# **REVIEW ARTICLE**

# Trigger Point Injections for Chronic Non-Malignant Musculoskeletal Pain: A Systematic Review

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#### ABSTRACT-

*Objective.* This systematic review assessed the available published evidence on the efficacy and safety of using trigger point injection (TPI) to treat patients with chronic non-malignant musculoskeletal pain that had persisted for at least 3 months.

*Methods.* All published systematic reviews or randomized controlled trials detailing the use of TPI in patients with chronic, non-malignant musculoskeletal pain (persisting for >3 months) were identified by systematically searching literature databases and the Websites of various health technology assessment agencies, research registers, and guidelines sites up to July 2006.

*Results.* Although no systematic reviews were identified, 15 peer-reviewed randomized controlled trials met the inclusion criteria. However, deficiencies in reporting, small sample sizes, and marked inter-study heterogeneity precluded a definitive synthesis of the data. TPI is a safe procedure when used by clinicians with appropriate expertise and training. It relieved symptoms when used as a sole treatment for patients with chronic head, neck, shoulder, and back pain or whiplash syndrome, regardless of the injectant used, and may be a useful adjunct to intra-articular injection in the treatment of osteoarthritis pain. Although the addition of TPI to stretching exercises augments treatment outcomes, this was also true of other therapies such as ultrasound and laser.

*Conclusion.* The efficacy of TPI is no more certain than it was a decade ago as, overall, there is no clear evidence of either benefit or ineffectiveness. The only advantage of injecting anesthetic into trigger points may be to reduce the pain of the needling process, which may not be an insignificant benefit.

Key Words. Systematic Review; Myofascial Trigger Point; Myofascial Pain Syndrome; Chronic Pain; Trigger Point Injection

#### Introduction

C hronic pain affects between 10% and 20% of the North American population, with 45% of Americans requiring treatment each year for pain at a cost of US\$85–90 billion [1]. Approximately

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47% of chronic pain is of musculoskeletal origin, which covers many diagnostic categories including whiplash, fibromyalgia, myofascial pain syndrome, tension headache, and low back pain [2,3].

Trigger points, which are usually associated with myofascial pain syndrome, are hyperirritable areas of tissue that are tender when compressed and can give rise to referred pain [4]. They can cause muscle spasm, stiffness, shortening, and fatigue, which hinder muscle lengthening, impair muscle coordination, and reduce range of motion and muscle strength [5–9].

Numerous methods, non-invasive such as stretching, massage, ischemic compression, laser therapy, heat, acupressure, ultrasound, and pharmacological treatments have been used to alleviate chronic musculoskeletal pain, but no single strategy has proved universally successful [5,6,10,11]. Of the invasive therapies, trigger point injection (TPI) is the technique most commonly used [12]. TPI, or direct wet needling, involves injecting fluid directly into the trigger point [6]. The main objective of TPI is to inactivate the trigger point, thereby reducing pain and restoring function. TPI is most often used to facilitate physical therapy, but is also employed for fast pain relief or as a diagnostic tool for determining whether pain originates from trigger points [10,12,13]. Other needling therapies include indirect wet needling in which fluid is injected into the skin or subcutaneous tissue over the trigger point; direct dry needling where a needle is aimed directly at the trigger point; and indirect dry needling in which a needle is placed superficially or deep into classic acupuncture points, or over the tender spot, but not directly into the trigger point [6,14].

Injecting a trigger point is painful, but addition of a local anesthetic to the injected fluid can reduce the pain and irritation caused by the needling [10,15]. However, this does not alleviate the pain caused by the brief, but strong, local twitch response unless the anesthetic is used as a nerve block and injected prior to treatment [16]. A variety of fluids have been injected into trigger points including water, saline, local anesthetics, vitamin B solutions, long-acting corticosteroids, acetylsalicylate, ketorolac, and botulinum toxin [9,12,17].

Currently, opinion on the optimal technique and treatment regimen for TPI varies between practitioners and is largely based on clinical experience [10]. Although the effects of needling on trigger points have been demonstrated at the molecular level [18], the etiology and pathogenesis of trigger points have yet to be elucidated and the precise mechanism by which TPI inactivates the trigger point is still unknown. This uncertainty, together with the fact that many consider dry needling to be as effective as TPI, has led to the suggestion that TPI has little value beyond placebo effect. Therefore, the aim of this review is to assess the available published evidence on the efficacy and safety of using TPI to treat patients with chronic non-malignant musculoskeletal pain.

# Methods

This report is an updated précis of a systematic review conducted by the Health Technology Assessment Unit of the Alberta Heritage Foundation for Medical Research on behalf of the Alberta Health Ministry [19].

# Inclusion Criteria

Full peer-reviewed systematic reviews or randomized controlled trials (RCTs) detailing the use of TPI in patients with chronic non-malignant pain of musculoskeletal origin (including non-malignant disorders of the skeletal system such as osteoarthritis) that had persisted for at least 3 months [20] were included for analysis. Studies on patients with pain secondary to a defined systemic disease, such as cancer or diabetes, were excluded unless the data subset for the patients with chronic musculoskeletal pain could be separated from the aggregate data. An article was deemed to be a systematic review if it met the five criteria outlined by Cook et al. [21]: 1) focused clinical question; 2) explicit search strategy; 3) use of explicit, uniformly applied selection criteria; 4) use of a quality tool to appraise the included studies; and 5) qualitative or quantitative data synthesis. The included studies must have reported at least one posttreatment efficacy or safety outcome common to all the interventions assessed to allow for intergroup comparisons. The comparator intervention was any medical, mechanical, or surgical intervention designed to treat patients with chronic musculoskeletal pain. Placebo and no treatment comparisons were also included, as were studies comparing different treatment regimens within the TPI modality.

## Literature Search Strategy

Relevant studies were identified by searching PubMed, EMBASE, CINAHL, *The Cochrane Library*, Science Citation Index, AMED, BIOSIS, and the Websites of various health technology assessment agencies, research registers, and guideline clearinghouses from root to July 2006. HealthSTAR, SUMSearch, Google.com, Copernic.com, and AlltheWeb.com were also searched for grey literature. No language restriction was applied. The bibliographies of all articles retrieved were manually searched for relevant references that may have been missed in the database searches.

Study selection was conducted by one reviewer (AS) based on study abstracts or, in cases of uncertainty, the full-text article. For studies in which the

 Table 1
 Study quality assessment criteria

|                   | Stu       | dy Characteristic  |
|-------------------|-----------|--|
| Patient selection | A.<br>B1. | Were the eligibility criteria specified?<br>Was randomization performed<br>adequately?       |
|                   | B2.       | Was treatment allocation concealed?  |
|                   | C.        | Were the groups similar at baseline?   |
| Interventions     | D.        | Were the index and control interventions   |
|                   | E.        | explicitly described?<br>Were co-interventions avoided or                                    |
|                   | ⊑.        | comparable?  |
|                   | E         | Was the patient blinded to the   |
|                   | ••        | intervention?  |
| Outcome           | G.        | Was the outcome assessor blinded to the  |
| measurement       | 0         | intervention?  |
|                   | Н.        | Were the outcome measures relevant?  |
|                   | Ι.        | Were adverse events described?   |
|                   | J.        | Was the withdrawal/dropout rate described and acceptable?                                    |
|                   | K1.       | Was a short-term follow-up measurement performed?  |
|                   | K2.       | Was a long-term follow-up measurement  |
|                   |           | performed?   |
|                   | L.        | Was the timing of the outcome  |
|                   |           | assessment comparable in both groups?  |
| Statistics        | Μ.        | Was the sample size for each group   |
|                   |           | described?   |
|                   | N.        | Did the analysis include an intention-to-<br>treat analysis?                                 |
|                   | Ο.        | Were point estimates and measures of variability presented for the primary outcome measures? |

Internal validity criteria: b, e, f, g, h, j, l, n; external validity criteria: a, c, d, i, k; statistical criteria: m, o.

definition of chronic pain was unclear, the authors were contacted to verify whether any of the study participants had chronic pain of less than 3 months' duration when treatment began.

## **Quality Assessment**

Studies were assessed independently by two reviewers (AS, BG) using a quality assessment checklist [22] that was modified by removing two items (1. Was the care provider blinded?; 2. Was compliance acceptable?); blinding of the care provider is often not possible in TPI and compliance is not a relevant issue when TPI is the sole treatment (Table 1). Some instructions were supplemented with more detailed descriptions from Downs and Black [23]. The questions were discussed by the reviewers prior to assessing the studies, and any unresolved disagreements were referred to a third reviewer for mediation. Given the potential dangers of using numerical scores to evaluate the quality of trials [24,25], the studies were scored with a nominal rating scale. The scientific quality of any systematic reviews and metaanalyses identified was to be assessed using the Oxman and Guyatt [26] checklist.

For descriptive purposes, the *quality* of the included studies was categorized as good, moderate, or poor according to the total number of criteria met (Tables 1 and 2).

- Internal validity (N = 9)—good (≥7 criteria met), moderate (4–6 criteria met), poor (<4 criteria met).
- External validity (N = 6)—good (≥5 criteria met), moderate (3 or 4 criteria met), poor (<3 criteria met).

## Data Extraction and Analysis

Safety and efficacy data were extracted by one reviewer (AS) using standardized data extraction forms developed a priori. When overlapping patient groups were reported, only the article quoting the most complete data set was used. Indicators of treatment efficacy included changes in range of motion, pain pressure threshold at the trigger point, and pain intensity. Although assessment of safety was a subsidiary aim of the review, it was considered pertinent to tabulate safety outcomes because TPI is invasive and can, in rare instances, be hazardous.

Data analysis was per-protocol. That is, the denominator used to calculate proportions was the number of patients remaining in the study at each follow-up period and did not include dropouts or withdrawals. The small number of studies and heterogeneity of treatment regimens, inclusion criteria, and follow-up periods made it impossible to conduct a meta-analysis. Instead, the findings of the studies were summarized and the *strength of the evidence* was categorized as follows [27].

- Strong—consistent findings from at least two good quality RCTs.
- Moderate—findings from one good quality RCT, or consistent findings from one good quality RCT and one RCT of lower quality, or consistent findings from multiple RCTs of poor to moderate quality.
- Limited—findings from one moderate quality RCT or one poor quality trial RCT.
- Conflicting—inconsistent findings among multiple RCTs of any quality.

When possible, results were expressed as the relative risk (RR) and risk difference (RD) plus 95% confidence interval (CI) for dichotomous data, and as the weighted mean difference (WMD) and standardized mean difference (SMD) for continuous data using RevMan 4.2.9 (The Cochrane Collaboration 2003). Results were interpreted

|                                     | Quality Criter  | ia  |                |      |              |
|-------------------------------------|-----------------|-----|----------------|------|--------------|
|                                     | Internal Validi | ty  | External Valio | dity | Statistical  |
| Study                               | (9 criteria)    |     | (6 criteria)   | -    | (2 criteria) |
| Head, neck, shoulder, and back pain |                 |     |                |      |              |
| Cheshire et al. [29]                | <b>√</b> 6/9    | Μ   | <b>√</b> 4/6   | М    | <b>√</b> 1/2 |
|                                     | $\times$ 3/9    |     | $\times 2/6$   |      | × 1/2        |
| Esenyel et al. [39]                 | <b>√</b> 5/9    | Μ   | <b>√</b> 4/6   | Μ    | ✓ 2/2        |
| ,                                   | $\times 4/9$    |     | × 2/6          |      |              |
| Ferrante et al. [30]                | <b>√</b> 3/9    | Р   | <b>√</b> 3/6   | М    | √ 2/2        |
|                                     | $\times$ 6/9    |     | $\times$ 3/6   |      |              |
| Ferrante et al. [34]                | ✓ 8/9           | G   | ✓ 4/6          | М    | ✓ 2/2        |
|                                     | × 1/9           |     | $\times 2/6$   |      |              |
| Graboski et al. [40]                | √ 6/9           | М   | √ 4/6          | М    | ✓ 2/2        |
|                                     | × 3/9           |     | × 2/6          |      |              |
| Kamanli et al. [37]                 | √ 3/9           | Р   | √ 4/6          | М    | <b>√</b> 1/2 |
|                                     | × 6/9           |     | × 2/6          |      | × 1/2        |
| Kiralp et al. [38]                  | √ 5/9           | М   | √ 4/6          | М    | √ 2/2        |
|                                     | × 3/9           |     | × 2/6          |      |              |
|                                     | NA 1/9          |     |                |      |              |
| Müller & Stratz [35]                | √ 6/9           | М   | √ 3/6          | М    | √ 2/2        |
|                                     | × 3/9           |     | × 3/6          |      |              |
| Wheeler et al. [32]                 | √ 6/9           | М   | √ 5/6          | G    | <b>√</b> 1/2 |
|                                     | × 3/9           |     | × 1/6          | -    | × 1/2        |
| Wheeler et al. [36]                 | √ 4/9           | М   | ✓ 6/6          | G    | √ 2/2        |
|                                     | × 5/9           |     |                | -    |              |
| Whiplash syndrome                   |                 |     |                |      |              |
| Byrn et al. [28]                    | <b>√</b> 7/9    | G   | <b>√</b> 4/6   | М    | <b>√</b> 1/2 |
| 2) ot a [20]                        | × 2/9           |     | × 2/6          |      | × 1/2        |
| Freund & Schwartz [41,42]           | √ 6/9           | М   | √ 3/6          | М    | √ 2/2        |
|                                     | × 3/9           |     | × 3/6          |      | • _/_        |
| Craniofacial pain                   |                 |     | 1000           |      |              |
| McMillan et al. [43]                | <b>√</b> 4/9    | М   | √ 3/6          | М    | <b>√</b> 1/2 |
| Momman of all [10]                  | × 5/9           |     | × 3/6          |      | × 1/2        |
| Cervicogenic headache               | X 0/0           |     | / 0/0          |      | X 1/2        |
| Schnider et al. [31]                | <b>√</b> 4/9    | М   | ✓ 6/6          | G    | ✓ 1/2        |
|                                     | × 5/9           | 141 | • 0/0          | 9    | × 1/2        |
| Osteoarthritis                      | / 0/0           |     |                |      | /            |
|                                     | √ 5/9           | М   | √ 5/6          | G    | √ 2/2        |
|                                     |                 | 141 |                | 9    | * _/_        |
| Yentür et al. [33]                  | ✓ 5/9<br>× 4/9  | М   | ✓ 5/6<br>× 1/6 | G    | √2           |

Table 2 Summary of study quality assessment results

Key:  $\checkmark$  = criterion met;  $\times$  = criterion not met.

NA = criterion was not applicable or possible to apply because of the nature of the intervention.

G = good, M = moderate, P = poor.

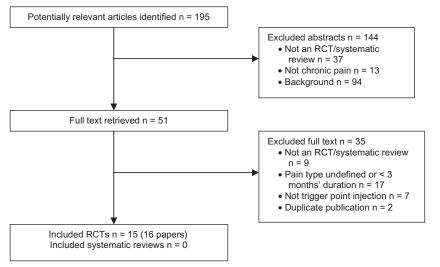
such that the index intervention was better than the control intervention when the upper limit of the 95% CI was <1 for the RR and <0 for the RD, WMD, and SMD. The converse was true when the lower limit of the 95% CI was >1 or >0, respectively. Where comparisons are written in the form A vs B in the tables, B is considered the "control".

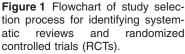
#### Results

Fifty-one potentially relevant studies were identified (Figure 1), but on closer examination of the full text articles, only 15 RCTs met the inclusion criteria of the review (Table 3). No systematic review was identified. Details of the excluded studies are available from the corresponding author. In six studies, the data presentation precluded calculation of the WMD [28–33]. Ten of the 15 studies had very small sample sizes, with less than 20 patients in each study arm.

# Methodological Quality of Included Studies Head, Neck, Shoulder, and Back Pain

Four double-blind RCTs [32,34–36], one singleblind RCT [37], two non-blinded RCTs [38,39], and three randomized double-blind crossover trials [29,30,40] assessed TPI in patients with head, neck, shoulder, and/or back pain. The internal validity of the ten trials ranged from poor to good (Table 2). This was largely due to inadequate reporting of aspects of study design, such as the method of randomization and allocation concealment and how withdrawals and dropouts were handled, together with a lack of detail on whether the outcome assessor was blinded or whether





co-interventions were used. Unfortunately, even though the studies may have been conducted appropriately, it is not apparent from the articles, which cast some doubt on the veracity of the data. The external validity was good in two studies [32,34,36] and moderate in the other eight [29,30,35,37–40]. The main deficiency in the latter eight studies was a failure to report adverse events or patient baseline parameters. Two studies [38,40] did not describe the criteria used for selecting the injection site, which raises uncertainty as to whether the trigger points were correctly identified. Point estimates or measures of variability for the primary outcomes were not reported in two studies [29,32].

## Whiplash Syndrome

The two double-blind RCTs [28,41,42] involving patients with whiplash syndrome had moderate to good internal validity. Once again, the primary shortcoming was a lack of information on cointerventions and the method of randomization used. The external validity of the studies was moderate since neither specified any criteria for patient selection. One study [28] did not report baseline parameters for the patient groups or measures of variability for the primary outcomes. The other study [41,42] had a relatively short follow-up period.

# Craniofacial Pain, Cervicogenic Headache, and Osteoarthritis

The remaining three RCTs [31,33,43] had moderate internal validity. It was unclear from the study methods how withdrawals and dropouts were handled and whether randomization or allocation concealment was adequate. Two studies [31,33] had good external validity. The third study [43] was of moderate quality, largely due to an extremely short follow-up period and deficiencies in the reporting of baseline patient parameters and adverse events. Two studies [31,43] did not clearly describe the sample size for each treatment group in the results section.

# Evidence for the Efficacy and Safety of Trigger Point Injection

# Head, Neck, Shoulder, and Back Pain

Trigger Point Injection with Local Anesthetic

A randomized crossover trial [30] compared sphenopalatine ganglion block (SPGB) with placebo SPGB and an internal standard (TPI with lidocaine). TPI with lidocaine was more effective than either SPGB or placebo SPGB in relieving myofascial pain up to 1 week after treatment. A similar number of patients in both treatment groups experienced a placebo response. However, it is likely that co-interventions confounded these results. As TPI was the internal standard therapy against which active SPGB was compared, it is possible that the benefit of TPI was overestimated by comparing it with an ineffective alternative treatment rather than a true placebo or no treatment control.

Another RCT [35] compared prilocaine TPI with TPI using a type 3 serotonin  $(5-HT_3)$  receptor antagonist (tropisetron) injected into a single trigger point. Both treatments achieved similar reductions in pain intensity scores 7 days after injection (Table 4). Approximately half of the patients in each treatment group were considered

|   | ourninary or included randomized corniomed | uneu mais  |                       |  |                        |   |
|---|--|--|-----------------------|--|------------------------|---|
| Study   | Study Design                               | Intervention   | Number of<br>Patients | Pain Duration                                      | Length of<br>Follow-up | Co-interventions  |
| Head, neck, shoulder, and back pain<br>Cheshire et al. [29]         | oain<br>Randomized double-blind            | TPI (normal saline) then TPI (botulinum toxin A)   | ю                     | Mean 3.5 years                                     | 16 weeks               | Neither muscle relaxants nor physical exercise  |
| Esenyel et al. [39]   | crossover trial<br>Non-blinded RCT         | TPI (botulinum toxin A) then TPI (normal saline)<br>Neck-stretching exercises<br>Utrasound puts stretching exercises   | 30 3<br>30 3<br>30 3  | Mean 3 years<br>Range 6 months<br>to 7 years       | 3 months               | was prescribed during the study.<br>Unclear   |
| Ferrante et al. [30]  | Randomized double-blind<br>crossover trial | FT (1.% nuocarrie) puts stretching exercises<br>SPGB then TPI (1% lidocaine) then SPGB<br>placebo<br>SPGB placebo then TPI (1% lidocaine) then<br>SPGB   | 13<br>13              | ≥6 months  | 1 week                 | Patients permitted to continue preexisting<br>therapies and medication during the study.  |
| Ferrante et al. [34]  | Double-blind RCT                           | TPI with saline plus physical therapy<br>TPI with 10 U botulinum toxin A plus physical<br>therapy<br>TPI with 25 U botulinum toxin A plus physical<br>therapy<br>TPI with 50 U botulinum toxin A plus physical | 35<br>32<br>34<br>31  | ⊵6 months  | 12 weeks               | Patients weaned from all pain medications 2<br>weeks before treatment. During the study,<br>patients received physical therapy and a<br>standardized pharmacologic regimen<br>consisting of: amitriptyline, ibuprofen, and<br>propoxyphene-acetaminophen napsylate. |
| Graboski et al. [40]  | Randomized double-blind<br>crossover trial | urerapy<br>TPI (0.5% bupivicatine) plus stretching exercises<br>TPI (25 U botulinum toxin A) plus stretching<br>exercises  | თდ                    | ≥3 months  | 10 weeks               | Patients permitted to continue preexisting<br>medication during the study but recorded<br>amounts and doses   |
| Kamanli et al. [37]   | Single-blind RCT                           | Dry needdoor<br>Dry needdoor<br>TPI (0.5% lidocaine) plus stretching exercises<br>TPI (10–20 U botulinum toxin A) plus stretching<br>exercises   | 0100                  | Mean 2.7 years<br>Mean 4.1 years<br>Mean 4.2 years | 4 weeks                | None  |
| Kiralp et al. [38]  | Non-blinded RCT                            | Laser process<br>Laser process<br>TPI (2% prilocaine) plus streiching exercises  | 23                    | Mean 2.8 years<br>Mean 2.3 vears                   | 6 months               | Analgesics not permitted during the study.  |
| Müller & Stratz [35]  | Double-blind RCT                           | TPI with 0.5% prilocaine<br>TPI with 5 mo trobisetron  | 16<br>17              | ≥3 months  | 8 weeks                | Unclear   |
| Wheeler et al. [32]   | Double-blind RCT                           | TPI with normal saline<br>TPI with 50 U botulinum toxin A<br>TPI with 100 U botulinum toxin A  | = = =                 | Mean 2.9 years<br>Mean 2.6 years<br>Mean 2.9 vears | 4 months               | Unclear   |
| Wheeler et al. [36]   | Double-blind RCT                           | TPI with normal saline<br>TPI with botulinum toxin A   | 24                    | Mean 9.3 years                                     | 16 weeks               | Physical therapy was not permitted during the study.  |
| Whplash syndrome<br>Byrn et al. [28]                                | Double-blind RCT                           | TPI with sterile water<br>TPI with saline  | 20                    | 4–6 years  | 8 months               | The majority of the patients were already<br>undergoing physiotherapy and/or taking<br>analgesics, benzodiazepines, or<br>antidepressants, unclear<br>antidepressants, unclear  |
| Freund & Schwartz [41,42]   | Double-blind RCT                           | TPI with saline<br>TPI with 100 U botulinum toxin A  | 12<br>14              | >6 months  | 4 weeks                | were communed during the study.<br>No other treatments permitted during the study<br>period.  |
| Craniotacial pain<br>McMillan et al. [43]<br>Convisionaris headache | Double-blind RCT                           | Simulated dry needling plus simulated TPI<br>Simulated TPI plus dry needling<br>TPI (1% procaine) plus simulated dry needling  | 10<br>10              | ≥3 months  | 24 hours               | No other medication or treatment permitted during the study.  |
| Schnider et al. [31]  | Double-blind RCT                           | TPI (normal saline) plus physical therapy<br>TPI (botulinum toxin A) plus physical therapy   | 16<br>17              | Mean 6.1 years<br>Mean 6.1 years                   | 12 weeks               | The majority of the patients were taking<br>medications at the start of the study; unclear if<br>these treatments were continued during the<br>study.   |
| Usteoarthritis<br>Yentür et al. [33]                                | Single-blind RCT                           | Intra-articular injection with sodium hyaluronate<br>TPI (0.5% lidocaine) plus intra-articular injection   | 16<br>17              | ≥1 year  | 21 days                | No other treatments permitted during the study.   |

Table 3 Summary of included randomized controlled trials

RCT = randomized controlled trial; SPGB = sphenopalatine ganglion block; TPI = trigger point injection.

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| Study         Pain Score (VAS)         Pain Pressure<br>Threshold (kg/cm²)         Subjective Function         Medication Usage           Esenyel et al. [39]         FU = 3 months<br>Scale 0-10         FU = 3 months<br>Scale 0-10         FU = 3 months         Scale 0-10         WMD 0.27 [0.05 to 0.49]         SVMD 0.27 [0.05 to 0.49]         SVMD 0.42 [-1.96 to -0.87]         SVMD 0.42 [-1.96 to -0.87]         SVMD 0.54 [0.05 to 1.04]           TPI (lidocaine) +<br>stretching vs stretching<br>TPI (lidocaine) +<br>stretching vs         SMD 0.14 [-1.48 to -0.71]         SMD 0.52 [0.03 to 1.01]         SMD 0.04 [-0.42 to 0.51]         SMD 0.052 [0.03 to 0.43]           Ferrante et al. [34]         FU = 12 weeks<br>Scale 0-100         FU = 12 weeks         FU = 12 weeks         FU = 8 weeks<br>Use of rescue medication<br>(number of pills ingest)           TPI (botulinum toxin 10 U)<br>vs satine TPI<br>sy statine TPI<br>sy statine TPI         SMD 0.03 [-0.44 to 0.50]         SMD -0.36 [-0.98 to 0.03]         SMD -0.36 [-0.85 to 0.52]           TPI (botulinum toxin 25 U)<br>vs Stile TPI         SMD 0.06 [-0.43 to 0.54]         SMD -0.36 [-0.85 to 0.33]         SMD -0.36 [-0.85 to 0.52]           SMD 0.06 [-0.43 to 0.54]         SMD 0.06 [-0.43 to 0.54]         SMD -0.36 [-0.85 to 0.52]         SMD -0.36 [-0.85 to 0.52]           Vs satine TPI         SMD 0.06 [-0.43 to 0.54]         SMD -0.36 [-0.85 to 0.52]         SMD -0.30 [-0.27 to 0.26]         SMD 0.47 [-0.22 to 0.75]           VMD 1.20 [-5.53 to 1.22]         SMD  |  |
|--|--|
| Scale 0–10         Scale 0–10           US plus stretching vs         WMD 2.270 [-3.55 to -1.85]         WMD 0.27 [0.05 to 0.49]           stretching vs         SMD -1.42 [-1.96 to -0.87]         SMD 0.54 [0.05 to 1.04]           TPI (lidocaine) +         SMD 0.132 [-1.85 to -0.78]         SMD 0.23 [0.03 to 0.43]           stretching vs         SMD 0.4 [-0.42 to 0.51]         SMD 0.54 [0.05 to 0.43]           TPI (lidocaine) +         SMD 0.4 [-0.42 to 0.51]         SMD -0.04 [-0.30 to 0.22]           stretching vs         SMD 0.4 [-0.42 to 0.51]         SMD -0.07 [-0.53 to 0.39]           US + stretching         FU = 12 weeks         FU = 12 weeks           Scale 0-100         SMD 0.04 [-0.42 to 0.51]         SMD -0.45 [-0.94 to 0.03]           vs saline TPI         SMD 0.09 [-12.55 to 18.35]         SMD -0.45 [-0.94 to 0.03]           vs saline TPI         SMD 0.09 [-12.54 to 15.94]         SMD -0.36 [-0.83 to 0.12]           vs saline TPI         SMD 0.06 [-0.43 to 0.54]         SMD -0.12 [-0.55 to 1.25]           vs saline TPI         SMD 0.06 [-0.43 to 0.54]         SMD -0.22 [-0.25 to 1.25]           vs saline TPI         SMD 0.06 [-0.43 to 0.54]         SMD -0.14 [-0.52 to 1.25]           vs SMD 0.06 [-0.43 to 0.54]         SMD -0.14 [-0.52 to 1.25]         SMD -0.21 [-0.55 to 1.40]           vs SMD 0.05 [-0.41]         SMD -0.04 [-0.  |  |
| US plus stretching vs<br>stretching         WMD -2.70 [-3.55 to -1.85]<br>MD -1.42 [-1.96 to -0.87]<br>SMD 0.54 [0.05 to 1.04]<br>WMD 0.23 [0.03 to 0.43]<br>SMD 0.52 [0.03 to 0.43]<br>SMD 0.54 [-0.53 to 0.39]           TPI (lidocarine) +<br>stretching vs<br>US + stretching<br>Vs stretching         SMD 0.4 [-0.42 to 0.51]<br>SMD 0.04 [-0.42 to 0.51]<br>SMD 0.07 [-0.53 to 0.39]         FU = 8 weeks<br>Use of rescue medication<br>(number of pills ingest<br>per group)           TPI (biotulinum toxin 10 U)<br>vs saline TPI<br>SMD 0.09 [-0.39 to 0.57]<br>SMD 0.09 [-0.39 to 0.57]         SMD 0-4.5 [-0.44 to 0.03]<br>SMD -0.45 [-0.44 to 0.03]<br>SMD -0.45 [-0.44 to 0.03]<br>SMD 0.03 [-0.44 to 0.50]         WMD -1.10 [-2.53 to 0.33]<br>SMD -0.36 [-0.85 to 0.12]<br>SMD 0.03 [-0.44 to 0.50]<br>SMD 0.03 [-0.44 to 0.50]<br>SMD 0.03 [-0.44 to 0.50]<br>SMD 0.03 [-0.44 to 0.54]<br>SMD 0.03 [-0.44 to 0.54]<br>SMD 0.04 [-0.52 to 0.35]<br>SMD 0.02 [-0.25 to 1.25]<br>SMD 0.02 [-0.25 to 0.41]<br>SMD 0.02 [-0.25 to 0.5]<br>SMD 0.02 [-0.25 to 0.78]<br>SMD 0.04 [-0.34 to 0.62]<br>SMD 0.14 [-0.34 to 0.62]<br>SMD 0.29 [-1.70 to 0.33<br>SMD 0.43 [-0.77 to 0.33]<br>SMD 0.43 [-0.77 to 0.33]<br>SMD 0.43 [-0.77 to 0.33<br>SMD 0.43 [-0.77 to 0.33]<br>SMD 0.43 [-0.77 to 0.33<br>SMD 0.43 [-0.77 to 0.33<br>SMD 0.43 [-0.77 to 0.33<br>SMD 0.43 [-0.37 to 0.30<br>SMD 0.47 [-0.31 to 1.26]<br>SMD 0.4 |  |
| Ferrante et al. [34]         FU = 12 weeks<br>Scale 0-100         FU = 12 weeks<br>Scale 0-100         FU = 12 weeks<br>Scale 0-100         FU = 8 weeks<br>Use of rescue medicator<br>(number of pills ingest<br>per group)           TPI (botulinum toxin 10 U)<br>vs saline TPI         WMD 2.90 [-12.55 to 18.35]<br>SMD 0.09 [-0.39 to 0.57]         WMD -1.50 [-3.06 to 0.06]<br>SMD -0.45 [-0.94 to 0.03]         WMD -34.60 [-78.83 to 1.92]           TPI (botulinum toxin 25 U)<br>vs saline TPI         WMD 0.90 [-12.69 to 14.49]         WMD -1.10 [-2.53 to 0.33]         WMD -11.70 [-59.76 to 3.93]           TPI (botulinum toxin 50 U)<br>vs saline TPI         SMD 0.03 [-0.44 to 0.50]         SMD -0.35 [-0.83 to 0.12]         SMD -0.35 [-0.89 to 4.93]           TPI (botulinum toxin 50 U)<br>vs saline TPI         SMD 0.06 [-0.43 to 0.54]         SMD -0.14 [-0.62 to 0.35]         SMD -0.02 [-0.50 to 0.41]           TPI (botulinum toxin 25 U)<br>vs saline TPI         SMD 0.06 [-0.43 to 0.54]         SMD 0.40 [-0.98 to 1.78]         SMD 0.02 [-0.25 to 0.47]           TPI (botulinum toxin 10 U)<br>vs TPI (botulinum toxin<br>10 U)         SMD -0.07 [-0.55 to 0.41]         SMD 0.40 [-0.37 to 0.62]         SMD 0.43 [-0.07 to 0.93]           TPI (botulinum toxin<br>10 U)         SMD -0.04 [-0.54 to 0.45]         SMD 0.29 [-0.21 to 0.78]         SMD 0.43 [-0.07 to 0.93]           TPI (botulinum toxin<br>10 U)         SMD 0.03 [-0.45 to 0.52]         SMD 0.18 [-0.30 to 0.67]         SMD 0.12 [-0.37 to 0.60]           TPI (botulinum toxin<br>10 U)         SMD 0.03 [-0.45 to 0.52   |  |
| TPI (botulinum toxin 10 U)       WMD 2.90 [-12.55 to 18.35]       WMD -1.50 [-3.06 to 0.06]       WiMD -34.60 [-78.83 to 15]         vs saline TPI       SMD 0.09 [-0.39 to 0.57]       SMD 0.09 [-0.39 to 0.57]       SMD 0.03 [-0.48 to 0.03]       SMD -0.36 [-0.85 to 0.13]         TPI (botulinum toxin 50 U)       ws aline TPI       SMD 0.03 [-0.44 to 0.50]       SMD -0.36 [-0.83 to 0.12]       SMD -0.11 [-0.59 to 0.30]         TPI (botulinum toxin 50 U)       ws aline TPI       SMD 0.06 [-0.43 to 0.54]       SMD -0.14 [-0.62 to 0.35]       SMD -0.02 [-0.50 to 0.44]         vs saline TPI       SMD 0.06 [-0.43 to 0.54]       SMD 0.04 [-0.98 to 1.78]       SMD -0.02 [-0.50 to 0.47]         vs saline TPI       SMD 0.06 [-0.43 to 0.54]       SMD 0.14 [-0.34 to 0.62]       SMD -0.27 [-0.22 to 0.75]         vs TPI (botulinum toxin 50 U)       wMD -1.20 [-15.37 to 12.97]       WMD 1.00 [-0.72 to 2.72]       SMD 0.43 [-0.07 to 0.93]         vs TPI (botulinum toxin 10 U)       SMD -0.04 [-0.54 to 0.45]       SMD 0.29 [-0.21 to 0.78]       SMD 0.43 [-0.07 to 0.93]         TPI (botulinum toxin 10 U)       WMD 0.80 [-11.33 to 12.93]       WMD 0.60 [-1.00 to 2.20]       WMD 0.43 [-0.07 to 0.93]         vs TPI (botulinum toxin 10 U)       SMD 0.03 [-0.45 to 0.52]       SMD 0.18 [-0.30 to 0.67]       SMD 0.12 [-0.37 to 0.60]         redut & Schwartz [41,42]       FU = 4 weeks       Scale 0-10       Vernon-Mior scale  |  |
| TPI (botulinum toxin 50 U)<br>vs TPI (botulinum toxin<br>10 U)       WMD -1.20 [-15.37 to 12.97]<br>SMD -0.04 [-0.54 to 0.45]       WMD 1.00 [-0.72 to 2.72]<br>SMD 0.29 [-0.21 to 0.78]       WMD 33.10 [-4.62 to 70<br>SMD 0.43 [-0.07 to 0.93]         TPI (botulinum toxin<br>10 U)       WMD 0.80 [-11.33 to 12.93]<br>vs TPI (botulinum toxin<br>25 U)       WMD 0.80 [-11.33 to 12.93]<br>SMD 0.03 [-0.45 to 0.52]       WMD 0.60 [-1.00 to 2.20]<br>SMD 0.18 [-0.30 to 0.67]       WMD 10.20 [-31.95 to 5]<br>SMD 0.12 [-0.37 to 0.60]         Freund & Schwartz [41,42]       FU = 4 weeks<br>Scale 0-10       FU = 4 weeks<br>Vernon-Mior scale       FU = 4 weeks<br>Vernon-Mior scale         TPI (botulinum toxin<br>100 U) vs saline TPI<br>Graboski et al. [40]       SMD -0.08 [-0.85 to 0.69]       SMD 0.47 [-0.31 to 1.26]<br>Composite of two VAS scores<br>(scale 0-10)       Analgesic consumption<br>score (scale 0-6)  | 0.12]<br>to 36.36]<br>0.36]<br>o 43.89]<br>0.47]<br>o 63.79] |
| TPI (botulinum toxin 50 U)<br>vs TPI (botulinum toxin<br>25 U)       WMD 0.80 [-11.33 to 12.93]<br>SMD 0.03 [-0.45 to 0.52]       WMD 0.60 [-1.00 to 2.20]<br>SMD 0.18 [-0.30 to 0.67]       WMD 10.20 [-31.95 to 55]<br>SMD 0.12 [-0.37 to 0.60]         Freund & Schwartz [41,42]       FU = 4 weeks<br>Scale 0-10       FU = 4 weeks<br>Vernon-Mior scale       FU = 4 weeks<br>Vernon-Mior scale       FU = 4 weeks<br>Vernon-Mior scale         TPI (botulinum toxin<br>100 U) vs saline TPI<br>Graboski et al. [40]       SMD -0.08 [-0.85 to 0.69]       SMD 0.47 [-0.31 to 1.26]<br>Composite of two VAS scores<br>(scale 0-10)       Analgesic consumption<br>score (scale 0-6)   |  |
| Freund & Schwartz [41,42]         FU = 4 weeks<br>Scale 0-10         FU = 4 weeks<br>Vernon-Mior scale           TPI (botulinum toxin<br>100 U) vs saline TPI<br>Graboski et al. [40]         WMD -4.10 [-45.34 to 37.14]         WMD 3.20 [-1.70 to 8.10]           SMD 0.08 [-0.85 to 0.69]         SMD 0.47 [-0.31 to 1.26]         SMD 0.47 [-0.31 to 1.26]           Graboski et al. [40]         Composite of two VAS scores<br>(scale 0-10)         Analgesic consumption<br>score (scale 0-6)  | -  |
| TPI (botulinum toxin         WMD -4.10 [-45.34 to 37.14]         WMD 3.20 [-1.70 to 8.10]           100 U) vs saline TPI         SMD -0.08 [-0.85 to 0.69]         SMD 0.47 [-0.31 to 1.26]           Graboski et al. [40]         Composite of two VAS scores (scale 0-10)         Analgesic consumption score (scale 0-6)  |  |
|  | n  |
| TPI (25 U botulinum         WMD 1.20 [-1.83 to 4.23]         WMD -0.33 [-1.27 to 0.6           toxin) + stretching vs         SMD 0.26 [-0.42 to 0.94]         SMD -0.23 [-0.91 to 0.4           0.5% bupivacaine TPI +<br>stretching         SMD 0.26 [-0.42 to 0.94]         SMD -0.23 [-0.91 to 0.4   |  |
| Kamanli et al. [37] FU = 4 weeks FU = 4 weeks<br>Scale 0-10  |  |
| TPI (0.5% lidocaine) +         WMD -3.17 [-5.27 to -1.07]         WMD 0.57 [-0.14 to 1.28]           exercises vs dry         SMD -1.27 [-2.25 to -0.29]         SMD 0.68 [-0.23 to 1.59]           needling + exercises         SMD -1.27 [-2.25 to -0.29]         SMD 0.68 [-0.23 to 1.59]   |  |
| TPI (botalinum toxin 10 U) WMD -2.44 [-4.38 to -0.50] WMD 0.18 [-0.52 to 0.88]<br>+ exercises vs dry SMD -1.03 [-2.01 to -0.06] SMD 0.22 [-0.68 to 1.12]<br>needling + exercises   |  |
| TPI (botulinum toxin 10 U) WMD 0.73 [-0.51 to 1.97] WMD -0.39 [-1.11 to 0.33]<br>+ exercises vs TPI (0.5% SMD 0.49 [-0.42 to 1.41] SMD -0.46 [-1.38 to 0.45]<br>lidocaine) +<br>exercises  |  |
| Kiralp et al. [38] FU = 6 months FU = 6 months<br>Scale 0–10   |  |
| TPI (prilocaine) +         WMD 0.26 [-0.56 to 1.08]         WMD -0.21 [-3.18 to 2.76]           exercises vs laser +         SMD 0.18 [-0.42 to 0.78]         SMD -0.04 [-0.64 to 0.56]           exercises         secrcises         SMD 0.18 [-0.42 to 0.78]         SMD -0.04 [-0.64 to 0.56]   |  |
| McMillan et al. [43] FU = 24 hours after third FU = 24 hours after third treatment treatment Scale 0–100 Masseter muscle   |  |
| Simulated TPI + dry         WMD 6.00 [-13.84 to 25.84]         WMD 0.30 [-0.09 to 0.69]           needling vs simulated         SMD 0.25 [-0.63 to 1.13]         SMD 0.64 [-0.26 to 1.55]           TPI + simulated dry         needling         SMD 0.25 [-0.63 to 1.13]         SMD 0.64 [-0.26 to 1.55]   |  |
| TPI (procaine) +         WMD 9.00 [-14.39 to 32.39]         WMD 0.30 [0.08 to 0.52]           simulated dry needling vs         SMD 0.32 [-0.56 to 1.21]         SMD 1.13 [0.17 to 2.09]           simulated TPI +         simulated dry needling         SMD 1.13 [0.17 to 2.09]  |  |
| TPI (procaine) + simulated<br>dry needling vs simulated<br>TPI + dry needling         WMD 3.00 [-22.17 to 28.17]         WMD 0.00 [-0.42 to 0.42]           Müller & Stratz [35]         FU = 7 days         SMD 0.10 [-0.78 to 0.98]         SMD 0.00 [-0.88 to 0.88]   |  |
| Scale 0–10           TPI (prilocaine) vs TPI         WMD –2.06 [-24.18 to 20.06]           (tropisetron)         SMD –0.06 [-0.74 to 0.62]           Wheeler et al. [36]         FU = 16 weeks   |  |
| Scale 0–100           TPI (botulinum toxin 50 U)         WMD 7.20 [-2.53 to 16.93]         WMD 0.00 [-1.42 to 1.42]           vs saline TPI         SMD 0.43 [-0.17 to 1.02]         SMD 0.00 [-0.59 to 0.59]  |  |

| Table 4 | Weighted and standardized n | mean differences for | most commonly re | ported efficacy outcomes |
|---------|-----------------------------|----------------------|------------------|--------------------------|
|         |                             |                      |                  |                          |

[] = 95% confidence interval. FU = follow-up; US = ultrasound; WMD = weighted mean difference; SMD = standardized mean difference; TPI = trigger point injection; VAS = visual analog scale.

responders and had more than a 35% reduction in pain score. However, 8 weeks after treatment, significantly more patients in the tropisetron group had experienced pain relief, compared with those in the prilocaine group (RR 4.24, 95% CI 1.07–16.70; RD 0.40, 95% CI 0.12–0.69).

Esenvel et al. [39] compared a combination of neck stretching and either TPI with lidocaine or ultrasound therapy with neck stretching alone. Relatively young patients were assessed to rule out degenerative disc or joint disease. Combined TPI with lidocaine and neck stretching therapy achieved the same improvement in pain symptoms as combined ultrasound/neck stretching therapy, and both treatments were more effective than neck stretching exercises alone, 2 weeks and 3 months after treatment. However, it was impossible to tell whether TPI required more treatment sessions to achieve this result than ultrasound, which was administered over 10 separate treatment sessions. It was also unclear if the results were confounded by co-interventions.

Kiralp et al. [38] reported that both prilocaine TPI and laser treatment, performed in conjunction with stretching exercises, produced significant improvements in pain pressure threshold and pain intensity immediately after treatment and at 6 months' follow-up. However, there was no detectable difference in the degree of improvement between the two groups.

An RCT [37] comparing stretching exercises plus either TPI (lidocaine) or dry needling found that, while the mean pain pressure threshold and pain at the trigger point improved in both groups, patients who underwent lidocaine TPI had significantly lower trigger point pain compared with the dry needling group (WMD -0.93, 95% CI -1.55to -0.31) 4 weeks after treatment. Scores for subjective pain, fatigue, and work disability significantly decreased after treatment with lidocaine but were unaffected by dry needling.

#### Trigger Point Injection with Botulinum Toxin

Three RCTs [32,34,36], two of which were supported by the Allergan Corporation [32,36], showed that botulinum toxin type A, administered in concentrations ranging from 10 U to over 200 U during one treatment session, and saline TPI were equally effective in reducing pain and disability up to 4 months after treatment. In one study [32], a small number of patients (13 in total) from each treatment group requested a further TPI at the end of the study and received 100 U of botulinum toxin. The patients who had previously received a botuli-

num toxin injection were more likely to report a benefit from the second botulinum toxin treatment than those who had initially received saline TPI.

A randomized crossover trial [29] comparing botulinum toxin with saline TPI in six patients reported equivocal results. Four of the six patients experienced a reduction in both pain and muscle spasm after botulinum toxin treatment, but not after saline injection. For the remaining two patients, one reported no change in pain symptoms after either treatment, while the other responded favorably to both. Generally, symptom relief occurred within 1 week after treatment and continued for 5–6 weeks after TPI. In contrast, the beneficial effect in the patient who responded to both treatments lasted for only 3-4 weeks after injection. Although patient outcome was not affected by the order in which the injections were received, a crossover effect was seen in one patient, which suggests that the washout period may have been too short.

Another double-blind randomized crossover trial [40] compared stretching exercises combined with either botulinum toxin or bupivicaine TPI. Once pain severity reached at least 75% of its pre-treatment level for two consecutive weeks, patients underwent a 2-week washout period and were then treated with the other solution. There was no difference between the two treatments with respect to magnitude of pain relief, speed or duration of pain relief, function, amount of medication used, or satisfaction with treatment. While there was no difference in cost of care between the two treatments, the cost of the botulinum toxin injectant was 500 times greater than for bupivicaine.

Similar results were found in an RCT [37] that compared botulinum toxin TPI with TPI (lidocaine) or dry needling, all performed in conjunction with stretching exercises. While the mean pain pressure threshold and pain at the trigger point improved in all three groups, patients who underwent botox TPI had significantly higher trigger point pain compared with the lidocaine group (WMD 0.82, 95% CI 0.11-1.53) 4 weeks after treatment. However, the botox TPI group had a higher pre-treatment trigger point pain score than the lidocaine group, which may have affected the results. Scores for subjective pain, fatigue, and work disability significantly decreased after treatment with botox or lidocaine, but remained unchanged after dry needling.

There was no difference in adverse effects reported among the treatments except for one study [37], which found that patients experienced less discomfort during TPI with botulinum toxin or saline than dry needling (Table 5). However, cutting edge hypodermic needles were used for dry needling, which are thought to cause more pain than the non-cutting acupuncture needles commonly used in clinical practice.

# Whiplash Syndrome

Byrn et al. [28] administered multiple TPIs to patients with whiplash syndrome (Table 6), according to need, during a maximum of three treatment sessions over a 2-month period. The symptoms of whiplash syndrome were significantly improved after TPI with sterile water, compared with saline, 3 months after treatment. However, the effect was not durable at 8 months' follow-up. Mean pain intensity scores and mobility were also significantly better following sterile water injection, compared with saline, both immediately after treatment and at the 8-month assessment. However, it is unclear if co-interventions were used. More patients in the saline group needed the maximum of three treatments and required more injections, compared with the sterile water group. Because up to three treatments were administered within the first 2 months of the study, according to patient need, the period of time between the last treatment and the follow-up assessment may have varied by up to 2 months for some patients.

In another RCT [41,42], patients receiving botulinum toxin had a significant decrease in mean pain intensity and an increase in mean total range of motion 4 weeks after treatment, whereas the slight improvement observed in the saline group was not statistically significant. There was no significant improvement in subjective function in either treatment group after 4 weeks. TPI with botulinum toxin was no more effective than saline TPI at reducing pain, improving subjective function, or increasing range of motion (WMD 35.00 degrees, -8.09 to 78.09).

## Craniofacial Pain

McMillan et al. [43] compared combined procaine TPI and dry needling with combinations of sham TPI and sham dry needling. The results suggested that procaine TPI combined with simulated dry needling offers little beyond a placebo effect, although it is unclear whether the sham procedures were truly inactive. Combined TPI and dry needling was not assessed. In addition, the follow-up period for this study was only 24 hours after each treatment over a study period of 3 weeks. As the location of the active trigger points changed between treatment sessions, it is likely that the injections were deactivating the trigger points effectively.

## Cervicogenic Headache

One RCT [31] assessing physical therapy combined with either botulinum toxin TPI or saline TPI found no significant changes in sagittal range of motion, biofeedback measurements, or daily analgesic intake over time in either group. Both treatments produced improvements in headache severity, headache-free days per month, and headache hours per day, but the degree of change was similar in each group. There was a statistically non-significant trend toward improvement in the number of headache-free days and headache hours per day in the botulinum toxin group, compared with the saline group, but in the absence of a control group that received only physical therapy it is impossible to tell what contribution TPI made to the overall treatment effect. In addition, co-interventions may have confounded the results.

# Osteoarthritis

Yentür et al. [33] showed that intra-articular injection combined with lidocaine TPI of any of 15 leg muscle trigger points was more effective than intra-articular injection alone in relieving pain and improving knee function in a highly selected group of older patients with knee osteoarthritis.

# Discussion

# Efficacy/Effectiveness of Trigger Point Injection

TPI relieved symptoms when used as a sole treatment for patients with whiplash syndrome or chronic head, neck, shoulder, and back pain, regardless of the injectant used, but was not more effective than other less invasive treatments such as laser and ultrasound (Table 6). There was some suggestion that sterile water is better than saline as an injectant, and that 5-HT<sub>3</sub> receptor antagonist may be superior to local anesthetic. Botulinum toxin is significantly more expensive but not more effective than saline or lidocaine, whereas TPI with either lidocaine or botulinum toxin provided greater symptom relief than dry needling.

TPI with lidocaine may be a useful adjunct to intra-articular injection in the treatment of joint pain caused by osteoarthritis, compared with intra-articular injection alone. Very limited evidence suggested that the combined use of simulated dry needling and TPI with procaine offers no

| Table 5         Relative risk and risk difference for most commonly reported safety outcomes   | e for most commonly reported   | safety outcomes   |   |   |  |
|--|--|---|---|---|--|
|  | Post treatment Outcomes  |   |   |   |  |
| Study  | Side Effects   | Weakness in<br>Non-injected Muscle                                  | Mild Local Pain at<br>Injection Site  | Mild Local Pain Opposite<br>Injection Site                          | Flu-like Symptoms                        |
| Byrn et al. [28]<br>TPI (saline) vs TPI (water)<br>Cheshire et al. [29]<br>TPI (botulinum toxin) vs TPI (saline)<br>Ferrante et al. [34]<br>TPI (botulinum toxin) vs saline TPI  | FU = 3 months<br>None reported in either group<br>FU = 16 weeks<br>None reported in either group |   |   |   | FU = 12 weeks<br>RR 2.57 [0:14 to 48.57] |
| Freund & Schwartz [41,42]<br>TPI (botulinum toxin 100 U) vs saline TPI<br>Kamanli et al., 2005 [37]<br>TPI (0.5% lidocaine) + exercises vs dry<br>needling + exercises           | FU = 4 weeks<br>None reported in either group  |   | FU = 4 weeks<br>RR 0.25 [0.07 to 0.90]<br>RD -0.60 [-0.95 to -0.25]                                       |   |  |
| TPI (botulinum toxin 10 U) + exercises vs<br>dry needling + exercises<br>TPI (botulinum toxin 10 U) + exercises vs<br>TPI (0.5% lidocaine) + exercises                           |  |   | RR 0.06 [0.00 to 0.98]<br>RD -0.80 [-1.08 to -0.52]<br>RR 0.22 [0.01 to 4.05]<br>RD -0.20 [-0.48 to 0.08] |   |  |
| Kiralp et al. [38]<br>TPI (prilocaine) + exercises vs<br>lacar + evervises   | FU = 6 months<br>None reported in either group   |   |   |   |  |
| Müller & Stratz [35]<br>TPI (prilocaine) vs TPI (tropisetron)  | FU = 8 weeks<br>None reported in either group  |   |   |   |  |
| Schnider et al. [31]<br>TPI (botulinum toxin) + PT vs TPI<br>(seline) + PT   |  |   | FU = 12 weeks<br>RR 2.83 [0.12 to 64.89]<br>RD 0.06 [_0.09 to 0.21]                                       |   |  |
| Wheeler et al. [32]<br>TPI (botulinum toxin) vs saline TPI   |  | FU = 4 months<br>RR 2.61 [0.14 to 50.09]<br>PD 0.00 F 0.04 to 0.261 |   | FU = 4 months<br>RR 2.61 [0.14 to 50.09]<br>PD 0.00 [ 0.08 to 0.26] |  |
| Yentür et al. [33]<br>TPI (lidocaine) + IA vs IA   | FU = 21 days<br>None reported in either group  |   |   |   |  |
| [] = 95% confidence interval.<br>[] = follow-up; IA = intra-articular injection; PT = physical therapy; RD = risk difference; RR = relative risk; TPI = trigger point injection. | /sical therapy; RD = risk difference; RR -   | = relative risk; TPI = trigger point                                | t injection.  |   |  |

| Treatment                                      | Condition                          | Comparator  | Study  | Evidence  |
|--|------------------------------------|---|--|---|
| TPI (water)                                    | Whiplash syndrome                  | TPI (saline)  | Byrn et al. [28]   | Limited evidence that water TPI is more<br>effective than saline TPI.<br>No difference in safety between the two<br>treatments.<br>Follow-up = 8 months   |
| TPI (LA)                                       | Head, neck, shoulder,<br>back pain | Sphenopalatine<br>ganglion block  | Ferrante et al. [30]   | Linited evidence that lidocaine TPI is<br>more effective than sphenopalatine<br>ganglion block.<br>Safety outcomes not reported.<br>Follow-up = 1 week  |
|  |                                    | TPI (tropisetron)   | Müller & Stratz [35]   | Limited evidence that TPI (tropisetron) is<br>more effective than TPI (LA) in<br>relieving pain.<br>No difference in safety between the two<br>treatments.  |
| TPI (LA) + stretching                          | Head, neck, shoulder,              | Stretching  | Esenyel et al. [39]  | Follow-up = 8 weeks<br>Limited evidence of no difference in   |
|  | back pain                          | Ultrasound + stretching<br>Laser + stretching<br>Dry needling +<br>stretching | Kamanli et al. [37]<br>Kiralp et al. [38]                          | effectiveness between TPI (LA) and<br>laser or ultrasound. Combined TPI/neck<br>stretching and ultrasound/neck<br>stretching were more effective than<br>neck stretching alone. TPI (LA) was<br>more effective than dry needling.<br>No difference in safety between TPI (LA)<br>and laser. TPI (LA) caused less<br>discomfort at injection than dry<br>needling. |
| TPI (LA) + simulated                           | Craniofacial pain                  | Simulated TPI + dry   | McMillan et al. [43]   | Follow-up range = 4 weeks to 6 months<br>Limited evidence of no difference in   |
| dry needling                                   |                                    | needling<br>Double sham<br>treatment  |  | effectiveness between the treatments.<br>Safety outcomes not reported.<br>Follow-up = 24 hours  |
| TPI (LA) + intra-<br>articular injection       | Osteoarthritis pain<br>(knee)      | Intra-articular injection   | Yentür et al. [33]   | Limited evidence that TPI + intra-articular<br>injection is more effective than<br>intra-articular injection alone.<br>No difference in safety between the two<br>treatments.   |
|  |                                    |   |  | Follow-up = 21 days   |
| TPI (botulinum toxin)                          | Head, neck, shoulder,<br>back pain | TPI (saline)<br>TPI (different<br>botulinum toxin<br>concentrations)          | Cheshire et al. [29]<br>Wheeler et al. [32]<br>Wheeler et al. [36] | Moderate evidence of no difference in<br>safety or effectiveness between<br>botulinum toxin TPI and saline TPI,<br>regardless of botulinum toxin<br>concentration (50 U to over 200 U).<br>Limited evidence of no difference in<br>safety or effectiveness between 50 U<br>and 100 U of botulinum toxin.<br>Follow-up range = 16 weeks                            |
|  | Whiplash syndrome                  | TPI (saline)  | Freund & Schwartz<br>[41,42]                                       | Limited evidence of no difference in<br>safety or effectiveness between the two<br>treatments.  |
| TPI (botulinum<br>toxin) + physical<br>therapy | Cervicogenic<br>headache           | TPI (saline) + physical<br>therapy  | Schnider et al. [31]   | Follow-up = 4 weeks<br>Limited evidence of no difference in<br>safety or effectiveness between the two<br>treatments.<br>Follow-up = 12 weeks   |
|  | Head, neck, shoulder,<br>back pain |   | Ferrante et al. [34]   | Limited evidence of no difference in<br>safety or effectiveness between the two<br>treatments, regardless of botulinum<br>toxin concentration (10 U to over 50 U).<br>Follow-up = 12 weeks  |
| TPI (botulinum<br>toxin) + stretching          | Head, neck, shoulder,<br>back pain | TPI (LA) + stretching<br>Dry needling +<br>stretching                         | Graboski et al. [40]<br>Kamanli et al. [37]                        | Moderate evidence of no difference in<br>safety or effectiveness between<br>botulinum toxin TPI and TPI (LA),<br>regardless of botulinum toxin<br>concentration (10 U to 25 U).<br>Limited evidence that botulinum toxin TPI<br>is more effective and causes less<br>discomfort than dry needling.<br>Follow-up range = 4 to 10 weeks                             |

 Table 6
 Summary of the evidence for trigger point injection

LA = local anesthetic; TPI = trigger point injection.

obvious clinical benefit beyond a placebo effect in the treatment of chronic craniofacial pain. The effectiveness of TPI for the treatment of cervicogenic headache is unclear.

The very different, and sometimes inadequately reported, treatment regimens used in the included RCTs precluded any specific determinations on the most effective needling technique or the optimal dose or intensity of TPI therapy. Synthesizing the evidence for a single TPI modality, such as TPI with local anesthetic, was also problematic because of the variation in types and concentrations of injectants used in the RCTs. Some solutions cause more pain on injection than others, and a painful injection is likely to cause a greater placebo response than a benign one [28,44].

Most of the included studies attempted to quantify the effects of TPI as a stand-alone therapy, rather than in the adjunct capacity in which it is routinely used in clinical practice. Thus, it is possible that the effectiveness of TPI was underestimated. Although there is some suggestion that the addition of TPI to stretching exercises in patients with chronic head, neck, shoulder, and back pain augments treatment outcomes, this was also true of stretching plus other therapies such as ultrasound and laser. The absence of a "no treatment" or "stretching alone" control arm made it impossible to assess what contribution, if any, TPI made to patient outcomes [37,38,40].

## Safety of Trigger Point Injection

TPI appears to be a relatively safe procedure when used by clinicians with appropriate expertise and training as very few adverse events were reported in the included RCTs. However, most RCTs are ill equipped to detect rare outcomes in procedures with a high safety profile. Thus, some unusual, and potentially dangerous, complications following TPI have only been published in case reports. These include: 1) cervical epidural abscess that required urgent cervical laminectomy [45]; 2) accidental intrathecal injection resulting in pneumocephalus [46]; 3) muscle atrophy at the injection site [47]; 4) pneumothorax that necessitated needle aspiration and chest tube drainage [48]; and 5) development of asystole in a patient with a history of panic attacks [49].

#### Training, Accreditation, and Reimbursement

As there is currently no satisfactory objective biochemical, electromyographic, or diagnostic imaging test available for diagnosing trigger points [50–53], their identification still largely relies upon

the knowledge and palpatory skill of the examiner [51,53]. Identifying trigger point(s) and implementing appropriate rehabilitation measures are the most demanding aspects of myofascial pain management for the practitioner. To date, no medical specialty provides formal undergraduate or postgraduate training in the diagnosis and treatment of myofascial trigger points, and no standards for training and practice have been established [4]. There is a clear need to develop a validated, standardized teaching method that is effective in training both expert and non-expert physicians to reliably identify trigger points and safely perform TPI [54-56]. In North America, there is only one formal course that offers comprehensive training in myofascial pain diagnosis, manual treatment, and needling techniques [57].

The majority of position statements and practice guidelines for the treatment of non-malignant chronic pain recommend an interdisciplinary approach to treatment [58]. TPI is generally considered an adjunctive rather than a primary treatment for chronic musculoskeletal pain, and its routine, solitary use in patients with chronic pain syndrome is not recommended [59-62]. When TPI is used as the primary therapy, patients may become dependent on it for pain relief [5], which may divert them from tackling the underlying factors causing and perpetuating their pain. Thus, it is important that physicians are aware of the danger of relying on TPI as a sole treatment for chronic non-malignant musculoskeletal pain and ensure that suitable postinjection follow-up with remedial stretching or exercise therapy, at a minimum, is conducted.

Provision of a training and accreditation program, for practitioners wishing to practice in the field of myofascial pain, by professional bodies such as the American College of Physicians, the College of Family Physicians of Canada, or the Royal College of Physicians and Surgeons of Canada would be helpful. Linking the successful completion of such training and subsequent accreditation to the ability to apply for reimbursement privileges could curb the potential overuse and misuse of TPI therapy. In order to achieve this goal, however, more research needs to be done to establish credible diagnostic criteria and evidencebased treatment protocols.

#### Considerations for Further Research

To date, the safety and efficacy data most commonly quoted for TPI in patients with chronic non-malignant musculoskeletal pain are usually derived from studies that did not define the term "chronic pain" [63,64], only recorded outcomes for acute pain [65], or pooled patient outcomes for acute and chronic pain [66]. When the most commonly used definition of chronic pain [20] is applied to the published RCTs on TPI, the dearth of evidence on its efficacy becomes apparent. Many questions regarding the use of TPI therapy for patients with chronic non-malignant musculoskeletal pain have yet to be addressed satisfactorily (Table 7). The effectiveness of TPI must be established before assessing the effectiveness of variations within the modality, such as comparing different injectants and needling technique.

A prospective blinded RCT, which is considered the most scientifically rigorous method of evaluating a new therapy [67], is often not applicable or feasible in studies of treatments for chronic musculoskeletal pain. In the case of TPI, it is sometimes difficult to blind patients to the therapy they received and impossible to conceal this from the clinicians administering it, unless different injectants are being compared. In addition, outcomes can be affected by variations in the degree of interaction and rapport that each clinician achieves with the patient during the treatment sessions, and by differences in treatment and patient management regimens that may exist between centers.

Nonetheless, there are many ways to augment the scientific rigor of a study on TPI (Table 7). Strict eligibility criteria for patient selection, particularly with respect to the definition of chronic pain (>3 months' duration), are essential because there is an 80% to 90% probability that patients with acute pain will recover spontaneously within 3 months of pain onset. This can significantly confound results when the active treatment is compared with a placebo or sham treatment group that has an inherently high recovery rate [65].

A control group is essential in TPI studies because of the significant placebo effect associated with subcutaneous needle insertion and injection

| Study Characteristic         | Description  |  |
|------------------------------|--|--|
| Objective                    | Questions not yet satisfactorily addressed include:  |  |
|                              | 1. What is the best control for TPI studies?   |  |
|                              | <ol><li>Is there a difference between TPI and non-specific injection of fluid into the region surrounding the<br/>trigger point?</li></ol>   |  |
|                              | <ol> <li>How strong is the placebo effect in TPI? Is TPI more effective than dry needling or no treatment?</li> <li>Does the needling technique or type, concentration, or volume of fluid injected affect outcomes?<br/>What is the safest and most effective injectant?</li> </ol> |  |
|                              | 5. Is there a cumulative dose response to TPI? What is the minimum dose/intensity required to achieve a clinically significant effect?   |  |
|                              | 6. What is the optimum TPI regimen (frequency, treatment duration, number of injections per session, needle size/type)?  |  |
|                              | 7. For botulinum toxin, is TPI of the affected muscles more effective than injecting their antagonists? Is non-specific injection more effective than injecting the trigger point?   |  |
| Inclusion/exclusion criteria | Strict, clearly defined eligibility criteria; chronic pain defined in terms of pain duration prior to enrollment.  |  |
| Patient group                | Comprehensive clinical description of patients using a universally accepted grading scale.   |  |
|                              | Provide baseline demographic data, functional status; document activity level, concurrent conditions, and cointerventions.   |  |
| Randomization                | Describe method used to generate and implement the allocation sequence (who generated the sequence, enrolled participants, assigned groupings).  |  |
|                              | Statistically compare treatment groups for potential prognostic factors, such as pain duration, depression, educational and employment status, naivety to TPI.   |  |
| Blinding                     | Identify who was blinded to group assignment.  |  |
| Intervention                 | Describe how trigger points were identified. Ideally, use two examiners blinded to treatment allocation to<br>identify the trigger points; report inter-examiner reliability.  |  |
|                              | Comprehensive description of treatment regimen: trigger point location; needle type; number of needle insertions; whether twitch was response elicited; volume and type of injectant (also diluent if applicable); number and frequency of treatments.                               |  |
| Control                      | "No treatment" control arm or "co-intervention only" control arm if TPI is combined with another intervention<br>(e.g., stretching).   |  |
| Sample size                  | (e.g., stretching).<br>Document participant flow; give reasons for dropouts/exclusions.  |  |
|                              | Document participant flow; give reasons for dropouts/exclusions.<br>Ideally, ensure a large enough sample to accommodate potential placebo effect.   |  |
| Outcomes                     | Assessed by independent observers blinded to treatment allocation.   |  |
|                              | Include changes in daily functioning, work status, and health-care utilization; objective measures of pain<br>relief and physiological outcomes. Report estimated effect size and its precision.   |  |
| Adverse events               | Report all adverse events/side effects for each study group.   |  |
| Follow-up                    | Assessment intervals and duration of follow-up must be tailored to capture all potential treatment outcomes<br>and be identical for all study groups.  |  |

Table 7 Points to consider when designing trials to evaluate trigger point injection (adapted from [72,73])

#### Trigger Point Injection Systematic Review

[43,68], but some consider including a "no treatment" control group for patients suffering from chronic musculoskeletal pain to be unethical. Thus, debate continues over what the most appropriate inert control or placebo treatment is. Ideally, a placebo should equalize the nonspecific effects of the treatment, such as physical contact, and maintain the illusion that the patient is receiving the active treatment, while exerting little or no specific treatment effect itself [69,70]. However, there is currently no placebo or sham treatment available for TPI that fulfills all of these criteria, particularly as obvious choices for a sham treatment (such as nonspecific dry or wet needling) or a physiologically inert control (TPI with saline or water) are considered by many to be active therapies [69–71]. Only one of the included RCTs used a control treatment that was truly inert [30].

A common deficiency in the included RCTs was inadequate reporting. This can be remedied in future studies if the Consolidated Standards of Reporting Trials' recommendations [72] are followed in tandem with the Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) [73]. The STRICTA guidelines, in particular, cover specific aspects of reporting that are peculiar to needling therapies.

#### Conclusions

TPI is a relatively safe procedure when used by clinicians with appropriate expertise and training, but there is no clear evidence in the medical literature of either benefit or ineffectiveness. TPI was generally analyzed as a stand-alone treatment, so its value within the multidisciplinary approach to chronic pain management that is currently advocated in clinical practice is unclear. Further expansion of the evidence base for TPI must come from RCTs that address the inherent challenges of assessing the effectiveness of injection therapies.

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#### Authors' Note

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