

STUDY PROTOCOL

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The effectiveness and cost-evaluation of manual therapy and physical therapy in patients with sub-acute and chronic non specific neck pain. Rationale and design of a Randomized Controlled Trial (RCT)

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Abstract

Background: Manual Therapy applied to patients with non specific neck pain has been investigated several times. In the Netherlands, manual therapy as applied according to the Utrecht School of Manual Therapy (MTU) has not been the subject of a randomized controlled trial. MTU differs in diagnoses and treatment from other forms of manual therapy.

Methods/Design: This is a single blind randomized controlled trial in patients with sub-acute and chronic non specific neck pain. Patients with neck complaints existing for two weeks (minimum) till one year (maximum) will participate in the trial. 180 participants will be recruited in thirteen primary health care centres in the Netherlands. The experimental group will be treated with MTU during a six week period. The control group will be treated with physical therapy (standard care, mainly active exercise therapy), also for a period of six weeks. Primary outcomes are Global Perceived Effect (GPE) and functional status (Neck Disability Index (NDI-DV)). Secondary outcomes are neck pain (Numeric Rating Scale (NRS)), Eurocol, costs and quality of life (SF36).

Discussion: This paper presents details on the rationale of MTU, design, methods and operational aspects of the trial.

Trial registration: ClinicalTrials.gov Identifier: NCT00713843

Background

Neck pain is one of the most common complaints of the musculoskeletal system.

Approximately two thirds of the population will at some point in their life experience neck pain [1]. Prevalence rises with age in both sexes and is highest at ages between 50 and 59. In general women suffer from neck complaints twice as often as men.

Prevalence of neck complaints is between 10% and 15% [2]. In the Netherlands, the point prevalence in absolute figures, calculated in the year 2000, amounted

to 594,000 males and 1,013,700 females registered with chronic neck complaints [3]. Systematic reviews showed a considerable heterogeneity in prevalence of neck complaints. Fejer et al found a range of the one-month prevalence from 15.4% to 41% [4]. Hogg-Johnson found a range from 15.4% to 45.3% among adults, interfering with activities ranged from 7.5% to 41.5% [5]. Bot showed an incidence of 23.1 per 1000 person-years of neck symptoms in a Dutch national survey of general practice [6].

The total costs related to neck pain in the Netherlands added up to approximately 668 million Euros in 1996. Direct medical costs amounted to 160 million Euros (23% of the total costs related to neck complaints) [2].

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Allied health care (such as occupational therapy and physical therapy) made up the largest proportion of the direct costs (84%) [2]. As such, neck pain forms a significant personal and economical problem.

Neck pain can be caused by traumata (specifically traffic accidents), infections, tumours, congenital defects and inflammations; however in many cases it is not possible to determine the underlying cause. In these cases neck pain will be regarded as 'non-specific neck pain'.

In case of acute neck pain the general practitioner (GP) will usually not take immediate action. Pain medication might be prescribed [7]. Research by Vos indicates that 51% of patients having neck pain are referred to physical therapy or manual therapy [7].

These figures may differ internationally because of different referral policy.

If the complaints are persistent (for six months or longer) it appears that the average discomfort perceived will remain fairly stable [8]. It is clinically and economically relevant to ensure that patients do not end up in this chronic phase.

Level of evidence manual therapy

In 2004 Gross et al made a meta-analysis of Randomized Controlled Trials (RCTs) in which the effect of manipulations and mobilizations for mechanical neck complaints was investigated [9]. In cases of a single manipulation session or several sessions (3 to 11 weeks) of manipulations or mobilizations compared to a control group or when mobilizations were compared to other forms of therapy, moderate evidence was found that this gave no results in the short term for acute, sub-acute and chronic mechanical neck problems.

When manipulation and mobilization were compared to withholding treatment, the results showed a tendency towards a positive effect of manipulation and mobilization. Mobilisation and manipulation compared to placebo or control groups showed a nonsignificant result [9].

Their conclusions were that the evidence did not favour manipulation and/or mobilisation done alone or in combination with various other physical medicine agents; when compared to one other, neither was superior.

As for the costs of care, there was moderate evidence that manual therapy was less expensive than other forms of care in acute, sub-acute and chronic neck complaints with or without headache or cervical radicular signs [9].

In 2007, Vernon et al published a systematic review of applying manual therapy in cases of neck pain [10]. Little evidence was found about the application of manual therapy for acute neck pain (existing less than four weeks) [10]. There was moderate- to high-quality evidence that subjects with chronic neck pain show

clinically important improvements from a course of spinal manipulation or mobilization, using intragroup changes [11]. The Task Force on Neck Pain stated that manual therapy or exercise therapy was not clearly superior to one other in either short- or long-term [12].

In some countries manual therapy has been included in the guidelines for treatment of neck pain [11].

In summary, reviews showed that manual therapy is an effective method (intragroup changes)(specially in sub acute and chronic neck pain) but compared to controls there is in general no clear evidence that one of them is superior (intergroup changes).

Research in the Netherlands

In the Netherlands, the effectiveness and cost-effectiveness of treatments with manual therapy and physical therapy (PT) compared with counselling of the general practitioner (GP) for non-specific neck pain was investigated in a RCT [13].

MT consisted of mobilizing techniques as described by Van der El en Di Fabio [14,15]. Low-amplitude, high-velocity thrust techniques were not applied. After seven weeks, perceived recovery was 68% for MT, 51% for PT and 36% for GP treatment. MT scored statistically significantly better than the other interventions. PT scored better than GP, although this difference was non-significant. At one year follow-up there were no statistically significant differences between the groups for pain and impediment (global perceived effect after one year 72% MT, 63% PT and 56% GP) [16]. MT was significantly more cost-effective than treatment by the GP and physical therapy [17]. The total costs per patient, including absence from work and costs of health care utilisation, amounted to €447 for MT, €1297 for PT and €1379 for GP.

In later research by Pool et al manual therapy (MT) was compared with exercise therapy with behaviour graded activity (BGA) in people with neck complaints [18]. Pool found neither clinically relevant nor statistically significant differences. 89.4% in the BGA group and 86.5% in the MT group showed positive global perceived effect after 52 weeks.

So, although the systematic reviews did not clearly show an effect of manual therapy for neck pain, two Dutch studies found that manual therapy is more cost-effective than physiotherapy and GP counselling, and equally effective as an extensive exercise therapy with behaviour graded activity programme. However, in both Hoving's and Pool's studies other forms of manual therapy than MTU were used [13,19].

Manual therapy according to the Utrecht School (MTU)

MTU is based on assessing the patient's individual preference of functioning by documenting and interpreting

their natural asymmetry in anatomical form, posture and movements.

The normal asymmetry and variability of human form and movement function have been specified in research [20-26]. These studies showed that many movements are carried out asymmetrically. These asymmetrical forms can be related to the asymmetrical movement function.

In addition to the general diagnostics, MTU is characterized by specific diagnostics. By means of this specific manual-therapeutic analysis the individual preference of functioning model of the patient is drawn up through documentation and interpretation of the individual asymmetry in form, posture and movement [27,28]. Some explanations of the measurements and movements are: (preferred) hand folding; (preferred) arm folding; which eye is master eye; leg use in (preferred) kicking of a ball. The purpose here is to describe the optimal direction and position of movement axes for all joints according to this model.

When composing this model, firstly the individual characteristics (a number of preferred movements, a number of asymmetrical aspects of posture and form) are assessed. Documentation, notation and interpretation of these characteristics take place according to a protocol.

The objective of MTU is to optimise the positioning of movement axes in the joints. To achieve this, three-dimensional movements in the joints are executed repeatedly. To purpose fully position the movement axes the therapist should (repeatedly) perform passive joint movements with low velocity and high accuracy. In addition to examining the individual preference of movement, exploratory examination is carried out to recognise possible red flags and to determine the treatment indication.

Treatment is based on preferred movements found in the patient and the interpretation according to the protocol of these movements and not on the complaint of the patient. It is executed by applying passive articular movements in the spinal joints and the joints of the extremities. During this process physiological joint limitations are carefully observed; traction or high-velocity movements will not be applied, as may be the case in other forms of manual therapy [29].

The diagnostic examination of other forms of manual therapy focuses on joint function, stability, movement patterns, range of movement, and the severity of disorders [30]. To diagnose the patients complaints, palpation of passive accessory and passive intervertebral movements are used. The results yield information as to tenderness (pain), restricted intersegmental motion (stiffness), and spasm (muscle tension) [29-31].

In general, other manual therapies, as described by Veen et al, are directed primarily to the complaints of patients, particularly the main complaint [29,32].

Trial Objectives

The primary objective is to compare the short-term effectiveness (7 weeks) and long-term effectiveness (52 weeks) of MTU with physical therapy in patients with sub-acute and chronic neck pain with regard to global perceived effect, functioning and pain.

The cost-effectiveness of manual therapy compared with physiotherapy will also be evaluated.

Methods/Design

Design and setting

This research is a single-blinded randomized controlled trial with cost-evaluation. A central research centre is set up in the Radboud University Nijmegen Medical Center, the Netherlands, housing a central investigator, an advisor, an independent physician, a statistician and a blinded research assistant entering data.

There are twelve locations where patients are treated. All of these are primary health care centres for manual and/or physical therapy. Each local centre will have a manual therapist, a physical therapist and a research assistant.

Ethical approval

Ethical approval was obtained from the Medical Ethics committee CMO Arnhem-Nijmegen (NL21128.091.08).

Inclusion and exclusion

Males and females aged between 18 and 70 years having neck pain for at least two weeks and with the last episode started at maximum of 52 weeks ago are eligible. Neck pain is the primary pain at the time of inclusion and must be provoked and reproduced as mechanical neck pain by movement or posture of the neck. Participants may have cervicogenic headache and radiation to the elbow. Exclusion criteria are: presence of red flags such as specific neck pain caused by cervical radiculopathy, entrapment neuropathy, myelopathy, unexplained fever, unexplained weight loss, nocturnal persistent pain, general malaise [33]; surgery of the cervical spine; pregnancy; whiplash trauma (in the past or recent, as cause of the complaint); physical conditions seriously impeding treatment (such as amputations, being wheelchair bound, illness); insufficient knowledge and command of the Dutch language for answering the questionnaires (to be judged by the research assistant); therapeutic treatment for neck pain in the previous three months such as physical therapy, manual therapy, osteopathy, chiropractics and acupuncture.

Sample size

The sample size is based on one of the two primary outcome variables, Neck Disability Index (NDI) and Global Perceived Effect (GPE). The GPE is chosen, because this outcome variable needs the largest group of participants. Previous studies have shown that the effect of manual therapy on GPE is 68.3% [13] and 70.1% [18].

A 20% difference on the GPE scale is considered clinically relevant. Based on $\alpha = .05$ and an 80% power ($\beta = 0.2$) 76 participants per intervention group are required.

With regard to prospective drop outs (15%), 90 participants per group will be recruited in this trial. A similar sample size was used in previous research [19,34,35].

Interventions

MTU (experimental intervention)

During the first consultation the manual therapist enquires about the complaints of the patient. The manual therapist conducts a number of measurements according to protocol, thus registering the natural asymmetry in form, posture and movement (see figure 1).

By means of an interpretation according to the protocol the measurements are translated into preferred movements in the patient's joints. During treatment these preferred movements are executed by the manual therapist in the patient's joints. The treatment techniques used by the manual therapist are very gentle mobilizations, without high velocity thrust techniques and are in general painless. In MTU it is common to give advice and recommend exercise.

A treatment session lasts between 30 and 60 minutes. In this trial treatment is repeated after one or two weeks. The maximum number of sessions is six.

The manual therapist has a minimum of five years of working experience.

Physical therapy (comparison intervention)

At the first appointment the physical therapist enquires about the complaints. The physical therapist conducts a complaint related function examination, after which treatment goals are determined. Treatment can consist of active exercises, manual traction or stretching and massage. The aims of exercises are improvement of strength, mobility and movement coordination. Specific manual mobilization techniques, known as manual-therapeutic techniques, are not a part of physiotherapeutic treatment. Treatment sessions take place no more than twice a week with a maximum of nine sessions; session duration is approximately 30 minutes. In each session the physical therapist will spend a minimum of twenty minutes on active exercise therapy combined with instruction.

To prevent overlap with MTU, physical therapists are selected who are not (also) trained as manual therapists or have started this training.

The physical therapist has at least five years of working experience.

Figure 1 contains the description of the experimental and control intervention.

Co-interventions

During the intervention period of the trial, participants will not receive treatment other than the ones allocated. Patients are free to use medication prescribed either by a physician or of their own choice. Participants are allowed to withdraw from the treatment at any time. Continuation of the treatment and co-interventions are registered.

Outcome

In the choice of primary and secondary outcome the ICF (International Classification of Functioning, Disability and Health) components have been taken into account. These cover the following categories: bodily functions, anatomical properties; activities and participation; external factors; personal factors [36].

Primary outcome

Global Perceived Effect (GPE) measures overall improvement or worsening. Measuring of GPE will be done by scoring a 7-point ordinal scale (ranging from much worse to complete recovery) [37,38]. The GPE measures patient subjective global improvement and has a high face validity [39]. In routine clinical practice it is important, since it would not make sense to classify a patient as improved or deteriorated against the patient's own personal assessment [39,40]. Functioning is the second primary outcome. The Neck Disability Index Dutch Version (NDI-DV) is a questionnaire containing 10 items. All items are related to daily functioning and functions. The maximum score is 50; the higher the score the more limitations. Validity and reliability of the NDI are good [41,42] and so is the responsiveness [42-44].

Secondary outcomes

To assess neck pain intensity the Numeric Rating Scale (NRS) will be used. This scale (11 points) measures the pain intensity experienced by the patient in the previous week. Dalton et al argued for standardization of pain measuring by means of the 11-point Numeric Rating Scale (NRS) [45]. The Visual Analogue Scale (VAS) and the NRS are the most cited pain measures, largely because they are simple to use. The NRS is a sensitive instrument, comparable with the VAS [46,47] or more sensitive than the VAS [48]. The NRS has been chosen on the basis of administrative aspects rather than for statistical power. It has been proved to be more comprehensible for patients [45-47,49,50]. Also the NRS is valid for verbal patient questioning [51].

The general health questionnaire (SF36) will be used to put together a detailed health profile on the basis of scores on eight health dimensions as well as a sum score on both physical and mental health [52].

	Item	MTU (Experimental)	PT (Control)
Diagnostic process	Interview and clinical tests.	Yes	Yes
	Test and measuring of total mobility	Yes, only to evaluate the treatment	Yes
	Testing muscle tension	No	Yes
	Testing muscle strength	Only in case of expected neurological entrapments	Yes
	Testing coordination	No	Yes
	Analysing individual preference of movement	Yes	No
	Analysing asymmetric posture and movements	Yes	No
Therapeutic process	Planning and intervention of the treatment	Yes	Yes
	Active exercise to increase total mobility	Only to stimulate the function	Yes
	Active exercise to increase muscle tension in neck and shoulder muscle	No	Yes
	Active exercise to increase muscle strength	No	Yes
	Active exercise to optimize stability	No	Yes
	Active exercise to optimize coordination	No	Yes
	Massage therapy	No	Yes
	passive angular arthrokinematic three dimensional mobilizations of the joints	Yes	No, only global mobilizations
	Treatment of total body function	Yes	Is not common
	Informing and advising the patient	Yes	Yes
	Evaluation of the treatment	Yes	Yes
	Ending treatment	Yes	Yes

Figure 1 Shows the differences of the intervention between the experimental group MTU (Manual therapy Utrecht) and the control group PT (physical therapy).

Table 1 Timing of measurements

measurements	Baseline T0	T3	T7	T13	T26	T39	T52
In- and exclusion	X						
Demographic data	X						
GPE		X	X	X	X		X
NDI-DV	X	X	X	X	X		X
NRS pain	X	X	X	X	X		X
SF-36	X		X				X
Side effect		X	X	X			
EuroQol5D		X	X	X	X	X	X
Costs		X	X	X	X	X	X

GPE = Global Perceived Effect (7-points scale); NDI-DV = Dutch version Neck Disability Index; NRS = Numeric Rating Scale for pain; SF36 = short form -36 quality of life questionnaire

The EuroQol5D is a standardized, non-disease-specific instrument for describing and valuing health states. It has the additional possibility of converting the descriptive data into values for economic (cost-effectiveness) analysis by linking patients' health state descriptions to empirical valuations of health states obtained from the general population [53]. EuroQol5D is simple to use, valid, responsive to change and reliable instrument for group comparisons [54-56]. The EuroQol5D is a two-part instrument. Part one records self-reported problems on each of five 'domains': mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each domain is divided into three levels of severity corresponding to no problem, some problem and extreme problem. Part two of the questionnaire records the subject's self-assessed VAS rating of health.

Participants are to fill in questions about (partial) disablement/return to work (if applicable), use of analgesic (types of and quantities), medical consultation during treatment and follow-up, costs and side effects [57,58].

The patient will fill in the questionnaires at baseline, 3, 7, 13, 26, 39 and 52 weeks after treatment has started (see table 1).

Procedure

Recruitment

The GP and therapists will send in patients suitable to include. See the flow chart in figure 2. The GP and therapists inform the patient about the aim of the study and present an information brochure. If the patient is willing to participate in the study, the GP or therapist contacts the local research assistant (LRA).

The LRA schedules an appointment with the patient. The patient will be informed again by the LRA about the contents and objectives of the study. After this, the LRA conducts a diagnostic examination according to protocol. Training and an instructional DVD is provided by the NECKprojectgroup to the LRA to ensure a correct intake procedure.

The purpose of the intake procedure is to assess inclusion and exclusion criteria. Should the patient be eligible, he/she is informed about how to fill in the questionnaires either digitally or on paper. After signing the informed consent, randomisation takes place. The patient receives an envelope with the name and address of the (local) therapist that will provide the treatment. The patient makes an appointment with the therapist in attendance and starts treatment. The LRA has no further contact with the patient in relation to this trial.

All questionnaires are sent either digitally or by mail to the central blinded investigator.

Randomisation, blinding and allocation

Block randomisation will take place through the computer after pre-stratification on the basis of prognostic aspects for the complaints: level score of the main complaint (scale 10: <7 or ≥ 7) and age (< 40 or ≥ 40 years) [59,60].

Four groups are formed which are randomized for both intervention groups. The randomisation scheme will be generated by the central computer. The LRA is blinded for the randomisation.

Treatment with physical therapy and MTU will take place at different locations. The investigator in charge of the database has no access to the key of the combination patient data - research number - treatment allocation. In the case of missing data the computer system will automatically generate an email to the participant directly or to the secretary of the NECKprojectgroup. The computer or secretary will send the patient a standard reminder. None of the therapists know the patient number(s).

The data from the questionnaires filled in digitally on <http://www.neckproject.nl> are sent directly to the database of the central researcher. The researcher is blinded from patients' data and type of intervention. The questionnaires filled in by hand are sent to a central freepost address. These lists are entered into the database by a secretary. Loss of data should be prevented by actively reminding the patient by email, mail or telephone.

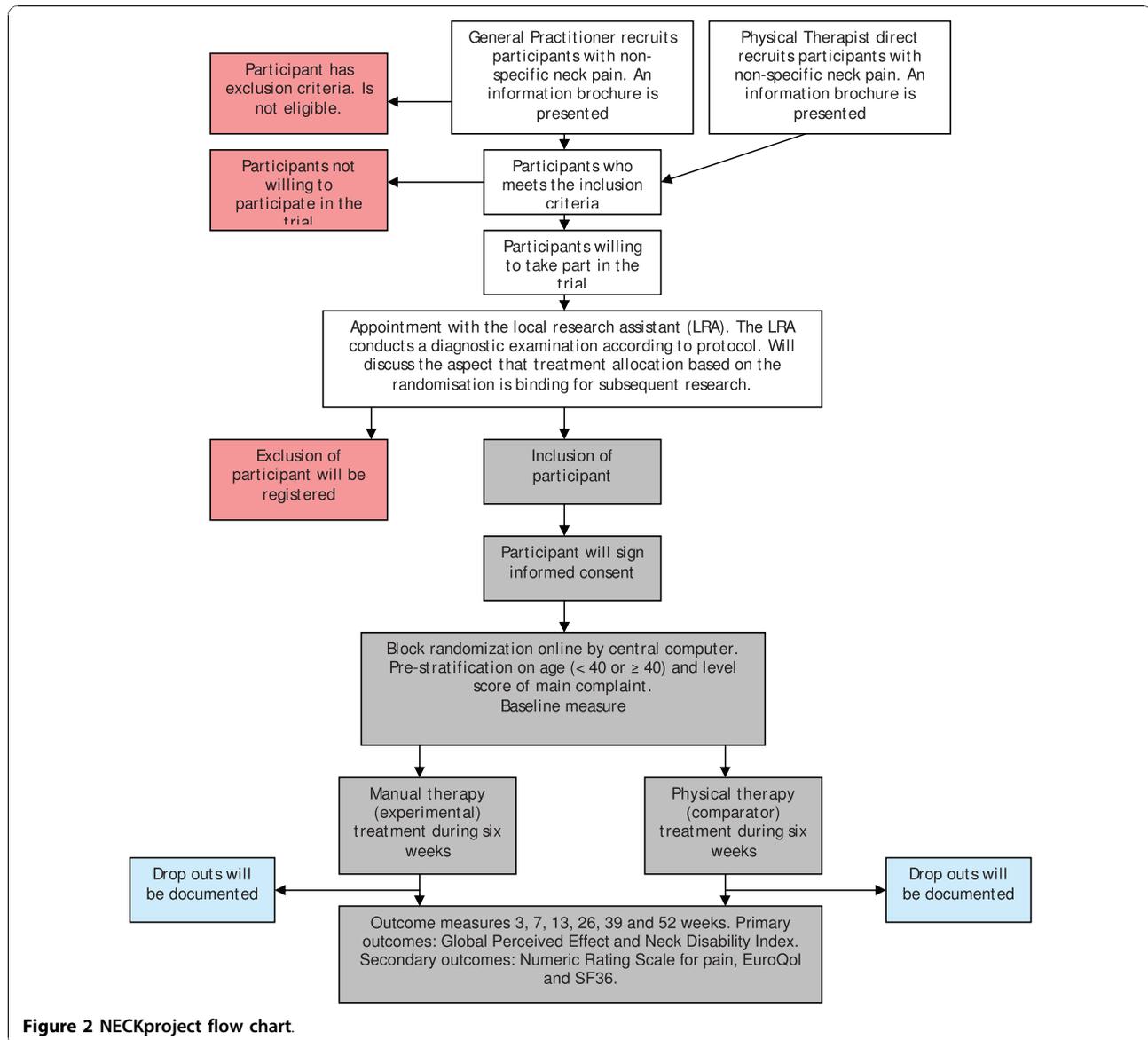


Figure 2 NECKproject flow chart.

Patients who fill in the forms digitally will automatically receive a reminder by email. Patients who fill in the lists by hand will receive them through the post. The secretary will attend to this.

Each treatment sessions will be registered by using standard forms filled in by the therapist. By doing spot checks the information received about the content of the treatment session will be inspected by the researcher from the UMC St Radboud.

Visitations will take place to ensure the therapists in attendance are keeping to the research protocols.

Side effects

All side-effects, both reported spontaneously by patients and noticed by the therapist, are registered. Any serious side-effects are registered and reported to the Medical

Ethic Commission in charge, according to the rules of this organisation.

Statistics

Descriptive statistics

Demographic data (gender, average age, disability/fitness, duration of complaints, headache of cervical origin, use of medication and other items) will be presented.

Outcomes will be presented per group (baseline, MTU, physical therapy) in mean, standard deviation and 95% confidence interval.

Multi-variate analysis

An ANOVA will be used to analyze differences between conditions per person (within subject) and per group (between groups).

Descriptive statistics will be applied to make a comparison between the baseline data of the manual therapy and the physical therapy groups and to assess whether the randomisation has been successful. Group differences between the interventions with a 95% confidence interval will be calculated for all outcome measures.

The statistical analyses will be carried out according to the intention-to-treat principle, whereby the patients are analysed in the intervention group in which they were originally placed. The differences between groups will be tested by ANOVA/mixed model (continuously) and by the Chi-Square test for dichotomous variables.

Multi-variate regression analysis will be used to test the influence of the baseline variables on the outcomes.

For the primary outcome measure Global Perceived Effect (GPE) a selection can be made between responders (positive effect) and non-responders (no or negative effect) to the treatment received.

The data will be processed by SPSS/SAS statistical software.

Discussion

In working with local centres, locally approaching the GPs by the manual therapists and physical therapists, we expect to be able to have the required number of participants minimally within one year after the start. Trial recruitment started in September 2008.

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Authors' contributions

RG, HK, HL, LA, JM, MT and RO were responsible for the design of the trial. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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