Deep tissue massage, strengthening and stretching exercises, and a combination of both compared with advice to stay active for subacute or persistent non-specific neck pain: A cost-effectiveness analysis of the Stockholm Neck trial (STONE)

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ABSTRACT

Objective: To evaluate the cost-effectiveness of deep tissue massage (‘massage’), strengthening and stretching exercises (‘exercises’) or a combination of both (‘combined therapy’) in comparison with advice to stay active (‘advice’) for subacute and persistent neck pain, from a societal perspective.

Methods: We conducted a cost-effectiveness analysis alongside a four-arm randomized controlled trial of 619 participants followed-up for one year. Health-related quality of life was measured using EQ-5D-3L and costs were calculated from baseline to one year. The interventions were ranked according to quality adjusted life years (QALYs) in a cost-consequence analysis. Thereafter, an incremental cost per QALY was calculated.

Results: In the cost-consequence analysis, in comparison with advice, exercises resulted in higher QALY gains, and massage and the combined therapy were more costly and less beneficial. Exercises may be a cost-effective treatment compared with advice to stay active if society is willing to pay 17 640 EUR per QALY. However, differences in QALY gains were minimal; on average, participants in the massage group spent a year in a state of health valued at 0.88, exercises: 0.89, combined therapy: 0.88 and, advice: 0.88.

Conclusions: Exercises are cost-effective compared to advice given that the societal willingness to pay is above 17 640 EUR per year in full health gained. Massage and a combined therapy are not cost-effective. While exercise appeared to have the best cost/benefit profile, even this treatment had only a modest benefit and treatment innovation is needed. Advice to stay active remains as a good therapeutic alternative from an economical perspective.

1. Introduction

Neck pain is a leading cause of disability worldwide and it is especially high among people between 25 and 64 years old (Vos et al., 2016). Since most people with neck pain are in working age, this translates into high costs for the society due to productivity loss (SBU, 2000). In Sweden in 2017, neck pain accounted for 4% (95% CI 3.3–4.8%) of the total years lived with disability and its burden is increasing (Institute for Health Metrics and Evaluation). Although most costs due to neck pain come from productivity loss (Landen Ludvigsson et al., 2016), the associated healthcare utilization are also an important source of expenditures. Health care costs are higher for care related to subacute and
chronic then for acute neck pain (Horn and Fritz, 2018).

The evidence suggest that non-pharmacological therapies are effective for the clinical management of neck and associated disorders (Côté et al., 2016). Recommended interventions for non-acute neck pain include massage (Koren and Kalichman, 2018) and exercises (Côté et al., 2016; Skillgate et al., 2007). Results from the STONE trial suggest that deep tissue massage and strengthening and stretching exercises are more effective in improving self-perceived recovery than advice to stay active in patients with disabling subacute and chronic non-specific neck pain (Skillgate et al., 2019).

Few studies have evaluated the cost-effectiveness of non-pharmacological therapies and none have specifically evaluated massage for neck pain from an economical perspective. The existing evidence regarding its cost-effectiveness is inconclusive (Driessen et al., 2012). Nonetheless, massage for low back pain has been shown not to be cost-effective when provided alone, but it is cost-effective when combined with exercises (Hollinghurst et al., 2008). On the other hand, exercises provided alone (Hollinghurst et al., 2008) or in combination with advice (Velde et al., 2016) are cost-effective for neck pain. In addition, one session of education is cost-effective for whiplash associated disorders (Velde et al., 2016). An economic evaluation of these types of therapies for disabling non-specific neck pain is warranted.

This study evaluates the cost-effectiveness of deep tissue massage, strengthening and stretching exercises, or a combination of both compared with advice to stay active for subacute and persistent non-specific neck pain from a societal perspective.

2. Material and methods

2.1. Study design

We conducted the Stockholm Neck (STONE) trial, a randomized controlled trial to determine the effectiveness of deep tissue massage therapy (hereafter massage), strengthening and stretching exercises (hereafter exercises), a combination of deep tissue massage and strengthening and stretching exercises (hereafter combined therapy), compared with advice to stay active (Skillgate et al., 2015). The study included subjects aged 18–70 years with subacute (30–90 days duration) or persistent (≥ 90 days duration) disabling neck pain with or without headache and/or radiating symptoms. Those with pain intensity <2/10 and pain-related disability <1/10 on the Numerical Rating Scales (NRS) were not included (Côté et al., 2016; Von Korff et al., 1992). A study coordinator prepared blocks of sequentially numbered sealed envelopes (40 for each intervention). Participants were randomly allocated to one intervention when they contacted the study coordinator. The intervention was revealed after baseline assessment at the research clinic. Blinding of participants or therapists was not possible due to the nature of the interventions. The recruitment and data collection occurred between Nov 2015 and Nov 2017. The sample size was calculated to detect a relative risk of 1.2–1.3 at 12 months follow-up for a minimal clinically important improvement in pain intensity and pain-related disability. A more detailed description of the trial’s methodology is provided elsewhere (Skillgate et al., 2015, 2019).

2.2. Interventions

All interventions were provided by naprapaths (medical professionals who focus on the management of musculoskeletal pain with a combination of manual therapy, exercise and/or advice) either under training (but with experience in the provision of massage and physical training) or licensed. The therapists underwent training sessions (3-h sessions twice) and regular supervision to ensure a standardized provision of all the interventions in the STONE trial. The number of sessions followed the usual practice in primary care in Sweden and were considered to be sufficient to achieve the purpose of the interventions; up to six sessions within six weeks were offered to the participants in the massage, exercises and combined therapy groups and up to three sessions in the advice to stay active group. All the sessions were provided individually.

2.2.1. Exercises (strengthening and stretching exercises)

Exercises targeted the following muscle groups: deep flexors of the neck, chest musculature, scapula musculature, jaw musculature and extensors of the neck. The sessions lasted 35 min on average. In addition to the supervised sessions, participants were advised to repeat the provided exercises at home. To facilitate that the execution of the exercises followed a proper technique, they were filmed with their own smartphone during the supervised sessions.

2.2.2. Massage (deep tissue massage)

The components of the deep tissue massage therapy were: massage of muscles of the neck, upper back, jaw and chest, as well as management of active and latent points producing concordant signs and stretching of chest. The techniques used were effleurage, firm motion involving compression and pressure release and deep muscle/fascia massage to areas that produced concordant symptoms. The sessions lasted 35 min on average.

2.2.3. Combined therapy (combination of strengthening and stretching exercises and deep tissue massage)

The combined therapy started with the same techniques as in the exercises groups and finished with the techniques in the massage group. Similar to the exercises group, in addition to the supervised sessions, participants were advised to repeat the provided exercises at home. Sessions lasted 50 min divided equally to the two modalities.

2.2.4. Advice (advice to stay active)

The intervention in the advice group consisted of a motivating discussion using evidence-based information on spinal pain in addition to an educational booklet. The advice group was the control group. Sessions lasted 20–25 min.

2.3. Outcomes

Participants filled out questionnaires at baseline, seven weeks, three months, six months and one year. We measured health-related quality of life using the EQ-5D-3L questionnaire (Group TE, 1990) (not measured at seven weeks), and based on this, utility was calculated using Swedish experience-based utility values (using the time trade-off method (Burstrom et al., 2014).

Pain intensity and pain-related disability were measured with numerical rating scales (NRS) from the Chronic Pain Questionnaire (Von Korff et al., 1992); information on perceived recovery (Kamper et al., 2010) as well as sickness absence were also collected. These outcomes were, however, not included in the economic evaluation. A more detailed description of procedures and findings regarding the effectiveness of the interventions (in terms of pain intensity, pain-related disability, perceived recovery and sickness absence) has been reported elsewhere (Skillgate et al., 2015, 2019).

2.4. Cost calculation

We collected information on direct medical costs (interventions, appointments with different health providers and prescribed drugs), direct non-medical costs (over the counter medication, neuropathic medication and time allocated to attend appointments) and indirect costs (sickness absence). Costs used in the economic evaluation were calculated as a product of items of resources used. The unit cost of each type of item associated with the therapy as described in the section below. All the costs were collected in Swedish crowns (SEK) and converted to Euros (1 EUR = 9.94 SEK (X-RATES, 2017)) for the year 2017/2018 (which correspond to the period in which the randomized
controlled trial was conducted) and no discounting was applied since the interventions and the follow-ups occurred within one year.

2.4.1. Healthcare utilization

Direct medical and non-medical costs were calculated by multiplying the number of each resource use at the individual level with its corresponding unit cost. No hospitalizations costs were recorded. Visits to physiotherapists and medical doctors are subsidized by the Swedish healthcare system and patients usually pay a copayment only. We assigned the fee paid by the patients plus the compensation given by the city council (Svensk Forfattningssamling, 2017a, 2017b). The cost of the interventions in the trial were obtained from market prices of visits to naprapaths, depending on the duration of the intervention, rather than from a direct calculation based on salaries, overhead costs, supplies and others, since that information was not available. The cost of imaging was calculated from the average of the market prices in Stockholm. For prescribed and over the counter (OTC) medication, we took the selling price available on The Dental and Pharmaceutical Benefits Agency (TLV from its name in Swedish). For naturopathic medications, price information was obtained from the local and online retailers and assigned to each participant individually. The Swedish healthcare system subsidizes prescribed medications, imaging and appointments with medical doctors, physiotherapists and, to some extent, psychotherapists (high-cost threshold) in order to protect patients from high expenditures (1177 Vårdguiden, 2015). This reduction in costs was taken into account during the cost calculations.

The unit costs assigned were as follows: 1019 SEK/appointment with a medical doctor (103 EUR), 564 SEK/appointment with a physiotherapist (57 EUR), 661 SEK/appointment with a naprapath (67 EUR), 607 SEK/appointment with a chiropractor (61 EUR), 657 SEK/appointment with an osteopath (66 EUR), 506 SEK/appointment with a masseur (51 EUR), 863 SEK/appointment with a psychotherapist (87 EUR), 159 SEK/session of Yoga or similar interventions (16 EUR), 546 SEK/appointment with other providers not listed above (mostly alternative medicine or fitness-related) (55 EUR), 609 SEK for x-rays (61 EUR), 1795 SEK for computerized tomographies (181 EUR), 2428 SEK for magnetic resonances (244), 10.6 SEK/day for prescribed medications on average (1.1 EUR), 5.7 SEK/day for over the counter medications on average (0.6 EUR), and 7.8 SEK/day for naturopathic medications on average (0.8 EUR).

2.4.2. Production loss and opportunity costs

Indirect costs were included in terms of losses to paid production (i.e., sickness absence). Participants reported the number of days they had been off work due to neck pain. We followed the human capital approach (SBU, 2017) (the value of people’s contribution is based on what they are paid) to calculate the cost of production loss. We multiplied the number of days off work by the mean salary based on the self-reported occupation (Statistics Sweden, 2018). Students and pensioners were assigned zero as value and volunteer time was deemed minimal.

Since we did not have specific information on means of transportation to and from the clinic or whether they used that time from work (or leisure time), no costs for that concept were assigned. However, overtime cost was used for the time invested in attending appointments, both the ones provided as part of the trial and the ones incurred by the participants after that. An hour was assumed for each attended appointment and the average salary for Sweden was used (33 700 SEK 3391 EUR). (Statistics Sweden).

A typical month was assumed to consist of 21 working days or 168 h.

2.5. Analyses

A recommended broader societal perspective on the impact of resource use was followed when conducting the economic evaluation. This implies that all relevant costs and effects of the intervention and non-specific neck pain are considered, regardless of who pays or benefits. An intention to treat principle was followed (SBU, 2017). Costs and benefits were analyzed within one year horizon (the RCT followed participants for one year) (Drummond et al., 2005). No discounting was applied (Drummond et al., 2005). Quality-Adjusted Life Years (QALYs) were calculated over one year using the standard calculation method (area under the curve) (Drummond et al., 2005). Quality of life is measured at 0 and 1. A QALY is equivalent to one year in perfect health (Drummond et al., 2005). Thereafter, a cost-consequence analysis (Kamlet, 1992) was performed in order to trim off strongly dominated alternatives, ranked by QALYs. If one of the interventions resulted in larger effects and higher cost than the next one in the QALYs-based rank, the relative cost-effectiveness of the intervention was calculated in terms of incremental cost-effectiveness ratio (ICER) by dividing the incremental costs by the incremental QALYs.

In order to account for the missing values in costs and QALYs, we did multiple imputation using QALYs at baseline (baseline utility) and provided intervention as predictors. We used predictive mean matching to impute QALYs and a regression function to impute data on costs. The economic value of providing an intervention was represented by the ICER. The differences in costs and QALYs between therapies was visually represented in a cost-effectiveness plane by using bootstrapping with 5000 replications. Seemingly unrelated regression was used to calculate the bootstrapped total costs and QALYs. To summarize the impact of uncertainty on the ICER, a cost-effectiveness acceptability curve (CEAC) was used to show the probability that the intervention will be cost-effective at different willingness to pay thresholds. All analyses were performed using Microsoft Excel and Stata 14.1 (StataCorp, 2015).

2.5.1. Sensitivity analysis

An a posteriori sensitivity analysis was performed by excluding the costs from sickness absence. We observed that this item showed the highest difference between therapies. In addition, we observed differences at baseline in terms of the proportion of persons reporting sickness absence the past six months (Advice 23%, 95% CI: 16–32; Massage 29% 95% CI: 21–38; Exercises 31% 95% CI: 23–39 and, Combined therapy 31% 95% CI: 23–39). This supported the decision for conducting the sensitivity analysis. An ICER and a CEAC were obtained using the same procedures as in the main analysis.

2.6. Flow of participants in the STONE trial

After assessment of eligibility, 619 subjects were included in the study (Fig. 1). After randomization, 145 subjects were allocated to the massage group, 159 to the exercises group, 168 to the combined therapy group and 147 to the advice group. The drop-out rate was higher in the advice group (21%) (Fig. 1). There were no differences in baseline demographic characteristics in between dropouts and those remaining in the study (P-values > 0.05).

2.7. Ethics

Participants gave their consent to participate in the STONE trial and for their data to be analyzed. The trial was approved by the Regional Ethics Committee in Stockholm (Registration number: 2014/755-31/3). The trial was registered 3 July 2014 with registration number ISRCTN01453590.

3. Results

Most participants were females, the mean age was 46 years, most participants had completed more than 12 years of education, the most common occupations were managerial or those requiring a high university degree (Table 1). Most participants had had neck pain for at least one year and reported a gradual onset of pain. The advice group had lower proportion of persons reporting at least one day of sickness
absence related to neck pain in the past six months (Table 1).

### 3.1. Effectiveness

Health-related quality of life improved in all groups at all follow-ups compared to measurements at baseline. The average values ranged between 0.846 and 0.898, indicating an overall good health related quality of life with little variation. No differences between groups were observed (All p-values > 0.05) (Table 2).

### 3.2. Costs

Cost were calculated from the start of the interventions and for 52 weeks follow-up (Table 3). The largest contributor to the cost of the
interventions was production lost due to sickness absence. This was higher in the massage (8642 SEK  870 EUR) and in the combined therapy (4694 SEK  472 EUR) groups, and the lowest in the advice group (2524 SEK  254 EUR). The costs for the combined therapy was higher (4009 SEK  404 EUR) since the duration of each session was longer compared with other interventions. On the other hand, advice was the cheapest (1352 SEK  136 EUR). Physiotherapists and masseurs were the providers most often visited by the participants during the year following the intervention. Participants in the exercises group spent less money on appointments with other care providers compared with the other intervention groups (2961 SEK (298 EUR) compared to 4433 SEK (446 EUR) in the massage group, 4146 SEK (417 EUR) in the advice group and 3567 SEK (359 EUR) in the combined therapy group). The number of days used prescribed medications seemed to be lower when exercises were provided (alone or in combination with massage). No apparent differences were observed between the groups in the use of over the counter or natural medications (Table 3).

3.3. Cost-consequence analysis

Table 4 presents the cost-consequence analysis of the interventions in the STONE trial. The interventions were ranked according to the QALYS over one year. Exercises had the highest total area under the curve, followed by advice, combined therapy and massage. However, the differences between the groups were small: massage 0.8817, exercises 0.8930, combined therapy 0.8840 and, advice 0.8844.

3.4. Incremental cost-effectiveness ratio from cost-effectiveness analysis

As result of the cost-consequence analysis, a comparison between exercises and advice to stay active in terms of the ICER was further performed using a cost-effectiveness approach for resource allocation decisions.

Table 4 Cost-consequence analysis of the interventions in the STONE trial.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>QALY*</th>
<th>Cost</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercises</td>
<td>0.8930</td>
<td>11 781 SEK (1186 EUR)</td>
<td></td>
</tr>
<tr>
<td>Advice to stay active</td>
<td>0.8844</td>
<td>10 265 SEK (1033 EUR)</td>
<td></td>
</tr>
<tr>
<td>Combined therapy</td>
<td>0.8840</td>
<td>14 663 SEK (1476 EUR)</td>
<td></td>
</tr>
<tr>
<td>Massage therapy</td>
<td>0.8817</td>
<td>19 669 SEK (1979 EUR)</td>
<td></td>
</tr>
</tbody>
</table>

*Calculated with the area under the curve approach. (After adjusting for the high-cost threshold.

Table 3 Mean number of units (as specified below) and mean cost and standard deviations per person over a year by treatment arm. All costs in Euros. 1 EUR  9.94 SEK for the period 2017/2018.

<table>
<thead>
<tr>
<th></th>
<th>Advice (n 147)</th>
<th>Massage (n 145)</th>
<th>Exercises (n 159)</th>
<th>Combined (n 168)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Units</td>
<td>Mean Costs</td>
<td>Mean Units</td>
<td>Mean Costs</td>
</tr>
<tr>
<td>Direct medical costs</td>
<td>(SD)</td>
<td>(SD)</td>
<td>(SD)</td>
<td>(SD)</td>
</tr>
<tr>
<td>Interventions provided</td>
<td>2.4 (0.8)</td>
<td>136 (46)</td>
<td>5.8 (0.8)</td>
<td>384 (53)</td>
</tr>
<tr>
<td>therapists, sessions</td>
<td></td>
<td></td>
<td>5.0 (1.6)</td>
<td>331 (105)</td>
</tr>
<tr>
<td>Physician appointments</td>
<td>0.6 (1.6)</td>
<td>61 (169)</td>
<td>0.7 (2.2)</td>
<td>74 (200)</td>
</tr>
<tr>
<td>Physiotherapist</td>
<td>1.7 (5.3)</td>
<td>94 (301)</td>
<td>2.4 (6.6)</td>
<td>137 (375)</td>
</tr>
<tr>
<td>appointments</td>
<td></td>
<td></td>
<td>1.0 (3.5)</td>
<td>56 (197)</td>
</tr>
<tr>
<td>Chiropractors appointments</td>
<td>0.4 (1.6)</td>
<td>22 (97)</td>
<td>0.6 (2.2)</td>
<td>36 (136)</td>
</tr>
<tr>
<td>Osteopaths appointments</td>
<td>0.1 (0.3)</td>
<td>3 (22)</td>
<td>0.2 (1.1)</td>
<td>10 (73)</td>
</tr>
<tr>
<td>Naprapaths appointments</td>
<td>1.4 (3.2)</td>
<td>90 (216)</td>
<td>0.9 (2.1)</td>
<td>57 (142)</td>
</tr>
<tr>
<td>Masseurs appointments</td>
<td>1.9 (4.1)</td>
<td>96 (210)</td>
<td>1.4 (2.5)</td>
<td>69 (128)</td>
</tr>
<tr>
<td>Diagnostic aids</td>
<td>0.2 (0.6)</td>
<td>17 (67)</td>
<td>0.2 (0.7)</td>
<td>16 (61)</td>
</tr>
<tr>
<td>Other providers</td>
<td>0.8 (3)</td>
<td>33 (169)</td>
<td>1.2 (6.2)</td>
<td>46 (301)</td>
</tr>
<tr>
<td>Prescribed medications,</td>
<td>30.3 (76.6)</td>
<td>26 (75)</td>
<td>30.0 (70)</td>
<td>20 (64)</td>
</tr>
<tr>
<td>days</td>
<td></td>
<td></td>
<td>21.9 (57.7)</td>
<td>20 (70)</td>
</tr>
<tr>
<td>Direct medical costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-medical costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTC medications, days</td>
<td>39.3 (64.9)</td>
<td>16 (27)</td>
<td>36.2 (47.7)</td>
<td>19 (36)</td>
</tr>
<tr>
<td>Natural medications, days</td>
<td>16.0 (46.4)</td>
<td>23 (97)</td>
<td>19.3 (59.8)</td>
<td>17 (77)</td>
</tr>
<tr>
<td>Leisure time, hours</td>
<td>9.3 (10.8)</td>
<td>187 (219)</td>
<td>13.3 (13.3)</td>
<td>268 (268)</td>
</tr>
<tr>
<td>Indirect costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sickness absence, days</td>
<td>1.6 (5.4)</td>
<td>254 (939)</td>
<td>6.3 (22.5)</td>
<td>870 (3543)</td>
</tr>
<tr>
<td>Total costs</td>
<td>–</td>
<td>1059 (1468)</td>
<td>–</td>
<td>2023 (4207)</td>
</tr>
<tr>
<td>Total costs, adjusted</td>
<td>–</td>
<td>1033 (1412)</td>
<td>–</td>
<td>1979 (4104)</td>
</tr>
</tbody>
</table>

NOTE: Data is not normally distributed. However, median and percentile 25-percentile 75 values are equal to 0 in most cases. Therefore, mean and SD are presented instead.

* For example, radiographies, computerized tomography or magnetic resonance.
1 Could refer to psychologists, psychotherapists, coaches or providers of alternative medicine.
2 Different types of medications. The type was taken into account to calculate the costs assuming standard doses.
3 Adjusting for high cost reductions for high cost or chronic diseases.
The ICER between exercises and advice to stay active was 175 295 SEK per QALY gained (17 640 EUR). The cost-effectiveness plane showed that 63% of the bootstrapped Costs-QALYs pair units lied in the upper right quadrant (more costly and more effective), 25% indicated dominance (less costly and more effective), 11% indicated that exercises were dominated by advice and 1% indicated lower costs and less effectiveness (Fig. 2).

The cost effectiveness acceptability curve showed that the probability that exercises can be considered cost-effective is about 65% at a hypothetical willingness to pay threshold of 500 000 SEK (50 315 EUR) per QALY. Similarly, it would have a 70% probability of being considered cost effective at a threshold of one million SEK per QALY. No noticeable further increases in such probability were observed at higher thresholds (Fig. 3).

3.5. Sensitivity analyses

When the costs from sickness absence are removed, the total cost of exercises decreased from 11 781 SEK (1186 EUR) to 8528 SEK (858 EUR) and the cost of advice therapy decreased from 10 265 SEK (1033 EUR) to 7741 SEK (779 EUR) and; the incremental costs decreased from 1516 SEK (153 EUR) to 787 SEK (79 EUR). The Incremental cost effectiveness ratio is in that case, 91 512 SEK per QALY gained (9209 EUR)) instead of previously 175 295 SEK per QALY gained (17 640 EUR). The cost-effectiveness plane shows slightly higher percentage of incremental costs – incremental QALYs pairs in the lower right quadrant area (29% instead of 25%). The CEAC is steeper in its first portion, indicating higher probability of being considered cost-effective at lower thresholds of willingness to pay per QALY (Supplementary Figs. 1 and 2).

4. Discussion

In this economic evaluation, we examined the cost-effectiveness of deep tissue massage, strengthening and stretching exercises, or a combination of both compared with advice to stay active for subacute and persistent non-specific neck pain from a societal perspective. We observed that exercises were the most cost-effective in terms of QALYs and that massage and combined therapy were more costly and less effective. In addition, assuming a willingness to pay equal to 500 000 SEK (50 315 EUR) per gained QALY (SBU, 2017), the probability of exercise to be considered cost-effective in reference to advice is above 60%. Although The Swedish National Board of Health and Welfare does not have an official threshold of costs per QALY to consider an intervention cost-effective, and the willingness to pay varies depending on the severity of the disease, there is consensus around the mentioned cut-off, above which it is considered a high cost per QALY (SBU, 2017).

We observed that costs due to sickness absence were lower in the advice group, likely due to a lower sickness absence already at baseline (referring to the past six months) in this group, despite the randomization. Although the differences were not statistically significant, it is likely that this might have had an influence in the overall results. However, the sensitivity analysis excluded cost of sickness absence, showing an even lower incremental costs between exercises and advice, indicating a higher likelihood of exercises to be considered cost-effective. On the other hand, massage showed the least effectiveness in terms of QALYs and the highest cost, driven to a large extend by the costs due to productivity loss. The reference intervention in the STONE
trial, advice to stay active, dominated combined therapy and deep tissue massage. Therefore, we think that advice to stay active should be considered a good alternative from an economical perspective considering that the differences in QALYs between the groups were small and not significant at any time point during the one-year follow-up.

The advice group received up to three sessions, instead of up to six as in the other three groups and they were shorter and therefore, less costly. However, we observed that individuals allocated to the advice group had a tendency to use additional health services to a higher extent, which translates into higher out-of-pocket costs with an intervention focused on self-management. In spite of this, the intervention was overall, less costly from a societal perspective.

4.1. Comparison with other studies

A recent systematic review with meta-analysis reported that supervised exercises might be cost-effective for neck pain when compared with usual care but no statistical significant differences were found (Miyanomo et al., 2018; Korthals-de Bos et al., 2003). In addition, exercises may be more costly and less effective than manual therapy, or if compared against home exercises for chronic neck pain (Miyanomo et al., 2018). In our study, we observed that exercise therapy is cost-effective. An additional study from Sweden compared neck specific exercises (with and without a behavioral intervention) to prescribed physical activity. The authors reported that neck specific exercises alone were cost-effective from a Swedish societal perspective, but not when combined with a behavioral intervention (Landen Ludvigsson et al., 2017).

In our study, adding deep tissue massage to the exercises resulted in higher costs and less effectiveness than advice to stay active. Only one previous study evaluated cost-effectiveness of massage (Tuina massage technique) alongside an RCT. (Pach et al., 2018). In that study, authors claim that massage might be cost-effective compared to a waiting list. However, several methodological weaknesses, as acknowledged by the authors, limit further comparisons (Pach et al., 2018). Although we did not distinguish between whiplash associated disorders and neck associated disorders in our analyses, our results are also in line with a study showing that education is cost-effective for whiplash associated disorders (Velde et al., 2016).

4.2. Strengths and limitations

We used a standardized instrument (EQ-5D-3L) for calculation of QALYs (Group TE, 1990). QALYs is a valid and widely used measure of effect for the purpose of economic evaluations, since it makes it possible for decision makers to compare across different diseases when it comes to resource allocation (Dolan, 1997). Furthermore, there is evidence showing that EQ-5D is appropriate for detecting responsiveness in chronic pain and musculoskeletal conditions (Payakachat et al., 2015).

Although there are various methods to calculate QALYs, such as regression models, which adjust for baseline values, (Gabrio et al.) we chose to obtain QALYs by calculating the total area under the curve following recommendations from the literature (Drummond et al., 2005). The health state preferences were measured in patients using a generic instrument and valid Swedish preference values were elicited using the time trade-off method to increase the generalizability of the economic evaluation.

There was uncertainty surrounding the costs derived from healthcare utilization. We took an average of the market prices available instead of participant-reported cost diaries. However, efforts were made to obtain precise estimates by assigning costs at the individual level. We cannot rule out the risk of errors in the estimation of costs due to information bias. Similarly, we did not obtain the exact use of medications, therefore we made assumptions based on usual recommended dosage per day and we might have over- or underestimated the costs. Nevertheless, we do not think such errors occurred to a greater extent in any of the arms, given the study design. On the other hand, such estimation of costs from market prices in Stockholm facilitates the generalizability of our results to the general population compared to if we had based our cost calculations based on only the clinic where the therapies took place.

Participants receiving exercises and a combined therapy were given the recommendation of repeating the exercise routines at home. Despite registering the number of times participants performed the exercises, we did not assign any opportunity cost to it. We made that decision considering that such exercises could be done simultaneously with other activities and it would have been difficult to know how much time was allocated for it. Moreover, assigning costs would have introduced imbalance since the advice group received education on multiple self-care options as well. It is likely that they performed, among other, home exercises. Unfortunately, this was not measured.

Although the dropout rate was higher in the advice to stay active group, the follow-up rate was very good overall and no differences were observed in terms of baseline characteristics between those who dropped out and those who remained in the study (p-value > 0.05 for various baseline characteristics; data not shown). Nonetheless, we did multiple imputation of the costs (in 12% of the costs at three months, 16% at six months and 19% at 12 months) and the QALYs (in 16% of the sample) following recommendations on conducting cost-effectiveness analyses (Burton et al., 2007).

Finally, the sample size was calculated to detect a difference between the treatment arms regarding the primary outcomes: a minimal clinically important improvement in pain intensity and a minimal clinically important improvement in pain-related disability. Therefore, the differences in terms of QALYs might not be captured in the present analyses due to lack of power.

5. Conclusions

Exercise is cost-effective compared to advice to stay active for subacute or persistent neck pain if the societal willingness to pay is above 17 640 EUR per QALY (175 000 SEK). Deep tissue massage only and a combination of deep tissue massage and stretching and strengthening exercises are not cost-effective for subacute or persistent neck pain. While exercise appeared to have the best cost/benefit profile, even this treatment had only a modest benefit and treatment innovation is needed. Advice to stay active remains as a good therapeutic alternative from an economical perspective.

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Declaration of competing interest

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.msksp.2020.102109.

References

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