

Effectiveness of Proprioceptive Neuromuscular Facilitation on Pain Intensity and Functional Disability in Patients with Low Back Pain: A Systematic Review and Meta-Analysis

Mohammadreza Pourahmadi, PhD, PT, Mohammad Sahebalam, BSc, PT, MSc Student, and Rasool Bagheri, PhD, PT

Abstract

Background:

This systematic review aimed to investigate the effectiveness of proprioceptive neuromuscular facilitation (PNF) training on back pain intensity and functional disability in people with low back pain (LBP).

Methods:

Totally, five electronic databases, including PubMed/Medline (NLM), Scopus, Google Scholar, PEDro, and Cochrane Central Register of Controlled Clinical Trials were searched up to October 31, 2018. Clinical trials with a concurrent comparison group (s) that compared the effectiveness of PNF training with any other physical therapy intervention were selected. Publication language was restricted to English language articles. Methodologic quality was assessed using the PEDro scale. The measures of continuous variables were summarized as Hedges's *g*.

Results:

In total, 20 eligible trials were identified with 965 LBP patients. A large effect size (standardized mean difference [SMD]=-2.14, 95% confidence interval [CI]=3.23 to -1.05) and significant effect were observed favoring the use of PNF training to alleviate back pain intensity in patients with LBP. Moreover, large effect size and the significant result were also determined for the effect of PNF training on functional disability improvement (SMD=-2.68, 95% CI=-3.36 to -2.00) in population with LBP. A qualitative synthesis of results indicated that PNF training can significantly improve sagittal spine ROM. Statistical heterogeneity analysis showed that there was considerable statistical heterogeneity among the selected trials for the primary outcomes ($I^2 \geq 86.6\%$).

Conclusion:

There is a low quality of evidence and weak strength of recommendation that PNF training has positive effects on back pain and disability in LBP people. Further high-quality randomized clinical trials regarding long-term effects of PNF training versus validated control intervention in a clinical setting is recommendable.

Key Words: Low back pain, Meta-analysis, PNF, Proprioceptive neuromuscular facilitation, Review

Introduction

Low back pain (LBP) is a major global challenge and a quite common symptom in populations worldwide that happens in all age groups from children to the elderly population (1, 2). The Global Burden of Disease Study 2017 reported that between 2007 and 2017, the number of all-age years lived with disability (YLDs) attributed to LBP increased by 17.5% (95% uncertainty interval 16.2-19.0%) (3). Several factors have been suggested as potential causes of LBP, including disturbances in trunk proprioception, as well as abdominal and paraspinal muscle weakness (4-6). Therefore, physical therapy interventions, which enhance trunk proprioception, as well as abdominal and back muscle function may optimize clinical and physiological outcomes, thereby improving the quality of life in patients with LBP (7).

Nonpharmacologic interventions are offered as first-line options in patients with chronic LBP since fewer harms are associated with these types of interventions, compared to pharmacologic options (8). Exercise therapy is one of the conservative treatment modalities most frequently used in LBP by physical therapists (9, 10). Bekkering et al. (2003) recommended exercise therapy as the first-line treatment for LBP (11). Proprioceptive neuromuscular facilitation (PNF) training is often used in order to promote or hasten neuromuscular responses by stimulating proprioceptors (7, 12, 13).

The PNF training was first introduced by Margaret (Maggie) Knott (physical therapist) and Herman Kabat (physician) in the 1940s and early 1950s to treat neuromusculoskeletal disorders (14, 15). The primary purpose of this treatment is to help

patients enhance movement efficiency and achieve their highest level of functioning (16). The PNF utilizes the body's proprioceptive system and reflexes to inhibit or facilitate muscle contraction (14). Moreover, the PNF techniques are frequently used in the clinical and athletic environments to improve active and passive range of motion (ROM) and agility to enhance motor performance and rehabilitation (17). According to Sharman et al., (2006) the PNF techniques may be effective stretching techniques when the aim is to increase ROM at least in the short-term (17). Furthermore, it has been reported that the PNF techniques can help improve the overall functional ability of patients, such as muscular strength, muscular endurance, joint mobility, joint stability, neuromuscular control, balance, and coordination (18, 19).

To date, 10 specific PNF techniques have been developed and are used by physical therapists worldwide (16). These techniques include rhythmic initiation, replication (also known as hold relax active motion), stretch through the range, stretch at beginning of range, rhythmic stabilization (also known as alternating isometric contractions), a combination of isotonic (also known as agonist reversals), dynamic reversals (also known as slow reversals), stabilizing reversals, hold relax, and contract relax (16). However, the most common types of PNF techniques used in the literature for LBP patients consist of rhythmic stabilization and a combination of isotonic (7). The rhythmic stabilization technique utilizes the alternating isometric contractions of agonists and antagonists against resistance, and no motion is allowed during this technique (20). The combination of isotonic is used when the purpose is to enhance the ability to execute controlled purposeful movements (Kofotolis and Kellis, 2006). It involves the performance of alternating concentric, isometric, and eccentric contractions and is used to improve muscle strength and ROM (21).

In addition to PNF techniques, the PNF movement patterns are functional movements, which are frequently used in daily and sports activities (22). The PNF patterns are characterized by spiral (three-dimensional) and diagonal movements as a result of synergistic muscle activation (22). It has been hypothesized that these exercises may be better suited for improving performance than conventional single-direction or single-plane weight-training programs (17).

Control of the spine is complex and relies on well-coordinated and deep-trunk musculature (23). The PNF patterns, which are a form of neuromuscular control exercises, can aid in restoring control, coordination, and strength of the muscles that control and support the spine, thereby improving pain control (8). Byström et al. (2013) also showed that neuromuscular control exercises resulted in improvements in function in the short and long term; however, the size of the effect was small (24).

A systematic review and meta-analysis conducted by Tong et al. (2017) showed that patients with LBP have altered lumbar spine proprioception, compared to controls (25). Lederman (2010) stated that changes in proprioceptive acuity after musculoskeletal injuries could be due to a competition between nociception and proprioception for central "attention," occurring at reflexive and cognitive levels (26). The PNF training may improve local joint control and muscle sensitivity by enhancing the sensitivity of muscle spindle and Golgi tendon organs, which are responsible for proprioception (27, 28). Accordingly, back pain is expected to be decreased as a result of improved lumbar proprioception (27). Furthermore, poor trunk muscle endurance and excessive fatigability of lumbar paraspinal muscles are often associated with chronic LBP (29). It has been reported that the PNF training may enhance trunk muscle flexibility, strength, and endurance, thereby providing further support to the effectiveness of PNF training for back pain and functional disability improvement (29).

Although PNF techniques and patterns are currently used in clinical practice and research settings for the treatment of LBP patients, no systematic review has yet focused on this topic. A recent narrative review summarized the available evidence for this rehabilitation concept and reported that there was a substantial body of literature, which supported the use of PNF training as a comprehensive rehabilitation concept (16). However, it should be noted that the study conducted by Smedes et al. (2016) is a literature review the design of which does not recommend the use of PNF training (16). In addition, this narrative review did not assess the efficacy of PNF training for specific populations (16). As a result, for the first time, this study was performed to systematically review the literature in order to assess the effectiveness of PNF training on LBP.

Materials and Methods

This systematic review process followed the guidelines of the PRISMA statement, and it was registered on the PROSPERO register (PROSPERO; CRD42018097303) (30). It is worth mentioning that patient consent and ethical approval were not required for this systematic review.

Identification and selection of studies

Search strategy

A comprehensive search was conducted in Pubmed/Medline (NLM), Scopus, Google Scholar, PEDro, and Cochrane Central Register of Controlled Clinical Trials from the earliest date until October 31, 2018. Electronic search strategies were developed based on the combined keywords, including “clinical trial”, “PNF”, and “low back pain” to identify English-language studies that evaluated PNF training for adult patients (≥ 18 years) with LBP. The language of publication was restricted to English since Morrison et al. (2012) reported no significant differences between pooled treatment effects in English-language restricted meta-analyses and languages other than English-inclusive meta-analyses in medicine (31). The search strategy was developed around two concepts with medical subject headings terms and keywords adapted to individual databases. Appendix S1 presents the details of the PubMed database search syntax. Reference checking, citation tracking in Google Scholar, and manual searching of ahead-of-print listing in journals of selected articles were performed to ensure that all relevant studies were included. After the search, all articles were imported into Endnote (version X8.1; Clarivate Analytics, PA, USA), and the duplicates were removed. In total, two reviewers (M.P. and M.S.) independently investigated the titles and abstracts of the Endnote library, and disagreements were settled by consensus. After title and abstract screening, full-text articles of potentially suitable trials were obtained to assess their eligibility.

Eligibility criteria

The eligibility criteria were defined according to Patient, Intervention, Comparator, Outcome, Study criteria, and objectives of this study [Table 1].

Criteria	Inclusion
P	The population was composed of adult patients (≥ 18 years of age) with low back pain or discomfort localized below the third lumbar and above the sacrum for at least one day (32, 33).
I	The PNF is a rehabilitation technique that is used to stimulate proprioceptors in order to produce the desired movement of the

Table 1

PICOS criteria for the study

Types of participants

Participants of this study comprised adult patients of both genders with any type of LBP (acute (<4 weeks), subacute (between 4 and 12 weeks), and chronic (>12 weeks) [Table 1].

Types of interventions

Studies in which PNF techniques and/or PNF patterns were used to decrease back pain or functional disability in patients with LBP were included in this study [Table 1].

Types of outcome measures

The co-primary outcome measures were back pain and functional disability [Table 1].

- The pain was defined as back pain intensity assessed at the time point closest to the end of treatment (35). Pain intensity could be measured with a continuous, self-report scale (e.g., visual analog scale [VAS]), numeric pain rating scale (NPRS), Borg verbal rating pain scale), or a rating scale within a composite measure of back pain (e.g., McGill Pain Questionnaire). The studies that used other measurement tools were not excluded.
- Functional disability was defined as loss of low back-specific function measured at the end of treatment. A functional disability could be measured with a continuous, self-report scale (e.g., Roland Morris Disability Questionnaire [RMDQ]), Oswestry Disability Index [ODI], modified ODI, or Quebec back pain disability score). The studies that used other measurement tools were not excluded.
- The secondary outcome of the measure was spine ROM [Table 1]. The ROM was defined as vertebral column flexion and extension ROM. The spine ROM could be measured with the Schober test, flexicurve technique, and inclinometer. The studies that used other measurement tools were not excluded.

Quality assessment

The methodological quality of the selected trials was assessed by two reviewers (M.P. and M.S.) independently according to the PEDro scale (36). Item 1 demonstrates the external validity (or ‘generalizability’ or ‘applicability’ of the study) and is not considered in the total PEDro score. Items 2-9 refer to the internal validity of a study, and items 10-11 present adequate statistical information to enable proper interpretation of the findings [Appendix S2]. Primary studies, which received scores of ≥ 6 on the PEDro scale, were classified as ‘high quality’ studies. Trials with a PEDro score of 4-5 were classified as ‘fair quality’

studies, and trials with scores of ≤ 3 were classified as 'poor quality' studies (23). A Cohen's kappa coefficient (κ) with a corresponding 95% confidence interval (CI) was used to evaluate the level of inter-rater agreement (0-0.20=poor; 0.21-0.40=fair; 0.41-0.60=moderate; 0.61-0.80=good; and 0.81-1=very good) (37). The consensus was reached in case of disagreement.

Data extraction

Data abstraction from the selected trials was undertaken independently by two non-blinded reviewers (M.P. and M.S.) using a standardized and pre-piloted data extraction form. The abstracted data included the description of trial characteristics, such as author name, publication year, country, study design, sample size, the status of health, mean age, body mass index, body mass, stature, gender, outcome measures, description of interventions, and key findings. Following the completion of this phase, one reviewer (M.P.) double-checked the extracted data to avoid any inaccuracies or omissions in the data extracted.

Statistical Methods

Measures of treatment effect

The measures of continuous variables are summarized as Hedges's g , if the same primary outcomes were used in the included studies. Since the selected studies had small sample sizes, this effect size was used to calculate standardized mean differences. Effect sizes were calculated using the 'metan' package of Stata software (version 14; Stata Corp., College Station, TX, USA) (38). The data used for estimating effect sizes include sample sizes, means, and standard deviations, both at baseline and post-treatment, for all groups (i.e., treatment and comparison). If continuous outcomes measures were different between trials, the pooled effects were presented with Hedges's g ; however, the different outcome measures were first converted to a 0 to 100 scale (34). All outcome variables were continuous. For the measurement of effect sizes, three levels were defined as small effect size ($SMD < 0.40$), medium effect size ($0.40 \leq SMD \leq 0.70$) or large effect size ($SMD > 0.70$) (34). A clinically important treatment effect was considered when the magnitude of the summary measure was at least medium (34).

Unit of Analysis Issues

When multiple comparisons of one clinical trial were included in one meta-analysis, the 'shared' group was split into two groups with smaller sample sizes to avoid overestimating the number of patients that would create a unit-of-analysis error (39).

Assessment of Statistical Heterogeneity

Statistical heterogeneity among the eligible studies was assessed using the I^2 statistic and Cochran's Q test (χ^2) as recommended by the Cochrane Handbook for Systematic Reviews of Interventions (40). The I^2 statistic were interpreted according to the following guide: 0-40%=no important statistical heterogeneity; 30-60%=moderate statistical heterogeneity; 50-90%=substantial statistical heterogeneity; 75-100%=considerable statistical heterogeneity (41). Statistical heterogeneity was considered before performing a meta-analysis. If I^2 values were $>50\%$, and there was an overlap between the CIs in visual inspection of the forest plot (eyeball test), the results were combined into a meta-analysis using a random-effects model (DerSimonian-Laird method) (23).

Assessment of publication bias

Assessment of publication bias was conducted using the Begg and Mazumdar's rank correlation test and the funnel plot method (23, 42). A P -value < 0.05 for Begg and Mazumdar's test indicated significant statistical publication bias. Moreover, Duval and Tweedie 'trim and fill' method was performed to investigate the potential influence of a reporting bias (43).

Sensitivity analysis

Sensitivity analysis using the leave-one-out method was performed to determine the effect of each study on the pooled results (37). In addition, if I^2 values were higher than 50%, the 'hetred' package in Stata software (version 11; Stata Corp., College Station, TX, USA) was used to assess the change in between-study heterogeneity when one or more outlier studies were excluded from the calculations (44). Furthermore, subgroup analysis was performed to assess the effectiveness of each PNF exercise or pattern on pain and functional disability improvement in patients with LBP.

Data synthesis

Considering that the selected articles shared basic methodological aspects (e.g., all were clinical trials with a comparison group), and that original studies included individuals with similar characteristics (e.g., patients with LBP), they were pooled for the meta-analysis. Stata software (version 14; Stata Corp., College Station, TX, USA) was employed to perform the meta-

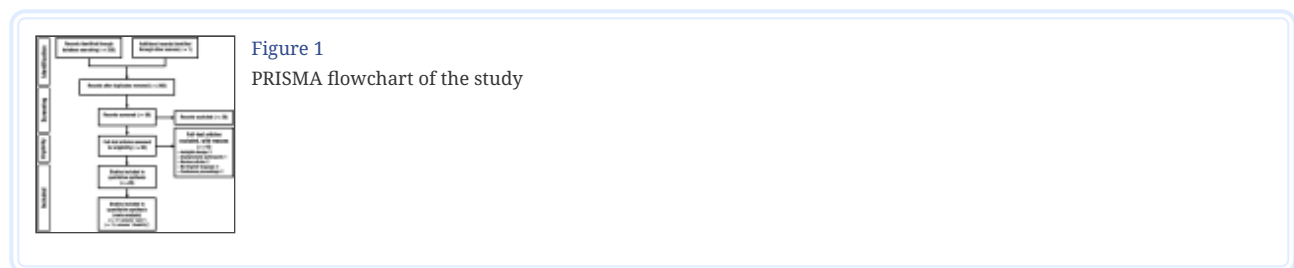
analysis for the primary outcomes of this study. When the trials were sufficiently homogenous, a meta-analysis was performed for the time points of short (<3 months after randomization), intermediate (3-12 months after randomization), and long-term (≥ 12 months after randomization) follow-up. If there were multiple time points at which the primary outcomes were measured within the same category, a time point was utilized closest to the end of the treatment, 6 months, or 12 months (34).

The overall quality of the evidence and strength of the recommendations were assessed using GRADE, which was applied for those primary outcomes included in the meta-analysis (45). The downgrading process was performed considering 5 domains, including study limitations (e.g., methodological quality/risk of bias), inconsistency (e.g., heterogeneity between trials findings), indirectness of evidence (including other populations or use of surrogate outcomes), imprecision (e.g., small sample size) and reporting bias (e.g., publication bias). The quality of evidence was classified as (i) high quality: further trials are unlikely to change the estimate of effect; the PEDro scale indicated no risks of bias and all domains in the GRADE tool were fulfilled; (ii) moderate quality: further trials are likely to have a significant impact on the estimate of effect, and one of the domains in the GRADE tool was not fulfilled; (iii) low quality: further trials are likely to change the estimate; 2 of the domains were not fulfilled in the GRADE tool; and (iv) very low quality: we are uncertain about the estimate of treatment effect; 3 of the domains in the GRADE tool were not fulfilled (45). The assessment of the strength of recommendations for the primary outcomes was by the quality of evidence, patient value preferences, the balance between desirable and undesirable effects, and wise use of resources (45). Differences in the strength of recommendation were discussed in a consensus meeting.

Results

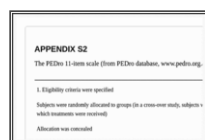
The flow of studies through the review

Figure 1 illustrates the search results. A total of 256 studies were retrieved from different databases, and 30 full-text articles were screened for eligibility. It is worth mentioning that one study was not a controlled/clinical study, and two studies used single-subject experimental research designs (46-48). Moreover, one study included healthy subjects, and two studies were published in the Korean language (49-51). Regarding the study design, two studies were review articles, and two studies were conference proceedings (14, 16, 52, 53). Therefore, 20 studies met our inclusion criteria and were finally considered for this review (7, 18, 21, 27, 29, 54-68). In total, three studies examined three or four-arm comparisons, and other studies compared PNF training with any other physical therapy intervention (i.e., educational booklet, exercise, electrotherapy, and manual or release techniques (7, 18, 21, 27, 29, 51, 54-57, 60-67). Out of 20 studies, 12 articles compared PNF training with different forms of exercises (i.e., core stabilization, strengthening, McKenzie exercise, and ball exercise (18, 27, 44, 54, 55, 57, 60, 62-64, 66-68).



Overview of participant characteristics

Appendix S3 provides a summary of the number of included participants as well as their health status, age, and gender. A total of 965 patients with LBP were originally included in the 20 studies, and 12 studies recruited chronic LBP (CLBP) patients (7, 21, 29, 51, 56, 57, 61, 62, 64, 65, 68). Furthermore, one study enrolled mechanical LBP patients, one study included patients with post-partum lumbopelvic pain, two studies recruited non-specific LBP patients, and one study recruited acute and subacute patients with intervertebral disc injury (27, 54, 63, 66, 67). Franklin et al. (2013) and Kotteeswaran et al. (2014) did not provide detailed information on the LBP sub-classification (55, 59). In three studies, female patients were included, and two studies enrolled only male patients with LBP (21, 27, 29, 60, 67). The mean age of the population in the eligible studies at baseline ranged from 22.53 to 60.80 years. Moreover, six trials provided limited information regarding demographic characteristics (27, 57, 59, 61, 65, 68). Finally, sample size determination was only described in three trials (7, 56, 64).



APPENDIX S2

The PEDro 11-item scale (from PEDro database, www.pedro.org.au)

Methodology considerations and outcome measures

Out of 20 studies, nine articles have been conducted in India, whereas the remaining clinical trials were from South Korea (51, 54, 62, 68), Greece, Iran, Poland, and Thailand (7, 21, 27, 29, 55-57, 59-61, 63-67) [Appendix S3]. Furthermore, five of the included studies were randomized controlled trials, and the other 15 were randomized clinical trials (7, 18, 21, 27, 29, 54-68). The PNF techniques were used in 12 studies, whereas the PNF patterns were utilized in five studies, and three studies used both PNF techniques and PNF patterns (7, 18, 21, 27, 29, 54-68). The most common PNF techniques used in the eligible trials were the combination of isotonic and rhythmic stabilization (7, 21, 27, 29, 55, 57, 58, 60, 63, 64, 66, 67). Except for one study, all other studies have evaluated pain intensity in patients with LBP (7, 18, 21, 27, 29, 54-68). Additionally, 13 trials have investigated functional disability as the primary outcome (7, 18, 21, 27, 29, 55, 56, 58, 60, 63-65, 67). Measurement of spine ROM was performed in seven studies (18, 21, 29, 55, 56, 60, 63). In the majority of the retrieved studies, total treatment duration varied from three to six weeks (7, 18, 21, 27, 29, 54-64, 67, 68). However, in a study performed by Mistry et al. (2015), treatments were delivered for 10 sessions over 6 months. The LBP patients generally performed three sets of 15 repetitions of each PNF exercise (7, 21, 27, 29, 54-58, 60, 63, 65).

Quality assessment

Table 2 tabulates the results of the quality assessment. The level of inter-rater agreement of quality assessment was good ($\kappa=0.76\pm 0.22$). In terms of quality assessment, a median PEDro score of 4 (interquartile range=2-5) indicated a fair methodological quality of the included studies. More specifically, of the 20 trials, three studies were of high quality according to the PEDro scale (7, 29, 64). In total, eight studies were rated as fair quality, and nine studies (18, 21, 27, 29, 54-62, 65, 67, 68) were graded as low quality. Criteria that were not met most frequently were allocation concealment, blinding of patients, therapists, and assessors, and intention-to-treat analysis. The percentage of trials that met each of the PEDro scale items is presented in Table 2.

Item	Number of studies
1. Randomized	5
2. Double-blind	5
3. Allocation concealment	5
4. Blinding of patients	5
5. Blinding of therapists	5
6. Blinding of assessors	5
7. Intention-to-treat analysis	5
8. Parallel design	5
9. Concurrent	5
10. Follow-up	5
11. Loss to follow-up	5

Table 2

Study quality according to the PEDro scale

Effects of interventions

Since the study carried out by Kofotolis et al. (2008) had more than two groups, the present study was divided into two studies (rhythmic stabilization plus transcutaneous electrical nerve stimulation [TENS] vs. TENS alone) (29). In addition, the study conducted by Kofotolis and Kellis (2006) was divided into two studies (rhythmic stabilization vs. normal daily activities, and a combination of isotonic vs. normal daily activities) (21).

Effects on back pain intensity

Totally, 15 out of 20 trials reported back pain intensity at baseline and short-term follow-up (7, 21, 27, 29, 54-60, 62, 63, 67, 68). Moreover, two trials evaluated back pain at baseline and intermediate-term follow-up, and one study did not assess back pain intensity (18, 65, 68). In addition, two trials did not report the number of patients in each group or sufficient data on back pain intensity to enable statistical pooling (61, 66). Therefore, three studies were excluded from the meta-analysis (18, 61, 66). The PNF training was found to be effective in alleviating back pain intensity at short-term follow-up, compared to other physical therapy interventions (SMD=-2.06; 95% CI=-3.24 to -0.88) [Figure 2A]. However, in the two studies that assessed back pain intensity at intermediate-term, the effect size of PNF training was large but not significant (SMD=-2.80) with a range from -6.67 to 1.07 [Figure 2A] (64, 65). Finally, the summary measure indicated large significant between-group differences on mean change scores for back pain intensity at post-treatment (SMD=-2.14; 95% CI=-3.23 to -1.05) [Figure 2A]. The effect size of each study is presented in Figure 2A.

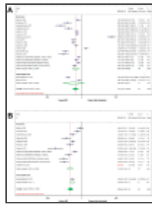


Figure 2

Forest plot of comparison: PNF training versus all other physical therapies, outcome: A; pain, and B; disability. =effect size for one trial; horizontal line=95% confidence interval; =pooled effect size for all trials

Furthermore, the result demonstrated that the effect of PNF training on improving back pain intensity in patients with LBP was clinically important (SMD=-2.14). Standard statistical tests for statistical heterogeneity indicated that there was considerable statistical heterogeneity in back pain intensity among the eligible studies ($\chi^2=519.35$, $P=0.00$, $I^2=96.5\%$).

Effects on functional disability

Out of 20 trials, 10 studies reported functional disability scores at baseline and short-term follow-up (7, 18, 21, 27, 29, 55, 56, 58, 60, 63). Only one randomized clinical trial examined disability at baseline and intermediate-term follow-up (64). Moreover, nine studies did not evaluate disability (54, 57, 59, 61, 62, 65-68). The results of the meta-analysis showed that PNF training was effective in reducing disability at short-term (SMD=-2.74; 95% CI=-3.53 to -1.96) and intermediate-term (SMD=-2.24; 95% CI=-2.80 to -1.68) follow-ups, compared to other physical therapy interventions [Figure 2B]. The overall pooled SMD showed large significant between-group differences on mean change scores for disability at post-treatment (SMD=-2.68; 95% CI=-3.36 to -2) [Figure 2B]. The effect size of each study is presented in Figure 2B.

Moreover, the result showed that the effect of PNF training on improving functional disability in people with LBP was clinically important (SMD=-2.68). Standard statistical tests for heterogeneity demonstrated that there was considerable statistical heterogeneity in functional disability among the selected trials ($\chi^2=81.93$, $P=0.00$, $I^2=86.6\%$).

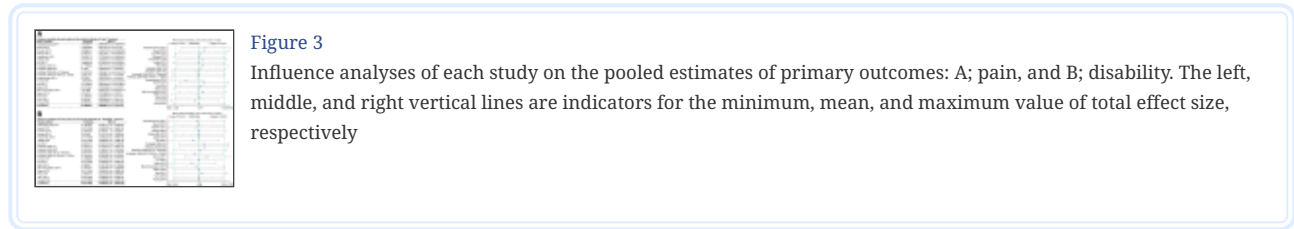
Effects on spine ROM

The meta-analysis was not performed for the secondary outcome (i.e., spine ROM) since the eligible studies used various instruments for measuring sagittal spine ROM. Therefore, a qualitative synthesis of results was performed. A recently published study compared PNF techniques (rhythmic stabilization and combination of isotonic) with core stabilization exercises performed on a Swiss ball (63). The result indicated that PNF techniques and core stabilization exercises were effective in improving lumbar flexion (mean difference [MD]=8.5°±0.7°; and MD=10.2°±0.6°, respectively) and extension (MD=5.2°±0.2°; and MD=5.2°±0.7°, respectively) ROM in patients with CNLBP (63). Hosseinifar et al. (2016) showed that PNF patterns significantly increased lumbar flexion (MD=1.8±0.75 cm) and extension (MD=0.87±0.09 cm) ROM after four weeks (56) [Table 2]. In another study, Park and Seo (2014) evaluated the effects of scapular and pelvic PNF patterns on lumbar sagittal plane ROM (18). The result of the present study indicated that lumbar flexion (MD=1±1.6 cm) and extension (MD=12±1 cm) significantly increased after the intervention in the experimental group (18). However, the difference in lumbar ROM in the comparison group was not significant after the intervention ($P>0.05$) (18). A study conducted by Franklin et al. (2013) reported that the combination of isotonic of trunk flexors significantly improved trunk flexion (MD=2.83±0.18 cm) and extension (MD=1.34±0.04 cm) ROM in patients with chronic LBP (55). Furthermore, Kumar et al. (2011) demonstrated that the combination of isotonic combined with conventional physical therapy can increase lumbar flexion (MD=3.51±1.09 cm) and extension (MD=1.05±0.25 cm) ROM, compared to conventional physical therapy alone in recurrent mechanical CLBP patients (60). There is also evidence that rhythmic stabilization technique and rhythmic stabilization technique combined with TENS can increase lumbar flexion (MD=2.8±3.2 cm; and MD=1.6±1 cm, respectively) and extension (MD=3±0.4 cm; and MD=7±4.1 cm, respectively), compared to TENS alone or placebo treatment at eight-week follow-up (29). Finally, Kofotolis and Kellis (2006) compared two PNF techniques (rhythmic stabilization and combination of isotonic) with lumbar flexion-extension ROM (21). After eight weeks, both rhythmic stabilization and combination of isotonic groups showed significant improvements (MD=8±0.1 cm, and MD=8.1±2.8 cm, respectively), compared to the control group (21).

Sensitivity analysis

The impact of individual trials on the overall meta-analysis estimates was evaluated. The results of leave-one-out sensitivity analysis revealed that the eligible trials had influences on the pooled SMDs of pain outcome ranging from -2.98 (95 % CI=-3.72 to -2.24) after excluding the study conducted by Tanvi et al. (2013) to -2.51 (95 % CI=-3.28 to -1.73) after excluding the study performed by Areeudomwong et al. (2017) (7) [Figure 3A]. Moreover, for the outcome “functional disability”, the sensitivity analysis demonstrated that the eligible studies had also an influence on the pooled SMDs ranging from -2.87 (95 % CI=-3.52 to

-2.22) after excluding the study by Malla et al. (2018) (63) to -2.45 (95 % CI=-3.07 to -1.82) after excluding the study carried out by Kumar et al. (2011) (60) [Figure 3B].



The sensitivity analysis for pain outcome by the ‘hetred’ command showed that 10 studies should be excluded to reduce the *I*² to <50% (7, 54-56, 58-60, 62, 64, 67) [Table 3A]. For the outcome “functional disability”, the ‘hetred’ command indicated that five studies were the source of heterogeneity (21, 29, 58, 60, 63) [Table 3B].

Study	Drop	I ²
A; Pain		
Kotzevski et al. (2014)	1	93
Saari et al. (2012)	2	96
Marcusson et al. (2011)	3	98
Stroobant et al. (2017)	4	99

Table 3

Sensitivity analysis for heterogeneity

Subgroup analyses of PNF types were performed for the primary outcomes. Due to the limited number of studies in each PNF type, a conclusive result could not be achieved. However, the results showed that a combination of PNF techniques and patterns had a greater beneficial effect on pain reduction than a PNF technique or pattern alone. Furthermore, the contract-relax technique improved functional disability more than other PNF techniques or patterns in patients with LBP [Figure 4].



Quality of evidence and strength of recommendation

The quality of evidence for the primary outcomes was investigated using the GRADE tool [Table 4]. For the outcome “pain”, there was low-quality evidence (downgraded due to study limitations (i.e., poor quality studies), inconsistency, publication (or reporting) bias, and upgraded due to large effect size) that PNF training could decrease pain in patients with LBP. For the outcome “functional disability”, there was low-quality evidence (downgraded due to study limitations (i.e., poor quality studies), inconsistency, publication (or reporting) bias, and upgraded due to large effect size) that PNF training could improve functional disability in patients with LBP. The strength of recommendation was weak for the primary outcomes (i.e., pain and functional disability).

*Downgraded one level as the majority of studies scored 1 on the PEDro scale
†Downgraded one level as the I ² value was > 50% (23)
‡Upgraded one level due to reported publication bias (7)
§Upgraded one level due to large effect size (6)
The quality of each study is indicated by the size of the boxes and the number of the boxes were filled (for each different level of evidence)

Assessment of publication bias

Evidence of publication bias was found for pain and disability outcomes as the funnel plots showed asymmetries [Figure 4]. Furthermore, the Begg and Mazumdar’s rank correlation tests also demonstrated that publication bias was significant for pain ($z=2.24, P=0.02$) and disability ($z=2.54, P=0.01$) outcomes. However, the application of the trim and fill method did not identify any missing study, and therefore, left the pooled estimates unchanged.

APPENDIX S1. Search strategy for PubMed/Medline (NLM).

((("muscle stretching" AND exercise*) OR (static AND stretching) OR (passive AND stretching) OR (relaxed AND stretching) OR (static-passive AND stretching) OR ("static passive" AND stretching) OR (isometric AND stretching) OR (active AND stretching) OR (static-active AND stretching) OR ("static active" AND stretching) OR (ballistic AND stretching) OR (dynamic AND stretching) OR ("proprioceptive neuromuscular facilitation") OR (PNF) OR (PNF AND stretching) OR ("proprioceptive neuromuscular facilitation" AND stretching)) AND ((low* AND "back pains") OR (low* AND "back pain") OR ("low back" AND pain*) OR ("lower

stretch tolerance have been proposed in the literature as possible mechanisms of increasing ROM following the application of the PNF techniques (17, 77).

The second main result of this review is that considerable statistical heterogeneity was evident across the eligible trials for the primary outcomes. The possible explanations for this considerable heterogeneity may be the differences in the included trials regarding the control intervention, differing patients' baseline characteristics, number of cases and controls, and variations in the dosage and duration of treatment.

To evaluate the presence of publication bias in this review, two funnel plots were generated [Figure 4]. The Begg and Mazumdar's rank correlation tests showed that publication bias was evident in the meta-analysis of the selected studies. The possible explanations could be the quality of included studies, non-published trials with negative results, or those showing no different findings, small sample size, and the number of trials in each separate meta-analysis.

A narrative review conducted by Smedes et al. (2016) recommended that well-designed clinical trials that are comprehensively detailed are required to investigate the efficacy of PNF training in rehabilitation (16). In a similar vein, our study showed that only 20% of total eligible studies were deemed high quality, and the majority of the included studies only evaluated the short-term effects of PNF training on pain and disability in patients with LBP (7, 29, 56, 64).

There are some limitations to our systematic review that should be acknowledged. The results of the studies included in this review mainly refer to short-term changes after intervention. Therefore, it is impossible to draw robust conclusions about the efficacy of PNF training at long-term follow-up. Moreover, a limited number of clinical trials were available to investigate the effectiveness of PNF training on LBP at intermediate-term follow-up. This limits the conclusions that can be derived from the meta-analyses. In addition, the majority of selected studies did not conduct a power analysis to estimate the required sample size. Therefore, the external validity of the results may be compromised. The eligible studies presented several methodological limitations. The most frequent limitations were related to non-blinding methods, allocation concealment, and intention-to-treat analysis. Finally, database searching was limited to English language articles, which might be suggestive of publication bias.

Future randomized controlled trials should consider the methodological limitations observed in the trials selected for this systematic review in order to improve their methodological quality. Moreover, future studies including an appropriate number of participants should investigate intermediate- and long-term follow-up of patients with LBP treated by PNF training.

According to the clinical trials included in this systematic review, it can be concluded that although the effects of the primary outcomes were large, there was the low quality of evidence revealing the positive effects of PNF training on back pain intensity and functional disability in patients with LBP. The strength of recommendation was also weak. In the current systematic review, the statistical heterogeneity analysis showed that there was considerable statistical heterogeneity among the eligible trials for the primary outcomes (χ^2 with $P < 0.05$ and $I^2 > 75\%$ for both primary outcomes). Due to the lack of sufficient data on lumbar ROM, a formal meta-analysis was impossible. However, a qualitative synthesis of evidence indicates that PNF training can improve lumbar spine ROM in the population with LBP. Further high-quality randomized controlled trials should assess the long-term effects of PNF training on back pain intensity, functional disability, and lumbar ROM in patients with LBP. Finally, it is recommended that clinicians use a combination of PNF techniques and patterns in patients with LBP to improve back pain.

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Mohammadreza Pourahmadi, PhD, PT,¹ Mohammad Sahebalam, BSc, PT, MSc Student,¹ and Rasool Bagheri, PhD, PT²

¹Department of Physiotherapy, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran

²Neuromuscular Rehabilitation Research Center, Semnan University of Medical Sciences, Semnan, Iran

Corresponding Author: Mohammadreza Pourahmadi, Department of Physiotherapy, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran. Email: pourahmadipt@gmail.com

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