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Bibliographic Data	
Authors	Louw A, Zimney K, Puentedura EJ, and et al.
Title	The efficacy of pain neuroscience education on musculoskeletal pain: A systematic review of the literature
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Other information if relevant	

Methods	
Aim of study	To evaluate the effectiveness of pain neuroscience education (PNE) treatment on pain, function, disability, psychosocial factors, movement, and healthcare utilization in individuals with chronic musculoskeletal (MSK) pain.
Design	Narrative systematic review of randomized clinical trials

PICOS	
Population from which participants are drawn	Adults 18 years or older with chronic musculoskeletal (MSK) pain resulting from multiple pain conditions such as low back pain, chronic fatigue syndrome, fibromyalgia, lumbar radiculopathy awaiting lumbar surgery, and chronic neck pain. Fibromyalgia studies were excluded from this critique.
Intervention being evaluated	Pain neuroscience education or therapeutic neuroscience education is an educational model of teaching that aims to explain to patients the biological and physiological processes involved in a pain experience and, more importantly, defocus the issues associated with the anatomical structures. Duration of each session ranged from 30 minutes to 4 hours and frequency ranged from a one-time educational session to multiple sessions spread out over the course of treatment.
Comparison or control intervention	Usual medical care, various group education classes, back anatomy education, exercise classes, mobilization or manipulation, The Back Book, dry-needling, and aquatic exercise.
Outcomes	Primary outcomes of the included studies were pain, function, psychosocial factors, movement, and healthcare utilization. Pain and function were the primary outcomes evaluated in this review. No limitation was set on specific measurement tools utilized to examine effect on these outcomes.

Study types	Only randomized controlled trials, excluding trials with other study designs

Study selection	
Search date of literature review	2002 through August 2015
Databases in literature search	Biomed Central, BMJ.com, CINAHL, the Cochrane Library, NLM Central Gateway, OVID, ProQuest (Digital Dissertations), PsycInfo, PubMed/Medline, ScienceDirect, and Web of Science. Reference lists of the selected articles were reviewed for additional references not identified in the primary search.
How authors assessed study quality (risk of bias and other considerations	Critical appraisal of each included study was conducted by determining the level of evidence on the Australian National Health and Medical Research Council (NHMRC) Hierarchy of Evidence (National Health and Medical Research Council, 1999). Methodological quality of the design and reporting of each study was assessed against the PEDro scale. A high-quality study was defined as scoring positive on a minimum of 50% (5/10) of the 10 items.
Additional information if relevant	The clinical relevance of each of the pooled results was also assessed. Mean changes between pre- and post-treatment (and 95% CI) were calculated for the RCTs. Pain reduction of at least 20% was considered as clinically important.

Results	
Number of studies screened	25,911 records were screened
Number of studies selected for analysis of results	13 RCTS were selected with 734 participants. Eight studies were from the current review search and 5 studies were from the previous 2011 review. Included studies were published between 2002 and 2015. Study sample sizes ranged from 12 to 105 participants. Mean age was 41.7 years and 70% of subjects were female.
Whether authors elected to perform meta-analysis to pool study results statistically and type of meta-analysis done (fixed effect or random effects, heterogeneity, etc)	No meta-analyses were conducted. Due to the heterogeneous nature of the systematic review's outcome measures and differing control groups, results were posted in narrative form. Outcomes were defined as "positive" (experimental group obtained a significantly greater improvement than the control group), "neutral" (there were no statistically significant differences between the groups), or "negative" (the control group obtained a significant greater improvement than the experimental group). An alpha of $p < 0.05$ was used to define a significant outcome measure.

Quality of studies as assessed by authors	All the studies scored a 6/10 or higher on the PEDro scale demonstrating good methodological quality. Five studies scored a 9 or 10 on the PEDro scale. The blinding of subjects and those that administered the therapy were the most common criteria not met. All 13 trials met the criteria for adequate randomization, allocation concealment, and outcome measures were similar at baseline. All 13 trials attempted to blind the outcome assessor, but only 6 studies blinded the participants. Eleven trials provided adequate information about missing data and kept this below 15% for outcomes. All included RCTs reported between group differences and effect sizes.
Effect sizes reported for primary outcomes (mean differences, standardized mean differences, response ratios, etc)	- Data from one trial (57 participants) showed greater pain reduction and greater improvement in disability in the PNE group compared with usual care. At one month, the decrease in pain on the Numeric Pain Rating Scale (NRS) was significantly different between the 2 groups ($P < 0.01$ mean difference, 1.5 pts. 95% CI: 0.7-2.3), and at one year follow-up, this significant difference in pain reduction was maintained (MD=1.9, 95% CI: 1–2.8). Both groups improved in disability with mean improvement of the PNE group over usual care of 3.9 points on the Roland Morris Disability Questionnaire (RMDQ) (95% CI: 2.0–5.8). For both pain and disability, these were clinically meaningful differences. - One trial (41 participants) compared individually delivered PNE to group delivered PNE. Both groups showed significant and clinically important reductions in pain on the NRS. Individual education group showed a treatment effect of 3.1 (95% CI: 1.8–4.2) on the NRS at the conclusion of the 4-week intervention and the group education group showed a 2.7 (95% CI: 1.6–3.9) reduction on the NRS. Even though group differences were statistically significant, they were not clinically important (MD = 1.0 (95% CI: 0.3–2.0). For disability, between-group change favored the individual PNE group with a mean effect of 2.4 (95% CI: 0.8–4.2) on the RMDQ. - One trial (94 participants) compared PNE/cognitive functional therapy with a manual therapy and exercise group. Both groups showed significant improvement in pain on the NRS with the PNE group showing statistically ($p < 0.001$) superior outcomes compared with the manual/exercise group at 3 and 12 months follow-up. The mean difference between groups for 3 and 12 months, respectively, for the NRS were 2.1 (95% CI: 2.7–1.4) and 1.3 (95% CI: 2.1–0.5), both statistically and clinically meaningful results. Both groups showed significant improvement in function over time on the Oswestry Disability Index (ODI). The PNE group had a significant ($p <0.001$) mean difference improvement in function of −9.7 (95% CI: −12.7 to −6.7) at 3 months and −8.2 (95% CI: −12.6 to −3.8) at 12 months compared with the manual/exercise group ODI score. These ODI scores are just short of the MCID of 10 points. The PNE group showed an overall ODI improvement over 12 months of 13.7 (95% CI: 11.4–16.1; $p < 0.001$) which was clinically significant.

Effect sizes reported for primary outcomes (mean differences, standardized mean differences, response ratios, etc) continued	- Data from one trial (58 participants) showed greater improvement in disability in the PNE group compared with the back education group. The PNE group improved in RMDQ by 2 points (95% CI: 0.4–3.6) compared with the control group post-treatment. - Analysis showed that both groups in one trial (79 participants) had pain reductions on the NRS and improved disability on the Patient-Specific Functional Scale (PFSF) over time, but there was no significant effect between groups on pain or disability with reading either the PNE book or advice from the control book. Increased knowledge about pain biology in the PNE group over advice group ($p < 0.01$) was seen with an effect size of Cohen $d = 1.7$. - Data from one trial (62 participants) showed greater pain reduction in the PNE group compared with the control group at 3 months, but not at 6 weeks. Visual analog (VAS) change at 3 months for PNE group was -25.4 ± 26.7 compared with the control group (-6.6 ± 30.7) and the difference (MD = 18.8) between groups was statistically and clinically important. Results showed there was no statistically significant or clinically important difference between the PNE group and the control group on improving disability at 6 weeks ($p = 0.83$) or 3 months ($p = 0.09$). A greater percent of participants in the PNE group reported benefits for functional disability at 6 weeks and 3 months with only the 3 months follow-up showing significant ($p = 0.034$) findings.
Effect sizes reported for additional outcomes	Healthcare Utilization - In one trial, at 1 year follow–up, the PNE group made 3.6 ± 2 (mean ± SD) healthcare center visits for low back pain, which was statistically less ($p < 0.001$) than the usual care group who made 13.2 ± 5 visits. - In another trial, overall healthcare costs for medical treatment at 1 year follow-up was less for the PNE group (mean = $2,678.57, SD =$3,135.30) compared with the usual care group (mean= $4,833.48, SD = $3,256.00) $p = 0.007$).

Authors' Conclusions	
Key conclusions of study authors	- The results of this updated systematic review of PNE for chronic MSK disorders supports strong evidence for the use of PNE in reducing pain, improving patient knowledge of pain, improving function and lowering disability, reducing psychosocial factors, enhancing physical movement, and minimizing healthcare utilization. Even though the included studies were heterogeneous in nature, no PNE study showed any outcome to be worse than the control groups, thus implying a significant risk–benefit ratio in favor of PNE. - The quality and number of the studies is substantially increased in the current review compared to the past update by Louw (2011). This review used only higher-level RCTs, and no lower level studies were included. This review provided high quality evidence. - Only three studies reported one year outcomes, and all three studies showed a significant reduction of healthcare utilization 1 year after PNE. - This review strongly suggests that the combination of PNE with movement, be it passive and/or active, may be key in the success of PNE. PNE education alone may not be effective in reducing pain ratings or sufficient for change. - In the future, there is a need to focus on more long-term studies on the efficacy of PNE, and the combination of PNE and movement in order to measure its true impact.
Comments by DOWC staff	- Based on 5 high quality and relevant studies that meet our criteria, this review found that PNE had clinically important effects for pain reduction, improved disability, and reduced healthcare utilization compared with either usual care, exercise, other education or another control group in chronic MSK disorders. - The premise of pain neuroscience education is to have patients view their pain differently or reconceptualize their pain. The patient may still experience pain, but they equate it to sensitization of the nervous system versus the health of the tissues. This reconceptualization imparts a message of "despite the pain," it is worthwhile to move, exercise, and continue in daily activities and not necessarily seek additional care for the sensitization (pain). This behavior change is the key to changing any patient's healthcare status, and is reflected in healthcare utilization. PNE was shown to be effective in reducing healthcare utilization. Results from two studies demonstrated significantly reduced healthcare visits and costs for medical treatment for patients one year after PNE. - The PEDro scale does not downgrade the quality of the trial due to imprecision related to a small sample size. Some of the included studies were truly small and imprecise, and would have scored lower on the PEDro scale had sample size been taken into consideration.

Comments by DOWC staff (continued)

- This review highlights the possible differences between PNE as a stand-alone treatment versus PNE combined with exercise and/or manual therapy. In five studies, patients received only PNE, but none of these studies produced decreased pain ratings, whereas 5 of the 6 studies that combined PNE with a physical intervention were able to produce a significant reduction in pain ratings. This suggests that PNE may not be effective alone and is most successful when combined with active interventions.
- Thus, while there is some evidence for the effectiveness of PNE for MSK disorders, there is no conclusive evidence that it is superior to other forms of treatment or exercises.
- The non-specific effects of personalized attention given in individualized delivered PNE may have contributed to the overall effectiveness of the intervention. It is noteworthy to mention that none of the control subjects received the level of attention given the PNE participants.
- The trials included in this review showed some variability in the populations included, but this does not appear to affect the generalizability of the findings.
- The main limitation of this review was the heterogonous studies regarding design, patient populations, outcome measures, and educational delivery methods which prevented meta-analyses from being conducted. Other limitations included some trials with small sample sizes (3 studies had less than 40 participants), and lack of longer follow-up periods.
- Only 3 of the trials reported long-term outcomes at one year, which would be important to consider for patients with chronic MSK pain.
- Minor or no adverse events were reported in the included trials.
- Future studies should include larger studies in order to reduce wide confidence intervals resulting in nonsignificant results, and some standardization of the factors that lead to high heterogeneity among the studies.

Assessment by DOWC	
Overall assessment as suitability of evidence for the guideline ☐ High quality ☒ Adequate ☐ Inadequate	Adequate quality systematic review supporting good evidence that pain neuroscience education combined with a physical intervention is more effective in reducing pain, improving disability, and reducing healthcare utilization compared with either usual care, exercise, other education or another control group for the treatment of patients with chronic musculoskeletal pain.
If inadequate, main reasons for recommending that the article not be cited as evidence	

Additional references if relevant

- Louw A, Diener I, Butler DS, Puentedura EJ. 2011 The effect of neuroscience education on pain, disability, anxiety, and stress in chronic musculoskeletal pain. Archives of Physical Medicine and Rehabilitation 92: 2041–2056.