Neural tissue management provides immediate clinically relevant benefits without harmful effects for patients with nerve-related neck and arm pain: a randomised trial

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Question: What are the benefits and harms of neural tissue management in the short term for treating nerve-related neck and arm pain? Design: Randomised controlled trial. Participants: Sixty participants with non-traumatic nerve-related neck and unilateral arm pain were randomised to experimental (n = 40) or control (n = 20) groups. Intervention: Both groups were advised to continue usual activities. The experimental group also received education, manual therapy, and nerve gliding exercises in 4 treatments over 2 weeks. Outcome measures: Primary outcomes were participant-reported improvement and worsening on a Global Rating of Change scale. Secondary outcomes were neck pain, arm pain, the Neck Disability Index, the Patient-Specific Functional Scale, and adverse events related to treatment. Follow-up occurred 3–4 weeks after baseline. Results: Numbers needed to treat favoured the experimental intervention for participant-reported improvement (2.7, 95% CI 1.7 to 6.5), neck pain (3.6, 95% CI 2.1 to 10), arm pain (3.6, 95% CI 2.1 to 10), Neck Disability Index (4.3, 95% CI 2.4 to 18.2), and Patient-Specific Functional Scale (3.0, 95% CI 1.9 to 6.7). The prevalence of worsening in the experimental (13%) and control (20%) groups were not different (RD –7%, 95% CI –28 to 13). Adverse events had minimal impact on daily activities and did not reduce the chance of improving with the experimental intervention (RR = 1.03, 95% CI 0.58 to 1.84). Conclusion: These results enable physiotherapists to inform patients that neural tissue management provides immediate clinically relevant benefits beyond advice to remain active with no evidence of harmful effects. Trial registration: ACTRN 12610000446066. [Nee RJ, Vicenzino B, Jull GA, Cleland JA, Coppieters MW (2012) Neural tissue management provides immediate clinically relevant benefits without harmful effects for patients with nerve-related neck and arm pain: a randomised trial. Journal of Physiotherapy 58: 23–31]

Key words: Spinal nerves, Upper limb neurodynamic test, Manual therapy, Nerve gliding, Neurodynamic treatment

Introduction

One month prevalence rates for activity-limiting neck pain range from 7.5% to 14.5% in the general population (Hogg-Johnson et al 2008, Webb et al 2003). Neck pain spreading down the arm is more common than neck pain alone and is associated with higher levels of self-reported disability (Daffner et al 2003). One mechanism for neck pain spreading down the arm is the sensitisation of neural tissues (Bogduk 2009).

Evidence on the benefits and harms of physiotherapy interventions for nerve-related neck and arm pain is needed (Carlesso et al 2010a, Miller et al 2010). Neural tissue management is one physiotherapy intervention advocated for nerve-related neck and arm pain (Butler 2000, Childs et al 2008, Elvey 1986). Neural tissue management uses specific positions and movements of the neck and arm to reduce nerve mechanosensitivity, resolve symptoms, and restore function (Butler 2000, Coppieters and Butler 2008, Elvey 1986). Physiotherapists have been advised to apply neural tissue management carefully to minimise the chance that treatment will aggravate sensitised neural tissues (Butler 2000, Elvey 1986, Hall and Elvey 2004).

Despite it being a recommended intervention (Childs et al 2008), it is unclear whether a multi-session neural tissue management program can change the short-term natural history of nerve-related neck and arm pain. Allison et al (2002) conducted the only randomised controlled trial that addressed this question. Although within-group analyses showed significant changes in pain and function for the treatment group but not the control group, the lack of a between-group analysis meant that no conclusive statement could be made about the effects of neural tissue management (Boutron et al 2010). However, Gross et al (2004) conducted a between-group analysis on these data in their systematic review. Standardised mean differences favoured neural tissue management over no intervention for improving pain and function but were not statistically significant. Low statistical power related to the small sample (treatment = 17, control = 10) may explain these non-significant results. A randomised controlled trial with a larger sample is needed to determine whether neural tissue management can

What is already known on this topic: Neck pain spreading down the arm is common and disabling.

What this study adds: Four sessions of neural tissue management over two weeks increased the number of people who experienced substantial reductions in neck pain, arm pain, and self-reported activity limitations. Adverse events such as aggravation of pain or headache were typically brief, non-disabling, and were not associated with poorer outcomes at four weeks.
change the short-term natural history of nerve-related neck and arm pain. Additionally, as with other physiotherapy interventions for the cervical spine, detailed information about adverse events related to neural tissue management is needed (Carlesso et al 2010a).

Thus, the research questions for this study were:

1. For patients with nerve-related neck and arm pain, what are the benefits and harms of neural tissue management compared to advice to remain active in the short term?
2. What are the characteristics (type, frequency, onset, duration, severity) of any adverse events that patients relate to neural tissue management?
3. Does experiencing an adverse event reduce a patient’s chance of benefiting from neural tissue management?

Method

Design

A randomised controlled trial was conducted. A detailed protocol has been published elsewhere (Nee et al 2011). Participants were randomised to receive advice to remain active and neural tissue management (experimental group) or advice to remain active only (control group). The Queensland Clinical Trials Centre prepared the randomisation list with a random number generator. Randomisation occurred in blocks of 12 without stratification. Participants were assigned to the experimental or control group in a 2:1 ratio to increase the data available for a separate analysis to develop a model that predicts the likelihood of improvement with neural tissue management (Nee et al 2011). Allocation was concealed. Group assignments were sealed in sequentially numbered, opaque envelopes by a research assistant who was not involved in data collection. Another independent research assistant revealed the group assignment to each participant after the baseline assessment. Neural tissue management involved a standardised program of four treatments over two weeks. Outcomes were measured at baseline and at a follow-up four weeks later. Adverse events that participants related to neural tissue management were documented with a questionnaire administered at the second through fourth treatments and at follow-up. Baseline and follow-up data were collected at a research laboratory within a tertiary academic institution. The examiner who collected baseline and follow-up data was blinded to group assignments. It was not possible to blind participants or the physiotherapists who provided interventions.

Participants, therapists, centres

Participants were recruited from the general community through advertisements in local newspapers and electronic newsletters. Eligible participants were aged 18–60 years with non-traumatic neck and unilateral arm pain that spread below the deltoid tuberosity. Symptoms had to have been present for at least four weeks and preceded by a pain-free period of four weeks or longer (de Vet et al 2002). Participants’ average levels of neck and arm pain during the previous week were recorded on separate 11-point numeric pain rating scales (Jensen et al 1994). The mean of these two scores had to be ≥3/10 for participants to enter the trial.

Participants’ symptoms had to be reproduced by the upper limb neurodynamic test for the median nerve (ULNT1\textsubscript{MEDIAN}) and changed by structural differentiation (contralateral neck sidebending or releasing wrist extension) (Butler 2000, Elvey 1997). This ULNT1\textsubscript{MEDIAN} response suggested that participants’ symptoms were at least partly related to increased nerve mechanosensitivity (Butler 2000, Hall and Elvey 2004). Participants with two or more abnormal neurological findings (decreased strength, reflex, or sensation) at the same nerve root level (C5 to T1) were excluded. It has been suggested that these two enrolment criteria would select participants who would be considered appropriate candidates for neural tissue management (Butler 2000, Elvey 1986, Hall and Elvey 2004).

Additional exclusion criteria were: bilateral arm symptoms, symptoms or signs suggestive of cervical myelopathy, physiotherapy intervention for neck and arm pain within the previous six weeks, previous neck or upper limb surgery, and medical red flags (Childs et al 2004) that suggested serious pathology. Self-report outcomes required that participants were proficient in speaking and reading English. Consecutive participants who met all enrolment criteria and provided informed consent entered the trial.

Physiotherapists (n = 8) who provided neural tissue management had postgraduate qualifications in musculoskeletal physiotherapy and attended a two-hour training session prior to initiating the trial. Physiotherapists were located at eight private physiotherapy practices in the local metropolitan area. Participants assigned to the experimental group received treatment at the most convenient location.

Intervention

All participants were advised to continue their usual activities after the baseline assessment. Baseline medication use was documented and participants were allowed to continue use of over-the-counter or prescription medications for their symptoms as needed or as instructed by their medical practitioner.

Neural tissue management was based on principles proposed by Elvey (1986) and Butler (2000). Along with advice to continue their usual activities, participants assigned to the experimental group received an educational component, manual therapy techniques, and a home program of nerve gliding exercises. The educational component attempted to reduce unnecessary apprehension participants may have had about neural tissue management (Butler 2000). The manual therapy techniques and nerve gliding exercises have been advocated for reducing nerve mechanosensitivity (Butler 2000, Coppieters and Butler 2008, Elvey 1986).

The educational component emphasised two points. First, examination findings suggested that participants’ symptoms were at least partly related to nerves in the neck and arm that had become overly sensitive to movement. Second, neural tissue management techniques would move the nerves in a gentle and pain-free manner, aiming to reduce this sensitivity. The manual therapy techniques included a contralateral cervical lateral glide and a shoulder girdle oscillation combined with active cranio cervical flexion to elongate the posterior cervical spine (Elvey 1986). The home program of nerve gliding exercises involved a ‘sliding’ and a ‘tensioning’ technique for the median nerve and cervical nerve roots (Coppieters and Butler 2008). In the ‘sliding’ technique, a movement that lengthened the median nerve bed (elbow and wrist extension) was counterbalanced by a movement that shortened the nerve bed (neck lateral flexion...
or rotation toward the symptomatic arm). The ‘tensioning’ technique only used movements that lengthened the median nerve bed (elbow and wrist extension alone or combined with neck lateral flexion or rotation away from the symptomatic arm). Shoulder abduction angles up to 90 degrees were used to preload the neural tissues during manual therapy techniques and nerve gliding exercises. Neural tissue management techniques were prescribed to not provoke participants’ symptoms. A gentle stretching or pulling sensation that settled immediately after the technique was the maximum sensory response allowed. Detailed protocols for applying neural tissue management techniques have been described previously (Nee et al 2011).

To verify that neural tissue management did not worsen a participant’s condition, physiotherapists monitored the body diagram, the mean numeric pain rating score for current, highest, and lowest levels of arm pain during the previous 24 hours (Cleland et al 2008), and the Patient-Specific Functional Scale (Westaway et al 1998) at the start of each treatment. Any indication that a participant’s condition may have worsened (new report of numbness or tingling, ≥ 1 point increase in arm pain, or ≥ 1 point decrease in average Patient-Specific Functional Scale score) required the physiotherapist to recheck strength, reflexes, and sensation to make sure the participant did not have two or more abnormal neurological findings. The physiotherapist and participant discussed and documented whether they felt any exacerbation was related to neural tissue management or to some other change in activity level. Neural tissue management was stopped if an exacerbation occurred that was associated with the development of two or more abnormal neurological findings. The participant was monitored after the follow-up assessment and referred for medical management as necessary. Data were retained for statistical analysis in accordance with intention-to-treat principles (Moher et al 2010).

Participants assigned to the control group received only advice to continue their usual activities. This provided a measure of the natural history of nerve-related neck and arm pain. To encourage these participants to remain in the study for the 4-week control period without treatment, they were advised that they would receive treatment afterwards, as shown in Figure 1. After the trial, they received four complimentary treatments from one of the trial’s physiotherapists. Interventions were at the physiotherapists’ discretion and no data were collected.

**Outcome measures**

The primary outcome for the benefits of neural tissue management was participant-reported improvement on a 15-point Global Rating of Change scale. The scale spans from –7 (‘a very great deal worse’) to 0 (‘no change’) to +7 (‘a very great deal better’) (Jaeschke et al 1989). Participants who reported a change ≥ +4 (at least ‘moderately better’) at follow-up were classified as ‘improved’. This represents at least moderate improvement in the participant’s condition (Jaeschke et al 1989).

Secondary outcomes for the benefits of neural tissue management were improvements in impairments in neck and arm pain intensity and reduced participant-reported activity limitations. Neck and arm pain intensity were measured by mean numeric pain rating scores for the participant’s current, highest, and lowest levels of pain during the previous 24 hours (Cleland et al 2008). Participant-reported activity limitations were measured by the Neck Disability Index (Vernon and Moir 1991) and the Patient-Specific Functional Scale (Westaway et al 1998).

The Global Rating of Change was also the primary outcome for harms related to neural tissue management. Participants with a change ≤ –2 (at least ‘a little worse’) at follow-up were classified as ‘worse’. Secondary outcomes included the number of participants who stopped neural tissue management early because they developed two or more abnormal neurological signs during an exacerbation that they and the physiotherapist related to neural tissue management and adverse events that participants related to neural tissue management.

An adverse event was defined as aggravation of existing symptoms or provocation of other unpleasant sensations after each neural tissue management treatment session (Carlesso et al 2010b, Hurwitz et al 2004). Participants described the characteristics (type, onset, duration, severity) of each adverse event on a questionnaire administered at the second through fourth treatments and at follow-up.

**Data analysis**

The difference in prevalence of ‘improvement’ (Global Rating of Change ≥ +4) and ‘worsening’ (Global Rating of Change ≤ –2) between the experimental and control groups were the primary analyses for the benefits and harms of the intervention. ‘Worst case’ intention-to-treat and ‘complete case’ analyses were performed (Moher et al 2010, Sterne et al 2009). In the ‘worst case’ analysis for benefit, participants who did not return for follow-up were classified as ‘not improved’ if assigned to the experimental group and ‘improved’ if assigned to control. For harm, participants who did not return for follow-up were classified as ‘worse’ if assigned to the experimental group and ‘not worse’ if assigned to control. ‘Complete case’ analyses included only participants who completed follow-up. The risk difference (RD) and 95% CI quantified the size of any difference in prevalence of improvement or worsening between the groups. When the 95% CI for a RD did not contain zero, the point estimate for the beneficial or harmful effect was reported as a number needed to treat (NNT) or number needed to harm (NNH) with a 95% CI.

Differences between groups in follow-up scores for neck pain, arm pain, Neck Disability Index, and Participant-Specific Functional Scale were the secondary analyses for the benefits of neural tissue management. Neck pain, arm pain, and Neck Disability Index were analysed with separate analyses of covariance (ANCOVA). Follow-up scores in each ANCOVA were adjusted by using the baseline score as the covariate (Vickers and Altman 2001). Because Participant-Specific Functional Scale activities were different for each participant, these change scores were analysed with an unpaired t-test. The size of any treatment effect was reported as the difference between group means and a standardised mean difference, each with a 95% CI. The latter allowed a comparison to previously reported treatment effects of neural tissue management (Gross et al 2004). To further aid the interpretation of any treatment effects related to these secondary outcomes (Dworkin et al 2009), NNTs with 95% CIs were calculated for the number of participants who achieved clinically important change scores for neck and arm pain (≥ 2.2 points) (Young et al 2010), Neck Disability...
Research

Volunteers who responded to recruitment advertisements screened for nerve-related neck and unilateral arm pain (n = 587)

Excluded (n = 527)
• unable to contact (n = 58)
• no clinic locations convenient (n = 41)
• age > 60 yr (n = 37)
• traumatic consent (n = 6)
• location of symptoms (n = 157)
• composite pain rating < 3/10 (n = 48)
• physiotherapy in previous 6 wk (n = 58)
• previous neck or upper limb surgery (n = 21)
• negative median nerve neurodynamic test (n = 83)
• ≥ 2 abnormal neurological signs (n = 3)
• decided not to participate (n = 13)
• not fluent in English (n = 1)
• congenital hand deformity in uninvolved limb prevented bilateral comparison (n = 1)

Volunteers who responded to recruitment advertisements screened for nerve-related neck and unilateral arm pain (n = 587)

Lost to follow-up (n = 2)
• changed work schedule prevented attendance at treatments with neural tissue management and participant decided not to attend follow-up (n = 2)

Week 0

Measured neck and arm pain intensity over previous 24 hr and participant-reported activity limitations with Neck Disability Index and Patient-Specific Functional Scale

Randomised in 2:1 ratio (n = 60)
(n = 40)                                                                                             (n = 20)

Experimental Group
• advice to remain active
• brief education
• manual therapy
• nerve gliding exercises
• 4 treatments over 2 wk

Control Group
• advice to remain active

Lost to follow-up (n = 2)
• no reason given (n = 1)
• hospitalised for an unrelated medical issue (n = 1)

Week 4

Measured participant-reported improvement or worsening with the Global Rating of Change scale, neck and arm pain intensity over the previous 24 hr, and participant-reported activity limitations with Neck Disability Index and Patient-Specific Functional Scale

(n = 38)                                                                                             (n = 18)

Participation in study completed

Received 4 physiotherapy treatments (Physiotherapist determined intervention)

Figure 1. Design and flow of participants through the trial.
The characteristics of adverse events related to neural tissue management were reported with descriptive statistics. A risk ratio (RR) with a 95% CI was calculated to determine whether experiencing an adverse event reduced a participant’s chance for being improved at follow-up. Only ‘complete case’ analyses were performed on secondary outcomes for the benefits and harms of neural tissue management.

The sample size was based on having 80% power to detect a 33% difference in the prevalence of ‘improvement’ between groups ($p \leq 0.05$). This translates to a NNT $\leq 3$, which was considered a clinically important treatment effect for changing the short-term natural history of nerve-related neck and arm pain. Assuming a prevalence of ‘improvement’ in the control group of 10% and an overall drop-out rate of 10%, the trial required 84 participants (experimental = 56, control = 28).

**Results**

**Flow of participants through the trial**

Participants were recruited from July 2009 through July 2011. Of the 587 volunteers who responded to recruitment advertisements, 60 entered the trial. Although the *a priori* sample size was 84, recruitment stopped at 60 because time constraints did not allow data collection to extend beyond two years. The flow of participants through the trial and reasons for the loss to follow-up of two participants from the experimental group (5%) and two from the control group (10%) are presented in Figure 1.

Participants’ baseline characteristics are presented in Table 1. Those in the experimental group had their symptoms for longer and were more likely to be using medication. Control group participants were slightly more likely to report symptoms below the elbow and that arm symptoms were worse than neck symptoms. There were no important differences between groups in baseline scores for neck pain, arm pain, or Neck Disability Index.

**Compliance with the trial method**

Follow-up visits for some participants occurred at three weeks rather than four, but there was no significant difference in the time from baseline to follow-up between the experimental (mean 24 days, SD 4) and control (mean 25 days, SD 2) groups. All participants who completed follow-

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**Table 1. Baseline characteristics of participants.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (n = 60)</th>
<th>Exp (n = 40)</th>
<th>Con (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n female (%)</td>
<td>38 (63)</td>
<td>26 (65)</td>
<td>12 (60)</td>
</tr>
<tr>
<td>Age (yr), mean (SD)</td>
<td>47 (9)</td>
<td>47 (8)</td>
<td>48 (9)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²), mean (SD)</td>
<td>26.7 (4.4)</td>
<td>27.3 (4.7)</td>
<td>25.7 (3.7)</td>
</tr>
<tr>
<td>Duration of symptoms (wk), median (IQR)</td>
<td>26 (12 to 77)</td>
<td>32 (15 to 104)</td>
<td>18 (8 to 39)</td>
</tr>
<tr>
<td>Symptoms distal to elbow, n (%)</td>
<td>46 (77)</td>
<td>29 (73)</td>
<td>17 (85)</td>
</tr>
<tr>
<td>Arm symptoms worst, n (%)</td>
<td>20 (33)</td>
<td>11 (28)</td>
<td>9 (45)</td>
</tr>
<tr>
<td>Reported numbness or tingling, n (%)</td>
<td>32 (53)</td>
<td>20 (50)</td>
<td>12 (60)</td>
</tr>
<tr>
<td>Using medication for symptoms, n (%)</td>
<td>27 (45)</td>
<td>23 (58)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Neck pain previous 24 hrs (0 to 10), mean (SD)</td>
<td>4.2 (2.0)</td>
<td>4.3 (1.7)</td>
<td>4.1 (2.4)</td>
</tr>
<tr>
<td>Arm pain previous 24 hrs (0 to 10), mean (SD)</td>
<td>4.0 (1.6)</td>
<td>4.0 (1.6)</td>
<td>4.1 (1.6)</td>
</tr>
<tr>
<td>Neck Disability Index (0 to 50), mean (SD)</td>
<td>12.5 (4.4)</td>
<td>12.7 (4.2)</td>
<td>12.1 (4.7)</td>
</tr>
</tbody>
</table>

Exp = experimental (neural tissue management), Con = control (advice to remain active)

Index ($\geq$ 7 points, 0 to 50 scale) (MacDermid et al 2009), and Patient-Specific Functional Scale ($\geq$ 2.2 points) (Cleland et al 2006, Young et al 2010).

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![Figure 2](image-url)
up received treatment as described except for one (3%) in the experimental group and one (5%) in the control group. The experimental group participant received only three treatments, which meant that the 38 participants in this group who completed follow-up received 151 treatments. Between treatments three and four, this participant experienced an exacerbation of symptoms related to an unusual amount of heavy lifting at work. The participant exhibited two abnormal neurological signs when assessed prior to the fourth treatment and therefore was not treated. The exacerbation and neurological signs were not related to neural tissue management in the opinion of the participant and physiotherapist and had resolved when the participant attended follow-up less than a week later. The control group participant attended four chiropractic treatments. Global Rating of Change scores indicated that neither participant was ‘improved’ or ‘worse’ at follow-up. These participants were analysed with their assigned group.

### Effect of intervention

The distribution and frequency of Global Rating of Change scores at follow-up are presented in Figure 2.

### Table 2. ‘Worst case’ and ‘complete case’ analyses of number and proportion of participants in each group reporting a Global Rating of Change score classified as an ‘improvement’ or ‘worsening’.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Exp</th>
<th>Con</th>
<th>Risk difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘Improved’ at follow-up (GROC ≥ +4), n / group n (%)</td>
<td>21/40 (53)</td>
<td>3/20 (15)</td>
<td>–38% (–16 to –60)</td>
</tr>
<tr>
<td>‘Worst case’ intention-to-treat analysis</td>
<td>21/38 (55)</td>
<td>1/18 (5)</td>
<td>–50% (–31 to –69)</td>
</tr>
<tr>
<td>‘Complete case’ analysis</td>
<td>5/40 (13)</td>
<td>4/20 (20)</td>
<td>–7% (–28 to 13)</td>
</tr>
<tr>
<td>‘Worse’ at follow-up (GROC ≤ –2), n / group n (%)</td>
<td>3/38 (8)</td>
<td>4/18 (22)</td>
<td>–14% (–35 to 7)</td>
</tr>
</tbody>
</table>

### Table 4. ‘Complete case’ analysis of mean (SD) follow-up scores for neck pain, arm pain and Neck Disability Index and mean (SD) change in Patient-Specific Functional Scale scores for each group, mean (95% CI) difference between groups, and standardised mean difference (95% CI) between groups.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Exp (n = 38)</th>
<th>Con (n = 18)</th>
<th>Difference between groups</th>
<th>Standardised mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck pain previous 24 hrs (0 to 10)</td>
<td>2.6 (2.4)</td>
<td>4.2 (2.2)</td>
<td>–2.1</td>
<td>–0.9 (–0.5 to –1.3)</td>
</tr>
<tr>
<td>Arm pain previous 24 hrs (0 to 10)</td>
<td>2.4 (2.1)</td>
<td>4.0 (1.9)</td>
<td>–1.5</td>
<td>–0.7 (–0.3 to –1.1)</td>
</tr>
<tr>
<td>Neck Disability Index (0 to 50)</td>
<td>8.9 (5.4)</td>
<td>11.2 (5.0)</td>
<td>–3.4</td>
<td>–0.6 (–0.2 to –1.0)</td>
</tr>
<tr>
<td>Patient-Specific Functional Scale change score (0 to 10)</td>
<td>2.0 (2.1)</td>
<td>0.4 (1.0)</td>
<td>2.1</td>
<td>0.9 (0.5 to 1.3)</td>
</tr>
</tbody>
</table>

### Table 5. ‘Complete case’ analysis of number of participants (%) in each group who achieved clinically important change scores for impairments in pain intensity and participant-reported activity limitations, and number needed to treat (95% CI).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Exp (n = 38)</th>
<th>Con (n = 18)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck pain previous 24 hrs (0 to 10) (decrease ≥ 2.2 points)</td>
<td>13 (34)</td>
<td>1 (6)</td>
<td>3.6 (2.1 to 10.0)</td>
</tr>
<tr>
<td>Arm pain previous 24 hrs (0 to 10) (decrease ≥ 2.2 points)</td>
<td>13 (34)</td>
<td>1 (6)</td>
<td>3.6 (2.1 to 10.0)</td>
</tr>
<tr>
<td>Neck Disability Index (0 to 50) (decrease ≥ 7 points)</td>
<td>11 (29)</td>
<td>1 (6)</td>
<td>4.3 (2.4 to 18.2)</td>
</tr>
<tr>
<td>Patient-Specific Functional Scale (0 to 10) (increase ≥ 2.2 points)</td>
<td>15 (39)</td>
<td>1 (6)</td>
<td>3.0 (1.9 to 6.7)</td>
</tr>
</tbody>
</table>
The experimental intervention changed the short-term natural history of nerve-related neck and arm pain. ‘Worst case’ intention-to-treat and ‘complete case’ analyses are presented in Table 2. Individual participant data are presented in Table 3 (see eAddenda for Table 3). These risk differences show that ‘improvement’ occurred significantly more often among participants in the experimental group (Table 2). The ‘worst case’ analysis indicates that for every three patients treated, one more patient would achieve ‘improvement’ than would otherwise occur (95% CI 1.7 to 6.5). The ‘complete case’ analysis indicates that for every two patients treated, one more patient would achieve ‘improvement’ than would otherwise occur (95% CI 1.5 to 3.3). Although nearly 60% of the experimental group were using medication at baseline, there was no relationship between medication use and improvement in this group (RR 1.02, 95% CI 0.56 to 1.84). Analyses of follow-up scores for pain and activity limitations added medication use and duration of symptoms as covariates to account for baseline differences between groups. Therefore, Patient-Specific Functional Scale change scores were analysed with an ANCOVA rather than an unpaired t-test. The experimental group had better follow-up scores for pain and activity limitations with ‘moderate’ standardised mean differences (≥0.6 but < 1.2) (Hopkins 2011) (Table 4). NNT values show that substantially greater proportions of participants in the experimental group achieved clinically important change scores for neck pain, arm pain, Neck Disability Index, and Patient-Specific Functional Scale (Table 5). Individual participant data for these outcomes are again presented in Table 3 (see eAddenda for Table 3).

There was no evidence to suggest that neural tissue management was harmful. ‘Worst case’ intention-to-treat and ‘complete case’ analyses showed no difference in the prevalence of worsening between groups (Table 2). Additionally, no participants had to stop neural tissue management early because of an exacerbation and associated adverse events.

### Table 6. Characteristics of unpleasant sensations that constituted adverse events that participants related to neural tissue management.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unpleasant sensations (n = 82)</th>
<th>Participants experiencing the unpleasant sensation during one or more adverse events (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aggravation of neck pain</td>
<td>17 (21)</td>
<td>14 (37)</td>
</tr>
<tr>
<td>Aggravation of arm pain</td>
<td>14 (17)</td>
<td>12 (32)</td>
</tr>
<tr>
<td>Aggravation of other symptomsa</td>
<td>5 (6)</td>
<td>5 (13)</td>
</tr>
<tr>
<td>Arm weakness</td>
<td>9 (11)</td>
<td>5 (13)</td>
</tr>
<tr>
<td>Tiredness or fatigue</td>
<td>11 (13)</td>
<td>7 (18)</td>
</tr>
<tr>
<td>Headache</td>
<td>14 (17)</td>
<td>11 (29)</td>
</tr>
<tr>
<td>Dizziness or imbalance</td>
<td>2 (2)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Fainting</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>2 (2)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Blurred or impaired vision</td>
<td>2 (2)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>3 (4)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Confusion or disorientation</td>
<td>1 (1)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Depression or anxiety</td>
<td>2 (2)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Time of onset after treatment, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30 min</td>
<td>40 (49)</td>
<td></td>
</tr>
<tr>
<td>30 min to 4 hr</td>
<td>18 (22)</td>
<td></td>
</tr>
<tr>
<td>4 to 24 hr</td>
<td>20 (24)</td>
<td></td>
</tr>
<tr>
<td>&gt; 24 hr</td>
<td>4 (5)</td>
<td></td>
</tr>
<tr>
<td>Duration, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10 min</td>
<td>6 (7)</td>
<td></td>
</tr>
<tr>
<td>10 min to 1 hr</td>
<td>12 (15)</td>
<td></td>
</tr>
<tr>
<td>1 to 24 hr</td>
<td>47 (57)</td>
<td></td>
</tr>
<tr>
<td>&gt; 24 hr</td>
<td>17 (21)</td>
<td></td>
</tr>
<tr>
<td>Intensity (0 to 10 numeric rating scale), mean (SD)</td>
<td>4.7 (2.1)</td>
<td></td>
</tr>
<tr>
<td>Restriction of home or work activities, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>24 (29)</td>
<td></td>
</tr>
<tr>
<td>A little</td>
<td>48 (59)</td>
<td></td>
</tr>
<tr>
<td>A lot</td>
<td>10 (12)</td>
<td></td>
</tr>
</tbody>
</table>

a numbness, tingling
Adverse events
Sixteen participants (42%) reported an adverse event that they related to neural tissue management after 29 of the 151 treatments (19%). Questionnaires were returned for 25 of the 29 adverse events. The characteristics of these adverse events are summarised in Table 6. On average, an adverse event consisted of three to four unpleasant sensations (82 unpleasant sensations over 25 adverse events). Aggravation of neck or arm pain and headache were most common. Nearly all (95%) unpleasant sensations started within 24 hours of the previous treatment session and approximately 80% lasted < 24 hours. Importantly, no additional treatments were needed for any unpleasant sensation and 88% of unpleasant sensations had little or no impact on participants’ daily activities. Furthermore, experiencing an adverse event did not reduce a participant’s chance of benefiting from neural tissue management because there was no difference in improvement rates for participants who did (9/16, 56%) and did not (12/22, 55%) experience an adverse event (RR = 1.03, 95% CI 0.58 to 1.84).

Discussion
This randomised controlled trial examined the benefits and harms of neural tissue management as an intervention for nerve-related neck and arm pain. Low NNTs and moderate standardised mean differences show that neural tissue management produced clinically important benefits for participant-reported improvement, pain intensity, and activity limitations at short-term follow-up when compared to advice to remain active. There was no evidence to suggest that neural tissue management was harmful. The prevalence of worsening was similar for the experimental and control groups, and no participants had to stop neural tissue management early because of an exacerbation that they and the physiotherapist related to treatment. Although several participants experienced adverse events that they related to neural tissue management, these events would be categorised as ‘mild’ because they did not require additional treatment, usually lasted < 24 hours, had minimal impact on daily activities, and did not reduce a participant’s chance of improving with neural tissue management (Carlesso et al 2011, Carnes et al 2010). The proportion of participants assigned to neural tissue management who experienced an adverse event and the characteristics of these events are similar to those reported previously for manual therapy for patients with neck pain (Hurwitz et al 2004). The results of this trial enable physiotherapists to have informed discussions with patients about the short-term benefits and harms of neural tissue management for nerve-related neck and arm pain.

Standardised mean differences for pain were similar to results from the trial by Allison and colleagues (2002) (≥ 0.7 versus 0.71), while those for activity limitations were larger (≥ 0.6 versus 0.34) (Gross et al 2004). The consistently favourable results for neural tissue management support the hypothesis that the lack of statistical significance in this previous trial was due to the small sample.

The size and source of the sample, comparison to advice to remain active, and short-term follow-up are potential limitations of our study. Time constraints prevented enrolment of the a priori sample of 84 participants. Although we anticipated that approximately 10% of volunteers would enter the trial, the response to each recruitment advertisement was lower than expected. Enrolment stopped at 60 participants because data collection could not extend beyond two years. The concern with early stoppage of a trial is that any treatment effect may reflect a ‘random high’ in the data rather than the ‘true’ effect (Moher et al 2010). We suggest that the large benefit of neural tissue management for participant-reported improvement in the short term is unlikely to be a ‘random high’ in the data because the ‘worst case’ intention-to-treat analysis still revealed a NNT of three with a relatively narrow 95% CI. Clinicians should remember that participants were recruited from the general community when interpreting our results. However, we are unaware of any data showing that treatment effects differ when samples with the same enrolment criteria are recruited from the general community rather than the clinic.

Because advice to remain active was the control condition, it is unclear whether observed benefits of neural tissue management reflect non-specific effects due to interacting with a physiotherapist or participants’ expectations, effects specific to neural tissue management, or to some combination. While discriminating non-specific from specific treatment effects is deemed important, establishing that neural tissue management can change the natural history of nerve-related neck and arm pain was a necessary prerequisite (Bialosky et al 2011). Assuming that a credible comparison intervention can be developed to measure non-specific effects accurately, future research should try to quantify the relative contributions that non-specific and specific effects make to the benefits of neural tissue management. Future research should also determine whether neural tissue management provides benefits in the longer term.

eAddenda: Table 3 available at jop.physiotherapy.asn.au

Ethics: The University of Queensland Medical Research Ethics Committee approved this study. All participants gave written informed consent before data collection began.

Competing interests: The authors have no competing interests.

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References


