TITLE

The effects of Tai Chi and neck exercises in the treatment of chronic non-specific neck pain: A randomized controlled trial

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DISCLOSURES

Peter Wayne is the founder and sole owner of the Tree of Life Tai Chi Center. Peter Wayne's interests were reviewed and managed by the Brigham and Women's Hospital and Partner's HealthCare in accordance with their conflict of interest policies.
All other authors have no interests to disclose.

ABSTRACT

This study aimed to test the efficacy of Tai Chi for treating chronic neck pain.

Subjects with chronic non-specific neck pain were randomly assigned to 12 weeks of group Tai Chi or conventional neck exercises with weekly sessions of 75-90 minutes, or a wait-list control. The primary outcome measure was pain intensity (visual analog scale, VAS). Secondary outcomes included pain on movement, functional disability, quality of life, well-being and perceived stress, postural and interoceptive awareness, satisfaction and safety.

Altogether, 114 participants were included (91 females, 49.4±11.7 years). After 12 weeks Tai Chi participants reported significantly less pain compared to the wait list (average difference in mm VAS: -10.5; 95%CI:-20.3,-0.9;p=0.033). Group differences were also found for pain on movement, functional disability and quality of life compared to wait list. No differences were found for Tai Chi compared to neck exercises. Patients' satisfaction with both exercise interventions was high, and only minor side effects were observed.

Tai Chi was more effective than no treatment in improving pain in subjects with chronic non-specific neck pain. Since Tai Chi is probably as effective as neck exercises it may be considered a suitable alternative to conventional exercises for those with a preference towards Tai Chi.

Trial registration: ClinicalTrials.gov, registry number: NCT02222051, URL: http://clinicaltrials.gov/show/NCT02222051

PERSPECTIVE

This article presents results of a randomized controlled trial comparing Tai Chi, conventional neck exercises and no treatment for chronic non-specific neck pain. Results indicate that Tai Chi exercises and conventional neck exercises are equally effective in improving pain and quality of life therefore representing beneficial interventions for neck pain.

KEY WORDS

Neck pain; Chronic pain; Tai Chi; neck exercises; spinal exercises; randomized controlled trial; efficacy

INTRODUCTION

Musculoskeletal pain syndromes, such as back and neck pain, are common public health problems in industrialized countries, which most people experience at some point in their life [2, 22]. The lifetime prevalence of chronic neck pain is approximately 50%, and it is associated with both substantial societal and individual burden [13-15, 54]. Exercise therapy has been found beneficial for chronic non-specific neck pain, with no differences regarding the type of exercise including isometric or isotonic neck strengthening or endurance exercises [29, 45]. However, stretching exercises, have been reported to have only limited effects [24]. Complementary medicine exercise approaches such as yoga and qigong have also been found efficacious for neck pain [16, 42, 47, 53] , providing patients with alternatives to conventional exercises. Tai Chi is a low-impact mind-body exercise originating in China, that integrates dynamic musculoskeletal, breathing, and meditation training [61]. Tai Chi is regularly utilized for health purposes [3, 40], and a growing body of evidence [66] supports its potential to benefit subjects suffering from back pain [26], rheumatological disorders [32, 39, 57, 58], or psychological disorders [59]. Despite the fact that musculoskeletal disorders including neck pain have been found predictive of Tai Chi use [3], no study to date has investigated its effects in subjects with chronic non-specific neck pain. Furthermore Tai Chi as well as conventional neck exercises can easily be taught in larger groups, with groups not only offering social support [10], but also being less costly than individual treatments.

This study aimed to investigate the efficacy of group Tai Chi compared to group neck exercises and no treatment to improve neck pain, disability and quality of life in subjects with chronic non-specific neck pain. The primary hypothesis was that Tai Chi was superior to no treatment to improve chronic non-specific neck pain after

12 weeks of intervention. The secondary hypothesis aimed to explore whether there Tai Chi was more or less effective compared to conventional neck exercises regarding the reduction of neck pain.

METHODS

Ethical approval and trial registration

The trial was conducted between September 2014 and March 2015 in the Department of Complementary and Integrative Medicine in Essen, Germany. The study was approved by the ethics committee of the University Hospital Essen (approval number: 13-5672-BO) and registered at ClinicalTrials.gov (registry number: NCT02222051), prior to subject recruitment.

Design

This was a randomized controlled three-armed parallel group trial. Tai Chi was compared to a wait list control group and another active control intervention (neck exercises). Both active interventions were offered in a group format, i.e. 10-15 participants per group met once weekly for a 75-90 minute intervention for 12 weeks in total. To minimize personality bias, both groups were led by the same instructor, a graduate sport scientist at MSc level and certified Tai Chi master who is experienced in working with subjects suffering from back and neck pain. Both active interventions followed a manual prepared prior to the trial; and participants were provided with written material to foster self-practice at home, which was recommended for at least 15 minutes per day. Measurements were conducted at weeks 0, 12 and 24, with 12 weeks defined as primary outcome measure time point.

Participants

Subjects were recruited via local newspaper advertisements, with a research assistant screening interested people by phone to assess their eligibility. Subjects who met the inclusion criteria were then invited for an in-person assessment where they were received detailed written information about the study, and their written informed consent was obtained. A study physician checked subjects' medical histories, examined their physical health and examined cervical flexibility and neurological function (sensitivity, motor function and reflexes) to exclude subjects presenting with red flags for prolapse or protrusion. The physician also checked subjects' medical records, e.g. any laboratory findings, x-rays or MRI results that subjects provided. If they met all study eligibility criteria, subjects were included in the trial.

Trial participants were required to be at least 18 years of age and to have chronic non-specific neck pain for at least three consecutive months for at least five days a week. They also had to report moderate pain of 45 mm or higher on a visual analog scale ranging from 0 to 100 mm (VAS) [31], with 100 mm described as "worst neck pain imaginable". Patients with other musculoskeletal pain, such as arm pain or lower back pain, in addition to neck pain as defined above were eligible.

The trial exclusion criteria included neck pain caused by trauma, disc protrusion, whiplash, congenital deformity of the spine, spinal stenosis, neoplasm, inflammatory rheumatic disease, neurological disorder, or active oncologic disease, severe affective disorder, addiction and psychosis. In addition, subjects who were pregnant or who had had invasive treatment of the spine within the previous four weeks (e.g. acupuncture, injections), or spinal surgery within the previous year, or had initiated or modified their drug regimen recently or were taking opiates were excluded. Finally, subjects with regular practice of Tai Chi, Qigong or Yoga in the

past 6 months, or those with any disability precluding exercise practice, were also excluded.

Randomization and allocation procedure

Participants were allocated to one of three groups in order of appearance adopting a computer-generated (Random Allocation Software, version 1.0.0) non-stratified block randomization with randomly varying block sizes. The trial coordinator who was not involved in participants' outcome assessments prepared sealed opaque envelopes with randomization assignments. Envelopes were labeled according to the study participant's ID number, and for eligible participants, envelopes were opened in ascending order by the study physician to determine the group allocation. Neither participants nor the interventionist were blinded to the intervention, however the outcome assessor was blinded to the group allocation at 12 and 24 weeks.

Intervention

After baseline measurements and randomization, participants were given pain and medication logs, and were provided with their respective intervention time table.

Tai Chi

Participants in the Tai Chi group met once weekly for a 75-90 minute session for 12 weeks in total. The Tai Chi intervention was based on a popular and internationally recognized Yang style (13 forms from Mantak Chia) [9]. Each session included a warm-up of 5-10 minutes, the Tai Chi form practice, and 5-10 minutes relaxation at the end. Tai Chi forms followed explicit protocols outlined in a training manual, as required during teacher training certification [9]. Sessions also included educational units and breathing exercises; and they were accompanied by relaxation music. Participants received illustrated written information that covered movement

sequences learned in the previous session. They were asked to practice Tai Chi outside of classes for at least 15 minutes each day. This length of home practice was chosen to increase compliance with, and memorization and reinforcement of the exercises taught in class. Fifteen minutes of home practice is also a common recommendation for beginner Tai Chi students.

Wait list control group

Participants in this group were advised to continue their usual activities and therapies, but not to initiate any new therapeutic regimen for symptom management. At the trial's end, participants in the wait list group were offered as a courtesy the option to participate in a Tai Chi and neck exercise group.

Neck exercises

Participants in the neck exercise group met once weekly for a 60-75 minute session for 12 weeks in total. This group was instructed in neck exercises, which were similar to those taught in rehabilitation programs containing exercises and education for a healthy back. Classes contained basic training of ergonomic principles (bodily alignment while standing); proprioceptive exercises; and isometric and dynamic mobilization, stretching and strengthening neck and core exercises (Table S1, Figure S1). Similar to Tai Chi, the sessions opened with 5-10 min. warm-up exercises and ended with relaxation exercises. Participants also received illustrated and written information that covered the most important exercises; and they were asked to execute the exercises for at least 15 minutes each day. This intervention was to control for effects due to increased levels of physical activity and the group setting in the Tai Chi group.

Assessment

Participants' *Expectation*

At the assessment visit all participants rated their expectations that Tai Chi or neck exercises would be able to improve their neck pain on a 0-10 numerical rating scale (NRS) [48] with 10 indicating 'highest possible expectation'. Expectation was included as covariate in the analysis.

Attendance and home practice

Attendance rate was measured using a record of attendance in each class. Home practice was assessed using a daily log, where participants filled in daily practice time during the 12 week study period themselves.

Questionnaires

A variety of questionnaires were utilized to investigate the effects of interventions on pain, disability and quality of life in chronic neck pain, as recommended by IMMPACT statement [19]. Furthermore, outcomes related to stress, well-being, and interoceptive and postural awareness were measured, as these behaviors are actively targeted by Tai Chi.

Current pain intensity was measured using a 0-100 mm visual analog scale from the German Pain Questionnaire [35, 44] with 0 mm indicating 'no neck pain at all' and 100 mm indicating 'worst neck pain imaginable'.

Participants were also asked to indicate the level of pain, which they would render tolerable in general on a 0-100 mm visual analog scale. This was used to determine whether participants could be considered 'responders' regarding their own level.

To measure pain on movement (POM) [38], participants were asked to flex, extend, laterally flex and laterally rotate their necks to the left and right. The evoked

pain was measured on a 100 mm VAS, for each direction. An average pain on movement score was then calculated from these data for each participant. The POM has been found valid and reliable [38].

Participants' functional neck-related disability was measured using the Neck Disability Index (NDI) [17, 52]. This 10-item questionnaire determines how participants see their neck pain affecting their daily activities. The maximum score is 50. Scores of less than four indicate no disability; 5-14 indicate mild disability, 15-24 moderate disability and 25-34 severe disability. Scores above 35 indicate complete perceived disability.

Health-related quality of life was assessed using the Short Form 36 Health Survey Questionnaire (SF-36) [6]. This widely used comprehensive 36-item questionnaire yields an 8-scale health profile as well as two component summaries of physical and mental health-related quality of life.

Psychological wellbeing was measured using the Questionnaire on the Assessment of Physical Wellbeing (FEW-16) [34]. This questionnaire comprises four subscales, each containing four items: stress resistance, ability to enjoy, vitality and inner peace

The degree to which participants perceived their lives as stressful was determined using the German Version of the Perceived Stress Scale (PSS) [7, 11] which consists of 10 items. Participants indicate how often they have found their lives unpredictable, uncontrollable, and overloaded in the last month; higher scores are indicative of higher perceived stress in life.

The Postural Awareness Scale (PAS) was used to determine the degree of consciousness towards body posture and movement patterns that might contribute

to the development of chronic neck pain (Manuscript in preparation). The instrument consists of 5 items each on 2 scales, which are: conscious effort and automatic awareness; and it has shown good psychometric properties (Manuscript in preparation). Conscious effort includes items that describe a low degree of awareness of body posture, which can only be made aware with conscious effort. The automatic awareness characterizes an automatic awareness of body posture that is present in general and without efforts. While larger scores on the conscious effort scale indicate difficulties in achieving awareness, larger scores on the automatic awareness indicate more presence in general.

Interoception, i.e. the sensitivity towards stimuli originating from within the body, was measured using the Multidimensional Assessment of Interoceptive Awareness instrument (MAIA) [4, 41] which consists of 40 items that results in eight separate dimensions of interoceptive awareness; and higher scores each represent higher awareness.

Daily log

All participants used a log to record the intensity of their neck pain (VAS), whether they exercised and whether they took analgesics or received other treatments for their neck pain. Analgesic consumption and concomitant treatments were analyzed by their frequency, and for analgesics, also by the defined daily doses were calculated [63].

Satisfaction with interventions

At the end of each 12 week study period participants were asked to judge how beneficial their respective treatment was on a 100 mm visual analog scale with 100 mm indicating ‘highest benefit possible’. They were also asked whether they would

utilize this intervention in the future and whether they would recommend it to family or friends on a 'yes'/'no' basis.

Safety

Participants were asked to report any adverse event during the study period, even if considered insignificant (e.g. having a cold). Adverse events were defined in accordance with Good Clinical Practice [20] as any untoward medical occurrence; i.e. any abnormal laboratory finding, symptom or disease temporally associated with study intervention, whether or not caused by the intervention. All adverse events were recorded by the study coordinator; and participants experiencing such events were asked to see the study physician to assess their import and initiate any necessary response.

Primary and secondary outcome measures

The primary outcome measure was pain intensity after 12 weeks as measured by the visual analog scale (VAS). Secondary outcome measures included pain intensity (VAS) after 24 weeks; pain on movement (POM), functional disability (NDI), quality of life (SF-36), well-being (FEW16), stress (PSS-10), postural (PAS) and interoceptive awareness (MAIA) after 12 and 24 weeks; and pain intensity (VAS) and medication from the daily log, compliance, satisfaction and safety. At 12 weeks the numbers of responders, i.e. participants experiencing at least 30% or 50% pain reduction, and participants reaching their own tolerance level of pain were analyzed.

Sample size calculation

The calculation for the required sample size was based on a trial that investigated the effects of Qigong for chronic neck pain in comparison to a usual care group [47]. Given an effect size of Cohen's d=0.69 and a two-sided 5% level t-

test, 34 participants would be needed per group to detect such group difference between the active intervention and a non-treated control group with a statistical power of 80%. Since no data were available for the comparison of Tai Chi vs. conventional exercise the same group size was used for that comparison. We planned to include 114 participants in this trial, assuming a potential loss of analytical power due to participant withdrawal.

Statistical analysis

All analyses were based on the intention to treat population, i.e. each participant providing baseline data was included in the final analysis. Missing data were completed using the Markov chain Monte Carlo multiple imputation method in SPSS. A set of 50 imputations was generated, and the mean score was used for the analyses.

The primary outcome was analyzed using a univariate analysis of covariance (ANCOVA) which modeled the post-treatment outcome as a function of treatment group (classified factor), and the respective baseline value (linear covariate). A gatekeeper stepwise analysis [18] was conducted to preserve the overall false positive rate; starting with the comparison Tai Chi vs. no treatment; followed by Tai Chi vs. neck exercises. Using this stepwise procedure, no alpha level adjustment for the primary outcome was necessary to maintain the overall type I error rate of 5% [21, 67]. Within this model the treatment effect was estimated, accompanied with a 95% confidence interval. The p-value was based on a two-sided t-test within this statistical model. For categorical variable x^2 tests were used to determine group differences.

Secondary outcomes were analyzed using the same statistical method, however secondary outcomes were reported exploratively only, and no p-values are

reported. Results from the daily log were analyzed using repeated measures ANOVA. Therefore weekly averages of pain intensity, medication use and concurrent treatments were calculated. In cases where interaction effects were observed, exploratory post-hoc tests were applied.

All analyses were performed using the Statistical Package for Social Sciences software (IBM SPSS Statistics for Windows, release 22.0. Armonk, NY: IBM Corp.).

RESULTS

Participants

Of the 195 subjects initially screened by telephone, 126 subjects were seen by the study physician, of whom 114 were enrolled and subsequently randomized. The most common reasons for excluding subjects were not meeting the inclusion criteria, scheduling issues or lost interest in the study. During the twelve week intervention 21 participants were lost to follow-up, three in Tai Chi, and nine each in the neck exercise group and nine in the wait list control group. Despite multiple attempts to contact study participants, reasons for withdrawal could not be determined in all cases, but those who provided reasons stated scheduling problems, lost interest or adverse events as reasons. During the follow-up period another four participants were lost. Since all participants provided baseline data, 114 participant data sets could be analyzed (see figure 1 for CONSORT flowchart).

Baseline characteristics

Participants were 49.4±11.7 years on average; and 91 women and 23 men were included (see table 1). Levels of education were mixed; and the majority of participants were employed at the time of the study. Participants most commonly had

received physiotherapy for symptom management, and approximately half of them reported receiving prior medication for neck pain. Injections and treatment within a rehabilitation center were reported by only a minority. Participants reported an average pain intensity of 50.7±20.4 mm VAS at baseline; and that they would consider a pain level of 20.9±12.7 mm VAS as tolerable. Efficacy expectations towards the interventions were quite high (7.3±1.5 for Tai Chi and 6.5±1.7 for neck exercises).

Outcome measures

Primary outcome measure:

Analysis of pain intensity revealed a significant group difference between Tai Chi and the wait list control group (difference -10.5, 95% CI: -20.3, -0.9, p=0.033) after 12 weeks (see table 2). No group difference was found between Tai Chi and neck exercises (difference 3.4; 95% CI: -9.5, 12.3; p=0.450) (see table 2).

After 12 weeks 24 (63.2%), 27 (73.0%) and 15 (38.5%) subjects in Tai Chi, neck exercises and the wait list group showed a pain reduction equal to or higher than 30% (p=0.007). A reduction in pain of 50% or higher was reported by 14 (36.8%), 17 (45.9%) and 6 (15.4%) participants in Tai Chi, neck exercises and the wait list, respectively (p=0.014). The proportion of participants reporting a reduction of pain of 50% or higher, when their own self-reported limits of pain tolerability were accounted for, showed very similar patterns: 14 (36.8%), 16 (43.2%) and 6 (15.4%) participants in Tai Chi, neck exercises and wait list, respectively (p=0.023).

Secondary outcome measures:

Group differences between Tai Chi and the wait list control were still present after 24 weeks regarding neck pain intensity (difference -10.6, 95% CI: -20.9, -0.3),

pain on movement (POM), disability (NDI) and quality of life (SF-36) (see table 3). No differences were found for psychological well-being, stress and interoceptive awareness (see tables 2 and 3), but for the postural awareness subscale *active efforts* (see tables 2 and 3) for Tai Chi compared to the wait list control group. Compared to neck exercises, no group differences were found for any of the outcomes (see tables 2 and 3).

Adherence

Participants of the Tai Chi course attended 7.6±3.4 sessions on average, those in the neck exercise 5.4±4.1 sessions. As can be seen in figure 1, there were nine participants in the neck exercise group that did not attend any session at all, while participants in the Tai Chi group were more adherent. Course attendance in general was average to good in Tai Chi, with at least 50% attendance rate during the course; however attendance rate in neck exercises was significantly lower (Mann-Whitney-U, p=0.017), mainly due to the nine participants that did not attend any of the classes. In both groups a steady decline of attendance could be observed (see figure 2). Together, the number of adherent participants (at least 80% attendance) was 26 (68.4%) and 15 (40.5%) in Tai Chi and neck exercises, respectively.

Daily log

The weekly home practice was comparable between the groups, with participants practicing Tai Chi for 44.9±10.7 minutes (range: 19-59) and neck exercises for 33.1±9.6 minutes (range 13-48) on average (see figure 3a). A steady decline in pain intensity was found in Tai Chi and neck exercises, but not in the wait list (see figure 3b). Analysis revealed an interaction effect of time and group; and differences between groups occurred after seven weeks, with pain ratings in Tai Chi

and neck exercises being lower than those in the wait list for most time points afterwards. Analysis of other drug therapies revealed that the average daily doses of analgesics were low; participants took less than 20% of the recommended daily dosage on average (see figure 3c).

An interaction effect of time and group was found, with participants in neck exercises reporting the highest intake compared to Tai Chi in weeks 1-4, however from week 5 those differences had disappeared. Participants received approximately two concomitant therapies per week, with no differences between the groups (see figure 3d). Concomitant therapies mainly included massages and the application of heat without differences between the groups.

Satisfaction with interventions

Participants reported high perceived benefit of both interventions (Tai Chi: 70.6±29.6 mm; neck exercises: 72.9±30.0 mm) as well as satisfaction after 12 weeks (Tai Chi: 76.1±28.9 mm; neck exercises: 80.0±27.7 mm). In total 85.7% and 88.0% of participants reported that they would consider using Tai Chi and neck exercises again; and 94.2% and 100% would consider recommending Tai Chi and neck exercises to family and friends respectively.

Safety

A total of 14 minor adverse events were recorded during the study. In Tai Chi, four participants presented with upper respiratory tract infections, one reported a single migraine attack, two complained of Achilles tendon pain, and one participant fell and got bruises at home (not during practice). In neck exercises four upper respiratory tract infections occurred and one participant each experienced knee pain and vertigo. Serious adverse events occurred in six trial participants: one participant

in the Tai Chi group each reported meniscal tear after running and was infected with mononucleosis. One participant each in the neck exercise group reported infection with mononucleosis, idiopathic sudden sensorineural hearing loss (before the intervention started), appendicitis and dental root infection. All participants with serious adverse events were under medical treatment at their respective physicians.

Except for knee and Achilles tendon pain, and migraine, all other adverse events were considered unlikely to be related to exposure to Tai Chi or neck exercises by the study physician. No participant in the wait list control group reported adverse events.

DISCUSSION

This trial found that a 12-week Tai Chi course was more effective than no treatment in addressing neck pain, functional disability and quality of life after 12 and 24 weeks. It was however neither superior nor inferior to a 12-week intervention of conventional neck exercises. Participants were highly satisfied with both active interventions, and except for minor side effects, the interventions were well accepted and tolerated.

Scientific evidence

Studies have investigated effects of exercise on neck pain before [24], however we are not aware of any studies to date that have evaluated the effects of Tai Chi for chronic neck pain despite Tai Chi being regularly used for neck pain. Studies have however investigated the efficacy of Qigong, a mind-body exercise very similar to Tai Chi [27, 37, 47, 53], for chronic neck pain. In one study Rendant and colleagues [47] compared the effects of Qigong to those of neck exercises and usual care in 123

subjects with chronic neck pain. The authors found that 18 sessions of Qigong over the course of 6 months were superior to usual care, but not compared to the neck exercises. While their design and sample were mostly comparable to our current study, our study only used traditional Tai Chi forms without specific focus on neck and shoulder function. Another study by Trott et al. [53] investigated the effects of Qigong for elderly subjects with chronic neck pain. The study reported that after 24 sessions within 12 weeks no differences between Qigong and usual care or neck exercises were reported. Participants however reported increased relaxation, and calmness [27] which were not found in our study.

In addition to neck pain, Tai Chi has been investigated in subjects with chronic back pain [26], with rheumatologic disorders such as osteoarthritis of the knee [5, 39, 57], the fibromyalgia syndrome [32, 58], and rheumatoid arthritis [51, 55, 56]. Patients with such disorders frequently benefit from Tai Chi, as do elderly subjects with enhanced risk of falls and fractures [23]. Tai Chi has also been found beneficial for several neurological [1, 12, 49, 68], psychological [59] and cardiovascular conditions [65].

The modes of action of Tai Chi are not understood completely, they might include general effects due to exercise such as increased flexibility and mobility of structures; improved muscle strength and endurance, increased tensile strength of ligaments and capsules; increased cardiovascular function, reduced stress, anxiety and depression; and changes in health beliefs and health related locus of control [33]. Tai Chi in particular may act via improved postural control as indicated by increases in balance and reduced falls [8, 25, 46, 50, 64]. Specific mechanisms of postural control relevant to neck pain may be better muscle tone due to increased muscle strength [28, 30, 36] and better kinesthetic control due to improved interoceptive or proprioceptive awareness [43]. Results of this study showed that subjects had fewer difficulties

regarding awareness of their posture after Tai Chi classes, however, no changes were found in interoceptive awareness. It can further be assumed that the meditative character might improve psychological well-being, stress and depressive mood [59], however no such correlations were observed in our current study. To establish the exact mechanisms of Tai Chi further rigorous research is warranted [62].

We also found Tai Chi as well as neck exercises to be quite safe, with only a few temporary minor side effects reported. This parallels recent systematic reviews considering Tai Chi and neck exercises to be safe interventions for populations with chronic pain and other chronic medical conditions [33, 60]. Of note, Tai Chi as well as conventional neck exercises can be practiced at home at low cost and with no need for special equipment; however at least during the initial stages of training, introductory courses are recommended to assure proper adoption of training principles.

Strengths and limitations

The strengths of the study include the randomized study design; the pre-defined sample size and the use of different comparators including an expert-designed neck exercise group. The use of standardized measurement instruments and the inclusion of the most important outcomes in relation to chronic neck pain, and the evaluation of concomitant medication and treatments are additional strengths of the trial.

Limitations include the lack of blinding of participants and physicians which is a general problem in non-pharmacological interventional trials. However expectations towards both active interventions were comparable indicating no major detection bias. Another limitation may exist given the initial withdrawal rate in the

neck exercise group, the general withdrawal rate during the trial and the adherence rate which was sufficient at best for neck exercises. Withdrawal rate for exercises was substantially higher than in other comparable trials [26, 47, 53]. Possible reasons might include different patient preferences towards neck exercises and Tai Chi in the samples, or specific differences in trial sites and subjects. Satisfaction was high in those participating in both Tai Chi and neck exercises indicating suitability of both exercise programs. Furthermore both classes were conducted by the same instructor, which on one hand may eliminate personality biases, but on the other hand, may have increased the probability of information contamination across groups. Results may also allow for only limited inference of efficacy of either intervention. The study was primarily powered to detect differences between Tai Chi and usual care, and it may have been underpowered for the comparison to neck exercises. Furthermore sample size was not nearly sufficient to conduct non-inferiority testing. And lastly, the follow-up did not exceed 24 weeks, which does not allow for conclusive judgment of long-term effects.

Future studies

Despite preliminary evidence of the efficacy of Tai Chi for chronic neck and back pain, further studies are necessary to confirm and extend those findings. Findings of this study indicate that Tai Chi had a clinically modest effect on average pain scores, however more than one in three participants reported a pain reduction by 50%. Further trials should not only apply larger sample to secure sufficient power for head to head comparisons of different exercise interventions, they might also include non-inferiority tests to confirm equality of interventions. Future trials should also determine the maximal possible benefit from Tai Chi, and identify subjects' characteristics and factors associated with improvement of neck pain. Other studies

might also evaluate whether Tai Chi training might be able to prevent the development of neck pain. Since many people use CD/DVDs or the internet to learn Tai Chi, advantages and disadvantages to these home-based interventions should also be evaluated.

Practical implications

Neck strengthening and stretching exercises are regularly recommended for subjects with chronic neck pain. If future studies confirm that Tai Chi is effective and safe, it could be recommended to subjects with a specific preference towards complementary medicine exercise techniques, or with subjects who want a participate in a practice that has a larger focus on body awareness and spirituality. However the decision for either must also be based upon availability and costs.

Conclusion

Twelve weeks of Tai Chi is more effective than no treatment to improve pain, disability, quality of life and postural control in subjects with chronic non-specific neck pain. Since Tai Chi proved to be equally efficacious and safe as conventional neck exercises, it may be considered a suitable alternative for subjects with chronic neck pain.

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FIGURE LEGENDS

Figure 1: Consort flow chart of patient recruitment

Figure 2: Weekly attendance rate during the 12-week study period, in % of study participants who attended the class

Figure 3: Data from the daily log including a) weekly home practice time in minutes, mean±SE ; b) pain intensity ratings during the 12-week study period, measured by a numerical rating scale, weekly average, mean±SE; c) average defined daily dose according to the WHO of concomitant analgesics, mean±SE; and d) weekly average of concomitant therapies (other than study interventions), %±SE

Figure S1: Illustration of exercises

TABLES

Table 1: Baseline characteristics of trial patients according to study arms

Table 2: Results of the statistical comparison between the groups at week 12. Scores are presented as Mean±SD; group differences are estimations from the ANCOVA with 95% Confidence Intervals (CI).

Table 3: Results of the statistical comparison between the groups at week 24. Scores are presented as Mean±SD; group differences are estimations from the ANCOVA with 95% Confidence Intervals (CI).

Table S1: List of neck exercise class content

REFERENCES

1. Amano S, Nocera JR, Vallabhajosula S, Juncos JL, Gregor RJ, Waddell DE, Wolf SL, Hass CJ. The effect of Tai Chi exercise on gait initiation and gait performance in persons with Parkinson's disease. *Parkinsonism Relat Disord.* 19:955-960, 2013

2. Binder A. The diagnosis and treatment of nonspecific neck pain and whiplash. *Eura Medicophys.* 43:79-89, 2007

3. Birdee GS, Wayne PM, Davis RB, Phillips RS, Yeh GY. T'ai chi and qigong for health: patterns of use in the United States. *J Altern Complement Med.* 15:969-973, 2009

4. Bornemann B, Herbert BM, Mehling WE, Singer T. Differential changes in self-reported aspects of interoceptive awareness through 3 months of contemplative training. *Front Psychol.* 5:1504, 2014

5. Brismee JM, Paige RL, Chyu MC, Boatright JD, Hagar JM, McCaleb JA, Quintela MM, Feng D, Xu KT, Shen CL. Group and home-based tai chi in elderly subjects with knee osteoarthritis: a randomized controlled trial. *Clin Rehabil.* 21:99-111, 2007

6. Bullinger M, Kirchberger I: SF-36. Fragebogen zum Gesundheitszustand. Handanweisung, Hogrefe, Göttingen, 1998.

7. Büssing A, Recchia DR. Spiritual and Non-spiritual Needs Among German Soldiers and Their Relation to Stress Perception, PTDS Symptoms, and Life Satisfaction: Results from a Structural Equation Modeling Approach. *J Relig Health.* 55:747-764, 2015

8. Chen WW, Sun WY. Tai chi chuan, an alternative form of exercise for health promotion and disease prevention for older adults in the community. *Int Q Community Health Educ.* 16:333-339, 1996

9. Chia M, Li J: The Inner Structure of Tai Chi: Mastering the Classic Forms of Tai Chi Chi Kung, Destiny Books, Rochester, VT, 2005.

10. Christensen U, Schmidt L, Budtz-Jorgensen E, Avlund K. Group cohesion and social support in exercise classes: results from a danish intervention study. *Health Educ Behav.* 33:677-689, 2006

11. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav.* 24:385-396, 1983

12. Corcos DM, Comella CL, Goetz CG. Tai chi for patients with Parkinson's disease. *N Engl J Med.* 366:1737-1738; author reply 1738, 2012

13. Cote P, Cassidy JD, Carroll L. The Saskatchewan Health and Back Pain Survey. The prevalence of neck pain and related disability in Saskatchewan adults. *Spine (Phila Pa 1976).* 23:1689-1698, 1998

14. Cote P, Hogg-Johnson S, Cassidy JD, Carroll L, Frank JW. The association between neck pain intensity, physical functioning, depressive symptomatology and time-to-claim-closure after whiplash. *J Clin Epidemiol.* 54:275-286, 2001

15. Cote P, van der Velde G, Cassidy JD, Carroll LJ, Hogg-Johnson S, Holm LW, Carragee EJ, Haldeman S, Nordin M, Hurwitz EL, Guzman J, Peloso PM, Bone, Joint Decade - Task Force on Neck P, Its Associated D. The burden and determinants of neck pain in workers: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976).* 33:S60-74, 2008

16. Cramer H, Lauche R, Hohmann C, Lüdtke R, Haller H, Michalsen A, Langhorst J, Dobos G. Randomized-controlled trial comparing yoga and home-based exercise for chronic neck pain. *Clin J Pain.* 29:216-223, 2013

17. Cramer H, Lauche R, Langhorst J, Dobos GJ, Michalsen A. Validation of the German version of the Neck Disability Index (NDI). *BMC Musculoskelet Disord.* 15:91, 2014

18. Dmitrienko A, Tamhane AC, Wang X, Chen X. Stepwise gatekeeping procedures in clinical trial applications. *Biom J.* 48:984-991, 2006

19. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, Kerns RD, Stucki G, Allen RR, Bellamy N, Carr DB, Chandler J, Cowan P, Dionne R, Galer

BS, Hertz S, Jadad AR, Kramer LD, Manning DC, Martin S, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robbins W, Robinson JP, Rothman M, Royal MA, Simon L, Stauffer JW, Stein W, Tollett J, Wernicke J, Witter J. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain.* 113:9-19, 2005

20. Edwards IR, Biriell C. Harmonisation in pharmacovigilance. *Drug Saf.* 10:93-102, 1994

21. Feise RJ. Do multiple outcome measures require p-value adjustment? *BMC Med Res Methodol.* 2:8, 2002

22. Fejer R, Kyvik KO, Hartvigsen J. The prevalence of neck pain in the world population: a systematic critical review of the literature. *Eur Spine J.* 15:834-848, 2006

23. Gillespie LD, Robertson MC, Gillespie WJ, Sherrington C, Gates S, Clemson LM, Lamb SE. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev.* 9:CD007146, 2012

24. Gross A, Kay TM, Paquin JP, Blanchette S, Lalonde P, Christie T, Dupont G, Graham N, Burnie SJ, Gelley G, Goldsmith CH, Forget M, Hoving JL, Bronfort G, Santaguida PL. Exercises for mechanical neck disorders. *Cochrane Database Syst Rev.* 1:CD004250, 2015

25. Hackney ME, Wolf SL. Impact of Tai Chi Chu'an practice on balance and mobility in older adults: an integrative review of 20 years of research. *J Geriatr Phys Ther.* 37:127-135, 2014

26. Hall AM, Maher CG, Lam P, Ferreira M, Latimer J. Tai chi exercise for treatment of pain and disability in people with persistent low back pain: a randomized controlled trial. *Arthritis Care Res (Hoboken).* 63:1576-1583, 2011

27. Holmberg C, Rappenecker J, Karner JJ, Witt CM. The perspectives of older women with chronic neck pain on perceived effects of qigong and exercise therapy on aging: a qualitative interview study. *Clin Interv Aging.* 9:403-410, 2014

28. Hong Y, Li JX, Robinson PD. Balance control, flexibility, and cardiorespiratory fitness among older Tai Chi practitioners. *Br J Sports Med.* 34:29-34, 2000

29. Hurwitz EL, Carragee EJ, van der Velde G, Carroll LJ, Nordin M, Guzman J, Peloso PM, Holm LW, Cote P, Hogg-Johnson S, Cassidy JD, Haldeman S, Bone, Joint Decade - Task Force on Neck P, Its Associated D. Treatment of neck pain: noninvasive interventions: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976).* 33:S123-152, 2008

30. Jacobson BH, Chen HC, Cashel C, Guerrero L. The effect of T'ai Chi Chuan training on balance, kinesthetic sense, and strength. *Percept Mot Skills.* 84:27-33, 1997

31. Jensen MP, Chen C, Brugger AM. Interpretation of visual analog scale ratings and change scores: a reanalysis of two clinical trials of postoperative pain. *J Pain.* 4:407-414, 2003

32. Jones KD, Sherman CA, Mist SD, Carson JW, Bennett RM, Li F. A randomized controlled trial of 8-form Tai chi improves symptoms and functional mobility in fibromyalgia patients. *Clin Rheumatol.* 31:1205-1214, 2012

33. Kay TM, Gross A, Goldsmith CH, Rutherford S, Voth S, Hoving JL, Bronfort G, Santaguida PL. Exercises for mechanical neck disorders. *Cochrane Database Syst Rev.* 8:CD004250, 2012

34. Kolip P, Schmidt B. Der Fragebogen zur Erfassung körperlichen Wohlbefindens (FEW16). Konstruktion und erste Validierung. *Zeitschrift für Gesundheitspsychologie.* 7:77-87, 1999

35. Korb J, Pfingsten M. Der deutsche Schmerzfragebogen - implementierte Psychometrie. *Schmerz.* 17:S47, 2003

36. Lan C, Lai JS, Chen SY, Wong MK. 12-month Tai Chi training in the elderly: its effect on health fitness. *Med Sci Sports Exerc.* 30:345-351, 1998

37. Lansinger B, Larsson E, Persson LC, Carlsson JY. Qigong and exercise therapy in patients with long-term neck pain: a prospective randomized trial. *Spine (Phila Pa 1976).* 32:2415-2422, 2007

38. Lauche R, Cramer H, Langhorst J, Michalsen A, Dobos GJ. Reliability and validity of the pain on movement questionnaire (POM) in chronic neck pain. *Pain Med.* 15:1850-1856, 2014

39. Lauche R, Langhorst J, Dobos G, Cramer H. A systematic review and meta-analysis of Tai Chi for osteoarthritis of the knee. *Complement Ther Med.* 21:396-406, 2013

40. Lauche R, Wayne P, Dobos G, Cramer H. Prevalence, patterns, and predictors of Tai Chi and Qigong use in the US: Results from a nationally representative survey. *J Altern Complement Med.* 22:336-342, 2016

41. Mehling WE, Price C, Daubenmier JJ, Acree M, Bartmess E, Stewart A. The Multidimensional Assessment of Interoceptive Awareness (MAIA). *PLoS One.* 7:e48230, 2012

42. Michalsen A, Traitteur H, Ludtke R, Brunnhuber S, Meier L, Jeitler M, Bussing A, Kessler C. Yoga for chronic neck pain: a pilot randomized controlled clinical trial. *J Pain.* 13:1122-1130, 2012

43. Moseley GL. Graded motor imagery for pathologic pain: a randomized controlled trial. *Neurology.* 67:2129-2134, 2006

44. Pfingsten M, Nagel B, Emrich O, Seemann H, Lindena G, Korb J. Deutscher Schmerzfragebogen. Handbuch. Available at: http://www.kedogs.de/download/DSF-Manual.pdf. 2007

45. Philadelphia P. Philadelphia Panel evidence-based clinical practice guidelines on selected rehabilitation interventions for neck pain. *Phys Ther.* 81:1701-1717, 2001

46. Province MA, Hadley EC, Hornbrook MC, Lipsitz LA, Miller JP, Mulrow CD, Ory MG, Sattin RW, Tinetti ME, Wolf SL. The effects of exercise on falls in elderly patients. A preplanned meta-analysis of the FICSIT Trials. Frailty and Injuries: Cooperative Studies of Intervention Techniques. *JAMA.* 273:1341-1347, 1995

47. Rendant D, Pach D, Ludtke R, Reisshauer A, Mietzner A, Willich SN, Witt CM. Qigong versus exercise versus no therapy for patients with chronic neck pain: a randomized controlled trial. *Spine (Phila Pa 1976).* 36:419-427, 2011

48. Sherman KJ, Cherkin DC, Erro J, Miglioretti DL, Deyo RA. Comparing yoga, exercise, and a self-care book for chronic low back pain: a randomized, controlled trial. *Ann Intern Med.* 143:849-856, 2005

49. Taylor-Piliae RE, Hoke TM, Hepworth JT, Latt LD, Najafi B, Coull BM. Effect of Tai Chi on physical function, fall rates and quality of life among older stroke survivors. *Arch Phys Med Rehabil.* 95:816-824, 2014

50. Tse SK, Bailey DM. T'ai chi and postural control in the well elderly. *Am J Occup Ther.* 46:295-300, 1992

51. Uhlig T, Fongen C, Steen E, Christie A, Odegard S. Exploring Tai Chi in rheumatoid arthritis: a quantitative and qualitative study. *BMC Musculoskelet Disord.* 11:43, 2010

52. Vernon H, Mior S. The Neck Disability Index: a study of reliability and validity. *J Manipulative Physiol Ther.* 14:409-415, 1991

53. von Trott P, Wiedemann AM, Ludtke R, Reishauer A, Willich SN, Witt CM. Qigong and exercise therapy for elderly patients with chronic neck pain (QIBANE): a randomized controlled study. *J Pain.* 10:501-508, 2009

54. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V, Abraham J, Ackerman I, Aggarwal R, Ahn SY, Ali MK, Alvarado M, Anderson HR, Anderson LM, Andrews KG, Atkinson C, Baddour LM, Bahalim AN, Barker-Collo S, Barrero LH, Bartels DH, Basanez MG, Baxter A, Bell ML, Benjamin EJ, Bennett D, Bernabe E, Bhalla K, Bhandari B, Bikbov B, Bin Abdulhak A, Birbeck G, Black JA, Blencowe H, Blore JD, Blyth F, Bolliger I, Bonaventure A, Boufous S, Bourne R, Boussinesq M, Braithwaite T, Brayne C, Bridgett L, Brooker S, Brooks P, Brugha TS, Bryan-Hancock C, Bucello C, Buchbinder R, Buckle G, Budke CM, Burch M, Burney P, Burstein R, Calabria B,

Campbell B, Canter CE, Carabin H, Carapetis J, Carmona L, Cella C, Charlson F, Chen H, Cheng AT, Chou D, Chugh SS, Coffeng LE, Colan SD, Colquhoun S, Colson KE, Condon J, Connor MD, Cooper LT, Corriere M, Cortinovis M, de Vaccaro KC, Couser W, Cowie BC, Criqui MH, Cross M, Dabhadkar KC, Dahiya M, Dahodwala N, Damsere-Derry J, Danaei G, Davis A, De Leo D, Degenhardt L, Dellavalle R, Delossantos A, Denenberg J, Derrett S, Des Jarlais DC, Dharmaratne SD, Dherani M, Diaz-Torne C, Dolk H, Dorsey ER, Driscoll T, Duber H, Ebel B, Edmond K, Elbaz A, Ali SE, Erskine H, Erwin PJ, Espindola P, Ewoigbokhan SE, Farzadfar F, Feigin V, Felson DT, Ferrari A, Ferri CP, Fevre EM, Finucane MM, Flaxman S, Flood L, Foreman K, Forouzanfar MH, Fowkes FG, Franklin R, Fransen M, Freeman MK, Gabbe BJ, Gabriel SE, Gakidou E, Ganatra HA, Garcia B, Gaspari F, Gillum RF, Gmel G, Gosselin R, Grainger R, Groeger J, Guillemin F, Gunnell D, Gupta R, Haagsma J, Hagan H, Halasa YA, Hall W, Haring D, Haro JM, Harrison JE, Havmoeller R, Hay RJ, Higashi H, Hill C, Hoen B, Hoffman H, Hotez PJ, Hoy D, Huang JJ, Ibeanusi SE, Jacobsen KH, James SL, Jarvis D, Jasrasaria R, Jayaraman S, Johns N, Jonas JB, Karthikeyan G, Kassebaum N, Kawakami N, Keren A, Khoo JP, King CH, Knowlton LM, Kobusingye O, Koranteng A, Krishnamurthi R, Lalloo R, Laslett LL, Lathlean T, Leasher JL, Lee YY, Leigh J, Lim SS, Limb E, Lin JK, Lipnick M, Lipshultz SE, Liu W, Loane M, Ohno SL, Lyons R, Ma J, Mabweijano J, MacIntyre MF, Malekzadeh R, Mallinger L, Manivannan S, Marcenes W, March L, Margolis DJ, Marks GB, Marks R, Matsumori A, Matzopoulos R, Mayosi BM, McAnulty JH, McDermott MM, McGill N, McGrath J, Medina-Mora ME, Meltzer M, Mensah GA, Merriman TR, Meyer AC, Miglioli V, Miller M, Miller TR, Mitchell PB, Mocumbi AO, Moffitt TE, Mokdad AA, Monasta L, Montico M, Moradi-Lakeh M, Moran A, Morawska L, Mori R, Murdoch ME, Mwaniki MK, Naidoo K, Nair MN, Naldi L, Narayan KM, Nelson PK, Nelson RG, Nevitt MC, Newton CR, Nolte S, Norman P, Norman R, O'Donnell M, O'Hanlon S, Olives C, Omer SB, Ortblad K, Osborne R, Ozgediz D, Page A, Pahari B, Pandian JD, Rivero AP, Patten SB, Pearce N, Padilla RP, Perez-Ruiz F, Perico N, Pesudovs K, Phillips D, Phillips MR, Pierce K, Pion S, Polanczyk GV, Polinder S, Pope CA, 3rd, Popova S, Porrini E, Pourmalek F, Prince M, Pullan RL, Ramaiah KD, Ranganathan D, Razavi H, Regan M, Rehm JT, Rein DB, Remuzzi G, Richardson K, Rivara FP, Roberts T, Robinson C, De Leon FR, Ronfani L, Room R, Rosenfeld LC, Rushton L, Sacco RL, Saha S, Sampson U, Sanchez-Riera L, Sanman E, Schwebel DC, Scott JG, Segui-Gomez M, Shahraz S, Shepard DS, Shin H, Shivakoti R, Singh D, Singh GM, Singh JA, Singleton J, Sleet DA, Sliwa K, Smith E, Smith JL, Stapelberg NJ, Steer A, Steiner T, Stolk WA, Stovner LJ, Sudfeld C, Syed S, Tamburlini G, Tavakkoli M, Taylor HR, Taylor JA, Taylor WJ, Thomas B, Thomson WM, Thurston GD, Tleyjeh IM, Tonelli M, Towbin JA, Truelsen T, Tsilimbaris MK, Ubeda C, Undurraga EA, van der Werf MJ, van Os J, Vavilala MS, Venketasubramanian N, Wang M, Wang W, Watt K, Weatherall DJ, Weinstock MA, Weintraub R, Weisskopf MG, Weissman MM, White RA, Whiteford H, Wiersma ST, Wilkinson JD, Williams HC, Williams SR, Witt E, Wolfe F, Woolf AD, Wulf S, Yeh PH, Zaidi AK, Zheng ZJ, Zonies D, Lopez AD, Murray CJ, AlMazroa MA, Memish ZA. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 380:2163-2196, 2012

55. Waite-Jones JM, Hale CA, Lee HY. Psychosocial effects of Tai Chi exercise on people with rheumatoid arthritis. *J Clin Nurs.* 22:3053-3061, 2013

56. Wang C. Tai Chi improves pain and functional status in adults with rheumatoid arthritis: results of a pilot single-blinded randomized controlled trial. *Med Sport Sci.* 52:218-229, 2008

57. Wang C, Schmid CH, Hibberd PL, Kalish R, Roubenoff R, Rones R, McAlindon T. Tai Chi is effective in treating knee osteoarthritis: a randomized controlled trial. *Arthritis Rheum.* 61:1545-1553, 2009

58. Wang C, Schmid CH, Rones R, Kalish R, Yinh J, Goldenberg DL, Lee Y, McAlindon T. A randomized trial of tai chi for fibromyalgia. *N Engl J Med.* 363:743-754, 2010

59. Wang F, Lee EK, Wu T, Benson H, Fricchione G, Wang W, Yeung AS. The effects of tai chi on depression, anxiety, and psychological well-being: a systematic review and meta-analysis. *Int J Behav Med.* 21:605-617, 2014

60. Wayne PM, Berkowitz DL, Litrownik DE, Buring JE, Yeh GY. What do we really know about the safety of tai chi?: A systematic review of adverse event reports in randomized trials. *Arch Phys Med Rehabil.* 95:2470-2483, 2014

61. Wayne PM, Kaptchuk TJ. Challenges inherent to t'ai chi research: part I--t'ai chi as a complex multicomponent intervention. *J Altern Complement Med.* 14:95-102, 2008

62. Wayne PM, Kaptchuk TJ. Challenges inherent to t'ai chi research: part II-defining the intervention and optimal study design. *J Altern Complement Med.* 14:191-197, 2008

63. WHO Collaborating Centre for Drug Statistics Methodology: Guidelines for ATC classification and DDD assignment 2010, Oslo, 2009.

64. Wolfson L, Whipple R, Derby C, Judge J, King M, Amerman P, Schmidt J, Smyers D. Balance and strength training in older adults: intervention gains and Tai Chi maintenance. *J Am Geriatr Soc.* 44:498-506, 1996

65. Xu F, Letendre J, Bekke J, Beebe N, Mahler L, Lofgren IE, Delmonico MJ. Impact of a program of Tai Chi plus behaviorally based dietary weight loss on physical functioning and coronary heart disease risk factors: a community-based study in obese older women. *J Nutr Gerontol Geriatr.* 34:50-65, 2015

66. Yang GY, Wang LQ, Ren J, Zhang Y, Li ML, Zhu YT, Luo J, Cheng YJ, Li WY, Wayne PM, Liu JP. Evidence base of clinical studies on Tai Chi: a bibliometric analysis. *PLoS One.* 10:e0120655, 2015

67. Zhang J, Quan H, Ng J, Stepanavage ME. Some statistical methods for multiple endpoints in clinical trials. *Control Clin Trials.* 18:204-221, 1997

68. Zhang TY, Hu Y, Nie ZY, Jin RX, Chen F, Guan Q, Hu B, Gu CY, Zhu L, Jin LJ. Effects of Tai Chi and Multimodal Exercise Training on Movement and Balance Function in Mild to Moderate Idiopathic Parkinson Disease. *Am J Phys Med Rehabil.* 94:921-929, 2015

Table 1: Baseline characteristics of trial participants according to study arms

Item	**Tai Chi N=38**	**Neck Exercises N=37**	**Wait list N=39**
Age in years	52.0±10.9	47.0±12.3	49.2±11.7
Gender n (female) / n (male)	28/10	31/6	32/7
BMI in kg/m^2	27.2±4.0	25.8±6.0	26.4±4.6
Marital status			
Single	6	6	5
In relationship, married	27	28	29
Separated, divorced, widowed	5	3	5
Education			
< High school	20	14	18
High school	7	12	9
University degree	11	11	12
Employment			
Unemployed	4	1	2
Employed	32	32	32
Retired (health related)	2 (0)	4 (1)	5 (1)
Previous therapies, received			
Medication	13	21	24
Physiotherapy	20	24	30
Operation to the spine	1	0	0
Injections	11	8	14
Rehabilitation center	8	8	5
Efficacy expectation			
Expectation (0-10) towards resp. intervention	7.3±1.5	6.5±1.7	
Pain			
Recent pain intensity	54.2±20.5	46.2±19.2	51.5±21.1
Pain considered tolerable	21.7±14.5	20.5±11.7	20.7±12.1

Table 2: Results of the statistical comparison between the groups at week 12. Scores are presented as Mean±SD; group differences are estimations from the ANCOVA with 95% Confidence Intervals (CI).

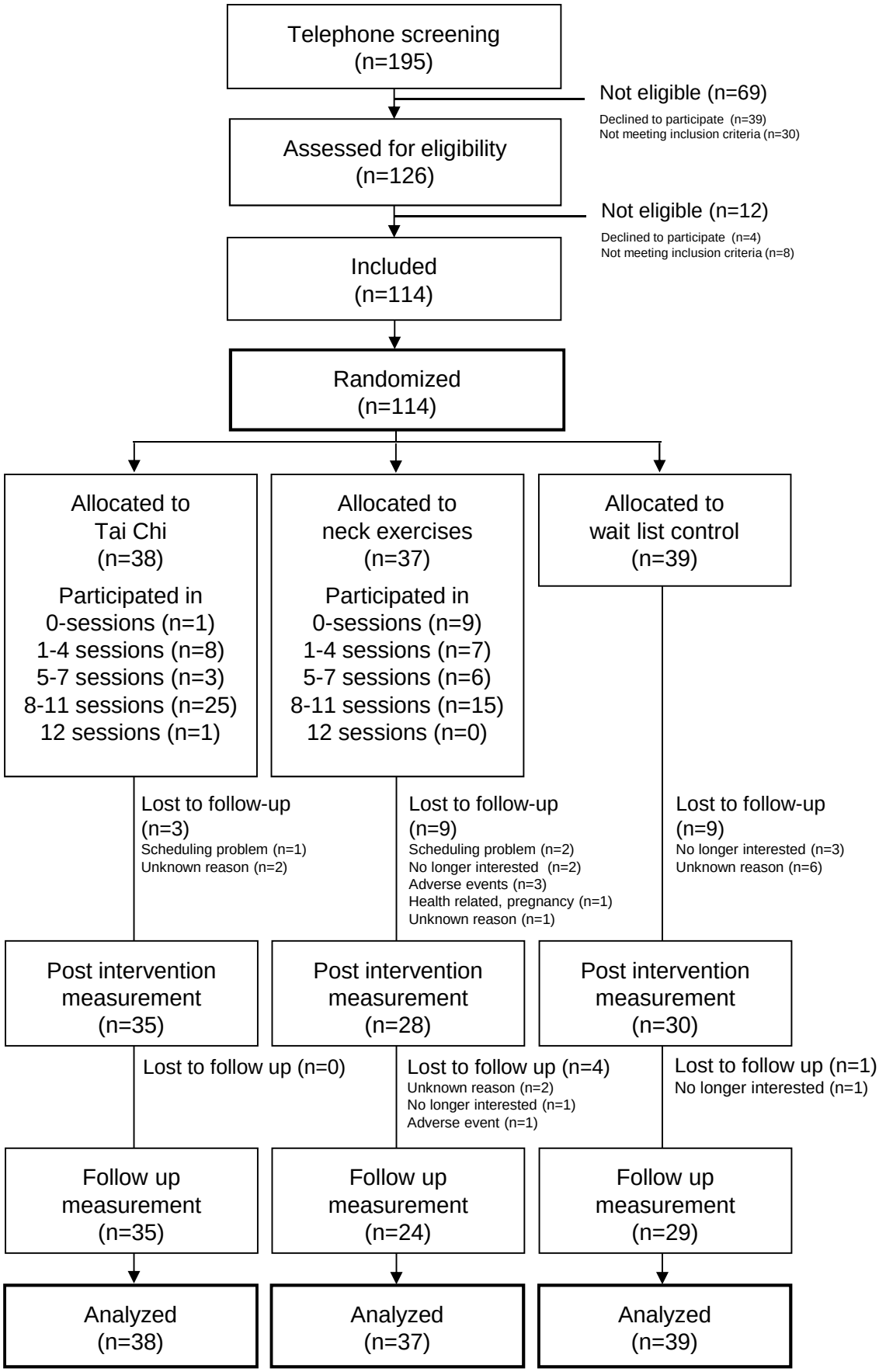
	Tai Chi		**Wait list**		**Neck Exercises**		**Estimated difference between Tai Chi and Wait list (95%CI)**	**Estimated Difference Between Tai Chi and Neck exercises (95%CI)**
	Week 0	Week 12	Week 0	Week 12	Week 0	Week 12		
Primary Outcome								
Pain intensity (mm VAS)	54.2±20.4	32.4±23.5	51.5±21.1	41.8±22.5	46.2±19.2	25.2±18.3	-10.5 (-20.3; -0.9); p=0.033	3.4 (-5.5;12.3); p=0.450
Secondary Outcomes								
Pain on movement (POM)								
Pain on movement (Mean score)	43.1±19.2	28.2±20.4	41.3±19.7	39.1±16.5	43.6±14.6	25.8±13.8	-12.0 (-18.7 ; -5.4)	3.7 (-3.2;10.6)
Disability								
NDI total score (0-100)	30.8±8.0	21.5±12.2	29.3±8.2	27.5±11.4	30.1±9.8	22.7±9.3	-7.2 (-11.7;-2.7)	-1.7 (-5.9;2.4)
Disability in days (VAS)	3.0±4.5	1,5±2.3	2.9±3.8	2.1±2.4	4.2±5.1	1.9±3.2	-0.6 (-1.6; 0.4)	-0.1 (-1.3;1,0)
Everyday function (VAS)	31.1±24.7	18.3±21.5	30.0±21.8	27.7±19.5	29.3±19.7	17.9±14.3	-9.9 (-17.8;-2.1)	-0.2 (-7.7;7.2)
Leisure (VAS)	38.6±23.8	21.7±25.9	39.5±22.8	32.1±22.8	32.9±20.2	18.4±25.9	-9.9 (-19.0;-0.7)	0.7 (-9.0;7.7)
Quality of life (SF-36)								
Physical component summary	44.13±7.0	47.3±9.1	43.6±7.3	42.9±5.4	41.8±7.4	45.2±5.4	4.1 (1.1;7.0)	0.1 (-5.1;5.3)
Mental component summary	46.3±10.3	46.8±11.9	46.9±10.5	46.1±10.7	46.9±8.3	47.7±8.5	1.1 (-2.9;5.1)	-1.2 (-15.1;12.7)
Physical functioning	78.5±13.1	81.1±17.1	79.1±13.6	74.6±19.3	77.4±15.4	80.3±111.5	7.0 (0.1;13.9)	3.0 (-3.9;9.8)
Physical role functioning	62.5±32.8	70.0±37.6	53.2±33.0	53.4±31.7	51.4±34.8	66.1±28.2	11.3 (-2.2;24.8)	4.0 (-2.0;10.1)
Bodily Pain	46.3±25.6	58.5±18.4	50.6±18.1	50.3±11.8	45.1±13.4	55.2±12.3	9.1 (2.1;16.0)	2.0 (-4.0;8.0)
General Health Perception	68.3±14.7	70.7±15.7	67.4±19.0	64.5±18.0	64.4±17.6	64.6±15.4	5.6 (-0.0;11.3)	5.1 (-3.7;13.8)

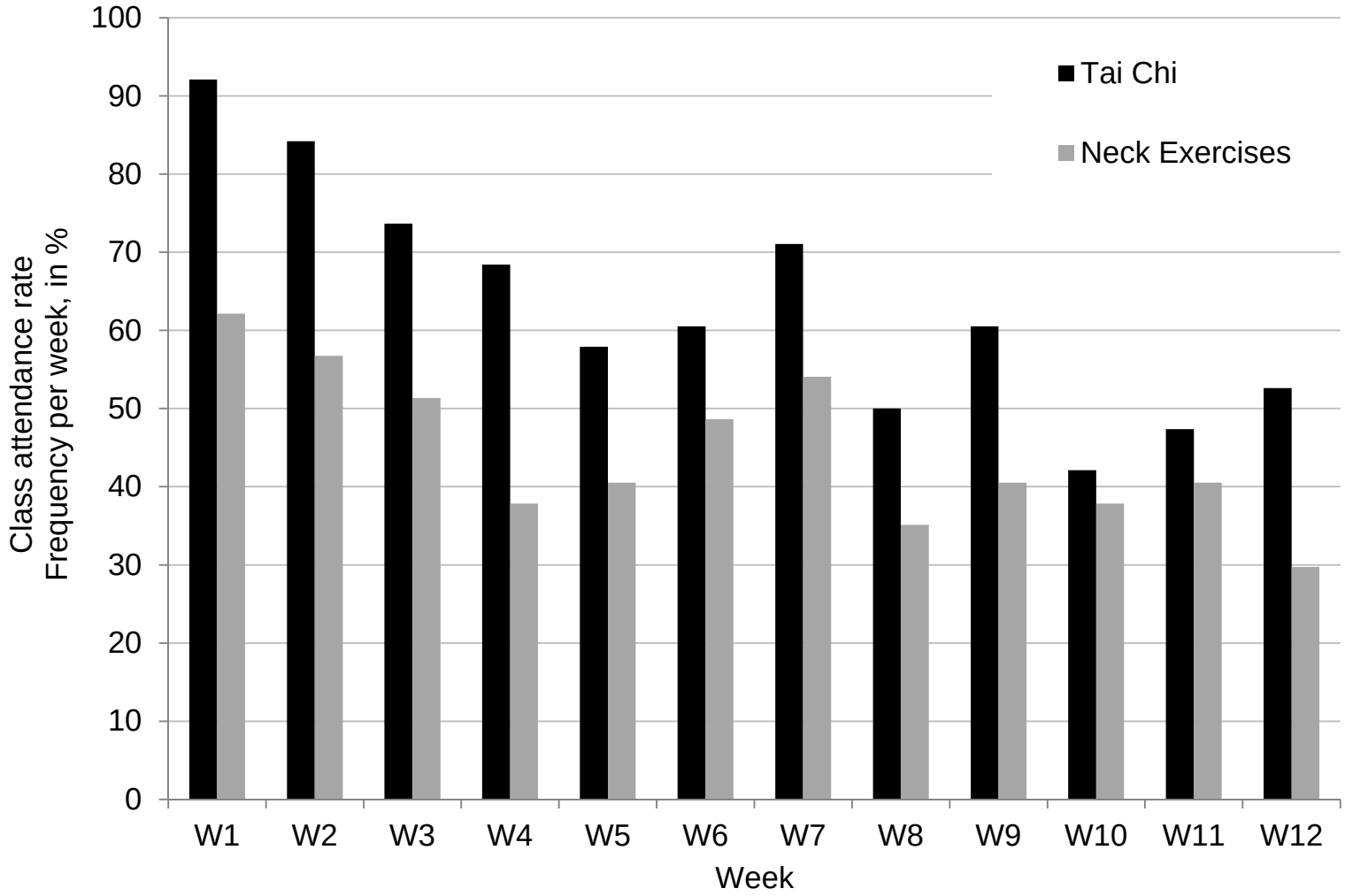
Vitality	51.4±15.5	56.5±17.4	49.9±17.4	49.7±17.0	48.2±15.0	52.5±14.7	5.5 (0.5;10.5)	-0.6 (-16.0;14.7)
Social role functioning	73.0±24.1	79.2±23.8	75.6±19.9	70.3±19.8	68.9±19.7	72.6±16.9	10.2 (1.6;18.9)	-2.7 (-7.9;2.6)
Emotional role functioning	64.0±36.7	68.3±41.6	70.9±39.9	62.9±38.7	72.1±32.9	72.1±28.1	8.5 (-8.3;25.2)	0.7 (-2.3;3.7)
Mental health	68.9±16.1	67.8±18.6	66.8±16.4	65.9±17.7	68.2±12.6	69.9±14.2	0.1 (-5.2±5.3)	-0.5 (-4.2;3,2)
Psychological well-being								
HADS_Anxiety	6.9±3.8	6.5±4.7	6.7±3.7	6.7±3.2	6.0±3.0	5.5±3.1	-0.5 (-1.5;0.5)	0.1 (-1.1;1.3)
HADS_Depression	3.8±2.9	3.9±3.8	4.5±3.0	4.9±3.4	3.8±2.4	3.8±2.3	-0.4 (-1.4; 0.6)	-0.0 (-1.1;1.0)
General Well-being								
FEW Resilience	12.9±3.6	12.9±3.3	12.4±3.6	12.0±3.6	12.1±4.0	12.1±3.2	-0.5 (-0.5;1.5)	0.3 (-0.9;1.5)
FEW Vitality	9.0±5.3	10.2±5.0	8.9±5.2	9.0±4.1	9.6±4.4	9.8±3.9	1.2 (-0.3;2.6)	0.8 (-0.8;2.4)
FEW Ability to Enjoy	12.3±3.9	12.9±3.7	12.6±3.5	12.0±3.5	12.2±3.0	12.3±3.1	1.1 (0.1;2.0)	0.6 (-0.7;1.8)
FEW Ease of Mind	10.4±4.7	11.4±4.6	10.9±3.9	11.0±3.8	11.4±3.8	11.3±3.8	0.7 (-0.3;1.8)	0.8 (-0.4;2.1)
Stress								
PSS Sum score	17.5±7.0	16.9±7.2	17.0±6.6	16.3±6.1	15.9±6.4	15.5±5.4	0.3 (-1.8;2.4)	0.3 (-1.7;2.3)
Interoceptive Awareness								
MAIA Noticing	3.5±0.7	3.7±0.7	3.5±0.7	3.4±0.7	3.5±0.6	3.5±0.7	0.2 (-0.0;0.5)	0.2 (-0.1;0.5)
MAIA Not -Distracting	1.6±0.9	1.8±0.8	1.6±0.8	1.7±0.8	1.6±1.0	1.8±0.9	0.1 (-0.2;0.4)	-0.1 (-0.4;0.3)
MAIA Not-Worrying	2.5±1.0	2.7±1.0	2.3±1.0	2.4±1.0	2.5±1.0	2.6±0.9	0.1 (-0.3;0.4)	0.1 (-9.3;0.4)
MAIA Attention Regulation	2.6±0.9	3.0±0.8	2.4±0.7	2.6±0.8	2.6±0.7	2.7±0.8	0.2 (-0.0;0.5)	0.2 (-0.1;0.5)
MAIA Emotional Awareness	3.8±0.7	3.8±0.8	3.5±1.0	3.5±0.8	3.6±0.8	3.6±0.7	0.2 (-0.1;0.5)	0.1 (-0.2;0.4)
MAIA Self-regulation	2.5±1.0	2.9±1.0	2.3±1.1	2.6±0.8	2.4±0.9	2.7±0.8	0.2 (-0.1;0.5)	0.1 (-0.2;0.4)
MAIA Body Listening	2.2±1.0	2.8±1.0	2.0±0.9	2.4±0.9	2.0±1.0	2.3±0.9	0.3 (-0.1;0.6)	0.4 (-0.0;0.7)
MAIA Trusting	3.1±1.1	3.4±1.0	3.0±1.2	3.0±1.2	3.2±0.9	3.4±0.9	0.3 (0.0;0.6)	0.1 (-0.2;0,4)
Postural Awareness								
PAS conscious efforts	4.98±1.10	4.46±1.14	5.27±0.84	5.20±0.90	5.28±0.83	4.74±0.91	-0.6 (-0.9;-0.2)	-0.2 (-0.6;0.3)
PAS automatic awareness	3.51±1.07	3.90±1.04	3.64±1.09	3.77±1.00	3.52±1.11	3.77±0.82	0.2 (-0.2; 0.6)	0.1 (-0.2;0.5)

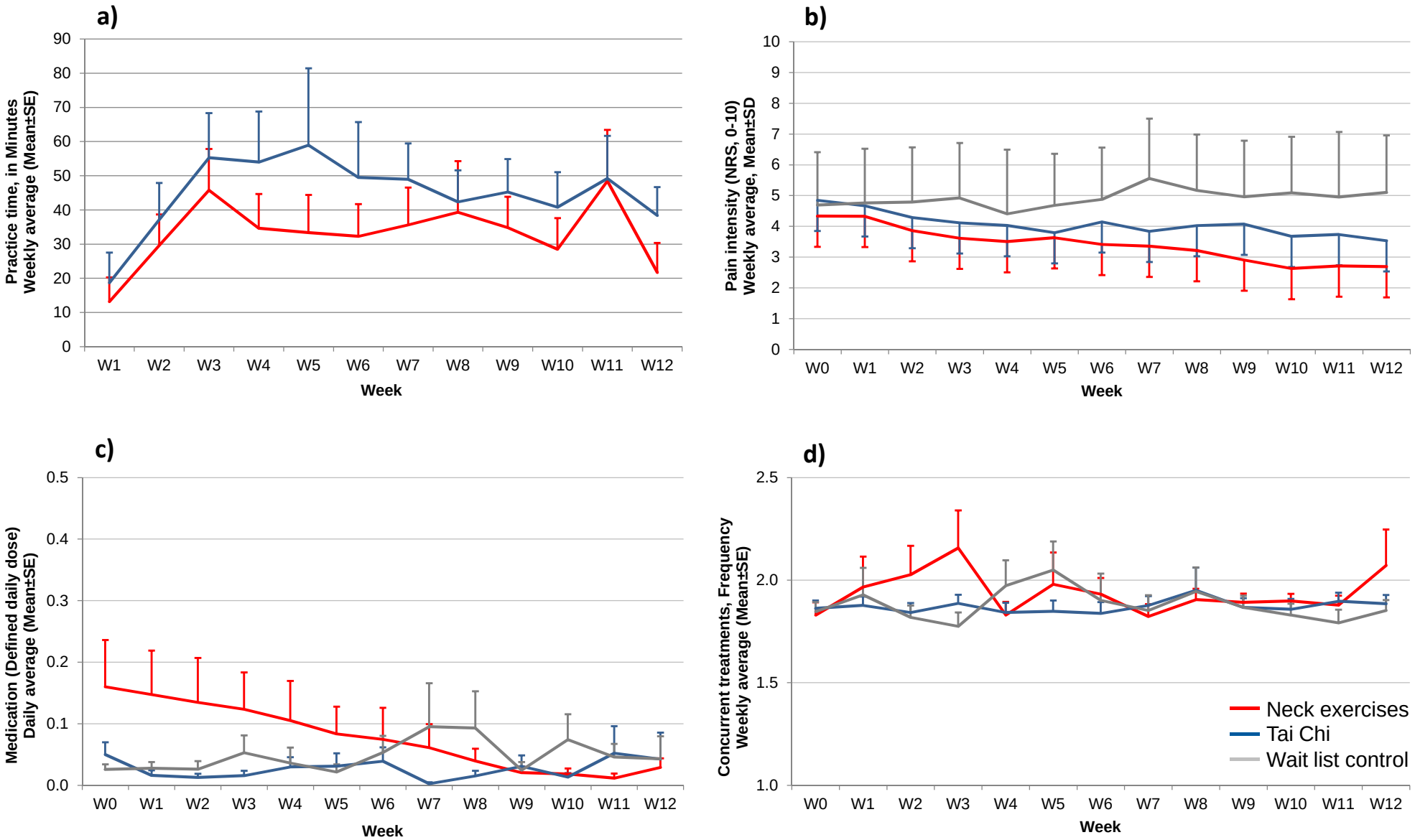
Table 3: Results of the statistical comparison between the groups at week 24. Scores are presented as Mean±SD; group differences are estimations from the ANCOVA with 95% Confidence Intervals (CI).

	Tai Chi		Wait list		Neck Exercises		Estimated difference between Tai Chi and Wait list (95%CI)	Estimated difference between Tai Chi and Neck exercises (95%CI)
	Week 0	Week 24	Week 0	Week 24	Week 0	Week 24	Week 24	Week 24
Primary Outcome								
Pain intensity (mm VAS)	54.2±20.4	35.0±27.7	51.5±21.1	44.6±20.0	46.2±19.2	33.1±20.9	-10.6 (-20.9; -0.3)	-0.5 (-11.8;10.7)
Secondary Outcomes								
Pain on movement (POM)								
Pain on movement (Mean score)	43.1±19.2	29.1±19.0	41.3±19.7	45.5±19.7	43.6±14.6	34.9±14.4	-14.3 (-22.0;-6.7)	-5.6 (-13.0;1.8)
Disability								
NDI total score (0-100)	30.8±8.0	24.3±14.1	29.3±8.2	29.4±12.7	30.1±9.8	25.1±12.9	-6.6 (-11.6;-1.6)	-1.4 (-6.7;4.0)
Disability in days (VAS)	3.0±4.5	1.9±3.4	2.9±3.8	2.7±3.0	4.2±5.1	2.7±3.7	-0.8 (-2.2;0.6)	-0.4 (-1.8;1.0)
Everyday function (VAS)	31.1±24.7	22.0±24.3	30.0±21.8	29.6±20.5	29.3±19.7	24.4±19.6	-8.0 (-17.5;1.5)	-2.9 (-12.6;6.9)
Leisure (VAS)	38.6±23.8	26.6±27.3	39.5±22.8	31.1±21.2	32.9±20.2	24.7±21.1	-4.1 (-14.2;6.0)	-0.8 (-11.1;9.5)
Quality of life (SF-36)								
Physical component summary	44.13±7.0	46.5±8.9	43.6±7.3	42.0±8.0	41.8±7.4	44.0±7.5	4.1 (0.8;7.5)	1.6 (-4.8;8.0)
Mental component summary	46.3±10.3	47.0±12.2	46.9±10.5	46.4±10.13	46.9±8.3	46.9±9.1	1.0 (-3.1;5.2)	0.3 (-12.0;12.6)
Physical functioning	78.5±13.1	79.6±17.0	79.1±13.6	74.0±19.1	77.4±15.4	77.2±17.3	6.0 (-0.9;13.0)	1.0 (-7.0;9.0)
Physical role functioning	62.5±32.8	67.7±37.1	53.2±33.0	49.9±23.9	51.4±34.8	60.2±30.6	12.7 (-1.2;26.6)	4.4 (-2.5;11.4)
Bodily Pain	46.3±25.6	58.6±22.4	50.6±18.1	53.6±15.8	45.1±13.4	56.9±15.8	6.8 (-1.4;15.1)	2.8 (-4.8;10.3)
General Health Perception	68.3±14.7	68.3±16.1	67.4±19.0	59.7±18.5	64.4±17.6	61.9±18.1	8.1 (11.5;14.6)	4.6 (-4.6;13.9)
Vitality	51.4±15.5	55.6±20.4	49.9±17.4	47.6±20.1	48.2±15.0	50.7±17.8	6.6 (-0.0;13.3)	6.0 (-8.7;20.7)

Social role functioning	73.0±24.1	77.9±24.6	75.6±19.9	68.9±22.8	68.9±19.7	71.2±20.5	10.3 (0.6;19.9)	-1.6 (-7.3;4.0)
Emotional role functioning	64.0±36.7	68.4±36.1	70.9±39.9	65.2±37.4	72.1±32.9	65.4±32.1	5.2 (-10.8;21.3)	0.7 (-2.2;3.6)
Mental health	68.9±16.1	68.4±20.0	66.8±16.4	65.9±16.7	68.2±12.6	69.4±15.0	0.7 (-4.8;6.2)	0.6 (-3.2;4.4)
Psychological well-being								
HADS_Anxiety	6.9±3.8	6.1±4.5	6.7±3.7	6.7±3.4	6.0±3.0	5.5±3.1	-0.8 (-2.0;0.4)	-0.3 (-1.3;0.7)
HADS_Depression	3.8±2.9	4.1±3.8	4.5±3.0	5.4±4.0	3.8±2.4	4.1±2.8	-0.8 (-1.9;0.4)	-0.1 (-1.2;1.1)
General Well-being								
FEW Resilience	12.9±3.6	12.6±3.4	12.4±3.6	11.9±3.5	12.1±4.0	11.7±4.0	0.4 (-0.7;1.5)	0.5 (-0.9;1.9)
FEW Vitality	9.0±5.3	10.2±4.9	8.9±5.2	8.9±4.4	9.6±4.4	10.1±4.1	1.2 (-0.6;2.9)	0.3 (-1.4;2.1)
FEW Ability to Enjoy	12.3±3.9	12.2±3.4	12.6±3.5	12.0±3.7	12.2±3.0	11.5±3.7	0.4 (-0.6;1.4)	0.6 (-0.7;2.0)
FEW Ease of Mind	10.4±4.7	10.9±4.5	10.9±3.9	11.0±3.8	11.4±3.8	10.9±3.8	0.3 (-1.0;1.6)	0.6 (-0.7;2.0)
Stress								
PSS Sum score	17.5±7.0	16.5±8.5	17.0±6.6	16.2±6.0	15.9±6.4	15.3±6.8	-0.1 (-2.6;2.4)	0.0 (-2.7;2.7)
Interoceptive Awareness								
MAIA Noticing	3.5±0.7	3.4±0.8	3.5±0.7	3.4±0.7	3.5±0.6	3.3±0.7	0.1 (-0.2;0.4)	0.1 (-0.2;0.5)
MAIA Not -Distracting	1.6±0.9	1.6±0.8	1.6±0.8	1.8±0.8	1.6±1.0	1.7±0.9	-0.2 (-0.5;0.1)	-0.1 (-0.4;0.2)
MAIA Not-Worrying	2.5±1.0	2.6±0.9	2.3±1.0	2.5±1.1	2.5±1.0	2.5±0.9	-0.1 (-0.4;0.3)	0.1 (-0.2;0.4)
MAIA Attention Regulation	2.6±0.9	2.8±0.7	2.4±0.7	2.6±0.8	2.6±0.7	2.7±0.8	0.1 (-0.2;0.3)	0.1 (-0.2;0.4)
MAIA Emotional Awareness	3.8±0.7	3.8±0.7	3.5±1.0	3.5±0.7	3.6±0.8	3.6±0.7	0.2 (-0.1;0.4)	0.2 (-0.1;0.4)
MAIA Self-regulation	2.5±1.0	2.8±1.1	2.3±1.1	2.5±0.8	2.4±0.9	2.4±0.9	0.2 (-0.2;0.5)	0.2 (-0.1;0.6)
MAIA Body Listening	2.2±1.0	2.5±0.9	2.0±0.9	2.4±0.8	2.0±1.0	2.1±0.9	0.0 (-0.3;0.3)	0.2 (-0.1;0.6)
MAIA Trusting	3.1±1.1	3.2±0.9	3.0±1.2	3.0±1.1	3.2±0.9	3.1±1.1	0.1 (-0.2;0.4)	0.2 (-0.1;0.5)
Postural Awareness								
PAS conscious efforts	4.98±1.10	4.55±1.00	5.27±0.84	5.15±0.84	5.28±0.83	4.90±1.09	-0.4 (-0.6;-0.1)	-0.1 (-0.5;0.2)
PAS automatic awareness	3.51±1.07	3.58±0.84	3.64±1.09	3.63±1.02	3.52±1.11	3.47±1.13	0.0 (-0.4; 0.4)	0.1 (-0.3;0.5)


Telephone screening
(n=195)
Not eligible (n=69)
Declined to participate (n=39)
Not meeting inclusion criteria (n=30)
Assessed for eligibility
(n=126)
Not eligible (n=12)
Declined to participate (n=4)
Not meeting inclusion criteria (n=8)
Included
(n=114)
Randomized
(n=114)
Allocated to
Tai Chi
(n=38)
Participated in
0-sessions (n=1)
1-4 sessions (n=8)
5-7 sessions (n=3)
8-11 sessions (n=25)
12 sessions (n=1)
Allocated to
neck exercises
(n=37)
Participated in
0-sessions (n=9)
1-4 sessions (n=7)
5-7 sessions (n=6)
8-11 sessions (n=15)
12 sessions (n=0)
Allocated to
wait list control
(n=39)
Lost to follow-up
(n=3)
Scheduling problem (n=1)
Unknown reason (n=2)
Lost to follow-up
(n=9)
Scheduling problem (n=2)
No longer interested (n=2)
Adverse events (n=3)
Health related, pregnancy (n=1)
Unknown reason (n=1)
Lost to follow-up
(n=9)
No longer interested (n=3)
Unknown reason (n=6)
Post intervention
measurement
(n=35)
Post intervention
measurement
(n=28)
Post intervention
measurement
(n=30)
Lost to follow up (n=0)
Lost to follow up (n=4)
Unknown reason (n=2)
No longer interested (n=1)
Adverse event (n=1)
Lost to follow up (n=1)
No longer interested (n=1)
Follow up
measurement
(n=35)
Follow up
measurement
(n=24)
Follow up
measurement
(n=29)
Analyzed
(n=38)
Analyzed
(n=37)
Analyzed
(n=39)


100
90
80
70
60
50
40
30
20
10
0
Class attendance rate
Frequency per week, in %
Tai Chi
Neck Exercises
W1
W2
W3
W4
W5
W6
W7
W8
W9
W10
W11
W12
Week


a)
Practice time, in Minutes
Weekly average (Mean±SE)
90
80
70
60
50
40
30
20
10
0
W1 W2 W3 W4 W5 W6 W7 W8 W9 W10 W11 W12
Week
b)
Pain intensity (NRS, 0-10)
Weekly average, Mean±SD
10
9
8
7
6
5
4
3
2
1
0
W0 W1 W2 W3 W4 W5 W6 W7 W8 W9 W10 W11 W12
Week
c)
Medication (Defined daily dose)
Daily average (Mean±SE)
0.5
0.4
0.3
0.2
0.1
0.0
W0 W1 W2 W3 W4 W5 W6 W7 W8 W9 W10 W11 W12
Week
d)
Concurrent treatments, Frequency
Weekly average (Mean±SE)
2.5
2.0
1.5
1.0
W0 W1 W2 W3 W4 W5 W6 W7 W8 W9 W10 W11 W12
Week
Neck exercises
Tai Chi
Wait list control

HIGHLIGHTS

Tai Chi provides moderate benefit for patients with chronic non-specific neck pain.

Tai Chi exercises appear to be as effective as conventional exercises for neck pain.

After 12 weeks a pain reduction of ≥50% was observed by 36.8% in the Tai Chi group.

A pain reduction of ≥50% was observed by 45.9% after conventional neck exercises.

Tai Chi and conventional neck exercises appear to be safe and well tolerated.