Dutch injection versus surgery trial in patients with carpal tunnel syndrome (DISTRICTS): protocol of a randomised controlled trial comparing two treatment strategies

Wijnand A C Palmbergen,1,2 Rob M A de Bie,1 Tim W H Alleman,3 Esther Verstraete,4 Korne Jellema,5 Wim I M Verhagen,6 Geert J F Brekelmans,7 Godard C W de Ruiter,5 Diederik van de Beek,1 Corianne A J M de Borgie,8 Rob de Haan,8 Roy Beekman,9 Camiel Verhamme1

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common peripheral neuropathy and is characterised by paresthesia, pain, numbness and sometimes weakness of the affected hand. Corticosteroid injections and surgery are the most common treatment options for patients with CTS.1–6 Clinical studies suggest that a surgical intervention is more effective than a steroid intervention for relieving symptoms of CTS.5,7,8 However, many neurologists initiate treatment with a steroid injection, because they consider this very easy to perform and relatively safe. Also, it is possible that with a corticosteroid injection, the need for surgery is avoided. It remains unclear with which intervention CTS treatment should be initiated.6 The lack of comparative knowledge regarding the best treatment strategy for CTS is also reflected in considerable practice variation in the treatment of CTS worldwide.9,10 Due to this practice variation, it is likely that many of the patients with CTS receive suboptimal treatment, resulting in higher societal costs. The objective of this study is to compare the clinical effectiveness and cost-effectiveness of a treatment strategy starting with a corticosteroid injection versus initial surgery.
with surgery compared with starting with a corticosteroid injection.

**METHODS AND ANALYSIS**

**Study design**

The Dutch Injection versus Surgery TRIal in patients with CTS (DISTRICTS) is an investigator-initiated, multicenter, open-label randomised controlled trial (RCT) with a follow-up of 18 months. Approximately 30 Dutch hospitals will be including participants. Data regarding baseline characteristics, treatment and follow-up assessments are collected according to a predefined protocol. Participants are randomised to the treatment strategy starting with surgery (surgery group) or to the treatment strategy starting with a corticosteroid injection (injection group). Figure 1 shows the study flow diagram conform Consolidated Standards of Reporting Trials guidelines.

Study monitoring and data management are performed in accordance with the International Conference on Harmonisation—Good Clinical Practice guidelines by the Clinical Research Unit of the Amsterdam UMC, AMC. The DISTRICTS was registered at [http://www.controlledtrials.com](http://www.controlledtrials.com) before start of the study.

The DISTRICTS started in December 2016 and is expected to end in June 2023.

**Study participants**

Inclusion criteria are: patients with clinically suspected CTS, which is confirmed by electrophysiological or sonographic testing and for which surgery and injection are both potential treatment options. The symptoms of CTS have to be present for at least 6 weeks and treatment should be initiated within 6 weeks following inclusion. Participants have to be 18 years or older at time of examination. Patients can participate for the most affected hand only in case both hands are eligible. Exclusion criteria are: previous surgery for CTS on the ipsilateral wrist, an injection for CTS in the ipsilateral wrist less than 1 year ago, previous participation in the DISTRICTS, clinical or neurophysiological suggestion that the symptoms are due to another diagnosis, not able to comprehend Dutch self-report questionnaires, pregnancy, follow-up not possible, legally incompetent adults and no informed consent. Potential participants will be recruited from neurology outpatient clinics.

Different strategies to improve participant enrolment are used such as creating nationwide awareness of the DISTRICTS with a strong commitment of the Dutch Association of Neurology, regular and tailored contacts with participating centres, making expense allowance available and providing tools such as instruction videos to increase successful participant enrolment.

Recruitment of participants started in November 2017. We aim to finish inclusion in November 2021.

**Patient and public involvement**

Prior to starting the DISTRICTS, we invited the Netherlands Patients Federation to discuss the protocol and subsequently incorporated their advice. Because a Dutch patients society specific for CTS does not exist, further input was given by the Netherlands Repetitive Strain Injury society. No patients were involved in the recruitment and conduct of the study. Study participants will receive the results of the study by mail.

**Study procedures and randomisation**

After referral to the neurology outpatient clinics, potential participants will be informed about the study with an information letter. The local clinician evaluates a potential participant for eligibility. Subsequently, the clinician will verify if the potential participant is fully informed about the study and will discuss enrolment in the study. Informed consent is obtained (see DISTRICTS patient information and consent form; online supplemental file 1). Baseline and demographic characteristics, such as sex, length, weight, unilateral or bilateral CTS symptoms, duration of symptoms, severity of symptoms, associated underlying cause, previous corticosteroid injection for CTS in the ipsilateral wrist more than 1 year ago, are recorded, after which the participants will be randomised to either the surgery group or the injection group. In case a participant has bilateral CTS, the most affected hand will be included and treated in accordance with the study protocol. The preferred treatment and timing of treatment for the other hand is decided by the participant and the local clinician. If the symptoms in both hands are equally severe, the dominant hand will be included in the study. Participants will be randomised by the local
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, the participating centre will continue to refer the participating patients 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. The surgeon describes the surgical technique in the surgical report form.

Injection group
A neurologist or other qualified staff member will administer the corticosteroid injection. As we choose to stay as close as possible to daily practice, participating centres will use their local protocol for injection, often based on the previous literature.

The use of analgesics is allowed. Additional treatments are allowed following the initial treatment at the participant and physician’s discretion, and are not dictated by the protocol.

Baseline data collection is performed by local investigators. Participating centres send their report forms to the central data entry site. Follow-up questionnaires are sent 1 week before the upcoming follow-up timepoint. If the questionnaire is not returned within 2 weeks, a reminder and a new questionnaire will be sent. If there is no response within 1 week after the reminder, the patient will be contacted by telephone.

A central data manager performs and monitors data entry, and looks after timely questionnaire delivery. Data are checked for completeness. Patients will be contacted by telephone in case of missing data. In case of incomplete follow-up, effort is undertaken to collect the most relevant 18-month timepoint data. A separate data management plan was made to secure correct data entry, coding and storage.

Sample size
The long-term effectiveness (12 months) of surgery is estimated to be approximately 75% and the long-term effectiveness (12 months) of one to three injections, 38% to 61%. To our knowledge, there are scarce data available regarding the recovery rate in treatment strategies that may include combinations of different types of treatment at 18 months.

For the sample size calculation, we assume a recovery rate of 70% in the surgery group and 60% in the injection group. We consider this 10% difference in recovery rate the 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 initial surgery) and a proportion of 0.60 (recovery after initial corticosteroid injection) when the sample size in each group is 376 (752 participants in total). Anticipating a 20% attrition rate, we will include (376/0.80 =) 470 participants per treatment group, which are 940 participants in total.

Outcome measures
The primary outcome is the proportion of participants recovered at 18 months. Recovery is defined as having no or mild symptoms; that is, a score of less than eight points on the 6-item carpal tunnel symptoms scale (CTS-6).

Secondary outcomes are: time to recovery during 18-month follow-up, proportion of participants recovered at all timepoints during 18-month follow-up, symptom severity at all timepoints during 18-month follow-up, upper limb functioning at 18 months measured using the QuickDASH, severity of pain in the scar/palm and pain-related activity limitation during 18-month follow-up using the palmar pain scale, participant’s global perception of recovery at 18 months measured with a seven-point Likert-type item, participant’s satisfaction at 18 months measured with a seven-point Likert-type item, health-related quality of life at 18 months assessed with the EuroQol 5-level EQ-5D (EQ-5D-5L), number and type of additional treatments during 18-month follow-up, adverse events during 18-month follow-up, use of care and health-related costs during follow-up assessed with an adapted version of the Medical Consumption Questionnaire (iMCQ) and the Productivity Cost Questionnaire (iPCQ).

Data will be collected at baseline, 6 weeks and at 3, 6, 9, 12, 15 and 18 months (table 1). Baseline data are acquired during the visit at the neurology outpatient clinic. All other follow-up consists of participants completing self-report questionnaires, which are collected centrally.

Statistics
We will prepare an in-depth statistical analysis plan before the database is finalised, cleaned and locked. Briefly, the statistical analyses will be based on the
intention-to-treat principle. Baseline patient characteristics will be summarised using descriptive statistics. The primary outcome, the between-group difference in the proportion of participants recovered at 18 months, will be analysed using the Fisher's exact test. Recovery at 18 months is defined as scoring less than eight points on the CTS-6. Effect size will be expressed in a crude OR with its 95% CI. Additionally, the primary outcome will be analysed using logistic regression, including the three stratification variables into the model. Effect size will be expressed in an adjusted OR with its corresponding 95% CI. Only in case of disbalance in baseline characteristics arisen by chance, we will perform further multivariable analyses with inclusion of potentially confounding variables, such as age, gender, duration of symptoms and severity of symptoms, to assess their effect on primary outcome. To assess the robustness of our findings, we will also perform a sensitivity analysis. In this analysis, a participant will be classified as having recovered if (s)he scores less than nine points on the total CTS-6 and less than three points on any individual item of the CTS-6. We will perform the same unadjusted analysis of the redefined primary outcome as described above.

Formal statistical tests will not be performed to examine differences between the secondary outcomes in the treatment groups. Differences between the surgery and injection groups with regard to the secondary outcomes measured at single timepoints will be summarised using appropriate parameters, such as hazard ratios (expressing the between-group difference in time to recovery) and proportions, means or medians and presented with their corresponding 95% CIs. Differences between the surgery and injection groups with respect to longitudinally measured outcomes will be analysed using a generalised linear mixed-effect model with treatment group as a fixed-effect and an appropriate random-effect structure.

A two-sided p value < 0.05 will be considered statistically significant. All statistical analyses will be performed in the current version of IBM SPSS Statistics for Windows (IBM Corp).

**Table 1** Assessment schedule

| Inclusion and exclusion criteria | Inclusion | Baseline | 6 weeks | 3 months | 6 months | 9 months | 12 months | 15 months | 18 months |
|---------------------------------|-----------|----------|---------|----------|----------|----------|-----------|-----------|-----------|
| Baseline characteristics        |           |          |         |          |          |          |           |           |           |
| Symptom severity (CTS-6)        | x         |          |         |          |          |          |           |           |           |
| Upper limb functioning (QuickDash) | x         |          |         |          |          |          |           |           |           |
| Pain palm/scar (palmar pain scale) | x         |          |         |          |          |          |           |           |           |
| Perceived recovery (Likert-type) |           |          |         |          |          |          |           |           |           |
| Participant satisfaction (Likert-type) |           |          |         |          |          |          |           |           |           |
| Quality of life (EuroQol)       |           |          |         |          |          |          |           |           |           |
| Additional treatment            |           | x        |         |          |          |          |           |           |           |
| Adverse events                  | x         | x        |         |          |          |          |           |           |           |
| Care use (IMCQ, IPCQ)           |           | x        |         |          |          |          |           |           |           |

blank, no assessment; CTS-6, carpal tunnel symptoms scale; IMCQ, Medical Consumption Questionnaire; IPCQ, Productivity Cost Questionnaire; x, assessment.
and physiotherapist. Time off work and presenteeism will be obtained from the iPCQ. Both direct and indirect costs are included. Data will be collected at 3, 6, 12 and 18 months.

Differences between the interventions will be statistically evaluated with bias-corrected bootstrap analysis. 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.

We will extrapolate the outcomes of the economic evaluation using a budget impact analysis in accordance with the International Society for Pharmacoeconomics and Outcomes Research guidelines. 

DISCUSSION

This study compares the clinical effectiveness and cost-effectiveness of two treatments strategies in CTS, either starting with surgery or starting with a corticosteroid injection, but subsequently leaving additional treatment choices at the discretion of the patient and treating physician over a 1.5-year period.

In long-term follow-up (12 months), the effectiveness of surgery is estimated to be approximately 75%. In short-term follow-up (1 month), the effectiveness of a single corticosteroid injection is estimated to be approximately 75%, while in long-term follow-up, this is estimated to be 25%–50%. In case of one to three subsequent injections, the long-term effectiveness could be 38%–61%. This is not only in line with a study that showed that after recurrence of CTS complaints, but also in case of unresponsiveness to a first injection, around 70% improved with a second corticosteroid injection. Both treatments (ie, surgery and injection) differ regarding efficacy and side effects profile and their place relative to each other in the treatment of CTS is unknown. Potentially, a corticosteroid injection could postpone the benefit of a more effective treatment (ie, surgery), conversely a single injection or repeated injections could reduce the number of patients that require surgery.

Other treatments than corticosteroid injections and surgery are used for CTS, such as splints, laser therapy and ultrasound. Limited evidence showed that splints are more effective than no treatment in the short term, but a single corticosteroid injection showed superior clinical effectiveness at 6 weeks compared with night-resting splints in patients presenting in primary care. Still, splints can be used as treatment in specific circumstances, such as during pregnancy or patients with contraindications to surgery and corticosteroid injection. For all other CTS treatments, evidence is lacking.

It must be taken into consideration that our sample size is based on a 10% difference in recovery rate between both treatment strategies, which is considered the minimal clinically important difference. This assumption is based on expert opinion in conjunction with patient representatives, because we could not retrieve a scientifically underpinned threshold for the minimal clinically important difference in recovery rate in the literature.

To measure symptom severity and treatment outcome, we employed the CTS-6. The CTS-6 is an abbreviated and validated questionnaire derived from the Boston Carpal Tunnel Syndrome Questionnaire and highly responsive to change of symptoms. In the inclusion phase of the trial, a short scale diminishes the workload for the local clinician, thus increasing the chances that as many patients are included as possible, in the follow-up phase a short scale likely improves patient acceptance and increases the response rate.

The prospective economic evaluation will provide insight in the cumulative healthcare costs. These costs are expected to differ between the strategies, and important healthcare costs will be related to the improvement in recovery within the follow-up time from a societal perspective. A prospective study in primary care setting in England showed that corticosteroid injections were cost-effective over the use of night splints. A prospective study in neurological outpatient clinics in the Netherlands showed that initial surgery was more cost-effective than splinting. A retrospective single-centre study in the USA showed no difference between the direct cost of nonsurgical care of CTS from that of surgical treatment without preoperative splinting or therapy; however, CTS surgery was associated with favourable incremental cost-utility ratio. There are no prospective studies comparing cost-effectiveness of proposed long-term treatment strategies in CTS.

One of the inclusion criteria in our study is that surgery and injection are both considered as potential treatments for the CTS related symptoms. There is no evidence that symptom severity or the severity of abnormalities found with electrophysiological or sonographic studies clearly directs to either surgery or corticosteroid injection as initial treatment. Poor prognostic factors for recovery after corticosteroid injection might be duration of symptoms, positive Phalen’s test and thenar wasting, although evidence was inconclusive. There is no clear evidence that corticosteroid injections are not effective in severe CTS or that less severe CTS does not benefit from surgery. Other difficulties are that grading of severity of CTS is attempted based on electrophysiological criteria. These do not consider severity of symptoms and signs. No consensus about the most appropriate grading system has been reached. Furthermore, in ultrasound-confirmed patients with CTS, these data are not available.

To successfully complete the DISTRICTS, 940 participants have to be included. To date, more than 30 Dutch centres take part in realising this. Because the inclusion process is mostly performed during specialised and time-efficient carpal tunnel outpatient clinics, it will be a challenge for these centres to include this relatively large number of participants.

The trial design is unique for CTS being an open-label RCT with long-term follow-up and using validated
self-reported, patient relevant outcome measurements. The trial not just compares surgical decompression with one corticosteroid injection, but compares treatment strategies, which start with the initial, randomised, allocated treatment, followed by long-term clinical care as usual for 1.5 years. We did not blind for the initial allocated treatment (ie, initial treatment with surgery or injection) as we aim to compare treatment strategies and knowledge about the initial treatment could be essential for choosing a subsequent treatment. Also, blinding of patients with dummy surgery is not considered ethical in this context. 

With regard to outcome assessment, we chose for validated self-reported, patient relevant outcome measurements. Arguments to choose for these patient relevant outcome measures are that in CTS care, symptom perception is the most important determinant to seek treatment and also to determine treatment effectiveness. The self-report questionnaires allow the participant to report their symptoms, prevents hospital visits just for study reasons and also to determine treatment effectiveness. The self-report questionnaires allow the participant to report adverse events and additional care use. It should be taken into account that participants might report adverse events differently than clinicians. We considered secondary outcome measures such as sensory signs, strength, and neurophysiological and ultrasound measures, but none of these outcomes showed convincing evidence of being useful in addition while additional hospital visits and standardised assessments would be mandatory. Due to the open-label design, we are aware of the risk of bias in collecting unblinded endpoint measurements. Still, a prospective randomised open, blinded endpoint design was not chosen as a blinded physician assessing the outcomes would still need to ask the patient for symptom perception. An additional advantage of focusing patient relevant outcome measures based on self-reporting is that it may increase external validity of the results.

This study is innovative in the way it finally compares the clinical effectiveness and cost-effectiveness of two treatment strategies that have been daily clinical practice for years. The study results will have the potential to change the current CTS treatment strategies.

Ethics and dissemination
The DISTRICTS was approved by the Medical Ethical Committee of the Amsterdam University Medical Centers (study number 2017-171). The DISTRICTS is conducted according to the principles of the Declaration of Helsinki (version of 2013) and in accordance with the World Medical Association and other guidelines, regulations and acts. Study results will be disseminated in peer-reviewed journals and conferences. The study results will have the potential to change CTS treatment strategies.

Author affiliations
1Department of Neurology, Amsterdam UMC location University of Amsterdam, Amsterdam Neuroscience, Amsterdam, The Netherlands
2Department of Neurology, BovenIJ hospital, Amsterdam, The Netherlands
3Department of Neurology, Saint Jans Hospital Weert, Weert, The Netherlands
4Department of Neurology, Rijnstate Hospital, Arnhem, The Netherlands
5Department of Neurology, Haaglanden Medical Center, Den Haag, The Netherlands
6Department of Neurology, CWZ, Nijmegen, The Netherlands
7Department of Neurology, ETZ, Tilburg, The Netherlands
8Department of Epidemiology and Data Science, Amsterdam UMC location University of Amsterdam, Amsterdam, The Netherlands
9Department of Neurology, Zuyderland Medical Center, Heerlen, The Netherlands

Acknowledgements We thank the patient adviser Sandra Oudshoff for her valuable input in the design of the study.

Contributors WP, RdB, RdH, CdB and CV designed and planned the study in collaboration with the other members of the Dutch injection versus surgery trial in patients with carpal tunnel syndrome steering committee: TA, EV, KJ, WJ, GB, GdR, DvdB. RdB arranged the funding. WP drafted the manuscript of the study protocol. All authors gave feedback on the manuscript and approved the final manuscript.

Funding This is an investigator-initiated study. This work is supported by ZonMw, 837004025 and 1033011201005. The funder has no role in study design; collection, management, analysis and interpretation of data; writing of the report; and the decision to submit the report for publication, and will have no ultimate authority over any of these activities.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. For further details, please refer to the Methods and analysis section.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iD
Wijnand A C Palmbergen http://orcid.org/0000-0002-1785-4411

REFERENCES
1 Atroshi I, Flandell M, Hofer M, et al. Methylprednisolone injections for the carpal tunnel syndrome: a randomized, placebo-controlled trial. Ann Intern Med 2013;159:309–17.
2 Bland JDP. Treatment of carpal tunnel syndrome. Muscle Nerve 2007;36:167–71.
3 Dammers JW, Veering MM, Vermeulen M. Injection with methylprednisolone proximal to the carpal tunnel: randomised double blind trial. BMJ 1999;319:884–6.
4 Huisstede BM, Hoogvliet P, Randsdorp MS, et al. Carpal tunnel syndrome. Part I: effectiveness of nonsurgical treatments—a systematic review. Arch Phys Med Rehabil 2010;91:981–1004.
5 Huisstede BM, Randsdorp MS, Coert JH, et al. Carpal tunnel syndrome. Part II: effectiveness of surgical treatments—a systematic review. Arch Phys Med Rehabil 2010;91:1005–24.
6 Padua L, Coraci D, Erra G, et al. Carpal tunnel syndrome: clinical features, diagnosis, and management. Lancet Neurol 2016;15:1273–84.
7 Ly-Pen D, Andreu J-L, de Blas G, et al. Surgical decompression versus local steroid injection in carpal tunnel syndrome: a one-year, prospective, randomized, open, controlled clinical trial. Arthritis Rheum 2005;52:612–9.
Visser LH, Ngo Q, Groeneweg SJM, et al. Long term effect of local corticosteroid injection for carpal tunnel syndrome: a relation with electrodiagnostic severity. *Clin Neurophysiol* 2012;123:838–41.

Ryan D, Shaw A, Graham S. Variation in CCG policies for the treatment of carpal tunnel syndrome - Are CTS patients receiving equal standards of care across the country? *Bulletin 2017;99:28–31.

Expertteam Ziekenhuisszorg. Praktijkvariatierapport 7 aandoeningen electieve zorg, 2014. Available: https://docplayer.nl/2496605-Praktijkvariatierapport-7-aandoeningen-electieve-zorg-2014.html

Berger M, Vermeulen M, Koelman JHTM, et al. The long-term follow-up of treatment with corticosteroid injections in patients with carpal tunnel syndrome. when are multiple injections indicated? *J Hand Surg Eur Vol* 2013;38:634–9.

Atroshi I, Lyren P-E, Gummesson C. The 6-item CTS symptoms scale: a brief outcomes measure for carpal tunnel syndrome. *Qual Life Res* 2009;18:347–58.

Gummesson C, Ward MM, Atroshi I. The shortened disabilities of the arm, shoulder and hand questionnaire (QuickDASH): validity and reliability based on responses within the full-length DASH. *BMC Musculoskelet Disord* 2006;7:44.

Atroshi I, Lyren P-E, Ornstein E, et al. The six-item CTS symptoms scale and palmar pain scale in carpal tunnel syndrome. *J Hand Surg Am* 2011;36:788–94.

Herdmian M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;20:1727–36.

Bouwmans C, Krol M, Severens H, et al. The IMTA productivity cost questionnaire: a standardized instrument for measuring and Valuing health-related productivity losses. *Value Health* 2015;18:753–8.

Barber JA, Thompson SG. Analysis of cost data in randomized trials: an application of the non-parametric bootstrap. *Stat Med* 2000;19:3219–36.

Mauskopf JA, Sullivan SD, Annemans L, et al. Principles of good practice for budget impact analysis: report of the ISPOR Task Force on good research practices--budget impact analysis. *Value Health* 2007;10:336–47.

Meys V, Thiesen S, Rozeman S, et al. Prognostic factors in carpal tunnel syndrome treated with a corticosteroid injection. *Muscle Nerve* 2011;44:763–8.

Ashworth NL, Bland JDP. Effectiveness of second corticosteroid injections for carpal tunnel syndrome. *Muscle Nerve* 2013;48:122–6.

Page MJ, Massy-Westropp N, O’Connor D, et al. Splinting for carpal tunnel syndrome. *Cochrane Database Syst Rev* 2012;Cd010003.

Chesterton LS, Blagojevic-Bucknall M, Burton C, et al. The clinical and cost-effectiveness of corticosteroid injection versus night splints for carpal tunnel syndrome (INSTINCTS trial): an open-label, parallel group, randomised controlled trial. *Lancet* 2018;392:1423–33.

Korthals-de Bois IBC, Gerritsen AAM, van Tulder MW, et al. Surgery is more cost-effective than splinting for carpal tunnel syndrome in the Netherlands: results of an economic evaluation alongside a randomized controlled trial. *BMC Musculoskelet Disord* 2006;7:96.

Pomerance J, Zurakowski D, Fine I. The cost-effectiveness of nonsurgical versus surgical treatment for carpal tunnel syndrome. *J Hand Surg Am* 2009;34:1193–200.

Burton CL, Chesterton LS, Chen Y, et al. Clinical Course and Prognostic Factors in Conservatively Managed Carpal Tunnel Syndrome: A Systematic Review. *Arch Phys Med Rehabil* 2016;97:e831:836–52.

Chan L, Turner JA, Comstock BA, et al. The relationship between electrodiagnostic findings and patient symptoms and function in carpal tunnel syndrome. *Arch Phys Med Rehabil* 2007;88:19–24.

Sucher BM. Grading severity of carpal tunnel syndrome in electrodiagnostic reports: why grading is recommended. *Muscle Nerve* 2013;48:331–3.

Sambandam SN, Priyanka P, Gul A, et al. Critical analysis of outcome measures used in the assessment of carpal tunnel syndrome. *Int Orthop* 2008;32:497–504.

Smidt MH, Visser LH. Carpal tunnel syndrome: clinical and sonographic follow-up after surgery. *Muscle Nerve* 2008;38:987–91.

Schrijver HM, Gerritsen AAM, Strijers RLM, et al. Correlating nerve conduction studies and clinical outcome measures on carpal tunnel syndrome: lessons from a randomized controlled trial. *J Clin Neurophysiol* 2005;22:216–21.