ORIGINAL ARTICLE

Biomechanical and psychosocial exposures are independent risk factors for carpal tunnel syndrome: assessment of confounding using causal diagrams

Carisa Harris-Adamson,[1,2] Ellen A Eisen,[2] Andreas Neophytou,[2] Jay Kapellusch,[3] Arun Garg,[3] Kurt T Hegmann,[4] Matthew S Thiese,[4] Ann Marie Dale,[5] Bradley Evanoff,[5] Stephen Bao,[6] Barbara Silverstein,[6] Fred Gerr,[7] Susan Burt,[8] David Rempel[1,9]

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For numbered affiliations see end of article.

Correspondence to
Dr Carisa Harris-Adamson, University of California, San Francisco, 1301 South 46th Street, Bldg 163, Richmond, CA 94804, USA; carisa.harris-adamson@ucsf.edu

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ABSTRACT

Background Between 2001 and 2010, six research groups conducted coordinated prospective studies of carpal tunnel syndrome (CTS) incidence among US workers from various industries to estimate exposure–response relationships.

Objective This analysis examined the presence and magnitude of confounding between biomechanical and workplace psychosocial factors and incidence of dominant-hand CTS.

Methods 1605 participants, without CTS at enrolment, were followed for up to 3.5 years (2471 person-years). Demographic information, medical history and workplace psychosocial stress measures were collected at baseline. Individual workplace biomechanical exposures were collected for each task and combined across the workweek using time-weighted averaging (TWA). CTS case criteria were based on symptoms and results of electrophysiological testing. HRs were estimated with Cox proportional hazard models. Confounding was assessed using causal diagrams and an empirical criterion of 10% or greater change in effect estimate magnitude.

Results There were 109 incident CTS cases (IR=4.41/100 person-years; 6.7% cumulative incidence). The relationships between CTS and forceful repetition rate, % time forceful hand exertion and the Threshold Limit Value for Hand Activity Level (TLV-HAL) were slightly confounded by decision latitude with effect estimates being attenuated towards the null (10–14% change) after adjustment. The risk of CTS among participants reporting high job strain was attenuated towards the null by 14% after adjusting for the HAL Scale or the % time forceful hand exertions.

Conclusions Although attenuation of the relationships between CTS and some biomechanical and work psychosocial exposures was observed after adjusting for confounding, the magnitudes were small and confirmed biomechanical and work psychosocial exposures as independent risk factors for incident CTS.

What this paper adds

- The relationship between important biomechanical exposures of forceful hand exertion and incident carpal tunnel syndrome (CTS) was confounded slightly by decision latitude.
- The relationship between job strain and CTS was confounded slightly by the biomechanical factors Hand Activity Level (HAL) Scale and % time spent in forceful hand exertion.
- Psychological demand and decision latitude were not strongly correlated with measures of biomechanical exposure.
- Owing to missing data, prior analyses did not adjust for confounding by biomechanical and psychosocial exposures in the full cohort. However, based on the small degree of attenuation observed after adjustment, the previously reported exposure–response estimates would have persisted even after controlling for psychosocial or biomechanical exposures.
- Job strain and forceful hand exertion (analyst-rated peak hand force, forceful repetition rate and % time forceful hand exertion) are independent risk factors for CTS.

INTRODUCTION

Carpal tunnel syndrome (CTS) is a common work-related peripheral entrapment neuropathy of the median nerve at the wrist that results in high medical treatment costs, lost work time and associated disability.[1] Early studies of CTS lacked a common case definition, were usually cross-sectional in design and had limited ability to adjust for confounding due to small sample sizes.[2–6] To address this research gap, six research groups designed coordinated, multiyear, prospective epidemiological studies of US production and service workers from a variety of industries. Detailed participant-level data on biomechanical and work psychosocial exposures were combined with longitudinal assessment of symptoms, physical examination results, electrophysiological measures and personal health and sociodemographic data.[7] Data from each study were combined into one data set, yielding a cohort that was diverse and generalisable to service and manufacturing workers in the USA.

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A prior publication reported on the relationship between work psychosocial exposure and CTS.[8] In those analyses, high psychological job demand was associated with CTS risk (HR=1.57; 95% CI 1.06 to 2.33), and high decision latitude (control) was protective (HR=0.73; 95% CI 0.51 to 1.04). Participants with high job strain (simultaneous high demand and low control) had a nearly twofold increase in risk (HR=1.90; 95% CI 1.11 to 3.14) compared with those with low job strain (simultaneous high control and low demand), and participants with high social support had half of the risk of incident CTS compared with those with low social support (HR=0.54; 95% CI 0.31 to 0.95).

We also reported exposure–response relationships between several biomechanical risk factors and CTS incidence, including measures of forceful hand exertion.[9 10] Participants exposed to higher levels of hand force had a 50–117% increase in the rate of CTS, yet no such increase was observed for those exposed to higher levels of repetition or those spending more time in combinations of any hand exertion (exertions of any force).

One objective of combining data sets across studies was to have sufficient power to estimate exposure–response relationships between CTS and personal, biomechanical and psychosocial factors while minimising bias from confounding. However, since prior analyses maximised power by retaining larger sample sizes and adjusted models only by personal factors and dissimilar biomechanical exposures (for biomechanical models), none of them evaluated biomechanical exposure and work psychosocial exposures simultaneously (which would have resulted in a smaller sample). To assess the possibility that the relationship between work psychosocial exposure and CTS is confounded by biomechanical exposure, and the possibility that the observed association between biomechanical exposure and CTS is confounded by work psychosocial exposure, further analyses were warranted. The objective of the current analysis was to assess the presence and magnitude of confounding by noncausal pathways using a subset of the cohort who had biomechanical and work psychosocial information.

METHODS

Study participants and procedures

Participants

This cohort included participants enrolled in four different prospective studies with common data on personal, biomechanical and work psychosocial exposure previously pooled to increase statistical power and generalisability. Participants in each study were at least 18 years of age and employed at a company where workers performed hand-intensive activities. Details on the study design and methods for pooling exposure and health outcome data are available elsewhere.[7 11] A total of 1995 workers were eligible for participation (see online supplementary figure S1). Participants were excluded from the analyses if they met the case criteria for CTS or possible polyneuropathy at enrolment (ie, baseline), resulting in 1605 cohort participants.

Data collection

Questionnaires were administered to participants at enrolment to collect information on work history, demographics, medical history, musculoskeletal symptoms and work psychosocial stress. Biomechanical exposures were measured at the individual task level at enrolment and measured again if the job changed, thus creating a time series of biomechanical exposure information. Electrodiagnostic studies (EDS) of median and ulnar nerve function across the wrist were administered to either (1) all participants at baseline and annually or (2) to those reporting upper limb symptoms.[7] Follow-up assessments of symptoms and EDS were performed at different intervals across the four studies. Investigators responsible for collecting health outcome data were blinded to participant biomechanical and psychosocial exposure status.

Personal factors

Information on participant age, gender, body mass index (BMI), race/ethnicity, education, smoking status, hand dominance and comorbid medical conditions such as rheumatoid arthritis, diabetes mellitus and thyroid disease was collected. Prior carpal tunnel release surgery and disorders of the distal upper extremity were also assessed. General health was assessed on a five-point scale. The total number of years worked at the current employer was collected at study enrolment.

Work psychosocial factors

Information on work psychosocial factors was collected with scales from the Job Content Questionnaire (JCQ). The JCQ psychological job demand and decision latitude scales were each dichotomised by splitting the distributions at their respective median values. A four-category job strain variable was created by assigning participants to one of the four quadrants resulting from the two split distributions (ie, high demand, low control; low demand, low control; high demand, high control; and low demand, high control).[12] The a priori putative high job strain category was defined as the job strain quadrant characterised by high demand and low control. The job strain ratio was calculated by dividing the psychological demand score by the decision latitude score.

Biomechanical exposure

Seven measures of workplace biomechanical exposures collected at the task level for each participant were used in this analysis; three measures quantified singular exposures (peak hand force, total repetition rate, % time all exertions), three measures quantified concurrent exposures (Hand Activity Level (HAL) Scale, forceful repetition rate, % time forceful exertions) and one was a composite measure (American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value for Hand Activity Level (TLV-HAL)). Exposure estimates were based on a blinded trained analyst's observation of each participant performing his/her usual work tasks, measurement of hand forces, weights of tools, force matching required to complete each task, videotape analysis of the task and interviews of participants or their supervisors.

Estimates of the highest analyst-rated hand force required for each task (peak hand force) were made using the Borg CR-10 rating scale.[13] The repetitiveness of tasks and allowable recovery were estimated using the analyst-rated HAL Scale. Other temporal exertion patterns for repetition and duty cycle were determined by detailed time studies of task-level videos[11] and included (1) the number of all hand exertions per minute (total repetition rate), (2) the number of forceful hand exertions per minute (forceful repetition rate), (3) the per cent of time for all hand exertions (% time all exertions) and (4) forceful hand exertions (% time forceful exertions). Forceful exertions were defined as those requiring ≥9 N pinch force or ≥45 N of power grip force or a Borg CR-10≥2. Although three approaches to summarise task-level exposure at the job level have been previously described,[11] only time-weighted average (TWA) summary measures (which included information from all tasks performed) were used for this analysis.

Outcome

The study outcome was incident CTS of the dominant hand and required (1) symptoms of tingling, numbness, burning or pain in the thumb, index finger or long finger and (2) temperature-adjusted (32°C) EDS results demonstrating median mononeuropathy at the wrist.[7 14] Median mononeuropathy was defined as (1) peak median sensory latency >3.7 ms or onset median sensory latency >3.2 ms at 14 cm, (2) median distal motor latency >4.5 ms, (3) transcarpal sensory difference of >0.85 ms (difference between median and ulnar sensory nerve latency across the wrist) or (4) an absent sensory latency consistent with abnormal EDS *and* EDS evidence of normal ulnar nerve physiology (ie, ulnar sensory peak latency <3.68 ms). Participants with symptoms consistent with CTS and concurrent abnormal median *and* ulnar nerve EDS were classified as *possible polyneuropathy* and were censored at the time that the case definition criterion was met.[7] Individuals who were symptomatic without a subsequent EDS were censored at the last date of known CTS case status. Person-time was calculated as the number of days from enrolment to an abnormal EDS with symptoms or censoring due to possible polyneuropathy, dropout or study termination.

Analytical approach

To help guide this analysis, we constructed causal diagrams (directed acyclic graph (DAG)) to visually encode the hypothesised relationships between covariates, time-varying exposures and CTS (figure 1A, B), and used them to perform a pathway analysis. DAGs are useful tools to identify potential confounders that may bias observed exposure–response associations and to distinguish confounders from intermediate variables on the causal pathway for which adjustment is inappropriate.[15] A pathway analysis is a logical sequence of exploring causal and non-causal pathways between exposures, covariates and outcomes portrayed in a DAG to better understand the relationships among the variables. In a DAG, the points representing variables are called 'nodes' and causal pathways from one node to another are depicted with a line or arrow referred to as an 'edge'.[16] The directionality of the pathway is designated with an arrowhead. A directed or causal path is defined as an unbroken route traced along edges connecting adjacent nodes, entering through the tail and leaving through the arrowhead.[16] A bidirectional arrow indicating a common cause (U) of two nodes ($Biomech_1 \leftarrow U \rightarrow Psychsoc_1$) can represent multiple variables that were not or could not have been measured, yet were a common ancestor of two nodes, thus creating a non-causal pathway. Essentially, U depicts how one exposure–effect association can be confounded by another despite neither variable being a direct cause of each other. Non-causal pathways from exposure to the outcome include those in the opposite direction of an arrowhead (ie, a 'backdoor path'). To estimate the causal exposure–response relationship using a DAG, all non-causal paths need to be blocked by adjusting for appropriate variables. Adjustment through stratification or conditioning is indicated by a rectangle around the node. Pathways can also be blocked by 'colliders' (two arrows pointed to the same variable along the pathway of interest) and caution should be taken not to adjust for a collider which would then 'open' the non-causal pathway.[15] Additionally, adjustment should not be made for any intermediary variables (variables along the causal path and between the primary exposure of interest and the outcome). It is also important to separate exposures and other time-varying covariates into separate nodes by time. For example, when assessing the causal relationship between baseline psychosocial factors and CTS (figure 1B), it is reasonable to adjust for biomechanical exposure at baseline ($Biomech_1$) to block a non-causal backdoor pathway, but not to adjust for biomechanical exposure at time 2 ($Biomech_2$) since it is plausible that work psychosocial stress could cause someone to change his/her job, and thus his/her exposure, making subsequent biomechanical exposure ($Biomech_2$) an intermediary variable ($Psychsoc_1 \rightarrow Biomech_2 \rightarrow CTS$). This approach is based on the assumption that U does not cause CTS other than through measured variables on the DAG.

Although the causal pathways between work psychosocial exposures, biomechanical exposures and CTS were previously reported, the potential confounding of one class of exposures by the other was not investigated. For example, it is plausible that there is some unmeasured attribute, such as educational status (figure 1A, U), associated with biomechanical and work psychosocial exposures ($Biomech_1 \leftarrow U \rightarrow Psychsoc_1$), thus creating a backdoor pathway between biomechanical exposure at baseline and CTS through work psychosocial factors (figure 1A, $Biomech_1 \leftarrow U \rightarrow Psychsoc_1 \rightarrow CTS$). Therefore, reassessing the exposure–response relationship of interest (figure 1A, bold line) while adjusting for work psychosocial exposure at baseline provides important information about the presence and magnitude of potential confounding. Similarly, in the assessment of the relationship between work psychosocial factors and CTS (figure 1B, bold lines), adjusting for baseline biomechanical exposure (figure 1B, $Biomech_1$) may reduce confounding bias.

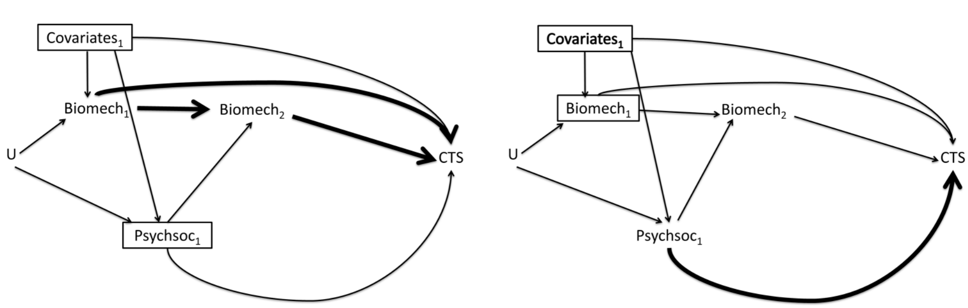

Figure 1 Directed acyclic graphs (DAGs) show the hypothesised relationship between baseline personal covariates, biomechanical and work psychosocial risk factors at up to two time points. U represents some unmeasured baseline variable related to the specific job someone chooses (such as educational status) that may be related to biomechanical and psychosocial exposure. (A) DAG shows the relationship between biomechanical exposure and carpal tunnel syndrome (CTS) (bolded line). (B) DAG shows the relationship between work psychosocial factors and CTS (bolded line).

Statistical analysis

Correlations between exposures were estimated using the Spearman rank correlation coefficient. HRs between exposures and incident CTS were estimated using Cox proportional hazards regression with robust CIs. Guided by DAGs, the models were adjusted for potential confounding by personal factors related to exposure and outcome that were not on the causal pathway. Using the forward stepwise procedure, variables were retained in the model if inclusion resulted in a change of the effect estimate of the primary exposure variable by 10% or more.[17] Ultimately, age, gender, BMI and study site were included in all models. Models where specific biomechanical exposures were the primary exposure of interest were adjusted for dissimilar biomechanical exposures (ie, exposures of a different type).[9] For example, the relationship between peak hand force and CTS was adjusted for total repetition rate and wrist posture, whereas the model assessing the relationship between forceful repetition rate and CTS was only adjusted for wrist posture. Assessment of confounding of one class of exposures by another (eg, biomechanical, work psychosocial) used the same process and criteria described above. All analyses were implemented with the Stata statistical package (Stata, College Station, Texas, USA).

RESULTS

Of the initial 1995 workers at baseline, 177 were excluded due to prevalent CTS (n=163) or possible polyneuropathy (n=14) at enrolment. Of the remaining 1818 eligible workers, 202 were excluded from the analyses due to lack of exposure data or loss to follow-up, resulting in a participation rate of 89.9% (n=1605) (see online supplementary figure S1). There were 109 (6.7%) incident CTS cases observed across 2471 person-years of follow-up with an incidence rate of 4.41 per 100 person-years (table 1). The mean age at baseline was 40.3 years (SD=10.8), and 90% reported no medical condition. The median number of years worked at the same company at baseline was 8.4 years (IQR=2–12) and most participants (79%) worked the day shift. The median follow-up time was 2 years (IQR=1–2.9). Biomechanical and psychosocial exposures varied widely across participants (see online supplementary table S1).

Among the biomechanical exposures, moderate-to-strong correlations were observed for measures that included some measure of force (table 2). None of the work psychosocial measures had correlations with any of the biomechanical measures of r>0.26.

When models estimating associations between biomechanical exposures and CTS were adjusted for psychological demand (table 3), effect estimates were minimally affected (1–4% change). However, when adjusted for decision latitude, effect estimates for forceful repetition rate, % time forceful exertion and the TLV-HAL decreased from 10% to 14% in comparison with associations without adjustment for decision latitude. There was a similar pattern for models adjusted for the job strain ratio; however, only the effect estimates for forceful repetition rate and CTS changed by more than 10%.

Owing to differences in the number of participants who were missing data, models varied in sample size. For clarity, only models of similar sample size are presented in table 4. Each adjusted model was compared with unadjusted models of the exact same cohort. All adjusted models in the same table had unadjusted models with virtually identical HRs; thus only one unadjusted model is shown. The effect estimates quantifying the relationship between psychological demand, decision latitude and CTS were slightly attenuated towards the null when adjusted for the % time forceful hand exertion (11%) and the HAL Scale (10%) (table 4). The effect estimates quantifying the relationship between high job strain and CTS had similar magnitudes of attenuation when adjusted for peak hand force, HAL Scale and % time forceful hand exertion.

Table 1 Demographic characteristics (%)

Demographics (cohort with exposure data) n (%)	Total N=1605 (%)	N	Cases (n)
Gender		1605	109
Male	888 (55)		51
Female	717 (45)		58
Age (years)		1605	109
<30	324 (20)		19
≥30 and <40	424 (26)		23
≥40 and <50	531 (33)		40
≥50	326 (20)		27
Ethnicity		1581	106
Caucasian	881 (55)		69
Hispanic	415 (26)		12
African-American	118 (7)		11
Asian	124 (8)		9
Other	43 (3)		5
Education		1596	108
Some high school or less	390 (24)		18
High school graduate or above	1206 (76)		90
Handedness		1605	109
Left handed	126 (8)		12
Right handed	1479 (92)		97
Body mass index		1599	109
Body mass index (<25)	542 (34)		23
Body mass index (≥25 and <30: overweight)	556 (35)		30
Body mass index (≥30: obese)	501 (31)		56
General health		1279	94
Very good or excellent	501 (39)		29
Good	584 (46)		49
Fair or poor	194 (15)		16
Medical condition		1605	109
No medical condition	1438 (90)		93
Current medical condition	167 (10)		16
Diabetes	61 (4)		5
Rheumatoid arthritis	23 (1)		0
Thyroid disease (hyper/hypo)	78 (5)		11
Pregnancy	12 (1)		0
Smoking status		1598	107
Never smoked	927 (58)		58
Currently smokes	415 (26)		31
Previously smoked	256 (16)		18

DISCUSSION

The purpose of this analysis was to replicate two prior prospective studies of a working population that assessed the relationship between personal, psychosocial and biomechanical factors and risk of CTS while using DAGs to guide an assessment for confounding. The most important finding in this analysis was that, although some bias did exist from confounding (ie, non-causal pathways), the magnitude was small and the 10% change in effect estimate criterion was rarely met. Further, the small changes in effect estimates could be due to

Table 2 Correlations between personal, biomechanical and work psychosocial exposure variables

	Psychological demand	Decision latitude	Total support	Job strain ratio	Peak hand force	HAL Scale	Repetition rate	Forceful repetition rate	% time total exertion	% time forceful exertion	ACGIH TLV for HAL
Psychological demand	1.00										
Decision latitude	−0.08	1.00									
Total support	−0.20	0.34	1.00								
Job strain ratio	0.84	−0.57	−0.32	1.00							
Peak hand force	0.09	0.04	0.10	0.06	1.00						
HAL Scale	0.22	0.18	0.18	0.08	0.47	1.00					
Total repetition rate	−0.04	−0.11	−0.25	0.04	−0.27	−0.28	1.00				
Forceful repetition rate	0.18	0.06	−0.05	0.13	0.56	0.39	0.21	1.00			
% time total exertion	−0.26	−0.02	−0.13	−0.18	−0.53	−0.56	0.57	−0.38	1.00		
% time forceful exertion	0.15	0.08	−0.01	0.09	0.53	0.33	0.17	0.91	−0.29	1.00	
ACGIH TLV for HAL	0.18	0.11	0.17	0.09	0.86	0.78	−0.37	0.60	−0.68	0.55	1.00

HAL, Hand Activity Level; TLV Threshold Limit Value.

Table 3 Biomechanical exposure and risk of CTS: (1) unadjusted for work psychosocial exposure and adjusted for (2) job strain ratio, (3) psychological demand and (4) decision latitude. All models (1–4) are adjusted for age, gender, BMI, study site and dissimilar biomechanical exposures[9]

	Cut-offs	Cohort	Cases	Unadjusted for work psychosocial exposure HR (95% CI)	Adjusted for job strain ratio HR (95% CI)	Adjusted for psychological demand HR (95% CI)	Adjusted for decision latitude HR (95% CI)
Peak force (CR-10)		1109	79				
Lower half	≤3		42	1.00	1.00	1.00	1.00
Upper half	>3		37	1.38 (0.85 to 2.26)	1.30 (0.79 to 2.13)	1.37 (0.84 to 2.24)	1.28 (0.78 to 2.08)
Total repetition rate		1109	79				
Lower half	≤16.4		47	1.00	1.00	1.00	1.00
Upper half	>16.4		32	1.03 (0.61 to 1.74)	0.96 (0.57 to 1.62)	1.01 (0.60 to 1.70)	0.97 (0.57 to 1.65)
% time all exertions		1109	79				
Lower half	≤68%		38	1.00	1.00	1.00	1.00
Upper half	>68%		41	1.18 (0.75 to 1.88)	1.19 (0.75 to 1.89)	1.19 (0.75 to 1.90)	1.16 (0.73 to 1.84)
HAL Scale		1370	90				
Lower half	≤4.4		41	1.00	1.00	1.00	1.00
Upper half	>4.4		49	1.90 (1.17 to 3.10)	1.82 (1.12 to 2.97)	1.89 (1.16 to 3.07)	1.79 (1.09 to 2.93)
Forceful repetition rate		1423	92				
Lower half	≤4.9		51	1.00	1.00	1.00	1.00
Upper half	>4.9		41	1.41 (0.87 to 2.30)	1.26 (0.75 to 2.12)	1.35 (0.82 to 2.24)	1.23 (0.74 to 2.05)
% time forceful exertions		1423	92				
Lower half	≤19%		43	1.00	1.00	1.00	1.00
Upper half	>19%		49	2.17 (1.36 to 3.46)	2.03 (1.26 to 3.26)	2.11 (1.32 to 3.39)	1.95 (0.62 to 1.96)
ACGIH TLV for HAL		1390	95				
Lower half	≤0.56		41	1.00	1.00	1.00	1.00
Upper half	>0.56		54	1.85 (1.20 to 2.86)	1.71 (1.10 to 2.66)	1.84 (1.19 to 2.84)	1.68 (1.07 to 2.62)

BMI, body mass index; HAL, Hand Activity Level; TLV Threshold Limit Value.

random fluctuations versus attenuation. Therefore, previously observed exposure–response relationships between biomechanical factors and CTS were not likely due to confounding by psychosocial factors, and previously observed exposure–response relationships between psychosocial factors and CTS were not likely due to confounding by biomechanical factors. Further, these findings suggest that it is perhaps unnecessary to be critical or dismissive of other studies that investigate the relationship between an upper extremity musculoskeletal disorder (UEMSD) (or at least CTS) and biomechanical exposure without adjusting for work psychosocial exposure, or vice versa, among cohorts similar to those of the current study. Rather, findings from the current large and generalisable study suggest that biomechanical exposure and work psychosocial exposure appear to be independent risk factors of incident CTS.

Psychological demand has been suggested as a surrogate measure for physical exertion.[18] Others have found that measures of work psychosocial stress and physical exertion are independently associated with health outcome measures.[19] None of the work psychosocial measures such as psychological demand or decision latitude or total support were strongly correlated with any measures of biomechanical exposures. Our data indicate that, in fact, they are independent of one another.

Table 4 Work psychosocial exposure and risk of CTS: (1) unadjusted for biomechanical exposure and adjusted for (2) peak hand force, (3) HAL Scale, (4) forceful repetition rate, (5) % time forceful exertions, (6) total repetition rate, (7) % time all exertions and (8) ACGIH TLV for HAL. All models (1–8) are adjusted for age, gender, BMI and study site

	Cut-offs	N	n	Unadjusted HR (95% CI)	Adjusted for peak hand force HR (95% CI)	Adjusted for HAL Scale HR (95% CI)	Adjusted for forceful repetition rate HR (95% CI)	Adjusted for % time forceful hand exertions HR (95% CI)
Psychological demand		1476	99					
Lower half	<31		40	1.00	1.00	1.00	1.00	1.00
Upper half	≥31		59	1.35 (0.91 to 2.01)	1.32 (0.89 to 1.97)	1.33 (0.89 to 1.97)	1.31 (0.87 to 1.97)	1.21 (0.80 to 1.83)
Decision latitude		1469	98					
Lower half	<60		42	1.00	1.00	1.00	1.00	1.00
Upper half	≥60		56	0.83 (0.55 to 1.26)	0.88 (0.58 to 1.34)	0.95 (0.62 to 1.45)	0.85 (0.55 to 1.31)	0.88 (0.58 to 1.35)
Job strain		1466	98					
Low strain			27	1.00	1.00	1.00	1.00	1.00
Passive strain			29	1.27 (0.74 to 2.16)	1.27 (0.75 to 2.16)	1.24 (0.73 to 2.09)	1.30 (0.75 to 2.23)	1.19 (0.68 to 2.09)
Active strain			13	1.11 (0.57 to 2.16)	1.07 (0.55 to 2.09)	0.93 (0.47 to 1.83)	1.16 (0.59 to 2.29)	1.11 (0.56 to 2.20)
High strain			29	1.51 (0.90 to 2.54)	1.41 (0.84 to 2.38)	1.32 (0.78 to 2.25)	1.46 (0.84 to 2.52)	1.34 (0.77 to 2.31)
Job strain ratio		1466	98					
Lower half	<0.53		42	1.00	1.00	1.00	1.00	1.00
Upper half	≥0.53		56	1.82 (1.23 to 2.71)	1.73 (1.15 to 2.61)	1.63 (1.08 to 2.45)	1.80 (1.18 to 2.76)	1.65 (1.07 to 2.54)

	Cut-offs	N	n	Unadjusted HR (95% CI)	Adjusted for total repetition rate HR (95% CI)	Adjusted for % time all hand exertions HR (95% CI)	Adjusted for ACGIH TLV for HALHR (95% CI)
Psychological demand		1176	84				
Lower half	<31		38	1.00	1.00	1.00	1.00
Upper half	≥31		46	1.15 (0.75 to 1.76)	1.14 (0.74 to 1.75)	1.14 (0.74 to 1.76)	1.31 (0.88 to 1.96)
Decision latitude		1482	83				
Lower half	<60		35	1.00	1.00	1.00	1.00
Upper half	≥60		48	0.83 (0.53 to 1.29)	0.84 (0.53 to 1.32)	0.84 (0.53 to 1.33)	0.95 (0.62 to 1.46)
Job strain		1479	83				
Low strain			25	1.00	1.00	1.00	1.00
Passive strain			23	1.10 (0.62 to 1.96)	1.10 (0.62 to 1.95)	1.10 (0.62 to 1.96)	1.27 (0.75 to 2.17)
Active strain			13	1.20 (0.61 to 2.36)	1.18 (0.60 to 2.31)	1.18 (0.60 to 2.34)	1.00 (0.50 to 1.98)
High strain			22	1.33 (0.75 to 2.35)	1.30 (0.73 to 2.32)	1.30 (0.73 to 2.32)	1.31 (0.77 to 2.22)
Job strain ratio		1165	83				
Lower half	<0.53		40	1.00	1.00	1.00	1.00
Upper half	≥0.53		43	1.62 (1.05 to 2.50)	1.60 (1.03 to 2.48)	1.59 (1.02 to 2.49)	1.63 (1.09 to 2.45)

BMI, body mass index; HAL, Hand Activity Level; TLV Threshold Limit Value.

When our first publication using the combined data set was published, we reported an increase in risk of CTS (HR=1.86; 95% CI 1.11 to 3.14) among those with high job strain and a protective effect (HR=0.54; 95% CI 0.31 to 0.95) of total support.[8] At that time, biomechanical exposures were not included in the analysis. Consequently, it was of interest to assess whether the findings were biased due to confounding from biomechanical exposures. Figure 1B shows that adjusting for biomechanical exposure at baseline blocks a non-causal pathway to CTS through some unmeasured attribute (U) that determines choice of work and thus is associated with biomechanical and work psychosocial exposure. From this analysis, it appears that adjusting for certain biomechanical exposures (HAL Scale or % time forceful hand exertions) could attenuate job strain effect estimates towards the null up to about 14%. Applying this magnitude of attenuation, the adjusted effect estimate would change from 1.86 to ∼1.65, still indicating an increase in risk of CTS among those with high job strain. Total support would have been negligibly affected since the changes in effect estimates in this subcohort were minimal and biased only slightly away from the null. Thus, it appears that high job strain is an important risk factor for CTS, and support from coworkers and supervisors is protective.

To maximise power and generalisability, two prior publications assessing the exposure–response relationship between biomechanical exposures and CTS[9 10] models did not control for potential confounding by work psychosocial measures. However, using the DAG in figure 1A, confounding by work psychosocial exposure could occur through a backdoor, non-causal pathway through some unmeasured variable (U). The magnitude of bias from not blocking this pathway was unknown. By using a smaller subset of individuals with complete data in this analysis, we found that the magnitude of the bias would have been minimal since most of the effect estimates in these fully adjusted models changed <10%. In fact, all biomechanical exposure effect estimates adjusted for psychological demand changed <5%. Decision latitude had the biggest impact with 9–14% reductions of effect estimates, resulting in slight attenuations towards the null. Decision latitude had the biggest impact on biomechanical measures that included some metric of force (peak hand force, forceful repetition rate, forceful hand exertions and TLV for HAL). It is plausible that there is some unknown factor associated with participant willingness to accept jobs requiring forceful hand exertion only if there is adequate decision latitude in performing such physically rigorous work. For example, U could include where participants grew up (and what jobs were available) or having parents who worked similar jobs. Thus, blocking the backdoor path through U (figure 1A) using decision latitude as the work psychosocial measure of choice may lead to slightly less biased effect estimates; however, the difference is negligible. In our prior analyses of biomechanical exposures and risk of CTS, there were strong associations between several measures of force and incident CTS, and those associations would have remained, albeit somewhat attenuated, had we adjusted for decision latitude in the larger cohort analysis. Of equal importance is that total repetition rate and % time all exertions, which were not associated with increased rate of CTS, were not confounded through U on a non-causal path. Therefore, it stands that total repetition rate and % time all exertions are not important independent risk factors for CTS in this cohort.

To corroborate our results by addressing the non-collapsibility of HRs, we developed logistic models for the exposure of interest and used them to develop inverse probability weights (IPWs) to standardise the population with respect to the potential confounder.[20] Results were very similar to the ones presented; for example, with respect to the model estimating the rate of CTS associated with psychological demand adjusting for the TLV-HAL using IPWs, HRs were nearly identical to the models conditional on TLV-HAL, and, similarly, slightly attenuated compared with the unadjusted model. Similarly, when estimating the rate of CTS associated with the % time forceful exertion adjusting for the decision latitude using IPWs, HRs were similar to models conditional on decision latitude and even closer to the unadjusted model. Thus, the use of conditional models presented no concerns of bias from the non-collapsibility properties of HRs in this analysis.

Although some data were missing at random, the reduction in sample size of some models was due to slight differences in study design across the four studies pooled. Some exposures, such as total repetition rate, were not collected for anyone within a particular study. Therefore, some analyses have different cohorts based on study design versus missing data that may have been differential to outcome or exposure status.

CONCLUSION

Measures of psychosocial exposure were not strongly correlated with biomechanical exposures. Decision latitude was a weak confounder of the relationship between certain biomechanical exposures (including forceful hand exertions) and the rate of CTS. The association between total support and incident CTS was not confounded by biomechanical exposures in this analysis. The HAL Scale and % time forceful hand exertion were weak confounders of the relationship between job strain and CTS. Despite not being able to adjust for confounding by biomechanical or psychosocial exposures in prior analyses using the larger pooled cohort, elevated effect estimates would have persisted after applying the same magnitude of confounding discovered in these analyses. Therefore, our prior findings that job strain, various measures of hand force (peak hand force, forceful repetition rate and % time forceful hand exertion) and the TLV-HAL increase the rate of CTS suggest they should be considered in future workplace intervention studies. Finally, it is worth noting that these results are from a pooled data set where each study group had actual investigator exposure and health outcome data collected from over 55 service and production companies across the USA. Thus, findings from this pooled Upper Extremity Musculoskeletal Disorders (UEMSD) Consortium are highly generalisable and should be taken into consideration when designing workplace injury prevention programmes.

Author affiliations
[1]Division of Occupational and Environmental Medicine, University of California, San Francisco, San Francisco, California, USA
[2]Department of Environmental Health Sciences, University of California Berkeley, Berkeley, California, USA
[3]Center for Ergonomics, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin, USA
[4]Rocky Mountain Center for Occupational and Environmental Health (RMCOEH), University of Utah, Salt Lake City, Utah, USA
[5]Division of General Medical Science, Washington University School of Medicine, Saint Louis, Missouri, USA
[6]Washington State Department of Labor and Industries, Safety and Health Assessment and Research for Prevention (SHARP) Program, Olympia, Washington, USA

[7]Department of Occupational and Environmental Health, University of Iowa, College of Public Health, Iowa City, Iowa, USA
[8]formerly with National Institute of Occupational Safety & Health, Atlanta, Georgia, USA
[9]Department of Bioengineering, University of California, Berkeley, Berkeley, California, USA

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Carisa Harris-Adamson, Ellen A Eisen, Andreas Neophytou, Jay Kapellusch, Arun Garg, Kurt T Hegmann, Matthew S Thiese, Ann Marie Dale, Bradley Evanoff, Stephen Bao, Barbara Silverstein, Fred Gerr, Susan Burt and David Rempel

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