Ergonomics

ISSN: 0014-0139 (Print) 1366-5847 (Online) Journal homepage: https://www.tandfonline.com/loi/terg20

The Strain Index (SI) and Threshold Limit Value (TLV) for Hand Activity Level (HAL): risk of carpal tunnelsyndrome (CTS) in a prospective cohort

A. Garg , J. Kapellusch , K. Hegmann , J. Wertsch , A. Merryweather , G. Deckow-Schaefer , E.J. Malloy & the WISTAH Hand Study Research Team

To cite this article: A. Garg , J. Kapellusch , K. Hegmann , J. Wertsch , A. Merryweather , G. Deckow-Schaefer , E.J. Malloy & the WISTAH Hand Study Research Team (2012) The Strain Index (SI) and Threshold Limit Value (TLV) for Hand Activity Level (HAL): risk of carpal tunnelsyndrome (CTS) in a prospective cohort, Ergonomics, 55:4, 396-414, DOI: 10.1080/00140139.2011.644328

To link to this article: https://doi.org/10.1080/00140139.2011.644328

Published online: 08 Mar 2012.

Ergonomics
Vol. 55, No. 4, April 2012, 396–414

The Strain Index (SI) and Threshold Limit Value (TLV) for Hand Activity Level (HAL): risk of carpal tunnel syndrome (CTS) in a prospective cohort

A. Garg[a]*, J. Kapellusch[a], K. Hegmann[b], J. Wertsch[c], A. Merryweather[b], G. Deckow-Schaefer[a], E.J. Malloy[d] and the WISTAH Hand Study Research Team

[a]*Center for Ergonomics, University of Wisconsin-Milwaukee, Milwaukee, WI 53201, USA;* [b]*Department of Family and Preventive Medicine, Rocky Mountain Center for Occupational & Environmental Health, University of Utah, Salt Lake City, UT 84108, USA;* [c]*Department of Physical Medicine & Rehabilitation, Medical College of Wisconsin, Milwaukee, WI 53226, USA;* [d]*Department of Mathematics & Statistics, American University, Washington, DC 20016, USA*

(*Received 29 December 2010; final version received 21 November 2011*)

A cohort of 536 workers was enrolled from 10 diverse manufacturing facilities and was followed monthly for six years. Job physical exposures were individually measured. Worker demographics, medical history, psychosocial factors, current musculoskeletal disorders (MSDs) and nerve conduction studies (NCS) were obtained. Point and lifetime prevalence of carpal tunnel syndrome (CTS) at baseline (symptoms + abnormal NCS) were 10.3% and 19.8%. During follow-up, there were 35 new CTS cases (left, right or both hands). Factors predicting development of CTS included: job physical exposure (American conference of governmental industrial hygienists Threshold Limit Value (ACGIH TLV) for Hand Activity Level (HAL) and the Strain Index (SI)), age, BMI, other MSDs, inflammatory arthritis, gardening outside of work and feelings of depression. In the adjusted models, the TLV for HAL and the SI were both significant per unit increase in exposure with hazard ratios (HR) increasing up to a maximum of 5.4 ($p = 0.05$) and 5.3 ($p = 0.03$), respectively; however, similar to other reports, both suggested lower risk at higher exposures. Data suggest that the TLV for HAL and the SI are useful metrics for estimating exposure to biomechanical stressors.

Practitioner Summary: This study was conducted to determine how well the TLV for HAL and the SI predict risk of CTS using a prospective cohort design with survival analysis. Both the TLV for HAL and the SI were found to predict risk of CTS when adjusted for relevant covariates.

Keywords: epidemiology; ergonomics; cohort; carpal tunnel syndrome; Strain Index; TLV for HAL

1. Introduction

Carpal tunnel syndrome (CTS) is the most common peripheral entrapment mononeuropathy and the United States (US) incurs approximately US$2 B in annual costs due to surgical releases (Stapleton 2006). The relationship between CTS and work has received considerable attention (Silverstein *et al*. 1987, 2006, 2009, 2010, Chiang *et al*. 1990, 1993, Bernard 1997, Bovenzi *et al*. 2005, Franzblau *et al*. 2005, Gell *et al*. 2005, Werner *et al*. 2005a, 2005b, Violante *et al*. 2007). CTS is among the larger drivers of worker's compensation costs, and is associated with significant lost time, lost productivity and disability (Stapleton 2006, Bureau of Labor Statistics 2008). In the United States, the annual incidence rate of CTS is 3.0 per 10,000 workers with a median of 28 days away from work (Bureau of Labor Statistics 2008). The mean worker's compensation cost has been estimated at $20,405 (National Council on Compensation Insurance [NCCI], Inc. 2005) and a mean of $10,000 in lost wages has been reported per CTS case (Foley *et al*. 2007).

There are many risk factors that have been reported for CTS including both occupational and non-occupational factors. The most prominent non-occupational factors include increasing age, female gender, obesity and diabetes mellitus (Silverstein *et al*. 1987, Stevens *et al*. 1988, de Krom *et al*. 1990, Nathan *et al*. 1992a, 1992b, Tanaka *et al*. 1995, Nordstrom 1997, Roquelaure *et al*. 1997, Solomon 1999, Boz 2004, Gell *et al*. 2005, Moghtaderi *et al*. 2005, Werner *et al*. 2005a, 2005b, Hegmann 2010). Occupational factors associated with increased risk of CTS include high levels of job physical exposure, particularly: forceful exertions, high repetition, awkward hand/wrist postures and hand/arm vibration (Moore and Garg 1995, Bernard 1997, Mani and Gerr 2000). It appears that these risk factors interact in a multiplicative manner. For example, exposure to both high force and high repetition is associated with greater risk than exposure to either high force or high repetition alone (Silverstein *et al*. 1987, 2006, Chiang *et al*. 1993, Bernard 1997, Violante *et al*. 2007).

*Corresponding author. Email: arun@uwm.edu

ISSN 0014-0139 print/ISSN 1366-5847 online

http://dx.doi.org/10.1080/00140139.2011.644328
http://www.tandfonline.com

Job analysis methods, such as Rapid Upper Limb Assessment (RULA), Threshold Limit Value for Hand Activity Level (TLV for HAL), the Strain Index (SI) and Occupational Repetitive Action (OCRA), have been proposed to evaluate the combinations of job physical exposure variables that expose a worker to an increased risk of distal upper extremity musculoskeletal disorders (DUE MSDs). Two of the most widely used quantitative tools to measure distal upper extremity (DUE) job physical exposures are likely (Dempsey *et al.* 2005, Spielholz *et al.* 2008): (i) the American conference of governmental industrial hygienists Threshold Limit Value (ACGIH TLV) for HAL (American Conference of Governmental Industrial Hygienists [ACGIH] Worldwide 2002) and (ii) the SI (Moore and Garg 1995). These tools offer summary measures of risk combining two or more job physical factors. The TLV for HAL includes two risk factors: an assessment of normalised peak force and an assessment of repetition (HAL) (American Conference of Governmental Industrial Hygienists [ACGIH] Worldwide 2002). The SI includes six putative risk factors (force, repetition, per cent duration of exertion, posture, speed of work and shift duration) and was derived from epidemiological and biomechanical data (Moore and Garg 1995). The SI places greater emphasis on force (Moore and Garg 1995), while the TLV for HAL appears to place about equal emphasis on peak force and HAL (American Conference of Governmental Industrial Hygienists [ACGIH] Worldwide 2002). Epidemiological studies of the TLV for HAL to predict risk of CTS have shown mixed results (Gell *et al.* 2005, Franzblau *et al.* 2005, Werner *et al.* 2005a, Violante *et al.* 2007). While several studies have shown a relationship between the SI score and risk of DUE MSDs (Moore and Garg 1995, Knox and Moore 2001, Moore *et al.* 2001, 2006, Silverstein *et al.* 2006), there are no prospective studies of the SI and risk of CTS.

The primary hypothesis of this study is that there is a relationship between job physical factors, measured by the ACGIH TLV for HAL and SI and risk of CTS.

2. Methods

This study was approved by the University of Wisconsin – Milwaukee Institutional Review Board (#03.02.059).

Workers for the study were recruited from 10 diverse production facilities of seven employers located in Midwest, USA (State of Wisconsin). Workers at these facilities performed a variety of operations including: (i) poultry processing, (ii) manufacturing and assembly of animal laboratory testing equipment, (iii) small engine manufacturing and assembly, (iv) small electric motor manufacturing and assembly (<1.5 kW, starting weight <0.1 kg and finished weight ≤ 9 kg), (v) commercial lighting assembly and warehousing, (vi) electrical generator manufacturing and assembly, (vii) metal automotive engine parts manufacturing (three facilities) and (viii) plastic and rubber automotive engine parts manufacturing and assembly. In all 10 facilities, the research team had an opportunity to explain the study and invite workers to participate during open meetings. A total of 672 of 894 workers who attended (75.2%) consented to participate (overall participation rate is unclear as the researchers only had access to those willing to attend the open meetings, although it is believed to be more than 50%). All production workers attending the meetings were eligible to participate in the study except those with unpredictable changes in job physical exposures (e.g. supervisors, clerical workers, maintenance/mechanics and forklift truck drivers).

Two different teams, blinded to one another, collected health outcomes and job physical exposure data at baseline and throughout the follow-up. Figure 1 depicts the sequencing of data collection.

2.1. *Worker health, demographics, hobbies, physical activities and psychosocial data collection and assessment*

At baseline, the health outcomes team administered a questionnaire, structured interview, physical examination and a nerve conduction study (NCS). The questionnaire was laptop-administered by occupational therapists and included information on (i) worker's demographics (age, gender, handedness, etc.), (ii) hobbies and outside of work activities (including frequency and duration of these), (iii) medical history (diabetes mellitus, thyroid disorders, high blood pressure, high cholesterol, MSDs, rheumatoid arthritis and other relevant diseases), (iv) psychosocial questions (physical exhaustion, mental exhaustion, depression, job satisfaction, family problems, supervisory, co-worker support, etc.) and (v) a few other questions (smoking, alcohol consumption, blood relatives with CTS, etc.) (Garg *et al.* 2010). Psychosocial questions were developed for use in the current study. The structured interview was administered by a trained occupational therapist and included: (i) current and in the prior month tingling and/or numbness in each digit, (ii) duration of tingling and/or numbness expressed as % of time symptomatic during the prior month and (iii) history of specific disorders including CTS, lateral epicondylitis, deQuervain's, flexor and extensor wrist tendonitis, and trigger digit. Symptoms and history of disorders were recorded for each hand separately. A standard physical examination of the neck to hand regions was performed by the same therapist who administered the structured interview (Garg *et al.* 2010). It included (i) palpation, (ii) physical manoeuvres and

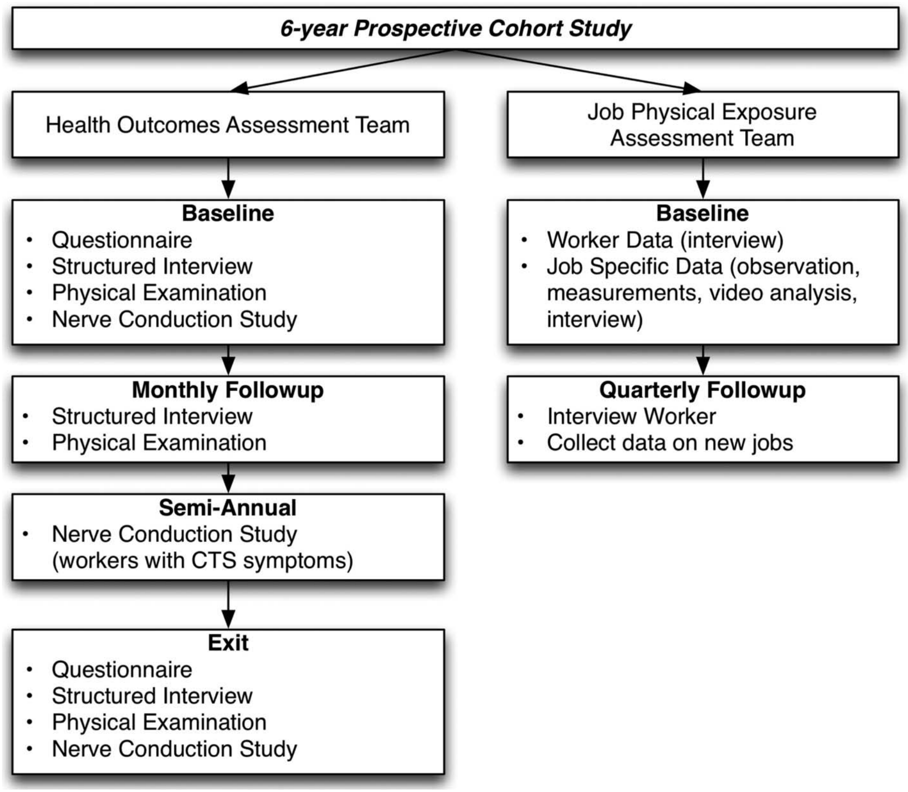

Figure 1. Data collection sequencing.

(iii) evaluation for signs of certain disorders such as rheumatoid arthritis. Height and weight were measured to calculate body mass indices (BMI).

During the monthly cohort follow-up, new symptoms of tingling and/or numbness in each finger, duration of these symptoms during the past month and changes in these symptoms were recorded with a structured interview. Every six months, those workers who had tingling or numbness were administered follow-up NCSs.

2.2. *Nerve conduction studies (NCS)*

Regardless of symptoms, all workers underwent a NCS of each hand at baseline. These were conducted by a board certified physiatrist who was blinded to the worker's symptoms and job physical exposures. The NCS protocol followed the recommendations of the American Association of Electrodiagnostic Medicine (2002). A minimal hand temperature of 30°C was assured before conducting NCSs. Standard antidromic sensory, motor and transcarpal (mixed nerve) studies were done for both the median and ulnar nerves bilaterally (Buschbacher 2000). Distances of 12 cm for sensory, 6 cm for motor and 8 cm for transcarpal studies were used with reference values of $\leq$0.55 ms for transcarpal delta (difference between the transcarpal sensory latencies for the median and ulnar nerves), $\leq$3.8 ms for sensory latency and $\leq$4.45 ms for motor latency. Workers with diffuse nerve conduction abnormalities (both the median and ulnar nerves) were excluded. Those workers with transcarpal delta $>$ 0.55 ms were classified as having an 'abnormal' NCS consistent with median mononeuropathy at the wrist. Workers classified as having 'abnormal NCS' may or may not have had abnormal median nerve sensory and/or motor latencies.

2.3. *CTS case definition*

The CTS case definition required: (i) symptoms (tingling and/or numbness) in at least two median nerve served digits (thumb, index finger, middle finger and/or ring finger), (ii) symptoms occurring on $\geq$25% of days during the preceding month, (iii) symptoms occurring for at least two or more consecutive monthly follow-up periods and (iv) an abnormal NCS consistent with median mononeuropathy recorded within six months of symptoms. Exact questions used to ascertain CTS symptoms are provided in Appendix 1.

A worker could have CTS either in the left, right or both hands for the person level analysis reported in this article. Those cases meeting the case definition at baseline, previously diagnosed as having CTS, or having undergone carpal tunnel release were excluded from eligibility for becoming an incident case. Those persons reporting symptoms due to an acute injury were excluded by censoring them as a non-event, one day before reporting the symptoms.

2.4. *Job physical exposure data collection*

Job physical exposure data were individualised and measured for each hand separately at baseline by ergonomic analysts who had been trained and standardised. Job information and rotation schedules were obtained through interviews with the workers and their supervisors by asking them how many different tasks each worker performed and the duration of each task. Data were collected for each task and included: (i) duration of each task and length of a work shift through worker and supervisor interviews, (ii) peak hand forces (Borg CR-10 scale; Borg 1982) separately rated by the analyst and worker and (iii) videotaping. Tasks with cycle time $\leq$ 2 min were recorded for at least 10 cycles and tasks with cycle time $>$ 2 min were recorded for 20–45 min, ensuring at least one complete cycle recorded. Videos were taken using a single camera but from three different camera angles. Tasks with cycle time $\leq$ 2 min were videotaped for at least three cycles from each of three angles, and tasks with cycle time $>$ 2 min were videotaped for at least 5 min from each of the three angles. Videos were analysed frame by frame to determine analyst overall force rating, temporal exertion requirements, hand/wrist postures and the speed of work. Expert ergonomists estimated overall force ratings for each hand/wrist to assign an overall intensity of exertion (force) rating for the SI score calculations (Moore and Garg 1995). Three different temporal exertion requirements were measured: (i) HAL rating using a verbal anchor scale (Latko 1997, American Conference of Governmental Industrial Hygienists [ACGIH] Worldwide 2002), (ii) number of efforts per minute and (iii) per cent duration of exertion (Moore and Garg 1995). Efforts per minute, per cent duration of exertion, speed of work and hand/wrist posture were measured using the SI methodology (Moore and Garg 1995).

Trained ergonomics analysts visited each worker every three months to assess job physical exposure changes. If either a worker or a supervisor reported a change in the job, physical exposures were reassessed using the same protocol utilised at baseline.

2.5. *Classifications of TLV for HAL and the SI*

TLV for HAL and the SI were computed for each task that a worker performed at baseline as well as for those tasks that changed during the follow-up period. Using the American Conference of Governmental Industrial Hygienists [ACGIH] Worldwide (2002) methodology, TLV for HAL score was calculated as: score = [analyst peak force rating on borg CR $-$ 10 Scale/(10 – HAL rating)]. We treated TLV for HAL score as a continuous variable. Then, using the American conference of governmental industrial hygienists (ACGIH) prescribed cut points, TLV for HAL scores were classified into one of the three categories: below the action limit (AL) (score $<$ 0.56), between the AL and TLV (0.56 $\leq$ score $<$ 0.78), and above the TLV (score $\geq$ 0.78).

The analyst's overall force rating, efforts/min, % duration of exertion, hand/wrist posture, speed of work and duration of task were used to calculate the SI score (Moore and Garg 1995). First, SI was treated as a continuous variable. Then, SI score was categorised into low risk (SI $\leq$ 6.1) and high risk (SI $>$ 6.1) based upon the most recent recommendation by Moore *et al*. (2006).

2.6. *Assigning exposure at the worker level*

Forty-seven per cent of workers performed more than one task during their workday or had job rotation. As there is no consensus method to quantify job exposures for a worker who performs two or more tasks (Garg and Kapellusch 2009a, 2009b), 'typical exposure' was used to assign worker exposure. Typical exposure was defined as exposure from the task the worker performed for the largest percentage of a work shift (i.e. quasi mode). Table 1 summarises exposure variables and metrics used to quantify job physical exposure.

2.7. *Statistical analyses*

The baseline and lifetime prevalence of CTS (person level analysis, CTS either in left, right or both hands) was determined and those workers were subsequently excluded from analyses. Time to first event of CTS was analysed

Table 1. Summary of job physical exposure variables and metrics from typical exposure.

Variable type	Variable (s)	Source	Reference
Force	Analyst peak force rating	Field measurement	Borg CR-10 scale
	Analyst overall force rating	Video analysis	Moore and Garg (1995)
Repetition	Cycle time (s)	Video analysis	–
	HAL rating	Video analysis	ACGIH (2002)
	Efforts/minute	Video analysis	Moore and Garg (1995)
Duty cycle	% Duration of exertion (%)	Video analysis	Moore and Garg (1995)
Speed of Work	Speed of work	Video analysis	Moore and Garg (1995)
Posture	Typical hand/wrist posture (SI rating)	Video analysis	Moore and Garg (1995)
TLV for HAL	Analyst peak force rating and HAL RATING	Calculated	ACGIH (2002)
SI	Analyst overall force rating, efforts/min, (%) duration of exertion, typical hand/wrist posture, speed of work (h/day)	Calculated	Moore and Garg (1995)

using survival analysis and incident cases were censored once they met the case definition for CTS. To account for changes in job physical exposure during follow-up, unadjusted univariate hazard ratios (HR) for incident cases of CTS and 95% confidence intervals for TLV for HAL and SI score were determined using Cox proportional hazard (PH) regression with time varying covariates (Cox 1972). All other covariates such as age, gender, BMI, hobbies, psychosocial factors and past medical history were treated as time independent covariates. Analyses were performed using the coxph() function in R-64 version 2.13.1 for Macintosh (R Development Core Team 2011).

The functional form of each continuous variable (age, BMI, SI score and TLV for HAL) was determined from Martingale residual plots (Therneau *et al.* 1990). The null Cox PH model was fit and the resulting Martingale residuals were plotted against each of the four continuous variables. Smoothed plots of the residuals provided approximate shapes of the covariate (Therneau *et al.* 1990). As different smoothing methods may suggest different functional forms (Lin *et al.* 1993), we examined loess and cubic smoothing splines as flexible means for estimating the shape (Ruppert *et al.* 2003). Results were consistent between smoothing methods. No transformation was suggested for BMI; however, age, TLV for HAL and SI score all exhibited a strong linear trend in the lower to mid-regions followed by a levelling off or a downward trend for the remaining values. To model the non-linearity in the upper region suggested by these plots, we included a linear spline term with a knot which gives the univariate Cox PH model: $\log(\text{HR}) = b_1 x + b_2(x - K)_+$; where x is the continuous variable of interest and the knot, K, was selected to be at approximately the point where the downward turn occurred in the residual plot. We used the closest quantile of cases to this point as the knot; while ensuring that at least five cases were in the upper region for stability of the estimates (the 50th percentile for age and SI score and the 90th percentile for TLV for HAL). The 'plus' notation on the spline term, $(x - K)_+$, indicates that this term is zero when $x - K \leq 0$.

Multivariate models were built to test whether TLV for HAL and SI were related to increased risk of CTS after controlling for potential confounders and/or effect modifiers (covariates). Multivariate models were constructed by first grouping all non-physical exposure variables (i.e. demographic, anthropometric, socioeconomic, hobbies, physical activities, psychosocial, history of other DUE disorders and other medical history; see Table 2), checking for colinearity and screening for biological plausibility. Potential covariates were those that: (i) were not collinear, (ii) were biologically plausible and (iii) had a univariate p-value ≤ 0.10 (Table 4). Due to the large number of resulting potential covariates (14 in total yielding 16,384 candidate models to fit and examine), a backward variable selection procedure was initially used to highlight those covariates most associated with CTS. This procedure was augmented by a check of the impact of removal on the Akaike Information Criterion (AIC) score (Akaike 1974) of the model. Variables were sequentially removed from the model based on the highest remaining p-value of variables in the model. If the reduced model had a lower AIC the variable was permanently removed, otherwise it was retained and the variable with the next highest p-value was removed. None of the covariates removed had $p \leq 0.10$ in multivariate models. Interactions between covariates and job physical factors were examined but could not be studied due to the small number of CTS cases.

Martingale residual plots from this final covariate model were examined to check the functional form of each exposure variable of interest (TLV for HAL and SI) and these were consistent with the forms suggested by the null model residual plots. Multivariate models were then fit by separately forcing the TLV for HAL and the SI using their respective linear spline functional forms. Subsequently, the categorical forms of TLV for HAL (American

Table 2. Potential confounders and/or effect modifiers considered for multivariate analyses of CTS.

Demographic	*Hobbies and activities*
Age	Aerobics
Gender	Walking
Handedness	Running
Marital status	Swimming
Pregnant at baseline	Bicycling
Currently smoke	Tennis
Ever smoked	Gardening
Alcohol consumption	Knitting
Anthropometric	Computer
Body mass index	Piano
Socioeconomic	Baseball
Education level	Basketball
Past medical history	Football (American)
Diabetes mellitus	Racquetball
High blood pressure	Weightlifting
High cholesterol	Maintenance
Rheumatoid and other inflammatory arthritis	Woodworking
Osteoarthrosis	Remodelling
Gout	Vibrating tools
Thyroid problem	Snow skiing
Kidney failure	Water skiing
Wrist fracture	Motorcycling
Baseline prevalence of DUE MSDs other than CTS (# of disorders)	Snow shovelling
Family history of CTS	Snow mobiling
Psychosocial	
Job satisfaction	
Feelings of depression	
General health compared to others	
Family problems	
Feel physically exhausted	
Feel mentally exhausted	
Employer cares	
Get along with co-workers	
Supervisor appreciation	
Recommend job to others	
Would take their job again	

Conference of Governmental Industrial Hygienists [ACGIH] Worldwide 2002) and the SI (Moore *et al*. 2006) were forced into the covariate model.

3. Results

Workers were recruited during the first 18 months from the beginning of the study. Out of 672 workers initially enrolled at baseline, 551 workers (82.0%) completed baseline data collection (Figure 2). Out of 551 workers 536 had at least one month of follow-up data. Out of these 536 workers, 28 workers had both symptoms of tingling and/or numbness and NCSs consistent with bilateral CTS and 27 with unilateral CTS. Nineteen workers had prior carpal tunnel release surgery (of which two were also baseline prevalent) and an additional 34 workers were told by a physician they had prior history of CTS. One worker was diagnosed with polyneuropathy. Excluding these 107 $(28 + 27 + 17 + 34 + 1)$, the cohort for this article included 429 workers who were eligible to become an incident case of CTS. The cohort was followed for an average of 37.8 ± 21.3 (range: 1.9–71.2) months. Over the six-year follow up period participation decreased, primarily due to plant closings and lay-offs.

Demographics of the cohort eligible for an incident case of CTS ($n = 429$) are summarised in Table 3. Most of the cohort was female (63.4%) and 67.1% were overweight (BMI = 25–29.9 kg/m^2) or obese (BMI $\geq$ 30.0 kg/m^2). Twelve (2.8%) reported being diabetic. A majority reported being physically active outside of work with participation in aerobic exercises and/or sports. Many had one or more hobbies such as gardening, knitting, maintenance work, remodelling and/or woodworking.

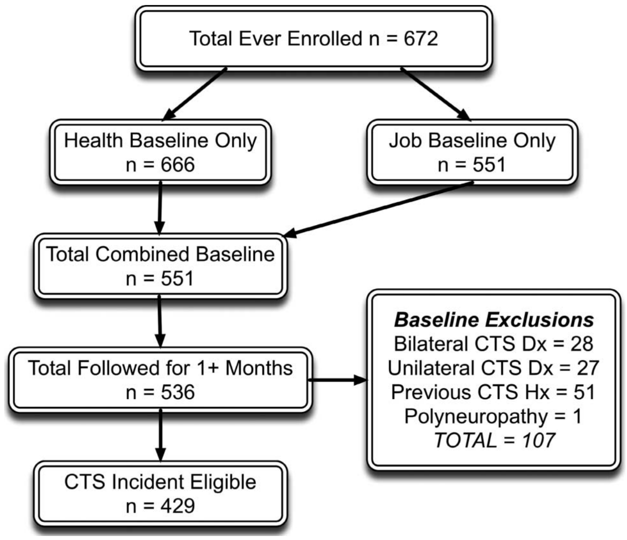

Figure 2. Subject enrolment and exclusion statistics.

Point prevalence of CTS at baseline was 10.3% and lifetime prevalence of CTS at baseline was 19.8%. During the average of 37.8 months of follow-up there were 35 new CTS cases ($n = 28$, 10.3% of females and $n = 7$, 4.5% of males) resulting in an incident rate of 2.55 cases per 100 person-years. Females had a higher CTS incidence rate than males, 3.23 versus 1.43 per 100 person-years respectively. All 35 cases indicated their tingling and numbness was either due to an 'unsure' ($n = 20$) cause or was thought to be work-related ($n = 15$). During follow-up there were two CTS incident cases among the 12 diabetics (16.7%).

Descriptive statistics for job physical exposure variables reported in Table 3 were calculated from physical exposures in the first time period of observation (baseline). However, univariate analyses reported for job physical exposure variables in Table 4 included data from all observation time periods (time-varying covariates).

Age, TLV for HAL and SI were fit with linear spline functions with a single knot, resulting in two spline terms for each variable. Estimated HR for first spline terms reported in Table 4 as well as in multivariate tables is $HR = e^{(\hat{b}_1)}$ for each unit increase in x up to $x = K$. Estimated HR for each unit increase in x for $x > K$ is $HR = e^{(\hat{b}_1 + \hat{b}_2)}$ (Appendix 2). The reported p-values for the second spline terms in Table 4 as well as multivariate tables are for a test of change in slope at the knot (i.e. $b_2 = 0$) in the linear spline transformed Cox PH model. Thus, this p-value *does not* correspond to the reported confidence intervals for second spline terms (i.e. 95% CI for $HR = e^{b1+b2}$) in Tables 4–8.

In Tables 5–8, an overall p-value is provided for each variable in the multivariate model. This p-value represents the significance of each variable in the final multivariate model using the likelihood ratio test.

Table 4 summarises the results from unadjusted univariate analyses for relevant covariates for determining possible predictors of increased risk of CTS in multivariate models. The statistically significant ($p \leq 0.05$) factors were: age, gender, BMI, family history of CTS, inflammatory arthritis, baseline prevalence of other DUE MSDs, feelings of depression, feelings of mental exhaustion after work, gardening and knitting. Osteoarthritis, wrist fracture, job satisfaction, perceived general health compared to others, supervisor shows appreciation and walking were marginally significant ($p \leq 0.10$).

Regarding univariate analyses of biomechanical measures of job physical exposures, when fitted with linear spline functions, TLV for HAL ($p = 0.11$) and SI ($p = 0.10$) were marginally significant. TLV for HAL as a categorical variable using the American Conference of Governmental Industrial Hygienists [ACGIH] Worldwide (2002) prescribed limits was not significant ($p = 0.61$). The SI as a categorical variable using the Moore *et al.* (2006) recommended limits ($SI \leq 6.1$ and $SI > 6.1$) was marginally significant ($p = 0.07$) (Table 4).

The multivariate Cox PH regression model for covariates included: age, BMI, number of specific DUE MSDs (other than CTS), rheumatoid/inflammatory arthritis, gardening and feelings of depression.

When introduced into the multivariate model of covariates TLV for HAL, treated as a continuous variable using a linear spline function, was statistically associated with increased risk of CTS ($p = 0.05$). The linear function showed that the risk increased up to TLV for HAL score of ≤ 1.25 ($HR = 3.85$ per unit increase, 95% $CI = 1.00$–14.86, $p = 0.05$) and then showed some evidence of a decrease in risk for TLV for HAL scores > 1.25 (Table 5). As a

Table 3. Descriptive statistics for covariates and job physical factors ($n = 429$).

Category	Variable	Categories	Mean ± SD (Range) or %
Demographic	Age (years)	–	41.2 ± 11.72 (18.7–68.1)
	Gender	Male	36.6
		Female	63.4
	Pregnant at baseline (Females only)	Yes	0.8
	Currently smoking	Yes	35.0
	Ever smoked	Yes	57.4
	Alcohol consumption	Yes	54.8
Anthropometric	Body Mass Index (BMI) kg/m^2	–	29.1 ± 6.80 (6.5–58.6)
Medical history	Diabetes mellitus	Yes	2.8
	High blood pressure	Yes	14.5
	High cholesterol	Yes	12.1
	Rheumatoid and/or inflammatory arthritis	Yes	4.7
	Osteoarthrosis	Yes	8.9
	Thyroid problem	Yes	4.2
	Wrist fracture	Yes	6.8
	Baseline prevalence of DUE MSDS other than CTS[1]	0	72.3
		1	17.5
		2	5.6
		3	3.2
		≥4	1.4
	Family history of CTS	Yes	18.4
Psychosocial	Job satisfaction	Very satisfied	19.6
		Somewhat satisfied	52.4
		Neither/Nor	23.8
		Somewhat/very dissatisfied[2]	4.2
	Feelings of depression	Never	24.0
		Seldom	57.1
		Often	17.7
		Always	1.2
	General health compared to others	Somewhat/much Better[2]	48.9
		The same	40.6
		Somewhat/much worse[2]	10.5
	Family problems	Never	21.2
		Seldom	56.6
		Often	17.3
		Always	4.9
	Physically exhausted	Never	13.3
		Seldom	50.3
		Often	29.6
		Always	6.8
	Mentally exhausted	Never	30.8
		Seldom	49.4
		Often/always[2]	19.8
	Employer cares	Strongly agree	21.4
		Agree	46.2
		Neither nor	19.1
		Disagree	8.2
		Strongly disagree	5.1
	Get along with co-workers	Never/seldom[2]	3.7
		Often	38.9
		Always	57.4
	Supervisor shows appreciation	Never	8.6
		Seldom	38.5
		Often	36.8
		Always	16.1
	Recommend their job to others	Strongly recommend	13.3
		Recommend	47.3
		Neither nor	26.1
		Discourage	8.2
		Strongly discourage	5.1

(*continued*)

Table 3. (*Continued*).

Category	Variable	Categories	Mean ± SD (Range) or %
	Would take the same job again	Very likely	21.2
		Likely	40.1
		Neither nor	13.0
		Unlikely	15.2
		Very unlikely	10.5
Hobbies/activities	Walking	Yes	46.8
Participation[3]	Gardening	Yes	53.6
	Knitting	Yes	21.2
	Computer	Yes	45.7
	Maintenance	Yes	20.5
	Remodelling	Yes	20.2
	Snow shovelling	Yes	50.2
Job physical factors[4]	Peak force rating (Borg CR-10)	–	3.7 ± 1.18 (0.5–10.0)
	Intensity of exertion (SI definition)	Light	57.8
		Somewhat hard	41.5
		Hard	0.7
		Very hard	0
		Maximum	0
	Cycle time (s)	–	247 ± 340.8 (4.0–2700)
	Median cycle time (s)		138.5
	Hand Activity Level (HAL)	–	5.1 ± 1.60 (1.0–9.0)
	Efforts per Minute	–	25.6 ± 14.57 (0.8–121.0)
	Duty cycle (%)	–	71.5 ± 17.83 (18.0–99.4)
	Speed of work (SI rating)	Very slow	0.0
		Slow	7.5
		Fair	90.4
		Fast	1.9
		Very fast	0.2
	Typical hand/wrist posture (SI rating)	Very good	0.2
		Good	5.8
		Fair	73.2
		Bad	19.4
		Very bad	1.4
	TLV for HAL (ACGIH limits)	$<$AL ($<$ 0.56)	22.8
		$\geq$AL– $<$ TLV	37.3
		$\geq$TLV ($\geq$0.78)	39.9
	TLV for HAL score[5]	–	0.86 ± 0.616 (0.07–6.00)
	SI Categories (Moore *et al.* 2006)	$\leq$6.1	28.2
		$>$6.1	71.8
	SI score	–	14.7 ± 12.21 (0.8–81.0)

Notes: [1]Distal Upper Extremity (DUE) Musculoskeletal Disorders (MSDs). These are: lateral epicondylalgia, medial epicondylalgia, deQuervain's, hand tendinitis (flexor or extensor) and trigger digit. [2]Categories combined due to small sample size. [3]Aerobics, Baseball, Basketball, Bicycling, Football (American), Motorcycling, Piano, Racquetball, Running, Snowmobiling, Snow Skiing, Swimming, Tennis, use of Vibrating Tools outside of work, Water Skiing, Weight Lifting, and Woodworking had less than 20% of workers participating and none were significant at $p \leq 0.10$. [4]Descriptive statistics are for first observation time period (baseline) only and these statistics do not include changes in exposure during the follow-up period. [5]TLV for HAL Score = [Analyst Peak Force Rating on Borg CR-10 Scale ÷ (10–HAL Rating)].

categorical variable using the American Conference of Governmental Industrial Hygienists [ACGIH] Worldwide (2002) prescribed limits, TLV for HAL was not significant ($p = 0.30$) (Table 6).

When the SI was introduced into the multivariate model of covariates and treated as a continuous variable using a linear spline function, it showed borderline association with increased risk of CTS ($p = 0.06$). The multivariate model showed that the risk for CTS increased with an increase in SI score up to $\leq$ 13.5 (HR = 1.13 per unit increase, 95% CI = 1.02–1.26, $p = 0.03$). With a further increase in SI score ($>$ 13.5), there was evidence of decreased risk (Table 7). In the multivariate model, SI as a categorical variable using the Moore *et al.* (2006) recommended limit was significant ($p = 0.03$) (Table 8).

Estimated risk of CTS (i.e. HR) for different levels of physical exposure, using unexposed as the reference, was calculated as $HR = e^{\hat{b}_1 x + \hat{b}_2 (x-K)_+}$. In the multivariate analyses, $\hat{b}_1$ and $\hat{b}_2$ were 1.348 and -3.478, respectively for TLV for HAL spline terms (footnote 4 of Table 5) and 1.123 and -1.141, respectively for the SI spline terms (footnote 3 of Table 7). These HRs are summarised in Table 9 for different levels of TLV for HAL and SI.

Table 4. Univariate Hazard Ratios for TLV for HAL, SI and Covariates ($n = 429$).

Category	Variable (overall p-value)	Categories	N (cases)	HR[1] (95% CI)	p-value
Demographic	Age (years) ($p = 0.009$)	Linear spline terms			
		Per year increase for age $\leq$ 44.3	247 (18)	1.102[2] (1.03–1.18)	0.008
		Per year increase for age > 44.3	182 (17)	0.955[2] (0.89–1.03)	0.02[3]
	Gender	Male	157 (7)	1.0	–
		Female	272 (28)	2.3 (1.00–5.25)	0.05
	Pregnant at baseline	No	270 (28)	1.0	–
		Yes	2 (0)	**	**
	Currently smoke	No	279 (21)	1.0	–
		Yes	150 (14)	1.3 (0.68–2.65)	0.39
	Ever smoked	No	183 (13)	1.0	–
		Yes	246 (22)	1.3 (0.67–2.63)	0.43
	Alcohol consumption	No	194 (14)	1.0	–
		Yes	235 (21)	1.3 (0.66–2.55)	0.45
Anthropometric	Body Mass Index (BMI) (kg/m^2)	Continuous-linear (per unit increase)	429 (35)	1.073 (1.03–1.12)	0.003
Medical history	Diabetes mellitus	No	417 (33)	1.0	–
		Yes	12 (2)	2.0 (0.49–8.49)	0.33
	High blood pressure	No	367 (31)	1.0	–
		Yes	62 (4)	1.2 (0.57–2.47)	0.65
	High cholesterol	No	377 (28)	1.0	–
		Yes	52 (7)	1.8 (0.78–4.11)	0.17
	Rheumatoid/inflammatory Arthritis	No	409 (30)	1.0	–
		Yes	20 (5)	3.8 (1.47–9.79)	0.006
	Osteoarthrosis	No	371 (29)	1.0	–
		Yes	38 (6)	2.2 (0.92–5.33)	0.08
	Thyroid problem	No	411 (32)	1.0	–
		Yes	18 (3)	2.0 (0.61–6.55)	0.25
	Wrist fracture	No	400 (30)	1.0	–
		Yes	29 (5)	2.4 (0.92–6.12)	0.07
	Baseline prevalence of DUE MSDs other than CTS (# of disorders) ($p = 0.003$)	0	310 (17)	1.0	–
		1–2	101 (15)	2.9 (1.45–5.83)	0.003
		$\geq$3	18 (3)	4.8 (1.39–16.37)	0.01
	Family history of CTS	No	350 (24)	1.0	–
		Yes	79 (11)	2.1 (1.04–4.35)	0.04
Psychosocial	Job satisfaction ($p = 0.08$)	Very satisfied	84 (3)	1.0	–
		Satisfied	225 (22)	2.9 (0.86–9.61)	0.31
		Neither/Nor	102 (7)	2.0 (0.52–7.76)	0.09
		Dissatisfied/V. dissatisfied[4]	18 (3)	7.2 (1.45–35.78)	0.02
	Feelings of depression ($p < 0.001$)	Never	103 (1)	0.1 (0.01–0.68)	0.02
		Seldom	245 (24)	1.0	–
		Often	76 (8)	1.1 (0.50–2.49)	0.78
		Always	5 (2)	5.2 (1.22–21.97)	0.02
	General health compared to others ($p = 0.10$)	Much better	67 (3)	1.0	–
		Somewhat better	143 (11)	1.6 (0.45–5.85)	0.45
		The same	174 (13)	1.7 (0.47–5.83)	0.43
		Somewhat/much worse[4]	45 (8)	3.04 (1.27-7.25)	0.03
	Family problems ($p = 0.77$)	Never	91 (5)	1.0	–
		Seldom	243 (22)	1.6 (0.62–4.31)	0.32
		Often	74 (6)	1.4 (0.44–4.73)	0.55
		Always	21 (2)	2.0 (0.39–10.30)	0.41
	Physically exhausted ($p = 0.21$)	Never	57 (3)	1.0	–
		Seldom	216 (15)	1.2 (0.36–4.28)	0.73
		Often	127 (12)	1.8 (0.50–6.23)	0.38
		Always	29 (5)	3.4 (0.81–14.18)	0.10
	Mentally exhausted ($p = 0.08$)	Never	132 (8)	1.0	–
		Seldom	212 (14)	1.1 (0.47–2.67)	0.80
		Often	83 (11)	2.7 (1.07–6.59)	0.04
		Always	12 (2)	3.7 (0.78–17.34)	0.10

(continued)

Table 4. (*Continued*).

Category	Variable (overall p-value)	Categories	N (cases)	HR[1] (95% CI)	p-value
	Employer cares ($p = 0.20$)	Strongly agree	92 (3)	0.3 (0.09–1.03)	0.06
		Agree	198 (20)	1.0	–
		Neither/Nor	82 (5)	0.6 (0.23–1.64)	0.33
		Disagree	35 (4)	1.5 (0.50–4.33)	0.48
		Strongly disagree	22 (3)	1.4 (0.42–4.74)	0.58
	Get along with co-workers ($p = 0.27$)	Never/seldom[4]	16 (1)	1.0 (0.13–7.58)	0.99
		Often	167 (18)	1.7 (0.88–3.40)	0.11
		Always	246 (16)	1.0	–
	Supervisor shows appreciation ($p = 0.09$)	Never	37 (7)	4.4 (1.13–16.90)	0.03
		Seldom	165 (10)	1.5 (0.42–5.60)	0.51
		Often	158 (15)	2.3 (0.67–8.04)	0.18
		Always	69 (3)	1.0	–
	Recommend their job to others ($p = 0.13$)	Strongly recommend	57 (1)	0.2 (0.03–1.54)	0.12
		Recommend	203 (16)	1.0	–-
		Neither/Nor	112 (9)	1.1 (0.47–2.43)	0.87
		Discourage	35 (5)	2.0 (0.73–5.44)	0.18
		Strongly discourage	22 (4)	2.5 (0.83–7.45)	0.10
	Would take the same job again ($p = 0.39$)	Very likely	91 (3)	1.0	–
		Likely	172 (17)	3.2 (0.93–10.81)	0.07
		Neither/Nor	56 (4)	2.3 (0.51–10.17)	0.28
		Unlikely	65 (6)	3.1 (0.78–12.46)	0.11
		Very unlikely	45 (5)	3.8 (0.90–15.78)	0.07
Hobbies/activities[5]	Walking	No	228 (13)	1.0	–
		Yes	201 (22)	1.9 (0.98–3.84)	0.06
	Gardening	No	199 (7)	1.0	–
		Yes	230 (28)	3.4 (1.47–7.70)	0.004
		No	338 (21)	1.0	–
	Knitting	Yes	91 (14)	2.5 (1.26–4.87)	0.009
	Computer	No	236 (22)	1.0	–
		Yes	193 (13)	0.7 (0.36–1.41)	0.33
	Maintenance	No	335 (30)	1.0	–
		Yes	94 (5)	0.6 (0.23–1.50)	0.26
Biomechanical stressors	TLV for HAL (ACGIH Limits) ($p = 0.61$)	$<$AL (<0.56)	98 (7)[6]	1.0	–
		$\geq$AL – $<$ TLV	160 (12)[6]	1.0 (0.39	0.99
		$\geq$TLV (≥ 0.78)	171 (16)[6]	1.4 (0.58	0.46
	TLV for HAL Score[7] ($p = 0.11$)	Linear spline terms			
		Per unit increase for score ≤ 1.25	393 (32)[6]	3.214[8] (0.78–13.22)	0.11
		Per unit increase for score > 1.25	36 (3)[6]	0.208[8] (0.02–2.69)	0.10[3]
	Strain Index (Moore *et al.* 2006 Limit)	SI ≤ 6.1	121 (6)[6]	1.0	–
		SI > 6.1	308 (29)[6]	2.2 (0.92–5.37)	0.07
	Strain Index ($p = 0.10$)	Linear spline terms			
		Per unit increase for SI ≤ 13.5	295 (22)[6]	1.111[9] (1.00–1.23)	0.05
		Per unit increase for SI > 13.5	134 (13)[6]	0.988[9] (0.95–1.03)	0.07[3]

Notes: [1]Hazard Ratio of 1.0 with no confidence interval indicates reference category for the variable. [2]For age, $\hat{b}_1 = 0.0967$ and $\hat{b}_2 = -0.1427$. $HR = e^{b_1 \cdot age}$ and $HR = e^{b_1 \cdot age + b_2(age-44.3)}$ for age ≤ 44.3 and > 44.3, respectively. HR per unit increase in age is e^{b1} for age ≤ 44.3 and e^{b1+b2} for age > 44.3 (See Appendix B). [3]This p-value is for the second spline term and represents a test for change in slope at the knot (i.e. $b_2 = 0$). Thus, this p-value *does not* correspond to the given confidence interval, which is for the HR (i.e. e^{b1+b2}) beyond the knot point. [4]Categories combined because there were either no observations, or no cases. [5]Aerobics, Baseball, Basketball, Bicycling, Football (American), Motorcycling, Piano, Racquetball, Remodelling, Running, Snowmobiling, Snow Shovelling, Snow Skiing, Swimming, Tennis, use of Vibrating Tools outside of work, Water Skiing, Weight Lifting and Woodworking had $< 20\%$ of workers participating or showed no statistically significant association with increased risk of CTS ($p \geq 0.40$). [6]For cases, 'n' is based upon exposure at the time a worker became a case. For non-cases, 'n' is based upon exposure at baseline. [7]TLV for HAL Score = [Analyst Peak Force Rating on Borg CR-10 Scale ÷ (10–HAL Rating)]. [8]For TLV for HAL, $\hat{b}_1 = 1.1676$ and $\hat{b}_2 = -2.7374$. $HR = e^{b_1 \cdot score}$ and $HR = e^{b_1 \cdot score + b_2(score-1.25)}$ for score ≤ 1.25 and > 1.25, respectively. HR per unit increase in score is e^{b1} for score ≤ 1.25 and e^{b1+b2} for score > 1.25 (see Appendix B). [9]For SI, $\hat{b}_1 = 0.1052$ and $\hat{b}_2 = -0.1168$. $HR = e^{b_1 \cdot SI}$ and $HR = e^{b_1 \cdot SI + b_2(SI-13.5)}$ for SI ≤ 13.5 and > 13.5, respectively. HR per unit increase in SI is $e^{b1}$for SI ≤ 13.5 and e^{b1+b2} for SI > 13.5 (See Appendix B). **Insufficient cases and/or observations for analysis.

Table 5. Multivariate model for risk of CTS with the TLV for HAL as continuous variable.

Variable (overall p-value)[1]	Category/function	N (cases)	Hazard ratio	95% CI	p-value
TLV for HAL Score[2] ($p = 0.05$)[1]	Spline terms	98 (7)[3]			
	Per unit score $\leq$ 1.25	160 (7)[3]	3.853[4]	1.00–14.86	0.05
	Per unit score > 1.25	171 (16)[3]	0.119[4]	0.00–3.39	0.09[5]
Covariates					
Age (years) ($p = 0.16$)[1]	Spline terms				
	Per unit age $\leq$ 44.3	247 (18)	1.076[6]	0.99–1.17	0.09
	Per unit age > 44.3	182 (17)	0.959[6]	0.89–1.04	0.10[5]
Body Mass Index(kg/m^{2})) ($p = 0.03$)[1]	Continuous (per unit increase)	429 (35)	1.068	1.02–1.12	0.003
Number of Specific DUE MSDs other than CTS ($p = 0.02$)[1]	0	310 (17)	1.0	–	–
	1–2	101 (15)	2.48	1.21–5.10	0.01
	≥3	18 (3)	3.51	0.95–12.90	0.06
Rheumatoid/inflammatory Arthritis ($p = 0.06$)[1]	No	409 (30)	1.0	–	–
	Yes	20 (5)	4.13	1.46–11.73	0.008
Gardening ($p = 0.02$)[1]	No	199 (7)	1.0	–	–
	Yes	230 (28)	3.05	1.28–7.25	0.01
Felt down, blue or depressed ($p = <0.001$)[1]	Never	103 (1)	0.08	0.01–0.59	0.01
	Seldom	245 (24)	1.0	–	–
	Often	76 (8)	0.92	0.40–2.09	0.84
	Always	5 (2)	6.89	1.45–32.85	0.02

Notes: [1]Overall significance associated with including each variable in the model using the likelihood ratio test. [2]TLV for HAL Score = [Analyst Peak Force Rating on Borg CR-10 Scale ÷ (10–HAL Rating)]. [3]For cases, 'n' is based upon exposure at the time a worker became a case. For non-cases, 'n' is based upon exposure at baseline. [4]For TLV for HAL, $\hat{b}_1 = 1.3487$ and $\hat{b}_2 = -3.4783$. $HR = e^{b_1 \cdot score}$ and $HR = e^{b_1 \cdot score + b_2(score - 1.25)}$ for score ≤ 1.25 and > 1.25 respectively. HR per unit increase in score is e^{b1} for score ≤ 1.25 and e^{b1+b2} for score > 1.25 (See Appendix B). [5]This p-value is for the second spline term and represents a test for change in slope at the knot (i.e. $b_2 = 0$). Thus, this p-value *does not* correspond to the given confidence interval, which is for the HR (i.e. e^{b1+b2}) beyond the knot point. [6]For age, $\hat{b}_1 = 0.0731$ and $\hat{b}_2 = -0.1147$. $HR = e^{b_1 \cdot age}$ and $HR = e^{b_1 \cdot age + b_2(age - 44.3)}$ for age ≤ 44.3 and >44.3 respectively. HR per unit increase in age is e^{b1} for age ≤ 44.3 and e^{b1+b2} for age > 44.3 (See Appendix B).

Table 6. Multivariate model for risk of CTS with the TLV for HAL as categorical variable using the ACGIH (2002) limits.

Variable (overall p-value)[1]	Category/function	N (cases)	Hazard ratio	95% CI	p-value
TLV for HAL ($p = 0.30$)[1]	<AL (<0.56)	98 (7)[2]	1.00	–	
	≥AL–<TLV	160 (12)[2]	1.44	0.55–3.76	0.46
	≥TLV (≥0.78)	171 (16)[2]	2.01	0.80–5.04	0.14
Covariates					
Age (years) ($p = 0.17$)[1]	Spline terms				
	Per unit age $\leq$ 44.3	247 (18)	1.077[3]	0.99–1.17	0.08
	Per unit age > 44.3	182 (17)	0.895[3]	0.78–1.02	0.11[4]
Body Mass Index (kg/m^{2}) ($p = 0.005$)[1]	Continuous (per unit increase)	429 (35)	1.070	1.02–1.12	0.002
Number of specific DUE MSDs (other than CTS) ($p = 0.02$)[1]	0	310 (17)	1.0	–	–
	1–2	101 (15)	2.45	1.21–5.08	0.01
	≥3	18 (3)	3.85	1.08–13.8	0.04
Rheumatoid/inflammatory Arthritis ($p = 0.02$)[1]	No	409 (30)	1.0	–	–
	Yes	20 (5)	4.07	1.43–11.58	0.008
Gardening ($p = 0.006$)[1]	No	199 (7)	1.0	–	–
	Yes	230 (28)	3.02	1.28–7.15	0.01
Felt down, blue or depressed ($p = < 0.001$)[1]	Never	103 (1)	0.08	0.01–0.62	0.02
	Seldom	245 (24)	1.0	–	–
	Often	76 (8)	0.99	0.44–2.24	0.99
	Always	5 (2)	8.19	1.69–39.72	0.009

Notes: [1]Overall significance associated with including each variable in the model using the likelihood ratio test. [2]For cases, 'n' is based upon exposure at the time a worker became a case. For non-cases, 'n' is based upon exposure at baseline. [3]For age, $\hat{b}_1 = 0.0738$, and $\hat{b}_2 = -0.1115$. $HR = e^{b_1 \cdot age}$ and $HR = e^{b_1 \cdot age + b_2(age - 44.3)}$ for age ≤ 44.3 and > 44.3, respectively. HR per unit increase in age is e^{b1} for age ≤ 44.3 and e^{b1+b2} for age > 44.3 (See Appendix B). [4]This p-value is for the second spline term and represents a test for change in slope at the knot (i.e. $b_2 = 0$). Thus, this p-value *does not* correspond to the given confidence interval, which is for the HR (i.e. e^{b1+b2}) beyond the knot point.

Table 7. Multivariate model for risk of CTS with the Strain Index as continuous variable.

Variable (overall *p*-value)[1]	Category/function	*N* (cases)	Hazard ratio	95% CI	*p*-value
Strain Index Score ($p = 0.06$)[1]	Spline terms	98 (7)[2]			
	Per unit SI $\leq$ 13.5	160 (12)[2]	1.131[3]	1.02–1.26	0.03
	Per unit SI $>$ 13.5	171 (16)[2]	0.982[3]	0.94–1.03	0.04[4]
Covariates					
Age (years) ($p = 0.19$)[1]	Spline terms				
	Per unit age $\leq$ 44.3	247 (18)	1.074[5]	0.99–1.17	0.09
	Per unit age $>$ 44.3	182 (17)	0.961[5]	0.89–1.04	0.12[4]
Body Mass Index (kg/m^2) ($p = 0.03$)[1]	Continuous (per unit increase)	429 (35)	1.066	1.02–1.11	0.004
Number of specific DUE MSDs (Other than CTS) ($p = 0.01$)[1]	0	310 (17)	1.0	–	–
	1–2	101 (15)	2.71	1.32–5.56	0.007
	$\geq$3	18 (3)	3.92	1.08–14.18	0.04
Rheumatoid/inflammatory Arthritis ($p = 0.09$)[1]	No	409 (30)	1.0	–	–
	Yes	20 (5)	3.66	1.32–10.16	0.01
Gardening ($p = 0.02$)[1]	No	199 (7)	1.0	–	–
	Yes	230 (28)	3.14	1.33–7.42	0.01
Felt down, blue or depressed ($p = <0.001$)[1]	Never	103 (1)	0.09	0.01–0.67	0.02
	Seldom	245 (24)	1.0	–	–
	Often	76 (8)	0.93	0.41–2.12	0.86
	Always	5 (2)	7.66	1.60–36.75	0.01

Notes: [1]Overall significance associated with including each variable in the model using the likelihood ratio test. [2]For cases, '*n*' is based upon exposure at the time a worker became a case. For non-cases, 'n' is based upon exposure at baseline. [3]For SI, $\hat{b}_1 = 0.1231$, and $\hat{b}_2 = -0.1413$. HR $= e^{b_1 \cdot SI}$ and HR $= e^{b_1 \cdot SI + b_2(SI-13.5)}$ for score ≤ 13.5 and >13.5, respectively. HR per unit increase in score is e^{b1} for SI ≤ 13.5 and e^{b1+b2} for SI $>$ 13.5 (See Appendix B). [4]This *p*-value is for the second spline term and represents a test for change in slope at the knot (i.e. $b_2 = 0$). Thus, this *p*-value *does not* correspond to the given confidence interval, which is for the HR (i.e. e^{b1+b2}) beyond the knot point. [5]For age, $\hat{b}_1 = 0.0711$, and $\hat{b}_2 = -0.1103$. HR $= e^{b_1 \cdot age}$ and HR $= e^{b_1 \cdot age + b_2(age-44.3)}$ for age ≤ 44.3 and >44.3 respectively. HR per unit increase in age is eb_1 for age ≤ 44.3 and e^{b1+b2} for age $>$ 44.3 (See Appendix B).

Table 8. Multivariate model for risk of CTS with the Strain Index as categorical variable using the recommended limit of SI = 6.1 (Moore *et al.* 2006).

Variable (overall *p*-value)[1]	Category/function	*N* (cases)	Hazard ratio	95% CI	*p*-value
Strain Index ($p = 0.03$)[1]	$\leq$6.1	121 (6)[2]	1.00	–	
	$>$6.1	308 (29)[2]	2.5	1.00–6.13	0.05
Covariates					
Age (years) ($p = 0.17$)[1]	Spline terms				
	Per unit age $\leq$ 44.3	247 (18)	1.076[3]	0.99–1.17	0.08
	Per unit age $>$ 44.3	182 (17)	0.962[3]	0.89–1.04	0.10[4]
Body Mass Index (kg/m^2) ($p = 0.01$)[1]	Continuous (per unit increase)	429 (35)	1.063	1.02–1.11	0.005
Number of specific DUE MSDs (other than CTS) ($p = 0.01$)[1]	0	310 (17)	1.0	–	–
	1–2	101 (15)	2.66	1.30–5.45	0.007
	$\geq$3	18 (3)	3.70	1.02–13.46	0.05
Rheumatoid/inflammatory Arthritis ($p = 0.02$)[1]	No	409 (30)	1.0	–	–
	Yes	20 (5)	4.14	1.48–11.59	0.007
Gardening ($p = 0.004$)[1]	No	199 (7)	1.0	–	–
	Yes	230 (28)	3.17	1.34–7.46	0.008
Felt down, blue or depressed ($p = <0.001$)[1]	Never	103 (1)	0.10	0.01–0.71	0.02
	Seldom	245 (24)	1.0	–	–
	Often	76 (8)	0.94	0.42–2.12	0.88
	Always	5 (2)	8.44	1.73–41.16	0.008

Notes: [1]Overall significance associated with including each variable in the model using the likelihood ratio test. [2]For cases, 'n' is based upon exposure at the time a worker became a case. For non-cases, 'n' is based upon exposure at baseline. [3]For age, $\hat{b}_1 = 0.0733$ and $\hat{b}_2 = -0.1123$. HR $= e^{b_1 \cdot age}$ and HR $= e^{b_1 \cdot age + b_2(age-44.3)}$ for age ≤ 44.3 and >44.3, respectively. HR per unit increase in age is $e^{b1}$for age ≤ 44.3 and e^{b1+b2} for age $>$ 44.3 (See Appendix B). [4]This *p*-value is for the second spline term and represents a test for change in slope at the knot (i.e. $b_2 = 0$). Thus, this *p*-value *does not* correspond to the given confidence interval, which is for the HR (i.e. e^{b1+b2}) beyond the knot point.

Table 9. Hazard ratio estimates for TLV for HAL and SI based on multivariate analyses.

TLV for HAL score	Hazard ratio[1]	Strain index score	Hazard ratio[1]
0.0	1.0	0	1.0
0.2	1.3	3	1.4
0.4	1.7	6	2.1
0.6	2.2	9	3.0
0.8	2.9	12	4.4
1.0	3.9	13.5[2]	5.3
1.2	5.0	15	5.1
1.25[2]	5.4	18	4.9
1.4	3.9	21	4.6
1.6	2.6	24	4.4
1.8	1.7	27	4.1
2.0	1.1	30	3.9
		45	3.0
		60	2.3
		75	1.7
		90	1.3

Notes: [1]HR estimates are from results in Tables 5 and 7 were calculated using the equation $e^{\hat{b}_1 x+\hat{b}_2(x-K)_+}$. [2]Value represents the knot point for the linear spline function.

Estimated peak HRs for TLV for HAL and the SI were 5.4 and 5.3, respectively (Table 9). Workers exposed to biomechanical stresses between 0.81 and 1.52 as measured by the TLV for HAL score and between 9 and 45 as measured by the SI score were had at least three times the risk of CTS as compared to those unexposed (Table 9).

4. Discussion

These results suggest that CTS has a complex, multifactorial etiology in manufacturing settings. These factors include: (i) job physical factors, (ii) worker demographics (age and obesity), (iii) co-morbidity (inflammatory arthritis and other DUE MSDs), (iv) psychosocial factors (feelings of depression) and (v) worker hobbies (gardening). Regarding job physical factors, in their continuous form, both the TLV for HAL and SI predicted risk of CTS with HRs up to 5.4 and 5.3, respectively (Table 9). The TLV for HAL showed no statistically significant association as originally constructed but was predictive when treated as a continuous function. When treated as a categorical variable (Moore *et al.* 2006), the SI was associated with increased risk of CTS with an HR of 2.5 (Table 8).

While the TLV for HAL and the SI use different definitions for force and repetition measurements, both methods have these two variables in common. This suggests that combinations of force and repetition (frequency and duration of exertion) are risk factors for CTS.

Many prior studies have reported associations with job physical factors; however, most studies were either retrospective, and/or had no objective CTS measurement (Silverstein *et al.* 1987, Chiang *et al.* 1990, 1993, Osorio 1994, Radecki 1994, Bernard 1997, Roquelaure *et al.* 1997, Bovenzi *et al.* 2005, Franzblau *et al.* 2005, Silverstein *et al.* 2006, Violante *et al.* 2007). Further, many of these studies either did not account for psychosocial factors, physical activities and hobbies outside of work and/or past medical history. This study addressed many of these weaknesses in prior studies through use of prospective methods, careful measurement of job physical factors, determination of disease status at baseline, reliance on nerve conduction studies (NCS), measured BMI and frequent follow-up of the cohort. It is possible that the strengths of associations shown in this study are greater than those reported in prior studies due to these detailed methods relying primarily on objective measurements.

4.1. Exposure assessment

Job physical exposures were assessed from typical tasks (i.e. a task performed for the largest duration of work shift when a worker rotated to two or more tasks). This method ignored physical exposure from other tasks performed by some of the workers during an entire work shift. Time-weighted average physical exposure for the SI and TLV for HAL was considered, but deemed inappropriate, as it would tend to dilute physical exposure (Garg and Kapellusch 2009a, 2009b). None of the currently available summary measures (including the ‘typical’ exposure used in this article) are expected to characterise job exposure completely and may result in exposure misclassification

(Garg and Kapellusch 2009a). For example, the time-weighted average approach will probably underestimate overall exposure, while the peak exposure approach may overestimate the overall exposure (Dempsey 1999, Garg and Kapellusch 2009a, 2009b). Thus, there is a need to develop a methodology, such as cumulative SI (Garg and Kapellusch 2009a) that would integrate stresses to distal upper extremity over an entire work shift from all different tasks that the worker performs during a work shift.

4.2. TLV for HAL

This study found that the TLV for HAL, when treated as a continuous variable, was predictive of increased risk of CTS (Table 5). Our findings are in agreement with those reported by Violante *et al.* (2007). The Violante *et al.* (2007) study showed that the TLV for HAL was associated with an increased risk of CTS using the ACGIH prescribed limits. However, using these same prescribed limits, three earlier studies found weak predictive abilities or trends towards predictive ability of the TLV for HAL (Franzblau *et al.* 2005, Gell *et al.* 2005, Werner *et al.* 2005a). When categorised using the ACGIH limits, the results of this study are consistent with these three earlier studies (Table 6). If the results (based on continuous analysis of TLV for HAL) of this study are replicated, it is suggested there be a consideration to reconfigure the AL and TLV risk categories for the TLV for HAL.

In this study, CTS risk increased with an increase in TLV for HAL score up to 1.25 and then decreased (Table 9). This decrease in risk might be due to survival bias with workers in the more physically demanding jobs migrating out of those jobs prior to development of disease, or other factors.

4.3. The Strain Index

A few studies have examined relationships between the Strain Index and risk of CTS (Moore and Garg 1995, Rucker and Moore 2002, Bovenzi *et al.* 2005, Moore *et al.* 2006, Silverstein *et al.* 2006) mostly using categorised values of SI. These studies have all reported an association between the SI score and prevalence or incidence of CTS. This study adds to a growing body of evidence that the Strain Index is a useful metric for estimating exposure to DUE biomechanical stressors.

Estimated HRs suggest that workers in this study were at an increased risk for CTS for SI scores up to approximately $SI \leq 100$ with peak risk occurring at $SI = 13.5$ (Table 9). The gradual decrease in CTS risk for physical exposures of $SI > 13.5$ might be due to survival bias; consistent with the TLV for HAL. Further, analyst overall force rating and under penalising frequency of exertion could have resulted in under-estimation of some SI scores.

In the SI methodology, the overall force rating requires the analyst to integrate the forces required to perform the task. For jobs where applied hand force levels are frequently changing within a task cycle (complex tasks), it becomes increasingly difficult for analysts to accurately provide an overall hand force rating. It is possible that analysts have underestimated or overestimated overall force requirements for some jobs. Thus, it is possible that analysts may have introduced non-differential exposure misclassification, which would be expected to bias towards the null. A well defined method to assign analyst's overall force rating is needed.

More than 60% of the jobs in this study required > 20 efforts per minute. The SI methodology caps the efforts multiplier at 20 efforts/min. Thus, these jobs might not have received appropriately high SI scores and this may have reduced the magnitude of the apparent dose–response relationship. The relationship between efforts/min and its multiplier needs to be further investigated and the multiplier may need revision.

4.4. Individual risk factors

Age, gender, BMI and pregnancy have been reported to be associated with increased risk of CTS (Nathan *et al.* 1992a, 1992b, Werner et al 1994, 2005a, Leclerc *et al.* 2001, Tanaka *et al.* 2001, Kouyoumdjian *et al.* 2002, Boz *et al.* 2004, Gell *et al.* 2005, Moghtaderi *et al.* 2005). This study found evidence of increased risk of CTS for age and BMI (Tables 4–8). Female gender was statistically significant in univariate ($HR = 2.3$, 95% $CI = 1.00–5.25$, $p = 0.05$), but not in multivariate analysis ($HR = 1.5$, 95% $CI = 0.62–3.57$, $p = 0.38$). Stratified analyses to quantify differences in risk factors for males and females were not possible due to the small number of male CTS cases (seven cases). This study was likely underpowered to determine risk of CTS from pregnancy as only 2/244 (0.82%) females were pregnant at baseline and 16/244 (6.6%) became pregnant during follow up.

This study found that baseline prevalence of inflammatory arthritis (including rheumatoid arthritis) was associated with an elevated risk for CTS. While Stevens *et al.* (1992) found an association between rheumatoid arthritis and prevalence of CTS, three other studies reported no statistical association with CTS (de Krom *et al.* 1990, Gell *et al.* 2005, Werner *et al.* 2005a). This study found no statistical association between diabetes mellitus and incident cases of CTS. This may be due to insufficient statistical power.

4.5. Other covariates

Aggregate DUE MSDs at baseline were associated with an increased risk of CTS. Leclerc *et al.* (2001) found no statistical association between baseline aggregate disorders and increased risk of CTS, while others have reported increased risk of CTS from any MSD (Ferry *et al.* 2000), upper extremity tendinitis (Gell *et al.* 2005) and wrist, hand and finger tendinitis (Werner 2005a).

Only a few studies have assessed psychosocial factors and no consistent associations have been identified (Bernard 1997, Nordstrom 1997, Leclerc 2001, Roquelaure 2001, Reading 2003, Gell *et al.* 2005, Werner *et al.* 2005a). This study found statistical significance for feelings of depression ($p < 0.001$) and suggests an association that requires further study.

Given the large number of covariates considered and the use of a backward selection process with an AIC-check to build the multivariate model in this study, *p*-values for non-physical exposure covariates are likely inflated and there might be (false-positive) associations that are unique to this cohort.

4.6. Strengths and weaknesses of the study

This study's strengths include: prospective methods, enrolments of large numbers of workers from diverse employers performing different work, assessments and measurements of numerous potential covariates, use of computerised structured interviews, reliance on NCSs at baseline and follow-ups, exclusions of pre-existing or prevalent cases, detailed quantification of job physical factors, blinding of team members, monthly health status follow-ups, quarterly job physical assessment follow-ups of the cohort and moderately long follow-up of the cohort. These methods appear likely to have resulted in stronger measures of effect than many prior studies, including a finding of a dose–response relationship between job physical factors and CTS.

Study limitations include that workers were primarily from manufacturing environments, thus the results might not be directly applicable in other environments, particularly to office settings. Further, within these manufacturing environments, the effect of facility/industry could not be evaluated due to small sample size (35 CTS cases and 10 facilities). Certain hobbies and physical activities such as gardening and snow shovelling are seasonal and therefore time dependent, but were treated as time-independent in this study due to data limitations. Some of the commonly reported risk factors such as diabetes, thyroid disease and pregnancy were likely inadequately assessed due to limited sample size of affected, eligible individuals, as study enrolments intentionally attempted to target one-third high, medium and low job physical demands to have adequate power to study job physical demands. Use of psychosocial questions developed for use in this study might have resulted in misclassification.

5. Conclusions

This study suggests a multifactorial etiology for CTS in manufacturing settings. These factors include job physical factors, age, BMI, co-morbidity of other DUE MSDs, inflammatory arthritis, gardening, and feelings of depression. Both the TLV for HAL and the SI predict increased risk of CTS and results suggest dose–response relationships.

Acknowledgements

The authors also wish to acknowledge the major contributions of the subjects and employers who allowed this team to measure and assess them for several years of their lives. The authors wish to recognise the contributions of the research team as follows:

University of Wisconsin-Milwaukee:
James C. Foster, MD, MPH; David L. Drury, MD, MPH; Suzanna Tomich, MS, CPE, OTR; Gail Groth, MS, OTR; Karen Wahlgren, MS, OTR; Melissa Lemke, MS Jessica Gin, MS; Prithima Reddy Mosaly, PhD; Vivek Kishore, MS; Priyank Gupta, MS; Meenu Sagar, BS; Christopher Hoge, BA; and Bridget Fletcher, BS

University of Utah:
Matthew S. Thiese, PhD, MSPH; Andrew Merryweather, PhD; Richard Sesek, PhD, CSP, MPH; Xiaoming Sheng, PhD; Richard Kendall, DO; Donald Bloswick, PhD, PE, CPE; Eric Wood, MD, MPH; Hannah Edwards, MD, MPH; Jeremy Biggs, MD, MSPH; William Mecham, MS, CPE, CSP; Ulrike Ott, MS; Steven J. Oostema, MS; Riann Robbins, MS; Atim Effiong, MS; and Richard Holubkov, PhD.

Medical College of Wisconsin
Kevin White, MD;

Texas A&M University
J. Steven Moore, MD, MPH

This study was funded, in part, by grants from the National Institute for Occupational Safety and Health (NIOSH/CDC), 1 U 01 OH007917-01 and NIOSH Education and Research Center training grant T42/CCT810426-10.

References

Akaike, H., 1974. A new look at the statistical model identification. *IEEE Transactions on Automatic Control*, 19 (6), 716–723.

American Association of Electrodiagnostic Medicine, 2002. American Academy of Neurology, American Academy of Physical Medicine and Rehabilitation. Practice parameter for electrodiagnostic studies in carpal tunnel syndrome: summary statement. *Muscle Nerve*, 25, 918–922.

American Conference of Governmental Industrial Hygienists (ACGIH) Worldwide, 2002. *Threshold Limit Values for chemical substances and physical agents in the work environment*. Cincinnati, OH: ACGIH Worldwide.

Bernard, B.P., 1997. *Musculoskeletal disorders and workplace factors: a critical review of epidemiologic evidence for work-related disorders of the neck, upper extremity, and low back, DHHS (NIOSH) Publication No. 97–141*. Cincinnati, OH: Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health.

Borg, G., 1982. Psychophysical bases of perceived exertion. *Medicine & Science in Sports & Exercise*, 14 (5), 377–381.

Bovenzi, M., Della Vedova, A., Nataletti, P., Alessandrini, B., and Poian, T., 2005. Work-related disorders of the upper limb in female workers using orbital sanders. *International Archives of Occupational and Environmental Health*, 78 (4), 303–310.

Boz, C., Ozmenoglu, M., Altunayoglu, V., Velioglu, S., and Alioglu, Z., 2004. Individual risk factors for carpal tunnel syndrome: an evaluation of body mass index, wrist index and anthropometric measurements. *Clinical Neurosurgery*, 106 (4), 294–299.

Bureau of Labor Statistics, 2008. *Nonfatal occupational injuries and illnesses requiring days away from work, 2007* [online]. U.S. Department of Labor. Available from: http://www.bls.gov/news.release/archives/osh2_11202008.pdf [Accessed 3 January 2012].

Buschbacher, R.M., 2000. *Manual of nerve conduction studies*. New York: Demos Publishing.

Chiang, H.C., Chen, S.S., Yu, H.S., and Ko, Y.C., 1990. The occurrence of carpal tunnel syndrome in frozen food factory employees. *Kao-Hsiung i Hsueh Ko Hsueh Tsa Chih [Kaohsiung Journal of Medical Sciences]*, 6 (2), 73–80.

Chiang, H.C., Ko, Y.-C., Chen, S.-S., Yu, H.-S., Wu, T.-N., and Chang, P.-Y., 1993. Prevalence of shoulder and upper-limb disorders among workers in the fish-processing industry. *Scandinavian Journal of Work, Environment & Health*, 19 (2), 126–131.

Cox, D.R., 1972. Regression models and life tables. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 34, 187–220.

Dempsey, P., 1999. Utilizing criteria for assessing multiple-task manual materials handling jobs. *International Journal of Industrial Ergonomics*, 24, 405–416.

Dempsey, P.G., McGorry, R.W. and Maynard, W.S., 2005. A survey of tools and methods used by certified professional ergonomists. *Applied Ergonomics*, 36 (4), 489–503.

de Krom, M.C., Kester, A.D., Knipschild, P.G., and Spaans, F., 1990. Risk factors for carpal tunnel syndrome. *American Journal of Epidemiology*, 132, 1102–1110.

Ferry, S., Hannaford, P., Warskyj, M., Lewis, M., and Croft, P., 2000. Carpal tunnel syndrome: a nested case-control study of risk factors in women. *American Journal of Epidemiology*, 151 (6), 566–574.

Foley, M., Silverstein, B., and Polissar, N., 2007. The economic burden of carpal tunnel syndrome: long-term earnings of CTS claimants in Washington State. *American Journal Industrial Medicine*, 50 (3), 155–172.

Franzblau, A., Armstrong, T.J., Werner, R.A., and Ulin, S.S, 2005. A cross-sectional assessment of the ACGIH TLV for Hand Activity Level. *Journal of Occupational Rehabilitation*, 15 (1), 57–67.

Garg, A. and Kapellusch, J., 2009a. Consortium pooled data job physical exposure assessment. *In*: *17th International Ergonomics Association world conference proceedings*, Beijing, China, 9–14 August.

Garg, A. and Kapellusch, J., 2009b. Applications of biomechanics for prevention of work-related musculoskeletal disorders. *Ergonomics*, 52 (1), 36–59.

Garg, A., Kapellusch, J., and Hegmann, K.T., 2010. *Upper limb musculoskeletal disorders: quantifying risk factors*. Final Report, Cooperative Agreement U01 OH007917, CDC (NIOSH), Atlanta.

Gell, N., Werner, R.B., Franzblau, A., Ulin, S.S., and Armstrong, T.J., 2005. A longitudinal study of industrial and clerical workers: incidence of carpal tunnel syndrome and assessment of risk factors. *Journal of Occupational Rehabilitation*, 15 (1), 47–55.

Hegmann, K.T. and Hughes, M.A., eds., 2010. American college of occupational and environmental medicine's occupational medicine practice guidelines. 3rd ed. Chapter 11: *Hand, wrist, forearm disorders*, Elk Grove Village, IL: American College of Occupational and Environmental Medicine Press.

Knox, K. and Moore, J.S., 2001. Predictive validity of the Strain Index in turkey processing. *Journal of Occupational & Environmental Medicine*, 43 (5), 451–462.

Kouyoumdjian, J.A., Zanetta, D.M.T., and Morita, M.P.A., 2002. Evaluation of age, BMI, and wrist index as risk factors for CTS. *Muscle & Nerve*, 25, 93–97.

Latko, W.A., Armstrong, T.J., Foulke, J.A., Herrin, G.D., Rabourn, R.A., and Ulin, S.S., 1997. Development and evaluation of an observational method for assessing repetition in hand tasks. *American Industrial Hygiene Association Journal*, 58 (4), 278–285.

Leclerc, A., Landre, M.-F., Chastang, J.-F., Niedhammer, I., and Roquelaure, Y., 2001. Upper-limb disorders in repetitive work. *Scandinavian Journal of Work, Environment & Health*, 27 (4), 268–278.
Lin, D.Y., Wei, L.J., and Ying, Z., 1993. Checking the cox model with cumulative sums of martingale-based residuals. *Biometrika*, 80 (3), 557–572.
Mani, L. and Gerr, F., 2000. Work-related upper extremity musculoskeletal disorders. *Primary Care: Clinics in Office Practice*, 27, 845–864.
Moghtaderi, A., Izadi, S., and Sharafadinzadeh, N., 2005. An evaluation of gender, body mass index, wrist circumference and wrist ratio as independent risk factors for carpal tunnel syndrome. *Acta Neurologica Scandinavica*, 112, 375–379.
Moore, J.S. and Garg, A., 1995. The Strain Index: a proposed method to analyze jobs for risk of distal upper extremity disorders. *American Industrial Hygiene Association Journal*, 56 (5), 443–458.
Moore, J.S., Rucker, N.P., and Knox, K., 2001. Validity of generic risk factors and the Strain Index for predicting non-traumatic distal upper extremity morbidity. *American Industrial Hygiene Association Journal*, 62 (2), 229–235.
Moore, J.S., and Garg, A., 2006. The validity and reliability of the Strain Index. *In*: *16th International Ergonomics Association world conference proceedings*, Maastricht, the Netherlands, 10–14 July.
Nathan, P.A., Meadows, K.D., Keniston, R.C., and Lockwood, R.S., 1992a. Longitudinal study of median nerve sensory conduction in industry: relationship to age, gender, hand dominance, occupational hand use, and clinical diagnosis. *Journal of Hand Surgery*, 17A (5), 850–857.
Nathan, P.A., Keniston, R.C., Myers, L.D., Meadows, K.D., 1992b. Obesity as a risk factor for slowing of sensory conduction of the median nerve in industry. A cross-sectional and longitudinal study involving 429 workers. *Journal of Occupational Medicine*, 34 (4), 379–383.
National Council on Compensation Insurance (NCCI), Inc., 2005. Carpal tunnel claims rank second among major lost time diagnoses. *NCCI Research Brief*, 3, April.
Nordstrom, D.L., Vierkant, R.A., DeStefano, F., and Layde, P.M, 1997. Risk factors for carpal tunnel syndrome in a general population. *Occupational and Environmental Medicine*, 54 (10), 734–740.
Osorio, A.M., Ames, R.G., Jones, J., Castorina, J., Rempel, D., Estrin, W. and Thompson, D., 1994. Carpal tunnel syndrome among grocery store workers. *American Journal of Industrial Medicine*, 25 (2), 229–245.
Radecki, P., 1994. The familial occurrence of carpal tunnel syndrome. *Muscle & Nerve*, 17 (3), 325–330.
Reading, I., Walker-Bone, Palmer, K.T., Cooper, C., and Coggon, D., 2003. Anatomic Distribution of Sensory Symptoms in teh Hand and Their Relation to Neck Pain, Psychosocial Variables, and Occupational Activities. *American Journal of Epidemiology*, 157 (6), 524–530.
R Development Core Team, 2011. *R: a language and environment for statistical computing* [online]. RFoundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0. Available from: http://www.R-project. org/ [Accessed 7 December 2011].
Roquelaure, Y., Mechali, S., Dano, C., Fanello, S., and Benetti, F., 1997. Occupational and personal risk factors for carpal tunnel syndrome in industrial workers. *Scandinavian Journal of Work, Environment & Health*, 23 (5), 364–369.
Roquelaure, Y., Mariel, J., Dano, C., Fanello, S., Penneau-Fontbonne, D., 2001. Prevalence, incidence and risk factors of carpal tunnel syndrome in a large footwear factory. *International Journal of Occupational and Environmental Health*, 14 (4), 357–367.
Rucker, N. and Moore, J.S, 2002. Predictive validity of the Strain Index in manufacturing facilities. *Applied Occupational and Environmental Hygiene*, 17 (1), 63–73.
Ruppert, D., Wand, M.P., and Carroll, R.J., 2003. *Semiparametric regression: cambridge series in statistical and probabilistic mathematics*. 1st ed. Cambridge: Cambridge University Press.
Silverstein, B., Fine, L.J. and Armstrong, T.J., 1987. Occupational factors and carpal tunnel syndrome. *American Journal of Industrial Medicine*, 11 (3), 343–358.
Silverstein, B., Foley, M., and Polissar, N., 2006. How well does the Strain Index predict carpal tunnel syndrome? *In*: *16th International Ergonomics Association world conference proceedings*, Maastricht, the Netherlands, 10–14 July.
Silverstein, B., Fan, Z.J., Smith, C.K., Bao. S., Howard, N., Spielholz, P., Bornauto, D.K., and Viikari-Juntara, E., 2009. Gender adjustment or stratification in discerning upper extremity musculoskeletal disorder risk? *Scandinavian Journal of Work, Environment & Health*, 35 (2), 113–126.
Silverstein, B., Fan, Z.J., Bonauto, D.K., Bao, S., Smith, C.K., Howard, N., and Viikari-Juntura, E., 2010. The natural course of carpal tunnel syndrome in a working population. *Scandinavian Journal of Work, Environment & Health*, 36 (5), 384–393.
Solomon, D.H., Katz, J. N., Bohn, R., Mogun, H. and Avorn, J., 1999. Nonoccupational risk factors for carpal tunnel syndrome. *Journal of General Internal Medicine*, 14 (5), 310–314.
Spielholz, P., Bao, S., Howard, N., Silverstein, B., Fan, J., Smith, C., and Salazar, C., 2008. Reliability and validity assessment of the Hand Activity Level Threshold Limit Value and Strain Index using expert ratings of mono-task jobs. *Journal of Occupational and Environmental Hygiene*, 5 (4), 250–257.
Stapleton, M.J., 2006. Occupation and carpal tunnel syndrome. *ANZ Journal of Surgery*, 76 (6), 494–496.
Stevens, J.C., Beard, C.M., O' Fallon, W.M., and Kurland, L.T., 1988. Carpal tunnel syndrome in Rochester, Minnesota, 1961 to 1980. *Neurology*, 38, 134–137.
Stevens, J.C., *et al*., 1992. Conditions associated with carpal tunnel syndrome. *Mayo Clinic Proceedings*, 67 (6), 541–548.
Tanaka, S., Wild, D.K., Seligman, P.J., Halperin, W.E., Behrens, V.J., and Putz-Anderson, V., 1995. Prevalence and work-relatedness of self-reported carpal tunnel syndrome among U.S. workers: analysis of the Occupational Health Supplement data of 1988 National Health Interview Survey [see comments]. *American Journal of Industrial Medicine*, 27 (4), 451–470.
Tanaka, S., Peterson, M., and Cameron, L., 2001. Prevalence and risk factors of tendinitis and related disorders of the distal upper extremity among U.S. workers: comparison to carpal tunnel syndrome. *American Journal of Industrial Medicine*, 39 (3), 328–335.
Therneau, T.M., Grambsch, P.M., and Fleming, T.R., 1990. Martingale-based residuals for survival models. *Biometrika*, 77, 147–160.

Violante, F.S., Armstrong, T.J., Fiorentini, C., Graziosi, F., Risi, A., Venturi, S., Curti, S., Zanardi, F., Cooke, R.M.T., Bonfiglioli, R., and Mattioli, S., 2007. Carpal tunnel syndrome and manual work: a longitudinal study. *Journal of Occupational and Environmental Medicine*, 49 (11), 1189–1196.

Werner, R.A., Albers, J.W., Franzblau, A. and Armstrong, T.J., 1994. The relationship between body mass index and the diagnosis of carpal tunnel syndrome. *Muscle & Nerve*, 17, 632–636.

Werner, R., Franzblau, A., Gell, N., Hartigan, A.G., Ebersole, M., Armstrong, T.J., 2005a. Incidence of carpal tunnel syndrome among automobile assembly workers and assessment of risk factors. *Journal of Occupational & Environmental Medicine*, 47, 1044–1050.

Werner, R.A., Franzblau, A., Gell, N., Hartigan, A.G., Ebersole, M., and Armstrong, T.J., 2005b. Risk Factors for visiting a medical department because of upper extremity musculoskeletal disorders. *Scandinavian Journal of Work, Environment & Health*, 31 (2), 132–137.

Appendix 1. Monthly follow-up questions used to ascertain symptoms of numbness/tingling*

During monthly follow-up, all workers were asked:

(1) 'Do you have any new numbness/tingling in your fingers?' Yes No
If 'yes', the following questions were asked for each finger of each hand:
(2) 'How many days ago did this numbness/tingling start?' _________days
For both new and ongoing symptoms, workers were asked:
(3) 'How many days have you had numbness/tingling in your finger since it started?'
All (100%) Most (75%) Half (50%) Few (25%) None (0%)
(4) 'How often do you have numbness/tingling upon awakening in the morning since it started?'
All (100%) Most (75%) Half (50%) Few (25%) None (0%)
(5) 'How often do you have numbness/tingling that wakes you up at night since it started?'
All (100%) Most (75%) Half (50%) Few (25%) None (0%)

*Questions 1 to 3 were used for the CTS case definition used in this article.

Appendix 2. Interpretation of coefficients in the Cox PHs model

- The general Cox PHs model with continuous or categorical covariates is: $\log(\mathrm{HR}) = b_1 x_1 + b_2 x_2 + \cdots + b_p x_p$
The estimated HR (i.e. change in risk) for each one unit increase of the first covariate (x_1) is $\mathrm{HR} = e^{\hat{b}_1}$. Similar interpretations hold for other continuous covariates. For categorical covariates, HR estimates are relative to the chosen reference category.
- A Cox PH model with a linear spline transformation of the x covariate (continuous) with a single spline term is: $\log(\mathrm{HR}) = b_1 x + b_2 (x - K)_+$
or, $\mathrm{HR} = e^{b1+b2(x-K)+}$
- The estimated change in risk for each unit increase of x up to $x = K$ is:
$HR = e^{\hat{b}_1}$.
- The estimated change in risk for each unit increase of x after $x = K$:
$HR = e^{\hat{b}_1+\hat{b}_2}$.
- Confidence intervals for the HRs can be found using the corresponding standard errors of the HR estimates.
- The p-value for a test of $b_2 = 0$ in the linear spline transformed Cox PH model tests for the significance of the change in slope for covariate values past the knot, $x > K$.

Note: The 'plus' notation on the spline term, $(x–K)_+$, indicates that this term is zero when $x - K \leq 0$. For additional information, please refer to: Collett, D. (2003) *Modelling Survival Data in Medical Research. Second Edition*. Chapman & Hall/CRC, Boca Raton, FL.