RHEUMATOLOGY

Original article

The effectiveness of corticosteroid injection *versus* night splints for carpal tunnel syndrome: 24-month follow-up of a randomized trial

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Abstract

Objectives. This follow-up study of the INSTinCTS (INjection *vs* SplinTing in Carpal Tunnel Syndrome) trial compared the effects of corticosteroid injection (CSI) and night splinting (NS) for the initial management of mild-to-moderate CTS on symptoms, resource use and carpal tunnel surgery, over 24 months.

Methods. Adults with mild-to-moderate CTS were randomized 1:1 to a local corticosteroid injection or a night splint worn for 6 weeks. Outcomes at 12 and 24 months included the Boston Carpal Tunnel Questionnaire (BCTQ), hand/wrist pain intensity numeric rating scale (NRS), the number of patients referred for and undergoing CTS surgery, and healthcare utilization. A cost–utility analysis was conducted.

Results. One hundred and sixteen participants received a CSI and 118 a NS. The response rate at 24 months was 73% in the CSI arm and 71% in the NS arm. By 24 months, a greater proportion of the CSI group had been referred for (28% *vs* 20%) and undergone (22% *vs* 16%) CTS surgery compared with the NS group. There were no statistically significant between-group differences in BCTQ score or pain NRS at 12 or 24 months. CSI was more costly [mean difference £68.59 (95% CI: −120.84, 291.24)] with fewer quality-adjusted life-years than NS over 24 months [mean difference −0.022 (95% CI: −0.093, 0.045)].

Conclusion. Over 24 months, surgical intervention rates were low in both groups, but less frequent in the NS group. While there were no differences in the clinical effectiveness of CSI and NS, initial treatment with CSI may not be cost-effective in the long-term compared with NS.

Key words: carpal tunnel syndrome, clinical trial, primary care

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Rheumatology key messages

- Corticosteroid injection and night splinting are safe and effective treatment options for mild-to-moderate carpal tunnel syndrome.
- Clinical effectiveness did not differ over 24 months, but night splinting may be more cost effective.
- Patient choice between a corticosteroid injection or night splinting can be encouraged in initial management decisions.

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Introduction

CTS is a symptomatic compression neuropathy of the median nerve at the wrist [1]. Clinical symptoms include localized pain and/or discomfort, paraesthesia, and functional loss. CTS is the most common peripheral entrapment neuropathy [2] with 36 patients per 10 000 person-years consulting with CTS in primary care in 2013 [3].

Management options are surgical or conservative (non-surgical). Surgical carpal tunnel decompression is usually offered to those with severe CTS or those not improving with conservative management. Conservative treatment options include local corticosteroid injections (CSI) and night splinting (NS), which are the most used conservative interventions and are recommended in national care pathways and guidelines [4, 5]. In one systematic review, 57–66% of affected people initially treated with a conservative approach were reported to eventually have required surgery [6].

Cochrane and other systematic reviews of randomized and quasi-randomized trials have evaluated the effectiveness of NS [7] and CSI for CTS [8, 9]. They found limited evidence that NS is more effective than no treatment in the short term (<3 months), but concerns were raised about allocation concealment and blinding [7]. There was evidence of short-term benefit from CSI compared with placebo injection or other conservative treatment options [8]. Evidence of longer-term benefit was insufficient, and reviews concluded that more research was needed.

We investigated the clinical and cost-effectiveness of CSI *vs* NS for CTS in the INSTinCTS (INjection *vs* SplinTing in Carpal Tunnel Syndrome) trial [10, 11]. We found significantly greater improvements in pain and function at 6 weeks with CSI than NS, although there were no significant between-group differences at 6 months. CSI was also cost effective over 6 months when compared with NS [10]. The aim of long-term trial follow-up was to compare the effect of CSI and NS on hand and wrist pain and function, the number of participants referred for and undergoing CTS surgery, and health care resource use, over 24 months [11].

Methods

Study design

INSTinCTS was a pragmatic, two-arm parallel group, open-label, randomized controlled trial conducted within the National Health Service (NHS). The trial was approved by the National Research Ethics Service Committee North West—Liverpool (UK; reference 13/NW/0280) and the Medicines and Healthcare products Regulatory Agency (European Clinical Trials Database, number 2013-001435-8). The trial protocol detailing the methods used, and the 6-week and 6-month findings have been published previously [10, 11].

Setting

Participants were recruited from 25 primary and community musculoskeletal clinics and services in England and Wales.

Eligibility criteria

Patients were eligible if they were aged 18 years or over and presented with mild to moderate CTS [12], diagnosed according to agreed standardized criteria [13]. Exclusion criteria included having severe CTS requiring urgent consideration of surgery or having received a CSI or NS for CTS within the preceding 6 months [11]. Written, informed consent was obtained from eligible patients who were interested in participating [11].

Randomization, blinding and procedures

Participants were randomly allocated on a 1:1 basis using permutated blocks of sizes two and four, pre-stratified by research site to either (i) one injection of 20 mg methylprednisolone acetate (as 20 mg of Depo-Medrone from 40 mg/ml; Pfizer Manufacturing Belgium NV; Puurs, Belgium) or (ii) resting night splint set at a neutral angle (0–20 degrees) (Beta Wrist Brace with CE marking; Promedics Orthopaedic; Port Glasgow, UK), to be worn at night for 6 weeks. Participants with bilateral CTS had their most severely affected wrist treated and reported as part of the trial. The contralateral wrist could be treated as per local protocol.

Randomization was completed by sites using Keele University Clinical Trial Unit's (CTU) web randomization service. The allocation sequence was not available to research team members. Neither clinicians nor patients could be blinded to treatment allocation. Treatment group allocation was masked up to the 6-week primary analysis.

Sample size

In order to detect a 15% greater improvement at the primary end point of 6 weeks, measured by the BCTQ, in the CSI group compared with NS [0.45 points, such as a 0.9-point (30%) reduction in the CSI group *vs* a 0.45-point (15%) reduction in the NS group, with pooled s.d. of 0.1], complete data was needed for 200 participants (100 in each treatment group), given 80% power and 5% two-tailed significance. By adopting an initial sample size that would allow for 15% lost-to-follow-up, 240 participants (120 participants in each treatment group) were needed [11]. A *post hoc* sample size calculation was not conducted for long-term analysis.

Data collection

Baseline data were collected from a self-completed questionnaire immediately before randomization. Subsequent postal questionnaires were mailed to participants at 6 weeks and 6, 12, and 24 months post-randomization. At each time point, two reminders were sent after 2 and 4 weeks to non-responders, and thereafter minimum data collection of the primary outcome measure and surgery for CTS by phone and/or post was obtained. Deceased participants or those who withdrew consent were no longer followed up, however their data up to that time point were used in the analysis.

Incident adverse events from either intervention were reported and assessed with clinical case report forms, participant self-report in follow-up questionnaires, or directly to the CTU or to their GP.

Outcomes

The primary outcome measure was the overall mean total score for hand and wrist symptom and function measured by the Boston Carpal Tunnel Questionnaire (BCTQ) (1–5 scale, higher scores indicating more severe symptoms and functional impairment) [14]. Other secondary outcome measures included hand/wrist pain intensity [numeric rating scale 0–10 (NRS)]; referral for CTS surgery; undergoing CTS surgery; health-related quality of life (EuroQoL: EQ-5D-5L) [15]; employment status; work performance (NRS); work absence (self-reported days absent from work due to CTS); healthcare utilization (primary and secondary care consultations, investigations and treatments, over-the-counter or pre-scribed medications, use of private healthcare due to CTS); and patient incurred costs due to CTS [11].

Analysis

Using data from the four follow-up points (6 weeks, 6, 12 and 24 months) a longitudinal mixed effect linear regression model examined the overall mean difference in outcome (BCTQ score and pain intensity) in the two treatment groups over the whole follow-up period adjusting for baseline outcome score and time point. The model then included an interaction term between treatment and time point to assess treatment effect at each time point. The treatment effect at each time point was estimated by summing the coefficients from the treatment effect and the interaction term. The models were further adjusted for age, gender and duration of symptoms. Patients with relevant outcomes reported on at least one follow-up time point, with available data for baseline adjustment factors, were eligible for corresponding analysis.

This approach was conducted to optimize use of the data for the repeated measure analysis and mitigate the influence of any further study attrition. The issue of treatment contamination over the course of the observed period remains, so results present the outcomes of patients initially treated with either corticosteroid injection or night splints.

The cumulative number (%) of participants requiring additional wrist splints or injections, referred for CTS surgery or undergoing CTS surgery were examined by treatment group. Only the first referral to surgery/surgical episode was taken into consideration.

Point estimates were accompanied by associated 95% CIs and all *P*-values <0.05 were considered to indicate statistical significance.

Economic evaluation

A cost–utility analysis was conducted from an NHS perspective, to determine the cost-effectiveness of night splints *vs* corticosteroid injection at 6, 12 and 24 months. Health-care resource use data were obtained from self-report questionnaires at 6, 12 and 24 months and valued using unit cost data obtained from standard UK sources [16–18]. We also estimated the cost of delivering both interventions.

All costs were valued at 2016–2017 prices. Outcomes were measured in quality-adjusted life-years (QALYs), which were estimated at 6, 12 and 24 months for each study participant, using EQ-5D-5L scores and the area under the curve approach. Imbalances in baseline utility (EQ-5D-5L) scores between the study arms were controlled for with a regression approach. Missing costs and EQ-5D-5L scores were accounted for using multiple imputation methodology. Twenty-five datasets were imputed using chained equations with predictive mean matching to ensure that imputed values do not go out of the plausible range. The coefficients were then pooled across the multiply imputed datasets using Rubin's rule to obtain single estimates of the corresponding population parameters [19, 20]. Cost and health outcomes (QALYs) at 24 months were discounted using the recommended discount rates of 3.5%.

An incremental analysis was undertaken, with differences in costs and QALYs expressed as an incremental cost-effectiveness ratio (ICER) of cost per additional QALY gained. Bootstrapping was used to quantify overall uncertainty, and 5000 paired estimates of mean differential costs and QALYs were estimated to construct cost-effectiveness acceptability curves. These show the probability of injection being cost-effective across a range of possible values of willingness to pay for an additional QALY at 6, 12 and 24 months. All analyses were performed using STATA v15 (StataCorp LLC, College Station, TX, USA).
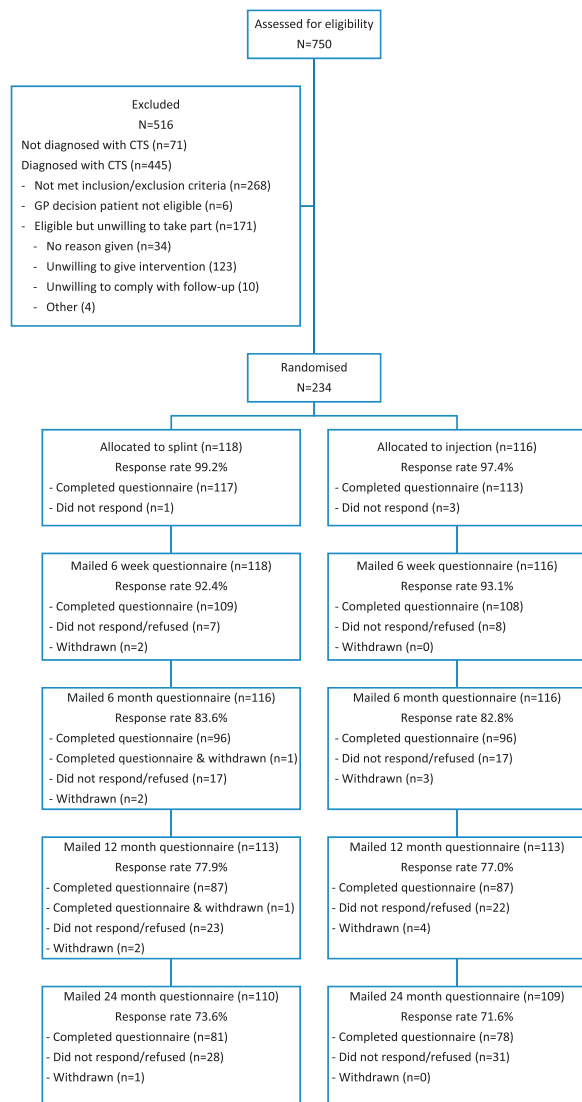
Patient and public involvement

Ten public contributors with lived experience of CTS were involved throughout this study (Supplementary Data S1, available at *Rheumatology* online). Their input and contributions shaped the delivery of the study and helped us consider how the findings should be disseminated to the wider public. One public contributor (A.H.) co-authored this paper and one sat on the Trial Steering Committee.

Results

Between 17 April 2014 and 31 December 2016, 750 patients were assessed for eligibility at either their general practice or community musculoskeletal clinic (Fig. 1). Two hundred and thirty-four participants (58% of the 405 eligible patients) gave informed consent to participate. One hundred and sixteen participants were randomly assigned to CSI and 118 to NS. As previously reported, demographics were similar between participants and eligible non-participants and between the CSI and NS groups [10]. The response rates at all time points were similar between the treatment arms. The 24-month response rate was 73% in the CSI arm and 71% in the NS arm.

Expected adverse reactions reported in the 6-week follow-up questionnaire or directly from participating

Fɪɢ. 1 Consort flow diagram over 24 months


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                    ┌─────────────────────┐
                    │ Assessed for        │
                    │ eligibility         │
                    │ N=750               │
                    └─────────────────────┘
  ┌──────────────────────────────────────────────┐
  │ Excluded                                       │
  │ N=516                                          │
  │ Not diagnosed with CTS (n=71)                  │
  │ Diagnosed with CTS (n=445)                     │
  │ - Not met inclusion/exclusion criteria (n=268) │
  │ - GP decision patient not eligible (n=6)       │
  │ - Eligible but unwilling to take part (n=171)  │
  │     - No reason given (n=34)                    │
  │     - Unwilling to give intervention (123)      │
  │     - Unwilling to comply with follow-up (10)   │
  │     - Other (4)                                 │
  └──────────────────────────────────────────────┘
                    ┌─────────────────────┐
                    │ Randomised          │
                    │ N=234               │
                    └─────────────────────┘
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Allocated to splint (n=118)	Allocated to injection (n=116)
Response rate 99.2%	Response rate 97.4%
- Completed questionnaire (n=117)	- Completed questionnaire (n=113)
- Did not respond (n=1)	- Did not respond (n=3)

Mailed 6 week questionnaire (n=118)	Mailed 6 week questionnaire (n=116)
Response rate 92.4%	Response rate 93.1%
- Completed questionnaire (n=109)	- Completed questionnaire (n=108)
- Did not respond/refused (n=7)	- Did not respond/refused (n=8)
- Withdrawn (n=2)	- Withdrawn (n=0)

Mailed 6 month questionnaire (n=116)	Mailed 6 month questionnaire (n=116)
Response rate 83.6%	Response rate 82.8%
- Completed questionnaire (n=96)	- Completed questionnaire (n=96)
- Completed questionnaire & withdrawn (n=1)	- Did not respond/refused (n=17)
- Did not respond/refused (n=17)	- Withdrawn (n=3)
- Withdrawn (n=2)	

Mailed 12 month questionnaire (n=113)	Mailed 12 month questionnaire (n=113)
Response rate 77.9%	Response rate 77.0%
- Completed questionnaire (n=87)	- Completed questionnaire (n=87)
- Completed questionnaire & withdrawn (n=1)	- Did not respond/refused (n=22)
- Did not respond/refused (n=23)	- Withdrawn (n=4)
- Withdrawn (n=2)	

Mailed 24 month questionnaire (n=110)	Mailed 24 month questionnaire (n=109)
Response rate 73.6%	Response rate 71.6%
- Completed questionnaire (n=81)	- Completed questionnaire (n=78)
- Did not respond/refused (n=28)	- Did not respond/refused (n=31)
- Withdrawn (n=1)	- Withdrawn (n=0)

sites have been reported previously [10]. There were seven serious adverse events after 6 months, three in the CSI group (two deaths from cryptogenic organizing pneumonia and heart failure, respectively, and one participant hospitalized for patella resurfacing) and four in the NS group (four participants hospitalized for myocardial infarction, fractured finger, total hip replacement and total knee replacement, respectively). All were considered unrelated to treatment.

Mean BCTQ and hand/wrist pain intensity scores decreased over time in both intervention groups (Table 1, Fig. 2). Overall, there was no difference in improvement of mean BCTQ score between treatment groups over the 24-month period [adjusted mean difference −0.10 (95% CI: −0.25, 0.04)]. The interaction term once added to the model suggested the treatment effect changed over time. Greater improvement in BCTQ score

in the CSI arm compared with the NS arm was observed at 6 weeks [−0.34 (−0.53, −0.14)], but the effect diminished and lost significance at 6 months [0.03 (−0.17, 0.24)], 12 months [−0.09 (−0.30, 0.12)] and 24 months [0.06 (−0.16, 0.28)].

Similarly, there was little overall difference in improvement of hand/wrist pain intensity score between the two treatment groups over the 24-month period [adjusted mean difference −0.02 (95% CI: −0.55, 0.50)]. Comparative treatment effect changed over time; greater reduction in pain in the CSI arm compared with NS arm was observed at 6 weeks [−0.98 (−1.72, −0.24)], but the difference diminished and lost significance at 6 months [0.76 (−0.02, 1.54)], 12 months [0.03 (−0.79, 0.85)] and 24 months [0.41 (−0.45, 1.26)].

During the 24-month follow-up period, 56 participants were referred for and 44 underwent carpal tunnel surgery. More participants in the CSI group than in the NS group were referred for (28% *vs* 20%) and underwent (22% *vs* 16%) carpal tunnel surgery (Table 2).

Use of additional wrist splints and injections reduced over the 24-month period (Table 3). Over the 24-month period, in the CSI group 13% wore a splint and 28% reported having a further corticosteroid injection; in the NS group 25% continued using splints and 18% subsequently had an injection.

With the exception of visits to a physiotherapist, which were higher in the CSI group, all other visits to health professionals were higher in the NS group (Table 4). Costs related to surgery, blood tests, MRI scans and wrist exercises were higher in the injection group. QALY scores at 24 months were higher in the NS than the CSI group (Supplementary Table S1, available at *Rheumatology* online).

From an NHS perspective, CSI was more costly and was associated with lower QALYs than NS at both 12 months [cost difference £113.15 (95% CI: −37.09, 279.21), QALY difference −0.003 (95% CI: −0.034, 0.027)] and 24 months [cost difference £68.59 (95% CI: −120.84, 291.24), QALY difference −0.022 (95% CI: −0.093, 0.045)] (Supplementary Tables S1, S2, and S4; Supplementary Figs S1 and S2, available at *Rheumatology* online). The 12- and 24-month probability of CSI being cost-effective compared with NS at the £20 000 per QALY threshold was 30% and 22%, respectively (Supplementary Figs S3 and S4, available at *Rheumatology* online). Therefore, NS may be more cost-effective at 12 and 24 months. There were no significant between group differences regarding time off work, work performance or overall productivity (Supplementary Table S3, available at *Rheumatology* online).

Discussion

Summary of findings

In this randomized trial, we found no differences in pain and function at 12- and 24-month follow-up between corticosteroid injection and night splinting used in the

TABLE 1 Treatment effect at each time point

	Mean score (s.d.) (*n* analysed)		Mean difference (95% CI)	
	Splint	Injection	Unadjusted (adjusted for time and baseline score)	Adjusted (adjusted for time, baseline score, age, sex and duration of symptoms)
Boston Carpal Tunnel Questionnaire[a]				
Overall treatment effect at 24 months[b]			−0.10 (−0.24, 0.05) (*P* = 0.178)	−0.10 (−0.25, 0.04) (*P* = 0.162)
Baseline	2.64 (0.64) (*n* = 105)	2.65 (0.72) (*n* = 100)	—	—
6 weeks	2.30 (0.77) (*n* = 102)	1.95 (0.82) (*n* = 95)	−0.33 (−0.53, −0.14) (*P* = 0.001)	−0.34 (−0.53, −0.14) (*P* = 0.001)
6 months	2.04 (0.72) (*n* = 92)	2.08 (0.79) (*n* = 83)	0.04 (−0.16, 0.24) (*P* = 0.702)	0.03 (−0.17, 0.24) (*P* = 0.744)
12 months	2.05 (0.80) (*n* = 78)	1.98 (0.88) (*n* = 78)	−0.09 (−0.30, 0.13) (*P* = 0.429)	−0.09 (−0.30, 0.12) (*P* = 0.406)
24 months	1.73 (0.76) (*n* = 73)	1.79 (0.79) (*n* = 70)	0.07 (−0.15, 0.29) (*P* = 0.552)	0.06 (−0.16, 0.28) (*P* = 0.578)
Hand/wrist pain intensity score[c]				
Overall treatment effect at 24 months[b]			−0.05 (−0.58, 0.47) (*P* = 0.841)	−0.02 (−0.55, 0.50) (*P* = 0.926)
Baseline	6.12 (2.21) (*n* = 108)	6.30 (2.01) (*n* = 108)	—	—
6 weeks	4.28 (2.62) (*n* = 106)	3.33 (2.67) (*n* = 105)	−1.02 (−1.76, −0.28) (*P* = 0.007)	−0.98 (−1.72, −0.24) (*P* = 0.009)
6 months	3.29 (2.74) (*n* = 94)	4.11 (3.01) (*n* = 92)	0.73 (−0.05, 1.51) (*P* = 0.068)	0.76 (−0.02, 1.54) (*P* = 0.058)
12 months	3.14 (2.74) (*n* = 85)	3.17 (2.93) (*n* = 83)	−0.02 (−0.84, 0.80) (*P* = 0.960)	0.03 (−0.79, 0.85) (*P* = 0.947)
24 months	2.40 (2.83) (*n* = 77)	2.81 (3.19) (*n* = 75)	0.39 (−0.46, 1.25) (*P* = 0.369)	0.41 (−0.45, 1.26) (*P* = 0.350)

[a]Boston Carpal Tunnel Questionnaire: higher scores indicating more severe symptoms and functional impairment. [b]The overall treatment effect of injection compared with splint at 24 months, not considering the time interaction term. [c]Hand/wrist pain intensity: higher scores indicate more pain.

initial treatment of mild to moderate carpal tunnel syndrome. We have previously reported greater improvement in pain and function in the CSI group at 6 weeks that had attenuated by 6 months [10]. There was continued symptomatic improvement in both the CSI and NS groups over 24 months. Surgical rates were low (one in four) overall but slightly higher in the CSI group compared with the NS group. While CSI was cost-effective from both an NHS and societal perspective over the first 6 months [10], the long-term results of this trial show that over 24 months NS may be more cost-effective.

The continued improvement over the 24-month observed period of symptoms and pain extended well beyond the active life of a single methylprednisolone injection or the expected effect of 6 weeks of NS. Therefore, a CSI may give more effective relief from symptoms in the short term, but either treatment is likely to be clinically effective in the longer term. There were few expected adverse reactions and no related serious adverse events, supporting the safety profile of both interventions.

Comparison to existing literature

Three other randomized controlled trials have compared the effectiveness of CSI and NS over varying periods of time [21–23]. Sevim *et al.* evaluated the effectiveness of CSI and NS in mild and moderate CTS, randomizing 120 patients with electrophysiologically confirmed CTS to either night splinting or beclomethasone injection. The trial excluded patients who were non-adherent with splinting but suggested that the adherent cohort showed significant clinical and electrophysiological improvements at 1 year while the injection groups did not [23]. Ucan *et al.* compared the use of splinting, splinting plus local steroid injection and open carpal tunnel release in patients with mild to moderate CTS with symptoms (and an electrophysiological diagnosis) for at least 6 months. At 3 months, all treatment modalities demonstrated improvement in patient reported and electrophysiological outcomes; however, at 6 months both measures deteriorated in the CSI and CSI with splinting group, while the CTR group continued to improve (BCTQ functional score $P = 0.03$) [21]. So *et al.* also compared the efficacy of CSI with NS in 50 patients with CTS. At 4 weeks, both the CSI and NS groups showed an improvement in the BCTQ symptom severity scale; however, only the CSI group showed improvement in function and patient satisfaction [22].

These trials were relatively small and set in a secondary care environment using case definitions that included electrophysiological criteria. It is therefore unlikely that these trials present robust evidence of the effectiveness of splinting *vs* corticosteroid injection generalizable to the primary care population, where patients can be assumed to present in the earlier stages of the condition. To our knowledge, our trial is the largest and

FIG. 2 Mean BCTQ (95% CI) over time
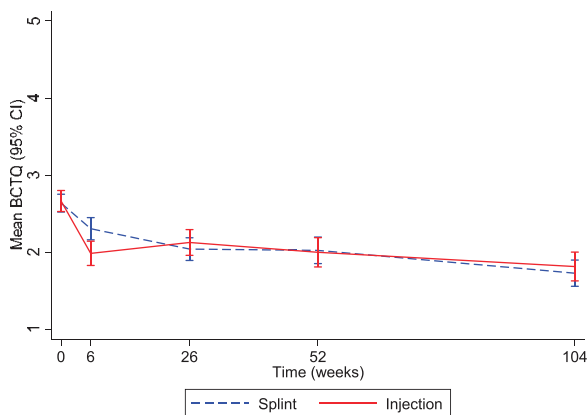
BCTQ: Boston Carpal Tunnel Questionnaire.

TABLE 2 Number of participants referred for surgery and undergoing had carpal tunnel surgery

	Injection (*n* = 116)		Splint (*n* = 118)	
	n (%)	Cumulative *n* (%)	*n* (%)	Cumulative *n* (%)
Referral for carpal tunnel surgery				
6 weeks	2 (1.72)	2 (1.72)	3 (2.54)	3 (2.54)
6 months	15 (12.93)	17 (14.66)	8 (6.78)	11 (9.32)
12 months	9 (7.76)	26 (22.41)	5 (4.24)	16 (13.56)
24 months	6 (5.17)	32 (27.59)	8 (6.78)	24 (20.34)
Underwent carpal tunnel surgery				
6 weeks	1 (0.86%)	1 (0.86%)	1 (0.85%)	1 (0.85%)
6 months	9 (7.76%)	10 (8.62%)	5 (4.24%)	6 (5.08%)
12 months	7 (6.03%)	17 (14.66%)	3 (2.54%)	9 (7.63%)
24 months	8 (6.90%)	25 (21.55%)	10 (8.47%)	19 (16.10%)

In the presence of missing data it was assumed referral to surgery/surgery did not occur.

TABLE 3 Number of additional wrist splints and wrist injections recorded by participants at follow-up beyond 6 weeks

	Injection	Splint
Treatments in the last 6 months recorded in the 6 month questionnaire[a]		
Splint	7/77 (9.09%)	19/79 (24.05%)
Injection	20/77 (25.97%)	13/79 (16.46%)
Treatments in the last 6 months recorded in the 12 month questionnaire		
Splint	7/68 (10.29%)	6/65 (9.23%)
Injection	13/68 (19.12%)	3/65 (4.62%)
Treatments in the last 12 months recorded in the 24 month questionnaire		
Splint	2/56 (3.57%)	1/61 (1.64%)
Injection	2/56 (3.57%)	4/61 (6.56%)
Cumulative total over 24 months[b]		
Splint	12/90 (13.33%)	23/90 (25.56%)
Injection	26/90 (28.89%)	17/90 (18.89%)

[a]May include the randomized treatment. [b]Denominator is based on providing this data in at least one follow-up questionnaire.

longest randomized comparison of the effectiveness of corticosteroid injection *vs* night splints for the treatment of mild to moderate CTS. It is also the first trial of its kind to be conducted in a primary care setting, where most patients with CTS symptoms are initially managed.

Our trial protocol dissuaded additional treatment, including referral for surgery, in the initial 6 weeks. After this time point, clinicians were encouraged to treat participants with ongoing symptoms as per usual care. The protocol itself should not therefore have impacted on referrals in the longer term. In total, 44 (18%) participants in our trial had undergone carpal tunnel surgery by 24 months. This proportion is similar to an observational study set in primary care electronic health records, which reported 27% of patients presenting in UK primary care had carpal tunnel surgery within 3 years of their initial presentation [3]. These surgical intervention rates from primary care and interface services are substantially lower than those reported in studies based in secondary care [6]. PALMS, a recent observational study, reported 64% of participants recruited from secondary care outpatient sites in England had carpal tunnel surgery by 18 months [24].

The discrepancies in the proportion of patients receiving surgery after initial conservative management are likely to be different between those treated in primary and secondary care for several reasons. One conclusion

TABLE 4 Mean (S.D.) NHS costs over 24 months (£) (complete case analysis)

	Cost, mean (S.D.), £		Difference (95% CI)
	Injection (*n* = 95)	Splint (*n* = 96)	
Health professionals			
GP visits	24.42 (39.98)	29.60 (46.66)	−5.18 (−17.12, 7.55)
Nurse visits	2.84 (14.45)	3.38 (14.38)	−0.53 (−4.55, 3.81)
Physiotherapist visits	13.26 (67.54)	11.72 (44.88)	1.54 (−12.18, 19.85)
Surgeon visit	28.74 (58.99)	30.47 (72.41)	−1.73 (−20.28, 17.11)
Rheumatologist visit	9.47 (56.42)	11.25 (39.72)	−1.78 (−14.41, 13.74)
Acupuncturist visit	—	1.88 (18.37)	−1.88 (−6.75, 0.00)
Occupational therapist visit	3.54 (14.58)	7.44 (33.93)	−3.90 (−11.64, 2.51)
Other health professionals	4.74 (23.13)	3.41 (16.65)	1.33 (−4.01, 7.71)
Investigations and interventions			
X-ray	1.81 (9.24)	3.59 (13.69)	−1.78 (−5.43, 1.18)
Blood test	1.26 (8.88)	1.18 (5.05)	0.08 (−1.46, 2.78)
Ultrasound	1.15 (7.94)	1.72 (12.49)	−0.56 (−4.29, 1.79)
MRI scan	12.08 (72.72)	3.42 (23.55)	8.67 (−2.51, 28.99)
Carpal tunnel surgery	415.22 (760.37)	354.86 (718.13)	60.36 (−140.66, 280.37)
Night splint during follow-up[a]	4.29 (15.91)	8.14 (17.95)	−3.85 (−8.52, 0.81)
Carpal tunnel injection during follow-up[a]	18.08 (29.54)	18.14 (43.64)	−0.06 (−11.92, 8.83)
Wrist exercises	15.63 (139.05)	1.41 (13.78)	14.23 (−2.57, 57.44)
Nerve conduction studies	36.47 (93.77)	30.93 (90.57)	5.54 (−20.35, 33.17)
Prescribed medication	5.05 (24.58)	20.03 (137.30)	−14.99 (−57.53, 2.41)

[a]Participants were asked, 'In the last 6 months have you had any investigations or treatments in the NHS, privately or tried yourself?' The number of wrist splints and injections recorded by participants in each arm of the trial over each 6-month period of follow-up are summarized in Table 3.

may be that those treated earlier have a better outcome, but consistent evidence for this is lacking [25]. A further assumption may be that treatment setting may dictate eventual surgical treatment, over clinical need. Again, evidence for this is lacking. Importantly, it is not possible to compare directly the patient reported outcome for each treatment option between these different types of studies, which would be required to make a definitive conclusion about overall patient benefit from CTS treatment.

Strengths and limitations

Strengths of this trial include collecting long-term outcomes with low attrition and a further full long-term health economic analysis. Limitations of the trial remain the absence of a no-treatment control group and no group receiving both interventions. The potential competing effect of a surgical intervention or further conservative management (e.g. a repeat corticosteroid injection or longer-term splint wearing) was not considered, given the small proportion of participants receiving further treatment and likely risk of confounding by indication. Further research should consider the additional participant reported benefit of combined CSI and NS, repeat CSI, longer term use of splints, and surgery.

Implications for clinical practice

More rapid initial improvement following corticosteroid injection led to it being more cost-effective from both an NHS and a societal perspective at 6 weeks; 12- and 24-month results further add to the preceding evidence of only short-term comparative effectiveness of CSI *vs* NS but that continuing improvement beyond 12 months can still be observed with either initial intervention. This is in line with many other studies of the effectiveness of local steroid injections [26], with short-term benefit but no long-term gain. This gives patients a clear choice: CSI is the treatment of choice if short-term benefit is required, but the patient needs to be counselled that it is unlikely to alter the overall course of the condition.

The idea of a one-off injection may seem preferable compared with wearing a NS for 6 weeks. Likewise, those who may be needle-phobic or for whom CSI are contraindicated may opt for NS. Patient choice must therefore be strongly advocated.

Conclusion

Over 24 months, while there were no differences in the clinical effectiveness of corticosteroid injection compared with night splinting, surgical intervention was slightly more frequent in the CSI group, and NS may be cost-effective when compared with CSI. Overall, surgical referral and intervention rates were low, but we cannot comment on the reasons for and outcomes of the surgical intervention. Patients receiving conservative treatment in a primary care setting for mild to moderate CTS can be reassured that fewer than one in four of them will need surgery over the next 2 years. Patients can be informed that symptoms are likely to improve over time and patient choice between CSI or NS can be encouraged in initial management decisions.

Acknowledgements

Data availability statement

Data for this study will be made available to others in the scientific community upon request after publication. Data will be made available for scientific purposes for researchers whose proposed use of the data has been approved by a publication committee. Data and documentation will be made available through a secure file exchange

platform after approval of proposal and a data transfer agreement is signed (which defines obligations that the data requester must adhere to with regard to privacy and data handling). Partially deidentified participant data limited to the data used for this work will be made available. For data access, contact the corresponding author.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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