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Carpal tunnel syndrome and work: time course of nerve impairment, incidence rates as sentinels of harmful occupational exposure, and prognosis

PhD dissertation

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PREFACE

This dissertation presents the work carried out in the years 2014 to 2017 at the Department of Occupational Medicine, Danish Ramazzini Centre, Aarhus University Hospital, the Department of Clinical Neurophysiology, Aarhus University Hospital and was funded by the Danish Working Environment Research Fund (grant no. 27-2013-03/20130023574).

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THE DISSERTATION IS BASED ON THE FOLLOWING PAPERS

Paper I Tabatabaeifar S, Svendsen SW, Johnsen B, Hansson GA, Fuglsang-Frederiksen A, Frost P. Reversible median nerve impairment after three weeks of repetitive work. Scand J Work Environ Health 2017;43(2):163-70. doi: 10.5271/sjweh.3619.

Paper II Tabatabaeifar S, Svendsen SW, Frost P. Carpal tunnel syndrome as sentinel for harmful hand activities at work: a nationwide Danish cohort study. [Manuscript]

Paper III Tabatabaeifar S, Svendsen SW, Johnsen B, Fuglsang-Frederiksen A, Frost P. Prognosis of symptoms and disability among patients with suspected carpal tunnel syndrome: influence of occupational mechanical exposures and abnormal median nerve conduction. [Manuscript]

LIST OF ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
AL	Action Limit
BMI	Body Mass Index
CI	Confidence Interval
CRS	The Civil Registration System
CTS	Carpal Tunnel Syndrome
DISCO-88	The Danish version of the International Standard Classification of Occupations from 1988
DISCO-08	The Danish version of the International Standard Classification of Occupations from 2008
DML	Distal Motor Latency
DNPR	The National Patient Register
ECM	The Employment Classification Module
EMG	Electromyography
HAL	Hand-Activity Level
HAVs	Hand-Arm Vibrations
ICD-10	The International Classification of Diseases, 10th revision
IR	Incidence Rate
JEM	Job Exposure Matrix
MCID	Minimal Clinical Important Difference
MNCV	Motor Nerve Conduction Velocity
MSDs	Musculoskeletal Disorders
NOMESCO	The Nordic Medico-Statistical Committee
MVE	Maximal Voluntary EMG activity
NCS	Nerve Conduction Studies
NCSP-D	The Danish version of the NOMESCO Classification of Surgical Procedures
NSAID	Non-Steroidal Anti-Inflammatory Drug
OR	Odds Ratio
OR_{adj}	Adjusted Odds Ratio
PR_{adj}	Adjusted Prevalence Ratio
SD	Standard Deviation
SES	Socioeconomic Status
SIR	Age-standardised Incidence Rate
SNCV2	Sensory Nerve Conduction Velocity digit 2
SNCV3	Sensory Nerve Conduction Velocity digit 3
TLV	Threshold Limit Value

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1. INTRODUCTION

Carpal tunnel syndrome (CTS) occurs when the median nerve, due to compression and traction in the carpal tunnel, causes symptoms and functional deficits in the innervated fingers.[1-3] Patients present with symptoms of tingling, numbness, pain, and fine motor skills problems. Some patients have nocturnal symptoms with awakening and shaking of their hands to alleviate symptoms.[1,4] Several clinical tests have been described in the diagnosis of CTS, but none of them are diagnostic on their own. Nerve conduction studies (NCS) in combination with relevant symptoms are believed to be the most accurate way of diagnosing CTS – but no diagnostic gold standard exists for CTS.[1,4-9]

In Denmark, with an adult population of around 4.3 million people, in 2016 app. 26,000 hospital contacts were under the diagnosis 'mononeuropathy of upper limb' of which CTS is by far the most common.[10]

Prevalence of CTS in general populations is reported with a high variation, ranging from 1% to 16%, depending on the definition of CTS.[4,9,11-13] In general, the prevalence of neurophysiological confirmed CTS is higher in working populations than in general populations; 5-21% for meat-packers and manufacturing vs. 1-5% in general populations.[14] The incidence rates (IRs) are also higher in working populations than in general populations. For example in studies from USA and Italy, IRs of 231 and 365 per 10,000 person-years, respectively, were found.[14,15] When compared to IRs from general population studies, which range from app. 5 to 70 per 10,000 person-years, it seems quite likely that risk factors for CTS are present among certain working populations.

Several systematic reviews and meta-analyses in the last decade have concluded that occupational exposures are risk factors for CTS.[16-20] The occupational exposures in question are exposures to hand-arms vibrations (HAVs), force exertion, repetition, and repetition in combination with force exertion. Limited evidence exists for wrist postures as an occupational risk factor.[16,18-21]

Little is known about the time relation between starting in a job that involves high mechanical exposures to the wrist and the development and course of median nerve dysfunction. And conversely, little is known about recovery of median nerve dysfunction after exposure termination. Three human studies indicate that CTS has a short induction period:

1. In Ohio, among newly hired pork processing employees who were followed, NCS showed impaired median nerve conduction after a mean of 64 work days.[22]

2. A study set in a lamb slaughter and processing plant in New Zealand, found that the majority of the workers who underwent surgery for CTS did so during their first three season of work, i.e. early in their career.[23]

3. A large American study found higher IRs of CTS among workers with less than 3 years of seniority compared to workers with more than three years seniority which also indicates that CTS occurs early in a worker's career.

A sentinel health event (SHE) is defined as a negative health indicator that signals the need for "scientific search for remediable underlying causes" of the negative health event in order to prevent future cases, death and reduce disability due to the SHE.[24,25] Occupational diseases can also be a SHE.[26] Sentinel health surveillance of the work environment by means of national administrative and medical registers may be attractive because national systems for recording and notification of occupational injuries suffer from general problems of under-reporting and potentially biased reporting due to legal aspects involving compensation.[13,27] Moreover, population-based health surveillance by questionnaires and clinical/or paraclinical examinations are labour intensive and expensive.[12,28,29] If workers are asked directly if their musculoskeletal disorders are caused by work, a substantial overestimation is likely to occur due to self-reported exposure to occupational risk factors are imprecise, usually inflated.[30-32] Exposure monitoring is also resource demanding, whether by direct technical measurements, observation, or self-report.

Although many patients undergo NCS on suspicion of CTS only little is known about the course of symptoms and disability, both overall and in relation to the result of NCS, choice of treatment, occupational biomechanical exposures, and lifestyle factors.[33] Despite the low level of evidence, a European multidisciplinary treatment guideline recommends that patients with CTS should reduce heavy work activities and avoid repetitive movements.[34]

Only a few studies, all with moderate to high risk of bias, have examined the course of untreated CTS and non-surgically managed CTS.[33] The studies found that 28%-68% of patients recovered or did not worsen if untreated.[33] Two of the studies found that app. one third of CTS patients had a clinical improvement after twelve months of follow-up.[35,36] Another study reported that about one third of 257 CTS patients were completely free of symptoms after a mean of six months.[37] These studies indicate that some CTS cases may be self-limiting and that an adaptation of the median nerve occurs.[33,36]

2. AIMS AND HYPOTHESIS

The primary aim of this dissertation was to evaluate the use of CTS as a signal disease of occupational exposures to harmful hand activities. Three studies were undertaken with the following specific aims:

Study I: To evaluate median nerve function in relation to three weeks of hand-intensive seasonal work.

We hypothesised that at the end of the work season median nerve conduction would be impaired and then recover within weeks.

Study II: To evaluate the use of IRs of CTS diagnoses as sentinels, which can identify occupational groups with high mechanical exposures to the wrist.

We hypothesised that elevated IRs of CTS within occupational groups signal harmful hand activities.

Study III: To evaluate occupational mechanical exposures and abnormal median nerve conduction as prognostic factors for symptoms and disability among patients with suspected CTS.

We hypothesised that high mechanical exposures were associated with poorer prognosis.

3. BACKGROUND

3.1 Carpal tunnel syndrome

CTS occurs when the median nerve, due to compression and traction in the carpal tunnel, causes symptoms and, in later stages, functional deficits in the innervated fingers.[1-3] The carpal tunnel is located at the wrist with the flexor retinaculum, aka the transverse carpal ligament, as its ceiling and the carpal bones as its walls. Nine flexor tendons and the median nerve pass through the tunnel.[1,2] The median nerve supplies the three radial digits, the radial side of digit four, and the radial two-thirds of the palm with sensory branches. It also innervates the thenar muscles with its motor branch in addition to the first and second lumbrical muscles. Patients present with symptoms of tingling, numbness, pain, and fine motor skills problems such as holding a pen or buttoning shirts. In theory, the sensory symptoms are limited to the innervated parts of the hand. Some patients have nocturnal symptoms with awakening and shaking of their hands to alleviate symptoms.[1,4] Several clinical tests have been described in the diagnosis of CTS, but none of them are diagnostic on their own and additional clinical or neurophysiological tests in the presence of relevant symptoms are required. The most used clinical tests are Tinel's sign and Phalen's manoeuvre.[1,4,38]

No diagnostic gold standard exists for CTS.[1,4-9] CTS is the most common nerve entrapment neuropathy accounting up to 90% of all entrapment neuropathies.[4] About 60% of the cases are bilateral and the dominant hand is often first affected.[39,40]

3.2 Carpal tunnel syndrome case definition

NCS in combination with relevant symptoms are believed to be the most accurate way of classifying CTS – but no gold standard case definition exists for CTS.[1,4-9] However a relative high degree of agreement has been found when different case definitions were applied in the same working population.[41] In 1998, an international consensus regarding case definitions of CTS in epidemiological studies was reached among experienced epidemiologists and clinicians who had done extensive research in the field of CTS.[5] Two sets of case definitions for CTS were proposed; one requiring the combination of NCS and symptom assessment, and another set, the combination of physical examination findings and symptom assessment when NCS are not available.[5]

Often in epidemiological studies of CTS, the Katz hand diagram is used to map symptom distribution[5,42] and the Levine questionnaire (aka Boston Carpal Tunnel Syndrome Questionnaire) is used to quantify symptom severity and functional deficits.[5,43] The Katz hand diagrams are usually classified as 'classic/probable', 'possible', and 'unlikely' CTS.[42]

The Levine questionnaire is side-specific and measures two components; symptom severity and functional status with 11 and 8 items, respectively. Each item is scored from 1 (least) to 5 (most severe). A mean is calculated for the symptom and function scores.[43]
Some studies have also used the Disabilities of the Arm, Shoulder and Hand questionnaire (DASH),[44] which wasn't specifically developed for CTS in contrast to the Levine questionnaire,[43] but for upper extremity musculoskeletal conditions.[44] DASH has been shown to have a comparable responsiveness and validity as an outcome instrument for CTS.[45,46] A validated and approved Danish translation of DASH was developed in 2010.[47] The DASH contains 30 items concerning the combined disability of both upper extremities and yields a score ranging from 0 to 100 with greater disability scoring higher.[47]

In nerve conduction studies (NCS), nerve function is assessed and can be quantified. In entrapment neuropathies, there will often be a delay of signal conduction through the nerve fibres at the point of the entrapment, which can be located using NCS.[4,38] NCS in the diagnosis of CTS examines motor and sensory function of the median nerve by applying a depolarising electrical stimulus to the skin over the median nerve at various anatomical locations, e.g. elbow or wrist. A nerve action potential propagate along the nerve giving rise to a sensory nerve action potential (SNAP) that can be recorded at another location over the nerve, and to a compound muscle action potential (CMAP) that can be recorded over the muscle innervated by the nerve. Both the SNAP and CMAP are recorded using surfaces electrodes placed at other locations along the nerve or over innervated muscles.[48] A number of different parameters are measured in a NCS of patient suspected of CTS. Those used in the diagnosis of CTS and in the electrodiagnostic case definitions used in papers I and III are explained here:
The distal motor latency (DML) is the time between the stimulation and the start of the CMAP at the distal part of the median nerve over a standard distance (from wrist to m. abductor pollicis brevis).[48] It is measured in milliseconds (ms). Longer latency indicates slowing of nerve conduction. In paper I, motor nerve conduction velocity (MNCV) is used to assess the motor nerve conduction in the forearm. MNCV is found as the difference in motor latency from stimulation at the elbow and the wrist, corresponding to the conduction time at the forearm, over the measured distance between the two stimulus sites. MNCV is measured in meters per seconds (m/s).
Sensory nerve conduction velocity (SNCV) is the conduction distance divided by the sensory latency where the sensory latency is the time from stimulating the nerve to the start of the sensory nerve action potential (SNAP). SNCV is measured in m/s and are found for digits 2 and 3.
To compare with a nerve not passing through the carpal tunnel, DML and SNCV for the distal part of ulnar nerve supplying m. abductor digiti minimi and digit 5 with sensory fibres, respectively, are

also examined. If the ulnar nerve is impaired in combination with the median nerve this could indicate a more generalised disorder, e.g. a polyneuropathy. Even though NCS are considered accurate in examining median nerve dysfunction, asymptomatic persons can have abnormal NCS findings, and vice versa, despite having symptoms suggestive of CTS, NCS can be without abnormal findings.[4,8,11]

3.3 Pathophysiology of carpal tunnel syndrome

The precise pathophysiological mechanisms leading to CTS are not clear but compression and traction are believed to be important factors.[2,49] There is evidence pointing to the compression of the median nerve is caused by an increase in the carpal tunnel pressure,[50,51] which may start a cascade of changes; initially oedema, microcirculation dysfunction and ischemia. Prolonged periods of increased carpal tunnel pressure are then believed to lead to alterations in the blood-nerve barrier, altered ion channel function and expression, thinning of myelin, and axonal degeneration.[1-4,52,53]

Occupational mechanical exposures to the wrist are believed to potentially lead to CTS through an increased pressure in the carpal tunnel which starts the abovementioned pathophysiological process (see section 3.5.1).[18,54]

Little is known about the time relation between starting in a job that involves high mechanical exposures to the wrist and the development and course of median nerve dysfunction. And conversely, little is known about recovery of median nerve dysfunction after exposure termination. Three human studies indicate that CTS has a short induction period:

1. In Ohio, among newly hired pork processing employees who were followed, NCS showed impaired median nerve conduction after a mean of 64 work days.[22]
2. A study set in a lamb slaughter and processing plant in New Zealand, found that the majority of the workers who underwent surgery for CTS did so during their first three season of work, i.e. early in their career.[23]
3. A large American study found higher IRs of CTS among workers with less than 3 years of seniority compared to workers with more than three years seniority which also indicate that CTS occurs early in a worker's career. Additionally it indicates that workers with more than 3 years of seniority are a selected population, i.e. healthy worker survivor bias is at play (see section 3.5.1).[55]

One study has examined median nerve recovery in non-operated workers with CTS: Bonfiglioli and colleagues re-examined assembly line workers with CTS after two years using NCS. They found that due to reduced exposures for five months preceding the follow-up, the workers tended to recover. Among the 32 who participated at baseline, they found only four cases at follow-up in contrast to the 14 cases at baseline.[56]

Median nerve impairment has also been studied in experimental animal studies including rats and monkeys. In rats it has been shown that impaired median nerve conduction occurs after 9-12 weeks of exposure to tasks characterized by high repetition and low force,[57,58] moderate repetition and high force,[59] and high repetition and high-force.[60] Recovery time was not studied in the referenced rat studies.[58,60]

In macaque monkeys, a close temporal association was found between 12-20 weeks of performing a moderately forceful, repetitive task and the development of abnormal NCS.[61,62] Recovery occurred 10-20 weeks after exposure cessation.[62] The authors found it unlikely that the observed changes would occur this quickly in humans.[61]

If, as the nonhuman primate model suggests, a short induction period is followed by a recovery phase among humans, and an impairment of nerve function is reversible in the first phases, early identification could be important to prevent chronicity. Another perspective is that surveillance of nerve function could be utilized as a sensitive assessment tool to direct workplace interventions in order to reach safe exposure levels.

3.4 Treatment, prognosis and course of untreated carpal tunnel syndrome

Treatment for CTS can be divided into surgical and non-surgical.

Ultrasound, splinting, manual therapy, corticosteroid injections, oral corticosteroids, diuretics, and non-steroidal anti-inflammatory drugs (NSAIDs), are some of the non-surgical treatments offered to CTS patients. Cochrane reviews about therapeutic ultrasound[63] and splinting[64] concluded that the evidence regarding their effectiveness as treatment options for CTS, is lacking when compared to other non-surgical treatments; and in case of splinting, compared to placebo. A systematic review,[65] a Cochrane systematic review,[66] and an update of UK evidence report[67] found inconclusive evidence for effectiveness of various manual therapy treatments for CTS, e.g. mobilisation of carpal bone, soft-tissue mobilisation and trigger point therapy. Likewise, limited evidence exists for ergonomic equipment in the treatment of CTS including ergonomic keyboards.[68] Steroid injection has been shown to relieve symptoms up to one month after injection compared to placebo, but significant symptom relief beyond this period has not been demonstrated. Limited evidence exists for the efficacy of NSAIDs or diuretics as treatments for

CTS.[65] The course of non-surgical managed CTS varies considerably and studies found that 58%-66% of patients underwent surgery after an initial 1-3 years of non-surgically management.[33]

Surgical intervention for CTS is broadly speaking divided into two types; open surgery and closed, endoscopic surgery. Modifications of both surgery types exist.[1,49] They all have the same purpose of increasing the volume of the carpal tunnel to relieve the pressure on the median nerve by dividing the flexor retinaculum.[1,49] There is limited evidence of differences in outcome and prognosis between the various surgical technique used,[39,69-71] however a Cochrane review concluded that patients operated with the endoscopic technique returned 8 days sooner to work (95% confidence interval (CI) 2-14 days).[72] Compared to splinting and NSAID plus hand therapy, there is significantly better symptom relief when treated surgically, but compared to steroid injections there is conflicting evidence regarding the effectiveness of surgery at short- and mid-term.[69,73] The prognosis of surgical treatment of CTS is generally good with 70%-90% of patients reporting satisfaction with the outcome.[71,74,75] A high degree of satisfaction and significant improvements were also found after a mean of 13 years of follow-up where 88% of 113 patients reported to be completely or very satisfied with the surgery.[76] A study with a mean of 10.5 years of follow-up found significant symptom and functional improvement assessed using the Levine questionnaire.[77] Interestingly, 58% of 71 asymptomatic patients fulfilled the study's NCS criteria of CTS, suggesting a discrepancy between improvements observed by the patient and NCS.[77]

A non-systematic literature review reported that normal NCS preoperatively, thenar muscle wasting, and diabetes among others were negative prognostic factor for outcome of carpal tunnel surgery.[74] The review concluded that in general, the quality of evidence was low for most of the studies on predictors of outcome.[74] Later published studies and other studies not included in the just-mentioned review, found smoking,[78] and monotonous repetitive work[79] was a negative prognostic factor but neither were in another recent study.[80] A large study of 462 patients associated high BMI with higher levels of symptoms and functional deficits pre- and postoperatively.[81] However, the degree of improvement was the same regardless of BMI.[81] Blue collar work[82,83] and adverse psychosocial exposures[83] may be associated with prolonged sickness absence after surgery for CTS, but the evidence is limited.[84]

Although many patients undergo NCS on suspicion of CTS very little is known about the overall course of symptoms, disability, influence of the result of NCS, choice of (no) treatment, occupational biomechanical exposures, and lifestyle factors on patient reported outcomes.[33] Despite the low level of evidence, a European multidisciplinary treatment guideline recommends that patients with CTS should reduce heavy work activities and avoid repetitive movements.[34] Especially the patients who undergo NCS but aren't diagnosed with CTS have not been studied well.

For patients evaluated on suspicion of CTS abnormal NCS had strong influence on treatment plans to include surgery.[7,85] It was also found that an abnormal NCS compared to a normal NCS may be a predictor of a positive outcome after surgery for CTS,[85] indicating that results of NCS influence treatment choice and may even be a predictor of prognosis.[7,85]

Compared with the non-surgical treatment options for CTS, surgery is likely the most effective option in the long term, albeit it remains unclear if surgery should be the first choice of intervention and if it should be related to the severity of the patient’s symptoms and disabilities.[1,69] It's been stated that the role of non-surgical interventions in the management of CTS are uncertain because it is unclear if they render surgery redundant or merely post-pone surgery.[86] Thus there is uncertainty about the most effective management strategy for CTS.[33,86] A pragmatic approach to the management of CTS would be using evidence-supported non-surgical treatment options or 'watchful waiting' as first choice taking into account the severity of symptoms, functional loss, and patient preference. The second step could be surgical treatment.[1,6,33,71]

Only a few studies have examined the course of untreated CTS. The evidence regarding course of untreated, and non-surgically managed, CTS is weak.[33] Burton and colleagues' review included four studies; two with moderate and two with high risk of bias. The studies found that 28%-68% of patients recovered or did not worsen if untreated.[33] The two studies with moderate risk of bias, found that approximately one third of CTS patients had a clinical improvement after twelve months of follow-up.[35,36] A study not covered by the aforementioned review also reported that approximately one third of 257 CTS patients were completely free of symptoms after a mean of six months.[37] These studies indicate that some CTS cases may be self-limiting and that an adaptation of the median nerve occurs[33,36] so a 'watchful waiting' period is not without its merit even though the length of the period is not defined by the current evidence available.[33]

A brief comment regarding the unit of analysis in a many of the clinical trials that report treatment outcomes and predictors hereof is warranted because CTS can be a bilateral condition. The majority of clinical trials do not account for bilaterality when designing, analysing and reporting the studies. I.e. a patient with bilateral CTS is included twice which 1) violates the common statistical assumption that there is independence between observations and 2) inflates the sample size which can result in a unit-of-analysis error leading to spurious statistical significance due to overly narrow CIs and artificially small p-values.[33,87,88] Statistical methods are available to account for the non-independence of observations, e.g. multilevel modeling,[87] however if the unit of analysis is clear at the level of random allocation (of wrists or of persons), then this would simplify the subsequent statistical analysis of the data.[88]

3.5 Epidemiology and risk factors

The reported incidences of CTS in general populations are quite varied, as can be seen in table 1.

The varying CTS incidences can be explained by many factors: different case definitions used in the studies, different settings, different time periods under study, differences in health-care seeking behaviour, differences in prevalence of CTS risk factors, e.g. diabetes and occupational exposures, and a true difference in CTS incidences between the countries.[8,33,89-91]

Gelfman et al. relied on symptoms only.[90] Even though they did a case review of 194 randomly sampled medical charts, and found that 80% fulfilled CTS symptom quality and location criteria, they did not adjust their age-standardised incidence rate (SIR) estimates accordingly. Of the sampled charts, 45% had an abnormal NCS consistent with median neuropathy. If an adjustment was done, the SIRs in the USA would still be high compared to the other countries. The authors believe the high SIRs indicate a high awareness of CTS in USA, and that attitudes regarding CTS have resulted in more patients presenting with symptoms indicative of CTS.[90]

The registers used in some of the studies in table 1 cover different aspects of the health care system. Some cover both the primary, secondary and tertiary sector,[89] while others only cover the primary sector.[92,93] The latter does not exclude the use of the secondary sector per se, e.g. if patients are referred to a hospital to have NCS performed. Also the diagnosis of CTS from registers is usually accepted at face value without the opportunity to verify the diagnosis.[92] The settings in which the studies originate from also differ with respect to health care sector; some are only from the primary sector[92,93] and others only from the secondary or tertiary sector.[40,94] As expected, including the secondary or tertiary sector restricts the case definition to include more than just symptoms and administrative data, resulting in reduced IRs of CTS.[40,94]

Table 1. General population studies reporting crude IRs and SIRs.

Author, year	Setting	Design	Case definition	Country	Year(s)	IRs (SIRs)[a]		W/M ratio
						Men	Women	
Atroshi et al., 2011[89]	Register study	Register based cohort study	CTS diagnosis according to The Skåne Health Care Register	Sweden (Skåne County)	2006-2008	18.2 (12.5)	42.8 (32.5)	2.4 (2.6)
Bland and Rudofler, 2003[40,90]	Sole regional provider of NCS	Cohort study	Clinician suspected CTS and abnormal NCS	UK (Canterbury, East Kent)	1992-2001	6.7 (6.0)	13.9 (11.8)	2.1 (2.0)
Bongers et al., 2007[90,93]	General practices	Register based cohort study	CTS diagnosis according to the first and second Dutch National Survey of General Practice (ICPC code N93)	The Netherlands	1987	6.0 (7.7)	19.0 (24.0)	3.2 (3.1)
					2001	9.0 (10.5)	28.0 (32.6)	3.1 (3.1)
Gelfman et al., 2009[89,90]	Register study	Register based cohort study	CTS diagnosis according to The Rochester Epidemiology Project medical record linkage system (ICD-8 code 357.2 and ICD-9 code 354.0) based on symptoms only	USA (Olmsted County, Minnesota)	1991-1995	- (26.4)	- (51.0)	- (1.9)
					1996-2000	- (28.1)	- (53.7)	- (1.9)
					2001-2005	- (30.3)	- (54.4)	- (1.8)
Jenkins et al., 2012[94]	Sole regional provider of orthopaedic hand service	Cohort study	Symptoms in combination with: abnormal NCS or thenar wasting or positive Tinel's or Phalen's sign	UK (Fife, Scotland)	2004-2010	4.8 (-)	9.3 (-)	1.9 (-)
Latinovic et al., 2006[90,92]	General practices	Register based cohort study	CTS diagnosis according to the General Practice Research Database (Read and Oxmis codes for CTS)	UK (Wales and England)	1992-2000	8.2 (7.8)	19.9 (19.2)	2.4 (2.5)
Mondelli et al., 2002[12,90]	Four public electromyographic laboratories	Cohort study	History and symptoms of CTS and abnormal NCS	Italy (Siena region, Tuscany)	1991-1998	13.9[b] (10.4)	50.6[b] (42.6)	3.6[b] (4.1)

Roh et al., 2010[91]	Register study	Register based nationwide cohort study	Physician diagnosed CTS without NCS	Korea	2005-2007	27.6 (-)	71.2 (-)	2.6 (-)
Roh et al., 2010[91]	Register study	Register based nationwide cohort study	Physician diagnosed CTS and abnormal NCS	Korea	2005-2007	5.8 (-)	13.8 (-)	2.4 (-)
Roquelaure et al., 2008[95]	Epidemiological surveillance	Cohort study	History and symptoms of CTS and abnormal NCS	France (Maine and Loire region)	2002-2004	6.0 (-)	14.0 (-)	2.3 (-)

[a] Direct age standardized to the 2000 US population according to Gelfman et al.[90]

[b] Direct age standardized to the World Health Organization European Standard Population.

ICD-8 and ICD-9, The International Classification of Diseases, 8th and 9th revision, respectively; IRs, incidence rates per 10,000 person-years; NCS, nerve conduction study; SIRs, age-standardised incidence rates per 10,000 person-years; W/M ratio, women/men ratio.

Prevalence of CTS in the general population is also reported with a high variation, ranging from 1% to 16%, depending on case definitions used.[4,9,11-13] E.g. in a Swedish study, 10.4% of men and 17.3% of women reported symptoms of CTS while the proportion who had both symptoms and clinical findings indicating CTS were 4.6% and 2.8%, respectively. If abnormal NCS was part of the case definition the prevalence was 2% and 3% for men and women, respectively.[11]
In general, the prevalence of neurophysiological confirmed CTS is higher in working populations than in general populations; 5-21% for meat-packers and manufacturing vs. 1-5% in general populations.[14] In a large Italian cohort study a two-year incidence of 3.6% and a baseline prevalence of 3.1% of CTS were found.[15] In USA, a pooled analysis of six prospective cohort studies found an incidence of 2.3% and a prevalence of 7.8%.[14] Both studies required diagnosed CTS by symptoms and abnormal NCS. The IRs are also higher in working populations than in general populations, and in some industries much higher. E.g. in the aforementioned studies from USA and Italy, IRs of 231 and 365 per 10,000 person-years, respectively, were found.[14,15] Compared to IRs from general population studies which range from app. 5 to 70 per 10,000 person-years (table 1) would indicate that occupation can be a risk factor in the development of CTS.

3.5.1 Occupational risk factors

Several systematic reviews and meta-analyses in the last decade have concluded that occupational exposures are risk factors for CTS.[16-20] So has an overview of systematic reviews in which the authors also did a meta-analysis of current research.[20] The occupational exposures in question are exposures to hand-arms vibrations (HAVs), force exertion, repetition (i.e. repetitive flexion and extension of the wrist), and repetition in combination with force exertion. Limited evidence exists for wrist postures as an occupational risk factor with inconsistent results between reviews.[16,18-21] In a recent meta-analysis analyses, Barcenilla et al. used two case definitions and found an association between wrist posture and CTS when using the less conservative case definition but not when the conservative case definition that required abnormal NCS, was used.[18]

An association between computer use and CTS was not found in several of the aforementioned reviews[16,19,20] and the topic remains controversial.[17,18,38,96-99] In an overview of systematic reviews from 2011, the authors found three[16,19,96] medium to high quality systematic reviews that all consistently concluded the epidemiological evidence for computer use and CTS occurrence is insufficient.[100] On this basis the authors concluded that there is insufficient evidence of a causal relationship between computer use and CTS occurrence.[100] A more recent scoping review made a firmer conclusion, namely that there is sufficient evidence of no association between computer use and CTS.[101]

In their meta-analysis Kozak and colleagues quantified the exposure-response relationship using the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value (TLV) for hand-activity level (HAL) based on four high quality studies.[20] In brief, the TLV for hand, wrist, and forearm consist of two components: HAL and peak hand force (PF).[102] HAL is a combined exposure estimate of 1) frequency of exertion (measured in exertions/second or in the reciprocal format, exertion period (seconds/exertion)) and 2) duty cycle (per cent), i.e. the distribution of work and recovery periods in a cycle. A HAL value (0-10) corresponds to different combinations of exertion frequency/exertion periods and duty cycles.

PF and HAL can be determined by different methods, e.g. by a trained observer or technical measurements. They can then be used to calculate a combined score with the following equation:[15,102-104]

$$\text{combined score} = PF/(10-HAL)$$

where a score of <0.56 is below the action limit (AL), a score of ≥0.56 and ≤0.78 is between AL and TLV, and a score of >0.78 is above the TLV according to the ACGIH.[15,102-104] Thus these three combined score categories correspond to low, moderate and high exposure categories.[15,20,102] Kozak and colleagues found a significant exposure-response relationship, with a relative risk (RR) of 1.5 (95% CI 1.02–2.31) and RR 2.0 (95% CI 1.46–2.82) for moderate and high risk, respectively, according to the combined score in the TLV for HAL framework.[20] In other words, Kozak and colleagues found a significant exposure-response relationship for the combined exposures repetition and force.[20] The referenced systematic reviews did not find any exposure-response relationships for any of the other occupational exposures.[16,18-20]

A recent large American cohort study of 2,474 workers published after Kozak et al.'s meta-analysis, found exposure-response relationships between several measures of forceful hand exertion, including force in combination with repetition, with HRs of approximately 1.8-2.2 and 1.5-1.6 for the high and medium exposed tertiles, respectively.[55] The TLV for HAL framework was not utilised in this study. When the analyses were divided in workers with less or more than 3 years of seniority, a healthy worker survivor bias was observed: workers with more than 3 years of seniority had lower risk of CTS compared to those with less than 3 years of seniority. This finding disappeared when using 5 or 7 year cut-points.[55] In another paper where the authors used the TLV for HAL framework, they found elevated risk in the moderate exposure category (i.e. between AL and TLV), but no further increase in risk as the exposure increased (i.e. above TLV).[103]

An Italian cohort was followed-up after two years[15] and after ten years.[104] In the first follow-up no healthy worker survivor bias was observed and an exposure-response association was found using the TLV for HAL framework,[15] unlike at the last follow-up where no increase in risk was found for exposures above TLV.[104] In the latter follow-up, the authors found an IR of 4.7 per 100 person-years among workers who reduced their exposures compared to an IR of 2.7 among those who did not reduce their exposures.[104] The relative magnitude of risk estimates in the American and Italian studies are comparable adding strength to the results.[103,104] It thus seems that there is evidence pointing to:

1. the existence of exposure-response association between combined exposures (repetitiveness and force exertion),
2. but the association has been complicated by healthy worker survivor bias.[55,105,106]
3. and that the current AL in the TLV for HAL framework does not sufficiently protect workers.[15,103,104]

3.5.2 Other risk factors

Non-occupational risk factors for CTS include a variety of factors, some of which are obesity,[107,108] diabetes,[108,109] previous upper extremity fractures,[4,110] inflammatory and degenerative joint diseases,[4,111] and, for women, pregnancy.[4,38,112] Recent meta-analyses found insufficient evidence of an association between CTS and smoking[113] or thyroid disease.[114] Previous associations found between CTS and thyroid disease might have been confounded by obesity among others, and suffered from publication bias.[114]

Overall IRs of CTS increases with age. In contrast to men, where IRs gradually increases with age, women tend to have a perimenopausal peak after progressively increasing IRs during the fertile years.[12,40,89-92,115] Hormonal factors, both pregnancy and menopause associated changes, are possible contributing factors to CTS being approximately 2-4 times more frequent among women than men (table 1). A systematic review of studies utilising NCS in pregnancy related CTS found that the symptoms resolved after one year in approximately half of the cases and in two-thirds after three years, thus leaving roughly 30% with persisting symptoms.[116]

Two studies compared biopsies from CTS cases with controls and found that oestrogen receptors were present in the flexor tendon synovial tissue and in the transverse carpal ligament.[117,118] Specifically, an increase in receptor expression was associated with increasing age with a peak around the menopausal age;[118] among post-menopausal women receptor expression was significantly higher in cases compared to controls.[117] In view of the histological[117,118] and epidemiological studies,[12,40,89-92,115] oestrogen, which is known to have anti-inflammatory properties,[117] seem to be part of the pathophysiology of CTS - at least among women during certain periods of life.

3.6 Assessment of occupational exposures

Occupational mechanical exposures can roughly speaking be assessed using four different techniques:

1. Self-report which is straightforward to utilise, e.g. in a questionnaire, and applicable in large study populations but has a great disadvantage which is recall bias.[30] Recall bias is especially troublesome in studies where the self-report of exposure is done at a time when the participants know their case status and thus could lead to differentiated misclassification.[30,119]
2. Direct or indirect observations of exposures can be simple (e.g. registration on a sheet using checklists) or advanced (video recordings which are analysed using specialised software); the latter are expensive, labour intensive, time consuming and may be more suitable to use in simulated tasks.[30,120] They are generally speaking not feasible in large study populations.
3. Technical measurements of exposures are accurate but measurements are difficult to apply in large study populations due to the same factors as advanced observations of exposures.[30]
4. Expert rated exposures, e.g. by a job exposure matrix (JEM), are inexpensive and applicable in large scale studies, however they are not as accurate as observations or technical measurements.[120,121] A combination of different assessment methods is also possible,[122] as is the inclusion of self-reported exposures in addition to expert rated exposures in a JEM.[121]

Another way to assess the level of exposure (low, moderate, high) could be by a proxy of exposure. E.g. if workers are piecework paid, payslips can be used to assess the level of exposure. However payslips do not let us infer about the quality of the exposure (repetition, force, etc.).

The assessment of occupational mechanical exposures can be done individually or at group level. Broadly speaking, individual-level exposure assessment can generate precise, but possibly biased estimates of associations,[123] unlike, in theory, when a group-level approach is used.[123,124] The resulting estimates of associations using a group-level approach are less precise, however almost unbiased.[123,124] Groups of workers can be constructed based on one or more common characteristics, e.g. job title, place of work, time period, etc.

3.7 Sentinel health event (occupational)

The concept of a sentinel health event (SHE) was conceived by Rutstein in 1976.[24] It is defined as a negative health indicator that signals the need for "scientific search for remediable underlying causes" of the negative health event in order to prevent future cases, death and reduce disability due to the SHE.[24,25] The SHE concept was later expanded to include occupational diseases, SHE occupational (SHE(O)).[26] Through literature survey the SHE(O) list was constructed in 1983[26] and later updated in 1991.[25] In essence the SHE(O) is a list of ICD-9 (the International Classification of Diseases, 9th revision) codes of known or possible work related diseases. SHE(O)s can be divided into two overall categories; in the first category, the diseases included have occupational exposures as their undoubtedly most dominant cause (e.g., asbestos induced mesothelioma and sinonasal cancer due to wood dust exposure). Diseases in the second category can be work-related, but may also not be work-related.[25,26]

One of the intended uses of the SHE(O) list was surveillance,[25,26] which diseases in both categories can be used for, i.e. surveillance of the work environment. In 1991 CTS was added to the SHE(O) list and is in the second category of SHE(O)s.[25] While a single disease case in the first category indicates that exposure to a specific detrimental occupational agent is extremely likely, in order to use diseases in the second category for surveillance, a group-based approach is necessary. E.g., elevated IRs of CTS in specific groups of workers may serve as a signal that could point to harmful occupational exposures to the wrist, and thereby guide and monitor the effects of preventive interventions.

Sentinel health surveillance of the work environment by means of national administrative and medical registers may be attractive because national systems for recording and notification of occupational injuries suffer from general problems of under-reporting and potentially biased reporting due to legal aspects involving compensation.[13,27] Moreover, population-based health surveillance by questionnaires and clinical/or paraclinical examinations require large efforts.[12,28,29] If workers are asked directly if their musculoskeletal disorders (MSDs) are caused by work, a substantial overestimation is likely to occur due to self-reported exposure to occupational risk factors are imprecise, usually inflated.[30-32] Exposure monitoring is also resource demanding, whether by direct technical measurements, observation, or self-report.

CTS has been used as a sentinel event for upper limb MSDs in an epidemiological surveillance program in the Pays de la Loire region of France in 2002-2004.[13,95] The aim of the program was to estimate the frequency of CTS in the general population due to an increased occurrence MSDs in France. The program included five sentinel physicians of the only four providers of NCS in the region. However one physician notified very few cases to the surveillance program and another physician left the network early resulting in incomplete catchment of cases in the study.[13,95] This is a testament to the vulnerability of such a setup which makes using readily available national administrative and medical registers in Denmark more appealing.

4. METHODS

4.1 Study overview

An overview of the methods and designs used in the three studies of this dissertation is given in table 2. Additional information on methods is available in the following sections and in greater detail in the appended papers I-III - particularly about the use of the JEM in studies II and III.

Table 2. Overview of methods and designs

	Study I	Study II	Study III
Title	Reversible median nerve impairment after three weeks of repetitive work	CTS as sentinel for harmful hand activities at work: a nationwide Danish cohort study	Prognosis of symptoms and disability among patients with suspected CTS: influence of occupational mechanical exposures and abnormal median nerve conduction
Design	Field study of a prospective cohort doing seasonal work	Register based nationwide cohort study	Prospective patient cohort study
Population	11 mink skinners	2,309,434 persons	361 patients
Follow-up	3-6 weeks post-season	2010-2013	9-12 months
Exposure	Mink skinning	Occupational mechanical exposures	Occupational mechanical exposures and personal factors
Exposure assessment	Technical measurements and payslips of no. of minks skinned day-by-day	JEM	JEM
Outcome	Median nerve function and CTS	First-time CTS diagnosis	Change of symptoms and disability
Outcome assessment	NCS	The DNPR	Questionnaire information (Levine and DASH)
Confounders	None	Sex specific analyses, age, pregnancy, diabetes	Age, sex, BMI, smoking, alcohol, surgery
Main analyses	Paired t-test	SIRs	Multivariate linear regression and Poisson's regression

BMI, body mass index; CTS, carpal tunnel syndrome; DASH, Disability of the Arm, Shoulder and Hand; DNPR, the Danish National Patient Register; IRs, incidence rates; JEM, job exposure matrix; NCS, nerve conduction studies; SIR, age-standardised incidence rates.

4.2 Study I

Design, population and setting

We conducted a prospective cohort study of 11 mink skinners from one mink skinning facility in Denmark, applying pre-, mid-, end-, and post-season NCS. Mink skinning is hand-intensive, seasonal work, which takes place during a few weeks each year, thus providing us with a natural experimental setting. The study took place from November 2014 to January 2015.

Exposure characteristics and outcome

Mink skinning was performed in day- and evening-shifts of 7.5 hours. For each participant, we obtained day-by-day accounts of the number of minks skinned from payslips and for 6 day-shift workers full shift exposure measurements of their dominant arm and hand were performed by ST. The day-by-day accounts of minks skinned were obtained to ensure that the days of measurement were representative for the whole season. The technical measurements consisted of postures and movements of the wrist using goniometers[125] and surface electromyography (EMG) of the forearm extensors to measure force exertion (percentage of maximal voluntary EMG activity (%MVE).[126,127] At all four occasions, NCS were performed by the same experienced technician according to the department standards. Age-specific reference values of the department were used to calculate z-scores for each participant.[128] A z-score was considered abnormal if larger than 1.96. The department's electrodiagnostic criteria for CTS were that at least two of the three z-scores for the median nerve DML, SNCV digit 2, and SNCV digit 3 were abnormal in the presence of normal ulnar nerve parameters.

Symptoms and disability

At pre-, end-, and post-season, the workers filled in a questionnaire which included the Katz hand diagram,[42] the Levine questionnaire,[43] and the Danish translation of the DASH questionnaire.[47] Please refer to section 3.2 for more details about the questionnaires and the hand diagram.

Case definition

Our CTS case definition required the department's electrodiagnostic criteria were fulfilled and that clinical criteria were fulfilled in terms of a Katz hand diagram classified as 'classic/probable' or 'possible'.[5,42]

Personal factors

For descriptive purposes, we collected questionnaire information on various personal and life-style factors.

Statistical analyses

To illustrate changes in NCS parameters over time, we plotted z-scores for each individual. We used paired t-test to evaluate intra-individual changes in NCS parameters and changes in Levine and DASH scores. Two-sample t-test was used to evaluate differences between the mean numbers of minks skinned per hour in day- and evening-shifts across the whole skinning season. Data was analysed using Stata 13 (StataCorp LP, College Station, Texas, USA).

Sample size calculation

We originally intended to include 16 mink skinners in order to detect a SNCV reduction of 2 m/s with a power and significance level of 0.80 and 0.05, respectively.

4.3 Study II

Design and registers used

Study II was a register based nationwide cohort study of the whole working population in Denmark. Due to the long history of collecting information on various aspects of life, including births, deaths, diseases, social conditions, working conditions, high-quality registers exist in Denmark.[129] An overview of the five registers used in study II is provided in table 3. A common shared feature is that they are nationwide and have (almost) complete coverage since they were established.

Table 3. Overview of the high-quality registers used in study II

Register	Start year	Variables used	Time span of used variables
The Civil Registration System (CRS)	1968	ID number; sex; dates of birth, death emigration and disappearance; region of residence	1945[a]-2013
The Employment Classification Module (ECM)	1976	ID number; DISCO-08 codes; socioeconomic status (SES)	2009-2012
The Danish National Patient Register (DNPR)	1977	ID number; date of CTS diagnosis[b]; date of CTS surgery[c]	1994-2013
The National Diabetes Register	2006	ID number; date of diabetes diagnosis	2006-2012
The Medical Birth Register	1968	ID number; date of child birth	2009-2012

ID number, 10 digit unique personal identification number consisting of birth date and a four digit sex specific code; DISCO-08 code, the Danish version of the International Standard Classification of Occupations from 2008; SES, persons classified as employed, unemployed or permanently outside labour market.

[a] CRS includes information for persons born before 1968.

[b] CTS diagnosis: Code DG56.0 according to ICD-10, the International Classification of Diseases, 10th revision.

[c] CTS surgery: Codes KACC51 and KACC61 according to NCSP-D, the Danish version of the Nordic Medico-Statistical Committee Classification of Surgical Procedures

Population

The cohort included all persons born in Denmark, excluding Greenland, between 1 January 1945 and 31 December 1994, who were alive and living in Denmark on 1 January 2009 according to the Civil Registration System. We excluded persons, who were diagnosed with CTS between 1 January 1994 and start of follow-up according to the DNPR, and persons who were permanently outside the labour market before start of follow-up, persons who were in the armed forces the entire period between 1 January 2009 and 31 December 2012 (the JEM did not provide exposure estimates for the armed forces), and persons who did not have at least 1 year of employment with a valid DISCO-08 code in this period according to the ECM.

Exposure and outcome

We validated the signal value of the IRs against exposure measures from an existing JEM based on experts' ratings of occupational arm and wrist exposures (the Hand-arm JEM). The JEM was reconfigured to be able to use the available DISCO-08 codes. To obtain year-by-year information on occupational mechanical exposures to the wrist for all cohort members, we linked each person's DISCO-08 code to the JEM. We collapsed the four exposure dimensions of the JEM (force, repetition, non-neutral wrist position, HAVs) into a single measure of wrist load (please refer to paper II for additional details).

Using the DNPR we identified first-time CTS diagnoses in terms of a primary discharge ICD-10 diagnosis code of G56.0. For descriptive purposes, we also identified first-time CTS surgeries in terms of surgery codes KACC51 (decompression and freeing of adhesions of median nerve) and KACC61 (endoscopic decompression and freeing of adhesions of median nerve) according to the Danish version of the Nordic Medico-Statistical Committee Classification of Surgical Procedures.

Statistical analyses

Sex-specific analyses were done. To obtain robust IR estimates, we constructed job groups by collapsing some of the more detailed categories in DISCO-08 into categories based on lower levels of detail within the same or the numerically closest four-, three-, or two-digit DISCO-08 code. The aim was to obtain at least 100 incident CTS diagnoses per constructed job group. We calculated crude IRs and SIRs for each constructed job group in addition to overall crude IRs. We used a one year time lag, i.e. used the DISCO-08 code in the preceding calendar year where information on CTS diagnosis (no/yes) was looked up (discrete follow up time of one year each) to make sure that the exposure happened before a possible CTS event.

To examine whether the SIRs were associated with the mean wrist load of the job groups, we plotted the mean wrist load against the SIRs together with the linear regression line and calculated the slopes with 95% CIs.

To evaluate the influence of the confounders diabetes, region of residence, and − for women - recent child birth on a first-time CTS diagnosis within job groups, we applied a logistic regression technique equivalent to discrete survival analysis; the resulting odds ratios (OR) can be interpreted as hazard ratios (HR).[130]

4.4 Study III

Design and population

We undertook a prospective cohort study and included patients aged 18-64 with suspected CTS, who were referred for NCS from 19 May 2015 to 29 April 2016. Exclusion criteria were inability to read or write Danish or to cooperate to the NCS and the subsequent clinical examination. After 9-12 months, a follow-up questionnaire was mailed.

Potential prognostic factors

The potential prognostic factors were abnormal nerve conduction of the median nerve evaluated by NCS and occupational mechanical exposures evaluated by linking the participants' job titles to the same Hand-arm JEM used in study II. We constructed the same single measure of wrist load as in study II. Experienced technicians performed NCSs with the use of the same age-specific reference values and electrodiagnostic criteria as in study I. Information on biomedical, personal- and lifestyle factors was extracted from the baseline questionnaire. Information on non-surgical treatment (splinting or corticosteroid injection) and surgery was extracted from the follow-up questionnaire.

Clinical examination and hand diagrams

For descriptive purposes, a standardised clinical examination of the neck and upper extremities including Tinel's and Phalen's test was performed by an experienced physician (ST). The result of the NCS was unknown to patient and examiner at the time of the examination. The baseline- and follow-up questionnaire included the Katz hand diagram,[42] which we classified as "classic/probable", "possible", or "unlikely" CTS.[5,42]

Outcome measures and statistical analyses

Our primary outcome measures were the changes in the Levine symptom and function scores between baseline and follow-up.[43] Our secondary outcome was the change in DASH score.[47] Additionally we analysed the outcomes as binary variables (yes/no) using minimal clinical important differences (MCID) from baseline to follow-up. We included one hand per person and used information for the dominant side in case of bilateral NCS. We applied crude and adjusted linear regression of the primary and secondary outcomes and the potential prognostic factorss. Prevalence of MCID in Levine symptom and function and of DASH scores were analysed using Poisson regression with robust error variance technique.[131]

5. RESULTS

The following section summarizes the main results of study I-III and presents additional results not in the appended papers.

5.1 Study I

11 male mink skinners participated and outside the skinning season, all were students or had jobs that did not entail repetitive movements. The task of mink skinning was characterized by a median extension of the wrist of 16º, a median velocity of wrist flexion/extension of 22 degrees/second, and force exertions of 11 %MVE. The skinning season lasted 22 calendar days. The mean number of days worked was 20.

All mink skinners had normal pre-season median nerve values. Nine of the 11 mink skinners showed changes in the direction of median nerve impairment during the skinning season with subsequent recovery. At end-season, five mink skinners had abnormally increased median nerve DML. Four and six participants had abnormally decreased SNCV digit 2 and SNCV digit 3, respectively. Five fulfilled our electrodiagnostic criteria for CTS at end-season.

From pre- to end-season, an increase in median nerve DML and a decrease in median SNCV digit 2 and SNCV digit 3 occurred; thus, sensory and motor changes occurred simultaneously. From end- to post-season, the changes reversed. There were no significant differences between pre- and post-season. There were no significant changes for the ulnar nerve.
The number with an ipsilateral hand diagram that was classified as 'classic/probable' or 'possible' was 2, 8, and 2, at pre-, end-, and post-season, respectively, and our case definition of CTS was fulfilled by 0, 4, and 0, respectively.

The mean Levine symptom score value of 1.3 (95% CI 1.0-1.7) at pre-season increased to 2.1 (95% CI 1.5-2.7) at end-season (P=0.022) and subsequently decreased to 1.3 (95% CI 0.9-1.7; P=0.012). All Levine function scores were about 1.1 with no significant changes. The development of the mean DASH score was parallel to the changes in the Levine symptom scores (see paper I).

5.2 Study II

The sex-specific study cohorts included 1,171,580 men and 1,137,854 women who were followed for 4,046,851 and 3,994,987 person-years, respectively. 4,405 cases of CTS were identified among men and 7,858 among women, corresponding to an IR of 10.9 (95% CI 10.6 to 11.2) per 10,000 person-years among men and 19.7 (95% CI 19.2 to 20.1) per 10,000 person-years among women. The number of CTS surgeries was 2,127 for men, including 30 operations that were not preceded by a registered CTS diagnosis (IR 5.3, 95% CI 5.0 to 5.5). Corresponding numbers for women were 4,311 and 61 (IR 10.8, 95% CI 10.5 to 11.1).

A wide range of SIRs were found. For men (table 3 in paper II), the SIRs ranged from 3.7 per 10,000 person-years for job group 21 ('health and legal professionals') to 23.7 for job group 90 ('civil engineering labourers'). For women (table 4 in paper II), the SIRs ranged from 10.1 for job group 20 ('science, business and information professionals') to 42.9 for group 80 ('operators and assemblers').

For both sexes, groups characterised by office and computer work (10-23 and 31-32 among men and 24, 26, and 31-41 among women) did not have elevated SIRs or odds. The job group ORs hardly changed when we adjusted for diabetes, region of residence, and child birth.

In the fully adjusted model, the ORs for diabetes were 1.8 (95% CI 1.6 to 2.0) for men and 2.0 (95% CI 1.8 to 2.2) for women. The OR for recent child birth was 1.8 (95% CI 1.6 to 2.0). Being in age groups 35-49 years and 50-65 years compared to 18-34 years yielded ORs of 2.0 (95% CI 1.8 to 2.2) and 2.8 (95% CI 2.6 to 3.1) for men and 2.4 (95% CI 2.2 to 2.6) and 3.5 (95% CI 3.3 to 3.8) for women.

For both sexes (figures 2 and 3 in paper II), there was a clear association between mean wrist load and SIRs with a steeper slope for men (beta=0.13 (95% CI 0.11 to 0.16) for men and 0.05 (95% CI 0.04 to 0.07) for women).

Additional results from study II are presented in the supplementary documents (section 12.1): the supplementary tables 1 and 2 show the contents of the constructed job groups. Figures of each of the four exposure dimensions covered in the Hand-arm JEM plotted against SIRs of CTS are provided in supplementary figures 1 to 8.

5.3 Study III

Of the 499 participants who provided baseline questionnaire data, 361 (72.3%) responded to the follow-up questionnaire. 187 participants had a normal NCS and 174 an abnormal. During follow-up, 21 participants (11.2%) and 95 participants (55.2%) with normal and abnormal NCS, respectively, underwent surgical treatment.

Additional results from study III are presented here: non-response descriptive statistics of baseline DASH scores, and results from uni- and multi variable linear regression of paired differences of improvements of DASH scores (table 4).

Overall non-responders and responders were comparable with respect to DASH score (26.5 (95% CI 23.6 to 29.4) vs. 24.9 (95% CI 23.1 to 26.7)). Stratified on NCS groups, non-responders with normal NCS had a higher DASH score compared to responders with normal NCS (29.9 (95% CI 26.0 to 33.8) vs. 25.0 (95% CI 22.3 to 27.6)). Conversely, non-responders with abnormal NCS had a lower DASH score compared to responders with abnormal NCS (20.9 (95% CI 16.9 to 24.8) vs. 24.8 (95% CI 22.3 to 27.3)).

No clear associations were found between the potential prognostic factors and change in the DASH score (table 4).

Table 4. Mean DASH score at baseline and at follow-up and results of uni- and multivariable linear regression of change scores. DASH score range is 0 (best) to 100 (worst).

	Mean score			Change score						
	N	**Baseline**	**Follow-up**	**Mean**	**$Diff_{crude}$**	**95% CI**	**$Diff_{model\ 1}$[a]**	**95% CI**	**$Diff_{model\ 2}$[b]**	**95% CI**
NCS result										
Normal	181	25.0	22.8	2.2	Ref.	-	Ref.	-	Ref.	-
Abnormal	168	24.4	18.3	6.1	3.9	0.9 to 6.8	3.5	0.14 to 6.8	2.5	-1.1 to 6.1
Wrist load										
Low	167	23.2	19.1	4.0	Ref.	-	Ref.	-	Ref.	-
Moderate	87	26.2	22.9	3.4	-0.7	-4.4 to 3.0	-0.7	-4.6 to 3.1	-0.8	-4.7 to 3.0
High	54	22.8	18.1	4.8	0.7	-3.6 to 5.1	-1.3	-6.2 to 3.6	-1.6	-6.5 to 3.3
Surgical treatment										
No	236	24.1	21.2	2.9	Ref.	-	-	-	Ref.	-
Yes	113	26.0	19.5	6.5	3.6	0.4 to 6.7	-	-	2.6	-1.3 to 6.5
Age (years)										
18-34	56	25.5	21.0	4.5	Ref.	-	Ref.	-	Ref.	-
35-49	128	25.0	19.8	5.1	0.6	-3.8 to 5.0	0.3	-4.8 to 5.4	0.3	-4.7 to 5.4
50-64	165	24.3	21.2	3.1	-1.4	-5.7 to 2.9	-2.2	-7.2 to 2.8	-2.3	-7.3 to 2.7
Sex										
Male	104	19.9	16.5	3.4	Ref.	-	Ref.	-	Ref.	-
Female	245	26.8	22.4	4.3	0.9	-2.3 to 4.1	-1.0	-4.8 to 2.9	-1.0	-4.9 to 2.8
BMI (kg/m^2)										
≥17-<25	140	23.7	18.7	5.0	Ref.	-	Ref.	-	Ref.	-
≥25-<30	108	23.5	20.2	3.3	-1.7	-5.2 to 1.8	-3.6	-7.4 to 0.3	-3.4	-7.3 to 0.4
≥30-48.9	93	26.8	22.9	3.9	-1.1	-4.8 to 2.6	-3.3	-7.4 to 0.8	-3.5	-7.6 to 0.6
Smoking status										
Never	159	22.4	18.6	3.8	Ref.	-	Ref.	-	Ref.	-
Current	66	30.8	28.0	2.9	-0.9	-5.0 to 3.1	-1.3	-5.9 to 3.2	-1.3	-5.8 to 3.2
Ex	112	23.9	18.5	5.3	1.5	-1.9 to 4.9	2.1	-1.6 to 5.9	2.3	-1.5 to 6.0
Alcohol consumption (units/week)										
≤1	154	29.8	24.8	5.0	Ref.	-	Ref.	-	Ref.	-
>1-<7	125	20.9	16.9	4.0	-1.0	-4.3 to 2.3	-2.6	-6.3 to 1.0	-2.7	-6.4 to 1.0
≥7-83	68	19.7	17.4	2.3	-2.7	-6.7 to 1.3	-3.0	-7.7 to 1.7	-3.1	-7.8 to 1.6

[a] Model 1: Adjustment for all the variables seen in the table except surgical treatment.
[b] Model 2: Adjustment for all the variables seen in the table.
Model 1 intercept is 7.5 (95% CI 1.1 to 13.9)
Model 2 intercept is 7.3 (95% CI 0.9 to 13.7)
BMI, body mass index. CI, confidence interval. NCS, nerve conduction studies.

6. DISCUSSION

6.1 Key findings

In study I we found that 20 days of hand-intensive seasonal work impaired the median nerve conduction in 9 of 11 mink skinners of whom 4 (36%) fulfilled our CTS case definition at end-season. The changes reverted to normal post-season. At pre-season, none of the mink skinners had abnormal NCS findings indicating that previous mink skinning seasons hadn't impaired the median nerve conduction.

In study II, we found sex-specific SIRs of CTS varied considerably between job groups. There was a clear association between higher job group SIRs of CTS and higher wrist load. The different slopes of the regression lines for men (the more steep) and women indicates that CTS rates increases faster among women in relation to increase in wrist load. Relative to teachers (the reference group) risk of CTS in the other job groups remained at the same level after controlling for diabetes, region of residence, and, for women, for recent child birth and in analyses restricted to participants with similar SES. We found no support for computer use in office work, increases the risk of CTS.

Study III found that an abnormal NCS among patients with suspected CTS was associated with more improvement in contrast to high occupational wrist load which resulted in less improvement. Improvement was also related to surgical treatment especially in case of abnormal NCS. The chance of MCID in outcome scores, was noticeably related to both abnormal NCS and surgical treatment. Wrist load was unrelated. None of the studied lifestyle and personal factors predicted the outcomes.
Findings at the clinical examination of the neck and upper extremities, and the Katz hand diagrams were unrelated with the results of the NCS indicating that for patients with suspected CTS clinical findings and symptom distribution in the hands have low discriminative properties with regards to median nerve impairment.

6.2 Methodological considerations

6.2.1 Exposure assessment

The aim of the technical measurements of the exposures in study I was to characterise the exposures during the task of mink skinning and not to make inferences about different levels of biomechanical exposures as potential risk factors for median nerve impairment. The exposure under study was the seasonal work as mink skinner.

In studies II and III we used the Hand-arm JEM. In study II the participants were linked to the JEM using DISCO-08 codes. In study III the self-reported job titles were converted to standardised occupational titles according to DISCO-88 which were linked to the JEM. Using a JEM is probably the only feasible way to have exposure estimates for the whole nationwide cohort in study II. If we used self-reported exposures in study III we would be in risk of recall bias, which we eliminated using the Hand-arm JEM.

The constructed job groups in study II could attenuate the association if the constructed job groups weren't homogenous and large exposure contrasts existed within the occupations grouped together. This could be of particular concern if smaller occupations with high exposure levels are grouped together with larger occupations with lower exposure levels. The basis of the constructed job groups was the participants DISCO-08 codes. The DISCO-08 codes are based on skills and "skill is defined as the ability to carry out the task and duties of a given job".[132,133] Skills may not reflect specific exposures.[134] To accommodate this aspect, previous JEMs developed in Denmark and Finland have used occupational titles instead of (D)ISCO codes.[122,134,135] Since occupational titles aren't available in any register in Denmark, it wasn't possible to use the participants' job titles in study II. Despite this, a clear association of higher SIRs of CTS and higher wrist load was found.

Also the way the Hand-arm JEM was constructed compensated to a large extent for the unavailability of occupational titles in study II. The Hand-arm JEM included exposure estimates according to DISCO-08 codes, DISCO-88 codes, and standardised occupational titles. There is a substantial overlap between DISCO-88 and DISCO-08 in both occupational codes and occupational titles. Each DISCO code can encompass more than one occupational title. The Hand-arm JEM's occupational section was constructed first which was the basis of the Hand-arm JEM's DISCO sections. During the construction of the Hand-arm JEM's occupational title section, the frequency of occupations in the Danish labour market was used as weights in the construction of the Hand-arm JEM's DISCO sections. Exposure estimates based on the Hand-arm JEM's occupational title section correlated highly with exposure estimates based on the Hand-arm JEM's DISCO-code sections.

Known limitations of using JEMs are 1) the inaccuracy of exposure estimates at the individual worker level due to e.g. variability between work places and work tasks 2) differences in exposures between men and women who have the same job and 3) variability between time periods.[136,137]

Concerning 1) a recent study of CTS found that the use of a JEM resulted in a modestly lower precision (wider CIs) but with similar effect sizes as found by individual observations of exposure.[121] A prospective study from 2018 compared the use of self-reported and JEM-derived physical and psychosocial exposures as predictors of musculoskeletal pain.[138] They generally found that associations obtained from the use of JEMs are comparable with associations obtained by using self-reported exposures.[138] A JEM of occupational mechanical exposures to the shoulder, the Shoulder JEM, was constructed by expert ratings like the Hand-arm JEM was.[122] The Shoulder JEM showed good validity of the expert rated exposure estimates when compared to technical measurements with respect to ranking of the occupations.[122] Four of the five experts who rated exposures in the Shoulder JEM also rated exposures in the Hand-arm JEM.[122,139]
A measurement-based JEM would have been preferable to an expert rated JEM, however one was not available. It would be difficult to convert expert rated JEM exposures into clinical practice of assessing patients' occupational exposures, especially if the correlation between expert-based exposure estimates and measured exposures are unknown. Consequently the use of many JEMs are limited to specific research questions and are inapplicable in clinical practice.

Regarding 2) Denmark has a profoundly sex-segregated labour market. Generally speaking, men and women work in different jobs, especially with respect to occupations that have biomechanical exposures. Examples hereof are nurses (females) and carpenters (males) in contrast to work in academia where sex-segregation is less profound as are the biomechanical exposures. The Hand-arm JEM did not include sex specific estimates, but because the labour market is profoundly sex-segregated, a possible exposure misclassification was there for limited.[139] In the Shoulder JEM,[122] the lack of sex specific exposure estimates was not found to be a problem. The validity of expert-rated job exposures was equal for men and women.[122] Nevertheless, when the measured sex-specific job exposures were compared, substantial differences were found in 4 of 10 job groups.[122] The Hand-arm JEM has not been validated with technical measurements as the Shoulder JEM, but it wouldn't be unexpected if similar discoveries were uncovered if a technical validation of the

Hand-arm JEM was done since studies have found different physiological load among men and women performing the same tasks.[140,141]

On closer examination of the association between SIRs of CTS and wrist load among women (figure 3 in paper II), the association would have been nicer if the three job groups with SIRs around 25 had a wrist load of app. 0.50 to 0.75. The three job groups in question are 51 ('shop sales assistants'), 52 ('child care workers') and 53 ('health care assistants'). It seems that these three job groups, which each consisted of a single occupation, were higher exposed than the experts who constructed the Hand-arm JEM, believed. Perhaps the three occupations in question were actually characterised by combinations of occupational exposures to the wrist that were difficult to rate. Thus expert-rated exposures are not without limitations.

On the subject of 3) the time period in studies II and III were of short duration (app. 7 years in total), the Hand-arm JEM was constructed in 2008 and later expanded in 2017. Therefor it seems unlikely that potential misclassification of exposures were due to the study periods or the age of the JEM.

6.2.2 Outcome definition

In study I the outcome of CTS was defined by a combination of abnormal NCS and symptoms. In the absence of a gold standard case definition for CTS,[1,4-9] we used the case definition which is regarded as the most accurate in the international consensus report about classifying CTS in epidemiological studies.[5]

In study II we identified first-time CTS diagnoses in terms of a primary discharge ICD-10 diagnosis code of G56.0 according to the DNPR. We had no means of verifying the diagnosis and studies of the validity of CTS diagnosis in the DNPR has yet to be performed. Nevertheless there was a very high correlation between carpal tunnel surgery and a CTS diagnosis; almost every single surgery case was preceded by a CTS diagnosis in the DNPR. In total app. half of the cases in study II underwent surgery which was almost identical to the proportion with abnormal NCS that underwent surgery in study III. Even though the diagnostic criteria of a CTS diagnosis in the DNPR can differ from hospital to hospital, we don't believe it would be systematically associated with occupational exposure. Hence any potential misclassification of outcome would be non-differentiated and attenuate the associations found.

In study III outcome assessment was based on the Levine CTS questionnaire[43] and the Danish version of the DASH questionnaire.[47] The primary outcome measures were the difference in the Levine symptom and function scores between baseline and follow-up. Secondary outcome was the corresponding difference in DASH score. Both questionnaires have shown good reliability, responsiveness and validity in patients with CTS.[43,45,46] However, no associations were found between the potential prognostic factors and change in the DASH score. This could likely be explained by the fact that the DASH measures the combined disability of both upper extremities and that the participants had mild disabilities. A fact supported by the lack of statistically significantly associations between the potential prognostic factors and the Levine function score . The study population was younger than the just-cited studies (mean 47.5 vs. 54-59 years),[43,45,46] and we included milder cases of CTS that were not operated. Also, in study III the baseline Levine scores were roughly 0.5 points lower, i.e. fewer symptoms and disabilities, than the cited studies in which all the patients were operated.[43,45,46]

6.2.3 Selection bias

The general principle in order for selection bias to occur is that the probabilities of selection are associated to both exposure and outcome. The just-mentioned selection is regarding the selection of participants from the source population.[119]

In study I, all participated at the pre- and end-seasonal occasions of NCS and filled in the questionnaires. Thus we had complete participation of all the mink skinners employed at the facility.

Selection bias is not expected to be a problem in study II due to a nation-wide cohort design where the study cohort equalled the source population. Any selection bias would be related to the completeness of the registers used, and they generally have high degree of completeness.[142-144] Thanks to the registers, we had detailed information on the reason why some were lost to follow-up. They died, emigrated or disappeared according to the CRS.[144] These three reasons for loss to follow-up are not likely to be associated with the probability of becoming a case later. Likewise, it is unlikely these reasons for loss to follow-up would be associated with exposure status.

Even though, the proportion followed up in study III was satisfactory (72.3%), drop out was associated with a normal NCS result. However, responders and non-responders did not differ with respect to baseline symptom and function scores and wrist load. Therefore, we think that the observed associations between abnormal NCS/high wrist load and the outcomes are unlikely to be inflated by selection bias.

6.2.4 Information bias

In study I we used objective methods, i.e. technical measurements, to characterise the exposures and obtained precise day-by-day account of number of minks skinned by each participant from their payslips to ensure that the work done on the days of measurement were representative for the whole season. The repeated measurements of outcome for each participant were also done using an quantifiable objective method and there were no missing data in any of the questionnaires. All these factors substantially reduced the risk of information bias. Also the subsequent analyses of the paired intra-individual changes of NCS parameters and of symptoms and disabilities, contributed to the reduction of risk of information bias.

The data quality of the registers used in study II could be a problem since the registers were not constructed with the purpose of being used for health research and are thus secondary data.[145] The contents, the used classification systems (e.g. different revisions of ICD), coverage (e.g. inclusion of private hospitals), and collection procedures may change over time.[145] Indeed they have, especially for the DNPR.[143] The time period studied in study II (1994-2013) was chosen so only one diagnostic classification system was used (ICD-10) in order to reduce the risk of information bias. However since the hospitals use the DNPR as a method of documentation to the authorities of what activities are performed and getting paid for said activities, there are substantial economic incentives to have complete and correct registration of activities.[143]

The DNPR only covers public and private hospital contact regardless of in- or outpatient contacts.[143] Patients diagnosed or treated in primary care or at specialists in private practise would only be included if a NCS at a hospital department was part of the diagnostic assessment. We might have missed CTS cases due to the diagnosis were done in the primary sector only. If persons in certain occupations were more prone to seek medical care in the primary sector than persons from other occupations, this would bias our association; especially if the persons in question are from low exposed occupations. Then the association of higher job group SIRs of CTS and higher wrist load would be overestimated. However, in Denmark, NCS are recommended in combination with clinical examination to diagnose CTS,[6] because it is believed to be more accurate,[1,5,6] and NCS are only performed at hospital departments.

In the DNPR we found that app. 1.4% of all operations weren't preceded with a registered CTS diagnosis. However in study III app. 11% of those with normal NCS were operated. This discrepancy could be due to changes in clinical practice, incomplete registration of surgeries in the DNPR, or that a proportion of patients diagnosed with CTS at a hospital were treated by private practising surgeons not covered by the DNPR. Changes in clinical practice was less likely during the short time span of studies II and III (app. 7 years), and in general surgical codes in the DNPR have been found to have a high validity.[146] A study of 9,364 house painters in Denmark 1994-2011 identified 155 first time diagnosis of CTS in the DNPR and additionally 55 cases (26%) with the service code 'nerve compression' in a register covering private practising surgeons.[147,148] The service code 'nerve compression' isn't limited to CTS, although it is the most common nerve entrapment, and the service code doesn't distinguish between diagnosis and surgical treatment of the nerve compression.[147,148] Therefor the true number of carpal tunnel surgery performed were probably higher than those found in study II. Recall that we studied CTS diagnosis as primary outcome in study II and obtained data on surgery for descriptive purposes only.

Workplaces are legally obligated to notify Statistics Denmark of the employee's DISCO-08 code.[149] From its salary register, Statistics Denmark generate the ECM, which includes information on the most important employment through the year, i.e. the employment that generated the highest income.[142] Although the ECM is considered to be of high quality,[142] there was a risk of exposure misclassification if a person had a second job with a different exposure profile than his/her primary job. We don't believe that an eventual exposure misclassification would be related to disease status and we would consider it as a non-differential misclassification. However, Denmark has a stable labour market with workers staying in the same field of work for long periods of time, and usually it isn't economical necessary in Demark to have two jobs, be that in the same field of work or not.

In study III assessment of occupational exposures were done independently with the use of the Hand-arm JEM, and the classification of the participants into groups of those with normal and abnormal NCS was done by objective measures of nerve impairment. Both of these factors eliminated the risk of recall bias and misclassification of the exposures. Treatment during follow-up was self-reported, however we find it unlikely that the information regarding surgery would suffer from recall bias since the time period to recall was a mere 9-12 months and the event to recall was not an insignificant one.

6.2.5 Confounding

Confounding is minimised in study I due to the natural experimental design of workers performing a highly standardised and monotonous task. More importantly though confounding was minimised due to the repeated NCS of the individual worker. In other words, the participants acted as their own controls with the same lifestyle and personal factors throughout the short study period.

In study II we had register information on the most important confounders, i.e. age, diabetes and (for women) recent child births. Analyses were performed sex-specific. Other lifestyle factors that are associated with CTS include obesity for which we had no data since no register contain these data. However by adjusting for diabetes, we also adjusted for any effects that obesity has through diabetes. This does not rule out the possibility of residual confounding, but by indirectly exploring the effect of obesity through sensitivity analyses restricting the cohort to SES groups 3 and 4, we found the that same pattern of associations remained. SES is associated with several lifestyle factors, and may act as a proxy for these lifestyle factors.[119] We did not have information on other risk factors for CTS, i.e. previous wrist fractures[4,110] or inflammatory and degenerative joint diseases,[4,111] but we think it is unlikely that these non-occupational risk factors would confound our findings and the overall pattern of higher SIRs of CTS were associated with higher levels of wrist load.

We determined sex and age in study III by the ID number each participant has according to the CRS. Information on lifestyle factors and medical history were self-reported. We thus had self-reported information on potential known confounders including carpal tunnel surgery.

6.3 Interpretation of findings

Study I added to the body of evidence that CTS can have a short induction period in relation to mechanical exposures to the wrist. For example if one starts in a job with high mechanical exposures to the wrist, or due to an increase in wrist exposures in a job already held. Study I also demonstrated that the median nerve impairment can resolve by itself after a period of exposure reduction. These findings can be used in clinical practice when advising patients; i.e. the condition is likely reversible if the exposures are reduced and if symptoms have been of short duration (weeks-months).

The mink skinners' exposures were not exceptionally high compared to other repetitive industrial work,[140,150-152] yet the proportion of mink skinners who fulfilled our case definition of CTS (36%) was markedly high. Previous cross-sectional studies of repetitive industrial work which used a similar case definition as ours, found lower prevalence of CTS among slaughterhouse workers (6.3%),[153] female supermarket cashiers (app. 8%),[154] and construction workers (3%).[155] The lower prevalence in the cited cross-sectional studies might be explained by a healthy worker survivor bias, modified work practices developed over time, and biological adaptation to exposures.

We calculated IRs of 10.9 (95% CI 10.6 to 11.2) and 19.7 (95% CI 19.2 to 20.1) per 10,000 person-years among men and women, respectively, during 2010-2013 which corresponded to a women-to-men ratio of 1.8. Roughly speaking, the IRs in study II lies in the middle tertile compared to previous general population studies of CTS. Our study population was restricted to participants aged 19 -65 years in contrast to the studies summarised in table 1[12,40,89-94] of which none but one had an upper age restriction; the exception was the study by Roquelaure et al. where age was restricted to 20-59 years.[156] In the only study where it was possible to approximate the proportion of cases older than 65 years old, app. 27% of the cases were so (Mondelli et al.[12]). We also required the participants in study II to have at least one year of employment during follow-up, which none of the studies in table 1 required. These factors in addition to the previous mentioned in section 3.5 probably explain the differences observed.

Several other studies have found that rates of CTS among women have a peak in the age group 50-59 years.[12,40,89-91,115] We found that women in age group 50-65 years had a markedly higher OR (3.5 (95% CI 3.3 to 3.8)) than women in age group 35-49 years (2.4 (95% CI 2.2 to 2.6)). If we had categorised age in narrower intervals, e.g. 5- or 10-year intervals, the ORs would likely have resembled the findings of the just-mentioned epidemiological studies more closely.[12,40,89-91,115] Some authors have suggested that the peak in question is due to hormonal changes.[115,117,118]

Study II's evaluation of IRs of CTS as sentinels of high mechanical occupational exposures was positive in the sense that there was a clear association of higher SIRs of CTS pointing to higher wrist load. The approach of using IRs of CTS as an occupational sentinel disease as done in study II, has the implicit prerequisite of access to readily available nationwide registers with both health and employment data. And that the health care system is tax-paid and equally accessible no matter socioeconomic status, as it is in Denmark. This limits the generalizability of our method to only a small handful of countries which is likely one of the main reasons why others haven't performed this evaluation before. Recall that the idea of using CTS as an occupational sentinel disease wasn't new.[13,25,27,156] However we believe that the association of high CTS rates as a signal of high wrist exposure to be generalizable, even though our methods may not be quiet so generalizable.

In study III, surgical treatment depended heavily on the result of NCS and was related to a more favourable prognosis. Controlling for surgery reduced the improvement associated with abnormal NCS, indicating that surgical treatment partly explained the favourable prognosis. Hence NCS seem to be an important factor when decisions about surgical treatment were made, as others have found as well.[7,85] NCS even provided prognostic information regarding the course of symptoms among patients referred for suspected CTS.

High wrist load was associated with poorer prognosis of symptoms. We found that surgical treatment was more common among those with high wrist load despite having a normal NCS. Among operated with abnormal NCS, the improvement in symptoms was of the same magnitude regardless of wrist load. However, the improvement among those who were operated despite a normal NCS, was smaller; especially in cases with high wrist load. The negative effect of a high wrist load may even have been underestimated due to few participants with high wrist load, mainly among women who accounted for 70% of the participants. Furthermore, patients with expected high wrist load may have reduced their exposures during follow-up.

None of the studied lifestyle and personal factors predicted the outcomes which are in accordance with existing literature on outcome predictors of carpal tunnel release surgery where inconsistent evidence on the effect of these factors is found.[78,80,81]

We believe that our results from study III can be generalized to other countries with a public and tax-paid healthcare system that also have a labour market similar to Denmark.

7. CONCLUSION

Median nerve impairment and subsequent CTS had a short induction period and was a potential reversible condition as shown in study I where we evaluated median nerve function in relation to three weeks of hand-intensive seasonal work. Our hypothesis that at the end of the work season median nerve conduction would be impaired and then recover post-season, was corroborated. These findings could be used in clinical practice when advising patients; i.e. the condition is likely reversible if the exposures are reduced and if symptoms have been of short duration (weeks-months).

As a novel approach we used readily available nationwide registers in study II to evaluate our hypothesis that the use of IRs of CTS as an occupational sentinel disease would point to job groups with high biomechanical exposures to the wrist. The results were in accordance with our hypothesis.

As shown in study III, if a patient suspected of CTS had an abnormal NCS, the chance of a more favourable prognosis was higher, partly because the choice of carpal tunnel surgery often relies on an abnormal NCS. However as hypothesised, high wrist exposure was associated with poorer prognosis which supports the recommendation for exposure reduction in case of high exposure.

8. PERSPECTIVES

The course of impaired median nerve conduction if the occupational mechanical exposures continued in study I, are unknown. The observed changes could resolve, e.g. due to biological adaptation, or deteriorate to a more severe impairment with prolonged recovery or perhaps even irreversibility. This could to be studied in a natural experimental setting if another seasonal hand-intensive occupation with a longer season could be found, or if healthy newly hired workers in a hand-intensive occupation are followed with repeated NCS.

As mentioned earlier, the validity of the CTS diagnosis in the DNPR used in study II is unstudied. A validation study could be conducted by validating diagnosis obtained from the DNPR against NCS data from the department of neurophysiology and calculate the positive predictive value of a registered CTS diagnosis in the DNPR. The time period under study could be expanded both retrospectively and prospectively with addition of data from the ECM and the DNPR in order to examine time trends of CTS and to corroborate the findings of study II in another study period. Using the data from study II it would be possible to examine the influence of cumulative exposures and risk of CTS with the underlying hypothesis that cumulative exposure to the wrist does not increase the risk of CTS as compared to short term exposures. Exposures to the wrist will often correlate with exposures to the shoulder,[157,158] thus there is potential to study if IRs of CTS as an occupational sentinel disease could predict occupational shoulder disorders.

To further study exposure-response relationship between biomechanical occupational exposures and CTS, a triple case-referent study was planned as part of this PhD project. The data has been collected with unforeseen long delays, but has not been analysed yet. Questionnaire data including job titles on app. 4,000 participants are waiting to be analysed. The study design and the Hand-arm JEM have previously been used in a similar study of ulnar neuropathy.[139]

In study III, we found that surgery and abnormal NCS were associated with more symptom improvement. Surgery could accelerate the natural, untreated, recovery of CTS as demonstrated in study I and in nonhuman primate models.[61,62] A subsequent follow-up questionnaire after an additional one or two years could shed more light on the course of CTS with and without treatment, and on the course of those with normal NCS, as suggested by a recent review on conservatively managed and untreated CTS.[33]

9. ENGLISH SUMMARY

Aim: Study I: to evaluate median nerve function in relation to three weeks of hand-intensive seasonal work and subsequent recovery.

Study II: to evaluate the use of incidence rates (IRs) of carpal tunnel syndrome (CTS) as sentinels, which can identify occupational groups with high biomechanical exposures to the wrist.

Study III: to evaluate occupational biomechanical exposures and abnormal nerve conduction as prognostic factors for symptoms and disability among patients with suspected CTS.

Methods: Study I was a prospective cohort study of 11 mink skinners during a three week long skinning season applying nerve conduction studies (NCS) pre-, mid-, end-, and post-season. To characterize the single task performed, full shift technical exposure measurements of 6 day-shift workers' dominant arm and hand were performed, i.e. postures and movements of the wrist using twin axis goniometers and bipolar surface electromyography of the forearm extensors to measure force exertion. We plotted z-scores obtained from NCS for each individual to illustrate the changes in NCS parameters over time, and used paired t-test to evaluate intra-individual changes in NCS parameters and changes in Levine and DASH scores.

Study II was a nationwide cohort study using data from Danish health and employment registers in which we identified first time diagnosis of CTS in 2010-2013. Using the participants' occupational codes (the Danish version of the International Standard Classification of Occupations from 2008; DISCO-08) we first constructed job groups by collapsing some of the more detailed categories in DISCO-08 into categories based on lower levels of detail in order to obtain robust IR estimates. We then validated the signal value of the age standardized IRs (SIRs) against exposure measures from an existing job exposure matrix (JEM) by first combining the four wrist exposures from the JEM into a single mean wrist load variable, and then by plotting the wrist load against the SIRs.

In study III we undertook a prospective study and included patients with suspected CTS referred for NCS. After the NCS they underwent a standardized clinical examination, filled in a baseline questionnaire, and were mailed a follow-up questionnaire after 9-12 months. Job title in the year before baseline was linked to a JEM to assess occupational mechanical exposures. Primary outcomes were symptoms and disability measured using Levine and DASH questionnaire. Data was analysed using linear regression and prevalence of minimal clinical important differences was analysed using Poisson regression.

Results: Study I showed that three weeks of mink skinning, which was characterized by being repetitive and not forceful, resulted in impaired median nerve conduction in 9 of 11 mink skinners. 4 fulfilled our case definition of CTS at end-season. Post-season the changes reverted to normal.

In study II we found 4,405 and 7,858 cases of CTS among men and women, respectively, among 4,046,851 and 3,994,987 person-years, yielding an IR of 10.9 (95% CI 10.6 to 11.2) per 10,000 person-years for men and an IR of 19.7 (95% CI 19.2 to 20.1) per 10,000 person-years for women. There was a clear association between higher SIRs of CTS and higher wrist load.

Among the 361 participants in study III, approximately 48% had an abnormal NCS of whom 55% were treated surgically during follow-up. Abnormal NCS was associated with a more favourable prognosis compared to patients with a normal NCS. Patients with high occupational wrist exposure obtained less improvement. Improvement was also related to surgical treatment especially in case of abnormal NCS. High wrist exposure seemed to predict surgery among those with normal NCS.

Conclusion: Median nerve impairment and subsequent CTS has a short induction period and is a potential reversible condition (study I), and SIRs of CTS seem to be a useful indicator of job groups with high biomechanical exposures to the wrist (study II). If a patient suspected of CTS has an abnormal NCS, the chance of a more favourable prognosis is higher, partly because the choice of carpal tunnel surgery often relies on an abnormal NCS. However, high wrist exposure was associated with less favourable prognosis (study III).

10. DANISH SUMMARY (DANSK RESUMÉ)

Formål: Studie I: at evaluere medianus nervens påvirkning og efterfølgende bedring efter tre ugers hånd-intensivt sæsonarbejde.

Studie II: at evaluere brugen af incidensrater (IR) af karpaltunnelsyndrom (KTS) som indikatorer for jobgrupper med høje biomekaniske eksponeringer af håndleddet.

Studie III: at evaluere arbejdsmæssige biomekaniske eksponeringer og abnorm nerveledning som prognostiske faktorer for symptomer og funktionsnedsættelse hos patienter mistænkt for KTS

Metoder: Studie I var et prospektivt kohorte studie af 11 minkpelsere, som blev fulgt gennem en tre ugers pelsningssæson. Der blev udført nerveledningsundersøgelser (NLU) præ-, midt-, slut- og post-sæson. For at karakterisere opgaven med at pelse mink lavede vi, gennem et helt skift, tekniske målinger af eksponeringer af dominante arm og hånd for 6 arbejdere i dag-skift. Vi målte stillinger og bevægelser af håndleddet vha. goniometri og vi målte kraftudfoldelsen i underarmens ekstensormuskler vha. bipolar overflade elektromyografi. Vi plottede z-scores fra NLU for hvert individ for at illustrere ændringerne i nerveledningsparametrene over tid, og brugte parrede t-test til at evaluere intra-individuelle ændringer i nerveledningsparametrene og ændringer i Levine og DASH scores.

Studie II var et nationalt registerbaseret kohortestudie med brug af data fra danske sundheds- og beskæftigelsesregistre, hvori vi fandt førstegangs KTS diagnoser i 2010-2013. For at opnå robuste IR estimater dannede vi først jobgrupper vha. deltagernes job koder (den danske version af International Standard Classification of Occupations fra 2008, DISCO-08): Vi brød nogle af de mere detaljerede kategorier i DISCO-08 ned i kategorier baseret på færre detaljer indenfor den samme eller numerisk tætteste fire-, tre- eller tocifrede DISCO-08 kode. Herefter validerede vi signalværdien af de aldersstandardiserede IR (SIR) op mod eksponeringsestimater fra en eksisterende jobeksponeringsmatrice (JEM). Først kombinerede vi de fire håndledseksponeringsestimater fra JEM'en til en enkelt gennemsnitlig håndleds-load variabel, hvorefter vi plottede håndleds-load variablen mod SIR.

I studie III udførte vi et prospektivt studie med inklusion af patienter henvist til NLU på mistanke om KTS. Efter NLU gennemgik patienterne en standardiseret klinisk undersøgelse, udfyldte et baseline spørgeskema og fik tilsendt et follow-up spørgeskema efter 9-12 måneder. Deres fagbetegnelse, året inden baseline, blev linket til en JEM for at vurdere arbejdsmæssige biomekaniske eksponeringer. Primære udfald var symptomer og funktionsnedsættelse vurderet

ved Levine og DASH spørgeskema. Data blev analyseret ved lineær regression og prævalens af mindste kliniske betydende forskel blev analyseret ved Poissons regression.

Resultater: Studie I viste at tre ugers minkpelsning, der var karakteriseret af at være repetitivt og ikke kraftfuldt, resulterede i nedsat nerveledning i medianus nerven hos 9 af 11 minkpelsere. Fire minkpelsere opfyldte vores case definition af KTS ved slut-sæson. Ved post-sæson havde ændringerne normaliseret sig.

I studie II fandt vi 4.405 og 7.858 KTS tilfælde blandt hhv. mænd og kvinder, iblandt 4.046.851 og 3.994.987 person-år resulterende i en IR på 10,9 (95% CI 10,6 til 11,2) per 10.000 person-år for mænd og en IR på 19,7 (95% CI 19,2 til 20,1) per 10.000 person-år hos kvinder. Der var en klar sammenhæng mellem højere KTS SIR og højere håndleds-load.

Blandt de 361 deltagere i studie III, havde ca. 48% en abnorm NLU hvoraf 55% blev opereret i follow-up perioden. Abnorm NLU var associeret med en mere favorabel prognose sammenlignet med patienter med normal NLU. Patienter med høje arbejdsmæssige håndledseksponeringer oplevede mindre fremgang. Fremgang var også relateret til kirurgisk behandling, specielt hvis NLU var abnorm var fremgangen stor. Blandt dem med normal NLU indikerede data at høje håndledseksponeringer prædikterede kirurgi.

Konklusion: Nedsat ledningsevne i medianus nerven og efterfølgende KTS har en kort induktions-periode og er en potentiel reversibel tilstand (studie I). KTS IR virker til at være en brugbar indikator af jobgrupper med høje biomekaniske håndledseksponeringer (studie II). Hos en patient mistænkt for KTS ses en bedre prognose hvis NLU er abnorm, muligvis pga. øget sandsynlighed for efterfølgende operation. Valget af operativt behandling af KTS baseres nemlig ofte på en abnorm NLU. Dog fandt vi at høje håndledseksponeringer var associeret med dårligere prognose (studie III).

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12. SUPPLEMENTARY DOCUMENTS

12.1 Supplementary tables and figures from study II

Supplementary tables 1 and 2 show occupational groups/titles in the constructed job groups for men and women, respectively.

Supplementary figures 1 to 8 show the four exposure dimensions in the Hand-arm JEM plotted against SIRs of CTS separately for men and women.

12.2 Baseline questionnaire used in study III (in Danish)

A modified version of the questionnaire was also used in study I.

12.3 Follow-up questionnaire used in study III (in Danish)

12.4 Clinical examination form used in study III (in Danish)

12.1 Supplementary tables and figures from study II

Supplementary table 1. Constructed job groups with labels, DISCO-08 codes, and occupational groups/titles for men 2010-2013.

Job group	Job group label	DISCO-08 occupational groups/titles
10	Managers	- 1 Managers
20	Science and information professionals	- 21 Science and engineering professionals - 25 Information and communications technology professionals
21	Health and legal professionals	- 22 Health professionals - 26 Legal, social and cultural professionals
22	Teachers	- 23 (excl. minor group 235) Teaching professionals
23	Business professionals	- 24 Business and administration professionals - 235 Other teaching professionals
30	Science and health associate professionals	- 31 Science and engineering associate professionals - 32 Health associate professionals - 34 Legal, social, cultural and related associate professionals
31	Financial and purchasing agents	- 331 Financial and mathematical associate professionals - 332 Sales and purchasing agents and brokers
32	IT technicians, business services and administrative workers	- 35 Information and communications technicians - 333 Business services agents - 334 Administrative and specialized secretaries - 335 Government regulatory associate professionals
40	General clerks	- 4 Clerical support workers
50	Services and sales workers	- 51 Personal services workers - 52 Sales workers
51	Care and protective workers	- 53 Personal care workers - 54 Protective services workers
60	Agricultural and fishery workers	- 6 Skilled agricultural, forestry and fishery workers
70	Carpenters	- 7115 Carpenters and joiners
71	Builders and painters	- 711 (excl. unit group 7115) Building frame and related trades workers - 713 Painters, building structure cleaners and related trades workers
72	Building finishers and metal workers	- 712 Building finishers and related trades workers - 721 Sheet and structural metal workers, moulders and welders, and related workers
73	Smiths	- 722 Blacksmiths, toolmakers and related trades workers
74	Mechanics	- 723 Machinery mechanics and repairers
75	Electricians	- 7411 Building and related electricians
76	Handicraft, garment and food processing workers	- 73 Handicraft and printing workers

12.1 Supplementary tables and figures from study II

Supplementary table 1 (cont.). Constructed job groups with labels, DISCO-08 codes, and occupational groups/titles for men 2010-2013.

		- 74 (excl. unit group 7411) Electrical and electronics trades workers - 75 Food processing, woodworking, garment and other craft and related trades workers
80	Truck drivers	- 8332 Heavy truck and lorry drivers
81	Operators	- 811 Mining and mineral processing plant operators - 812 Metal processing and finishing plant operators - 813 Chemical and photographic products plant and machine operators - 814 Rubber, plastic and paper products machine operators - 815 Textile, fur and leather products machine operators - 818 Other stationary plant and machine operators
82	Assemblers	- 82 Assemblers - 816 Food and related products machine operators - 817 Wood processing and papermaking plant operators
83	Drivers	- 83 (excl. unit group 8332) drivers and mobile plant operators
90	Civil engineering labourers	- 9312 Civil engineering labourers
91	Cleaners, food and elementary workers	- 91 Cleaners and helpers - 92 Agricultural, forestry and fishery labourers - 94 Food preparation assistants - 95 Street and related sales and services workers - 96 Refuse workers and other elementary workers
92	Storage labourers	- 933 Transport and storage labourers
93	Construction and manufacturing labourers	- 931 (excl. unit group 9312) Mining and construction labourers - 932 Manufacturing labourers
99	Unemployed and apprentices	Persons who are unemployed, apprentices or trainees some, but not all, of the follow-up period

Excl.: Excluding.

12.1 Supplementary tables and figures from study II

Supplementary table 2. Constructed job groups with labels, DISCO-08 codes, and occupational groups/titles for women 2010-2013.

Job group	Job group label	DISCO-08 occupational groups/titles
10	Managers	- 1 Managers
20	Science, business and information professionals	- 21 Science and engineering professionals - 24 Business and administration professionals - 25 Information and communications technology professionals
21	Health professionals	- 22 (excl. unit group 2221) Health professionals
22	Teachers	- 23 (excl. unit groups 2341 and 2343) Teaching professionals
23	Nurses	- 2221 Nursing professionals
24	Primary school teachers	- 2341 Primary school teachers
25	Pedagogues	- 2343 Pedagogical professionals*
26	Legal professionals	- 26 Legal, social and cultural professionals
30	Science and health associate professionals	- 31 Science and engineering associate professionals - 32 Health associate professionals - 34 Legal, social, cultural and related associate professionals
31	Financial, sales and business services agents	- 331 Financial and mathematical associate professionals - 332 Sales and purchasing agents and brokers - 333 Business services agents
32	IT technicians and administrative workers	- 35 Information and communications technicians - 334 Administrative and specialized secretaries - 335 Government regulatory associate professionals
40	General clerks	- 41 General and keyboard clerks
41	Customer service and other clerks	- 42 Customer services clerks - 43 Numerical and material recording clerks - 44 Other Clerical support workers
50	Services and sales workers	- 5 (excl. unit groups 5223 and 5311 and 5321 and 5322) Services and sales workers
51	Shop sales assistants	- 5223 Shop sales assistants
52	Child care workers	- 5311 Child care workers
53	Health care assistants	- 5321 Health care assistants
54	Home-based personal care workers	- 5322 Home-based personal care workers
60	Agricultural and fishery workers	- 6 Skilled agricultural, forestry and fishery workers
70	Craft workers	- 7 Craft and related trades workers
80	Operators and assemblers	- 8 Plant and machine operators and assemblers

12.1 Supplementary tables and figures from study II

Supplementary table 2 (cont.). Constructed job groups with labels, DISCO-08 codes, and occupational groups/titles for women 2010-2013.

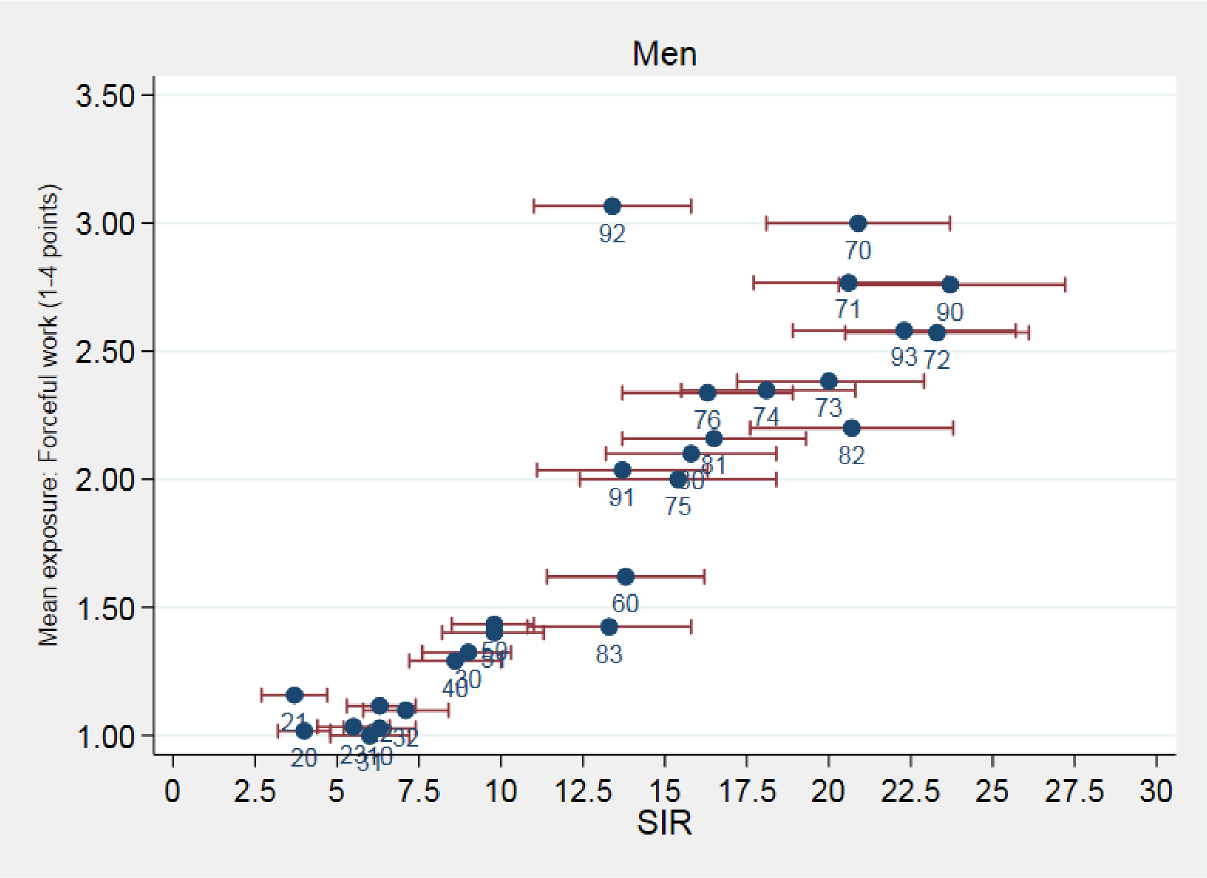
90	Cleaners	-	9112 Cleaners and helpers in offices, hotels and other establishments
91	Elementary occupations	-	9 (excl. unit group 9112) Elementary occupations
99	Unemployed and apprentices		Persons who are unemployed, apprentices or trainees some, but not all, of the follow-up period

Excl.: Excluding.

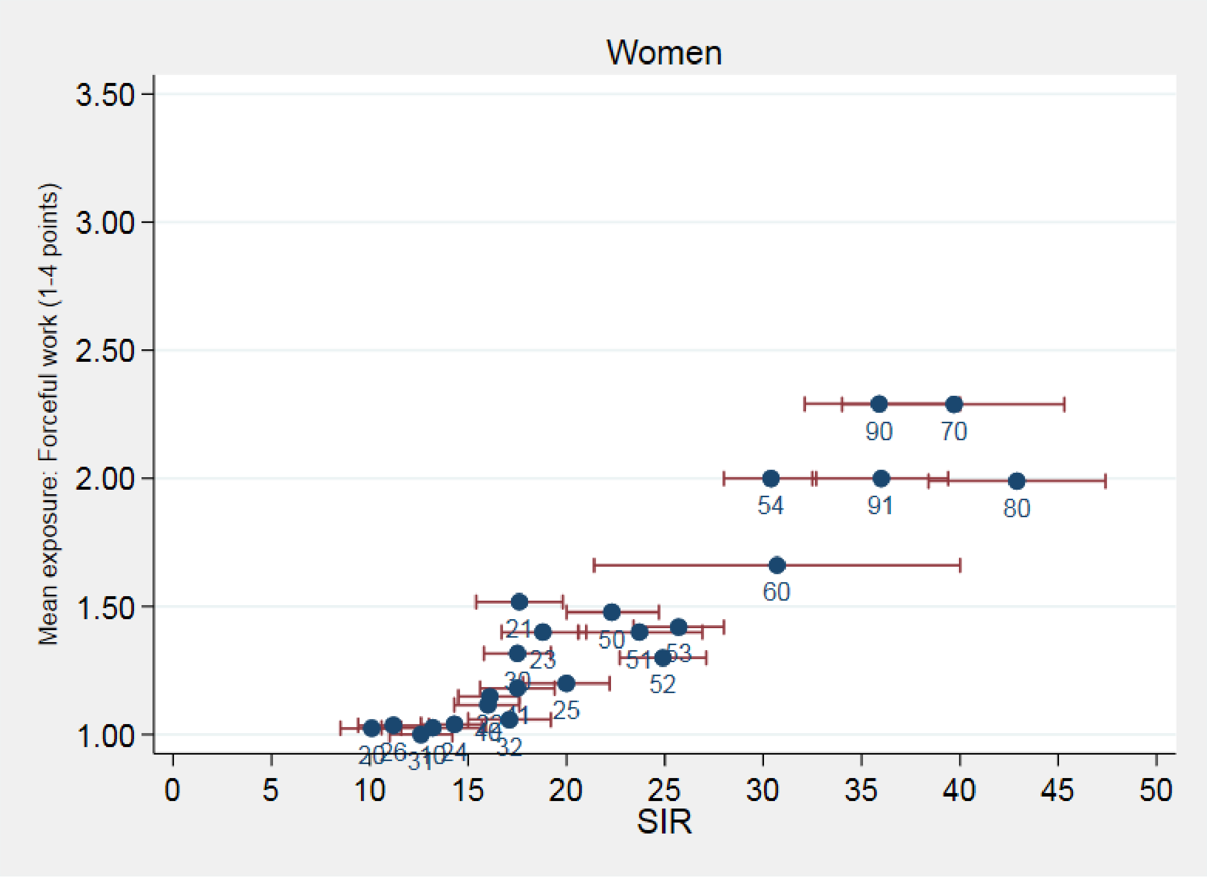
* 2343 “Pedagogical Professionals” is unique for DISCO-08 and does not exist in ISCO-08.

12.1 Supplementary tables and figures from study II

Supplementary figure 1. Force exposure vs. SIRs of CTS among men.

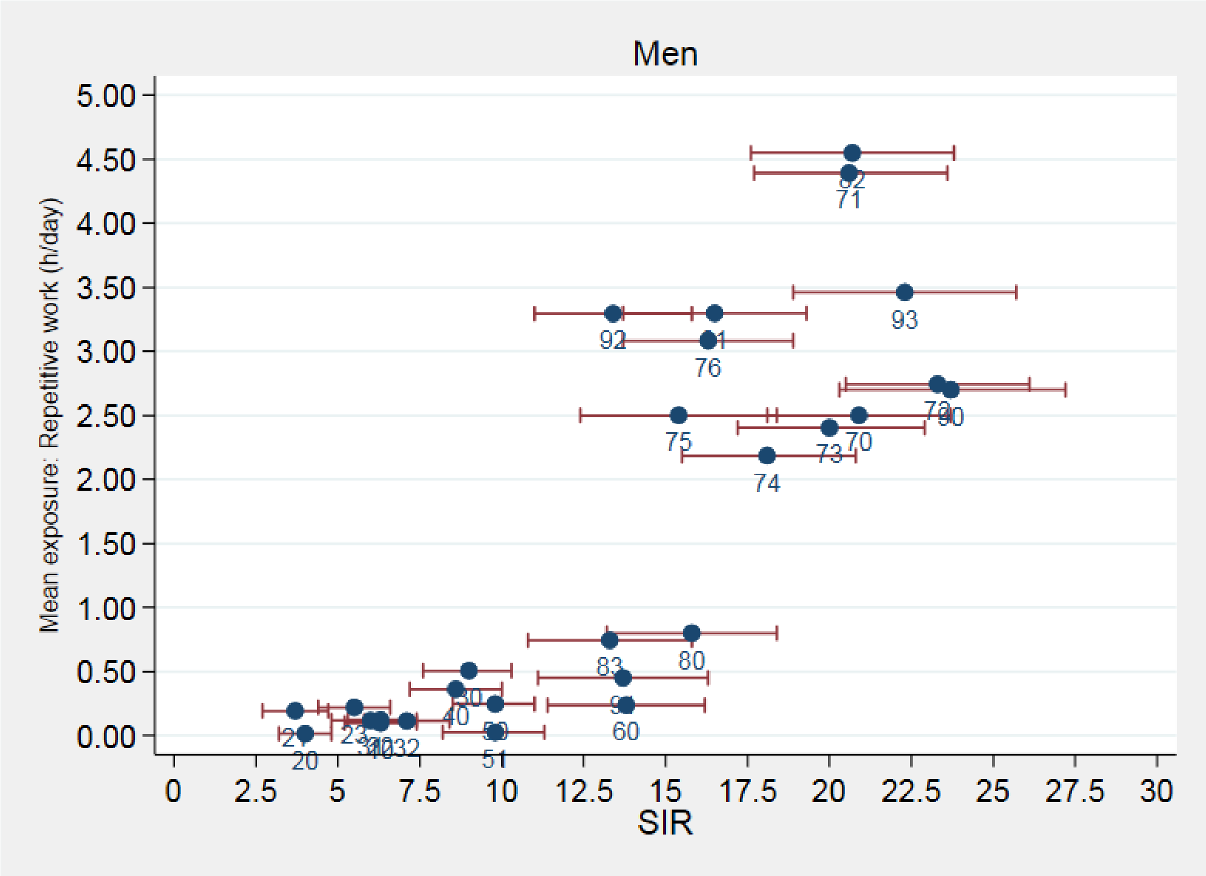


Supplementary figure 2. Force exposure vs. SIRs of CTS among women.

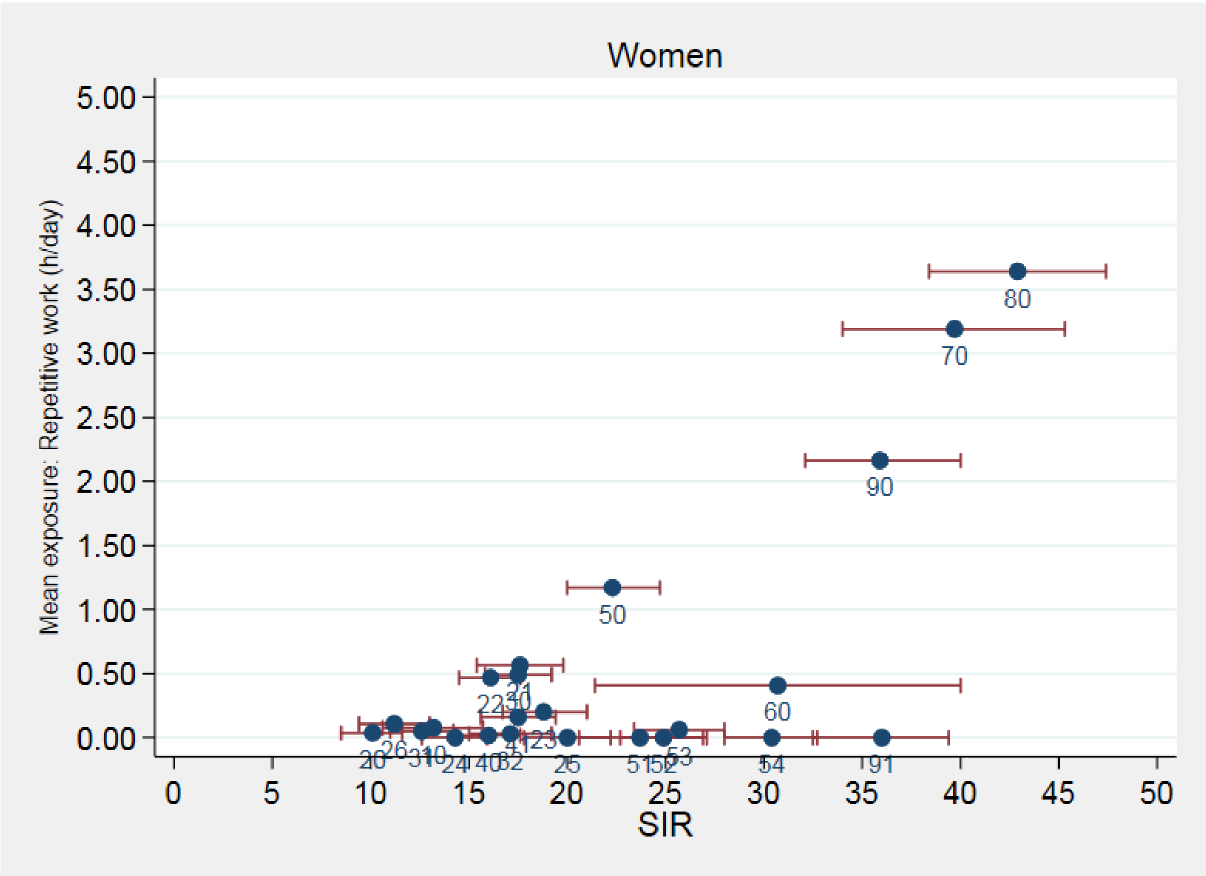


12.1 Supplementary tables and figures from study II

Supplementary figure 3. Repetitive work exposure vs. SIRs of CTS among men.

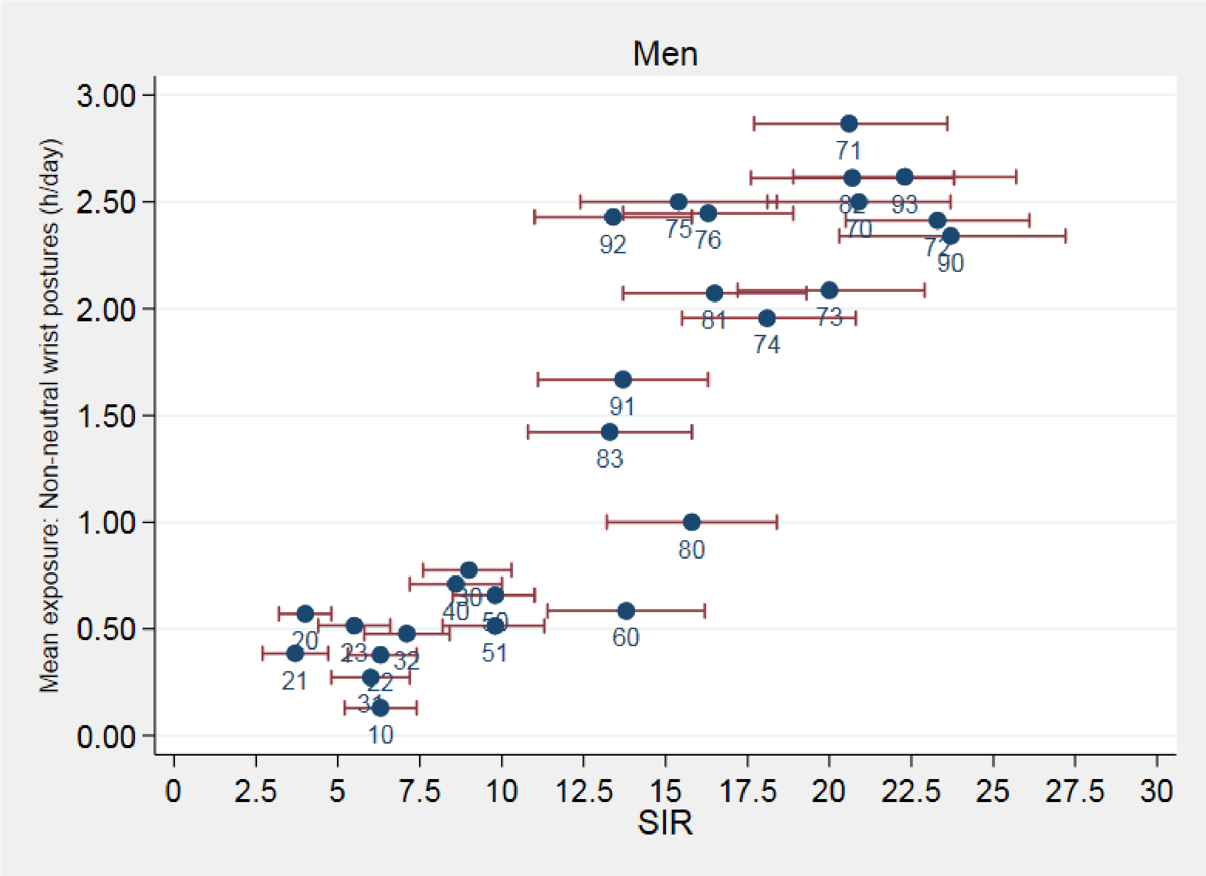


Supplementary figure 4. Repetitive work exposure vs. SIRs of CTS among women.

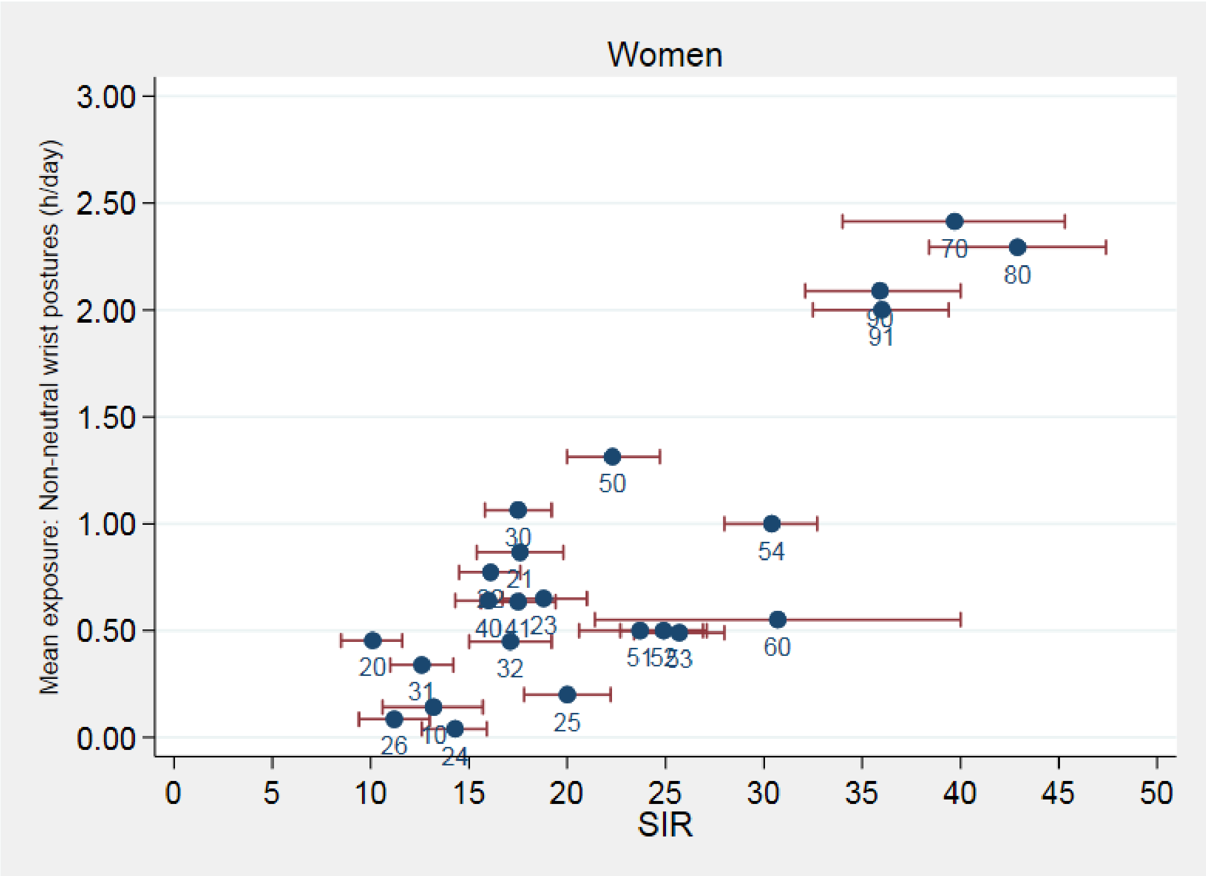


12.1 Supplementary tables and figures from study II

Supplementary figure 5. Non-neutral wrist posture exposure vs. SIRs of CTS among men.

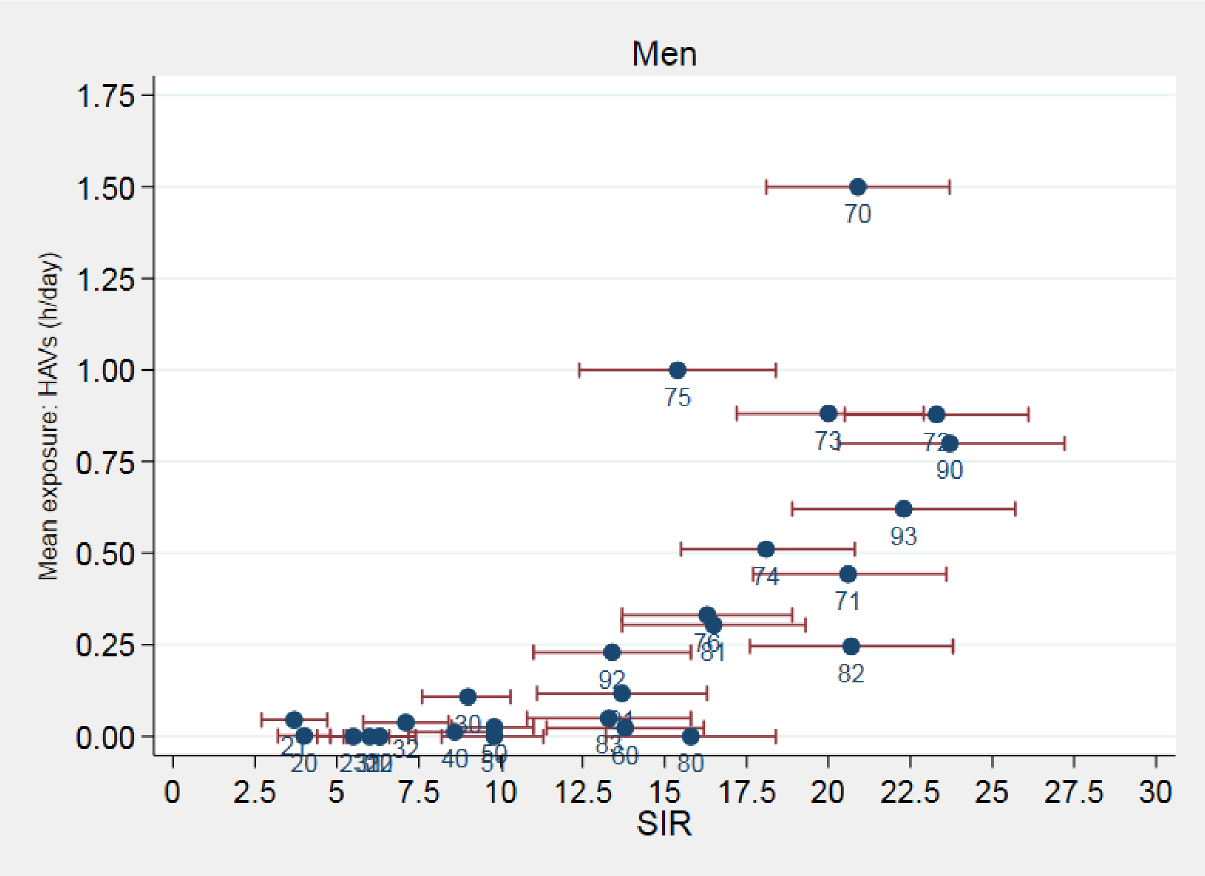


Supplementary figure 6. Non-neutral wrist posture exposure vs. SIRs of CTS among women.

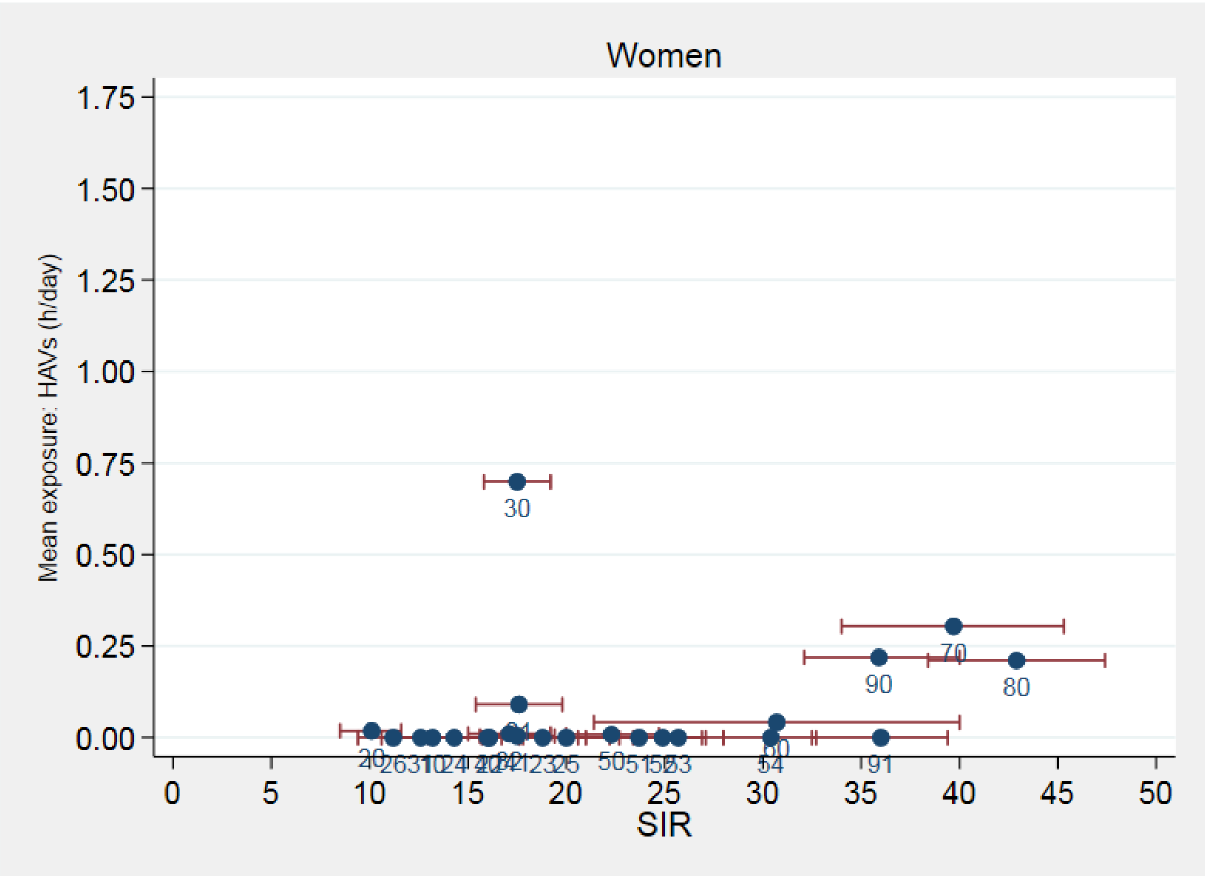


12.1 Supplementary tables and figures from study II

Supplementary figure 7. Hand-arm vibration exposure vs. SIRs of CTS among men.



Supplementary figure 8. Hand-arm vibration exposure vs. SIRs of CTS among women.



12.2 Baseline questionnaire used in study III (in Danish)

Dit CPR-nr.: |__|__|__|__|__|__|-|__|__|__|__|
Dato for besvarelse: |__|__| - |__|__| - |__|__|__|__| *(DD- MM-ÅÅÅÅ, fx "17-04-2015")*

SPØRGESKEMA TIL PATIENTER UNDERSØGT FOR SNURREN, PRIKKEN, SMERTER ELLER ANDET BESVÆR I HÅND OG FINGRE

12.2 Baseline questionnaire used in study III (in Danish)

Vejledning

Ved at udfylde dette spørgeskema deltager du i undersøgelsen af hvordan det går med dine gener i hånd og fingre på længere sigt.

Du kan læse mere om undersøgelsen på vedlagte informationsark.

Det er frivilligt at besvare spørgeskemaet
Manglende besvarelse vil ikke få konsekvenser for din behandling.

Dine svar behandles fortroligt
Undersøgelsen er tilmeldt Datatilsynet v/Region Midtjylland, og personer, der arbejder med undersøgelsen, har tavshedspligt. Resultaterne af undersøgelsen offentliggøres kun i en form, hvor enkeltpersoner ikke kan genkendes.

For at kunne undersøge forløbet af smerter og andre gener fra hånd og fingre, vil vi om ca. et år sende dig et nyt skema, med nogle af de samme spørgsmål til dit helbred.

Sådan udfylder du spørgeskemaet
De fleste skal bruge omkring 15 minutter på at udfylde skemaet. Vi vil bede dig svare på spørgsmålene efter de anvisninger, der er i spørgeskemaet. Brug venligst **sort** eller **blå** kuglepen. Sæt X og skriv tal så de er nemme at tolke, som vist i eksemplet nedenfor.

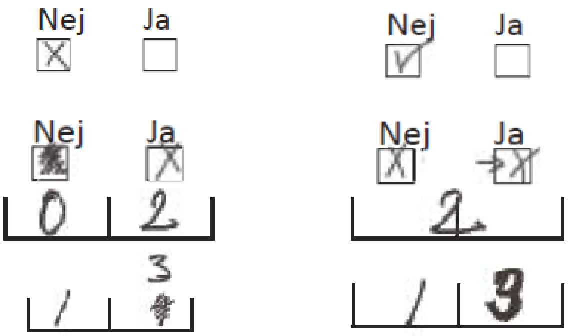
RIGTIGT **FORKERT**

Sæt tydelige X

Hvis et felt er **udfyldt forkert**,
Skraveres den pågældende kasse,
og krydset sættes det rigtige sted

Tallene skrives i felterne

Tallene rettes ved at overstrege det forkerte tal og skrive det rigtige ovenover



På bagsiden er der plads til kommentarer.

Når skemaet er udfyldt, bedes du aflevere det i receptionen.

Med venlig hilsen

Sorosh Taba
Læge, ph.d.-studerende
Arbejdsmedicinsk Klinik, Aarhus Universitetshospital

Birger Johnsen
Overlæge, ph.d.
Neurofysiologisk afdeling, Aarhus universitetshospital

12.2 Baseline questionnaire used in study III (in Danish)

Uddannelse og erhvervsstatus

1. Har du fuldført en uddannelse udover en skole- eller ungdomsuddannelse?
(Sæt X ved den længste uddannelse du har fuldført)

Nej (ufaglært)	☐
Et eller flere kortere kurser (specialarbejderkurser, arbejdsmarkedskurser m.v.)	☐
Faglært inden for håndværk, handel eller kontor m.v. (f.eks. lærlinge- eller EFG uddannelse)	☐
Kort videregående uddannelse indtil 3 år (f.eks. social- og sundhedsassistent, politibetjent, tekniker, merkonom)	☐
Mellemlang videregående uddannelse 3-4 år (f.eks. folkeskolelærer, journalist, socialrådgiver, fysioterapeut)	☐
Lang videregående uddannelse over 4 år (f.eks. civilingeniør, cand. mag., læge, psykolog)	☐
Anden uddannelse	☐
Hvis anden uddannelse, skriv med BLOKBOGSTAVER: ________________	

2. Hvad er din aktuelle erhvervsstatus?
(Sæt ét X)

I arbejde (som ansat eller selvstændig)	☐
Beskæftiget på særlige vilkår (fx aktivering, skånejob, fleksjob)	☐
Sygemeldt fra arbejde (heltids-/eller deltidssygemeldt)	☐
Sygemeldt fra arbejdsløshed	☐
På orlov fx (barsels-, forældre-, uddannelsesorlov)	☐
Arbejdsløs	☐
Elev, lærling eller studerende	☐
Folkepensionist, efterlønsmodtager eller førtidspensionist	☐
Andet	☐
Hvis andet, skriv med BLOKBOGSTAVER: ________________	

12.2 Baseline questionnaire used in study III (in Danish)

3. **Hvad har du arbejdet som siden 2010?**
Vær så præcis som muligt. Skriv fx "montør for køkkenfirma" i stedet for "montør" eller "fabriksarbejder på møbelfabrik" i stedet for "fabriksarbejder". Begynd med din seneste stillingsbetegnelse og gå tilbage i tiden til 2010.

	Fra årstal	Til årstal	Antal år
Arbejde nr. 1 (nuværende eller seneste arbejde): Jeg arbejder som – skriv stillingsbetegnelse: ________	|__|__|__|__|	|__|__|__|__|	|__|__|
Arbejde nr. 2 (foregående arbejde): Jeg arbejdede som – skriv stillingsbetegnelse: ________	|__|__|__|__|	|__|__|__|__|	|__|__|
Arbejde nr. 3: Jeg arbejdede som – skriv stillingsbetegnelse: ________	|__|__|__|__|	|__|__|__|__|	|__|__|
Arbejde nr. 4: Jeg arbejdede som – skriv stillingsbetegnelse: ________	|__|__|__|__|	|__|__|__|__|	|__|__|
Arbejde nr. 5: Jeg arbejdede som – skriv stillingsbetegnelse: ________	|__|__|__|__|	|__|__|__|__|	|__|__|

4. **Er du tilbøjelig til at støtte højre albue mod underlaget – fx mens du hviler hovedet i hånden, eller når du bruger computer?**
(Sæt ét X)

Nej	☐
Ja	☐
Ved ikke	☐

5. **Er du tilbøjelig til at støtte venstre albue mod underlaget – fx mens du hviler hovedet i hånden, eller når du bruger computer?**
(Sæt ét X)

Nej	☐
Ja	☐
Ved ikke	☐

Helbred

6. I løbet af <u>de sidste 12 måneder,</u> hvor meget har du alt i alt været generet af smerter eller ubehag i følgende kropsregioner?
(Sæt ét X i hver linje)

	Slet ikke	Meget lidt	Lidt	Noget	En del	Meget	Særdeles meget
a. Nakke	☐	☐	☐	☐	☐	☐	☐
b. Skuldre	☐	☐	☐	☐	☐	☐	☐
c. Lænderyg	☐	☐	☐	☐	☐	☐	☐
d. Albuer, underarme og/eller hænder	☐	☐	☐	☐	☐	☐	☐
e. Hofter, knæ og/eller fodled	☐	☐	☐	☐	☐	☐	☐

7. Har du, eller har du haft nogle af disse langvarige sygdomme?
(Sæt ét X i hver linje)

	Nej	Ja	Ved ikke
Sukkersyge	☐	☐	☐
Stofskiftesygdom	☐	☐	☐
Slidgigt eller leddegigt	☐	☐	☐
Kuldeudløste anfald af hvide fingre	☐	☐	☐
Håndeksem	☐	☐	☐
Andre langvarige sygdomme	☐	☐	☐
Hvis andre, skriv hvilke: ________________			

8. Hvordan synes du, dit helbred er alt i alt?
(Sæt ét X)

Fremragende	Vældig godt	Godt	Mindre godt	Dårligt
☐	☐	☐	☐	☐

12.2 Baseline questionnaire used in study III (in Danish)

Begge arme

I denne del af spørgeskemaet stiller vi dig spørgsmål om dine symptomer og din evne til at udføre visse aktiviteter. Vær venlig at svare på hvert eneste spørgsmål ved at sætte ét X svarende til det, der passer bedst til din tilstand i den forløbne uge. Hvis du ikke har haft lejlighed til at udføre en bestemt aktivitet i den forløbne uge, beder vi dig angive det svar, du mener ville dække bedst.
Det er uden betydning, hvilken hånd eller arm du anvender til at udføre aktiviteten; dit svar skal afspejle din evne til at udføre selve handlingen, uanset hvordan du gør det.

9. Vurder venligst, hvordan din evne til at udføre følgende handlinger har været i den forløbne uge ved at sætte et X i boksen under det svar, der passer bedst.
(Sæt ét X ud for hvert spørgsmål og besvar venligst alle spørgsmål)

	Ikke vanskeligt	Lidt vanskeligt	Noget vanskeligt	Meget vanskeligt	Umuligt
a. Åbne et marmeladeglas med stramt låg	☐	☐	☐	☐	☐
b. Skrive	☐	☐	☐	☐	☐
c. Dreje en nøgle i en lås	☐	☐	☐	☐	☐
d. Tilberede et måltid mad	☐	☐	☐	☐	☐
e. Skubbe en tung dør op	☐	☐	☐	☐	☐
f. Anbringe en genstand på en hylde over dit hoved	☐	☐	☐	☐	☐
g. Udføre tungt husarbejde (fx vaske vægge, vaske gulve)	☐	☐	☐	☐	☐
h. Arbejde i haven	☐	☐	☐	☐	☐
i. Rede seng	☐	☐	☐	☐	☐
j. Bære en indkøbspose eller en mappe	☐	☐	☐	☐	☐
k. Bære en tung genstand (over 5 kg)	☐	☐	☐	☐	☐
l. Skifte en elektrisk pære over hovedhøjde	☐	☐	☐	☐	☐
m. Vaske eller føntørre dit hår	☐	☐	☐	☐	☐
n. Vaske dig selv på ryggen	☐	☐	☐	☐	☐
o. Tage en sweater på	☐	☐	☐	☐	☐
p. Bruge en kniv til at skære mad ud	☐	☐	☐	☐	☐
q. Fritidsaktiviteter, der ikke er særlig anstrengende (fx kortspil, strikning, osv.)	☐	☐	☐	☐	☐

9. Fortsat	Ikke vanskeligt	Lidt vanskeligt	Noget vanskeligt	Meget vanskeligt	Umuligt
r. Fritidsaktiviteter, som sender en vis kraft eller stød gennem din arm, skulder eller hånd (fx golf, slag med hammer, tennis, osv.)	☐	☐	☐	☐	☐
s. Fritidsaktiviteter, som kræver fuld bevægelighed af din arm (fx frisbee, badminton, osv.)	☐	☐	☐	☐	☐
t. Klare transport (komme fra et sted til et andet)	☐	☐	☐	☐	☐
u. Dyrke sex	☐	☐	☐	☐	☐

10. Hvor *vanskeligt* har det været for dig i den <u>forløbne uge</u>, at omgås familie, venner, naboer og grupper pga. din arm, skulder eller hånd?
(Sæt ét X)

Slet ikke	Lidt	En del	Temmelig meget	Virkelig meget
☐	☐	☐	☐	☐

11. Har du i den <u>forløbne uge</u> været hæmmet i at udføre dit arbejde eller andre gøremål pga. din arm, skulder eller hånd?
(Sæt ét X)

Slet ikke hæmmet	Lidt hæmmet	En del hæmmet	Meget hæmmet	Ude af stand til
☐	☐	☐	☐	☐

12.2 Baseline questionnaire used in study III (in Danish)

12. Vær venlig at angive sværhedsgraden af følgende symptomer i den forløbne uge.
(Sæt ét X ud for hvert spørgsmål og besvar venligst alle spørgsmål)

	Ingen	Lidt	En del	Svær	Ekstrem
a. Smerte i din arm, skulder eller hånd	☐	☐	☐	☐	☐
b. Smerte i din arm, skulder eller hånd, når du laver noget bestemt	☐	☐	☐	☐	☐
c. Prikken i din arm, skulder eller hånd	☐	☐	☐	☐	☐
d. Svaghed i din arm, skulder eller hånd	☐	☐	☐	☐	☐
e. Stivhed i din arm, skulder eller hånd	☐	☐	☐	☐	☐

13. Hvor vanskeligt har det i den forløbne uge været for dig, at sove pga. smerter i din arm, skulder eller hånd?
(Sæt ét X)

Ikke vanskeligt	Lidt vanskeligt	Noget vanskeligt	Meget vanskeligt	Så vanskeligt at det forhindrer mig i at sove
☐	☐	☐	☐	☐

14. Jeg føler mig mindre effektiv, mindre sikker på mig selv, eller til mindre nytte pga. min arm, skulder eller hånd.
(Sæt ét X)

Helt uenig	Uenig	Hverken enig eller uenig	Enig	Helt enig
☐	☐	☐	☐	☐

Højre albue, underarm og hånd

I denne del af spørgeskemaet stiller vi dig spørgsmål om din højre arm.

15. Har du nogensinde haft brækket højre albue, underarm eller håndled?
(Sæt ét X)

Nej	☐
Ja	☐
Ved ikke	☐

16. Er du nogensinde blevet opereret i nogen af nedenstående regioner?
(Sæt ét X ud i hver linje)

	Nej	Ja	Ved ikke
Højre albue	☐	☐	☐
Højre underarm	☐	☐	☐
Højre håndled	☐	☐	☐
Højre hånd	☐	☐	☐

17. Er du nogensinde blevet opereret på grund af en nerve, der var kommet i klemme i højre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________

12.2 Baseline questionnaire used in study III (in Danish)

18. Er du <u>nogensinde</u> blevet behandlet med en skinne, på grund af en nerve der var kommet i klemme i <u>højre</u> arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv årstal: ______________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv årstal: ______________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv årstal: ______________

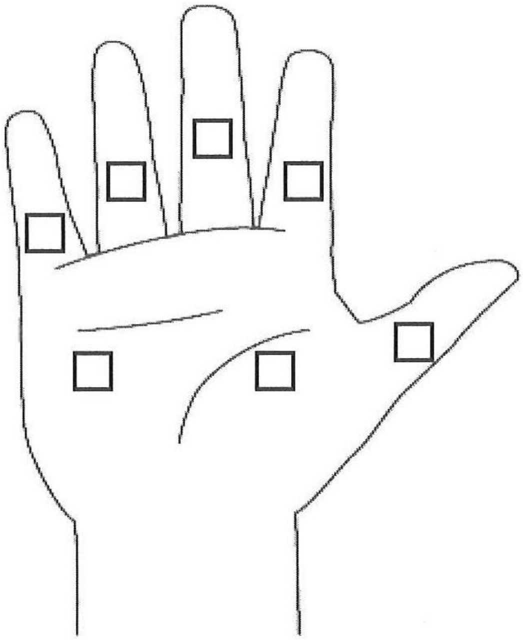
19. Er du <u>nogensinde</u> blevet behandlet med indsprøjtning, på grund af en nerve der var kommet i klemme i <u>højre</u> arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv årstal: ______________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv årstal: ______________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv årstal: ______________

12.2 Baseline questionnaire used in study III (in Danish)

20. Har du haft snurrende og prikkende fornemmelser i <u>højre</u> hånd inden for <u>de sidste 4 uger</u>?
(Sæt ét X)

Nej	☐	→ *Gå til spørgsmål 21*
Ja	☐	→ Vis med X på billedet, hvor du har haft snurrende og prikkende fornemmelser *(sæt gerne flere X, men kun i boksene)*



12.2 Baseline questionnaire used in study III (in Danish)

Følgende spørgsmål handler om dine symptomer fra højre hånd og håndled gennem et typisk døgn i løbet af de sidste 2 uger.

21. Hvor svære er dine hånd- eller håndledssmerter om natten?
(Sæt ét X)

Jeg har ikke hånd- eller håndledssmerter om natten	☐
Lette smerter	☐
Moderate smerter	☐
Svære smerter	☐
Meget svære smerter	☐

22. Hvor mange gange er du vågnet pga. hånd- eller håndledssmerter en typisk nat i løbet af de sidste 2 uger?
(Sæt ét X)

Aldrig	☐
Én gang	☐
To eller tre gange	☐
Fire eller fem gange	☐
Mere end fem gange	☐

23. Har du typisk hånd- eller håndledssmerter om dagen?
(Sæt ét X)

Jeg har aldrig hånd- eller håndledssmerter om dagen	☐
Jeg har lette hånd- eller håndledssmerter om dagen	☐
Jeg har moderate hånd- eller håndledssmerter om dagen	☐
Jeg har svære hånd- eller håndledssmerter om dagen	☐
Jeg har meget svære hånd- eller håndledssmerter om dagen	☐

24. Hvor mange gange har du hånd- eller håndledssmerter om dagen?
(Sæt ét X)

Aldrig	☐
En eller to gange om dagen	☐
Tre til fem gange om dagen	☐
Mere end fem gange om dagen	☐
Smerterne er konstante	☐

25. Hvor længe varer en episode med hånd- eller håndledssmerter om dagen i gennemsnit?
(Sæt ét X)

Jeg har aldrig hånd- eller håndledssmerter om dagen	☐
Mindre end 10 minutter	☐
10 til 60 minutter	☐
Mere end 60 minutter	☐
Smerterne er konstante gennem dagen	☐

26. Har du sovende fornemmelse (følelsesløshed) i din hånd?
(Sæt ét X)

Nej	☐
Jeg har en let sovende fornemmelse	☐
Jeg har en moderat sovende fornemmelse	☐
Jeg har en svær sovende fornemmelse	☐
Jeg har en meget svær sovende fornemmelse	☐

27. Har du nedsat kraft i din hånd eller dit håndled?
(Sæt ét X)

Ingen nedsat kraft	☐
Let nedsat kraft	☐
Moderat nedsat kraft	☐
Svært nedsat kraft	☐
Meget svært nedsat kraft	☐

28. Har du snurren og prikken i din hånd?
(Sæt ét X)

Ingen snurren og prikken	☐
Let snurren og prikken	☐
Moderat snurren og prikken	☐
Svær snurren og prikken	☐
Meget svær snurren og prikken	☐

29. Hvor svær er den sovende fornemmelse (følelsesløshed) eller snurrende fornemmelse i hånden om natten?
(Sæt ét X)

Jeg har ingen sovende eller snurrende fornemmelse om natten	☐
Let sovende eller snurrende fornemmelse om natten	☐
Moderat sovende eller snurrende fornemmelse om natten	☐
Svær sovende eller snurrende fornemmelse om natten	☐
Meget svær sovende eller snurrende fornemmelse om natten	☐

30. Hvor mange gange er du vågnet pga. sovende fornemmelse (følelsesløshed) eller snurrende fornemmelse i hånden en typisk nat i løbet af de sidste 2 uger?
(Sæt ét X)

Aldrig	☐
Én gang	☐
To eller tre gange	☐
Fire eller fem gange	☐
Mere end fem gange	☐

31. Har du besvær med at tage fat om eller bruge små ting såsom nøgler eller kuglepenne?
(Sæt ét X)

Intet besvær	☐
Let besvær	☐
Moderat besvær	☐
Meget besvær	☐
Virkelig meget besvær	☐

12.2 Baseline questionnaire used in study III (in Danish)

32. På en typisk dag i løbet af de sidste 2 uger, har du da haft besvær med at gennemføre følgende aktiviteter på grund af symptomer fra højre hånd og håndled?
(Sæt ét X i hver linje)

Aktivitet	Intet besvær	Let besvær	Moderat besvær	Meget besvær	Kan overhovedet ikke på grund af symptomer fra hånd og håndled
a. Skrive i hånden *(hvis du er højre håndet, ellers gå til **b.**)*	☐	☐	☐	☐	☐
b. Knappe knapper	☐	☐	☐	☐	☐
c. Holde en bog under læsning	☐	☐	☐	☐	☐
d. Holde en telefon	☐	☐	☐	☐	☐
e. Åbne (marmelade)glas	☐	☐	☐	☐	☐
f. Huslige pligter	☐	☐	☐	☐	☐
g. Bære indkøbsposer	☐	☐	☐	☐	☐
h. Badning og påklædning	☐	☐	☐	☐	☐

Venstre albue, underarm og hånd

I denne del af spørgeskemaet stiller vi dig spørgsmål om din venstre arm.

33. Har du nogensinde haft brækket venstre albue, underarm eller håndled?
(Sæt ét X)

Nej	☐
Ja	☐
Ved ikke	☐

34. Er du nogensinde blevet opereret i nogen af nedenstående regioner?
(Sæt ét X i hver linje)

	Nej	Ja	Ved ikke
Venstre albue	☐	☐	☐
Venstre underarm	☐	☐	☐
Venstre håndled	☐	☐	☐
Venstre hånd	☐	☐	☐

35. Er du nogensinde blevet opereret på grund af en nerve, der var kommet i klemme i venstre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________

36. Er du nogensinde blevet behandlet med en skinne, på grund af en nerve der var kommet i klemme i venstre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________

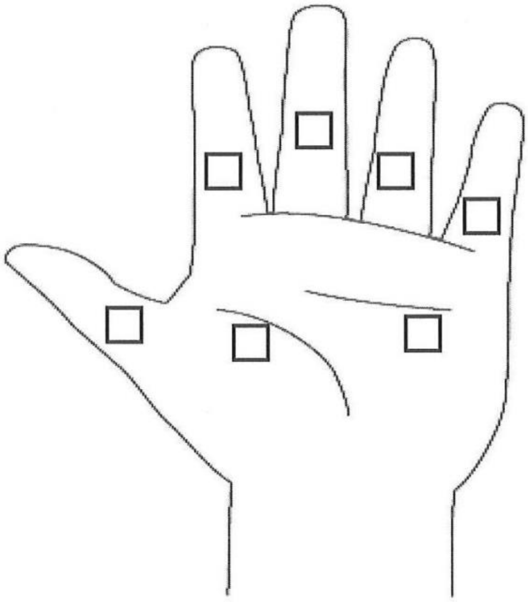
37. Er du nogensinde blevet behandlet med indsprøjtning, på grund af en nerve der var kommet i klemme i venstre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv årstal: ____________

12.2 Baseline questionnaire used in study III (in Danish)

38. Har du haft snurrende og prikkende fornemmelser i <u>venstre</u> hånd inden for <u>de sidste 4 uger</u>?
(Sæt ét X)

Nej	☐	→ *Gå til spørgsmål 39*
Ja	☐	→ Vis med X på billedet, hvor du har haft snurrende og prikkende fornemmelser *(sæt gerne flere X, men kun i boksene)*



12.2 Baseline questionnaire used in study III (in Danish)

Følgende spørgsmål handler om dine symptomer fra venstre hånd og håndled gennem et typisk døgn i løbet af de sidste 2 uger.

39. Hvor svære er dine hånd- eller håndledssmerter om natten?
(Sæt ét X)

Jeg har ikke hånd- eller håndledssmerter om natten	☐
Lette smerter	☐
Moderate smerter	☐
Svære smerter	☐
Meget svære smerter	☐

40. Hvor mange gange er du vågnet pga. hånd- eller håndledssmerter en typisk nat i løbet af de sidste 2 uger?
(Sæt ét X)

Aldrig	☐
Én gang	☐
To eller tre gange	☐
Fire eller fem gange	☐
Mere end fem gange	☐

41. Har du typisk hånd- eller håndledssmerter om dagen?
(Sæt ét X)

Jeg har aldrig hånd- eller håndledssmerter om dagen	☐
Jeg har lette hånd- eller håndledssmerter om dagen	☐
Jeg har moderate hånd- eller håndledssmerter om dagen	☐
Jeg har svære hånd- eller håndledssmerter om dagen	☐
Jeg har meget svære hånd- eller håndledssmerter om dagen	☐

42. Hvor mange gange har du hånd- eller håndledssmerter om dagen?
(Sæt ét X)

Aldrig	☐
En eller to gange om dagen	☐
Tre til fem gange om dagen	☐
Mere end fem gange om dagen	☐
Smerterne er konstante	☐

43. Hvor længe varer en episode med hånd- eller håndledssmerter om dagen i gennemsnit?
(Sæt ét X)

Jeg har aldrig hånd- eller håndledssmerter om dagen	☐
Mindre end 10 minutter	☐
10 til 60 minutter	☐
Mere end 60 minutter	☐
Smerterne er konstante gennem dagen	☐

44. Har du sovende fornemmelse (følelsesløshed) i din hånd?
(Sæt ét X)

Nej	☐
Jeg har en let sovende fornemmelse	☐
Jeg har en moderat sovende fornemmelse	☐
Jeg har en svær sovende fornemmelse	☐
Jeg har en meget svær sovende fornemmelse	☐

45. Har du nedsat kraft i din hånd eller dit håndled?
(Sæt ét X)

Ingen nedsat kraft	☐
Let nedsat kraft	☐
Moderat nedsat kraft	☐
Svært nedsat kraft	☐
Meget svært nedsat kraft	☐

46. Har du snurren og prikken i din hånd?
(Sæt ét X)

Ingen snurren og prikken	☐
Let snurren og prikken	☐
Moderat snurren og prikken	☐
Svær snurren og prikken	☐
Meget svær snurren og prikken	☐

47. Hvor svær er den sovende fornemmelse (følelsesløshed) eller snurrende fornemmelse i hånden om natten?
(Sæt ét X)

Jeg har ingen sovende eller snurrende fornemmelse om natten	☐
Let sovende eller snurrende fornemmelse om natten	☐
Moderat sovende eller snurrende fornemmelse om natten	☐
Svær sovende eller snurrende fornemmelse om natten	☐
Meget svær sovende eller snurrende fornemmelse om natten	☐

48. Hvor mange gange er du vågnet pga. sovende fornemmelse (følelsesløshed) eller snurrende fornemmelse i hånden en typisk nat i løbet af de sidste 2 uger?
(Sæt ét X)

Aldrig	☐
Én gang	☐
To eller tre gange	☐
Fire eller fem gange	☐
Mere end fem gange	☐

49. Har du besvær med at tage fat om eller bruge små ting såsom nøgler eller kuglepenne?
(Sæt ét X)

Intet besvær	☐
Let besvær	☐
Moderat besvær	☐
Meget besvær	☐
Virkelig meget besvær	☐

50. På en typisk dag i løbet af de sidste 2 uger, har du da haft besvær med at gennemføre følgende aktiviteter på grund af symptomer fra venstre hånd og håndled?
(Sæt ét X i hver linje)

Aktivitet	Intet besvær	Let besvær	Moderat besvær	Meget besvær	Kan overhovedet ikke på grund af symptomer fra hånd og håndled
a. Skrive i hånden *(hvis du er venstre håndet, ellers gå til **b.**)*	☐	☐	☐	☐	☐
b. Knappe knapper	☐	☐	☐	☐	☐
c. Holde en bog under læsning	☐	☐	☐	☐	☐
d. Holde en telefon	☐	☐	☐	☐	☐
e. Åbne (marmelade)glas	☐	☐	☐	☐	☐
f. Huslige pligter	☐	☐	☐	☐	☐
g. Bære indkøbsposer	☐	☐	☐	☐	☐
h. Badning og påklædning	☐	☐	☐	☐	☐

Psykisk arbejdsmiljø

51. Hvor stor indflydelse har du normalt på tilrettelæggelsen og udførelsen af dit arbejde?
(*Sæt ét X*)

Meget stor	Ret stor	Moderat stor	Ikke så stor	Ret lille	Meget lille
☐	☐	☐	☐	☐	☐

52. Hvor krævende synes du alt i alt, dit arbejde er?
(*Sæt ét X*)

Særdeles krævende	Meget krævende	Ret krævende	Noget krævende	Ikke så krævende	Meget lidt krævende
☐	☐	☐	☐	☐	☐

53. Hvis du har problemer på dit arbejde, kan du så få den nødvendige hjælp og støtte fra din ledelse?
(*Sæt ét X*)

Altid	Næsten altid	Som regel	Ofte	Af og til	Sjældent/ aldrig
☐	☐	☐	☐	☐	☐

54. Hvis du har problemer på dit arbejde, kan du så få den nødvendige hjælp og støtte fra dine kolleger?
(*Sæt ét X*)

Altid	Næsten altid	Som regel	Ofte	Af og til	Sjældent/ aldrig
☐	☐	☐	☐	☐	☐

12.2 Baseline questionnaire used in study III (in Danish)

Baggrund og levevaner

55. I hvilken grad har du inden for <u>den sidste uge, inklusiv i dag</u>, været plaget af:
(Sæt ét X ud for hvert spørgsmål og besvar venligst ale spørgsmål)

	Slet ikke	Lidt	Noget	En hel del	Særdeles meget
a. Hovedpine	☐	☐	☐	☐	☐
b. Svimmelhed eller tilløb til at besvime	☐	☐	☐	☐	☐
c. Smerter i hjerte eller bryst	☐	☐	☐	☐	☐
d. Lavtsiddende rygsmerter	☐	☐	☐	☐	☐
e. Kvalme eller uro i maven	☐	☐	☐	☐	☐
f. Muskelsmerter	☐	☐	☐	☐	☐
g. At du har svært ved at få vejret	☐	☐	☐	☐	☐
h. Anfald af varme- eller kuldefornemmelser	☐	☐	☐	☐	☐
i. Følelsesløshed eller en snurrende, fornemmelse i kroppen	☐	☐	☐	☐	☐
j. En klump i halsen	☐	☐	☐	☐	☐
k. At du føler dig svag i kroppen	☐	☐	☐	☐	☐
l. At dine arme eller ben føles tunge	☐	☐	☐	☐	☐

56. Hvis du er kvinde, har du været gravid inden for det seneste år?
(Sæt ét X)

Nej	☐
Ja	☐

57. Er du?
(Sæt ét X)

Højrehåndet	☐
Venstrehåndet	☐
Bruger begge hænder lige godt	☐

58.	**Hvor høj er du?**	|__|__|__| cm
59.	**Hvad vejer du?**	|__|__|__| kg

12.2 Baseline questionnaire used in study III (in Danish)

60. Har du dyrket sport mere end 1 time om ugen inden for det seneste år?
(Sæt ét X i hver linje)

	Nej	Ja
Ketsjersport (tennis, badminton, squash)	☐	☐
Håndbold	☐	☐
Cykling (medregn almindelig brug af cyklen som transportmiddel)	☐	☐
Roning	☐	☐
Andre sportsgrene	☐	☐
Hvis andre, skriv hvilke: ______________________________		

61. Har du nogensinde været <u>daglig ryger</u>?
(Sæt ét X)

Nej	☐	→ *Gå til spørgsmål 65*
Ja	☐	→ *Besvar næste spørgsmål*

62. Hvor mange år i alt du været <u>daglig ryger</u>? (Perioder med rygestop skal trækkes fra)

Ca. |__|__| år

63. Hvor meget har du røget i gennemsnit i de år, hvor du har været <u>daglig ryger</u>?
(Skriv ét tal i hver linje)

Cirka |__|__| cigaretter per dag

Cirka |__|__| cerutter eller cigarer per dag

Cirka |__|__| gram tobak per uge (en pakke indeholder typisk 50 gram)

64. Ryger du for tiden?
(Sæt ét X)

Nej	☐
Ja	☐

12.2 Baseline questionnaire used in study III (in Danish)

65. Hvor ofte drikker du alkohol?
(Sæt ét X)

Aldrig	☐	→ *Gå til spørgsmål 67*
1-3 gange om måneden	☐	→ *Besvar næste spørgsmål*
1 gang om ugen eller mere.	☐	→ *Besvar næste spørgsmål*
Ved ikke	☐	→ *Besvar næste spørgsmål*

66. Hvor meget øl, vin eller spiritus drikker du i gennemsnit om ugen?
(Skriv ét tal i hver linje)

Cirka |__|__| flasker almindelig øl
Cirka |__|__| flasker guldøl (stærk øl)
Cirka |__|__| glas rødvin, hvidvin eller rosévin
Cirka |__|__| glas hedvin (fx portvin)
Cirka |__|__| glas spiritus (fx snaps eller whisky)

67. Har du kommentarer, er du velkommen til at skrive dem her:

____

____

____

Mange tak for din besvarelse

12.3 Follow-up questionnaire used in study III (in Danish)

ID NR.: |__|__|__|

OPFØLGNINGS SPØRGESKEMA TIL PATIENTER UNDERSØGT FOR SNURREN, PRIKKEN, SMERTER ELLER ANDET BESVÆR I HÅND OG FINGRE

12.3 Follow-up questionnaire used in study III (in Danish)

Vejledning

Du modtager dette opfølgningsspørgeskema, fordi du for ca. et år siden var til undersøgelse for besvær i hånd og fingre på Neurofysiologisk Afdeling, Aarhus Universitetshospital. I den anledning deltog du i et forskningsprojekt, hvis formål var at belyse hvordan det går med besværet i din hånd og fingre på længere sigt. Dette spørgeskema skal bruges til at sammenligne dit besvær for ca. et år siden med nu.

Du kan læse mere om undersøgelsen på skemaets bagside.

De fleste vil bruge 10-15 minutter på at udfylde skemaet.

Det udfyldte spørgeskema lægges i vedlagte frankerede kuvert og sendes retur med posten.

Du bedes besvare spørgsmålene i den opstillede rækkefølge. Giv dig god tid til at læse spørgsmålene inden du svarer, og følg de vejledninger, der er undervejs.

Du vil sikkert komme i tvivl ved nogle af spørgsmålene, men det er vigtigt, at du svarer så godt, du kan alligevel, og at alle spørgsmålene besvares.

Du vil modtage en påmindelse om ca. 3 uger, hvis vi ikke har modtaget dit spørgeskema inden da.

Hvis du har spørgsmål til spørgeskemaet, er du velkommen til at kontakte undertegnede læge, Sorosh Taba på tlf. 7846 4719 (hverdage kl. 9-14) eller e-mail: sortab@rm.dk

Sådan udfylder du spørgeskemaet
Vi vil bede dig svare på spørgsmålene efter de anvisninger, der er i spørgeskemaet. Brug venligst sort eller blå kuglepen. Sæt X og skriv tal så de er nemme at tolke, som vist i eksemplet nedenfor.

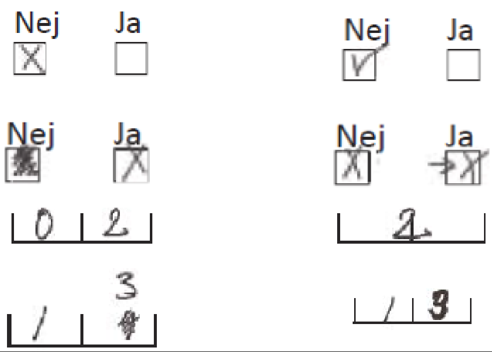
KORREKT **FORKERT**

Sæt tydelige X

Hvis et felt er **udfyldt forkert**, skraveres den pågældende kasse, og krydset sættes det rigtige sted

Tallene skrives i felterne

Tallene rettes ved at overstrege det forkerte tal og skrive det rigtige ovenover



Med venlig hilsen

Sorosh Taba, læge
Poul Frost, overlæge

Arbejdsmedicinsk Klinik,
Aarhus Universitetshospital

Susanne Wulff Svendsen, professor

Arbejdsmedicinsk Klinik,
Regionshospitalet Herning

Birger Johnsen, overlæge
Anders Fuglsang-Frederiksen, professor

Neurofysiologisk Afdeling,
Aarhus Universitetshospital

Erhvervsstatus

1. Hvad er din aktuelle erhvervsstatus?
(Sæt ét X)

I arbejde (som ansat eller selvstændig)	☐
Beskæftiget på særlige vilkår (fx aktivering, skånejob, fleksjob)	☐
Sygemeldt fra arbejde (heltids-/eller deltidssygemeldt)	☐
Sygemeldt fra arbejdsløshed	☐
På orlov fx (barsels-, forældre-, uddannelsesorlov)	☐
Arbejdsløs	☐
Elev, lærling eller studerende	☐
Folkepensionist, efterlønsmodtager eller førtidspensionist	☐
Andet	☐
Hvis andet, skriv med BLOKBOGSTAVER: ____________________	

2. Hvad er din aktuelle jobtitel?
Vær så præcis som muligt. Skriv fx "montør for køkkenfirma" i stedet for "montør" eller "fabriksarbejder på møbelfabrik" i stedet for "fabriksarbejder".

Jeg arbejder som – skriv stillingsbetegnelse:
____

12.3 Follow-up questionnaire used in study III (in Danish)

Helbred

3. I løbet af de sidste 12 måneder, hvor meget har du alt i alt været generet af smerter eller ubehag i følgende kropsregioner?
(Sæt ét X i hver linje)

		Slet ikke	Meget lidt	Lidt	Noget	En del	Meget	Særdeles meget
a.	Nakke	☐	☐	☐	☐	☐	☐	☐
b.	Skuldre	☐	☐	☐	☐	☐	☐	☐
c.	Lænderyg	☐	☐	☐	☐	☐	☐	☐
d.	Albuer, underarme og/eller hænder	☐	☐	☐	☐	☐	☐	☐
e.	Hofter, knæ og/eller fodled	☐	☐	☐	☐	☐	☐	☐

4. Hvordan synes du, dit helbred er alt i alt?
(Sæt ét X)

Fremragende	Vældig godt	Godt	Mindre godt	Dårligt
☐	☐	☐	☐	☐

Begge arme

I denne del af spørgeskemaet stiller vi dig spørgsmål om dine symptomer og din evne til at udføre visse aktiviteter. Vær venlig at svare på hvert eneste spørgsmål ved at sætte ét X svarende til det, der passer bedst til din tilstand i den forløbne uge. Hvis du ikke har haft lejlighed til at udføre en bestemt aktivitet i den forløbne uge, beder vi dig angive det svar, du mener ville dække bedst.
Det er uden betydning, hvilken hånd eller arm du anvender til at udføre aktiviteten; dit svar skal afspejle din evne til at udføre selve handlingen, uanset hvordan du gør det.

5. Vurder venligst, hvordan din evne til at udføre følgende handlinger har været i den forløbne uge ved at sætte et X i boksen under det svar, der passer bedst.
(Sæt ét X ud for hvert spørgsmål og besvar venligst alle spørgsmål)

		Ikke vanskeligt	Lidt vanskeligt	Noget vanskeligt	Meget vanskeligt	Umuligt
a.	Åbne et marmeladeglas med stramt låg	☐	☐	☐	☐	☐
b.	Skrive	☐	☐	☐	☐	☐
c.	Dreje en nøgle i en lås	☐	☐	☐	☐	☐
d.	Tilberede et måltid mad	☐	☐	☐	☐	☐
e.	Skubbe en tung dør op	☐	☐	☐	☐	☐
f.	Anbringe en genstand på en hylde over dit hoved	☐	☐	☐	☐	☐
g.	Udføre tungt husarbejde (fx vaske vægge, vaske gulve)	☐	☐	☐	☐	☐
h.	Arbejde i haven	☐	☐	☐	☐	☐
i.	Rede seng	☐	☐	☐	☐	☐
j.	Bære en indkøbspose eller en mappe	☐	☐	☐	☐	☐
k.	Bære en tung genstand (over 5 kg)	☐	☐	☐	☐	☐
l.	Skifte en elektrisk pære over hovedhøjde	☐	☐	☐	☐	☐
m.	Vaske eller føntørre dit hår	☐	☐	☐	☐	☐
n.	Vaske dig selv på ryggen	☐	☐	☐	☐	☐
o.	Tage en sweater på	☐	☐	☐	☐	☐
p.	Bruge en kniv til at skære mad ud	☐	☐	☐	☐	☐
q.	Fritidsaktiviteter, der ikke er særlig anstrengende (fx kortspil, strikning, osv.)	☐	☐	☐	☐	☐

5.	**Fortsat**	Ikke vanskeligt	Lidt vanskeligt	Noget vanskeligt	Meget vanskeligt	Umuligt
r.	Fritidsaktiviteter, som sender en vis kraft eller stød gennem din arm, skulder eller hånd (fx golf, slag med hammer, tennis, osv.)	☐	☐	☐	☐	☐
s.	Fritidsaktiviteter, som kræver fuld bevægelighed af din arm (fx frisbee, badminton, osv.)	☐	☐	☐	☐	☐
t.	Klare transport (komme fra et sted til et andet)	☐	☐	☐	☐	☐
u.	Dyrke sex	☐	☐	☐	☐	☐

6. Hvor *vanskeligt* har det været for dig i den <u>forløbne uge</u>, at omgås familie, venner, naboer og grupper pga. din arm, skulder eller hånd?
(Sæt ét X)

Slet ikke	Lidt	En del	Temmelig meget	Virkelig meget
☐	☐	☐	☐	☐

7. Har du i den <u>forløbne uge</u> været hæmmet i at udføre dit arbejde eller andre gøremål pga. din arm, skulder eller hånd?
(Sæt ét X)

Slet ikke hæmmet	Lidt hæmmet	En del hæmmet	Meget hæmmet	Ude af stand til
☐	☐	☐	☐	☐

8. Vær venlig at angive sværhedsgraden af følgende symptomer i den <u>forløbne uge</u>.
(Sæt ét X ud for hvert spørgsmål og besvar venligst alle spørgsmål)

		Ingen	Lidt	En del	Svær	Ekstrem
a.	Smerte i din arm, skulder eller hånd	☐	☐	☐	☐	☐
b.	Smerte i din arm, skulder eller hånd, når du laver noget bestemt	☐	☐	☐	☐	☐
c.	Prikken i din arm, skulder eller hånd	☐	☐	☐	☐	☐
d.	Svaghed i din arm, skulder eller hånd	☐	☐	☐	☐	☐
e.	Stivhed i din arm, skulder eller hånd	☐	☐	☐	☐	☐

9. Hvor vanskeligt har det i den forløbne uge været for dig, at sove pga. smerter i din arm, skulder eller hånd?
(Sæt ét X)

Ikke vanskeligt	Lidt vanskeligt	Noget vanskeligt	Meget vanskeligt	Så vanskeligt at det forhindrer mig i at sove
☐	☐	☐	☐	☐

10. Jeg føler mig mindre effektiv, mindre sikker på mig selv, eller til mindre nytte pga. min arm, skulder eller hånd.
(Sæt ét X)

Helt uenig	Uenig	Hverken enig eller uenig	Enig	Helt enig
☐	☐	☐	☐	☐

Højre albue, underarm og hånd

I denne del af spørgeskemaet stiller vi dig spørgsmål om din højre arm.

11. Er du inden for de sidste 12 måneder blevet opereret på grund af en nerve, der var kommet i klemme i højre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv dato: ____________

12. Er du inden for de sidste 12 måneder blevet behandlet med en skinne, på grund af en nerve der var kommet i klemme i højre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv dato: ____________

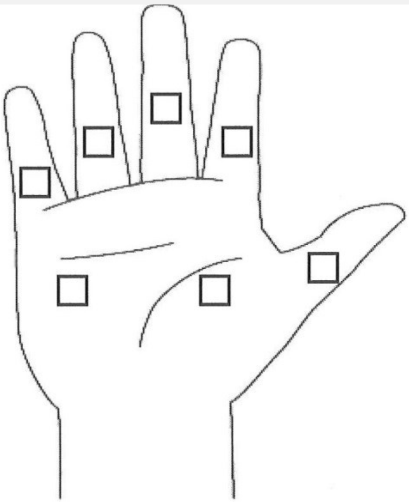
13. Er du inden for de sidste 12 måneder blevet behandlet med indsprøjtning, på grund af en nerve der var kommet i klemme i højre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv dato: ____________

12.3 Follow-up questionnaire used in study III (in Danish)

14. Har du haft snurrende og prikkende fornemmelser i <u>højre</u> hånd inden for <u>de sidste 4 uger</u>?
(Sæt ét X)

Nej	☐	→ *Gå til spørgsmål 15*
Ja	☐	→ Vis med X på billedet, hvor du har haft snurrende og prikkende fornemmelser *(sæt gerne flere X, men kun i boksene)*



12.3 Follow-up questionnaire used in study III (in Danish)

Følgende spørgsmål handler om dine symptomer fra højre hånd og håndled gennem et typisk døgn i løbet af de sidste 2 uger.

15. Hvor svære er dine hånd- eller håndledssmerter om natten?
(Sæt ét X)

Jeg har ikke hånd- eller håndledssmerter om natten	☐
Lette smerter	☐
Moderate smerter	☐
Svære smerter	☐
Meget svære smerter	☐

16. Hvor mange gange er du vågnet pga. hånd- eller håndledssmerter en typisk nat i løbet af de sidste 2 uger?
(Sæt ét X)

Aldrig	☐
Én gang	☐
To eller tre gange	☐
Fire eller fem gange	☐
Mere end fem gange	☐

17. Har du typisk hånd- eller håndledssmerter om dagen?
(Sæt ét X)

Jeg har aldrig hånd- eller håndledssmerter om dagen	☐
Jeg har lette hånd- eller håndledssmerter om dagen	☐
Jeg har moderate hånd- eller håndledssmerter om dagen	☐
Jeg har svære hånd- eller håndledssmerter om dagen	☐
Jeg har meget svære hånd- eller håndledssmerter om dagen	☐

18. Hvor mange gange har du hånd- eller håndledssmerter om dagen?
(Sæt ét X)

Aldrig	☐
En eller to gange om dagen	☐
Tre til fem gange om dagen	☐
Mere end fem gange om dagen	☐
Smerterne er konstante	☐

19. Hvor længe varer en episode med hånd- eller håndledssmerter om dagen i gennemsnit?
(Sæt ét X)

Jeg har aldrig hånd- eller håndledssmerter om dagen	☐
Mindre end 10 minutter	☐
10 til 60 minutter	☐
Mere end 60 minutter	☐
Smerterne er konstante gennem dagen	☐

20. Har du sovende fornemmelse (følelsesløshed) i din hånd?
(Sæt ét X)

Nej	☐
Jeg har en let sovende fornemmelse	☐
Jeg har en moderat sovende fornemmelse	☐
Jeg har en svær sovende fornemmelse	☐
Jeg har en meget svær sovende fornemmelse	☐

12.3 Follow-up questionnaire used in study III (in Danish)

21. Har du nedsat kraft i din hånd eller dit håndled?
(Sæt ét X)

Ingen nedsat kraft	☐
Let nedsat kraft	☐
Moderat nedsat kraft	☐
Svært nedsat kraft	☐
Meget svært nedsat kraft	☐

22. Har du snurren og prikken i din hånd?
(Sæt ét X)

Ingen snurren og prikken	☐
Let snurren og prikken	☐
Moderat snurren og prikken	☐
Svær snurren og prikken	☐
Meget svær snurren og prikken	☐

23. Hvor svær er den sovende fornemmelse (følelsesløshed) eller snurrende fornemmelse i hånden om natten?
(Sæt ét X)

Jeg har ingen sovende eller snurrende fornemmelse om natten	☐
Let sovende eller snurrende fornemmelse om natten	☐
Moderat sovende eller snurrende fornemmelse om natten	☐
Svær sovende eller snurrende fornemmelse om natten	☐
Meget svær sovende eller snurrende fornemmelse om natten	☐

24. Hvor mange gange er du vågnet pga. sovende fornemmelse (følelsesløshed) eller snurrende fornemmelse i hånden en typisk nat i løbet af de sidste 2 uger?
(Sæt ét X)

Aldrig	☐
Én gang	☐
To eller tre gange	☐
Fire eller fem gange	☐
Mere end fem gange	☐

25. Har du besvær med at tage fat om eller bruge små ting såsom nøgler eller kuglepenne?
(Sæt ét X)

Intet besvær	☐
Let besvær	☐
Moderat besvær	☐
Meget besvær	☐
Virkelig meget besvær	☐

12.3 Follow-up questionnaire used in study III (in Danish)

26. På en typisk dag i løbet af <u>de sidste 2 uger</u>, har du da haft besvær med at gennemføre følgende aktiviteter på grund af symptomer fra <u>højre</u> hånd og håndled?
(Sæt ét X i hver linje)

	Aktivitet	Intet besvær	Let besvær	Moderat besvær	Meget besvær	Kan overhovedet ikke på grund af symptomer fra hånd og håndled
a.	Skrive i hånden *(hvis du er højrehåndet, ellers gå til* ***b.****)*	☐	☐	☐	☐	☐
b.	Knappe knapper	☐	☐	☐	☐	☐
c.	Holde en bog under læsning	☐	☐	☐	☐	☐
d.	Holde en telefon	☐	☐	☐	☐	☐
e.	Åbne (marmelade)glas	☐	☐	☐	☐	☐
f.	Huslige pligter	☐	☐	☐	☐	☐
g.	Bære indkøbsposer	☐	☐	☐	☐	☐
h.	Badning og påklædning	☐	☐	☐	☐	☐

Venstre albue, underarm og hånd

I denne del af spørgeskemaet stiller vi dig spørgsmål om din venstre arm.

27. Er du inden for de sidste 12 måneder blevet opereret på grund af en nerve, der var kommet i klemme i venstre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv dato: ____________

28. Er du inden for de sidste 12 måneder blevet behandlet med en skinne, på grund af en nerve der var kommet i klemme i venstre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv dato: ____________

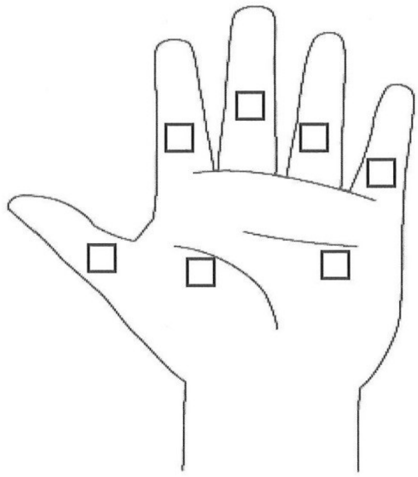
29. Er du inden for de sidste 12 måneder blevet behandlet med indsprøjtning, på grund af en nerve der var kommet i klemme i venstre arm?
(Hvis ja, sæt gerne flere X)

Nej	☐	
Ja, ved albuen	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, ved håndleddet	☐	Hvis ja, hvornår cirka? Skriv dato: ____________
Ja, andet sted	☐	Hvis ja, hvornår cirka? Skriv dato: ____________

12.3 Follow-up questionnaire used in study III (in Danish)

30. Har du haft snurrende og prikkende fornemmelser i venstre hånd inden for de sidste 4 uger?
(Sæt ét X)

Nej	☐	→ *Gå til spørgsmål 31*
Ja	☐	→ Vis med X på billedet, hvor du har haft snurrende og prikkende fornemmelser *(sæt gerne flere X, men kun i boksene)*



12.3 Follow-up questionnaire used in study III (in Danish)

Følgende spørgsmål handler om dine symptomer fra venstre hånd og håndled gennem et typisk døgn i løbet af de sidste 2 uger.

31. Hvor svære er dine hånd- eller håndledssmerter om natten?
(Sæt ét X)

Jeg har ikke hånd- eller håndledssmerter om natten	☐
Lette smerter	☐
Moderate smerter	☐
Svære smerter	☐
Meget svære smerter	☐

32. Hvor mange gange er du vågnet pga. hånd- eller håndledssmerter en typisk nat i løbet af de sidste 2 uger?
(Sæt ét X)

Aldrig	☐
Én gang	☐
To eller tre gange	☐
Fire eller fem gange	☐
Mere end fem gange	☐

33. Har du typisk hånd- eller håndledssmerter om dagen?
(Sæt ét X)

Jeg har aldrig hånd- eller håndledssmerter om dagen	☐
Jeg har lette hånd- eller håndledssmerter om dagen	☐
Jeg har moderate hånd- eller håndledssmerter om dagen	☐
Jeg har svære hånd- eller håndledssmerter om dagen	☐
Jeg har meget svære hånd- eller håndledssmerter om dagen	☐

12.3 Follow-up questionnaire used in study III (in Danish)

34. Hvor mange gange har du hånd- eller håndledssmerter om dagen?
(Sæt ét X)

Aldrig	☐
En eller to gange om dagen	☐
Tre til fem gange om dagen	☐
Mere end fem gange om dagen	☐
Smerterne er konstante	☐

35. Hvor længe varer en episode med hånd- eller håndledssmerter om dagen i gennemsnit?
(Sæt ét X)

Jeg har aldrig hånd- eller håndledssmerter om dagen	☐
Mindre end 10 minutter	☐
10 til 60 minutter	☐
Mere end 60 minutter	☐
Smerterne er konstante gennem dagen	☐

36. Har du sovende fornemmelse (følelsesløshed) i din hånd?
(Sæt ét X)

Nej	☐
Jeg har en let sovende fornemmelse	☐
Jeg har en moderat sovende fornemmelse	☐
Jeg har en svær sovende fornemmelse	☐
Jeg har en meget svær sovende fornemmelse	☐

12.3 Follow-up questionnaire used in study III (in Danish)

37. Har du nedsat kraft i din hånd eller dit håndled?
(Sæt ét X)

Ingen nedsat kraft	☐
Let nedsat kraft	☐
Moderat nedsat kraft	☐
Svært nedsat kraft	☐
Meget svært nedsat kraft	☐

38. Har du snurren og prikken i din hånd?
(Sæt ét X)

Ingen snurren og prikken	☐
Let snurren og prikken	☐
Moderat snurren og prikken	☐
Svær snurren og prikken	☐
Meget svær snurren og prikken	☐

39. Hvor svær er den sovende fornemmelse (følelsesløshed) eller snurrende fornemmelse i hånden om natten?
(Sæt ét X)

Jeg har ingen sovende eller snurrende fornemmelse om natten	☐
Let sovende eller snurrende fornemmelse om natten	☐
Moderat sovende eller snurrende fornemmelse om natten	☐
Svær sovende eller snurrende fornemmelse om natten	☐
Meget svær sovende eller snurrende fornemmelse om natten	☐

12.3 Follow-up questionnaire used in study III (in Danish)

40. Hvor mange gange er du vågnet pga. sovende fornemmelse (følelsesløshed) eller snurrende fornemmelse i hånden en typisk nat i løbet af de sidste 2 uger?
(Sæt ét X)

Aldrig	☐
Én gang	☐
To eller tre gange	☐
Fire eller fem gange	☐
Mere end fem gange	☐

41. Har du besvær med at tage fat om eller bruge små ting såsom nøgler eller kuglepenne?
(Sæt ét X)

Intet besvær	☐
Let besvær	☐
Moderat besvær	☐
Meget besvær	☐
Virkelig meget besvær	☐

12.3 Follow-up questionnaire used in study III (in Danish)

42. På en typisk dag i løbet af de sidste 2 uger, har du da haft besvær med at gennemføre følgende aktiviteter på grund af symptomer fra venstre hånd og håndled?
(Sæt ét X i hver linje)

	Aktivitet	Intet besvær	Let besvær	Moderat besvær	Meget besvær	Kan overhovedet ikke på grund af symptomer fra hånd og håndled
a.	Skrive i hånden *(hvis du er venstrehåndet, ellers gå til **b.**)*	☐	☐	☐	☐	☐
b.	Knappe knapper	☐	☐	☐	☐	☐
c.	Holde en bog under læsning	☐	☐	☐	☐	☐
d.	Holde en telefon	☐	☐	☐	☐	☐
e.	Åbne (marmelade)glas	☐	☐	☐	☐	☐
f.	Huslige pligter	☐	☐	☐	☐	☐
g.	Bære indkøbsposer	☐	☐	☐	☐	☐
h.	Badning og påklædning	☐	☐	☐	☐	☐

Psykisk arbejdsmiljø

43. Hvor stor indflydelse har du normalt på tilrettelæggelsen og udførelsen af dit arbejde?
(*Sæt ét X*)

Meget stor	Ret stor	Moderat stor	Ikke så stor	Ret lille	Meget lille
☐	☐	☐	☐	☐	☐

44. Hvor krævende synes du alt i alt, dit arbejde er?
(*Sæt ét X*)

Særdeles krævende	Meget krævende	Ret krævende	Noget krævende	Ikke så krævende	Meget lidt krævende
☐	☐	☐	☐	☐	☐

45. Hvis du har problemer på dit arbejde, kan du så få den nødvendige hjælp og støtte fra din ledelse?
(*Sæt ét X*)

Altid	Næsten altid	Som regel	Ofte	Af og til	Sjældent/ aldrig
☐	☐	☐	☐	☐	☐

46. Hvis du har problemer på dit arbejde, kan du så få den nødvendige hjælp og støtte fra dine kolleger?
(*Sæt ét X*)

Altid	Næsten altid	Som regel	Ofte	Af og til	Sjældent/ aldrig
☐	☐	☐	☐	☐	☐

Baggrund og levevaner

47. I hvilken grad har du inden for den sidste uge, inklusiv i dag, været plaget af:
(Sæt ét X ud for hvert spørgsmål og besvar venligst alle spørgsmål)

		Slet ikke	Lidt	Noget	En hel del	Særdeles meget
a.	Hovedpine	☐	☐	☐	☐	☐
b.	Svimmelhed eller tilløb til at besvime	☐	☐	☐	☐	☐
c.	Smerter i hjerte eller bryst	☐	☐	☐	☐	☐
d.	Lavt-siddende rygsmerter	☐	☐	☐	☐	☐
e.	Kvalme eller uro i maven	☐	☐	☐	☐	☐
f.	Muskelsmerter	☐	☐	☐	☐	☐
g.	At du har svært ved at få vejret	☐	☐	☐	☐	☐
h.	Anfald af varme- eller kuldefornemmelser	☐	☐	☐	☐	☐
i.	Følelsesløshed eller en snurrende, fornemmelse i kroppen	☐	☐	☐	☐	☐
j.	En klump i halsen	☐	☐	☐	☐	☐
k.	At du føler dig svag i kroppen	☐	☐	☐	☐	☐
l.	At dine arme eller ben føles tunge	☐	☐	☐	☐	☐

48. Ryger du for tiden?
(Sæt ét X)

Nej	☐
Ja	☐

49. Skriv venligst dato for besvarelse:

|__|__| - |__|__| - |__|__|__|__| *(DD- MM-ÅÅÅÅ, fx "17-02-2016")*

50. Har du kommentarer, er du velkommen til at skrive dem her:

____

____

Mange tak for din besvarelse

12.3 Follow-up questionnaire used in study III (in Danish)

Information om spørgeskemaet

Formål
Formålet med denne videnskabelige undersøgelse er at få mere viden om, hvordan det går med besværet i hånd og fingre på længere sigt. Undersøgelsen skal kortlægge, om helbredsforhold og forhold på arbejde eller i fritiden påvirker, hvordan det går. Resultaterne forventes at kunne bidrage til forbedret rådgivning af patienter, der undersøges på grund af snurren, prikken, stikken eller andet besvær i hånd og fingre.

Hvordan deltager jeg, og hvordan gennemføres undersøgelsen?
Du deltog i den første del af undersøgelsen lige efter din nerveledningsundersøgelse på Neurofysiologisk Afdeling, Aarhus Universitetshospital for ca. et år siden. Dengang udfyldte du et spørgeskema efter en kort lægeundersøgelse af din nakke, skulder, albuer og hænder. Den anden del af undersøgelsen er dette spørgeskema, hvor vi spørger om dit nuværende besvær, og om du er blevet behandlet herfor.

Hvad sker der med oplysningerne?
Vi vil gerne understrege, at alle oplysninger behandles fortroligt, og at der ikke videregives oplysninger, som kan føres tilbage til den enkelte person. Datatilsynet har givet tilladelse til undersøgelsen, og oplysningerne behandles efter lovens forskrifter.

Hvem laver undersøgelsen, og hvem betaler den?
Arbejdsmedicinsk Klinik og Neurofysiologisk Afdeling, Aarhus Universitetshospital og Arbejdsmedicinsk Klinik, Regionshospitalet Herning har taget initiativ til undersøgelsen. Undersøgelsen finansieres af Arbejdsmiljøforskningsfonden.

Deltagelse er frivillig
Deltagelse i spørgeskemaundersøgelsen er frivillig, og du kan uden begrundelse undlade at deltage. Du vil op til to gange kunne modtage en påmindelse om undersøgelsen, så vi undgår manglende besvarelser, som skyldes ren forglemmelse eller almindelig travlhed i hverdagen. Hvis du har spørgsmål er du velkommen til at kontakte læge, Sorosh Taba, på tlf.: 7846 4719 (hverdage kl. 9-14) eller på e-mail: sortab@rm.dk.

Med venlig hilsen

Sorosh Taba, læge
Poul Frost, overlæge

Arbejdsmedicinsk Klinik,
Aarhus Universitetshospital

Susanne Wulff Svendsen, professor

Arbejdsmedicinsk Klinik,
Regionshospitalet Herning

Birger Johnsen, overlæge
Anders Fuglsang-Frederiksen, professor
Neurofysiologisk Afdeling,
Aarhus Universitetshospital

12.4 Clinical examination form used in study III (in Danish)

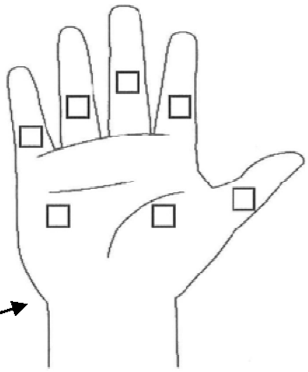
Skema til objektiv undersøgelse

Vejledning: (__): Sæt 'x' for ja/pos. (tom v. nej/neg.) **CPR-nr.:** ____________-______ Sp.sk. m. hjem? ___

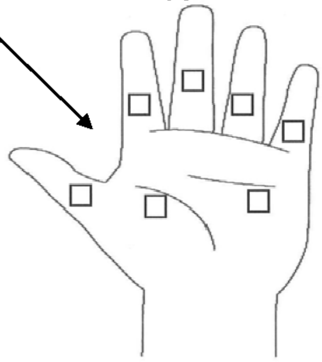
Dato:_____________ (DD-MM-ÅÅÅÅ) **Navn:**______________________________ Sp.sk. retur fra hjem?___

Columna cervicalis	**Aktiv bevægelighed**		
	Unormal?	(__)	
	Smerter?	(__)	
V unormal aktiv bevægelighed	**Passiv bevægelighed**		
	Unormal?	(__)	
	Smerter?	(__)	
		Hø	**Ve**
	Foramenkompressionstest	(__)	(__)
Nakke-skulderåg	**Atrofi?**	**Hø**	**Ve**
	Infraspinatus	(__)	(__)
	Supraspinatus	(__)	(__)
	Palpationsøm?	**Hø**	**Ve**
	Regio nuchae	(__)	(__)
÷ øm: ingen el let ømhed uden afværgereaktion	Levator scapulae	(__)	(__)
	Trapeziusrand	(__)	(__)
	Supraspinatus	(__)	(__)
+ øm: moderat til betydelig ømhed med afværgereaktion	Infraspinatus	(__)	(__)
	Pectoralis major	(__)	(__)
	Udstråling v palp af infraspinatus?	**Hø**	**Ve**
Udstråling til hånd/fingre	Hånddiagram	(__)	(__)
Skulder	**Aktiv bevægelighed**	**Hø**	**Ve**
	Unormal?	(__)	(__)
Arm svinges hel omgang	Smerter?	(__)	(__)
Laves v alle	**Sm v isometriske bevægelser?**	**Hø**	**Ve**
	Abduktion	(__)	(__)
	Udadrotation	(__)	(__)
a. Intet synligt udtryk for sm b. Synligt udtryk (fx grimasse) c. Afværgereaktion	**Impingement?**	(__)	(__)
Albue	**Palpationsøm?**	**Hø**	**Ve**
	Lateral epikondyl	(__)	(__)
	Mediale epikondyl	(__)	(__)
		Hø	**Ve**
V bevægelser over håndleddet	Ekstension mod modstand - smerter ved lat. epikondyl?	(__)	(__)
	Fleksion mod modstand - smerter ved med. epikondyl?	(__)	(__)
Ml med. epikondyl og olecranon	Tinels tegn ved albuen (Ulnaris)	(__)	(__)
Håndled	**Ømhed ved…**	**Hø**	**Ve**
Tenosynoviti/tendinit	Palpation?	(__)	(__)
	Håndtryk?	(__)	(__)
	Bevægelser over håndleddet?	(__)	(__)

Hø



Ve



12.4 Clinical examination form used in study III (in Danish)

	Kliniske test for KTS	**Hø**	**Ve**
	Tinels tegn	(__)	(__)
Holdes i 60 sek.	Phalens test	(__)	(__)
Hånd	**Atrofi?**	**Hø**	**Ve**
	Thenar	(__)	(__)
	Hypothenar	(__)	(__)
	Dorsale interosser	(__)	(__)
Med vatpind	**Unormal sensibilitet i hånd/fingre?**	**Hø**	**Ve**
	1. finger	(__)	(__)
	2. finger	(__)	(__)
	3. finger	(__)	(__)
	4. finger radial side	(__)	(__)
	4. finger ulnar side	(__)	(__)
	5. finger	(__)	(__)
Kraft i hånden	**APB (abductor pollicis brevis)**	**Hø**	**Ve**
n. medianus	Unormal?	(__)	(__)
	Dorsale 1. interos	**Hø**	**Ve**
n. ulnaris	Unormal?	(__)	(__)
		Hø	**Ve**
n. ulnaris	Froments tegn	(__)	(__)
n. ulnaris	Wartenburgs tegn	(__)	(__)

Froment's positive

13. ORIGINAL PAPERS

Paper I Tabatabaeifar S, Svendsen SW, Johnsen B, Hansson GA, Fuglsang-Frederiksen A, Frost P. Reversible median nerve impairment after three weeks of repetitive work. Scand J Work Environ Health 2017;43(2):163-70. doi: 10.5271/sjweh.3619.

Paper II Tabatabaeifar S, Svendsen SW, Frost P. Carpal tunnel syndrome as sentinel for harmful hand activities at work: a nationwide Danish cohort study. [In preparation to Occupational and Environmental Medicine]

Paper III Tabatabaeifar S, Svendsen SW, Johnsen B, Fuglsang-Frederiksen A, Frost P. Prognosis of symptoms and disability among patients with suspected carpal tunnel syndrome: influence of occupational mechanical exposures and abnormal median nerve conduction. [In preparation to Occupational and Environmental Medicine]

PAPER I

Reversible median nerve impairment after three weeks of repetitive work

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Original article

Scand J Work Environ Health – online first. doi:10.5271/sjweh.3619

Reversible median nerve impairment after three weeks of repetitive work

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Tabatabaeifar S, Svendsen SW, Johnsen B, Hansson G-Å, Fuglsang-Frederiksen A, Frost P. Reversible median nerve impairment after three weeks of repetitive work. *Scand J Work Environ Health* – online first. doi:10.5271/sjweh.3619

Objectives The aim of this study was to evaluate the development of impaired median nerve function in relation to hand-intensive seasonal work. We hypothesized that at end-season, median nerve conduction would be impaired and then recover within weeks.

Methods Using nerve conduction studies (NCS), we examined median nerve conduction before, during, and after engaging in 22 days of mink skinning. For a subgroup, we used goniometry and surface electromyography to characterize occupational mechanical exposures. Questionnaire information on symptoms, disability, and lifestyle factors was obtained.

Results The study comprised 11 male mink skinners with normal median nerve conduction at pre-season (mean age 35.7 years, mean number of seasons with skinning 8.9 years). Mink skinning was characterized by a median angle of wrist flexion/extension of 16º extension, a median velocity of wrist flexion/extension of 22 °/s, and force exertions of 11% of maximal voluntary electrical activity. At end-season, mean distal motor latency (DML) had increased 0.41 ms ($P<0.001$), mean sensory nerve conduction velocity (SNCV) digit 2 had decreased 6.3 m/s ($P=0.004$), and mean SNCV digit 3 had decreased 6.2 m/s ($P=0.01$); 9 mink skinners had decreases in nerve conduction, 5 fulfilled electrodiagnostic criteria and 4 fulfilled electrodiagnostic and clinical criteria (a positive Katz hand diagram) for carpal tunnel syndrome (CTS). Three to six weeks post-season, the changes had reverted to normal. Symptom and disability scores showed corresponding changes.

Conclusions In this natural experiment, impaired median nerve conduction developed during 22 days of repetitive industrial work with moderate wrist postures and limited force exertion. Recovery occurred within 3–6 weeks post-season.

Key terms carpal tunnel syndrome; CTS; nerve conduction study; occupational exposure.

Carpal tunnel syndrome (CTS) is an impairment of the median nerve at the wrist with symptoms including numbness, tingling, and pain in the radial part of the hand (1). Recent reviews have concluded that the risk of CTS is increased in relation to repetitive work, particularly in combination with force exertion, while the influence of wrist postures is less well-documented (2–5). Occupational mechanical exposures may lead to increased pressure in the carpal tunnel and traction of the median nerve, which may initiate a series of changes such as ischemic microcirculation injury, edema, alterations in the blood-nerve barrier, thinning of myelin, altered ion channel dynamics and expression, and axonal degeneration (1, 6, 7).

Little is known about the time relation between entry into a job that entails high mechanical exposures to the wrist and the development and course of median nerve impairment. To the extent that an impairment of nerve function is reversible in initial phases, early identification may be important to prevent chronicity. Another perspec-

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tive is that if a short induction period is followed by a reversible phase, surveillance of nerve conduction may be a responsive here-and-now assessment tool to guide workplace interventions to reach safe exposure intensities.

Two human studies have indicated a short induction period for CTS. One of the studies showed that surgery for CTS was most often performed within the first three seasons of work in a lamb slaughter and processing plant (8). In the other study, which followed newly hired pork processing employees, nerve conduction studies (NCS) showed signs of impaired median nerve conduction after an average of 64 work days (9). Recovery has been studied among assembly line workers with CTS, who tended to recover within two years, according to NCS after five months of reduced exposures (10).

Experimental animal studies have shown that 12 weeks of repetitive work with either high- or low-force exertion led to impaired median nerve conduction in rats (11, 12). In monkeys, a close temporal relationship was found between around 20 weeks of performing a moderately forceful, repetitive task and the development of abnormal NCS with subsequent recovery within weeks after exposure termination (13, 14). The authors found it unlikely that changes in humans would occur as rapidly (13).

The aim of this study was to evaluate median nerve function in relation to three weeks of hand-intensive seasonal work. We hypothesized that at end-season, median nerve conduction would be impaired and then recover within weeks.

Methods

Design and population

We conducted a prospective cohort study of 11 mink skinners from one mink skinning facility in Denmark, applying pre-, mid-, end-, and post-season NCS. Mink skinning is hand-intensive, seasonal work, which takes place during a few weeks each year, thus providing us with a natural experimental setting. We included mink skinners, who were Danish residents and could read and write Danish. Any previous physician-diagnosed CTS was an exclusion criterion. The Central Denmark Region Committees on Biomedical Research Ethics (record no. 1-10-72-263-14) and The Danish Data Protection Agency (record no. 1-16-02-84-14) approved the study. Written informed consent was obtained from all participants.

Exposure characteristics

Mink skinning was performed in day- and evening-shifts of 7.5 hours. For each participant, we obtained day-by-day accounts of the number of minks skinned from pay slips. Male and female minks had a weight of around four and two kilograms, respectively. From an adjacent table, the mink skinners grabbed one mink at a time using their left hand, and manually mounted it on a skinning machine. They pressed two buttons, one with each hand to activate the machine, and used a knife in their dominant hand to assist the last part of the skinning.

The same trained investigator performed full shift exposure measurements for the six day-shift workers; all measurements were dominant-sided. Postures and movements of the wrist were measured using SG75 twin axis goniometers (Biometrics Ltd., Cwmfelinfach, Gwent, UK) and recorded at a rate of 128 Hz using Mobi8-loggers (Twente Medical Systems International, Oldenzaal, The Netherlands) (15). To define 0° of flexion/extension and ulnar/radial deviation, the reference was a position with the forearm in pronation and the 3rd metacarpal bone aligned with the distal forearm's axis (16). For each participant, the goniometer data was processed to yield the 10th, 50th, and 90th percentiles of the angular distribution of wrist flexion/extension (º; negative and positive values denote extension and flexion, respectively), % time with non-neutral wrist postures defined as flexion/extension >45º or ulnar/radial deviation >20º (17), the median velocity of wrist flexion/extension (º/s), the repetitiveness defined as the mean power frequency (Hz; for a strictly cyclic movement, this is equal to the inverse of the cycle time) (18), and % time with no movement defined as an angular velocity <1 °/s.

Bipolar surface electromyography (EMG) of the forearm extensors was used to measure force exertion (19, 20). We placed Ag/AgCl electrodes with an active diameter of 6 mm and a center-to-center distance of 20 mm (VS, Medicotest A/S, Ølstykke, Denmark) over the bellies of mm. extensor carpi radialis longus et brevis, located by palpation during voluntary contraction with pronated forearm, at a distance of one-third the forearm length from the elbow. Data was recorded at 1024 Hz using Mobi8-loggers (Twente Medical Systems International, Oldenzaal, The Netherlands). Root mean square values of the EMG amplitudes were calculated for periods of 1/8 seconds to describe the muscular activity. Data was normalized to the maximal voluntary EMG activity (MVE) as measured during the highest of three measurements of maximum handgrip force (Jamar dynamometer, Sammons Preston, Bolingbrook, IL, USA). MVE was measured with the participant seated, the elbow flexed 90º and the upper arm vertical (21). Data was processed to yield the 10th, 50th, and 90th percentiles of the amplitude distributions and % time with muscular rest defined as an activity <0.5 % MVE.

All measurement data was analyzed using EMINGO, a program for analyzing EMG, inclinometry, and goniometry, developed by the Department of Occupational and Environmental Medicine, Lund, Sweden. During the measurement day, the participants logged the start and end time of breaks, and exposure measurements during breaks were excluded from the analysis.

Nerve conduction studies

Pre-, mid-, and end-season NCS were carried out at the mink skinning facility. Post-season NCS took place at a hospital department of clinical neurophysiology. Only the dominant side was examined. On all four occasions, the same experienced technician performed NCS using Keypoint.NET system, version 2.11 (Alpine Biomedical, Skovlunde, Denmark). The temperature of the hands was kept at a minimum of 34º Celsius by the use of an electrical heater and heat pads. The NCS followed the standard of the department: median nerve motor studies by stimulation at the wrist and elbow and recording from m. abductor pollicis brevis; ulnar nerve motor studies by stimulation at the wrist and recording from m. abductor digiti minimi; sensory studies with antidromic technique by stimulation of the median and ulnar nerves at the wrist and recordings from digits 2 and 3 for the median nerve and from digit 5 for the ulnar nerve with an active ring electrode around the middle of the proximal phalanx referred to a ring electrode around the middle of the intermediate phalanx. Motor nerve conduction in the distal parts of the nerves was assessed by the distal motor latency (DML) and in the forearm of the median nerve by motor nerve conduction velocity (MNCV). Sensory nerve conduction was assessed by the conduction velocity calculated as the conduction distance divided by the sensory latency. Compared with the use of sensory latency, the use of sensory nerve conduction velocity (SNCV) has the advantage that anatomical landmarks can be used for electrode placement omitting the need of a standard distance between stimulation and recording electrodes (22). We used the age-specific reference values of the department to calculate z-scores for each participant, ie, deviations from the reference values expressed in standard deviations (SD) (23). A z-score was considered abnormal if larger than 1.96. The department's electrodiagnostic criteria for CTS were that at least two of the three z-scores for median nerve DML, SNCV digit 2, and SNCV digit 3 were abnormal in the presence of normal ulnar nerve parameters. Cursors for latencies were set by the same investigator who was blinded to the order of the measurements.

Symptoms and disability

At pre-, end-, and post-season, the mink skinners completed a questionnaire which included a question on tingling sensations in the hand, the Katz hand diagram (24), the Levine questionnaire for the assessment of severity of symptoms and functional status in CTS (25), and the authorized Danish translation of the disabilities of the arm, shoulder and hand (DASH) questionnaire (26). We classified the Katz hand diagrams as "classic/probable", "possible", and "unlikely" CTS (24). The Levine questionnaire is side-specific and has two components: a symptom severity scale and a functional status scale with 11 and 8 items, respectively. Each item is scored from 1 (mildest) to 5 (most severe) and symptom and function scores are calculated as the mean for each scale (25). The DASH contains 30 items concerning the combined disability of both upper extremities and yields a score ranging from 0–100 with greater disability scoring higher (26).

Case definition

Our CTS case definition required that the department's electrodiagnostic criteria were fulfilled (see above) and that clinical criteria were fulfilled in terms of a Katz hand diagram classified as "classic/probable" or "possible" (27).

Personal factors

For descriptive purposes, we collected questionnaire information on number of previous seasons with mink skinning, height, weight, smoking, and alcohol consumption. We calculated pack-years of smoking and transformed alcohol consumption to units per week, where one unit was defined as 12 grams of alcohol. Body mass index (BMI) was calculated as weight/height squared (kg/m^2). We also had information on age.

Statistical analysis

To illustrate changes in NCS parameters over time, we plotted z-scores for each individual. We used paired t-test to evaluate intra-individual changes in NCS parameters and changes in Levine and DASH scores. There were no missing items in the Levine or DASH questionnaires. Two-sample t-test was used to evaluate differences between the mean numbers of minks skinned per hour in day and evening shifts across the whole skinning season. Data were analyzed using Stata 13 (StataCorp LP, College Station, TX, USA).

Sample size calculation

We originally intended to include 16 mink skinners in order to detect a SNCV reduction of 2 m/s with a power and significance level of 0.80 and 0.05, respectively.

Results

Table 1 shows characteristics of the 11 male mink skinners who participated. One was left-handed, the others right-handed. One participant had previously had surgery for ulnar neuropathy at the elbow, none of the participants had ever had wrist surgery, and none of them had diabetes, rheumatoid arthritis, or thyroid disease. Outside the skinning season, all were students or had jobs that did not entail repetitive movements.

Table 2 shows exposure characteristics of mink skinning based on goniometer measurements for six mink skinners during one day shift (mean recording duration 432 minutes) and surface EMG measurements for four (mean recording duration 427 minutes – for the remaining two, the measurements were lost because the electrodes loosened). Mink skinning was characterized by a median angle of wrist flexion/extension of 16º extension, a median velocity of wrist flexion/extension of 22 °/s, and force exertions of 11 % MVE.

During the measurements, the mean number of minks skinned per hour was 116. The mean for all the mink skinners across the whole season was 109 minks per hour with no significant difference between day- and evening-shifts (114 and 105 minks per hour, respectively; P=0.450). The skinning season lasted 22 calendar days and the 11 mink skinners worked a total of 220 days, ie, 20 days per participant on average. Four participants had a total of 4.5 sick days during the skinning season, none of which were related to upper-extremity symptoms.

Figure 1 shows the NCS values for each mink skinner from pre-season 10th November 2014 (N=11), through mid-season 24th November 2014 (N=10) and end-season 2nd December 2014 (N=11), to post-season 22nd December 2014 (N=2) and 14–15th January 2015 (N=7). All mink skinners had normal pre-season median nerve values. A total of nine skinners showed changes in the direction of median nerve conduction impairment during the skinning season and subsequent recovery. At end-season, five mink skinners had abnormally increased median nerve DML, and four and six had abnormally decreased SNCV from wrist to digit 2 and digit 3, respectively. Five fulfilled our electrodiagnostic criteria for CTS. One worker (depicted with gray lines and hollow squares in the online version of figure 1) had previously had a deep laceration of his 5th finger, resulting in ulnar nerve damage. There were no systematic changes of the ulnar NCS values.

Table 3 shows mean NCS values at the four measurement occasions and mean paired differences from pre- to end-season and from end- to post-season. From pre- to end-season, there was an increase in median nerve DML and a decrease in median SNCV from digits 2 and 3; thus, sensory and motor changes occurred simultaneously. There were no changes in median MNCV from elbow to wrist. From end- to post-season, the changes reversed. There were no significant differences between pre- and post-season; results not shown. Between pre- and mid-season, the only significant change was an increase in median nerve DML (P=0.002). There were no significant changes for the ulnar nerve.

At pre-season, 3 of the 11 mink skinners reported tingling sensations in their dominant hand. This number increased to 8 at end-season and returned to 2 out of 9 at post-season (2 of the mink skinners did not answer the post-season questionnaire). The corresponding numbers with hand diagrams that were classified as "classic/probable" or "possible" were 2, 8, and 2, and our case definition of CTS was fulfilled by 0, 4, and 0.

The Levine symptom score increased from 1.3 [95% confidence interval (95% CI) 1.0–1.7] at pre-season to 2.1 (95% CI 1.5–2.7) at end-season (P=0.022) and then returned to 1.3 (95% CI 0.9–1.7; P=0.012). All Levine function scores were around 1.1 with no significant changes (results not shown). The mean DASH score increased from 5.7 (95% CI -0.1–11.5) at pre-season to 10.4 (95% CI 4.3–16.6) at end-season (P=0.002) with a subsequent decrease to a post-season mean of 4.9 (95% CI -0.6–10.3, P=0.013).

Table 1. Pre-season characteristics of the participating 11 male mink skinners. [SD=standard deviation; IQR=interquartile range]

	Mean	SD	Median	IQR
Age, years	35.7	10.2		
Seasons with mink skinning			6.0	4.0–11.0
Height (cm)	183.2	5.7		
Weight (kg)	84.9	7.2		
Body mass index (kg/m^2)	25.3	1.7		
Smoking (pack-years)			8.1	0.0–15.0
Alcohol consumption (units/week)			3.0	1.8–5.0

Table 2. Wrist exposures during mink skinning. Simultaneous dominant-sided full-shift goniometer (N=6) and electromyography recordings (N=4) [a]. All participants were male. [SD=standard deviation; MVE=maximal voluntary electrical activity]

Wrist exposures	Measures	Mean	SD
Postures	Angular distribution of flexion/extension (°) [b]		
	10th percentile	-41	9
	50th percentile	-16	9
	90th percentile	12	6
	Non-neutral postures (% time)	19.7	10.5
Movements	Median velocity of flexion/extension (°/s)	22.4	3.4
	Repetitiveness (mean power frequency; Hz)	0.43	0.04
	No movement (% time <1 °/s)	1.1	0.7
Exertion of force	Extensor activity (% MVE)		
	10th percentile	0.8	0.4
	50th percentile	3.9	1.3
	90th percentile	11.2	3.8
	Extensor rest (% time <0.5 % MVE)	6.9	3.4

[a] Two measurements were lost because the electrodes loosened.
[b] Negative and positive values denote extension and flexion, respectively.

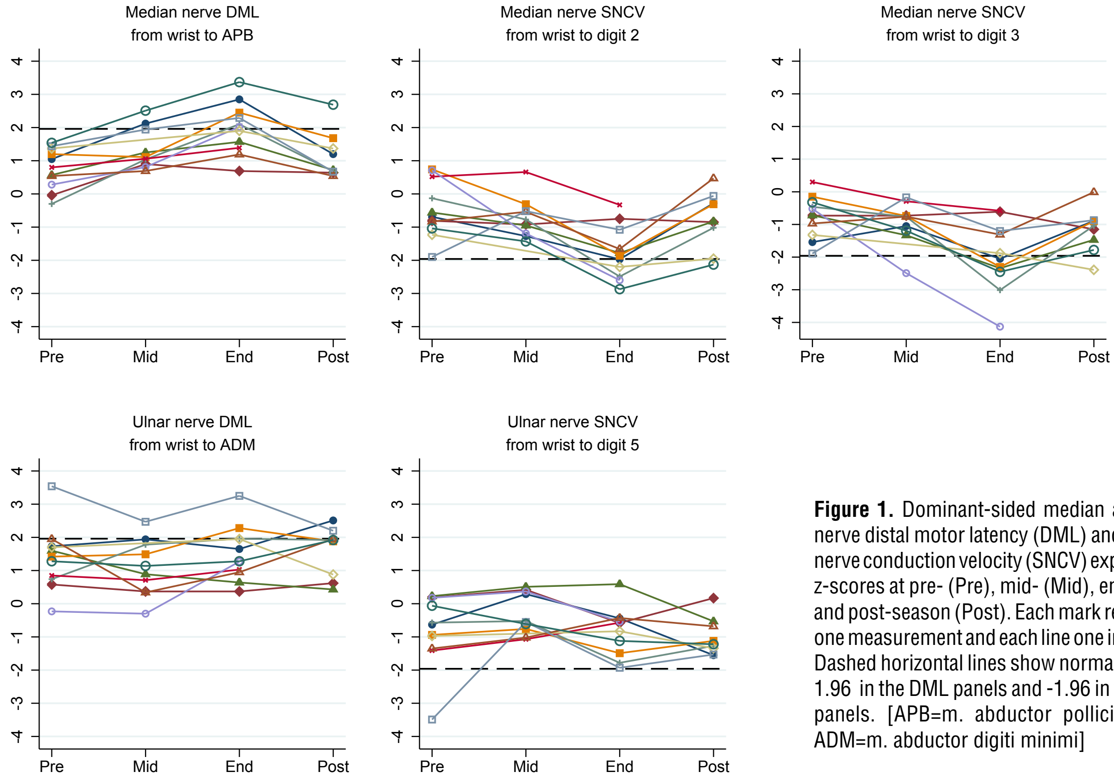

Figure 1. Dominant-sided median and ulnar nerve distal motor latency (DML) and sensory nerve conduction velocity (SNCV) expressed in z-scores at pre- (Pre), mid- (Mid), end- (End), and post-season (Post). Each mark represents one measurement and each line one individual. Dashed horizontal lines show normal limits; at 1.96 in the DML panels and -1.96 in the SNCV panels. [APB=m. abductor pollicis brevis; ADM=m. abductor digiti minimi]

Discussion

We found that 22 days of hand-intensive seasonal work led to impaired median nerve conduction in 9 of 11 mink skinners, 4 of whom fulfilled our case definition of CTS at end-season. The changes reverted to normal post-season. None of the mink skinners had abnormal pre-season NCS parameters, which indicates that median nerve conduction was not impaired by previous skinning seasons.

The study took advantage of a natural experiment provided by seasonal mink skinning, which allowed us to study nerve conduction and CTS symptoms in a targeted workforce with a highly standardized exposure pattern, a setup which has previously only been possible in experimental animal studies (13, 14). Even though the study population was small, the NCS changes were of a magnitude that enabled us to detect significantly decreased median nerve conduction and recovery. Since we used repeated NCS, the workers acted as their own controls, which minimized any confounding. A further strength was that the investigator who evaluated the NCS was blinded to the seasonal order of the examinations when he set the latency cursors.

We performed direct technical measurements of the exposures with equipment that has been used in several previous studies (17, 28–30). Regarding postures, work as a mink skinner was placed in the middle of the spectrum observed for repetitive industrial work with respect to wrist flexion/extension (28, 30), and the % time spent in non-neutral postures was lower than the value of 30% time reported for house painters in the only other study that has used this particular exposure measure (17). With respect to median velocity of wrist flexion/extension, values of 15–40 °/s have been measured for occupational groups with repetitive industrial work, which places work as a mink skinner in the middle of the spectrum, comparable to fish processing and wood industry workers (laminate production and parquet slats sorting) and below meat cutters and poultry workers (28, 30). Work as a mink skinner showed a higher median velocity of wrist flexion/extension than work as a house painter (15.7 °/s) (17) and office work (≤10 °/s) (28). The 90[th] percentile for % MVE was 11.2 for the mink skinners, which was lower than values of 15–35% MVE which have been reported for other groups with industrial repetitive work (28, 30) and actually comparable to office work. We only achieved four EMG measurements and we cannot rule out that we underestimated this exposure. However, the mink skinners did not experience their work as force requiring and an investigator who observed the work process rated the intensity of

Table 3. Nerve conduction parameters at pre- (Pre), mid- (Mid), end- (End), and post-season (Post) and differences from Pre to End and End to Post. There are minor differences between "Difference End to Post" and the difference between "End" and "Post" due to two participants with missing post-season measurements. [ADM=m. abductor digiti minimi; APB=m. abductor pollicis brevis; 95% CI=95% confidence interval; DML=distal motor latency (ms); MNCV=motor nerve conduction velocity (m/s); SNCV=sensory nerve conduction velocity (m/s)]

Nerve parameter (unit)	Pre N=11		Mid N=10		End N=11		Post N=9		Difference Pre–End			Difference End–Post		
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	P-value	Mean	95% CI	P-value
Median nerve														
DML, wrist – APB (ms)	3.30	3.12–3.47	3.48	3.30–3.66	3.71	3.51–3.90	3.42	3.20–3.65	0.41	0.27–0.56	$<10^{-3}$	-0.31	-0.45–0.17	$<10^{-3}$
MNCV, elbow – wrist (m/s)	59.3	56.4–62.1	60.7	57.6–63.9	59.6	56.9–62.2	59.2	56.6–61.9	0.3	-2.6–3.2	0.820	-0.5	-2.4–1.3	0.540
SNCV, wrist – digit 2 (m/s)	60.3	57.2–63.4	59.3	57.0–61.5	54.0	51.1–56.9	58.8	54.9–62.7	-6.3	-10.2–-2.5	0.004	5.2	7.9–2.5	0.002
SNCV, wrist – digit 3 (m/s)	59.2	56.8–61.6	58.5	55.9–61.1	53.0	49.2–56.7	57.0	53.4–60.7	-6.2	-10.6–-1.9	0.010	3.7	7.1–0.4	0.030
Ulnar nerve														
DML, wrist – ADM (ms)	2.66	2.46–2.85	2.57	2.39–2.74	2.69	2.54–2.85	2.72	2.56–2.87	0.04	-0.11–0.19	0.590	0.00	-0.16–0.16	1.000
SNCV, wrist – digit 5 (m/s)	58.8	55.1–62.6	61.5	59.1–64.0	59.0	56.5–61.5	57.5	54.8–60.2	0.2	-2.7–3.1	0.890	-1.18	-4.0–1.6	0.360

exertion as a 2 (somewhat hard) using a scale ranging from 1 (light) to 5 (near maximal), corresponding to % MVE values of 10–29% (31).

The exposure measures in our study can be compared to exposure–response relationships based on studies that have used identical methods for exposure assessment (17, 28). Among house painters, who had median velocities of wrist flexion/extension within a limited range (14–17 °/s), a Danish study of clinically diagnosed CTS suggested an adjusted incidence rate ratio for men of 1.15 per 1 °/s (17). A meta-regression of data from eight previous Swedish studies of male workers with a wide range of median velocities of wrist flexion/extension (3–35 °/s) showed an increase in the prevalence of clinically diagnosed CTS of 0.3% per 1 °/s (28). According to our judgment, the mink skinners' observed work pace would place them at a hand activity level of around 7 on the American Conference of Governmental Industrial Hygienists' scale, which ranges from 0 (hand idle most of the time; no regular exertions) to 10 (rapid, steady motion/difficulty keeping up or continuous exertion) (32). An Italian study of CTS confirmed by NCS among manual and non-manual workers found a hazard ratio of 1.8 for hand activity levels between 5.1 and 8.5, when compared to levels between 1.0 and 3.0 (33), and a comparable North American study found a hazard ratio of 1.3–1.5 for hand activity levels >4 (34). Thus, exposure intensities comparable to those of the mink skinners have previously been related to an increased risk of CTS.

Even though the mink skinners' wrist exposures were not exceptionally high as compared to other kinds of repetitive industrial work, nearly all of the participants exhibited decreases of nerve conduction across the carpal tunnel and a considerable fraction (36%) developed CTS. Previous cross-sectional studies that have used a case definition similar to ours have found a CTS prevalence of 6.3% among slaughterhouse workers (83% men) (35), around 8% among female supermarket cashiers (36), and 3% among construction workers (99% men) (37). The lower prevalence in those studies might be explained by a healthy worker survivor effect, modified work techniques developed over time, and biological adaptation to exposures. We do not know the course of impaired median nerve conduction in case of continued occupational mechanical exposures. The observed changes might resolve or increase to a more severe impairment with protracted recovery or even irreversibility; this remains to be studied.

Our findings agreed with the only other human study that we are aware of, which focused on the time course of median nerve impairment in relation to occupational activities (9). The proportion that displayed decreases of nerve conduction was not reported in that study, but animal studies have shown that the majority of the exposed individuals developed impaired median nerve conduction (13, 14). Our findings also showed that work-related impaired median nerve conduction may occur as rapidly in humans as animals. CTS in pregnancy is generally thought to be related to increased pressure in the carpal tunnel, and findings regarding CTS in pregnancy are in accordance with a short induction period and subsequent improvement (38–40). After surgery for CTS and even intra-operatively, rapid reversibility of NCS values has also been reported (41). Our study is unique in that it is the first to show that 22 days of repetitive industrial work can lead to impaired median nerve conduction and CTS with subsequent recovery. Quick reversibility suggests that other mechanisms than demyelination and axonal degeneration play a role in mild subacute CTS.

We have no reason to think that a replication of our study in other male or female populations with similar exposures would lead to substantially different results. For clinical practice, our findings implicate that patients who develop CTS in relation to a newly increase in occupational mechanical exposures can be informed that the condition is most likely reversible within weeks if the exposures are reduced. For national surveillance purposes, register information on CTS diagnosis and surgery may be used to identify job groups with high incidence rates, which suggest high exposure intensities. Within high-risk job groups, occupational health practitioners may use median NCS before and after workplace interventions to make sure that safe exposure intensity levels are reached.

In conclusion, this study took advantage of a natural experiment to evaluate median nerve function in relation to seasonal exposure to repetitive industrial work with moderate wrist postures and limited force exertion. The results showed that impaired median nerve conduction and CTS can develop in a considerable fraction of individuals during a few weeks of exposure and recover within weeks after exposure cessation.

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PAPER II

Carpal tunnel syndrome as sentinel for harmful hand activities at work: a nationwide Danish cohort study

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ABSTRACT

Objectives: To evaluate the use of incidence rates (IRs) of carpal tunnel syndrome (CTS) as sentinels that can identify occupational groups with high mechanical exposures to the wrist.

Methods: We conducted a nationwide register-based cohort study of all persons born in Denmark 1945–1994, who had at least 1 year of full-time employment 2009-2012. During follow-up 2010–2013, we identified first-time CTS diagnoses. To obtain robust IRs of CTS we established job groups and calculated sex-specific age-standardised IRs (SIRs) for each of these groups. To validate the CTS rates as signals, we linked occupational codes with a job exposure matrix, calculated a mean wrist load measure for each job group, and plotted the wrist load against the SIRs.

Results: 1,171,580 men and 1,137,854 women were followed for 4,046,851 and 3,994,987 person-years, respectively. 28 job groups were constructed for men and 24 for women. We identified 4,405 cases of CTS among men and 7,858 among women, yielding crude IRs of 10.9 and 19.7 pr. 10,000 years. For men, job group SIRs ranged from 3.7 to 23.7; for women from 10.1 to 42.9. For both sexes, there was a positive association between the SIRs and wrist load.

Conclusion: We found that sex specific SIRs of CTS varied substantially between job groups and higher SIRs pointed to job groups with higher wrist load. The results corroborated that elevated CTS rates may serve as sentinels of harmful hand activities.

Keywords

Epidemiological surveillance, job exposure matrix, occupational exposures, register study, upper extremity, wrist load.

INTRODUCTION

Carpal tunnel syndrome (CTS) has been suggested as an occupational sentinel disease,[1-3] i.e., a disease that signals a need for preventive measures in the working environment.[1, 4] Occupational sentinel diseases may be divided into diseases that are almost always caused by occupational exposures (e.g., mesothelioma caused by asbestos) and diseases that are likely to be so (e.g., CTS which may be caused by occupational mechanical exposures).[1] Diseases in both categories may be used for surveillance of the working environment, but while even a single case in the first category signals exposure to a specific harmful occupational agent, it takes more to interpret cases in the second category.

For diseases in the second category, sentinel-based surveillance has been attempted by asking workers if they believed their disease to be work-related or by requiring employers and healthcare-providers to report cases that they attributed to work.[5, 6] While such attempts have often been the best options available, they are inherently flawed by "the problem of attribution",[5] i.e., the fact that it is impossible to discern whether a particular case is work-related. This problem also pertains to national systems for recording of occupational diseases, which additionally suffer from under-reporting and potentially biased reporting due to legal aspects involving compensation[2] and public concern. The problem of attribution may be circumvented by an epidemiological approach, where elevated incidence rates (IRs) in specific groups of workers serve as sentinels.[2] CTS often leads to hospital visits for diagnosis and treatment (which is less likely for other distal upper limb disorders), and Denmark has high-quality registers of hospital discharge diagnoses and occupational codes, which lend themselves for epidemiological surveillance of IRs of CTS as sentinels.

To be useful as a signal, an occupational sentinel disease must be associated with known occupational risk factors. Occupational risk factors for CTS comprise forceful work, repetitive movements, hand-arm vibrations (HAVs), and – less well-documented - non-neutral postures of the wrist, along with combinations of these exposures.[7-9] The just-mentioned exposures are differentially distributed across the labour market, which means that it should be possible to establish sufficiently large and relatively homogeneously exposed occupational groups to ensure robust IR estimates, while still being able to capture relevant differences in IRs between groups. For the IR signal to be quickly responsive to effects of preventive interventions, a short induction period is necessary. We have recently found an induction period of CTS as short as three weeks in a study of workers engaged in seasonal work with repetitive movements of the wrist.[10] The IR signal will be delayed when captured from hospital-based registers,[11] but IRs of CTS diagnoses can still be expected to react to exposure changes within a few years at most.

IRs of CTS are higher among women than among men with reported female to male IR ratios of 1.8 to 3.6[12-14] and because the labour market in Denmark is markedly sex-segregated, sex-specific sentinel IRs have to be calculated. Furthermore, IRs of CTS increase with age in the working age range and age-distributions vary across occupational groups, which means that age must also be taken into account.[12-14] Other non-occupational risk factors for CTS include obesity,[15] diabetes,[16] and pregnancy,[17] while smoking does not seem to be a risk factor.[18] With the exception of obesity, Danish registers contain information about these possible confounders of the sentinel rates, which add to the potential value of IRs of CTS as sentinels for harmful hand activities.

If differences in IRs of CTS can be found across job groups, estimates of occupational wrist exposures are needed to validate the use of the IRs as sentinels. We have developed a hand-arm job exposure matrix (JEM), which is suitable for this purpose. The Hand-arm JEM was originally established for a study of ulnar neuropathy,[19-21] but has also proved useful in a study of prognosis after wrist injuries.[22]

The aim of this study was to evaluate the use of IRs of CTS diagnoses as sentinels, which can identify occupational groups with high mechanical exposures to the wrist. We hypothesised that elevated IRs of CTS within occupational groups signal harmful hand activities.

METHODS

Design and registers

We conducted a nationwide cohort study using Danish register data from the Civil Registration System,[23] the Employment Classification Module (ECM),[24] the Danish National Patient Register (DNPR),[25] the National Diabetes Register,[26] and the Medical Birth Register.[27] The DNPR contains information on all patient contacts with the public somatic hospital system from 1977, and from 2003 also patient contacts with private hospitals. Contacts with private practice specialists, e.g. orthopaedic surgeons, are not included in the DNPR.[25] The ECM provided individual year-by-year information on 1) occupational codes according to the Danish version of the International Standard Classification of Occupations from 2008 (DISCO-08), and 2) socioeconomic status (SES).[24]

Population

The cohort included all persons born in Denmark, excluding Greenland, between 1 January 1945 and 31 December 1994, who were alive and living in Denmark on 1 January 2009 according to the Civil Registration System. We excluded persons, who were diagnosed with CTS between 1 January 1994 and start of follow-up according to the DNPR, and persons who were permanently outside the labour market before start of follow-up, persons who were in the armed forces the entire period between 1 January 2009 and 31 December 2012 (the JEM did not provide exposure estimates for the armed forces), and persons who did not have at least 1 year of employment with a valid DISCO-08 code in this period according to the ECM. The Danish Data Protection Agency (record no. 1-16-02-84-14) and Statistics Denmark (project no. 703999) approved the study.

CTS diagnoses and CTS surgeries

From the DNPR, we identified first-time CTS diagnoses in terms of a primary discharge diagnosis code DG56.0 according to the International Classification of Diseases, 10th revision. For descriptive purposes, we also identified first-time CTS surgeries in terms of surgery codes KACC51 (decompression and freeing of adhesions of median nerve) and KACC61 (endoscopic decompression and freeing of adhesions of median nerve) according to the Danish version of the Nordic Medico-Statistical Committee Classification of Surgical Procedures.

Construction of job groups

To obtain robust incidence rate (IR) estimates, we constructed job groups by collapsing some of the more detailed categories in DISCO-08 into categories based on lower levels of detail within the same or the numerically closest four-, three-, or two-digit DISCO-08 code. The aim was to obtain at least 100 incident CTS diagnoses per constructed job group. We constructed 28 job groups for men and 24 for women. The occupational groups/titles in the constructed job groups can be seen in supplementary tables 1 and 2. Because of a markedly sex-segregated labour market in Denmark, seemingly identical constructed job groups differed according to sex with respect to the included occupational groups/titles. For men, it was possible to construct several job groups from DISCO-08 major groups 7, 8, and 9, e.g., carpenters (70), builders and painters (71), truck drivers (80), operators (81), and storage labourers (92). For women, it was possible to construct several job groups from DISCO-08 major groups 2 and 5, e.g., nurses (23), teachers (22 and 24), shop sales assistants (51), and care (52, 53, 54).

Occupational mechanical exposures

We validated the signal value of the CTS rates against exposure measures from The Hand-arm JEM. To obtain year-by-year information on occupational mechanical exposures to the wrist for all cohort members, we linked each person's DISCO-08 code to the JEM. The construction of the JEM has been described previously.[19] In brief, the JEM was based on mean values of five experts' ratings of occupational mechanical exposures for 806 occupational titles, which were divided into 169 groups of jobs with expected homogeneous exposure profiles. The JEM covered forceful work rated on a 5 point-scale (1-5),[28] where a higher score indicated higher force requirements, number of hours/day with repetitive movements of the elbow and/or wrist (excluding computer use), non-neutral postures of the elbow and/or wrist, and exposure to hand-arm vibrations (HAVs).[19] For this study, we had to reconfigure the JEM to be able to use the available DISCO-08 codes. One DISCO-08 code was not represented in the JEM, so we applied exposure estimates from a similar DISCO-08 code.

To obtain a single measure of wrist exposure, we first trichotomised three of the exposure estimates. The categories for force were 1-<1.5 (low), ≥1.5-<2.5 (medium), and ≥2.5-≤4 points (high), inspired by Moore and Garg's intensity of exertion[28] (no occupation in the JEM had a force rating of 5 points). The categories for repetition were 0-<2 (low), ≥2-<4 (medium), and ≥4 hours/day (high).[29] The categories for HAVs were 0-<0.25 (low), ≥0.25-<1 (medium), and ≥1-≤2.8 hours/day (high). Non-neutral postures were dichotomised as 0-<2 (low) and ≥2-≤7 hours/day (moderate) due to weaker evidence of an association with CTS.[7, 8, 30]

Next, we calculated a joint wrist exposure measure, wrist load. Wrist load was scored 0 if all four exposures were low, 1 if at least one exposure was medium and none were high, 2 if one of the exposures was high, and 3 if two or more were high. Years as unemployed or apprentice and years in the armed forces were allocated a wrist load of 0.

Potential confounders

The Civil Registration System[23] provided information on sex and region of residence. From the National Diabetes Register[26] we obtained dates of diabetes diagnosis and from the Medical Birth Register[27] we obtained dates of recent child birth. The 22 SES groups from the ECM were divided into five categories: (1) self-employed, (2) top managers and employees at upper level, (3) employees at intermediate level, (4) employees at basic level, (5) persons outside the labour market including unemployed,[31] and a sixth category with missing information on SES. A priori, we decided not to adjust for SES in the main analyses to avoid over adjustment due to expected correlations with wrist load.[31]

Statistical analyses

Men and women were analysed separately. Follow-up started on 1 January 2010 or on the date, when the person had been employed for at least one year after the age of 18, whichever came later, and ended on the date of a first-time CTS diagnosis, censoring due to the person's 65th birthday, death, disappearance, emigration, or 31 December 2013, whichever came first.

For each job group, we calculated sex-specific crude IRs (IR_{crude}) and standardised IRs (SIRs) using the sex-specific age distribution of person-time in the entire study population as the reference. Age was categorised as 18-34, 35-49, and 50-65 years.
To evaluate whether controlling for diabetes, region of residence, and recent child birth influenced the odds of a first-time CTS diagnosis within job groups, we applied a logistic regression technique equivalent to discrete survival analysis with follow-up intervals of 1 year using job group 22 'teachers' as the reference; the resulting odds ratios (OR) can be interpreted as hazard ratios (HR).[32] We constructed two models, one, which adjusted for age in categories as defined above and follow-up intervals, and another, which additionally adjusted for region of residence (five regions), diabetes (no/yes), and recent child birth (no/yes). In supplementary analyses, we entered age as a continuous variable instead of categorised. We used a one year time lag for time varying independent variables. To explore if the ORs for the job groups were similar within strata of SES, we conducted sensitivity analyses restricting the logistic regression to the two largest SES groups, groups 3 and 4, in which all job groups were present.

To validate the signal value of the SIRs against the JEM-based mean wrist load estimates, we plotted the mean wrist load against the SIRs together with the linear regression line. The slopes of the regression lines were calculated together with their 95% confidence intervals (CI). All analyses were performed on Statistics Denmark's research platform using STATA v13.1 (Stata Corp, College Station, Texas, USA).

RESULTS

Figure 1 shows the construction of the sex-specific study cohorts. A total of 1,171,580 men and 1,137,854 women were followed for 4,046,851 and 3,994,987 person-years, respectively. Tables 1 and 2 show sex-specific age distributions of person-time according to job groups. Table 2 also shows the distribution of recent child birth. The age distribution and the distribution of recent child birth differed across job groups.

In total, 4,405 cases of CTS were identified among men and 7,858 among women, corresponding to an incidence rate of 10.9 (95% CI 10.6 to 11.2) per 10,000 person-years among men and 19.7 (95% CI 19.2 to 20.1) per 10,000 person-years among women. The number of CTS surgeries was 2,127 for men, including 30 operations that were not preceded by a registered CTS diagnosis (IR 5.3, 95% CI 5.0 to 5.5). Corresponding numbers for women were 4,311 and 61 (IR 10.8, 95% CI 10.5 to 11.1).

Tables 3 and 4 show sex-specific IR_{crude}, SIRs, and adjusted ORs according to job groups. A wide range of SIRs is seen. For men, job groups with approximately doubled SIRs and odds were 60 ('agricultural and fishery workers') and 83 ('drivers'), while approximately tripled values were seen for groups 70 ('carpenters') and 74 ('mechanics'). For women, approximately doubled values were seen for groups 54 ('home-based personal care workers') and 90 ('cleaners'). For both sexes, the ORs were significantly increased from around group 50 and upwards and groups characterised by office and computer work (10-23 and 31-32 among men and 24, 26, and 31-41 among women) did not have elevated SIRs or odds. The job group ORs hardly changed when we adjusted for diabetes, region of residence, and child birth. In the fully adjusted model, the ORs for diabetes were 1.8 (95% CI 1.6 to 2.0) for men and 2.0 (95% CI 1.8 to 2.2) for women. The OR for recent child birth was 1.8 (95% CI 1.6 to 2.0). Being in age groups 35-49 years and 50-65 years compared to 18-34 years yielded ORs of 2.0 (95% CI 1.8 to 2.2) and 2.8 (95% CI 2.6 to 3.1) for men and 2.4 (95% CI 2.2 to 2.6) and 3.5 (95% CI 3.3 to 3.8) for women. Using age as a continuous variable did not change the job group ORs (results not shown). When restricting the logistic regression to SES groups 3 and 4, the same patterns were found for both sexes, but with 10-20% lower ORs for men and 20-25% lower ORs for women (results not shown).

Figures 2 and 3 depict job group specific mean wrist load against SIRs for men (figure 2) and women (figure 3). For both sexes, there was a clear association between mean wrist load and SIRs with a steeper slope for men (beta=0.13 (95% CI 0.11 to 0.16) for men and 0.05 (95% CI 0.04 to 0.07) for women).

DISCUSSION

In this nationwide cohort study, we found that sex-specific SIRs of CTS varied substantially between job groups and higher SIRs pointed to job groups with higher wrist load.

Our study benefited from a nationwide cohort and data from high quality registers with almost complete follow-up information.[23-27] We ensured that the job group information preceded the CTS diagnoses using a one year lag in the analyses. To the extent that the constructed job groups were not homogenously exposed, the signal value of IRs of CTS would be attenuated, but we did find a wide range of SIRs and a clear pattern that higher SIRs of CTS were associated with higher levels of wrist load.

We used the DNPR[25] to identify CTS diagnoses, which means that cases diagnosed in primary care or at private practising specialists would only be included if nerve conduction studies (NCS) were part of the diagnostic evaluation. In Denmark, NCS are recommended in combination with clinical examination to diagnose CTS, and NCS are only performed at hospital departments. The patterns of association remained when we restricted the analyses to SES groups 3 and 4 and we adjusted for region of residence to account for geographical clustering of specialists.

The patterns of associations between job groups and SIRs persisted after controlling for diabetes and recent child birth. Information on BMI was unavailable from the registers, but we adjusted for any effects of a high BMI that work through diabetes, and SES may act as a proxy for several lifestyle factors including a high BMI.[33] We did not have information on previous wrist fractures and rheumatoid arthritis,[34] but we find it unlikely that these non-occupational risk factors would confound our findings.

To validate the signal value of the SIRs, we used the Hand-arm JEM, which covered all job groups in the cohort. The JEM has been informative in studies of ulnar neuropathy[19-21] and wrist injuries.[22] The wrist load variable was constructed to capture the joint occupational mechanical exposures. A similar shoulder load variable has proved to predict (surgery for) subacromial impingement syndrome.[35]

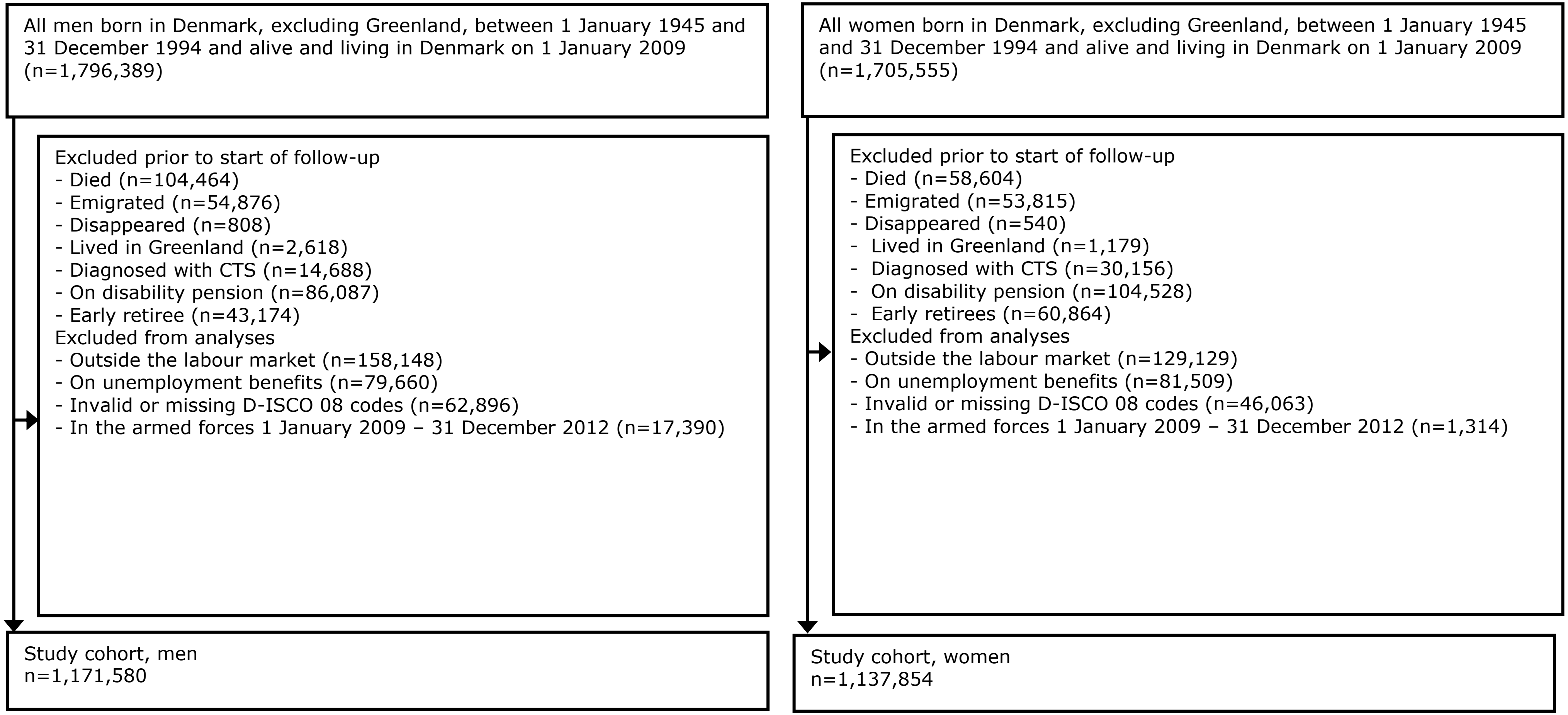
A Swedish general population register study, which included non-hospital cases, reported IRs of CTS diagnosis of 18.2 per 10,000 person-years for men and 42.8 per 10,000 person-years for women.[13] A general population study from Italy found SIRs of CTS diagnosis of 13.9 and 50.6 per 10,000 person-years for men and women, respectively.[12] Corresponding SIRs from a general population study from the US were 30.3 and 54.2 per 10,000 person-years.[36]The study populations in the just-mentioned studies included persons older than 65 years, which might explain why we found lower IRs; our study cohort was a younger, working population. Varying case definitions and differences in health-care seeking behaviour across countries may also play a part. However, these differences do not detract from the value of SIRs of CTS diagnoses as country-specific sentinels of harmful hand activities. We found no indications of an association between SIRs of CTS and office and computer work, which is in accordance with recent evidence.[37-39]

Exposure monitoring is resource demanding, be it by direct technical measurements, observation, or self-report, and population-based health surveillance by questionnaires and clinical/paraclinical examinations requires large efforts.[11, 12, 40] Sentinel-based surveillance of the working environment using epidemiological measures may therefore be an attractive add-on to other efforts, including reporting of occupational diseases, in countries with routinely collected register data on health and occupation.

Even though the register-based SIRs of CTS diagnoses may only represent the tip of the iceberg with respect to CTS, this does not reduce their sentinel value, and the epidemiological measures directly point to the job groups with the largest preventive potential. Exposures to the wrist will often correlate with exposures to the elbows and shoulder, meaning that CTS might be a sentinel of harmful upper extremity activities, not just harmful wrist activities. Calculation of robust SIRs requires relatively large job groups, which means that comprehensive changes of the working environment would be necessary to change the signals. Thus, routine national registers may be used to monitor SIRs of CTS as occupational sentinels to guide preventive efforts and potentially to monitor their effects. The sentinel approach should be transferable to other countries with easy access to hospitals and with nationwide registers comprising health and employment data.

In conclusion, the results corroborated our hypothesis that elevated SIRs of CTS diagnoses within occupational groups may serve as sentinels of harmful hand activities.

Figure 1. Sex specific flowcharts.



CTS, carpal tunnel syndrome.

Table 1. Age distribution of 4,046,851 person-years of follow-up 2010-2013 according to 28 job groups. Men.

Job group	Job group label	Age group, years					
		18-34		35-49		50-65	
		Person-years	%	Person-years	%	Person-years	%
10	Managers	19,315	7.4	124,713	47.9	116,553	44.7
20	Science and information professionals	47,460	18.7	127,890	50.4	78,409	30.9
21	Health and legal professionals	30,766	21.1	58,046	39.7	57,336	39.2
22	Teachers	51,182	23.3	84,530	38.5	83,923	38.2
23	Business professionals	33,120	19.8	74,705	44.7	59,439	35.5
30	Science and health associate professionals	32,840	17.5	85,339	45.4	69,933	37.2
31	Financial and purchasing agents	41,576	23.9	80,276	46.1	52,115	30.0
32	It technicians, business services and administrative workers	27,108	19.3	57,362	40.8	55,971	39.9
40	General clerks	63,145	34.4	63,998	34.8	56,634	30.8
50	Services and sales workers	133,972	45.4	81,787	27.7	79,536	26.9
51	Care and protective workers	77,781	43.6	54,194	30.4	46,603	26.1
60	Agricultural and fishery workers	15,987	16.2	35,999	36.5	46,704	47.3
70	Carpenters	48,398	42.7	35,383	31.2	29,629	26.1
71	Builders and painters	31,103	33.4	33,835	36.3	28,282	30.3
72	Building finishers and metal workers	34,217	29.5	49,204	42.5	32,433	28.0
73	Smiths	22,320	23.8	40,555	43.2	30,964	33.0
74	Mechanics	36,339	35.4	38,135	37.2	28,102	27.4
75	Electricians	31,018	40.6	27,769	36.4	17,551	23.0
76	Handicraft, garment and food processing workers	24,403	26.8	37,766	41.4	29,030	31.8
80	Truck drivers	15,238	16.8	38,128	42.0	37,475	41.3
81	Operators	14,292	17.1	34,824	41.7	34,490	41.3
82	Assemblers	19,398	23.2	34,272	41.0	29,970	35.8
83	Drivers	14,275	15.5	32,192	34.9	45,910	49.7
90	Civil engineering labourers	15,475	19.4	29,112	36.5	35,147	44.1
91	Cleaners, food and elementary workers	32,384	38.3	26,994	31.9	25,243	29.8
92	Storage labourers	30,103	33.1	33,962	37.3	26,880	29.6
93	Construction and manufacturing labourers	22,499	30.6	27,510	37.4	23,614	32.1
99	Unemployed and apprentices	230,111	61.4	80,117	21.4	64,566	17.2
Total		1,195,812	29.5	1,528,597	37.8	1,322,442	32.7

The specific DISCO-08 occupational groups/titles in the job groups can be seen in supplementary table 1.

Table 2. Age and child birth distribution of 3,994,987 person-years of follow-up 2010-2013 according to 24 job groups. Women.

		Age group, years							
		18-34		35-49		50-65		Child birth	
Job group	Job group label	Person-years	%	Person-years	%	Person-years	%	Person-years	%
10	Managers	10,001	11.6	42,683	49.3	33,887	39.1	2,322	2.7
20	Science, business and information professionals	36,987	21.5	91,405	53.0	44,045	25.5	9,199	5.3
21	Health professionals	31,019	22.8	61,153	44.9	43,997	32.3	8,308	6.1
22	Teachers	53,123	21.7	101,785	41.5	90,328	36.8	10,681	4.4
23	Nurses	31,389	20.7	63,191	41.7	57,145	37.7	7,215	4.8
24	Primary school teachers	42,531	21.9	83,357	42.9	68,623	35.3	9,293	4.8
25	Pedagogues	38,379	25.0	66,917	43.5	48,389	31.5	7,074	4.6
26	Legal professionals	35,403	26.6	59,491	44.7	38,134	28.7	7,966	6.0
30	Science and health associate professionals	50,098	23.1	92,187	42.5	74,865	34.5	8,898	4.1
31	Financial, sales and business services agents	46,103	23.8	92,395	47.6	55,694	28.7	8,486	4.4
32	It technicians and administrative workers	20,463	11.5	79,462	44.6	78,222	43.9	4,210	2.4
40	General clerks	48,064	21.8	93,800	42.5	79,106	35.8	5,811	2.6
41	Customer service and other clerks	50,037	26.3	78,463	41.3	61,695	32.4	5,997	3.2
50	Services and sales workers	83,878	44.7	63,625	33.9	40,308	21.5	6,180	3.3
51	Shop sales assistants	104,829	62.6	38,518	23.0	24,043	14.4	5,623	3.4
52	Child care workers	80,635	37.3	73,147	33.8	62,527	28.9	5,230	2.4
53	Health care assistants	37,607	21.2	56,789	32.0	83,308	46.9	4,637	2.6
54	Home-based personal care workers	66,642	32.2	67,625	32.7	72,836	35.2	5,461	2.6
60	Agricultural and fishery workers	3,846	28.4	5,126	37.9	4,554	33.7	457	3.4
70	Craft workers	15,580	31.4	21,894	44.1	12,136	24.5	1,561	3.2
80	Operators and assemblers	13,421	15.9	37,155	44.1	33,732	40.0	1,656	2.0
90	Cleaners	31,565	32.8	34,765	36.1	29,937	31.2	1,860	1.9
91	Elementary occupations	25,393	21.1	37,869	31.4	57,313	47.5	1,573	1.3
99	Unemployed and apprentices	264,862	66.1	85,001	21.2	50,595	12.6	22,859	5.7
Total		1,221,855	30.6	1,527,803	38.2	1,245,329	31.2	152,557	3.8

The specific DISCO-08 occupational titles and occupational groups included in the job groups can be seen in supplementary table 2.

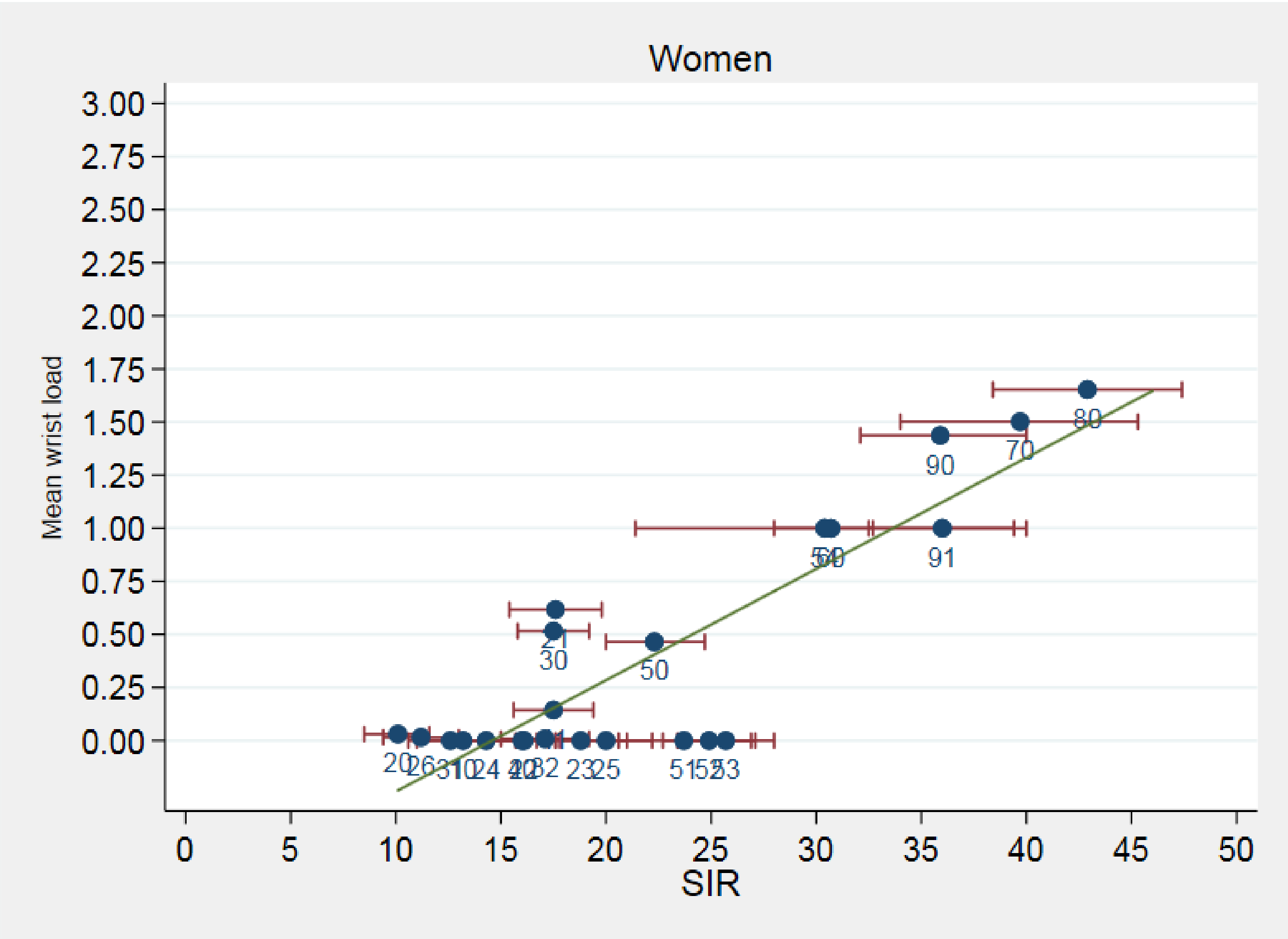
Figure 2. Mean wrist load versus age standardised incidence rates (SIRs) of carpal tunnel syndrome in 28 job groups[a]. Marker labels are job groups.

The slope of the regression line is: 0.13 (95% CI 0.11 to 0.16). Men.

[a] The occupational groups/titles in the job groups can be seen in supplementary table 1.

Figure 3. Mean wrist load versus age standardised incidence rates (SIRs) of carpal tunnel syndrome in 24 job groups[a]. Marker labels are job groups.

The slope of the regression line is: 0.05 (95% CI 0.04 to 0.07). Women.



[a] The occupational groups/titles in the job groups can be seen in supplementary table 2.

Table 3. Carpal tunnel syndrome (CTS) in Denmark 2010-2013. Crude incidence rate (IR_{crude}) per 10,000 person-years, age-standardised incidence rate (SIR) per 10,000 person-years, and adjusted odds ratios (OR[a]), according to 28 job groups. Men.

Job group	Job group label	Person-years	CTS number	IR_{crude}	95% CI	SIR	95% CI	$OR_{age\ adj}$[b]	95% CI	$OR_{fully\ adj}$[c]	95% CI
10	Managers	260,581	188	7.2	6.3-8.3	6.3	5.2-7.4	0.9	0.8-1.2	0.9	0.8-1.2
20	Science and information professionals	253,759	110	4.3	3.6-5.2	4.0	3.2-4.8	0.6	0.5-0.8	0.7	0.5-0.8
21	Health and legal professionals	146,148	57	3.9	3.0-5.1	3.7	2.7-4.7	0.6	0.4-0.8	0.6	0.4-0.8
22	Teachers	219,635	152	6.9	5.9-8.1	6.3	5.3-7.4	Ref.	-	Ref.	-
23	Business professionals	167,264	98	5.9	4.8-7.1	5.5	4.4-6.6	0.8	0.7-1.1	0.9	0.7-1.1
30	Science and health associate professionals	188,112	180	9.6	8.3-11.1	9.0	7.6-10.3	1.3	1.1-1.7	1.3	1.1-1.6
31	Financial and purchasing agents	173,967	102	5.9	4.8-7.1	6.0	4.8-7.2	0.9	0.7-1.1	0.9	0.7-1.1
32	It technicians, business services and administrative workers	140,441	114	8.1	6.8-9.8	7.1	5.8-8.4	1.1	0.9-1.5	1.1	0.9-1.4
40	General clerks	183,777	151	8.2	7.0-9.6	8.6	7.2-10.0	1.3	1.0-1.6	1.3	1.0-1.6
50	Services and sales workers	295,294	248	8.4	7.4-9.5	9.8	8.5-11.0	1.4	1.2-1.8	1.4	1.2-1.7
51	Care and protective workers	178,578	149	8.3	7.1-9.8	9.8	8.2-11.3	1.4	1.1-1.8	1.4	1.1-1.8
60	Agricultural and fishery workers	98,690	145	14.7	12.5-17.3	13.8	11.4-16.2	2.0	1.6-2.5	1.9	1.5-2.3
70	Carpenters	113,410	224	19.8	17.3-22.5	20.9	18.1-23.7	3.3	2.7-4.1	3.3	2.7-4.0
71	Builders and painters	93,220	188	20.2	17.5-23.3	20.6	17.7-23.6	3.2	2.6-3.9	3.1	2.5-3.8
72	Building finishers and metal workers	115,854	266	23.0	20.4-25.9	23.3	20.5-26.1	3.6	2.9-4.4	3.4	2.8-4.2
73	Smiths	93,839	192	20.5	17.8-23.6	20.0	17.2-22.9	3.0	2.5-3.8	2.8	2.3-3.5
74	Mechanics	102,576	180	17.6	15.2-20.3	18.1	15.5-20.8	2.8	2.3-3.5	2.7	2.2-3.4
75	Electricians	76,338	105	13.8	11.4-16.7	15.4	12.4-18.4	2.3	1.8-3.0	2.3	1.8-2.9
76	Handicraft, garment and food processing workers	91,199	150	16.5	14.0-19.3	16.3	13.7-18.9	2.5	2.0-3.1	2.4	1.9-3.0
80	Truck drivers	90,841	155	17.1	14.6-20.0	15.8	13.2-18.4	2.4	1.9-2.9	2.2	1.7-2.7
81	Operators	83,606	146	17.5	14.9-20.5	16.5	13.7-19.3	2.4	1.9-3.0	2.3	1.8-2.9
82	Assemblers	83,627	178	21.3	18.4-24.7	20.7	17.6-23.8	3.1	2.5-3.9	2.9	2.3-3.6
83	Drivers	92,377	133	14.4	12.2-17.1	13.3	10.8-15.8	1.9	1.5-2.4	1.8	1.4-2.3
90	Civil engineering labourers	79,734	196	24.6	21.4-28.3	23.7	20.3-27.2	3.4	2.7-4.2	3.2	2.6-4.0
91	Cleaners, food and elementary workers	84,621	109	12.9	10.7-15.5	13.7	11.1-16.3	2.1	1.6-2.7	2.1	1.6-2.7
92	Storage labourers	90,945	117	12.9	10.7-15.4	13.4	11.0-15.8	2.0	1.6-2.6	1.9	1.5-2.4
93	Construction and manufacturing labourers	73,623	163	22.1	19.0-25.8	22.3	18.9-25.7	3.4	2.7-4.3	3.2	2.5-4.0
99	Unemployed and apprentices	374,794	209	5.6	4.9-6.4	8.9	7.6-10.2	1.1	0.9-1.4	1.1	0.9-1.4

[a] The OR can be interpreted as a HR.
[b] Adjusted for age in three categories and follow-up intervals. Job group 22 (teachers) was used as reference.
[c] Additionally adjusted for region of residence and diabetes.
The specific DISCO-08 occupational groups/titles in the job groups can be seen in supplementary table 1.

Table 4. Carpal tunnel syndrome (CTS) in Denmark 2010-2013. Crude incidence rate (IR_{crude}) per 10,000 person-years, age-standardised incidence rate (SIR) per 10,000 person-years and adjusted odds ratios (OR[a]), according to 24 job groups. Women.

Job group	Job group label	Person-years	CTS number	IR_{crude}	95% CI	SIR	95% CI	$OR_{age\ adj}$[b]	95% CI	$OR_{fully\ adj}$[c]	95% CI
10	Managers	86,571	128	14.8	12.4-17.6	13.2	10.6-15.7	0.8	0.6-1.0	0.8	0.7-1.0
20	Science, business and information professionals	172,437	169	9.8	8.4-11.4	10.1	8.5-11.6	0.6	0.5-0.7	0.6	0.5-0.8
21	Health professionals	136,169	249	18.3	16.2-20.7	17.6	15.4-19.8	1.1	0.9-1.3	1.1	1.0-1.3
22	Teachers	245,236	423	17.3	15.7-19.0	16.1	14.5-17.6	Ref.	-	Ref.	-
23	Nurses	151,725	308	20.3	18.2-22.7	18.8	16.7-21.0	1.2	1.1-1.4	1.2	1.1-1.4
24	Primary school teachers	194,511	297	15.3	13.6-17.1	14.3	12.6-15.9	0.9	0.8-1.1	0.9	0.8-1.1
25	Pedagogues	153,685	315	20.5	18.4-22.9	20.0	17.8-22.2	1.3	1.1-1.5	1.3	1.1-1.5
26	Legal professionals	133,028	147	11.1	9.4-13.0	11.2	9.4-13.0	0.7	0.6-0.9	0.7	0.6-0.9
30	Science and health associate professionals	217,150	405	18.7	16.9-20.6	17.5	15.8-19.2	1.1	0.7-1.3	1.1	1.0-1.3
31	Financial, sales and business services agents	194,102	246	12.7	11.2-14.4	12.6	11.0-14.2	0.8	0.7-0.9	0.8	0.7-0.9
32	It technicians and administrative workers	178,147	340	19.1	17.2-21.2	17.1	15.0-19.2	1.0	0.9-1.2	1.0	0.9-1.2
40	General clerks	220,970	376	17.0	15.4-18.8	16.0	14.3-17.6	1.0	0.9-1.1	1.0	0.9-1.2
41	Customer service and other clerks	190,195	340	17.9	16.1-19.9	17.5	15.6-19.4	1.1	1.0-1.3	1.1	1.0-1.3
50	Services and sales workers	187,811	361	19.2	17.3-21.3	22.3	20.0-24.7	1.4	1.2-1.6	1.4	1.2-1.6
51	Shop sales assistants	167,390	264	15.8	14.0-17.8	23.7	20.6-26.9	1.4	1.2-1.6	1.4	1.2-1.6
52	Child care workers	216,309	502	23.2	21.3-25.3	24.9	22.7-27.1	1.6	1.4-1.8	1.5	1.4-1.8
53	Health care assistants	177,704	514	28.9	26.5-31.5	25.7	23.4-28.0	1.6	1.4-1.9	1.6	1.4-1.8
54	Home-based personal care workers	207,103	636	30.7	28.4-33.2	30.4	28.0-32.7	1.9	1.7-2.2	1.9	1.7-2.2
60	Agricultural and fishery workers	13,526	42	31.1	23.0-42.0	30.7	21.4-40.0	1.9	1.4-2.6	1.9	1.4-2.6
70	Craft workers	49,610	192	38.7	33.6-44.6	39.7	34.0-45.3	2.6	2.2-3.0	2.5	2.1-3.0
80	Operators and assemblers	84,308	389	46.1	41.8-51.0	42.9	38.4-47.4	2.6	2.3-3.0	2.5	2.2-2.9
90	Cleaners	96,267	340	35.3	31.8-39.3	35.9	32.1-40.0	2.3	2.0-2.6	2.2	1.9-2.6
91	Elementary occupations	120,575	469	38.9	35.5-42.6	36.0	32.5-39.4	2.2	1.9-2.5	2.1	1.9-2.4
99	Unemployed and apprentices	400,458	406	10.1	9.2-11.2	17.2	15.3-19.0	0.9	0.8-1.1	0.9	0.8-1.1

[a] The OR can be interpreted as a HR.
[b] Adjusted for age in three categories and follow-up intervals. Job group 22 (teachers) was used as reference.
[c] Additionally adjusted for region of residence, diabetes, and recent child birth.
The specific DISCO-08 occupational groups/titles in the job groups can be seen in supplementary table 2.

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PAPER III

Prognosis of symptoms and disability among patients with suspected carpal tunnel syndrome: influence of occupational mechanical exposures and abnormal median nerve conduction

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ABSTRACT

Objectives: To evaluate occupational mechanical exposures and abnormal median nerve conduction as prognostic factors for symptoms and disability among patients with suspected carpal tunnel syndrome (CTS).

Methods: We conducted a prospective study of 18-64 year-old patients with suspected CTS referred for nerve conduction studies (NCS). Participants completed a questionnaire at baseline and after 9-12 months. Information on job titles was combined with a job exposure matrix to assess wrist load. The primary outcomes were the Levine symptom and function scores and the secondary outcome was the Disability of the Arm, Shoulder and Hand (DASH) score. We used linear regression to analyse changes in the scores and Poisson regression to analyse prevalence ratios of minimal clinically important differences (MCID) between baseline and follow-up.

Results: A total of 361 (72.3%) completed follow-up. The Levine symptom score improved less in case of high wrist load (-0.33 points; 95% confidence interval (CI): -0.61 to -0.05). Abnormal NCS were associated with larger improvement (0.21 points; 95% CI: 0.00 to 0.42) and also with a higher prevalence of MCID in Levine and DASH scores (e.g. the prevalence ratio for MCID in the Levine function score was 2.59; 95% CI: 1.78 to 3.78). Improved symptom and function scores were related to surgical treatment, especially in case of abnormal NCS.

Conclusion: Among patients with suspected CTS, high wrist load predicted less improvement, while abnormal NCS predicted larger improvement and a higher prevalence of MCID in symptom and function scores, which was partly explained by surgical treatment.

Keywords

Clinical examination, job exposure matrix, mononeuropathy, nerve conduction study, prospective cohort study, upper extremity

INTRODUCTION

Upper limb symptoms suggestive of carpal tunnel syndrome (CTS) are common in working aged people[1] and often lead to referral for nerve conduction studies (NCS). In accordance with clinical guidelines, the diagnosis of CTS is frequently based on the combination of symptoms and the result of the NCS.[2-4] The diagnostic use of NCS complies with criteria recommended for epidemiologic studies.[5, 6] In the Swedish general population, 10% of men and 17% of women reported symptoms indicating CTS, while the proportion that also had abnormal NCS was 2 to 3%.[1] In a study of patients referred for NCS on suspicion of CTS due to extensive numbness and tingling, Tinel's sign at the wrist and a positive Phalen's test, the proportion with abnormal NCS was 67%.[7]

Little is known about the prognosis of symptoms and disability among patients with suspected CTS, both overall and in relation to the result of NCS, choice of treatment, occupational mechanical exposures, and lifestyle factors.[8] For patients evaluated on suspicion of ulnar neuropathy, occupational mechanical exposures to the elbow/hand, abnormal ulnar NCS, female sex, and a body mass index (BMI) ≥30 kg/m^2 were negative prognostic factors.[9]

Among patients evaluated on suspicion of CTS, abnormal NCS clearly favoured the choice of surgical treatment[10, 11] and predicted a more favourable outcome with respect to symptoms after surgery.[11] With regard to symptom relief after surgery, one study found that smoking was a negative prognostic factor,[12] while another study found that monotonous repetitive work was a negative prognostic factor,[13] but findings have been inconsistent.[14] A high BMI has been associated with symptoms and impairment pre- and postoperatively, but did not influence the improvement.[15] Blue collar work[16, 17] and adverse psychosocial exposures[17] may be associated with prolonged sickness absence after surgery for CTS, but the evidence is limited.[18] Despite low level of evidence, a European multidisciplinary treatment guideline recommends that patients with CTS should reduce heavy work activities and repetitive movements.[4]

The aim of this study was to evaluate occupational mechanical exposures and abnormal median nerve conduction as prognostic factors for symptoms and disability among patients with suspected CTS. We hypothesised that high mechanical exposures were associated with poorer prognosis.

METHODS

Design and population

We undertook a prospective study of consecutive patients referred to a hospital department of neurophysiology for NCS on suspicion of CTS. From 19 May 2015 to 29 April 2016, we invited patients aged 18-64 years. The baseline data collection comprised clinical examination of the neck and upper extremities, NCS, and a questionnaire. A follow-up questionnaire was mailed after 9-12 months (non-responders could be reminded twice). Exclusion criteria were inability to read or write Danish and to cooperate in the NCS and the subsequent clinical examination. According to Danish legislation, observational studies that use questionnaire or clinical data only do not require approval from the Danish system of health research ethics committees (request number: 84/2015). The Danish Data Protection Agency approved the study (j. no.: 1-16-02-84-14).

Potential prognostic factors

Nerve conduction studies NCS were performed by experienced technicians using the Keypoint.NET system, version 2.33 (Dantec Keypoint, Natus Neurology, Middleton, USA). The NCS procedure has been described in details elsewhere.[19] We used age-specific reference values of the department to calculate z-scores for each participant, i.e. deviations from the reference values expressed in standard deviations (SD).[20] We considered a z-score as abnormal if larger than 1.96 for distal motoric latency (DML) or smaller than -1.96 for sensory nerve conduction velocities (SNCV). If it was not possible to record a motor or sensory response, DML or SNCV was considered abnormal too. The department's electrodiagnostic criteria for an abnormal NCS are that at least two of the three z-scores for median DML and SNCV digits 2 and 3 are abnormal in the presence of normal ulnar nerve DML and SNCV digit 5.

To assess occupational mechanical exposures, we linked questionnaire information on job title the year before baseline with a job exposure matrix (JEM) based on five experts' ratings. The Hand-arm JEM was originally developed for a study of ulnar neuropathy[21] and has also been used to study prognosis after wrist injuries.[22] The construction of the JEM has been described elsewhere.[21] The JEM covers forceful work rated from 1 (low) to 5 (high)[23] and duration of work per day with repetitive movements of the elbow and/or wrist (excluding computer use), non-neutral wrist postures, and hand-arm vibrations (HAVs).[21] We constructed a joint wrist load variable, which represented the just-mentioned exposures either individually or in different combinations.[24] Wrist load was categorised as low, medium, and high.[24] For patients who were unemployed or outside the labour market, the exposures were coded as missing.

Baseline questionnaire information was obtained on height, weight, smoking, alcohol consumption, hand dominance, diabetes, thyroid disease, previous elbow, forearm or wrist fractures, and education level. The baseline questionnaire also included questions on psychosocial work factors (job demands, job control, and social support from leader and colleagues) in terms of single item questions with a 6 point scale.[25] Job demands, job control and social support were dichotomised into high/low values. Information on non-surgical treatment (splinting or corticosteroid injection) and surgery was obtained from the follow-up questionnaire.

Clinical examination and hand diagrams

For descriptive purposes, a clinical examination of the neck and upper extremities was performed by an experienced physician (ST) according to a written protocol. At the time of the examination, the result of the NCS was unknown to patient and examiner. The presence/absence was recorded of: reduced range of motion (ROM) and pain during active movement of the cervical spine and shoulders (painful arc), palpation tenderness of the neck/shoulder muscles (trapezius, levator scapulae, supra- and infraspinatus), trigger points in the infraspinatus muscle eliciting tingling sensations in the ipsilateral hand, impingement test a.m. Hawkins,[26] palpation tenderness at the common tendon attachments to the humeral epicondyles,[27] Tinel's sign at the elbow (tingling provoked by percussing the ulnar nerve at its sulcus), wrist pain during resisted flexion, extension, and gripping, Tinel's sign at the wrist, a positive Phalen's test,[28] thenar atrophy, reduced sensibility of the fingers, and reduced strength of the abductor pollicis brevis and first dorsal interosseous muscles. If presence of reduced ROM and pain during active movement of the cervical spine was recorded, a foraminal compression test was performed.

The baseline- and follow-up questionnaires included the Katz hand diagram,[29] which we classified as "classic/probable", "possible", or "unlikely" CTS.[5] We considered the diagrams positive if they were classified as at least possible CTS.

Outcome measures

Outcome assessment was based on the Levine (or Boston) CTS questionnaire,[30] which we translated into Danish, and the validated Danish version of Disability of the Arm, Shoulder and Hand (DASH) questionnaire.[31] The Levine questionnaire is side-specific and has two dimensions: a symptom severity scale with 11 items and a functional status scale with 8 items. Each item is scored from 1 (mildest) to 5 (most severe) and symptom and function scores are calculated as the mean for each scale.[30] The DASH questionnaire contains 30 items concerning the combined disability of both upper extremities and yields a score ranging from 0 (best) to 100 (worst).[31]

Our primary outcome measures were the changes in the Levine symptom and function scores between baseline and follow-up. Our secondary outcome was the change in DASH score. Additionally, we analysed the prevalence of minimal clinical important differences (MCID) from baseline to follow-up. For the Levine symptom and function scores we applied MCIDs of ≥1.0 and ≥0.7 points, respectively.[32] For the DASH score, we applied an MCID of ≥15 points.[33]

Statistical analyses

We included one hand per person. In case of bilateral NCS, we used information for the dominant side. Patients with missing information on hand dominance (n=4) were classified as right-handed. Age was categorised as 18-34, 35-49, and 50-64 years. BMI was calculated as weight/height squared (kg/m^2) and categorised as ≥17-<25, ≥25-<30, and ≥30-48.9 kg/m^2.

We applied crude and adjusted linear regression of the primary and secondary outcomes including a priori chosen potential prognostic variables, i.e. wrist load and the result of NCS. Model 1 additionally included age, sex, BMI, smoking status, and alcohol consumption. Model 2 included the variables in model 1 and surgery during follow-up. We performed supplementary analyses including the variables from model 2 together with psychosocial work factors and education level. We also performed crude linear regression analyses of change in outcome measures according to surgery status separately for participants with normal NCS and abnormal NCS.

The prevalence ratios of MCID in the Levine symptom and function scores and in the DASH score were analysed using Poisson regression with robust error variance technique.[34] Finally, the effect of surgery on the MCID outcomes was analysed according to the result of NCS using the group with normal NCS who did not undergo surgery as the reference. All Poisson analyses were adjusted for the same explanatory variables as those in linear regression model 1.

RESULTS

Figure 1 displays the flowchart of the study. A total of 499 (79.7%) provided baseline information and 361 (72.3%) responded at follow-up. Non-responders at follow-up (n=138) were younger (mean 41.4 vs. 47.5 years) and more often males (42.8 vs. 29.6%). Overall, and within categories of wrist load, non-responders were comparable with respect to Levine scores (results not shown). Normal NCS were more common among non-responders (62.3 vs. 51.8%) while distributions of the clinical characteristics were similar (results not shown).

Among responders at follow-up, 48.2% had an abnormal NCS result at baseline. The mean DML of the median nerve was 3.2 ms (SD 0.5) for participants with normal NCS and 4.8 ms (SD 1.2) otherwise. For SNCV digit 2 the corresponding means were 59.4 m/s (SD 7.0) and 39.8 m/s (SD 7.6) and for SNCV digit 3, 59.3 m/s (SD 7.1) and 38.2 m/s (SD 8.0). The mean of the ulnar DML was 2.4 ms (SD 0.2) in both groups and the mean SNCV digit 5 was 60.4 m/s (SD 5.3) and 60.6 m/s (SD 4.8), respectively.

Table 1 displays baseline characteristics of the study population according to the result of the NCS. Participants with abnormal NCS were older, had higher BMI, and more often had vocational education and moderate/high wrist load. Among men, the three most frequent jobs with high wrist load were carpenters, bricklayers, and smiths. Among women it was electronic assemblers, house painters, and storage labourers. Participants with abnormal NCS more frequently underwent bilateral NCS and had a dominant-sided condition. Table 1 also shows that surgical treatment during follow up was strongly related to abnormal NCS. In case of abnormal NCS, the proportions with surgery were around 55% irrespective of wrist load, while in case of normal NCS 9.2% with low, 9.8% with moderate, and 22.7% with high wrist load underwent surgery. In both NCS groups, approximately 9% received non-surgical treatment.

Table 2 shows clinical findings and wrist/hand symptoms according to the result of the NCS; the two groups were similar. None of the participants had a positive foraminal compression test. At follow-up, 60.5% had a positive Katz hand diagram in the group with normal NCS against 51.2% in the group with abnormal NCS.

Table 3 shows the results for the Levine symptom score. An overall improvement was seen. Increased improvement was related to abnormal NCS and surgical treatment, and when adjusted for surgical treatment (model 2), the increased improvement related to abnormal NCS (model 1) was reduced. Higher wrist load was associated with less improvement. Age, sex, and lifestyle factors did not influence prognosis. The same was true of psychosocial work factors and education level (results not shown). As seen in table 4, the results for the Levine function score showed the same tendencies although not statistically significantly. No associations were found between the potential prognostic factors and change in the DASH score (results not shown).

An MCID in the Levine symptom score was obtained by 32.7% (normal NCS 18.7%, abnormal NCS 47.7%); $PR_{adjusted}$ 2.59 (95% CI 1.78 to 3.78). For the Levine function score, the percentage was 21.3% (normal NCS 12.8%, abnormal NCS 30.5%); $PR_{adjusted}$ 2.60 (95% CI 1.53 to 4.42). For the DASH score, the percentage was 21.3% (normal NCS 15.5%, abnormal NCV 28.6%); $PR_{adjusted}$ 1.79 (95% CI 1.12 to 2.86). An MCID in the DASH score was also negatively associated with age ≥50-<65 years; $PR_{adjusted}$ 0.54 (95% CI 0.31 to 0.95). There was no association between wrist load and lifestyle factors and any of the MCIDs.

An MCID in each of the three scores was significantly associated with surgery. For those with abnormal NCS, the $PR_{adjusted}$ related to surgery reached 4.59 (95% CI 2.93 to 7.19) for the Levine symptom score, 3.33 (95% CI 1.78 to 6.23) for the Levine function score, and 2.66 (95% CI 1.59 to 4.46) for the DASH score. Even in the subgroup with no surgery, abnormal NCS was associated with an MCID in Levine symptom score (PR 1.96, 95% CI 1.11 to 3.45) and the Levine function score (PR 2.37, 95% CI 1.21 to 4.63). For those with normal NCS, surgery was associated with an MCID in the Levine symptom score only ($PR_{adjusted}$ 3.23, 95% CI 1.75 to 5.98).

DISCUSSION

Among patients with suspected CTS, high wrist load was a negative prognostic factor, while an abnormal NCS was a positive prognostic factor. Improved symptom and function scores were related to surgical treatment, especially in case of abnormal NCS.

The study took advantage of a cohort of consecutive patients, high percentages that responded at baseline and at follow up, independent assessment of wrist load based on a JEM, and NCS of median nerve impairment. Drop out was associated with a normal NCS result, but responders and non-responders did not differ with respect to baseline symptom and function scores and wrist load. Therefore, we think that the observed associations between abnormal NCS/high wrist load and the outcomes are unlikely to be inflated by selection bias.

Findings at clinical examination of the neck and upper extremities as well as the Katz hand diagram were not clearly related to the result of the NCS. In accordance with previous studies,[10, 11, 35] this indicates that for patients referred for NCS on suspicion of CTS, clinical examination and distribution of hand symptoms have low discriminative properties with respect to median nerve impairment.

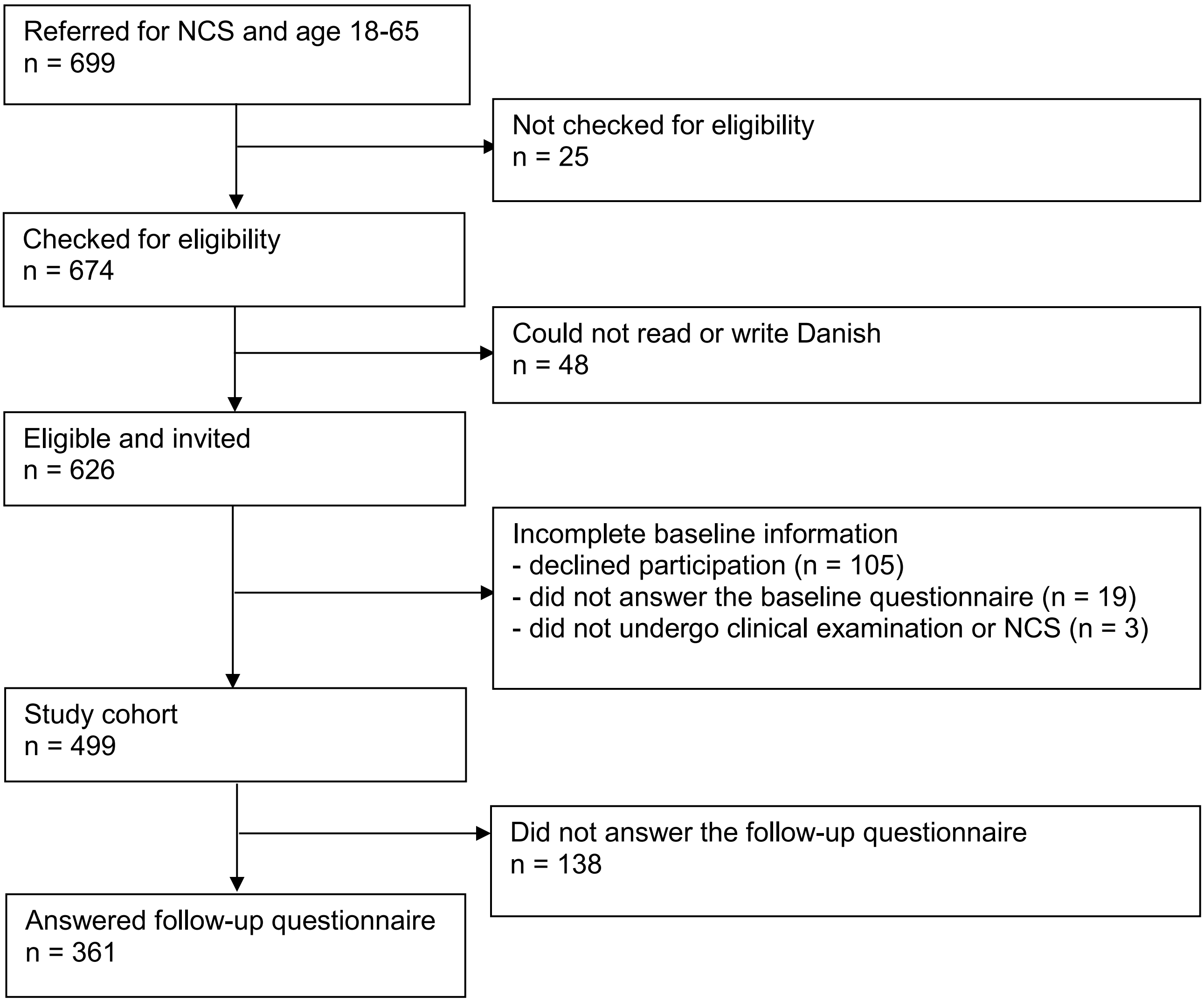
High wrist load was related to a poorer prognosis of symptoms. Surgery did not alleviate this, which could at least partly be explained by the fact that surgical treatment despite a normal NCS result was more common in case of high wrist load, and in this patient group, the improvement in symptoms was particularly small. The negative effect of a high wrist load may even have been underestimated due to few participants with high wrist load particularly among women who accounted for 70.4% of the participants.[24] Furthermore, patients with high wrist load may have reduced their exposures during follow-up.

An abnormal NCS was a positive prognostic factor and as reported in a previous study of patients with suspected CTS,{{827 Becker,S.J. 2014;828 Makanji,H.S. 2013;}} abnormal NCS predicted choice of CTS surgery. Surgical treatment was related to a more favourable prognosis. Adjusting for surgery reduced the improvement associated with abnormal NCS, indicating that surgical treatment partly explained the favourable prognosis. Thus, NCS plays an important role with respect to choice of treatment and even conveys prognostic information irrespective of choice of treatment among patients referred for suspected CTS.

In clinical studies of CTS outcome measures from USA and UK, preoperative Levine symptom and function scores of 3.0 to 3.4 and 2.6 to 3.0 have been reported.[30, 36] Postoperative scores were 1.9 to 2.0, yielding change scores of 1.0 to 1.5 and 0.7 to 1.0.[30, 36] In this study, the baseline Levine scores were around 0.5 points lower indicating fewer symptoms and consequently less room for improvement. The lower baseline scores may be explained by the study population being younger than in the studies cited (mean 48 vs. 57-59 years),[30, 36] and by our inclusion of milder cases of CTS that were not operated. We believe that our results can be generalised to other countries with a public and tax-paid healthcare system that also have a labour market similar to Denmark.

In conclusion, we found that abnormal NCS was related to a more favourable prognosis among patients with suspected CTS, partly because the choice of surgical treatment often relied on an abnormal NCS. High wrist load was a negative prognostic factor.

Figure 1. Flowchart.



NCS, nerve conduction studies

Table 1.Baseline characteristics of the study population and surgical treatment during follow-up according to result of nerve conduction studies (NCS) at baseline.

	NCS result			
	Normal n = 187		Abnormal n = 174	
	n	%	n	%
Age (years)				
18-34	38	20.3	21	12.1
35-49	69	36.9	62	35.6
50-<65	80	42.8	91	52.3
Sex				
Male	52	27.8	55	31.6
Female	135	72.2	119	68.4
BMI (kg/m^2)				
≥17-<25	87	46.5	59	33.9
≥25-<30	52	27.8	62	35.6
≥30-48.9	44	23.5	49	28.2
Missing	4	2.1	4	2.3
Smoking status				
Never	82	43.9	80	46.0
Current	42	22.5	30	17.2
Ex	57	30.5	58	33.3
Missing	6	3.2	6	3.5
Alcohol consumption (units/week)				
≤1	82	43.9	75	43.1
>1-<7	63	33.7	68	39.1
≥7-83	41	21.9	30	17.2
Missing	1	0.5	1	0.6
Bilateral NCS	72	38.5	96	55.2
Dominant-sided condition	135	72.2	144	82.8
Diabetes or thyroid disease	12	6.4	17	9.8
Previous ipsilateral upper extremity fracture	33	17.7	14	8.1
Education level				
Higher or medium-level	59	31.6	52	29.9
Vocational	83	44.4	98	56.3
Low	39	20.9	22	12.6
Missing	6	3.2	2	1.2
High job demands[a]	27	24.8	23	20.9
Low job control[a]	17	15.6	15	13.6
Low social support at work[a]	11	10.1	20	18.2
Wrist load[b]				
Low	98	52.4	77	44.3
Moderate	41	21.9	47	27.0
High	22	11.8	34	19.5
Missing	26	13.9	16	9.2
Surgical treatment during follow-up				
No	166	88.8	78	44.8
Yes	21	11.2	96	55.2

[a] Restricted to those working at baseline, n=219.
[b] Year before baseline.
BMI, body mass index.

Table 2. Baseline clinical findings and wrist/hand symptoms and according to result of nerve conduction studies (NCS) at baseline. Only ipsilateral findings.

	NCS result			
	Normal n = 187		Abnormal n = 174	
	n	%	n	%
Cervical spine				
Pain, active movement	49	26.2	33	19.0
Reduced ROM	12	6.4	9	5.2
≥3 tender points in neck-shoulder region	6	3.2	5	2.9
Trigger points in infraspinatus muscle	45	24.0	29	16.7
Shoulders				
Painful arc	37	19.8	24	13.8
Reduced ROM	22	11.8	15	8.6
Impingement	14	7.5	6	3.4
Elbow				
Lateral epicondylitis	3	1.6	3	1.7
Medial epicondylitis	2	1.1	2	1.1
Tinel's sign	37	19.8	28	16.1
Wrist				
Wrist pain	5	2.7	3	1.7
Tinel's sign	49	26.2	51[a]	29.7
Phalen's test positive	86[b]	49.7	109[c]	69.9
Hand				
Atrophy of thenar	5	2.7	12	6.9
Abnormal sensibility				
Digit 1	37	19.7	41	23.6
Digit 2	36	19.3	39	22.4
Digit 3	42	22.5	49	28.2
Digit 4 radial side	40	21.4	38	22.8
Digit 4 ulnar side	21	11.2	13	7.5
Digit 5	20	10.7	13	7.5
Reduced strength				
Abductor pollicis brevis	15[d]	8.1	12[e]	7.0
First dorsal interosseous muscle	14[d]	7.5	5	2.9
Katz hand diagram, baseline[f]				
Positive	155	90.6	168	97.1
Negative	16	9.4	5	2.9

N in footnotes a to e indicates no. of persons who could not participate in the respective tests:
[a] N = 2, [b] N = 14, [c] N = 18, [d] N = 1, [e] N = 3. [f] Missing not included in the proportions.
ROM, range of motion.

Table 3. Mean Levine symptom score at baseline and at follow-up and results of uni- and multivariable linear regression of change scores. Levine symptom score ranges from 1 (mildest) to 5 (most severe).

	Mean score			Change score						
	N	Baseline	Follow-up	Mean change	$Beta_{crude}$	95% CI	$Beta_{model\ 1}$ [a]	95% CI	$Beta_{model\ 2}$ [b]	95% CI
NCS result										
Normal	187	2.5	2.1	0.35	Ref.	-	Ref.	-	Ref.	-
Abnormal	172	2.7	1.8	0.87	0.52	0.34 to 0.70	0.51	0.30 to 0.71	0.21	0.00 to 0.42
Wrist load										
Low	174	2.5	1.9	0.60	Ref.	-	Ref.	-	Ref.	-
Moderate	88	2.6	2.0	0.56	-0.04	-0.27 to 0.19	-0.12	-0.35 to 0.12	-0.14	-0.36 to 0.08
High	55	2.6	2.0	0.60	0.00	-0.28 to 0.27	-0.23	-0.53 to 0.07	-0.33	-0.61 to -0.05
Surgical treatment										
No	243	2.4	2.1	0.33	Ref.	-	-	-	Ref.	-
Yes	116	2.9	1.7	1.15	0.82	0.64 to 1.00	-	-	0.76	0.53 to 0.98
Age (years)										
18-34	59	2.6	2.1	0.53	Ref.	-	Ref.	-	Ref.	-
35-49	129	2.6	2.0	0.61	0.08	-0.20 to 0.36	0.00	-0.31 to 0.30	0.01	-0.28 to 0.30
50-64	171	2.6	1.9	0.61	0.08	-0.18 to 0.35	-0.12	-0.42 to 0.18	-0.14	-0.43 to 0.14
Sex										
Male	107	2.6	1.9	0.66	Ref.	-	Ref.	-	Ref.	-
Female	252	2.6	2.0	0.57	-0.10	-0.30 to 0.11	-0.12	-0.35 to 0.12	-0.14	-0.36 to 0.08
BMI (kg/m^2)										
≥17-<25	145	2.5	1.9	0.55	Ref.	-	Ref.	-	Ref.	-
≥25-<30	113	2.6	2.0	0.57	0.02	-0.20 to 0.24	-0.10	-0.34 to 0.13	-0.06	-0.28 to 0.16
≥30-48.9	93	2.7	2.0	0.71	0.16	-0.07 to 0.39	0.06	-0.19 to 0.32	-0.01	-0.24 to 0.23
Smoking status										
Never	162	2.5	1.9	0.58	Ref.	-	Ref.	-	Ref.	-
Current	71	2.8	2.3	0.55	-0.03	-0.28 to 0.22	0.05	-0.22 to 0.32	0.04	-0.21 to 0.30
Ex	114	2.5	1.9	0.65	0.07	-0.14 to 0.29	0.04	-0.18 to 0.27	0.09	-0.12 to 0.31
Alcohol consumption (units/week)										
≤1	155	2.7	2.2	0.54	Ref.	-	Ref.	-	Ref.	-
>1-<7	131	2.5	1.8	0.64	0.09	-0.11 to 0.30	0.08	-0.15 to 0.30	0.06	-0.15 to 0.27
≥7-83	71	2.5	1.8	0.64	0.09	-0.16 to 0.34	0.18	-0.10 to 0.48	0.16	-0.11 to 0.43

[a] Model 1: Adjustment for all the variables seen in the table except surgical treatment.
[b] Model 2: Adjustment for all the variables seen in the table.
Model 1 intercept is 0.48 (95% CI 0.09 to 0.87)
Model 2 intercept is 0.44 (95% CI 0.07 to 0.80)
BMI, body mass index. CI, confidence interval. NCS, nerve conduction studies.

Table 4. Mean Levine function score at baseline and at follow-up and results of uni- and multivariable linear regression of change scores. Levine function score ranges from 1 (mildest) to 5 (most severe).

	Mean score			Change score						
	N	Baseline	Follow-up	Mean	Diff$_{crude}$	95% CI	Diff$_{model\ 1}$ [a]	95% CI	Diff$_{model\ 2}$ [b]	95% CI
NCS result										
Normal	185	2.0	1.9	0.07	Ref.	-	Ref.	-	Ref.	-
Abnormal	170	2.0	1.7	0.37	0.30	0.15 to 0.45	0.23	0.07 to 0.39	0.18	0.00 to 0.36
Wrist load										
Low	174	1.9	1.7	0.21	Ref.	-	Ref.	-	Ref.	-
Moderate	86	2.1	1.9	0.24	0.03	-0.15 to 0.22	0.05	-0.14 to 0.24	0.04	-0.15 to 0.23
High	55	1.9	1.8	0.09	-0.11	-0.33 to 0.10	-0.19	-0.43 to 0.05	-0.21	-0.45 to 0.03
Surgical treatment										
No	240	2.0	1.8	0.12	Ref.	-	-	-	Ref.	-
Yes	115	2.2	1.8	1.40	0.27	0.11 to 0.43	-	-	0.14	-0.05 to 0.33
Age (years)										
18-34	59	2.1	1.9	0.14	Ref.	-	Ref.	-	Ref.	-
35-49	128	2.0	1.8	0.21	0.07	-0.15 to 0.29	0.10	-0.15 to 0.34	0.10	-0.15 to 0.35
50-64	168	2.0	1.8	0.23	0.09	-0.13 to 0.30	0.08	-0.16 to 0.32	0.08	-0.17 to 0.32
Sex										
Male	106	1.7	1.6	0.16	Ref.	-	Ref.	-	Ref.	-
Female	249	2.1	1.9	0.23	-0.07	-0.24 to 0.09	-0.04	-0.23 to 0.15	-0.05	-0.24 to 0.14
BMI (kg/m^2)										
≥17-<25	144	1.9	1.8	0.18	Ref.	-	Ref.	-	Ref.	-
≥25-<30	110	2.0	1.8	0.23	0.04	-0.13 to 0.22	-0.02	-0.21 to 0.17	-0.01	-0.20 to 0.18
≥30-48.9	93	2.1	1.9	0.23	0.04	-0.14 to 0.23	-0.08	-0.28 to 0.12	-0.09	-0.29 to 0.11
Smoking status										
Never	159	2.0	1.7	0.25	Ref.	-	Ref.	-	Ref.	-
Current	70	2.2	2.2	0.05	-0.20	-0.40 to 0.00	-0.18	-0.40 to 0.04	-0.18	-0.40 to 0.04
Ex	114	1.9	1.7	0.22	-0.04	-0.21 to 0.13	-0.06	-0.25 to 0.12	-0.05	-0.24 to 0.13
Alcohol consumption (units/week)										
≤1	154	2.2	2.0	0.20	Ref.	-	Ref.	-	Ref.	-
>1-<7	129	2.0	1.7	0.29	0.09	-0.09 to 0.25	0.02	-0.16 to 0.21	0.02	-0.16 to 0.20
≥7-83	70	1.7	1.6	0.12	-0.09	-0.29 to 0.12	-0.01	-0.24 to 0.22	-0.02	-0.25 to 0.21

[a] Model 1: Adjustment for all the variables seen in the table except surgical treatment.
[b] Model 2: Adjustment for all the variables seen in the table.
Model 1 intercept is 0.12 (95% CI -0.19 to 0.44)
Model 2 intercept is 0.14 (95% CI -0.20 to 0.43)
BMI, body mass index. CI, confidence interval. NCS, nerve conduction studies

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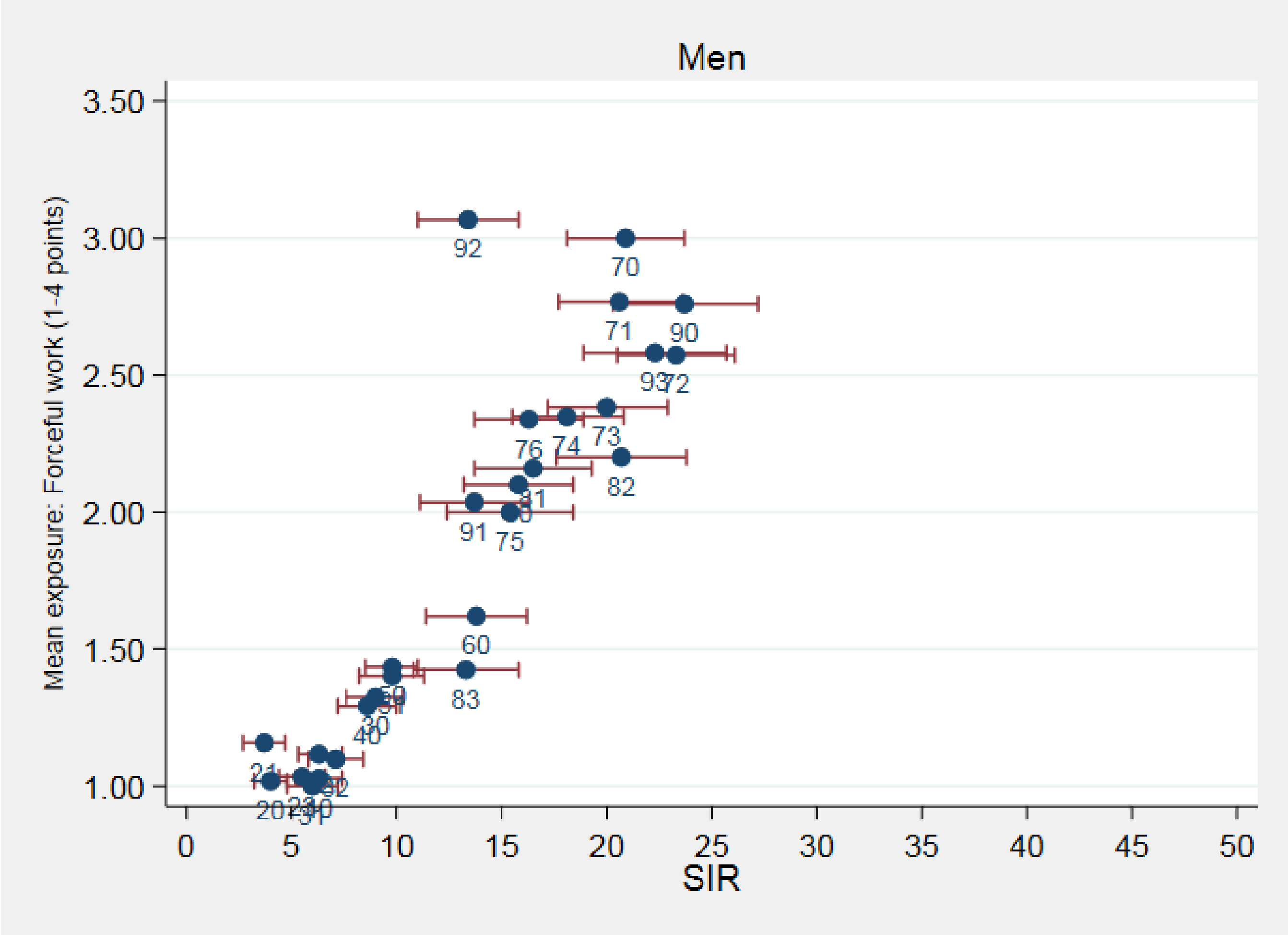
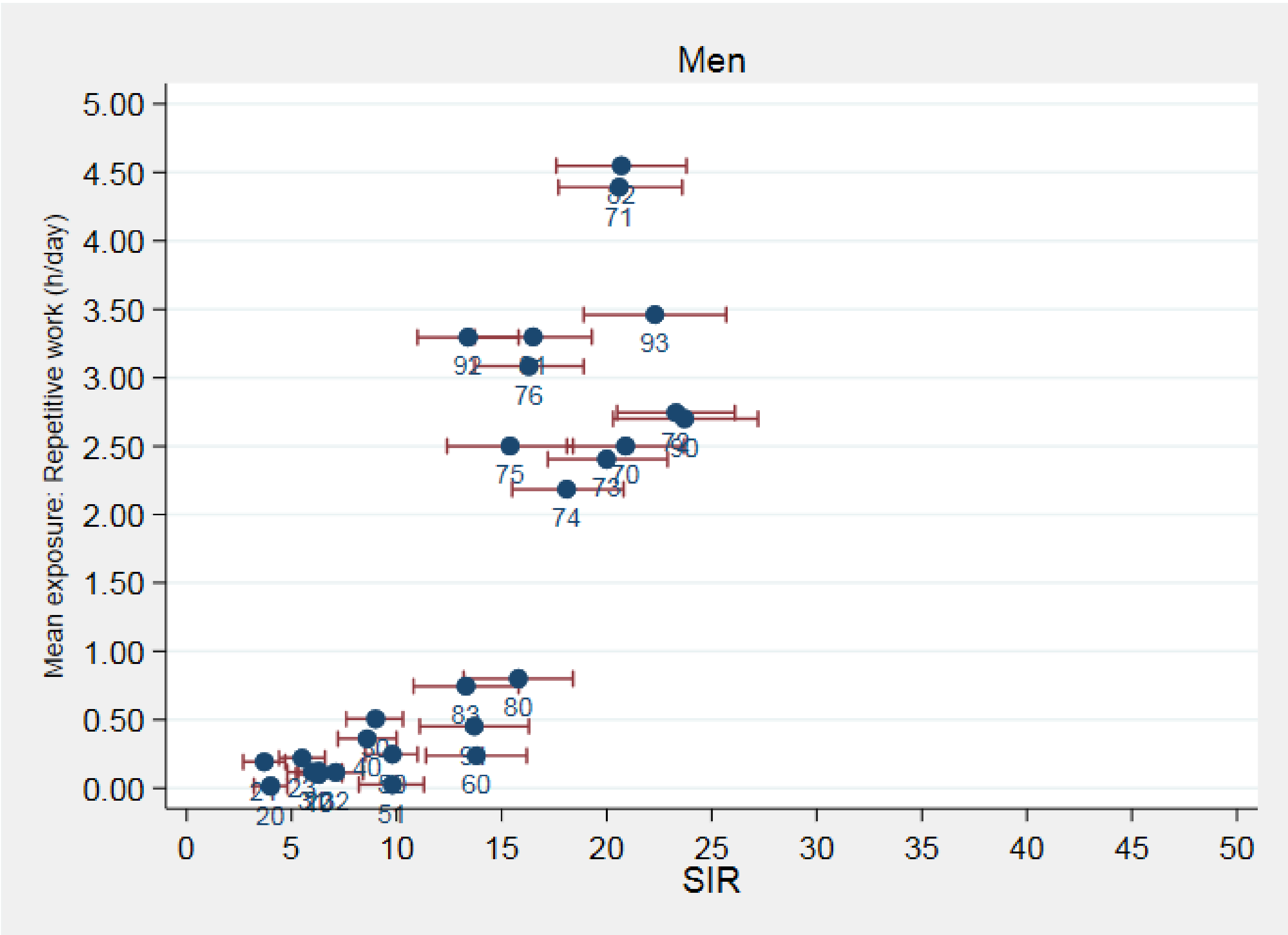
Corrected supplementary figure 1. Force exposure vs. SIRs of CTS among men.



Corrected supplementary figure 3. Repetitive work exposure vs. SIRs of CTS among men.



Corrected supplementary figure 5. Non-neutral wrist posture exposure vs. SIRs of CTS among men.

Corrected supplementary figure 7. Hand-arm vibration exposure vs. SIRs of CTS among men.