treinamento de resistência de membros inferiores é uma das principais ferramentas no tratamento da DPF, no entanto, o volume de treinamento (ou seja, a quantidade de exercício) ideal e/ou necessário para que se atinjam os benefícios clínicos permanece sem resposta na literatura. Objetivo: Examinar o efeito dose-resposta do volume de treinamento resistido de membros inferiores em mulheres com DPF. Métodos: Revisão sistemática com meta-regressão. Foram incluídos ensaios clínicos randomizados que utilizaram programas de treinamento resistido para membro inferiores em mulheres com diagnóstico de DPF. Os bancos de dados PEDro, PubMed, SPORTDiscus e Web of Science foram pesquisados desde o início até abril de 2022. Uma meta-análise avaliou o efeito do treinamento de resistência na dor (escala visual analógica ou escala numérica de dor) e função autorreferida (Anterior Knee Escala de Dor). As análises de meta-regressão univariável avaliaram a associação do efeito da diferença média após o treinamento de resistência com a idade dos pacientes, dor e função basal e nove variáveis relacionadas ao volume do treinamento de resistência. Resultados: Doze estudos (423 pacientes) foram incluídos. As intervenções resultaram em uma redução de 3,4 pontos (IC 95%: -3,9 a -2,8) na dor e um aumento de 12,5 pontos (IC 95%: 9,5 a 15,6) na função. Conclusão: O treinamento resistido de membros inferiores resulta em melhorias significativas na dor e na função autorreferida em mulheres com DPF. Programas com 2-3 sessões semanais foram associados a maiores reduções na dor. Programas com maior número de séries foram associados a maiores melhorias na função, com as melhores respostas com 17 a 27 séries por sessão três vezes por semana.



Palavras-chave: dor patelofemoral; dor anterior do joelho; terapia por exercícios; reabilitação, dose-resposta.

## ABSTRACT

Patellofemoral pain (PFP) is a very prevalent clinical condition, especially in women aged 18-40 years. It is characterized by pain in the patella region, mainly during daily activities such as walking, squatting, going up and down steps, kneeling. Lower limb resistance training is one of the main tools in the treatment of PFP, however, the ideal and/or necessary training volume (i.e., the amount of exercise) to achieve clinical benefits remains unanswered in the literature. Objective: To examine the dose-response effect of lower limb resistance training volume in women with PFP. Methods: Systematic review with meta-regression. Randomized clinical trials that used resistance training programs for the lower limbs in women diagnosed with PFP were included. The PEDro, PubMed, SPORTDiscus, and Web of Science databases were searched from baseline through April 2022. A meta-analysis evaluated the effect of resistance training on pain (visual analogue scale or numerical pain scale) and self-reported function ( Previous Knee Pain Scale). Univariate meta-regression analyzes assessed the association of the mean difference effect after resistance training with patients' age, pain and baseline function, and nine variables related to resistance training volume.Results: Twelve studies (423 patients) were included. The interventions resulted in a 3.4 point reduction (95% CI: -3.9 to -2.8) in pain and a 12.5 point increase (95% CI: 9.5 to 15.6) in pain. occupation. Conclusion: Lower limb resistance training results in significant improvements in pain and self-reported function in women with PFP. Programs with 2-3 sessions per week were associated with greater reductions in pain. Programs with the highest number of sets were associated with greater improvements in function, with the best responses with 17 to 27 sets per session three times a week.

Keywords: patellofemoral pain; anterior knee pain; exercise therapy; rehabilitation, dose-response.

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## LISTA DE ABREVIATURAS E SIGLAS

| | |
|---|---|
| APTA | American Physical Therapy Association |
| AKPS | Anterior Knee Pain Scale |
| DPF | Dor patelofemoral |
| NPS | Numerical Pain Scale |
| PEDro | Physiotherapy Evidence Database |
| PFP | Patellofemoral pain |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| SD | Standard Deviation |
| VAS | Visual Analogue Scale |

## SUMÁRIO

## 1. CONTEXTUALIZAÇÃO

A dor patelofemoral (DPF) é uma condição comum no joelho, que afeta principalmente adolescentes e adultos jovens, onde as mulheres têm uma incidência 2.2 vezes maior que homens (BOLING et al., 2010; RA et al., 2015). DPF é caracterizada por dor retro patelar (atrás da patela) ou peri-patelar (ao redor da patela). A dor ocorre principalmente quando a carga é exercida sobre os músculos que realizam extensão dos joelhos ao subir escadas, agachar-se, correr, andar de bicicleta ou ficar sentado com os joelhos flexionados (DAVIS IS, 2019; LANKHORST; BIERMA-ZEINSTRA; VAN MIDDELKOOP, 2013), muitas vezes dificultando ou impedindo a realização dessas atividades.

Diversos fatores foram relacionados à etiologia da DPF. Entre eles, fatores locais (contribuição da articulação patelofemoral), mecânica e tecidos adjacentes à dor, fatores distais (contribuição da mecânica do pé e tornozelo) e fatores proximais (contribuição da mecânica do quadril, pelve e tronco) (DAVIS IS, 2019). Contudo, a etiologia desta condição ainda não está clara. Dentre esses fatores, os déficits de força nas musculaturas extensora de joelho e abdutora e rotadora externa de quadril têm se mostrado fortemente associados à DPF, o que os torna alvo constante dos programas de reabilitação em pacientes com DPF (LANKHORST; BIERMA-ZEINSTRA; VAN MIDDELKOOP, 2013).

O diagnóstico da DPF é essencialmente clínico, associando os sintomas apresentados e excluindo outras patologias do joelho que causam dor na mesma localização (WILLY et al., 2019), como síndrome de Hoffa, síndrome de Osgood Schlatter, síndrome de atrito da banda iliotibial, tendinites, neuromas, lesões traumáticas, e patologias mais raras. Por isso a importância da observação dos sintomas associados a testes que mimetizam as funções diárias, como o agachamento.

Nessa população, a principal forma de conduzir o tratamento é conservadora (ou seja, sem a necessidade de uma intervenção cirúrgica). As intervenções conservadoras incluem órteses de joelho, órteses de pé (HOSSAIN et al., 2011), taping patelar (CALLAGHAN MJ, 2012) e terapia por exercício (WILLY et al., 2019). A terapia por exercícios compreende uma ampla gama de possibilidades. O último Guia de Prática Clínica demonstrou que os programas de terapia por exercício que se concentram em exercícios de força para membros inferiores, priorizando fortalecimento dos músculos quadríceps e póstero laterais do quadril, que apresentam um corpo de evidências mais extenso, de modo que esta abordagem é altamente recomendada para os programas de tratamento da DPF (WILLY et al., 2019). Estudos sugerem que indivíduos sintomáticos para DPF realizam atividades de sustentação de peso com uma flexão mínima do quadril, inclinando o tronco à frente (POWERS, 2010), levando a maiores demandas no músculo quadríceps e, consequentemente, maiores tensões articulares femoropatelares. Outras avaliações demonstraram aumento da adução de quadril (NAKAGAWA et al., 2012; WILLSON; DAVIS, 2008, 2009) e rotação interna (NAKAGAWA et al., 2012; SOUZA et al., 2010) durante tarefas funcionais. Esses movimentos têm sido relacionados à fraqueza dos músculos abdutores, rotadores externos e extensores de quadril (BALDON et al., 2011; DIERKS et al., 2008; SOUZA; POWERS, 2009), e acredita-se que essas alterações levam a um maior ângulo do valgo do joelho e, consequentemente, a uma maior pressão lateral na articulação femoropatelar. Além dos fatores relacionados a biomecânica, outros aspectos parecem ter influência na resposta dessa população ao tratamento. A relação com medo, evitação, hipervigilância e outros aspectos psicossociais ainda foi muito pouco explorada, como alertado no estudo de Piva e colaboradores (PIVA et al., 2009b) que ressaltaram a falta de estudos e validação de escalas para essa população e mais recentemente abordado no estudo de Crossley e colaboradores (CROSSLEY et al., 2019), onde reiteram a provável influência desses aspectos na resposta ao tratamento a importância de abordá-los, encorajando clínicos a incluírem questionários ainda que não específicos para avaliar características psicossociais.

Diversos estudos (BOLGLA et al., 2016; DE MARCHE BALDON et al., 2014; DOLAK et al., 2011; HERRINGTON; AL-SHERHI, 2007; KHAYAMBASHI et al., 2014; NAKAGAWA et al., 2008; ØSTERÅS et al., 2013; RABELO et al., 2017; SONG et al., 2009; VAN LINSCHOTEN et al., 2009) utilizaram o exercício de força para membros inferiores como intervenção em programas de reabilitação para pacientes com DPF, tendo como desfecho esperado a redução da dor e/ou melhora da funcionalidade. Analisando brevemente as evidências, pode-se concluir que há uma grande variabilidade entre os programas de treinamento, seja na sua duração em semanas, no número de séries e repetições, e no tipo de exercício realizado pelos pacientes. Considerando que estudos envolvendo treinamento resistido em indivíduos saudáveis demonstram haver uma relação entre o volume de treinamento e os ganhos de força e massa muscular (RALSTON GW et al., 2017; SCHOENFELD BJ, OGBORN D, KRIEGER JW, 2017), é razoável hipotetizar a existência de uma relação dose-resposta também na reabilitação de indivíduos com DPF.

Entretanto, apesar da extensa literatura demonstrando que o exercício é atualmente o melhor tratamento para pacientes com DPF, não temos conhecimento se há um volume de treinamento capaz de gerar maiores benefícios nessa população. O conhecimento acerca do volume de treinamento ideal e/ou necessária para gerar os benefícios da intervenção é fundamental para que os fisioterapeutas possam guiar seus programas de tratamento, prescrevendo a quantidade de exercícios de fortalecimento muscular mais adequada a seus pacientes. Portanto, se faz necessária uma investigação acerca do efeito dose-resposta do treinamento resistido nessa população.

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# 2. OBJETIVOS

## Objetivo Geral:

Investigar a relação dose-resposta do treinamento resistido de membros inferiores sobre o nível de dor de mulheres com dor patelofemoral.

## Objetivos específicos:

Investigar o efeito da idade sobre as respostas de dor em mulheres com dor patelofemoral submetidas a programas de treinamento resistido de membros inferiores;

Investigar o efeito do nível basal de dor sobre as respostas de dor em mulheres com dor patelofemoral submetidas a programas de treinamento resistido de membros inferiores;

Investigar o efeito do número de semanas e número total de sessões da intervenção sobre as respostas de dor em mulheres com dor patelofemoral submetidas a programas de treinamento resistido de membros inferiores;

Investigar o efeito da frequência semanal da intervenção sobre as respostas de dor em mulheres com dor patelofemoral submetidas a programas de treinamento resistido de membros inferiores;

Investigar o efeito do volume de séries utilizadas na intervenção sobre as respostas de dor em mulheres com dor patelofemoral submetidas a programas de treinamento resistido de membros inferiores;

Investigar o efeito do volume de repetições utilizadas na intervenção sobre as respostas de dor em mulheres com dor patelofemoral submetidas a programas de treinamento resistido de membros inferiores.

## 3 ARTIGO

Dose-response relationship of lower limb resistance training for treating woman with patellofemoral pain: a systematic review and meta-regression

(Formatado conforme normas do periódico Brazilian Journal of Physical Therapy – *Qualis A2, Fator de Impacto 4.762*)

**Dose-response effect of lower limb resistance training on pain and function of women with patellofemoral pain: A systematic review and meta-regression**

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# Dose-response effect of lower limb resistance training on pain and function of women with patellofemoral pain: A systematic review and meta-regression


## ABSTRACT

**Background:** Lower limb resistance training is a key component in the management of patellofemoral pain (PFP).

**Objective:** To examine the dose-response effect of lower limb resistance training volume in women with PFP.

**Methods:** PEDro, PubMed, SPORTDiscus, and Web of Science databases were searched from inception to April 2022. A meta-analysis assessed the effect of resistance training on pain (visual analogue scale or a numerical pain scale) and self reported function (Anterior Knee Pain Scale). Univariable meta-regression analyses assessed the association of the mean difference effect following resistance training with patients' age, baseline pain and function, and nine resistance training volume-related variables.

**Results:** Twelve studies (423 patients) were included. Interventions resulted in a reduction of 3.4 points (95% CI: -3.9 to -2.8) in pain and an increase of 12.5 points (95% CI: 9.5 to 15.6) in function. Changes in knee pain were associated with baseline pain ($\beta$= -1.0 ± 0.3, $P<0.001$) and weekly training frequency ($\beta$= 0.6 ± 0.2, $P$= 0.003). Changes in function were associated with total number of sets performed over the intervention ($\beta$= 0.1 ± 0.03, $P$= 0.033) and number of sets per session ($\beta$= 0.6 ± 0.3, $P$= 0.019).

**Conclusion:** Lower limb resistance training results in meaningful improvements in pain and self-reported function in women with PFP. Programs with 2-3 weekly sessions were associated with greater reductions in pain. Programs comprising a higher number of sets were associated with greater improvements in function, with the best responses with 17 to 27 sets per session thrice a week.


**Key Words:** Exercise therapy, strength training, knee, anterior knee pain, female.

## INTRODUCTION

Patellofemoral pain (PFP) is one of the main painful conditions affecting the knee of young adults, with the female population being twice as affected.1 PFP is characterized by pain around or behind the patella, which is aggravated by one or more activities that load the patellofemoral joint during weight bearing on a flexed knee (e.g., squatting, stair ambulation, jogging/running, hopping/jumping).[2] This often reduces the ability of those with PFP to perform sporting, physical activity and work- related activities pain-free, which can have a substantial impact on quality of life and burden of living with PFP such as loss of physical function, loss of self-identity, pain-related confusion and fear, and concern for the future.[2,3]

The most recent guideline from the American Physical Therapy Association (APTA)[3] recommends that exercise therapy for treating patients with PFP should include a combination of hip- and knee-targeted resistance exercises to reduce pain and improve patient-reported outcomes and functional performance. The APTA guideline also recommends that hip-targeted exercise therapy should focus on the posterolateral hip musculature (i.e., hip abductors and external rotators), while knee-targeted exercise therapy should focus quadriceps muscle including either weight- bearing (e.g., squats) or non-weight-bearing exercises (e.g., resisted knee extension).[3] However, there is a paucity of specific information on the amount of resistance exercise necessary for achieving better outcomes in this population. Although lower limb resistance training is currently considered a key component in the PFP management, further information on exercise prescription variables would be critical for improving the therapeutic benefit.

Resistance training volume (or dosage) is the product of the total number of exercises, sets and repetitions.[4] Although this is a critical factor for successfully improving health-related outcomes such as muscle size[5] and strength[6] in the general population, the role of resistance training volume is still unclear in patients with PFP. In a previous systematic review comprising 17 trials, Young et al.[7] did not observe a clear relationship of the duration of the program, frequency or number of sessions with improvements in pain and function in this population. However, the superiority of programs with a combination of hip- and knee-targeted exercises over programs with knee-targeted exercise has only been derived from studies prescribing a greater resistance training volume for patients treated with hip- and knee-targeted exercises.[8] In addition, Østerås et al.[9] indicated greater improvements in pain and function following a high volume of combined resistance and aerobic training compared to a low volume in patients with PFP, while Almeida et al.[10] did not observe differences between adding anteromedial or posterolateral hip musculature exercises to knee-targeted exercises when equalizing the resistance training volume. As a result, a more comprehensive assessment of the literature is necessary to clarify the dose-response effect of resistance training in PFP.

The aim of the present study was to systematically review and analyze whether the effects of lower limb resistance training on pain and self-reported function are influenced by the dose of resistance exercise prescribed (i.e., number of weeks, frequency, number of sessions, sets and repetitions) in women with PFP. Identifying a minimum or an optimal resistance training volume may help increase the efficacy of interventions and establish more precise recommendations for clinicians managing this population.

## METHODS

### Search strategy and study selection procedure

This systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO, XXX) and presented in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[11]

In this review, we included clinical trials examining the effects of lower limb resistance training in women with PFP. The primary outcome was pain assessed by a visual analogue scale (VAS) or a numerical pain scale (NPS), while self-reported function assessed by the Anterior Knee Pain Scale (AKPS) questionnaire was the secondary outcome. The exclusion criteria were: (1) studies involving males or mixed male and female samples not reporting specific information for female participants; (2) studies involving women over 45 years old; (3) studies not presenting information on resistance training programs such as exercise selection, number of sets and repetitions, and weekly frequency undertaken; and (4) studies published in a language other than English.

The date of the systematic search was April 15th, 2022, with no limitation for publication date. The search was conducted in the Physiotherapy Evidence Database (PEDro), PubMed, SportDiscus and Web of Science databases. The search strategy is presented in the **TABLE 1 (Supplementary File).** In addition, a manual search was undertaken in the references list provided in the selected studies. The Rayyan platform was used to remove duplicates and organize the studies assessed.[12] Eligibility was assessed independently and evaluated in duplicate (N.T.O and L.S.S.). Disagreements between reviewers were resolved by consensus.

## Data extraction

Data extraction was performed via a standardized form. Information such as mean age and conditioning status of participants (i.e., sedentary or physically active), number of weeks, number of sessions, weekly frequency, exercise selection, number of sets and repetitions performed from interventions were collected. Mean and standard deviation values at baseline and at the end of the resistance exercise program were extracted for pain and self-reported function outcomes. When a study did not present the information required for the present review, the authors were contacted. In studies comprising multiple lower limb resistance training groups, all groups were included for analyses.

## Quantification of resistance training volume

The volume of lower limb resistance training was quantified for single- or multi-joint exercises involving one or more muscle groups of the lower limbs and performed against an external load (e.g., free weights, weight machines, elastic bands, therapist manual resistance) or exercises using the patient's body weight. Only dynamic resistance exercises were quantified. For the resistance exercise volume, number of weeks (i.e., duration of the program), number of sessions (i.e., total number of exercise sessions scheduled), frequency (i.e., number of sessions per week), number of sets (i.e., total number of sets, average sets per week, and average sets per training session), and number of repetitions (i.e., total number of repetitions, average repetitions per week, and average repetitions per exercise session) were extracted and calculated for each training group included. Exercises with the maintenance of body position for a period (e.g., front/side planks, single leg balance) were not quantified, as well as cycling, running, walking, calisthenics or any kind of stretching-or balance-focused exercise. When necessary, authors were contacted for clarification about the exercises performed.

### Primary and secondary outcomes

Knee pain was assessed by studies using VAS (0-10 cm) or NPS (0-10 score) before and after the intervention period. Within the studies included, researchers had asked for patients inform their pain level in the week or fortnight prior to the assessment day, as well as the pain level while performing functional tasks at the time of the assessment. When a study assessed pain using both methods, the pain in the week/fortnight prior to the assessment was used for analysis. For the self-reported function outcome, studies using the AKPS before and after the intervention period were included. The AKPS is a patient-reported outcome measure (PROM) widely used in studies involving people with PFP. This questionnaire comprises 13 questions on symptoms and difficulty of performing common daily activities such as walking, running, squatting and climbing stairs. The score ranges from 0 to 100 points, with a score of 100 indicating no pain and/or functional limitations, and 0 indicating constant pain and severe functional limitations.[13] The mean and standard deviation (SD) of the values obtained in these outcomes were extracted for analyses.

### Risk of bias

The risk of bias was evaluated using the PEDro Scale, which is a reliable[14] and valid tool to measure the methodological quality of clinical trials.[14-16] Studies with a score greater than 6 were classified as having a lower risk of bias, while scores equal or less than 6 were classified as having a high risk of bias.[17]

**Statistical analysis**

For the meta-analysis, the pooled effect estimates from pain and function were obtained and expressed as mean difference and 95% confidence interval of baseline to the final assessment of the intervention group. A meta-analysis was conducted for all studies, and a subgroup analysis was provided based on physical activity conditioning status (i.e., sedentary vs. physically active). Calculations were performed using a random-effects model with the DerSimonian & Laird method.[18] Statistical significance was assumed when the mean difference effect was below a $P \leq 0.05$. Statistical heterogeneity was assessed using the Cochran Q test. A threshold P-value of 0.1 and values greater than 50% in $I^2$ were considered indicative of high heterogeneity.[19] We examined heterogeneity using the package 'dmetar' from R (function find.outlier)[20] by omitting studies in which the confidence intervals did not overlap the estimated pooled effect. Publication bias was explored by contour-enhanced funnel plots and Egger's test.[21]

Meta-regression models were undertaken to test the association between potential moderators of resistance training effects and outcomes of interest. We tested the association between the mean difference effect of interventions and the patients' average age, baseline levels of pain and function, and resistance training volume-related variables such as number of weeks, number of sessions, frequency, number of sets (i.e., total number of sets, average sets per week, and average sets per exercise session) and number of repetitions (i.e., total number of repetitions, average repetitions per week, and average repetitions per exercise session). Analyses were conducted using the package 'meta' from R.[20] Results presented for the outcome measures are after sensitivity analysis procedure adjustments.

## RESULTS

## Study selection

A total of 2,589 studies were retrieved from our search, with 1,404 potential records retained for screening after duplicate removals. After assessment for eligibility, 12 studies[10,22-32] (22 resistance training groups) were included for further analysis **(FIGURE 1).**

<< FIGURE 1 >>

## Characteristics of participants and interventions

In summary, a total of 423 participants with an average age ranging from 17 to 29 years were included. Six studies[10,22,26,30-32] included physically active participants, while 3 studies[27-29] included sedentary participants. Three studies[23–25] did not inform the physical activity conditioning status of participants. Regarding the primary outcome, the average value of pain at baseline ranged from 3.8 to 7.9 points out of 10. For the secondary outcome, the average value of function at baseline ranging from 61.8 to 77.4 points out of 100. Regarding the characteristics of the lower limb resistance training programs, the number of weeks ranged from 3 to 12 weeks, with frequencies from 2 to 7 days by week. As a result, the total number of sessions undertaken by the participants ranged from 12 to 42 sessions. The total volume of sets throughout the training program ranged from 42 to 600 sets, with 9 to 63 sets per week and 1 to 23 sets per session. In regard to the number of repetitions, a total of 1,080 to 7,680 repetitions were prescribed, with 90 to 994 repetitions per week and 30 to 270 repetitions per session. The characteristics of the individual studies are presented in **TABLE 2**, while further details on the type of resistance exercises performed in each trial are expressed in **TABLE 3 (Supplementary File).**

<<TABLE 2 >>

## Risk of bias

The PEDro scores of the included studies ranged from 4 to 8 points **(TABLE 4, Supplementary File)**. Eight studies[10,22,26–28,30–32] were classified as having low risk of bias (score >6), while 4 studies[23–25,29] were classified as having a high risk of bias (score ≤6).

## Effects and moderators of interventions on pain

Lower limb resistance training resulted in a significant reduction of 3.4 points (95% CI: -3.9 to -2.8) out of 10 in pain **(TABLE 5; FIGURE 2, Supplementary File).** The heterogeneity I2 was 89%, with no effect of publication bias (τ= 0.1, P= 0.951). After removing eight effect sizes which were considered outliers in the analysis[22,23,27–29,31,32] a significant reduction of 3.7 points (95% CI: -4.1 to -3.2) was observed, with a reduction in the heterogeneity I2 to 66% **(TABLE 5).** Publication bias was not observed after removing outliers (τ= 1.7, P= 0.125). This effect was consistent across sedentary and physically active participants **(TABLE 5).**

In the univariable meta-regression analyses, reductions in pain following resistance training were associated with baseline pain and weekly frequency **(TABLE 6)**. Participants experiencing higher levels of pain presented greater reductions following the interventions (β= -1.0 ± 0.3), and resistance training programs comprising a lower number of sessions per week promoted greater reductions in pain (β= 0.6 ± 0.2) **(FIGURE 3, Supplementary File)**. Changes in pain were not associated with the remaining variables **(FIGURE 3, Supplementary File).**

<<TABLE 5>>

<<TABLE 6>>

**Effects and moderators of interventions on self-reported function**

A significant increase of 12.5 points (95% CI: 9.5 to 15.6) out of 100 was observed in the AKPS questionnaire following resistance training programs **(TABLE 5; FIGURE 4, Supplementary File)**. Heterogeneity I2 was 75%, with no effect of publication bias (τ= 0.8, P= 0.449). After removing two effect sizes which were considered outliers in the analysis,28,32 an increase of 14.4 points (95% CI: 12.3 to 16.5 points) was observed **(TABLE 5)**. Heterogeneity was reduced to I2= 31%, and publication bias was not observed after removing outliers (τ= 0.2, P= 0.867). This effect was consistent across sedentary and physically active participants **(TABLE 5).**

In the univariable meta-regression analyses **(TABLE 7),** improvements in function following resistance training programs were associated with total number of sets and average number of sets per session **(FIGURE 5, Supplementary File).** A higher number of resistance exercise sets (β= 0.1 ± 0.03) and sets per exercise session (β= 0.6 ± 0.3) resulted in greater improvements in function, whereas the remaining variables did not explain the variance in function **(FIGURE 5, Supplementary File).**

<<TABLE 7>>

## DISCUSSION

The present review examined the dose-response effect of lower limb resistance training for treating women with PFP. There were four main findings. First, there was considerable variability in the resistance training dosage, with programs prescribing a wide range of exercise volumes in women with PFP. Second, lower limb resistance training interventions significantly reduced pain and improved self-reported function. Third, participants experiencing more pain at the baseline and resistance training programs comprising a low number of sessions per week were significantly associated with greater reductions in pain. Finally, a resistance training program with a higher volume (i.e., number of sets) was associated with greater improvements in self-reported function compared to a lower volume.

### ***Resistance training volume in women with PFP***

There is a lack of consensus on the minimal or optimal resistance training volume for managing women with PFP. Previous studies in this population have undertaken 9 to 81 resistance exercise sets per week. This 9-fold difference between studies prescribing low and high weekly volumes result in imprecisions for designing rehabilitation programs for patients with PFP and affects decision-making when establishing resistance training programs for this population. Another barrier to implementing such interventions in clinical practice is the poor reporting of exercise programs in previous studies.[33] During the screening phase, 18 studies were excluded due to insufficient information on the volume of exercise undertaken in resistance training programs. Therefore, future trials should provide sufficient information about prescribed and completed exercise volumes to better inform the design of subsequent studies and allow a valid interpretation of the results in the clinical setting.

**Overall effect of resistance training on pain and function**

In agreement with previous systematic reviews[8,34] our findings are that women with PFP experienced substantial improvements in pain and function following lower limb resistance training programs. Interestingly, the improvements of 3.4 points out of 10 in pain and 12.5 points out of 100 in function were above the minimal clinically important difference (MCID) of 2 and 10 points for patients with PFP, respectively.[35] These findings indicate that women with PFP can expect a remarkable reduction in pain following resistance training while presenting noticeable improvements in function. In addition, clinicians can help patients achieve meaningful benefits through resistance training, reducing the risk of physical disability and improving the quality of life and wellbeing.

### *Moderators of lower limb resistance training*

Regarding the moderators of resistance training effects on pain, we observed that women experiencing higher levels of knee pain achieved greater improvements following interventions. In addition, we did observe that a low weekly frequency (i.e., 2 or 3 resistance training sessions per week) was associated with greater reductions in pain. This information can be used for managing patients with severe symptoms, indicating that even adopting a low number of sessions per week may be sufficient to derive substantial reductions in pain. This is a feasible strategy to encourage patients and improve adherence to resistance training programs. Conversely, baseline levels of function had no association with changes in this outcome, suggesting that AKPS cannot be used as a tool to predict the patients' response to lower limb resistance training. Likewise, our meta-regression analysis indicates that young adult women with PFP were benefited from resistance training regardless of age. This result does not support that age should be used as a prognostic factor for outcomes related to pain and function in this population.

Interestingly, weekly frequency was the only resistance training volume-related variable significantly associated with changes in pain. Despite not being considered an optimal variable to represent training volume because of the high variability in the exercise volumes undertaken per session, our findings demonstrated that 2 or 3 sessions of resistance training per week were associated with the greatest analgesic effects.

Eighteen out of the 22 groups of women with PFP included in the current review performed 2 or 3 resistance training sessions per week, and both weekly frequencies resulted in pain reduction of >4 points[10,22,24,28–31] i.e., greater than twice the MCID for patients with PFP.[35] Conversely, we did not find any association between a high number of sets and repetitions with greater reductions in pain. Improvements of >4 points in pain were obtained with a wide range from 324 to 2728 sets per session (or 9 to 81 sets per week). As a result, a low volume of resistance training (e.g., below the median of 12 sets per session) 2 or 3 times a week may be a minimal and conservative approach that clinicians can initially prescribe for pain relief in women with PFP. This weekly frequency and minimal volume are likely feasible in most clinical settings and may be associated with greater attendance compared to more frequent and longer resistance training programs.

Greater increases in self-reported function were observed with higher volumes of lower limb resistance training in women with PFP. Improvements of >15 points in AKPS were observed in studies prescribing 3 sessions per week and a volume between 17 and 27 sets per session.[27,28,30] From a practical perspective, strategies to balance reductions in pain and gains in function while undergoing resistance training programs are necessary in women with PFP. Therefore, women with PFP could initially benefit from a low volume resistance training twice or thrice weekly to effectively reduce pain. This may help patients build upon compliance. Subsequently, goals such as improving function could be prioritized by introducing a higher volume of lower limb resistance training. Considering the approaches utilized in both research and clinical settings, we suggest that 3 sets per exercise for 6 to 9 lower limb resistance exercises with 3 sessions per week may optimize functional recovery of women with PFP. It is also noteworthy that resistance training studies prescribing 2 resistance training sessions per week and 9 to 15 sets per session found improvements in both pain and function outcomes.[10,31] Therefore, even when the patient has limited availability, positive effects can also be expected following less frequent and shorter resistance training programs, although a higher frequency and volume may still be preferable.

***Strengths and limitations***

To the best of our knowledge, this is the first systematic review and meta-regression examining the dose-response effect of resistance training volume in women with PFP. The strengths of the present study are: (1) the quantification of the resistance training volume, a widespread method utilized for different populations, but underestimated in the orthopedic and sports physical therapy field; and (2) the translation from our findings to practical recommendations for women with PFP. Moreover, in terms of future directions, our study indicates the need for investigating the dose-response effect of resistance training in other models of musculoskeletal rehabilitation such as traumatic injuries (e.g., ACL reconstruction) and overuse injuries (e.g., patellar and Achilles tendinopathies). However, we also have limitations. First, this review only included women with PFP. There is a lack of understanding on sex-related differences in resistance training response due to the paucity of well-designed studies with this goal, and it is unclear if resistance training prescription should be different between men and women.[36] Consequently, our results should not be extrapolated to men with PFP. Second, only assessments undertaken immediately after the intervention period were analyzed, thus the maintenance or residual effects of resistance training-induced gains remain to be determined in this population. Third, isometrics (e.g., planks, single leg balance) and other exercise interventions (e.g., stretching, balance/neuromuscular, aerobic exercises), as well as electrophysical agents (e.g., cryotherapy), analgesic drugs, and patients' education may have affected analyses on the dose-response of resistance training in women with PFP. Finally, we could not access the role of resistance training intensity (or load) because of the lack of or poor reporting of studies. This is a topic of great interest and deserves attention in future investigations.

## CONCLUSION

In conclusion, our findings are that a lower limb resistance training program result in meaningful improvements in pain and self-reported function in women with PFP. In addition, we identified specific moderators associated with more favorable responses. Women presenting with higher baseline pain experienced greater analgesic effect following resistance training, while programs with lower frequency (i.e., 2-3 times per week) were associated with greater reductions in pain. For function, resistance training programs comprising a higher number of sets were associated with greater improvements in this outcome. From a practical perspective, we suggest that a low volume of resistance training (i.e., <12 sets per session) twice or thrice weekly can be initially used to reduce pain. Subsequently, a higher volume of resistance training, between 17 to 27 sets per session (e.g., 3 sets of 6-9 exercises) thrice a week, can be introduced to improve function in women with PFP. These results are clinically relevant as women with PFP can be targeted based on baseline assessment and with specific resistance training programs to reduce pain and improve function.

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**FIGURES**

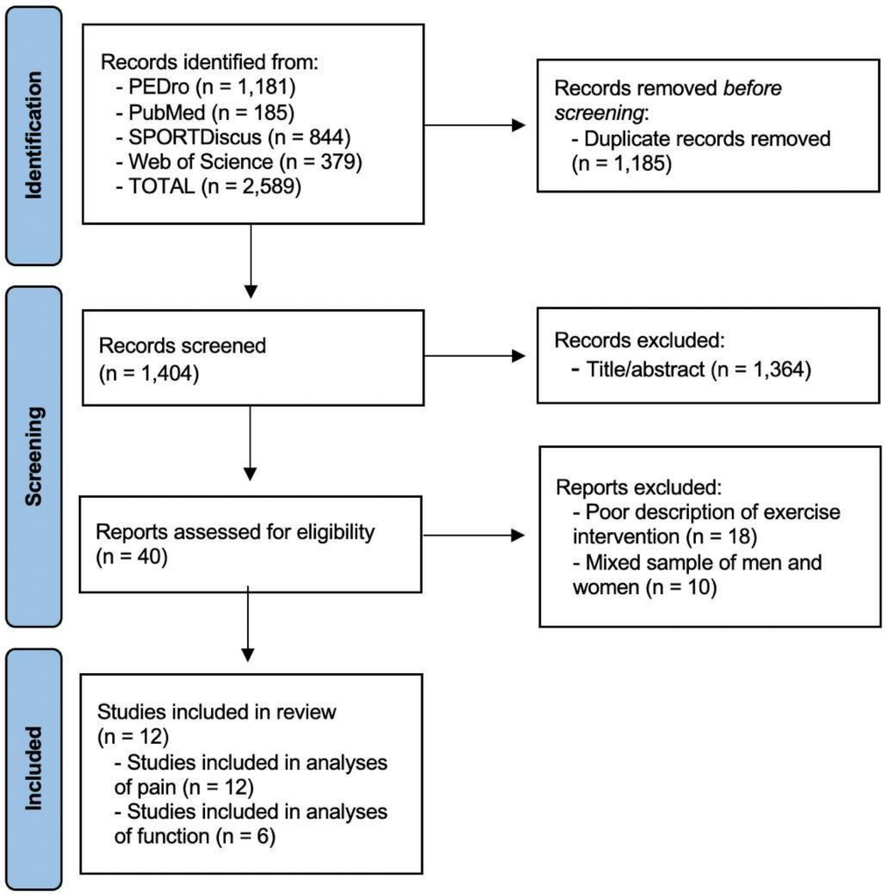


**FIGURE 1.** Flowchart of study selection process.

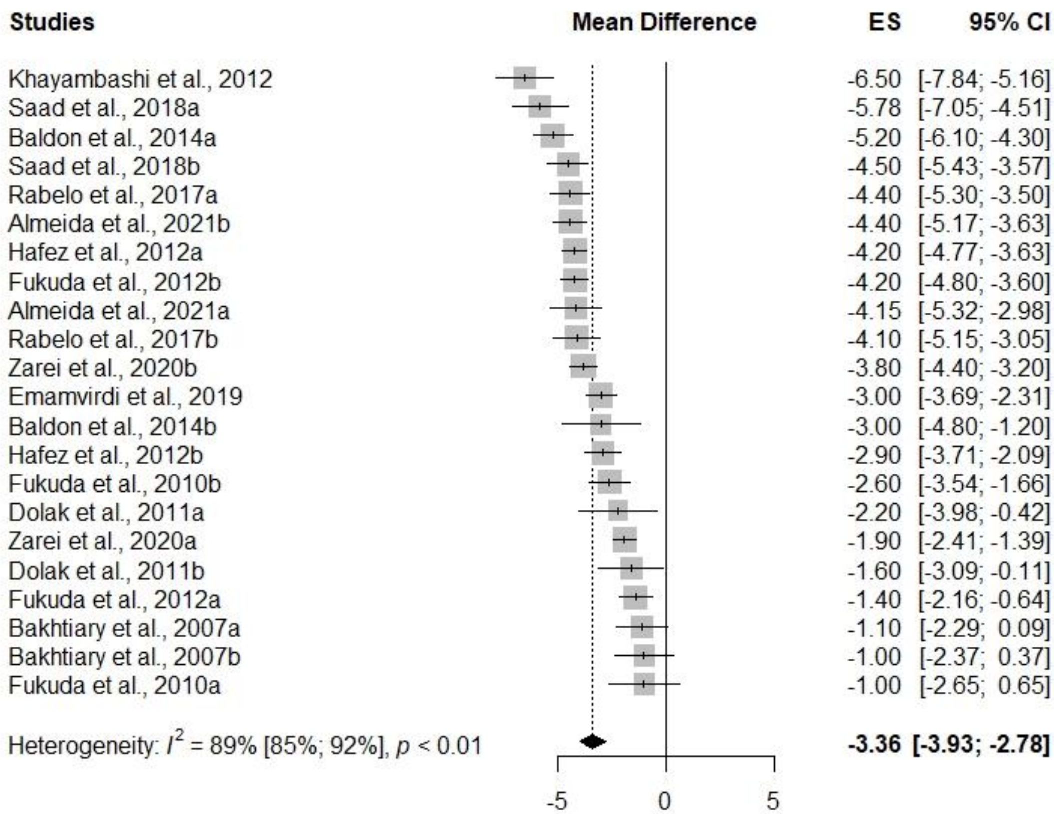


**FIGURE 2.** Changes in knee pain in women with patellofemoral pain following lower limb resistance training programs. Effect size (ES) and confidence interval (95% CI) presented in centimeters.

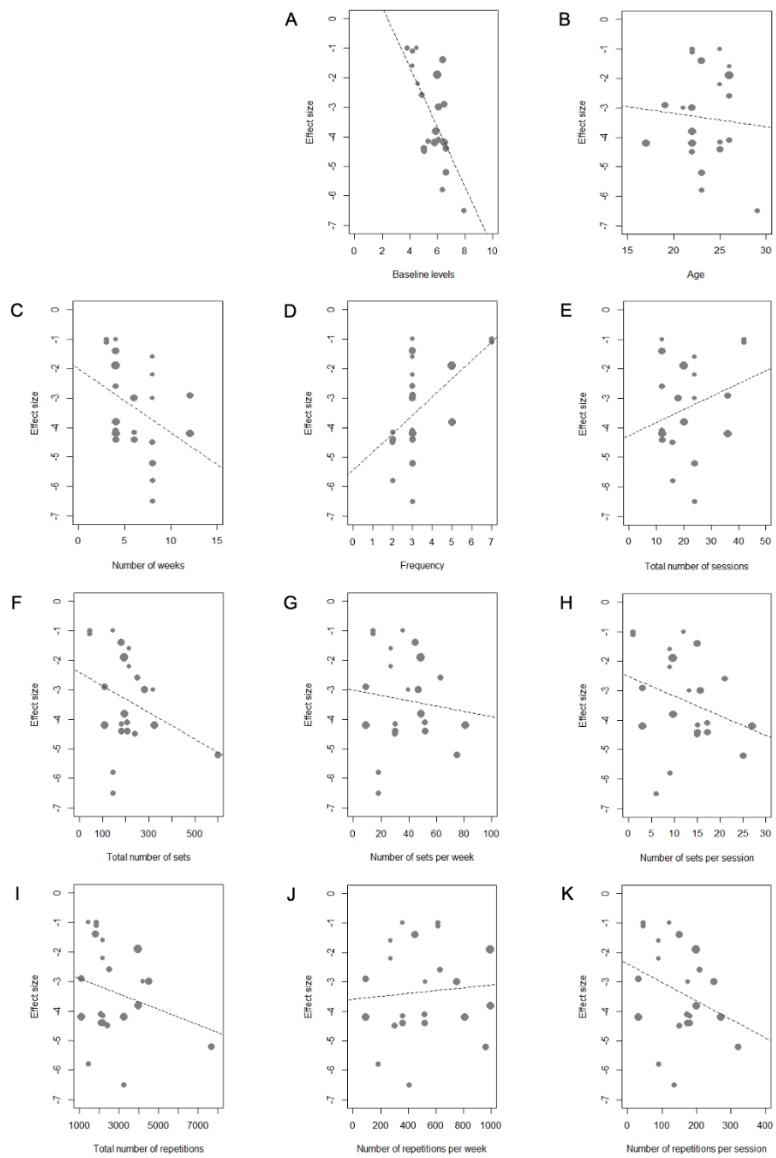


**FIGURE 3.** Univariable meta-regression on changes in knee pain and baseline pain (panel A), average age (panel B), number of weeks (panel C), frequency (panel D), total number of sessions (panel E), total number of sets (panel F), number of sets per week (panel G) and per session (panel H), total number of repetitions (panel I), number of repetitions per week (panel J) and per session (panel K). Each observation represents the weighted mean difference of knee pain between baseline and post-intervention assessment. The size of the circles is proportional to the inverse variance of each study in the pooled analysis.

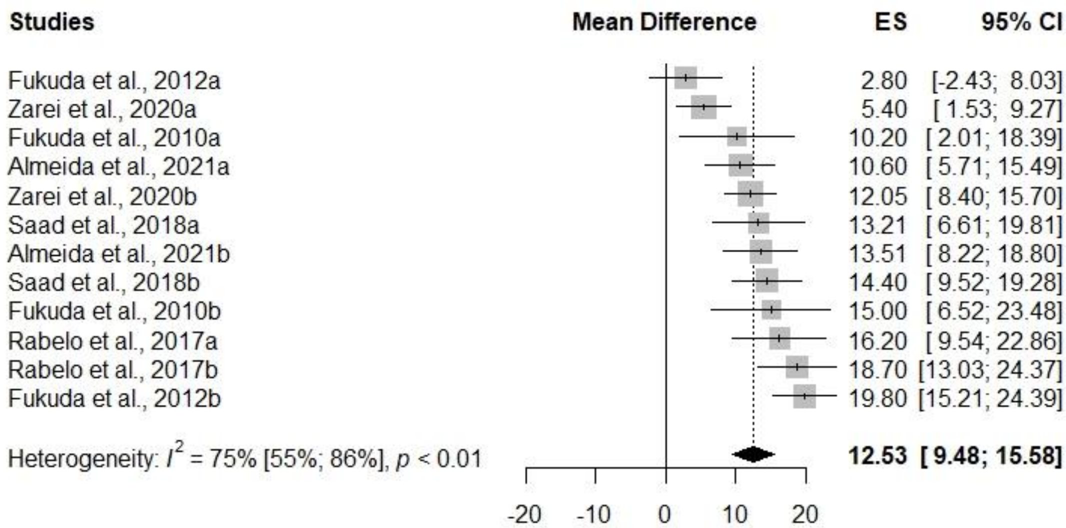


**FIGURE 4.** Changes in function in women with patellofemoral pain following resistance training programs. Effect size (ES) and confidence interval (95% CI) presented in AKPS points.

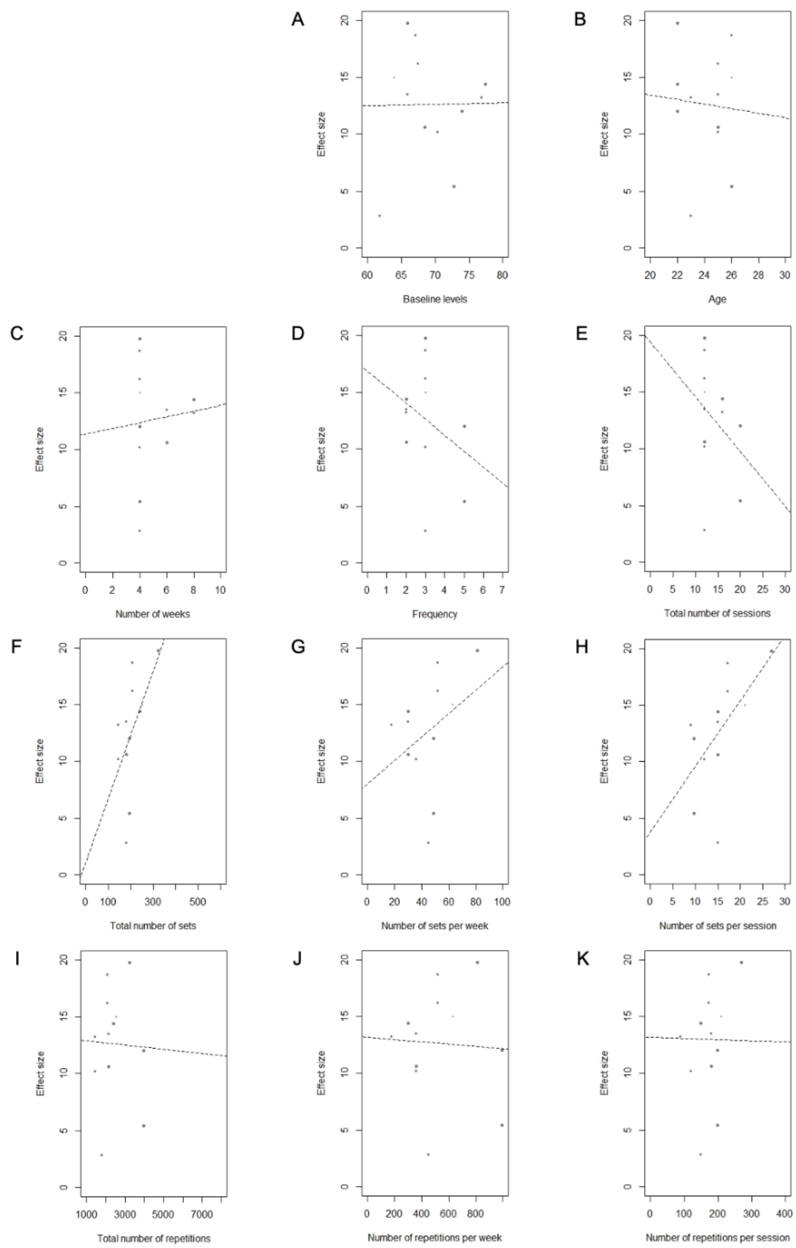


**FIGURE 5.** Univariable meta-regression on changes in patients' function and baseline function (panel A), average age (panel B number of weeks (panel C), frequency (panel D), total number of sessions (panel E), total number of sets (panel F), number of sets per week (panel G) and per session (panel H), total number of repetitions (panel I), number of repetitions per week (panel J) and per session (panel K). Each observation represents the weighted mean difference of knee pain between baseline and post-intervention assessment. The size of the circles is proportional to the inverse variance of each study in the pooled analysis.

# TABLES

**TABLE 1.** Search strategy.

| Database | Search strategy |
|---|---|
| Pedro | 1. exercise therapy AND patellofemoral pain syndrome.<br>2. exercise therapy AND knee pain.<br>3. exercise therapy AND patellofemoral pain.<br>4. physical therapy AND patellofemoral pain syndrome.<br>5. physical therapy AND knee pain.<br>6. physical therapy AND patellofemoral pain.<br>7. physiotherapy AND patellofemoral pain syndrome.<br>8. physiotherapy AND knee pain.<br>9. physiotherapy AND patellofemoral pain.<br>10. rehabilitation AND patellofemoral pain syndrome.<br>11. rehabilitation AND knee pain.<br>12. rehabilitation AND patellofemoral pain.<br>> advanced search, clinical trial<br>> individual searches |
| PubMed | exercise therapy[MeSH Terms] OR exercise therapy[Text Word] OR physical therapy [Text Word] OR physiotherapy [Text Word] OR rehabilitation [Text Word] AND "patellofemoral pain syndrome"[MeSH Terms] OR patellofemoral pain syndrome[Text Word] OR knee pain [Text Word] OR patellofemoral pain [Text word] |
| SPORTDiscus | 1. exercise therapy OR physical therapy OR physiotherapy OR rehabilitation<br>2. patellofemoral pain syndrome OR knee pain OR patellofemoral pain<br>> articles; English<br>> association of searches |
| Web of Science | 1 (TI=(exercise therapy OR physical therapy OR physiotherapy OR rehabilitation)) OR AB=(exercise therapy OR physical therapy OR physiotherapy OR rehabilitation) 2 (TI=(patellofemoral pain syndrome OR knee pain OR patellofemoral pain)) OR AB=(patellofemoral pain syndrome OR knee pain OR patellofemoral pain) 3 DT=(Article) 4 LA=(English)<br>> association of searches |

**TABLE 2.** Characteristics of studies examining lower limb resistance training programs on pain and function in women with patellofemoral pain.

| Study [Group] | Participants | | | | | Resistance training volume | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | Age | Profile | Baseline pain | Baseline function | # of weeks | Weekly frequency | # of sessions | Total # of sets | Sets per week | Sets per session | Total # of reps | Reps per week | Reps per session |
| Almeida et al. 2021 [A] | 26 | 25 | active | 5.3 ± 2.0 | 68.5 ± 8.2 | 6 | 2 | 12 | 180 | 30 | 15 | 2160 | 360 | 180 |
| Almeida et al. 2021 [B] | 26 | 25 | active | 5.0 ± 1.6 | 66.0 ± 10.0 | 6 | 2 | 12 | 180 | 30 | 15 | 2160 | 360 | 180 |
| Baldon et al. 2014 [A] | 15 | 23 | active | 6.6 ± 1.1 | NR | 8 | 3 | 24 | 558 | 70 | 23 | 7272 | 909 | 303 |
| Baldon et al. 2014 [B] | 16 | 21 | active | 6.1 ± 1.8 | NR | 8 | 3 | 24 | 318 | 40 | 13 | 4200 | 525 | 175 |
| Bakhtiary et al. 2007 [A] | 16 | 22 | NR | 4.2 ± 1.9 | NR | 3 | 7 | 42 | 42 | 14 | 1 | 1840 | 613 | 44 |
| Bakhtiary et al. 2007 [B] | 16 | 22 | NR | 3.8 ± 1.6 | NR | 3 | 7 | 42 | 42 | 14 | 1 | 1840 | 613 | 44 |
| Dolak et al. 2011 [A] | 17 | 25 | NR | 4.6 ± 2.5 | NR | 8 | 3 | 24 | 216 | 27 | 9 | 2160 | 270 | 90 |
| Dolak et al. 2011 [B] | 16 | 26 | NR | 4.2 ± 2.3 | NR | 8 | 3 | 24 | 216 | 27 | 9 | 2160 | 270 | 90 |
| Emamvirdi et al. 2019 | 32 | 22 | active | 6.1 ± 1.2 | NR | 6 | 3 | 18 | 282 | 47 | 16 | 4512 | 752 | 251 |
| Fukuda et al. 2010 [A] | 20 | 25 | sedentary | 4.5 ± 2.8 | 70.4 ± 12.5 | 4 | 3 | 12 | 144 | 36 | 12 | 1440 | 360 | 120 |
| Fukuda et al. 2010 [B] | 21 | 26 | sedentary | 4.9 ± 1.6 | 63.9 ± 11.7 | 4 | 3 | 12 | 252 | 63 | 21 | 2520 | 630 | 210 |
| Fukuda et al. 2012 [A] | 26 | 23 | sedentary | 6.4 ± 1.4 | 61.8 ± 9.0 | 4 | 3 | 12 | 180 | 45 | 15 | 1800 | 450 | 150 |
| Fukuda et al. 2012 [B] | 28 | 22 | sedentary | 5.8 ± 1.2 | 65.9 ± 8.5 | 4 | 3 | 12 | 324 | 81 | 27 | 3240 | 810 | 270 |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hafez et al. 2012 [A] | 20 | 17 | NR | 6.5 ± 1.1 | NR | 12 | 3 | 36 | 108 | 9 | 3 | 1080 | 90 | 30 |
| Hafez et al. 2012 [B] | 20 | 19 | NR | 6.5 ± 1.2 | NR | 12 | 3 | 36 | 108 | 9 | 3 | 1080 | 90 | 30 |
| Khayambashi et al. 2012 | 14 | 29 | sedentary | 7.9 ± 1.7 | NR | 8 | 3 | 24 | 144 | 18 | 6 | 3240 | 405 | 135 |
| Rabelo et al. 2017 [A] | 17 | 25 | active | 6.6 ± 1.0 | 67.5 ± 11.3 | 4 | 3 | 12 | 207 | 52 | 17 | 2070 | 518 | 173 |
| Rabelo et al. 2017 [B] | 17 | 26 | active | 6.1 ± 1.4 | 67.1 ± 7.6 | 4 | 3 | 12 | 207 | 52 | 17 | 2070 | 518 | 173 |
| Saad et al. 2018 [A] | 10 | 23 | active | 6.3 ± 1.9 | 76.9 ± 8.7 | 8 | 2 | 16 | 144 | 18 | 9 | 1440 | 180 | 90 |
| Saad et al. 2018 [B] | 10 | 22 | active | 5.1 ± 1.3 | 77.4 ± 5.5 | 8 | 2 | 16 | 240 | 30 | 15 | 2400 | 300 | 150 |
| Zarei et al. 2020 [A] | 20 | 26 | active | 6.0 ± 0.7 | 72.8 ± 6.5 | 4 | 5 | 20 | 195 | 49 | 10 | 3975 | 994 | 199 |
| Zarei et al. 2020 [B] | 20 | 22 | active | 5.9 ± 0.8 | 74.0 ± 6.4 | 4 | 5 | 20 | 195 | 49 | 10 | 3975 | 994 | 199 |

*Abbreviations: N, number of participants; NR, not reported; # number, [A] and [B], studies with two groups engaged in resistance training programs.*

**TABLE 3.** Exercises performed into the lower limb resistance training programs. Names of exercises were kept from the original studies.

| Study [Group] | Exercises |
|---|---|
| Almeida et al. 2021 [A] | Seated knee extension strengthening; Squatting, Hip abduction in side-lying; Clam with elastic resistance; Hip external rotation with elastic resistance; |
| Almeida et al. 2021 [B] | Seated knee extension strengthening; Squatting; Hip adduction in side-lying; Flex ring squeeze in side-lying; Hip internal rotation with elastic resistance; |
| Baldon et al. 2014 [A] | Lateral rotation in standing; Hip abduction/lateral rotation/extension in sidelying; Hip extension/lateral rotation in prone; Hip abduction/lateral rotation with slight knee and hip flexion in sidelying; Pelvic drop in standing; Hip lateral rotation in closed kinetic chain; Single-leg deadlift; Single-leg squat; Forward lunge; Prone knee flexion; Seated knee extension (90°-45° of knee flexion); |
| Baldon et al. 2014 [B] | Straight leg raise in supine; Seated knee extension (90°-45° of knee flexion); Leg press (0°-45° of knee flexion); Wall squat (0°-60° of knee flexion); Step-ups and step-downs from a 20-cm step; |
| Bakhtiary et al. 2007 [A] | Straight leg raise exercise: the subject should be in a supine position with hip and knee extended in the exercise limb and the nonexercise limb in hip and knee flexion. The subject was asked to lift the lower limb with extended knee until 45° hip flexion and hold it for 3– 4s, and then let it down for a 3–4s rest. |
| Bakhtiary et al. 2007 [B] | Semi-squat exercise: the subject was asked to stand on the lower limb to be exercised and hold onto a stable surface using their hand, while the nonexercise lower limb was in 90u hip and knee flexion. The subject was then ordered to flex the extended knee 15–20º and hold this position for 3–4s, then bring it to full extension and remain in this position for a 3–4s rest. |
| Dolak et al. 2011 [A] | Wall slides with resistance; Lateral step-downs off a 10-cm step; 2-leg calf raises; Single-leg mini-squats; Single-leg calf raises; Lunges to a 20.3-cm step; Sidelying combination hip abduction and external rotation; Standing hip abduction; Seated hip external rotation; Sidelying hip abduction; Quadruped hydrant (combined hip abduction and external rotation); |
| Dolak et al. 2011 [B] | Wall slides with resistance; Lateral step-downs off a 10-cm step; 2-leg calf raises; Single-leg mini-squats; Single-leg calf raises; Lunges to a 20.3cm step; Short arc quads; Straight leg raises; Terminal knee extensions; |
| Emamvirdi et al. 2019 | Squat in front of mirror (0°-60° of knee flexion); Squat (0°-60° of knee flexion); Lateral walk with elastic resistance around the forefoot; Strengthening the hip abductors with weightbearing (Trendelenburg); Squat with elastic resistance (0°-60° of knee flexion, resistance placed around the knees, stimulating the constant activation of the hip abductors and lateral rotators); Forward lunge in front of mirror; Modified forward lunge with elastic around the knee that is ahead ( activation of abductors and lateral rotators of the hip); Romanian deadlift; Lateral sliding without jumping; Hip lateral rotation; |
| Fukuda et al. 2010 [A] | Iliopsoas strengthening in non-weight bearing; Seated knee extension 90°-45°; Leg press 0°-45°; Squatting 0°-45°; |
| Fukuda et al. 2010 [B] | Iliopsoas strengthening in non-weight bearing; Seated knee extension 90°-45°; Leg press 0°-45°; Squatting 0°-45°; Hip abduction against elastic band (standing); Hip abduction with weights (sidelying); Hip external rotation against elastic band (sitting); |
| Fukuda et al. 2012 [A] | Seated knee extension from 90° to 45°; Leg press from 0° to 45°; Squatting from 0° to 45°; Single-leg calf raises; Prone knee flexion; |
| Fukuda et al. 2012 [B] | Seated knee extension from 90° to 45°; Leg press from 0° to 45°; Squatting from 0° to 45°; Single-leg calf raises; Prone knee flexion; |

| | |
|---|---|
| | Hip abduction with weights (sidelying); Hip abduction against elastic band (standing); Hip lateral rotation against elastic band (sitting); Hip extension (machine); |
| Hafez et al. 2012 [A] | Sit in the chair slowly. |
| Hafez et al. 2012 [B] | Seated knee extension (90° - 0°). |
| Khayambashi et al. 2012 | Isolated hip abductor strengthening with elastic tubing. |
| Rabelo et al. 2017 [A] | Side lying hip abduction; Side lying clam exercise; Seated knee extension (from 90° to 45°); Squatting (from 0° to 45°); Lateral band walks; Forward lunge; Pelvic drop in standing; |
| Rabelo et al. 2017 [B] | Side lying hip abduction; Side lying clam exercise; Seated knee extension (from 90° to 45°); Squatting (from 0° to 45°); Lateral band walks; Forward lunge; Pelvic drop in standing; Squatting (from 0° to 45°) with elastic band; Forward lunge with elastic band; Single leg squat (from 0° to 30°); |
| Saad et al. 2018 [A] | Straight Leg Raise; Seated knee extension (open kinetic chain exercise, 90º – 60º of knee flexion); Leg Press (closed kinetic chain exercise, 0º – 45º of knee flexion); |
| Saad et al. 2018 [B] | Straight Leg Raise in side lying; Supine Bridge on Ball; Seated Hip Abduction; Strengthening the extensors, abductors and hip external rotators at four support positions; |
| Zarei et al. 2020 [A] | Quadriceps exercise; Side-lying straight-leg raises; Side-lying clamshells; Mini-squats; Mini-lunge; Step-down; |
| Zarei et al. 2020 [B] | Quadriceps exercise; Side-lying straight-leg raises; Side-lying clamshells; Mini-squats; Mini-lunge; Step-down; |

**TABLE 4.** PEDro scores of included studies.

| Study | PEDro criteria | | | | | | | | | | | Final score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1* | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | |
| Almeida et al. 2021 | Y | Y | Y | Y | N | N | N | Y | Y | Y | Y | 7 |
| Baldon et al. 2014 | Y | Y | Y | Y | N | N | N | Y | Y | Y | Y | 7 |
| Bakhtiary et al. 2007 | N | Y | Y | Y | N | N | N | N | Y | Y | Y | 6 |
| Dolak et al. 2011 | Y | Y | N | Y | N | N | Y | N | Y | Y | Y | 6 |
| Emamvirdi et al. 2019 | Y | Y | Y | Y | N | N | N | Y | Y | Y | Y | 7 |
| Fukuda et al. 2010 | Y | Y | Y | Y | N | N | Y | Y | N | Y | Y | 7 |
| Fukuda et al. 2012 | Y | Y | Y | Y | N | N | Y | Y | Y | Y | Y | 8 |
| Hafez et al. 2012 | N | Y | N | Y | N | N | N | N | N | Y | Y | 4 |
| Khayambashi et al. 2012 | Y | Y | N | Y | N | N | N | Y | N | Y | Y | 5 |
| Rabelo et al. 2017 | Y | Y | Y | Y | N | N | Y | Y | Y | Y | Y | 8 |
| Saad et al. 2018 | N | Y | Y | Y | N | N | Y | Y | Y | Y | Y | 8 |
| Zarei et al. 2020 | Y | Y | Y | Y | N | N | Y | Y | Y | Y | Y | 8 |

*Abbreviations: N, no (criterion not satisfied); PEDro, Physiotherapy Evidence Database; Y, yes (criterion satisfied); 1 Eligibility criteria (* not used for score); 2 Subjects were randomly allocated; 3 Allocation was concealed; 4 Groups were similar at baseline; 5 There was blinding of all subjects; 6 There was blinding of all therapists who administered the therapy; 7 There was blinding of all assessors who measured at least one key outcome; 8 Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; 9 All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by 'intention-to-treat'; 10 The results of between-group statistical comparisons are reported; 11 The study provides both point measures and measures of variability.*

**TABLE 5.** Overall and subgroup resistance training effects on pain and function.

| | Random effect meta-analysis | | | | | Heterogeneity | | |
|---|---|---|---|---|---|---|---|---|
| | k value | n | ES | 95% CI | P-value | Q | $I^2$ | P- |
| **Pain** | | | | | | | | |
| **All groups** | 22 | 423 | -3.4 | -3.9 to -2.8 | <0.001 | 192.8 | 89% | <0.001 |
| Without outlier† | 14 | 286 | -3.7 | -4.1 to -3.2 | <0.001 | 38.7 | 66% | <0.001 |
| **Subgroup analysis** | | | | | | | | |
| | 5 | 109 | -3.2 | -4.8 to -1.5 | <0.001 | 64.0 | 94% | <0.001 |
| Physically active | 11 | 209 | -4.0 | -4.7 to -3.3 | <0.001 | 82.6 | 88% | <0.001 |
| **Function** | | | | | | | | |
| **All groups** | | | | | | | | |
| Overall effect | 12 | 241 | 12.5 | 9.5 to 15.6 | <0.001 | 43.4 | 75% | <0.001 |
| Without outlier† | 10 | 195 | 14.4 | 12.3 to 16.5 | <0.001 | 13.0 | 31% | 0.163 |
| **Subgroup analysis** | | | | | | | | |
| Sedentary | 4 | 95 | 12.0 | 3.1 to 20.8 | 0.008 | 23.6 | 87% | <0.001 |
| Physically active | 8 | 146 | 12.7 | 9.7 to 15.6 | <0.001 | 19.8 | 65% | 0.006 |

*Abbreviations: k, number of effect sizes; n, number of participants; ES, effect size; 95% CI, 95% confidence interval; Q, Cochran's Q test of heterogeneity $I^2$, percentage of variation across studies that is due to heterogeneity; †Adjustment after omitting studies in which the confidence intervals did not overlap the estimated pooled effect*

**TABLE 6.** Univariable meta-regression on changes in knee pain following intervention and demographic and resistance training program characteristics.

| | | | Univariable model | |
|---|---|---|---|---|
| | k | Range | β ± SE | P-value |
| Baseline pain | 22 | 3.8 – 7.9 | **-1.0 ± 0.3** | **<0.001** |
| Age | 22 | 17 – 29 | -0.1 ± 0.1 | 0.722 |
| Number of weeks | 22 | 3 – 12 | -0.2 ± 0.1 | 0.066 |
| Weekly frequency | 22 | 2 – 7 | **0.6 ± 0.2** | **0.003** |
| Number of sessions | 22 | 12 – 42 | 0.0 ± 0.0 | 0.188 |
| Total number of sets | 22 | 42 – 600 | -0.0 ± 0.0 | 0.107 |
| Sets per week | 22 | 9 – 81 | -0.0 ± 0.0 | 0.591 |
| Sets per session | 22 | 1 – 27 | -0.1 ± 0.1 | 0.145 |
| Total number of reps | 22 | 1,080 – 7,680 | -0.0 ± 0.0 | 0.238 |
| Reps per week | 22 | 90 – 994 | 0.0 ± 0.0 | 0.699 |
| Reps per session | 22 | 30 – 320 | -0.0 ± 0.0 | 0.131 |

*Abbreviations: k, number of effect sizes ; β, Regression coefficient; SE, standard error.*

**TABLE 7.** Univariable meta-regression on changes in patients' function following intervention and demographic and resistance training program characteristics.

| | | | Univariable model | |
|---|---|---|---|---|
| | k | Range | β ± SE | P-value |
| Baseline function | 12 | 62 – 77 | 0.0 ± 0.3 | 0.967 |
| Age | 12 | 22 – 26 | -0.2 ± 1.0 | 0.835 |
| Number of weeks | 12 | 4 – 8 | 0.3 ± 1.0 | 0.798 |
| Weekly frequency | 12 | 2 – 5 | -1.4 ± 1.4 | 0.323 |
| Number of sessions | 12 | 12 – 20 | -0.5 ± 0.5 | 0.300 |
| Total number of sets | 12 | 144 – 324 | **0.1 ± 0.03** | **0.033** |
| Sets per week | 12 | 18 – 81 | 0.1 ± 0.1 | 0.231 |
| Sets per session | 12 | 9 – 27 | **0.6 ± 0.3** | **0.019** |
| Total number of reps | 12 | 1,440 – 3,975 | -0.0 ± 0.0 | 0.918 |
| Reps per week | 12 | 180 – 994 | -0.0 ± 0.0 | 0.861 |
| Reps per session | 12 | 90 – 270 | -0.0 ± 0.0 | 0.861 |

*Abbreviations: k, number of effect sizes; β, Regression coefficient; SE, standard error.*

Conflict of Interest

Dose-response effect of lower limb resistance training on pain and function of women with patellofemoral pain: A systematic review and meta-regression

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Competing interests: The authors have no conflicts of interest to declare.

# 4 CONCLUSÃO GERAL

O presente estudo reforça o corpo de evidências acerca da efetividade de programas envolvendo treinamento resistido de membros inferiores sobre a redução do quadro álgico de mulheres com DPF. Ainda, a partir das informações extraídas dos estudos selecionados para análise, é evidenciado que um programa de treinamento resistido de membros inferiores, resulta em melhorias significativas na dor e função autorreferida em mulheres com PFP. Além disso, identificamos que as mulheres que apresentavam maior dor basal experimentaram maior efeito analgésico após o treinamento de resistência, enquanto programas com menor frequência (ou seja, 2-3 vezes por semana) foram associados a maiores reduções na dor. Para a função, programas de treinamento resistido com maior número de séries foram associados a maiores melhorias nesse resultado.

## 5 IMPACTOS DO TRABALHO

Esta Dissertação apresenta um estudo de revisão sistemática com meta-regressão acerca da relação dose-resposta do treinamento resistido de membros inferiores utilizado para o tratamento de mulheres com DPF. Enquanto investigações acerca do impacto do volume de treinamento sobre as respostas de sujeitos saudáveis já ocupam espaço na literatura científica há várias décadas, há uma evidente carência deste tipo de estudo em populações acometidas por desordens de natureza traumato-ortopédica. Portanto, um potencial impacto científico do presente estudo é o incentivo que o mesmo possa ter para que pesquisadores com interesse e expertise no tratamento de outras lesões traumato-ortopédicas desenvolvam análises semelhantes para que se descubra a existência ou não de uma “dosagem ideal” para o tratamento dos pacientes. Além disso, dado a inexistência de ensaios controlados randomizados comparando o efeito de diferentes volumes de treinamento sobre as respostas de mulheres com DPF, espera-se que os achados aqui reportados justifiquem a relevância de se desenvolver estudos originais com esse tema de pesquisa. Por fim, do ponto de vista clínico, esses resultados indicam que as mulheres com PFP podem ser direcionadas com base na avaliação inicial e com programas específicos de treinamento de resistência para reduzir a dor e melhorar a função. O principal impacto deste trabalho se constitui no alerta para que os fisioterapeutas adotem critérios para prescrição e passem a ter maior controle sobre o volume de exercícios que seus pacientes executam a cada sessão do programa de tratamento.