The Dutch Injection versus Surgery TRIal in Carpal Tunnel Syndrome patients

-DISTRICTS-

a multicenter open-label randomized controlled trial comparing two treatment strategies

Dutch CTS study group

PROTOCOL TITLE 'The Dutch Injection versus Surgery TRIal in Carpal Tunnel Syndrome patients'

Protocol ID	***837004025***
Short title	***DISTRICTS***
Version	***4.2***
Date	***27-06-2017***
Coordinating investigator/project leader	***Prof. dr. R.M.A. de Bie*** *Academisch Medisch Centrum*
Principal investigator	***Dr. C. Verhamme*** *Academisch Medisch Centrum*
Executing investigator	***Drs. W.A.C. Palmbergen*** *Zuyderland Medisch Centrum*
Participating Centers **See appendix 13.1 for investigators on site**	*Academisch Medisch Centrum* *Canisius-Wilhelmina Ziekenhuis* *Catharina Ziekenhuis* *Elisabeth-TweeSteden Ziekenhuis* *Elkerliek Ziekenhuis* *Haaglanden Medisch Centrum* *Maasstad Ziekenhuis* *Medisch Centrum Leeuwarden* *OLVG Amsterdam* *Radboudumc* *Rijnstate* *SJG Weert* *St. Antonius Ziekenhuis* *The Hand Clinic* *Zaans Medisch Centrum*

	Ziekenhuis St Jansdal *Zuyderland Medisch Centrum*
Dutch CTS study group	***Drs. T.W.H. Alleman*** ***Prof. dr. R.H.M.A. Bartels*** ***Prof. dr. D. van de Beek*** ***Dr. R. Beekman*** ***Prof. dr. R.M.A. de Bie*** ***Dr. K. Jellema*** ***Drs. W.A.C. Palmbergen*** ***Dr. W.I.M. Verhagen*** ***Dr. C. Verhamme*** ***Dr. E. Verstraete*** ***Prof. dr. L.H. Visser***
Sponsor:	***Prof. dr. R.M.A. de Bie***
Subsidising party	***Doelmatigheidsonderzoek ZonMw*** *Project nummer 837004025*
Independent expert	***Dr. P.J. Nederkoorn*** *Academisch Medisch Centrum* *Afdeling Neurologie*

PROTOCOL SIGNATURE SHEET

Name	Signature	Date
Head of Department: ***Prof. dr. I.N. van Schaik***		
Coordinating Investigator: ***Prof. dr. R.M.A. de Bie***		

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

AE	**Adverse Event**
AMC	**Academisch Medisch Centrum**
AR	**Adverse Reaction**
BCTQ	**Boston Carpal Tunnel Syndrome Questionnaire**
CBO	**Centraal BegeleidingsOrgaan**
CRF	**Case Report Form**
CRU	**Clinical Research Unit**
CTS	**Carpal Tunnel Syndrome**
CTS-6	**6-item carpal tunnel symptoms scale**
eCRF	**Electronic CRF**
EMG	**Electrodiagnostic testing**
GCP	**Good Clinical Practice**
IC	**Informed Consent**
METC	**Medisch Ethische Toetsing Commissie**
NVN	**Nederlandse Vereniging voor Neurologie**
QALY	**Quality-adjusted life year**
SAE	**Serious Adverse Event**
SPC	**Summary of Product Characteristics**
Sponsor	**The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.**
STZ	**Stichting Topklinische Ziekenhuizen**
WMO	**Wet Medisch-wetenschappelijk Onderzoek met Mensen**
ZBC	**Zelfstandig BehandelCentra**

SUMMARY

Rationale: carpal tunnel syndrome (CTS) is the most common peripheral neuropathy. The optimal treatment strategy is still unknown. This results in considerable practice variation in the treatment of CTS.

Objective: the objective is to investigate if initial surgical treatment of CTS results in a better outcome and is more cost-effective when compared to initial treatment with a steroid injection.

Study design: multicenter open-label randomized controlled trial.

Study population: adult patients with CTS.

Intervention: one strategy starts with surgical treatment and the other strategy starts with a steroid injection. The choice for possible subsequent treatments is at the patient and physician's discretion.

Main study parameters/endpoints: the primary objective is to assess if the treatment strategy starting with a surgical treatment results in a higher rate of recovery compared to starting treatment with a steroid injection. Recovery is defined as having no or mild CTS symptoms as measured with the 6-item carpal tunnel symptoms scale. Follow-up is 18 months.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: surgical treatment and steroid injections for CTS have been widely used treatments and patients will not be exposed to additional risks. The patient has to fill in eight self-report questionnaires in the course of 18 months. We estimate that this may take 4 hours (4x 0,7hrs + 4x 0,3hrs).

1. INTRODUCTION AND RATIONALE

Carpal tunnel syndrome (CTS) is the most common peripheral neuropathy and is characterized by pain, paresthesia, numbness, and weakness of the affected hand. The cause of CTS is entrapment of the median nerve at the wrist. There are no universally accepted criteria for diagnosing CTS. Electrodiagnostic testing (EMG) and sonography are both accurate tools to confirm the diagnosis.[1] The overall prevalence rate of electrophysiologically confirmed CTS in the Netherlands is 9.2% in women and 0.6% in men.[2] There are approximately 300,000 patients with CTS in The Netherlands.[3] Estimated costs for absenteeism due to CTS are 26,5 million euro/year.3 Treatment options for CTS include splinting, steroid injections, and surgical decompression.[4 5 6 7]

Splinting is effective in the short term. A Dutch study showed that 54% of CTS patients with nocturnal splinting had a general improvement after 3 months.[6] In the same study 75% experienced an improvement of symptoms in the long term, but 41% of patients had also received surgery by that time.[6] The conclusion of the study was that surgery resulted in better outcome than splinting.

Steroid injections have been proven to be efficacious in the short term and are relatively safe.[8] A Dutch study showed that 25% of patients had a persistent effect of a steroid injection after one year.[9] Another Dutch study showed that 67% of patients initially treated with a steroid injection required additional surgery within one year.[10] This was confirmed by a Swedish study in which more than 70% of patients that had a steroid injection for CTS needed surgery within the following year. Ninety-two percent of the patients allocated to placebo needed surgery within the first year.[8] Results of another study suggest that a second injection is as effective as the first one, but long-term prospective data are missing.[11]

Surgical treatment is efficacious in most patients. The reported efficacy however varies. In a pooled analysis of 209 studies (32,936 surgeries), 75% of patients considered their condition as improved, much better, or cured.[12] There is no difference in effectiveness between open carpal tunnel release and endoscopic release.[13]

In line with the above, a systemic review also suggested that surgical treatment is more effective than non-surgical interventions for relieving symptoms of CTS.**Error! Bookmark not defined.** However, most neurologists initiate treatment with a steroid injection because they consider this very easy to perform and safe. Often, a second steroid injection is performed if the result of the first injection proved to be unsatisfactory. If symptoms remain or

reoccur, patients are referred for surgical treatment. Because of the high frequency of persisting or reoccurring symptoms, this strategy may result in postponement of the more effective treatment, that is surgical treatment, which could lead to unnecessary health loss, work absenteeism, and costs. Patients with severe CTS are often primarily treated surgically,[7] though the best treatment strategy for severe CTS is also not known.

The lack of comparative knowledge regarding the best treatment strategy for CTS, that is starting with a surgical treatment or starting treatment with a steroid injection, is reflected in the concept NVN-guideline for CTS (2016), which states no preference for one of the two strategies.[14] All of the above contributes to the considerable practice variation in the treatment of CTS.[15] The objective of this study is therefore to assess the efficacy and cost-effectiveness of a treatment strategy starting with a surgical treatment compared to starting treatment with a steroid injection.

2. OBJECTIVES

2.1 Primary objective

The primary objective is to assess:

if the treatment strategy starting with a surgical treatment results in a higher recovery rate 18 months later when compared to starting treatment with a steroid injection.

2.2 Secondary objectives

Secondary objectives are to compare the treatment strategy that starts with a surgical treatment to the treatment strategy that starts with a steroid injection regarding:

A) time to recovery during 18 months of follow-up;

B) number of patients recovered at different time points during 18 months follow-up;

C) level of symptom severity at different time points during 18 months follow-up;

D) hand functioning at 18 months;

E) patient's global perception of recovery at 18 months;

F) patient satisfaction at 18 months;

G) quality of life at 18 months;

H) number of additional treatments during 18 months follow-up;

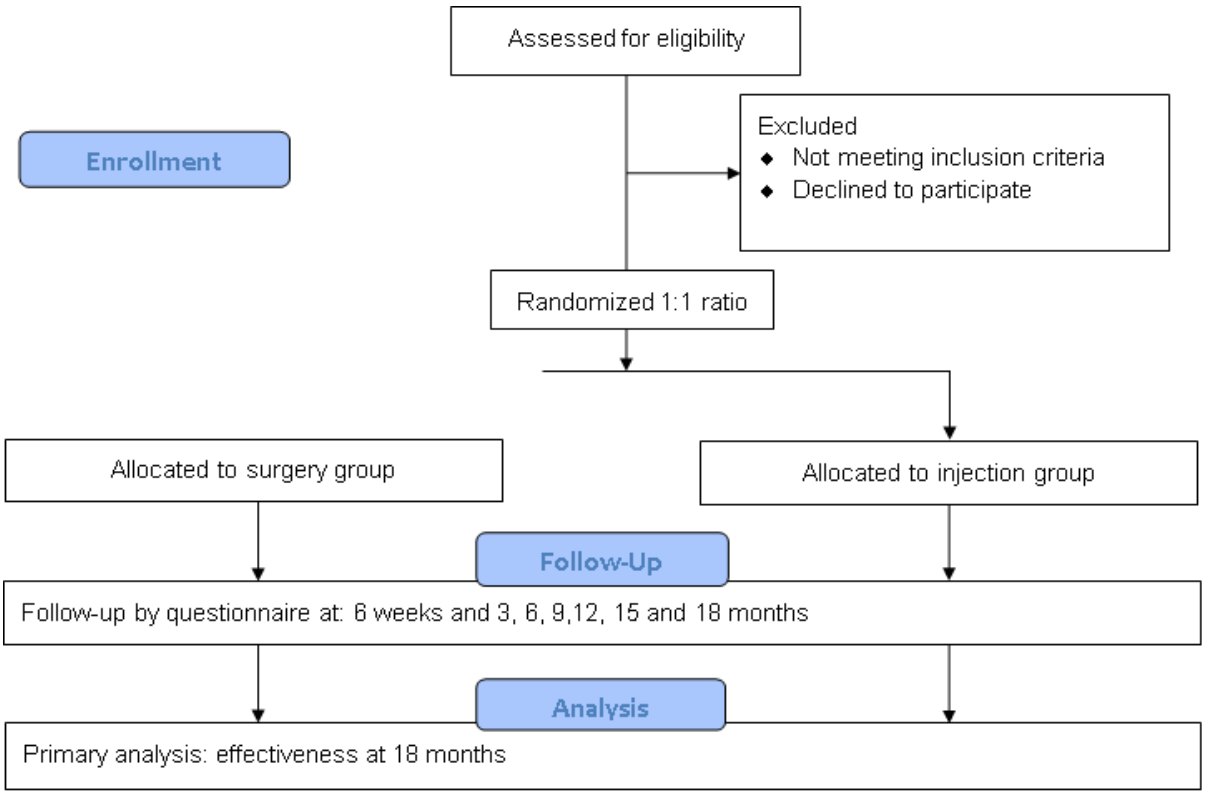
I) adverse events during 18 months follow-up;

J) use of care and health-related costs during 18 months follow-up.

3. STUDY DESIGN

The study is a multicenter open-label randomized controlled trial (Figure 1). The inclusion period will be 18 months. The follow-up of each patient is 18 months from randomization. The approximately 30 participating centers consist of university medical centers, STZ–hospitals (Stichting Topklinische Ziekenhuizen), general hospitals, and ZBC's (Zelfstandig behandelcentra) in the Netherlands.

Figure 1. Study flowchart



Secondary analysis:
- time to recovery
- number of patients recovered at different time points
- level of symptom severity at different time points
- hand functioning at 18 months
- patient's global perception of recovery at 18 months
- patient satisfaction at 18 months
- quality of life at 18 months
- number of additional treatments
- number of adverse events
- use of care and health-related costs

4. STUDY POPULATION

4.1 Population (base)

The overall prevalence of electrophysiologically confirmed CTS in the Netherlands is 9.2% in women and 0.6% in men.[2] General practitioners will refer patients with clinically suspected CTS to one of the at least 30 participating neurological outpatient clinics. All participating hospitals have special outpatient clinics for CTS, each treating more than 400 patients per year. This results in approximately 18,000 potential participants if the inclusion period is 1.5 years (30x400x1.5). We need 940 participants, which is 5.2% of the potential participants.

4.2 Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- 18 years or older at time of examination;
- clinically suspected CTS;
- symptoms being present for at least 6 weeks;
- electrophysiological or sonographic confirmed CTS according to the Dutch 'carpal tunnel syndrome guideline'*;[16]
- treatment within 6 weeks after inclusion;
- the patient can only be included for the treatment of one hand; this will be the hand with the most severe complaints or the dominant hand if both hands are equally affected.

* There is no consensus about findings with sonography in CTS. The current opinion of the DUTCH CTS study group is that a cross-sectional area of more than 11 mm^2 is abnormal and thus confirms a clinical suspicion of CTS. We recommend that the CSA of the wrist is also recorded.

4.3 Exclusion criteria

A subject who meets any of the following criteria will be excluded from participation in this study:

- follow-up not possible;
- history of ipsilateral wrist fracture/trauma/surgery;
- a previous history of injection or surgery for CTS;
- previously participating in the DISTRICTS;
- clinical or neurophysiological suggestion of another diagnosis, like:

  - cervical radiculopathy;
  - cervical myelopathy;
  - brachial plexopathy including thoracic outlet syndrome;
  - mononeuropathies, such as pronator teres syndrome;
  - polyneuropathy, including Hereditary Neuropathy with Liability to Pressure Palsies;
  - complex regional pain syndrome;
- secondary CTS due to a known underlying cause including, but not limited to:
  - thyroid disease;
  - rheumatoid arthritis;
  - diabetes mellitus;
  - dialysis due to kidney failure;
  - space-occupying lesion at the volar side of the wrist;
  - pregnancy;
- known allergy to corticosteroids;
- unable to comprehend Dutch self-report questionnaires;
- legally incompetent adults;
- no informed consent.

4.4 Sample size calculation

To date, there are no reliable data available regarding recovery in case of strategies that may include different treatments. We conservatively estimate that after 18 months 70% of patients in the surgery group and 60% of patients in the injection group are recovered.[10 12] A difference in recovery after 18 months of 10% is considered a minimal clinical important difference. A Fisher's exact test with a 0.05 two-sided significance level will have 80% power to detect the difference between a proportion of 0.70 (recovery after primary surgery) and a proportion of 0.60 (recovery after initial steroid injection) when the sample size in each group is 376 (752 patients in total). Anticipating on a 20% attrition rate, we will include (376 / 0.80 =) 470 patients per treatment group; 940 patients in total.

5. TREATMENT OF SUBJECTS

5.1 Investigational product/treatment

Patients will be randomly assigned to two treatment strategies. One strategy consists of starting with a surgical treatment (surgery group). The other strategy consists of starting with a steroid injection proximal to the carpal tunnel (injection group). If needed, these treatments can be followed by any additional treatments within the 18 months of follow-up such as a second injection or surgical treatment. Independent of the initial treatment performed, patients will receive the usual care at the discretion of their physician.

Surgery group — A certified surgeon or a qualified resident will perform the surgical treatment. As we choose to stay as close as possible to daily practice, participating center will continue to refer patient to their surgeon of choice, whether this be a neurosurgeon, plastic surgeon or other surgeon. Surgeons can use any proven surgical technique for decompression of the carpal tunnel.Surgical treatment will be a decompression of the median nerve at the carpal tunnel. As we aim to compare two intervention strategies, we choose to stay as close to daily practice as possible. This implicates that any proven surgical technique for decompression of the carpal tunnel can be used. In The Netherlands however, most surgeons use the standard open carpal tunnel release. This operation is performed in the ambulatory setting with field sterility and local anesthesia and without the need for an anesthesia provider. A tourniquet can be used. Open carpal tunnel release is performed by making a 2-3 cm long incision in the palm of the hand. The structures overlying the median nerve are divided and the transverse carpal ligament is cut under direct vision. Another, but less commonly used technique is the endoscopic carpal tunnel release. It is performed with one or two small incisions (portals) proximal and/or distal to the carpal tunnel. With aid of a camera, the surgeon obtains indirect access to the bottom surface of the transverse ligament. The ligament is cut from its lower surface with a knife, thus preserving the subcutaneous tissue and the overlying skin.

Injection group — The technique used for injections is as follows: injections will be given with a 3 cm long 0.7 mm needle as described by Dammers.[4] The site of injection will be at the volar side of the forearm 3-4 cm proximal to the wrist crease between the tendons of the radial flexor muscle and the long palmar muscle. In participants with a thin wrist the median nerve is close to the skin. In these participants the angle will be 10°. The angle will be larger, about 20°, in those with a thick wrist. In participants with well-developed muscles, the pronator quadratus muscle may push up the median nerve, so in a thick muscular arm the angle of introduction will also be flat, between 10° and 20°. The needle

is introduced slowly, and the participant will be instructed to say stop if he or she feels pins and needles or pain in the fingers. If a resistance is felt the needle will be withdrawn a few millimeters and then repositioned. The injection can be given without much pressure. After injection, the fluid bolus will be gently massaged towards the carpal tunnel.
The injection contains steroids. Each participating center is free in using their choice of brand and dosage of steroids, with or without local anesthetic.

5.2 Escape medication

The use of analgesics is allowed.

6. NON-INVESTIGATIONAL PRODUCT

6.1 Name and description of non-investigational product(s)

Steroid injections are widely used as treatment in patients with CTS. There are however a wide range of different brands and dosages used. Sometimes, the steroids are combined with a local anesthetic: usually lidocaine. The participating hospitals are not restricted in their choice of brands when using steroid injections. The following are some of the most commonly used steroids: methylprednisolone, betamethasone, hydrocortisone, dexamethasone, prednisolone, triamcinolone acetonide. Please see the Summery of Product Characteristics (SPC) for additional information (appendix 13.2).

6.2 Dosages, dosage modifications and method of administration

Participating centers are free to choose their own brand and dosage of steroids and use of local anesthetic provided. The method of administration is described in chapter 5.1.

6.3 Preparation and labeling of Non Investigational Medicinal Product

Each participating center will be responsible for providing and preparing their own steroid injections. As steroid injections are widely used as treatment for CTS, they are available in all participating clinics.

7. METHODS

7.1 Study parameters/endpoints

7.1.1 Main study parameter/endpoint

There is one main study parameter: number of patients recovered at 18 months after randomization.

Recovery is defined as having no or mild CTS symptoms as measured with the 6-item carpal tunnel symptoms scale (CTS-6).[17] The CTS-6 is a self-report disease-specific questionnaire referring to symptoms for a typical 24-hour period during the past two weeks. The CTS-6 is an abbreviated and validated questionnaire derived from the Boston Carpal Tunnel Syndrome Questionnaire (BCTQ) and highly responsive to change of symptoms.[18] It contains 6 questions about symptoms that patients may experience. Each item is scored 1 (no symptoms) to 5 (most severe symptoms). The summated score ranges from 6 to 30 points. The validated Dutch translation of the BCTQ[19] has been used to compose a Dutch version of the CTS-6 (appendix 13.3).

Recovery at 18 months is defined as scoring less than 8 points on the CTS-6.

Time to recovery is defined as the first time point after the last intervention (*e.g.*, splinting, steroid injection or surgical treatment) with a score of less than 8 points if this time point is followed by a score of less than 8 points at the next time point or if this is the last time point at 18 months. Recovery during follow-up is repeatedly determined at 6 weeks and 3, 6, 9,12, and 15 months after randomization.

7.1.2 Secondary study parameters/endpoints

Secondary outcomes are:

A) time to recovery. Time to recovery is defined as the first time point after the last intervention (*e.g.*, splinting, steroid injection or surgical treatment) with a score of less than 8 points if this time point is followed by a score of less than 8 points at the next time point or if this is the last time point at 18 months. Recovery during follow-up is repeatedly determined at 6 weeks and 3, 6, 9,12, and 15 months after randomization.

B) number of patients recovered at 6 weeks and 3, 6, 9,12, and 15 months after randomization;

C) level of symptoms severity at 6 weeks and 3, 6, 9,12, 15, and 18 months after randomization;

D) hand functioning at 18 months follow-up. The functional status is measured using the QuickDASH (appendix 13.4).[20] The scale measures upper extremity related disability on 11 items. Each item is scored 1 (no disability) to 5 (most severe disability). The summated score ranges from 11 to 55 points. The QuickDASH has been used in patients with CTS; [20]

E) patient's global perception of recovery at 18 months compared to baseline measured with a 7 point Likert-type item ranging from 1 (substantially deteriorated) to 7 (substantially recovered) (appendix 13.5);

F) patient satisfaction at 18 months measured with a 7 point Likert-type item ranging from 1 (very dissatisfied) to 7 (very satisfied) (appendix 13.5);

G) quality of life at 18 months as assessed with the EuroQol (EQ-5D-5L)(appendix 13.6).[21] The EuroQol consists of 5 items on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and all rated on a 5-point scale. Overall health is measured with a 20 cm vertical VAS (with endpoints labeled 'the best health you can imagine' and 'the worst health you can imagine');

H) number of additional treatments defined as every treatment initiated by the treating physician after initial treatment, such as but not limited to steroid injections, (re)surgery and splints (appendix 13.7) . Additional undergone treatments are determined at 6 weeks and 3, 6, 9,12,15, and 18 months;

I) adverse events defined as the number, nature, severity, duration and frequency of any adverse event throughout the course of the study (appendix 13.8) . Adverse events are determined at 6 weeks and 3, 6, 9,12,15, and 18 months;

J) use of care and health-related costs during follow-up, as assessed with the adapted Medical Consumption Questionnaire and the Productivity Cost Questionnaire (appendix 13.9). Data will be collected at 3, 6, 12 and 18 months.

7.2 Randomization, blinding and treatment allocation

Patients will be randomized by the local clinician using a centralized web-based application (ALEA). Eligible patients will be randomized in a 1:1 ratio to the initial surgical treatment (surgery group) or the initial steroid injection (injection group). Patients will be stratified for uni- or bilateral CTS symptoms. As this is an open label study, there is no need for predefined randomization breaking rules. The local clinician receives an email with the outcome of the randomization.

7.3 Study procedures

After signing informed consent the baseline characteristics are documented and verified by the local clinician or other authorized personnel. The following baseline characteristics will be recorded:

- sex;
- year of birth;
- dominant hand;
- symptoms, in terms of
  - a sensation of pins and needles with or without pain, and numbness in median nerve innervated area of the hand
  - above mentioned complaints at night, which wake the patient
  - increased or decreased symptoms during certain hand or wrist movements;
- duration of symptoms;
- most affected hand;
- results of physical examination;
- outcome of the electrophysiological investigation or the sonography;
- symptom severity (CTS-6 score);
- hand functioning (QuickDASH);
- quality of life;
- weight and length;
- contact information;
- type of outpatient clinic.

After baseline assessment patients will be randomized to treatment strategy starting with surgical treatment (surgery group) or the treatment strategy starting with steroid injection (injection group). Only one hand can be included in the trial. The hand with the most severe complaints will be included if a patient has bilateral CTS. If both hands have equally severe symptoms the dominant hand is included. The not included hand may receive treatment at the local clinicians discretion.

Follow-up consists of completing paper based self-report questionnaires, which have to be completed 6 weeks, and 3, 6, 9,12,15, and 18 months after randomization. For an overview of the questionnaires and the time points please see the assessment schedule (appendix 13.10).

Paper questionnaires are sent 1 week before the upcoming follow-up time point. If the questionnaire is not returned 2 weeks after initial sending a reminder and a new questionnaire will be sent. If there is no response 1 week after de reminder the patient will be called by telephone. Trained trial personnel will contact the patient and assess the

reason for not returning the questionnaire and ask if the patient would be willing to continue the follow-up assessments. If the patient agrees the questionnaire will be completed by telephone. If the patient does not want to participate the reason for drop-out will be registered. In case telephone contact cannot be established a questionnaire will be sent at the next follow-up time point.

7.4 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons.

7.5 Replacement of individual subjects after withdrawal

Subjects will not be replaced after withdrawal. An attrition rate of around 20% is anticipated.

7.6 Follow-up of subjects withdrawn from treatment

Subjects withdrawn from treatment will receive usual care.

7.7 Premature termination of the study

Reasons for premature termination of the study are not specified.

8. SAFETY REPORTING

8.1 Temporary halt for reasons of subject safety

In accordance to section 10, subsection 4, of the WMO, the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardize subject health or safety. The sponsor will notify the accredited METC without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the accredited METC. The investigator will take care that all subjects are kept informed.

8.2 AEs and SAEs

8.2.1 Adverse events (AEs)

Adverse events are defined as any undesirable experience occurring to a subject during the study, whether or not considered related to the trial procedure. All adverse events reported spontaneously by the subject or observed by the investigator or his staff will be recorded.

8.2.2 Serious adverse events (SAEs)

A SAE is any untoward medical occurrence or effect that

- results in death;
- is life threatening (at the time of the event);
- requires hospitalization or prolongation of existing inpatients' hospitalization;
- results in persistent or significant disability or incapacity;
- is a congenital anomaly or birth defect;
- any other important medical event that did not result in any of the outcomes listed above due to medical or surgical treatment but could have been based upon appropriate judgement by the investigator.

An elective hospital admission will not be considered as a serious adverse event.

The local investigator will report all SAEs in the patients Case Report Form (CRF). The principal investigator will report all SAEs to the sponsor and to the accredited METC that approved the protocol. As both surgical treatment and steroid injection are proven and relative safe therapies the SAEs will be reported annually through line listing.

8.3 Follow-up of adverse events

All AEs will be followed until they have abated or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures as indicated, and/or referral to the general physician or a medical specialist.
SAEs need to be reported till end of study within The Netherlands, as defined in the protocol

8.4 Data Safety Monitoring Board

Since this open label trail consist of two routine treatments applied in regular daily practice and participation in this study does not contain additional risks for the patient, we consider this trial as a low risk study. Therefore, no DSMB will be established.

9. STATISTICAL ANALYSIS

Statistical analyses will be based on the intention-to-treat principle. Baseline assessments and outcome parameters will be summarized using simple descriptive statistics. Continuous, normally distributed variables will be expressed as means and standard deviations; continuous, non-normally distributed and ordinal variables as medians (25th – 75th percentiles), and categorical variables as counts and percentages. Normality of data will be explored by a Normal Q-Q Plot and tested by the Shapiro-Wilk test. Outcome data on the 7-point Likert-type items (perceived recovery, patient satisfaction) will be considered ordinal. Where necessary we will use multiple imputations for handling missing data. In all analyses statistical uncertainty will be expressed in two-sided 95% confidence intervals. A two-sided p value less than 0.05 is considered statistically significant. We will not correct for multiple testing.

9.1 Primary study parameters

The difference in the proportion of patients (based on the CTS-6 cut-off score) recovered at 18 months will be analyzed using Fisher's exact test. In addition, logistic regression will be performed including treatment groups and the stratification variable (uni- or bilateral CTS symptoms) as independent variables. The effect size will be expressed in an adjusted odds ratio. The difference in time to recovery, the second primary outcome, between the treatment groups will be analyzed by plotting Kaplan-Meier curves and comparing them using the log-rank test. In addition, we will compare the treatment groups using Cox proportional hazards regression, with adjustment for the stratification variable. The effect size will be expressed in an adjusted hazard ratio.

9.2 Secondary study parameters

The difference in time to recovery between the treatment groups will be analyzed by plotting Kaplan-Meier curves and comparing them using the log-rank test. Hence, the analysis will deal correctly with potentially censored data. The differences in the proportions of patients recovered at the different time points during follow-up (6 weeks, 3, 6, 9, 12, and 15 months), requiring additional treatment and experiencing adverse events during 18 months follow-up will be analyzed using Fisher's exact test. Differences in symptom severity scores (full scoring range of the CTS-6) between the treatment groups and over all time points will be analyzed using a linear mixed model with treatment group membership as a fixed-effect and an appropriate random-effect structure. The perceived recovery scores and patient satisfaction scores at 18 months will be compared with the Mann-Whitney test. Differences in the mean changes in hand functioning (QuickDASH)

and overall level of quality of life (Euroqol-VAS) from baseline to 18 months will be analyzed using the two-sample t-test. In addition, we will analyze these treatment effects by performing multivariable linear regression with 18-month observations as the dependent variable, and treatment groups, the baseline values and the stratification variable as the independent variable.

9.3 Sensitivity analysis

We will perform a separate sensitivity analysis to evaluate whether the primary treatment effect (recovery at 18 months) changes if the definition of recovery is adapted. In this sensitivity analysis, a patient will be classified as having recovered if he or she scores less than nine points on the total CTS-6 and fewer than three points on any individual item of the CTS-6.

9.4 Cost effectiveness analysis (CEA)

We hypothesize that a treatment strategy starting with a surgical treatment in CTS patients will improve patient management and patient recovery, as defined. To assess the benefits and harms of both treatment strategies (*e.g.*, surgical treatment vs steroid injection) a prospective economic evaluation will be set up alongside the proposed RCT, providing insight in the cumulative health care costs associated with 18 months follow-up. All important health care costs will be related to the improvement in recovery within the follow-up time from a societal perspective.

9.4.1 Cost-analysis

Cost categories and overall costs will be compared between both intervention groups and where relevant, differences will be calculated, inclusive of 95% confidence intervals. The economic evaluation will be set-up as a cost-effectiveness analysis (CEA) using the primary outcome measure (recovery as defined) and a cost-utility analysis (CUA), with the costs per quality-adjusted life year (QALY) as the outcome. Utility will be measured using QALY values, derived from the EuroQol EQ-5D-5L. The time-horizon will be limited to the medium-term (*i.e.*, 18 months) and long-term (4 years in concordance with the BIA) study follow-up. Considering the time horizon discounting of costs (4%) and effects will be performed.

Additional costs as a result of comorbid conditions and protocol driven costs will be excluded. Costs will be expressed for the base year 2019. Unit costs from different calendar years will be indexed with general yearly consumer price indices.

9.4.2 Measurement

Cost-calculations will be set up to reflect a health service and a societal perspective and will be based on process components and actual resource use in routine practice during the study period considering surgical treatment and steroid injection (*e.g.*, hospital visits (surgery, steroid injections), outpatients visits, diagnostics examinations (EMG, sonography), additional drugs, additional treatment, rehabilitation, day-care treatment, and possible treatment of complications). Data on resources used are directly collected from the hospital information system, hospital databases, CRF's, patient files and (if applicable) financial reports. In addition, we will monitor the use of health care resources by the Medical Consumption Questionnaire (iMCQ) tailored to CTS patients. The adapted version of the iMCQ will be used to measure the volume of for example out-of-hospital consultations such as general physician and physiotherapist. Time off work and presenteeism will be obtained from the Productivity Cost Questionnaire (iPCQ). [22] The friction cost method will be applied to value the production losses in line with the Dutch costing guidelines. [23] Data will be collected at 3, 6, 12, and 18 months.

9.4.3 Unit costs

Both direct and indirect costs are included. Direct medical costs (net expenditure of health care resources) are defined as the volumes of health care resource utilization multiplied by calculated unit prices. Indirect costs include the opportunity costs (time spent receiving medical care) and the costs of productivity loss (iPCQ) and out-of-pocket expenses (iMCQ). All registered volumes within the participating centers will be valued according to standard current Dutch costing guidelines and market prices. [23] Deterministic and probabilistic sensitivity analysis will be used to explore uncertainty of key parameters.

9.4.4 Statistical analysis

Differences between the interventions will be statistically evaluated with bias-corrected bootstrap analysis.[24] Scenario-analysis will be performed to extrapolate the consequences of implementation and concrete performance of both interventions in the pointed population. The validity of the developed scenarios will be studied in a sensitivity analysis varying cost estimates and probabilities.

9.5 Budget impact analysis (BIA)

To assess the economic impact of the initial use of surgical treatment instead of steroid injection to achieve better recovery, we will extrapolate the outcomes of the economic evaluation in The Netherlands. Therefore a Budget Impact Analysis will be designed and executed in accordance with the ISPOR guidelines.[25] The analyses will be patient based, covering relevant health care costs observed during the 18 months follow-up period. The BIA will mainly estimate the annual financial impact from a governmental, health care provider and insurer perspective on the mid and long-term (up to four calendar years). The analysis will inform the health care decision makers responsible for the national budget. This will be based on data that reflect the size and characteristics of the CTS population, the effectiveness of both interventions, the related resource use and associated medical costs (based on charges). Implementation and budget-impact are anticipated to change over time. Where possible the deterministic sensitivity analyses will be based on 95% CI estimated for each differentiating input parameter (*e.g.*, unit costs, type of unit costs, recovery, re-interventions).

10. ETHICAL CONSIDERATIONS

10.1 Regulation statement

The DISTRICTS will be conducted according to the principles of the Declaration of Helsinki (version of 2013) and in accordance with WMO and other guidelines, regulations and Acts. Study monitoring and data management, will be performed in accordance with the International Conference on Harmonisation- Good Clinical Practice (GCP) guidelines. Randomization based on a centralized web-based application (ALEA) will be developed by the Academic Medical Center's Clinical Research Unit (CRU).

The Investigator will permit independent monitoring. Monitors will have access to all (electronic) CRF's and subject' medical records which are relevant to this trial. The purpose of monitoring is to oversee the progress of the clinical trial and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures, GCP-guidelines and the applicable regulatory requirements.

The approval of the ethics committees of the participating centers will be sought. The patients will receive written information about the study and they need to give their written informed consent. Before the start of the study, it will be registered at a trial register (http://www.controlled -trails.com; ISRCTN Register).

10.2 Recruitment and consent

Patient will be recruited both from the regular neurology outpatient clinics and from the specialized carpal tunnel outpatient clinics.

Patients from the regular neurology outpatient clinics with a clinical suspect CTS are verbally informed by their local clinician about the trial. Potential candidates receive an information letter from their local clinician about the trial, which they can read at home. After assessment with EMG and/or sonography, the local clinician evaluates a patient for eligibility, by checking the in- and exclusion criteria of the trial. Then he will verify if the patient is fully informed about the trial and will discuss enrolment in the study with the patient. The patient is given the opportunity to think over enrolment and ask questions. Then the local clinician will ask the patient to participate in the study. If the patient wants to participate he is asked to sign the informed consent form.

Patients form the specialized carpal tunnel outpatient clinics will be informed about potential enrolment in the trial with an information letter before their appointment. This is send to them along with their appointment information. They will also receive a questionnaire with basic questions about their characteristics and condition. After assessment with EMG and/or sonography the course is similar to that of the regular neurology outpatients as described above.

10.3 Benefits and risks assessment, group relatedness

Although surgery is considered more effective than steroid injections, most neurologists initiate treatment with steroid injections because they consider this easier applicable and safer. Because steroid injections may not so effective, especially regarding long-term effects, this strategy may only result in postponement of a more effective treatment, that is, a surgical treatment, and lead to unnecessary health loss and work absenteeism. Surgical treatment and steroid injection are proven, much used, low risk treatments. Patients will not be submitted to additional risks, only to the burden of follow-up self-report questionnaires.

10.4 Compensation for injury

The sponsor/investigator has received dispensation from the METC for the statutory obligation to provide additional insurance, because participating in the study is without additional risks.

11. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

11.1 Handling and storage of data and documents

The investigator will set up a Trial Master File at the beginning of the study. The list of essential documents will be in accordance with the GCP-guidelines. The essential documents that make up the file will be stored in a secure but accessible manner. All essential documents will be legible and accurate. The participating centers will keep copies of relevant documents, including essential center-specific documents.
For each randomized patient a paper case record form (CRF) will be completed and stored at the participating center. The CRF consists of a sequential set of instructions with provision for data recording. All randomized patients are identified by a Patient Identification Number (PIN) in combination with a center number. The local investigator will ensure that patients' anonymity is maintained. Paper CRFs and baseline self-report paper questionnaire will only be identified by a PIN in combination with a center number. The subject identification code list will be safeguarded by the local investigator. The paper CRF and baseline self-report paper questionnaire will be transferred to the electronic CRF (eCRF) which will be built in OpenClinica (GCP-proof application).

The patients' contact information is collected separately at the participating center and sent either by fax or email to the AMC. Patients' contact information is collected and stored in LDOT, which is a secure web-based tool designed to monitor the study logistics (GCP-proof application). The follow-up self-report paper questionnaires will be sent from the AMC to the patients. Follow-up self-report questionnaires will only be identified by a PIN in combination with a center number. After completion patients will return the questionnaires by mail and these will be added to the eCRF.

11.2 Monitoring and Quality Assurance

Academic Medical Center's CRU will provide independent monitoring.

11.3 Amendments

Amendments are changes made to the research after a favorable opinion by the accredited Academic Medical Center's METC has been given. All amendments will be notified to the Academic Medical Center's METC that gave a favorable opinion.

All substantial amendments will be notified to the METC and to the competent authority.

Non-substantial amendments will not be notified to the accredited METC and the competent authority, but will be recorded and filed by the sponsor.
Only substantial amendments that might change the willingness or risk of the subjects will result in a correction of the patient information and or informed consent form.

11.4 Annual progress report

The sponsor/investigator will submit a summary of the progress of the trial to the accredited METC once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial, serious adverse events/ serious adverse reactions, other problems, and amendments.

11.5 Temporary halt and (prematurely) end of study report

The investigator/sponsor will notify the accredited METC of the end of the study within a period of 8 weeks. The end of the study is when the last patient completes the last survey. The sponsor will notify the METC immediately of a temporary halt of the study, including the reason of such an action. In case the study is ended prematurely, the sponsor will notify the accredited METC within 15 days, including the reasons for the premature termination. Within one year after the end of the study, the investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited METC.

11.6 Public disclosure and publication policy

The authors aim to publish the results in high-impact peer-to-peer reviewed journals.

12. STRUCTURED RISK ANALYSIS

Both surgical treatments as well as steroid injections for the treatment of CTS have been widely used treatments, which are not innovative and low complex. Therefore patients will not be exposed to additional risks. The exclusion criteria, which include diseases that can mimic carpal tunnel syndrome, prevent patient from being submitted to unnecessary treatments. To summarize, the risk of this trial is considered negligible.

13. APPENDICES

13.1 Participating Centers and investigators on site

Academisch Medisch Centrum	Dr. C. Verhamme
Alrijne Ziekenhuis	Dr. E.L.L.M. de Schryver
Canisius-Wilhelmina Ziekenhuis	Dr. W.I.M. Verhagen
Catharina Ziekenhuis	Dr. B.F.L. van Nuenen
Elisabeth-TweeSteden Ziekenhuis	Prof. dr. L.H. Visser
Elkerliek Ziekenhuis	Dr. R. van Koningsveld
Haaglanden Medisch Centrum	Dr. K. Jellema
Maasstad Ziekenhuis	Drs. J. P. A. Samijn
Medisch Centrum Leeuwarden	Dr. F.G. van Rooij
OLVG Amsterdam	Dr. J. Visser
Radboud Universitair Medisch Centrum	Drs. J. Wijntjes
Rijnstate	Dr. E. Verstraete
SJG Weert	Drs. T.W.H. Alleman
St Antonius Ziekenhuis	Dr. O.J.M. Vogels
The Hand Clinic	Prof. dr. M.J.P.F. Ritt
Zaans Medisch Centrum	Drs. J. Citroen
Ziekenhuis St Jansdal	Dr. S.W. de Jong
Zuyderland Medisch Centrum	Dr. R. Beekman

13.2 Summary of Product Characteristics (SPC)

The SPCs of the following injectable steroids: methylprednisolone, betamethasone, hydrocortisone, dexamethasone, prednisolone, triamcinolone acetonide, are attached to this application in Adobe pdf format and is also available online on the site of the College ter Beoordeling van Geneesmiddelen (Medicines Evaluation Board) through the following link: http://www.cbg-meb.nl/

13.3 De 6-punts CTS symptoom schaal

De volgende vragen hebben betrekking op uw klachten die u gedurende een gebruikelijke dag en nacht ervaren heeft in de afgelopen twee weken (kruis eén vakje aan per klacht)

Hoe ernstig zijn de volgende klachten van uw hand?	Geen	Licht	Matig	Ernstig	Zeer ernstig
Pijn gedurende de nacht					
Pijn gedurende de dag					
Verdoofd gevoel of de tintelingen gedurende de nacht					
Verdoofd gevoel of de tintelingen gedurende de dag					

Hoe vaak werd u gedurende de nacht wakker door de volgende klachten in uw hand?	Nooit	Eenmalig	2 of 3 keer	4 of 5 keer	Meer dan 5 keer
Pijn					
Verdoofd gevoel of tintelingen					

13.4 QuickDASH

QUICKDASH-DLV

Beoordeel wat uw mogelijkheden zijn geweest om de volgende activiteiten te verrichten in de afgelopen week door het meest passende cijfer hieronder te omcirkelen.

		GEEN PROBLEEM	GERING PROBLEEM	PROBLEEM	ERNSTIG PROBLEEM	NIET MOGELIJK
1	Openen van een vastgedraaide pot.	1	2	3	4	5
2	Zwaar huishoudelijk werk verrichten (bv. stofzuigen en/of vloeren soppen).	1	2	3	4	5
3	Boodschappentas of aktetas dragen.	1	2	3	4	5
4	Rug wassen.	1	2	3	4	5
5	Een mes gebruiken om eten te snijden.	1	2	3	4	5
6	Vrijetijdsbesteding waarbij enige kracht of belasting uitgeoefend wordt op de arm, schouder of hand (golfen, doe het zelf, tennissen, etc.).	1	2	3	4	5

		GEEN PROBLEEM	GERING PROBLEEM	PROBLEEM	ERNSTIG PROBLEEM	NIET MOGELIJK
7	In hoeverre heeft uw arm, schouder of hand, problemen gegeven met de normale sociale activiteiten met familie, vrienden, buren of groepen in de afgelopen week? (omcirkel het cijfer)	1	2	3	4	5

		Absoluut niet beperkt	Enigszins beperkt	Matig beperkt	Veel beperkt	Onmogelijk
8	In hoeverre bent u beperkt geweest in uw werk of andere dagelijkse activiteiten ten gevolge van uw arm, schouder of hand probleem, gedurende de afgelopen week? (omcirkel het cijfer)	1	2	3	4	5

Geef de ernst van de onderstaande klachten aan gedurende de afgelopen week. (omcirkel het cijfer)

		GEEN	MILD	MATIG	ERNSTIG	EXTREEM
9	Pijn in uw arm, schouder of hand.	1	2	3	4	5
10	Tintelingen (spelden prikken) in arm, schouder of hand.	1	2	3	4	5

		GEEN PROBLEEM	GERING PROBLEEM	MATIG PROBLEEM	ERNSTIG PROBLEEM	IK KAN ER NIET VAN SLAPEN
11	Hoeveel moeite heeft u gehad met slapen ten gevolge van pijn in uw arm, schouder of hand, gedurende de afgelopen week? (omcirkel het cijfer)	1	2	3	4	5

13.5 Patient's perceived recovery and satisfaction

In de afgelopen 18 maanden bent u behandeld voor uw hand/pols klachten.
Er volgen nu twee vragen die gaan over het eindresultaat van deze behandeling(en).

Als u uw huidige klachten van uw hand/pols vergelijkt met uw klachten voorafgaande aan de behandeling(en), hoe beoordeelt u dan uw huidige klachten?
(Omcirkel het desbetreffende nummer)

Ten opzichte van vóór de behandeling(en) zijn mijn klachten nu:

1. veel erger geworden
2. erger geworden
3. een beetje erger geworden
4. niet verbeterd / niet erger geworden
5. een beetje verbeterd
6. verbeterd
7. sterk verbeterd

Hoe tevreden bent u nu over het resultaat van uw behandeling(en)?

1. zeer ontevreden
2. ontevreden
3. een beetje ontevreden
4. niet tevreden / niet ontevreden
5. een beetje tevreden
6. tevreden
7. zeer tevreden

13.6 EuroQol (EQ-5D-5L)

Zet bij iedere groep in de lijst hieronder een kruisje in het hokje dat het best past bij uw gezondheid VANDAAG.

MOBILITEIT

Ik heb geen problemen met lopen ❑
Ik heb een beetje problemen met lopen ❑
Ik heb matige problemen met lopen ❑
Ik heb ernstige problemen met lopen ❑
Ik ben niet in staat om te lopen ❑

ZELFZORG

Ik heb geen problemen met mijzelf wassen of aankleden ❑
Ik heb een beetje problemen met mijzelf wassen of aankleden ❑
Ik heb matige problemen met mijzelf wassen of aankleden ❑
Ik heb ernstige problemen met mijzelf wassen of aankleden ❑
Ik ben niet in staat mijzelf te wassen of aan te kleden ❑

DAGELIJKSE ACTIVITEITEN *(bijv. werk, studie, huishouden, gezins- en vrijetijdsactiviteiten)*

Ik heb geen problemen met mijn dagelijkse activiteiten ❑
Ik heb een beetje problemen met mijn dagelijkse activiteiten ❑
Ik heb matige problemen met mijn dagelijkse activiteiten ❑
Ik heb ernstige problemen met mijn dagelijkse activiteiten ❑
Ik ben niet in staat mijn dagelijkse activiteiten uit te voeren ❑

PIJN/ONGEMAK

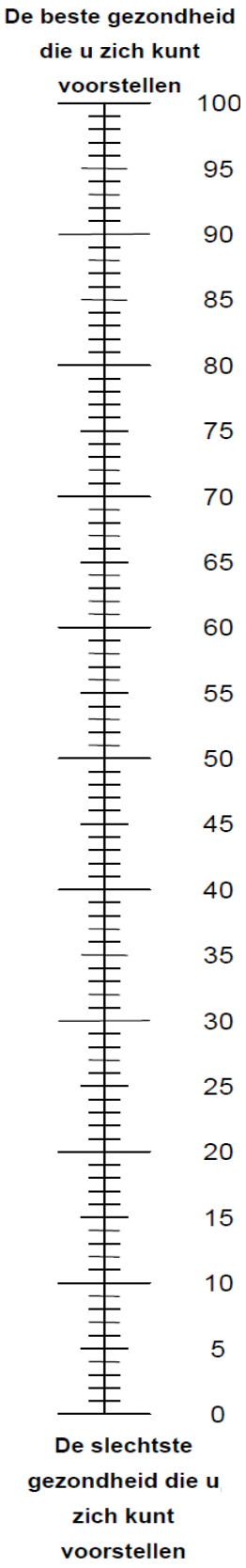
Ik heb geen pijn of ongemak ❑
Ik heb een beetje pijn of ongemak ❑
Ik heb matige pijn of ongemak ❑
Ik heb ernstige pijn of ongemak ❑
Ik heb extreme pijn of ongemak ❑

ANGST/SOMBERHEID

Ik ben niet angstig of somber ❑
Ik ben een beetje angstig of somber ❑
Ik ben matig angstig of somber ❑
Ik ben erg angstig of somber ❑
Ik ben extreem angstig of somber ❑

- We willen weten hoe goed of slecht uw gezondheid VANDAAG is.
- Deze meetschaal loopt van 0 tot 100.
- 100 staat voor de beste gezondheid die u zich kunt voorstellen.
  0 staat voor de slechtste gezondheid die u zich kunt voorstellen.
- Markeer een X op de meetschaal om aan te geven hoe uw gezondheid VANDAAG is.
- Noteer het getal waarbij u de X heeft geplaatst in onderstaand vakje.

UW GEZONDHEID VANDAAG = ☐



13.7 Additional treatments questionnaire

Heeft u sinds het vorige meet moment nog nieuwe behandelingen gehad voor uw hand/pols klachten?
(De injectie of operatie aan het begin van het onderzoek telt niet mee)
(Meerdere opties mogen aangekruist worden. Indien u meerdere dezelfde behandelingen heeft gehad, graag het aantal keer achter de behandeling zetten)

☐ geen nieuwe behandeling

☐ injectie ..... keer

☐ operatie ..... keer

☐ handspalk ..... keer

☐ fysio/ergotherapie ..... keer

☐ overige, welke? .... keer

Heeft u sinds het vorige meet moment nog nieuwe onderzoeken gehad voor uw hand/pols klachten?
(Meerdere opties mogen aangekruist worden. Indien u meerdere dezelfde onderzoeken heeft gehad, graag het aantal keer achter de behandeling zetten)

☐ geen nieuw onderzoek

☐ zenuwgeleidings- en/of spieronderzoek (EMG) ..... keer

☐ onderzoek met geluidsgolven (echografie) ..... keer

☐ beeldvorming (MRI of CT scan) ..... keer

☐ wel nieuw onderzoek, onbekend welke ..... keer

☐ overige, welke? .... keer

13.8 Adverse events questionnaire

Heeft u sinds het vorige meet moment nog nieuwe behandelingen gehad voor uw hand/pols klachten?
(De injectie of operatie aan het begin van het onderzoek telt niet mee)
(Meerdere opties mogen aangekruist worden. Indien u meerdere dezelfde behandelingen heeft gehad, graag het aantal keer achter de behandeling zetten)

☐ geen nieuwe behandeling

☐ injectie ..... keer

☐ operatie ..... keer

☐ handspalk ..... keer

☐ fysio/ergotherapie ..... keer

☐ overige, welke? .... keer

Heeft u in de afgelopen 3 maanden weleens in het ziekenhuis gelegen vanwege gezondheidsklachten als gevolg van het carpaletunnelsyndroom?
(U moest dus blijven slapen. Bijvoorbeeld omdat u geopereerd was en niet direct naar huis kon)

☐ Nee

☐ Ja, in totaal │__│__│ verpleegdagen

1. In welk ziekenhuis?.....
2. In welk ziekenhuis?.....
3. In welk ziekenhuis?.....

Met de onderstaande vragen willen we te weten komen of er <u>sinds het vorige meetmoment</u> nieuwe gezondheidsklachten zijn ontstaan.
(Het gaat om klachten aan de hand/pols waarmee u meedoet aan het onderzoek)
*(het gaat hierbij **niet** om de bekende klachten die bij uw carpaletunnelsyndroom horen)*

Heeft u:	Ja	Nee
nieuwe pijnklachten hand/pols/litteken	☐	☐
nieuw veranderd gevoel in hand	☐	☐
nieuwe verminderde kracht in hand	☐	☐
nieuwe verminderde vaardigheid hand	☐	☐
wond/huid probleem waarvoor extra behandeling nodig was	☐	☐

De volgende vragen gaan over klachten van de algemene gezondheid:

Heeft er in de afgelopen 3 maanden een nadelige gebeurtenis ten aanzien van uw algemene gezondheid plaatsgevonden?

☐ Nee

☐ Ja, namelijk

Nadelige gebeurtenis 1: .....
Nadelige gebeurtenis 2: .....
Nadelige gebeurtenis 3: .....

Heeft u in de afgelopen 3 maanden een arts geraadpleegd vanwege een nadelige gebeurtenis ten aanzien van uw algemene gezondheid?

☐ Nee

☐ Ja, namelijk *(noteer naam en specialisme)*

Arts 1: .....
Arts 2: .....
Arts 3: .....

Heeft u een behandeling moeten ondergaan vanwege deze nadelige gebeurtenis ten aanzien van uw algehele gezondheid?

☐ Niet van toepassing

☐ Nee

☐ Ja, namelijk

Behandeling 1: ..... |__|__| keer
Behandeling 2: ..... |__|__| keer
Behandeling 3: ..... |__|__| keer

Bent u hersteld van de nadelige gebeurtenis ten aanzien van uw algemene gezondheid?

☐ Niet van toepassing

☐ Nee

☐ Gedeeltelijk

☐ Ja

Bent u opgenomen geweest in het ziekenhuis vanwege de nadelige gebeurtenis ten aanzien van uw algemene gezondheid?
(indien het een spoedopname betreft graag dit aankruisen)

☐ Niet van toepassing

☐ Nee

☐ Ja, in totaal |__|__| verpleegdagen

In welk ziekenhuis?.....□ spoedopname

In welk ziekenhuis?.....□ spoedopname

In welk ziekenhuis?.....□ spoedopname

Is er volgens u een verband tussen de doorgemaakte nadelige gebeurtenis ten aanzien van uw algemene gezondheid en de behandeling die u heeft gehad in verband met uw hand/pols klachten?

☐ Niet van toepassing

☐ Nee

☐ Mogelijk

☐ Ja

13.9 Care Use

Vraag 14: Wat doet u in het dagelijkse leven?
(Kruis aan wat u de meeste tijd doet.)
□ Ik zit op school, ik studeer

□ Ik werk in loondienst

□ Ik ben zelfstandig ondernemer

□ Ik ben huisvrouw, huisman

□ Ik ben werkloos

□ Ik ben arbeidsongeschikt voor |__|__|__| %

□ Ik ben met pensioen of prepensioen

□ Ik doe iets anders, namelijk……..

Vraag 15: Hebt u nu betaald werk?
(in de ziektewet zijn geldt ook als betaald werk)
□ Nee (*Ga verder met vraag 25*)

□ Ja, we vragen naar uw eigen netto inkomen uit betaald werk.

LET OP: het gaan alleen om uw eigen inkomen, dus zonder dat van uw eventuele partner. U hoeft dus maar een van de volgende mogelijkheden in te vullen. Ga daarna door naar vraag 16.

☐ Mijn eigen netto inkomen uit betaald werk is ongeveer:
…….. Euro per week
…….. Euro per 4 weken
…….. Euro per maand
…….. Euro per jaar
☐ Ik weet mijn inkomen niet of wil het liever niet zeggen.

Vraag 16. Wat is uw beroep?
……

Vraag 17: Hoeveel uur per week werkt u? |__|__| uren per week
(Tel alleen de uren waarvoor u betaald wordt)

Vraag 18: Op hoeveel dagen in de week werkt u? Op |__|__| dagen per week

Vraag 19: Bent u in de afgelopen 4 weken afwezig geweest van uw werk vanwege gezondheidsklachten door het carpaletunnelsyndroom?
□ Nee (*ga verder met vraag 22*)

□ Ja, ik ben |__|__| dagen afwezig geweest
(Tel alleen de <u>werkdagen</u> in de afgelopen 4 weken)

Vraag 20: Was u langer dan de gehele periode van 4 weken afwezig van uw werk ten gevolge van gezondheidsklachten door het carpaletunnelsyndroom?
(*Het gaat om een aaneengesloten periode van werkverzuim)*
□ Nee (*ga verder met vraag 22*)

□ Ja (*ga verder met vraag 21*)

Vraag 21. Wanneer heeft u zich ziek gemeld?

|__|__| |__|__| |__|__|__|__|
d d m m j j j j

Vraag 22: Waren er in de afgelopen 4 weken dagen waarop u wel gewerkt heeft, maar tijdens uw werk last had van gezondheidsklachten door het carpaletunnelsyndroom?
□ Nee (*ga verder met vraag 25*)

□ Ja (*ga verder met vraag 23 en 24*)

Vraag 23: Op hoeveel dagen had u tijdens uw werk last van gezondheidsklachten door het carpaletunnelsyndroom*?*
(Tel alleen de werkdagen in de afgelopen 4 weken)
|__|__| werkdagen

Vraag 24: Op de dagen dat u last had kon u misschien niet zoveel werk doen als normaal. Hoeveel werk kon u op deze dagen gemiddeld doen?
(*Kijk naar de cijfers hieronder. Een 10 betekent dat u op deze dagen net zoveel kon doen als normaal. Een 0 betekent dat u op deze dagen niets kon doen. Zet een cirkel om het goede cijfer)*

Ik kon op deze dagen niets doen	Ik kon ongeveer de helft doen	Ik kon net zoveel doen als normaal

0 1 2 3 4 5 6 7 8 9 10

Vraag 25: Waren er dagen waarop u minder onbetaald werk kon doen vanwege gezondheidsklachten door het carpaletunnelsyndroom?
(*Het gaat om dagen in de afgelopen 4 weken)*
□ Nee (*ga verder met vraag 28*)

□ Ja (*ga verder met vraag 26 en 27*)

Vraag 26: Op hoeveel dagen was dit zo?
(*Tel alleen de dagen in de afgelopen 4 weken)*
|__|__| dagen

Vraag 27: Stel dat iemand, bijvoorbeeld uw partner, familielid of een bekende, u op deze dagen had geholpen. En al het onbetaalde werk wat u niet kon doen, voor u had gedaan. Hoeveel uur was die persoon hier op deze dagen dan gemiddeld mee bezig geweest?
Gemiddeld |__|__| uur op deze dagen

Vraag 28: Heeft u in de afgelopen 3 maanden één of meer van de volgende artsen of therapeuten bezocht als gevolg van het carpaletunnelsyndroom?

Huisarts	□	nee	□	ja,	|__|__| afspraken
Chirurg	□	nee	□	ja,	|__|__| afspraken
Neuroloog	□	nee	□	ja,	|__|__| afspraken
Fysiotherapeut	□	nee	□	ja,	|__|__| afspraken
Ergotherapeut	□	nee	□	ja,	|__|__| afspraken
Bedrijfsarts	□	nee	□	ja,	|__|__| afspraken
Anders, namelijk .....□		nee	□	ja,	|__|__| afspraken

Vraag 29: Heeft u de afgelopen 3 maanden vanwege klachten als gevolg van het carpaletunnelsyndroom gebruik gemaakt van betaalde thuiszorg of van onbetaalde hulp van familie, vrienden, buren of vrijwilligers?
(meer dan 1 antwoord mogelijk)
(Tel alle weken in de afgelopen 3 maanden bij elkaar op. Let op: een periode van 3 maanden telt 13 weken)
□ Nee

□Thuiszorg, hulp in de huishouding |__|__| weken |__|__| uren per week

□Thuiszorg, hulp bij persoonlijke verzorging |__|__| weken |__|__| uren per week

□Thuiszorg, verpleegkundige hulp |__|__| weken |__|__| uren per week

□Onbetaalde hulp van familie / vrienden / buren / vrijwilliger
|__|__| weken |__|__| uren per week

Vraag 30: Heeft u in de afgelopen 3 maanden vanwege gezondheidsklachten als gevolg van het carpaletunnelsyndroom medicijnen voorgeschreven gekregen?
□Nee
□Ja, de volgende medicatie heb ik voorgeschreven gekregen:

☐ ……

Aantal |__|__| per dag
Aantal mg |__|__||__|__| per tablet
Hoe lang gebruikt |__|__| dagen

☐ ……

Aantal |__|__| per dag
Aantal mg |__|__||__|__| per tablet
Hoe lang gebruikt |__|__| dagen

☐ ……

Aantal |__|__| per dag
Aantal mg |__|__||__|__| per tablet
Hoe lang gebruikt |__|__| dagen

Vraag 31: Heeft u na de behandeling in de afgelopen 3 maanden vanwege gezondheidsklachten aan de handen zelf nog extra kosten gemaakt zonder dat daar een vergoeding tegenover stond?
(meer dan 1 antwoord mogelijk).
□ Nee

□ Ja, namelijk .....

☐ Voor extra medicatie zoals pijnstillers ±|__|__|__| euro per maand

☐ Extra huishoudelijke hulp ±|__|__|__| euro per maand

☐ Reiskosten ±|__|__|__| euro per maand

☐ Anders, namelijk…… ±|__|__|__| euro per maand

Vraag 32: Welke wijze van vervoer heeft u gebruikt om van uw huis naar het ziekenhuis te gaan?
□ Auto
□ Openbaar Vervoer
□ Taxi
□Anders, namelijk.....

Vraag 33: Wat was de enkele reisafstand tussen uw huis en het ziekenhuis?

Deze afstand bedroeg |__|__|__| kilometer.

13.10 Assessment schedule

	inclusion	baseline	6 weeks	3 months	6 months	9 months	12 months	15 months	18 months
In- and exclusioncriteria	x								
Baseline characteristics		x							
Symptom severity (CTS-6)		x	x	x	x	x	x	x	x
Hand functioning (QuickDash)		x							x
Perceived recovery (Likert-type)									x
Patient satisfaction (Likert-type)									x
Quality of life (EuroQol)		x							x
Additional treatment			x	x	x	x	x	x	x
Adverse events			x	x	x	x	x	x	x
Care use				x	x		x		x

x = assessment, blank = no assessment

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