Clinical variables associated with recovery in patients with chronic tension-type headache following treatment with manual therapy

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Abstract
The aim of this study is (i) to describe the course of chronic tension-type headache (CTTH) in participants receiving manual therapy (MT) and (ii) to develop a prognostic model for predicting recovery in participants receiving MT. We evaluated the outcome of 145 adults with CTTH who received MT as participants in a previously published randomised clinical trial (n=41) or in a prospective cohort study (n=104). Assessments were made at baseline and at 8 and 26 weeks of follow up. Recovery was defined as a 50% reduction in headache days in combination with a score of ‘much improved’ or ‘very much improved’ for global perceived improvement. Potential prognostic factors were analysed by univariate and multivariate regression analysis. After 8 weeks 78 percent of the participants reported recovery following MT and after 26 weeks the frequency of recovered participants was 73%. Prognostic factors related to recovery were co-existing migraine, absence of multiple-site pain, greater cervical range of motion and higher headache intensity. In participants classified as being likely to be recovered, the posterior probability for recovery at 8 weeks was 92%, while for those being classified at low probability of recovery this posterior probability was 61%.

We concluded that the course of CTTH is favourable in participants receiving MT. The prognostic models provide additional information to improve prediction of outcome.

Key words: chronic tension-type headache, course, prognostic factors, manual therapy, cohort study
**Introduction**

Tension-type headache affects people worldwide. In Western society the point prevalence of chronic tension-type headache (CTTH) in adults varies between 2 and 5%. Tension-type headache affects daily functioning, resulting in limitations in performance and participation [17,25,27].

In primary care physical and manual therapy (MT) are regularly used treatments for tension-type headache. [12] The guideline for tension type headache of the European Federation of Neurological Societies recommends physical therapy as a valuable option for therapy in tension-type headache, although evidence for effectiveness of this intervention is limited [3,9]. Our recently published trial of the effectiveness of MT treatment in participants with CTTH showed promising results: after 8 weeks of MT, the mean reduction in days with headache (reported in a 2 week diary) was -9.1 days (sd 3.8) versus -2.7 days (sd 4.3) in the control group receiving usual care by their general practitioner. A 50% reduction of headache days was reported by 87.5% of the participants in the MT group versus 25% in the control group [6].

The effectiveness of MT could be further improved by selecting participants who are likely to show a favourable response to MT. Age, duration (hours/day <8.5) and frequency (<5.5 days/week) of headache and trigger points on cervical muscles were previously reported to be prognostic factors. Dichotomised scores on two subscales (bodily pain <47, vitality <47.5) of the SF 36 (Short Form 36, a self-administered questionnaire assessing health-related functions in 8 different domains, ranging from 0 =lowest to 100 =highest level of functioning) and dichotomised scores (<18 points) on the NDI (Neck Disability Index, scores ranging from 0 points= no disability to 50 =severe disability) have also been reported to be related to a successful response in participants with CTTH following two different physical treatments (trigger point massage or trigger point massage in combination with joint mobilisation) [10,11].

A multimodal manual therapy approach, including mobilisation, muscle strength exercises and posture correction is commonly used in the treatment of neck disorders and headache.

So far no studies have investigated prognostic indicators of a favourable outcome in participants with CTTH who have been treated with this multimodal treatment. Such prognostic information would help clinicians to estimate outcome in their patients.
Therefore, we aimed (i) to describe the course of symptoms in patients with CTTH receiving manual therapy and (ii) to develop a prognostic model for predicting recovery in participants with CTTH who receive manual therapy.

**Material and methods**

**Subjects**

We used data from a multi-centre pragmatic randomised clinical trial (RCT, Netherlands Trial Register nr TR 1074) and a parallel multi-centre prospective cohort study of participants with CTTH recruited from 14 general practices in an urban area near Amsterdam in The Netherlands [6].

For the RCT 41 participants were randomised to a MT intervention group, while 41 control participants received usual care from their general practitioner (GP). Hundred and four participants, who refused randomisation because of a preference for manual therapy, were entered into the cohort study. Participants in the cohort study fulfilled the same in- and exclusion criteria and received similar measurements and MT intervention as participants in the RCT. Data from the RCT and the cohort were used to describe the course of CTTH and to develop the prognostic model.

Inclusion criteria required participants to fulfil the CTTH criteria according to the classification of headaches of the International Headache Society (IHS) [28], which define CTTH as headache occurring on at least 15 days on average per month for a period of more than 3 months, and headache lasting for hours or continuous. Additionally, the headache has at least two of the following characteristics: (1) bilateral location; (2) pressing/tightening (non pulsating) quality; (3) mild or moderate intensity, not aggravated by normal physical activity such as walking or climbing stairs; and (4) both of the following: i. no more than one of photophobia, phonophobia or mild nausea, and ii. neither moderate or severe nausea nor vomiting. Participants had to be between 18 and 65 years of age.

Exclusion criteria were rheumatoid arthritis, suspected malignancy, pregnancy. According to the IHS classification of headache attributed to medication overuse [28], we excluded participants with an intake of either triptans, ergotamines or opioids on ≥10 days/month or simple analgesics on ≥15 days/month on a regular basis for ≥3 months.
Participants were also excluded if they had received MT treatment in the two months before the study, or were not able to read and write Dutch.

The selection and informed consent procedures, baseline- and follow-up measurements, and MT protocol of this study have been previously published [5]. The study protocol was approved by the Medical Ethics Committee of the VU University Medical Center in Amsterdam, The Netherlands.

**Potential prognostic factors**

A pre-selection of generic and specific prognostic factors was made, based on literature and clinical expertise. Generic prognostic factors for musculoskeletal disorders included pain severity at baseline, pain duration, multiple-site pain, previous pain episodes, age, disability and range of motion [22]. Specific prognostic factors, i.e. headache duration and headache frequency, were derived from a previous study on prognostic factors for the outcome of trigger point massage in adults with CTTH [10].

Central sensitisation may play a role in the pathogenesis for CTTH and migraine. Based on the supposed working mechanism of the MT treatment (i.e. modulation of central pain mechanism by improvement of cervical musculoskeletal function) we expected that co-existing migraine, neck flexor muscle endurance and algometry results could predict recovery and added these variables as potential prognostic factor. Co-existing migraine was defined as attacks of ‘a separate headache’ fulfilling the IHS criteria for migraine and not exceeding one attack on average per month to limit the frequency of days with migraine to a maximum of three days on the headache diary.

**Measurements**

Baseline measurements included a standardised history of headache, general health, a physical examination carried out by an independent research assistant, and several participant self-report measures.

**Outcome measures**

To determine the course of CTTH, we used a headache diary that was kept by the participants to register their headaches during a 2-weeks period before baseline and follow-up measurement. According to Blanchard et al. a 2-weeks period is sufficient to monitor tension type headache and recommended as outcome measurement in headache research [1,4]
All participants were asked to report improvement following treatment on the General Perceived Improvement (GPI) scale, a commonly used rating scale on global change, consisting of a 7-point Likert scale (0= very much worse 1= much worse, 2= somewhat worse, 3= no change, 4= somewhat improved, 5= much improved 6= very much improved) [19].

Potential prognostic factors
Headache was measured as headache intensity scored on an 11-point (0=no pain, 10 most severe) numerical rating scale [30]. Age, multiple-site pain, co-existing migraine, headache episode duration (hours/day) and total duration (years) of headache were obtained from a standardised headache questionnaire. Baseline disability and impact on daily activities were measured, respectively with the Headache Disability Inventory (HDI) and Headache Impact Test-6 (HIT-6). The HDI contains 25 questions on physical and emotional functioning with three possible response options: no= 0 points, sometimes= 2 points, yes= 4 points. A total score is computed by summarizing all scores, resulting in a total HDI score ranging from 0 (no disability) to 100 points (severe disability) [15]. The HIT-6 consists of 6 items (pain intensity, social functioning, role functioning, vitality, cognitive functioning and psychological distress) each with 5 response options (never: 6 points, rarely: 8 points, sometimes: 10 points, very often: 11 points, always: 13 points), with a total score ranging from 36 to 78 points [21]. The cervical active range of motion (AROM) was measured with the CROM-device as the sum of all motions [20,29]. Pressure algometry measurements were carried out with a Wagner FDK algometer with a 3.0 kg/cm pressure at four points at the left and right side: two points on the upper trapezius muscle and two points on the suboccipital muscle. Participants rated the severity of pain on an 11-point (0=no pain, 10 most severe pain) numerical rating scale. Scores for each pressure point were summarized into a total score ranging between 0 and 80 points [2,13,24]. The neck flexor muscle endurance was scored as the number of seconds the participant can raise his/her head from the table when lying on his/her back. This procedure for endurance of the neck flexor muscles was developed by Harris et al. [14].

Definition of recovery
To construct a definition of recovery a combination of two self-reported outcomes was used. Participants who scored a reduction of >50% in headache days on
their two-week diary and scored ‘much improved’ or ‘very much improved’ (score 5 and 6 on a 7-point Likert scale) for GPI, were considered to be recovered. All others were classified as being not recovered, at 8 and 26 weeks follow up.

**Manual therapy treatment**

**Manual therapists**

All participants received treatment from four participating manual therapists who had 10 years experience as manual therapist on average and all had completed an additional course on diagnosis and management of disorders of the cervical spine. They worked at three different locations and were registered members of the National Association of Manual Therapists. In two meetings, of two hours each, they were trained in all procedures of the treatment protocol and received a treatment manual including patient booklets with home exercises.

**Treatment protocol**

The MT treatment consisted of a maximum of nine sessions with duration of 30 minutes each, and aimed at three goals. At each session the manual therapist decided, depending on the participant’s condition and outcomes, which type of mobilisations or exercises were selected from the treatment protocol. The first goal was mobilisation of the cervical and upper-thoracic spine in flexion, extension, retraction and left and right rotation. The therapeutic procedures for these mobilisations were described in the treatment protocol and consisted of low and/or high-velocity mobilisation and also included also home-exercises. All mobilisations started with active mobilisation (hands-off techniques) and if necessary the manual therapist proceeded with passive mobilisations (hands-on techniques). In addition to mobilisation techniques, soft tissue techniques (muscle stretching, deep muscle frictions) could be used to reduce cervical muscular tension and pain.

The second goal was training of the endurance of the craniocervical muscles. This training consisted of low-load craniocervical muscle endurance exercises as described by Jull using a stabilizer [18]. In case a stabilizer could not be used, the participants were instructed, while lying on their back in a horizontal position, to pull their chin in (atlanto-occipital cervical flexion) and hold this position (isometric contraction) for 10-20 seconds. This exercise was also instructed in combination with retraction of the cervical spine in a sitting position. Participants were asked to perform these exercises at least two times a day.
The third goal of treatment was postural correction of the cervical and thoracic spine. In an upright sitting position the manual therapist instructed the participant to straighten the thoracic spine with a simultaneously retraction of the cervical spine. In all exercises of postural correction in sitting and standing position the craniocervical muscle endurance exercises were incorporated. The manual therapists underlined the importance of this posture correction. Besides posture correction exercises participants were given advice about their work place, especially to those who performed sedentary work during several hours a day.

Every participant received a booklet with a full description of all home-exercises and written instructions by the manual therapist on type, frequency and duration of the exercises. The participants were encouraged by their manual therapist to continue their exercises after their treatment period, focusing on retraction of the cervical spine and posture correction.

**Data analysis**

**Course of symptoms**

Descriptive statistics were used to describe the course of headache in terms of change in frequency of headache days and to describe the percentage of participants defined as recovered based on the combination of 50% reduction of headache days and a 5 or 6 score on GPI.

**Model development**

Data from all participants receiving MT were used to develop a prognostic model for recovery after 8 and 26 weeks. Univariate logistic regression analysis was used to assess the association of each of the 12 potential prognostic variables with recovery. Variables showing an association with a significance level of \( p < 0.15 \) were retained as potential predictors and entered into multivariate logistic regression analysis. A backwards manual step-wise selection procedure was used to form the most parsimonious combination of predictors for identifying patients with CTTH with a high probability of recovery during MT treatment. Bootstrapping techniques were used to estimate the amount of optimism in regression coefficients of the prognostic factors in the final model.

**Performance of the prognostic model**
The performance of the final prognostic model was studied in terms of discrimination, explained variance and calibration. Discrimination was assessed by calculating the area under the Receiver Operating Characteristic (ROC) curve (AUC) [7]. The explained variance was calculated as Nagelkerke’s $R^2$ while for calibration the Hosmer-Lemeshow test was applied [23]. To describe the accuracy of the prognostic model, we calculated positive and negative predictive values for the final prognostic model based on the cut-off point of the ROC curve indicating the optimal combination of sensitivity and specificity.

**Results**

Between June 2007 and March 2009 204 participants were recruited and follow-up measurements were completed in September 2009. Figure 1 summarizes recruitment and retention of participants throughout the study. Baseline characteristics of cohort and RCT participants were largely similar, except for a higher prevalence of co-existing migraine and multiple-site pain in the cohort group. (Table 1) Thirty-eight percent of all participants (42% in the cohort versus 29% in the trial) reported co-existing migraine, at 9 +/-15 days per year on average.

**Results at 8 weeks**

**Course of symptoms**

At 8 weeks the mean reduction in days with headache per 2 weeks of the MT participants (n=142) was -8.1(SD 3.7) days and 78% of the MT participants reported a 50% reduction in headache days in combination with a 5 or 6 score on the GPI.
Figure 1. Recruitment and retention of participants throughout the study.

Eligible participants informed and referred for screening n=204

Not meeting inclusion criteria n=18:
- pain medication-overuse (n=10)
- migraine >1 episodes per month (n=6)
- language (n=1)
- MT treatment <2 months (n=1)

Screening for inclusion:. n=204

Randomisation for randomised clinical trial (RCT) n=82

Manual therapy (MT): n=104
Received treatment: n=103
drop out: n=1

Manual Therapy (MT) : n=41
Received treatment: n=40
donot out: n=1

Usual Care (UC) n=41
Received treatment: n=40
donot out: n=1
Not used for analysis

Follow up at 8 weeks n=142
Lost to follow up: n=3 (reasons unknown: n=3)
Recovered : n=110

Follow up at 26 weeks n=128
Lost to follow up: n=17 (moved: n=2; reasons unknown: n=12)
Recovered: n= 93
Table 1. Comparability of all MT participants at baseline regarding headache characteristics and potential prognostic factors.

<table>
<thead>
<tr>
<th></th>
<th>MT Cohort (n=104)</th>
<th>MT RCT (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>38.0 (sd 12.1)</td>
<td>40.2 (sd 10.2) range: 18-64 range: 20-59</td>
</tr>
<tr>
<td>% male</td>
<td>20%</td>
<td>28%</td>
</tr>
<tr>
<td>Headache duration (years)</td>
<td>11.2 (11.3)</td>
<td>12.5 (10.7)</td>
</tr>
<tr>
<td>Headache days/2 weeks (headache diary)</td>
<td>11.3 (2.8)</td>
<td>12 (2.6)</td>
</tr>
<tr>
<td>Headache hours/day</td>
<td>13.0 (9.1)</td>
<td>12.8 (8.9)</td>
</tr>
<tr>
<td>Headache days/month &gt;5.5 days/week (y/n)</td>
<td>56%</td>
<td>70%</td>
</tr>
<tr>
<td>Headache intensity (NRS*:0-10 points)</td>
<td>7.6 (1.7)</td>
<td>7.5 (1.7)</td>
</tr>
<tr>
<td>% co-existing migraine present</td>
<td>42%</td>
<td>29%</td>
</tr>
<tr>
<td>% multiple-site pain present</td>
<td>76%</td>
<td>59%</td>
</tr>
<tr>
<td>Cervical active range of motion (Total sum of degrees all movements)</td>
<td>338.7 (57.9)</td>
<td>357.1 (42.3)</td>
</tr>
<tr>
<td>Algometry (Total NRS* score: 0-80 points)</td>
<td>32.9 (18.3)</td>
<td>28.1 (19.5)</td>
</tr>
<tr>
<td>Neck flexor muscle endurance (in seconds)</td>
<td>29.1 (24.8)</td>
<td>32.1 (26.6)</td>
</tr>
<tr>
<td>HIT-6 (36-78 points)</td>
<td>62.1 (5.3)</td>
<td>62.6 (5.4)</td>
</tr>
<tr>
<td>Headache Disability Inventory (0-100 points)</td>
<td>39.4 (20.4)</td>
<td>39.6 (21.9)</td>
</tr>
</tbody>
</table>

* NRS numerical rating scale; (sd) standard deviation

Prognostic model

The univariable associations of the selected twelve potential prognostic variables with outcome for all MT participants (n=142) are shown in Table 2. In the final multivariable regression model higher headache intensity, co-existing migraine, absence of multiple-site pain and greater cervical AROM were positively related to recovery (Table 3). The performance of this final model showed an AUC of 0.77 (CI 95%: 0.68 to 0.87; 0.74 after adjustment for optimism), an explained variance of 0.23 (0.17 after adjustment) and a Hosmer-Lemeshow test of p=0.15. With regard to the accuracy of the model, the optimal ROC showed a sensitivity of 64% (CI 95%: 54 to 72) and a specificity of 81% (CI 95%: 65 to 91). While the prior probability of recovery was 78%, in participants who were classified by the model as being likely to recover the posterior probability for recovery (positive predictive value) was 92% (95%CI: 84 to 96%). The negative
predictive value was 39% (95%CI: 29 to 52), which means that the posterior probability of recovery was 61% (100-39%) in those who were classified by the model as being at low probability of recovery.

**Table 2.** Potential prognostic variables, results of univariate logistic regression at 8 weeks (n=142).

<table>
<thead>
<tr>
<th></th>
<th>Recovered at 8 weeks n=110</th>
<th>Not recovered at 8 weeks n=32</th>
<th>B</th>
<th>Sig.</th>
<th>Odds Ratio (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>37.9 (sd 12)</td>
<td>42 (sd 10)</td>
<td>-.03</td>
<td>.09</td>
<td>.97 (.94 – 1.01)</td>
</tr>
<tr>
<td>Headache duration (years)</td>
<td>11.6 (11.8)</td>
<td>11.7 (9.3)</td>
<td>-.001</td>
<td>.95</td>
<td>.99 (.97 – 1.04)</td>
</tr>
<tr>
<td>Headache days/month &gt;5.5 days/week (y/n)</td>
<td>62%</td>
<td>59%</td>
<td>.102</td>
<td>.8</td>
<td>1.11 (.5 - 2.47)</td>
</tr>
<tr>
<td>Headache hours/day &gt;8.5 h/d (y/n)</td>
<td>56%</td>
<td>59%</td>
<td>-.16</td>
<td>.69</td>
<td>.85 (.38 – 1.9)</td>
</tr>
<tr>
<td>Headache intensity (NRS score: 0-10 points)</td>
<td>7.8 (1.6)</td>
<td>7 (1.9)</td>
<td>.24</td>
<td>.04</td>
<td>1.27 (1.02 – 1.6)</td>
</tr>
<tr>
<td>Co-existing migraine y/n</td>
<td>43%</td>
<td>25%</td>
<td>.81</td>
<td>.07</td>
<td>2.24 (.92 - 5.42)</td>
</tr>
<tr>
<td>Multi-site pain y/n</td>
<td>66%</td>
<td>88%</td>
<td>-1.31</td>
<td>.02</td>
<td>.27 (.09 - .82)</td>
</tr>
<tr>
<td>Cervical active range of motion. (Total sum of degrees all movements)</td>
<td>349.7 (51.6)</td>
<td>326 (58.8)</td>
<td>.09</td>
<td>.03</td>
<td>1.01 (1.00 - 1.02)</td>
</tr>
<tr>
<td>Algomtery (total NRS* score:0-80 points)</td>
<td>31.3 (18.6)</td>
<td>31.3 (19.5)</td>
<td>.00</td>
<td>.99</td>
<td>1.00 (.98 - 1.02)</td>
</tr>
<tr>
<td>Neck flexor muscle endurance (in seconds)</td>
<td>29.4 (25)</td>
<td>33.9 (27)</td>
<td>-.007</td>
<td>.38</td>
<td>.99 (.98 - 1.09)</td>
</tr>
<tr>
<td>HIT-6 (36-78 points)</td>
<td>62.6 (5.2)</td>
<td>60.8 (5.8)</td>
<td>.063</td>
<td>.1</td>
<td>1.07 (.99 - 1.15)</td>
</tr>
<tr>
<td>Headache Disability Inventory (0-100 points)</td>
<td>39.1 (21.2)</td>
<td>39.6 (19.7)</td>
<td>-.001</td>
<td>.91</td>
<td>.99 (.98 - 1.02)</td>
</tr>
</tbody>
</table>

(sd) standard deviation, * NRS numerical rating scale
Table 3. Course and prognostic factors for recovery after 8 and 26 weeks MT participants.

<table>
<thead>
<tr>
<th>Results after 8 weeks n=142</th>
<th>Results after 26 weeks n=128</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in days with headache on 2 weeks headache diary</td>
<td>-8.1(3.7)</td>
</tr>
<tr>
<td>% Recovered (n=142)</td>
<td>78%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prognostic factors and performance final model</th>
<th>Prognostic factors an performance final model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio</td>
<td>95%CI</td>
</tr>
<tr>
<td>Co-existing migraine present</td>
<td>2.58</td>
</tr>
<tr>
<td>Multiple-site pain present</td>
<td>0.18</td>
</tr>
<tr>
<td>Cervical active range of motion (Total sum of degrees all movements, OR per degree)</td>
<td>1.01</td>
</tr>
<tr>
<td>Headache intensity (NRS score: 0-10 points, 1.78 OR per point)</td>
<td>1.36</td>
</tr>
<tr>
<td>Area under the curve:</td>
<td>0.68 (CI 95%: 0.58 to 0.78)</td>
</tr>
</tbody>
</table>

Results at 26 weeks

Course of symptoms

The mean reduction in headache days per 2 weeks in MT participants (n=128) at 26 weeks was -8.4 (SD 4.1) days and 73% of the MT participants reported a 50% reduction in headache days in combination with a 5 or 6 score on the GPI.

Prognostic model

The final prognostic model included greater cervical AROM and greater neck flexor muscle endurance at baseline (Nagelkerke’s $R^2$ 0.13; Hosmer-Lemeshow p=0.66). (Table 3).

The ROC curve showed an AUC of 0.68 (95%CI: 0.58 to 0.78; 0.67 after adjustment for optimism) and reflected a sensitivity of 34.4% (95%CI: 25.4 to 44.7) and specificity of 89.5% (95%CI: 75.9 to 95.8).

With a prior probability of recovery of 73%, in participants who were classified by the model as being likely to recover the posterior probability for recovery (positive predictive value) was 88% (95%CI: 74 to 96). The negative predictive
value was 37% (95%CI: 28 to 47), indicating a posterior probability of recovery of 63% (100-37%) in those who were classified by the model as being at low probability of recovery.

Discussion

Main findings

The course of participants with CTTH at 8 weeks showed a reduction in headache days of 8.1 (SD 3.7) days measured on a 2 week diary. At 26 weeks the mean reduction in headache days was -8.4 (SD 4.1) days. At 8 weeks 78% of the participants met the definition of recovery and 73% after 26 weeks. A prominent finding is the sustained reduction in headache days after 26 weeks.

The prognostic models consisting of headache intensity, co-existing migraine, multiple-site pain, cervical AROM and neck flexor muscle endurance demonstrated moderate performance, with an AUC adjusted for over-optimism of 0.74 at 8 weeks and 0.67 at 26 weeks.

The models increased the posterior probability for recovery, with respectively 14% and 15% at 8 and 26 weeks to around 90%. In participants classified as having a poor outcome, the posterior probability for recovery was reduced by a similar amount (17% at 8 weeks and 10% at 26 weeks) to around 60%. Apparently, the favourable outcome in the short and long term in the great majority of participants receiving MT provides the most important information to the clinician. The prognostic models provide some additional information to improve prediction of outcome.

Comparison with literature

The reported reduction in headache days at both follow up moments is comparable to the findings of a randomised clinical trial by Ettekoven et al. in participants with CTTH receiving a similar approach including mobilisation, craniocervical exercises and posture correction [8].

The following pre-selected general prognostic variables were associated with recovery at 8 weeks follow-up: absence of multi-site pain, greater cervical AROM and higher pain intensity. We found no significant associations for age, pain duration and disability at baseline with recovery at either 8 or 26 weeks. Greater cervical AROM at baseline was the only prognostic factor consistently associated with recovery, which corresponds with other studies reporting on the prognostic value of cervical AROM in patients with CTTH [11,22].
The predictive value of greater cervical AROM, greater neck flexor muscle endurance and performance of the models (AUC 0.68) implies that response to treatment may be better in participants with normal function of the cervical spine than in participants with a severe dysfunction. Further analysis is needed to investigate to what extent the manual therapy treatment can influence AROM, and whether this subsequently leads to better patient outcomes in terms of headache frequency and recovery.

In contrast with the exploratory study of prognostic variables by Fernandez de las Penas et al. we found no association between baseline headache frequency (>5.5 days per week) or baseline headache duration (>8.5 hours per day) and outcome at 8 or 26 weeks follow up [10]. This lack of consistency may be the result of differences in several characteristics of this study, including differences in treatment (trigger point massage), differences in follow up period (1 month) and differences in definition of recovery (combination of 50% reduction in frequency or duration or intensity of headache and general perceived effect).

Co-existing migraine was found to be associated with recovery at 8 weeks, but was not associated with recovery at 26 weeks. We do not have an explanation for this unexpected finding. When developing a predictive model the aim is not to investigate the causal association between individual prognostic factors and outcome. The statistical approach identifies the combination of factors most likely to predict outcome and this process may result in unexpected associations for individual factors.

**Strengths and limitations**

As far as we know, our study is the first to evaluate the course and prognosis of adults with CTTH receiving MT treatment.

We prevented ‘overfitting’ of the prognostic model by including no more than one prognostic variable per 10-15 events and by adjusting the performance of our models for over-optimism. Furthermore, we had a limited loss to follow-up of 17 participants (12%) and we enhanced generalisibility by including participants with CTTH and migraine, a combination that co-exists in many adults with headache [16,26].

A limitation of the study is that, due to the modest size of the study, we could only analyze a limited number of potential prognostic factors. These potential prognostic factors had emerged from earlier studies [10,22] or were additional
variables related to the supposed working mechanisms of MT treatment. We did not measure psychological or work-related variables.

**Recommendations**
More research is needed to clarify the working mechanism of MT and to evaluate whether our results will hold in other settings and populations. We recommend including additional potential prognostic factors such as stressors and work-related variables in future studies.

In order to investigate whether the prognostic factors in this study are generic prognostic factors of outcome in participants with CTTH or that they predict a differential response to MT treatment (i.e. modify effect to MT treatment specifically), large randomised controlled trials are needed.

**Conclusion**
Participants with CTTH receiving MT showed a favourable course of symptoms at short and long term. Absence of multiple-site pain, co-existing migraine, higher headache intensity, greater cervical AROM and greater neck flexor muscle endurance were associated with recovery and could be useful for the clinician to improve prediction of outcome.

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References


