**FINAL PROGRESS REPORT**

**Grant Number:** 5R01OH010474-03

**Sponsor:** National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention

**Title**: Exposure Response Relationships for CTS and Epicondylitis from Pooled Data

**Project start and end dates:** 9/1/13 – 8/31/17


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Date of completion of Final Report: December 26, 2017

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## List of Terms and Abbreviations

| | |
|---|---|
| 1995 SI | 1995 Moore & Garg Strain Index |
| ACGIH | American Conference of Governmental Industrial Hygienists |
| AL | Action Limit |
| AU | American University |
| BLS | Bureau of Labor Statistics |
| BMI | Body Mass Index |
| CI | Confidence Interval |
| COSI | Composite Strain Index |
| CTS | Carpal Tunnel Syndrome |
| CUSI | Cumulative Strain Index |
| DUE | Distal Upper Extremity |
| EPI | Epicondylitis (either lateral or medial) |
| HAL | Hand Activity Level |
| HR | Hazard Ratio |
| IRR | Incident Rate Ratio |
| LEPI | Lateral Epicondylitis |
| LNI | Washington State Department of Labor and Industries |
| MEPI | Medial Epicondylitis |
| MSD | Musculoskeletal Disorder |
| NCS | Nerve Conduction Studies |
| OR | Odds Ratio |
| PEAK | Highest physical exposure task in a shift |
| PF | Peak Force |
| PR | Prevalence Ratio |
| P-Y | Person-Years |
| RSI | Revised Strain Index |
| TLV | Threshold Limit Value |

| | |
|---|---|
| TYPICAL | Most commonly (% of time) occurring task in a shift |
| TWA | Time Weighted Average |
| UU | University of Utah |
| UWM | University of Wisconsin - Milwaukee |
| WR | Wrist Ratio |

## Abstract

Carpal tunnel syndrome (CTS), and lateral (LEPI) and medial (MEPI) epicondylitis are burdensome occupational MSDs for workers and employers. Prior studies have examined risk factors but only limited information is available about quantified exposure-response relationships for these MSDs using detailed physical exposure data measured at the sub-task level.

Data were pooled from three research sites and included workers from 35 facilities in four US states. Demographic, psychosocial, and health outcomes data were collected on each worker and at least quarterly throughout follow-up. Workers were followed for up to 7 years. Detailed, occupational physical exposures were measured at baseline and regularly re-assessed for each task performed by each worker.

A total of 2,020 workers were available and complete data were pooled for 1,834 (90.8%) of them. Several workers (710) performed multi-task jobs (i.e., job-rotation) and performed an average of 5.1 tasks/worker during their work day. Exposure-response relationships were quantified for the 1995 Moore and Garg Strain Index (SI), the ACGIH TLV for HAL, and the Revised Strain Index (RSI) — a new physical exposure model developed as a part of this study. Unlike prior models, the RSI quantifies distal upper extremity (DUE) physical exposure for each sub-task performed, and for each task within a multi-task job.

The 1995 SI, the TLV for HAL, and the RSI exhibited strong exposure-response relationships with incidence of CTS, LEPI, MEPI, and EPI (i.e., combined LEPI or MEPI). Workers classified as having medium- or high- physical exposures were between 40% to 240% more likely to develop an incident case of one of these MSDs. HRs were higher for LEPI and MEPI than for CTS, suggesting that EPI might be more sensitive to physical exposure levels than CTS, or alternatively that non-occupational factors play a larger role in CTS pathology.

Workers with multi-task jobs were found to have higher physical exposures than those performing mono-task jobs and were at higher risk for CTS, LEPI, and MEPI. This suggests that job rotation, as currently practiced in industry, might not be an effective MSD intervention strategy.

Workers with higher physical exposures provided less positive psychosocial responses than those with lower exposures (e.g., reported having lower job satisfaction). This might explain why some studies of DUE MSDs have reported associations with psychosocial factors. Another noteworthy finding of this study was the association between cardiovascular disease (CVD) risk factors and prevalence of CTS, LEPI, and MEPI — providing further evidence of the complex pathologies of these occupational MSDs.

The findings of this study should help inform comprehensive MSD intervention strategies. Continuous exposure-response relationships provide a basis for companies to develop exposure policies. The RSI model provides a foundation for detailed design-level evaluation and decision making. Evidence of association between job organizational, biomechanical, and psychosocial factors provide insight into comprehensive workplace interventions. Association between CVD risk factors and occupational MSDs provides a basis and possible strategy for workplace wellness initiatives.

# Section 1: Final Progress Report

## 1.1 *Significant-Key Findings*

This project provides evidence of exposure-response relationships between: (i) the TLV for HAL, (ii) 1995 SI, and (iii) the newly developed RSI exposure models, and incidence of: (a) carpal tunnel syndrome (CTS), (b) lateral epicondylitis (LEPI), and (c) medial epicondylitis (MEPI). Results show that workers classified as having medium or high exposure levels were between 40% and 240% more likely to develop one of these MSDs. Effect sizes were relatively larger for LEPI and MEPI than for CTS, suggesting that EPI is more sensitive to physical exposure levels than CTS, or alternatively that there were more non-occupational factor influences on CTS.

Significant relationships were found between job organizational, biomechanical, and psychosocial factors. Increased biomechanical exposures were statistically associated with worse psychosocial responses. Given the consistent associations between physical exposure and MSDs, this finding might partially explain prior findings linking psychosocial factors to increased risk of MSDs.

Job rotation was associated with significantly higher biomechanical exposures and between 25% and 70% increased likelihood of MSD prevalence. Job rotation was significantly associated with relatively worse psychosocial measures and in particular worse job satisfaction. These findings raise questions regarding whether job rotation, as currently practiced in workplaces, has efficacy as an approach to MSD intervention.

Cardiovascular disease (CVD) risk factors were associated with common occupational MSDs. Cross-sectional analyses of Framingham CVD risk scores and CTS, LEPI and MEPI showed dose-response relationships with up to 4- to 7-fold increased risk estimates.

The findings of this project provide further evidence of complex, multifactorial pathologies for occupational MSDs and demonstrates the need for further epidemiological studies specifically designed to address the influence of job organizational and psychosocial factors as well as more comprehensive direct measures of personal health, such as traditional measures of CVD risk.

## 1.2 *Translation of Findings*

A major product of this research is the Revised Strain Index (RSI) distal upper extremity (DUE) physical exposure quantification method. The RSI is a discrete model that accounts for each exertion within each task, and each task within each job. The RSI's comprehensive approach requires fewer assumptions and subjective measurements. This should prove more repeatable and reliable than surveillance-based risk assessments models such as the TLV for HAL and 1995 SI. The RSI's discrete calculations are sensitive to small task improvements that are made systematically over time and thus the RSI is compatible with continuous-improvement design strategies used by many engineering teams in manufacturing environments.

The RSI is open-source and thus companies can program it into their existing design systems. Companies could then use the RSI to rapidly compare design and intervention alternatives at the level of individual exertion patterns, tool types, production system approaches, etc. Based on our findings, companies should reduce exposures to RSI ≤ 15.0 in order to reduce biomechanical exposure to an acceptable level.

We provide continuous exposure-response relationships between physical exposure and incidence of MSDs. Companies and governmental agencies can use these to develop physical exposure policies and/or regulations. We have published the methods we use to generate these continuous exposure-response relationships in an open-access journal and included a tutorial and example code so that other occupational epidemiologists can more easily provide continuous exposure-response relationships.

With regard to surveillance of MSDs, we performed a comprehensive comparison of the TLV for HAL and the 1995 SI — the most widely used DUE assessment tools in the United States an beyond. These findings show that the tools are likely measuring different aspects of exposure and are best used in concert. Doing so will help employers to better identify at-risk workers and more effectively direct their intervention efforts.

Job rotation is a commonly used strategy to reduce the risk of MSDs. However, job rotation alone is likely not effective and might be increasing risk in many organizations and/or complicating production planning. If used, it is advised that workers not simply rotate from one high exposure task to another, but rather rotate to tasks with differing levels of exposure or at least tasks that require different muscle groups. These findings show that a single high-exposure task performed in a day, even for relatively short duration, may cause MSDs. Thus, even short duration tasks that exceed RSI scores of 15.0 should be targeted for intervention, regardless of whether job rotation is used.

CVD risk factors were associated with increased prevalence of MSDs and thus wellness programs targeted at reducing CVD risk might be effective at reducing MSD risk.

### *1.3 Research Outcomes-Impact*

Simple approaches to DUE MSD prevention and intervention, such as job rotation, appear unlikely to be effective in the long-term. The RSI and continuous exposure-response relationships provide a basis for detailed biomechanical exposure measurement and continuous improvement. Similar to quantitative quality control programs, this type of comprehensive and systematic approach to occupational MSD intervention and prevention can be expected to reduce workers' compensation costs, lost time due to occupational MSDs, and short- and long-term MSD related disability within companies that choose to use the strategy and tools.

# Section 2: Scientific Report

## *2.1 Background*

Workplace distal upper extremity (DUE) musculoskeletal disorders (MSDs) are prevalent, disabling and expensive.[1] For example, lost time cases had a severity rate of 2,647 lost workdays for CTS, and 765.5 for epicondylitis per 10,000 FTEs. CTS is the most common peripheral entrapment mononeuropathy, is among the larger drivers of worker's compensation costs (e.g., surgical releases cost $2B/year), and is associated with significant lost time, lost productivity, and disability.[2,3] In the United States (U.S.), the annual incidence rate of CTS is 3.0/10,000 workers with a median of 28 days away from work [3], mean worker's compensation cost of $20,4056 and a mean of $10,000 in lost wages per CTS case.[4]

While many risk factors have been suggested for CTS, work-related risk factors are not well quantified.[5] Similarly, work-related risk factors for lateral epicondylitis (LEPI) and medial epicondylitis (MEPI) are understudied and not well documented. Several problems have contributed to limitations and inconsistencies in the literature, including: (i) reliance on retrospective methods;[6-8] (ii) use of job titles or imprecise exposure estimates; (iii) imprecise techniques to quantify complex physical exposures for tasks with varying forces and/or job rotation (e.g., average force); (iv) use of small and /or non-representative samples of workers and industries; and (v) lack of objective outcomes measures, such as physical maneuvers and nerve conduction studies (NCS).[8,9]

### 2.1.1 DUE MSDs and Job Risk Factors

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.[7,10,11]

A force greater than 4 kg during gripping, high peak force (PF), and sustained forceful movement of the wrist are associated with CTS.[12-24] Repetition or hand activity has been found to be a risk factor in many studies,[12-18,20,22] while other studies have found no association.[5,25-31] Recently, Harris-Adamson et al. [24] found association between forceful frequency and duration of exertions and CTS, but frequency and duration of exertion per se. Posture alone has not been found to be a risk factor in many studies,[7,12,24,31] although a few studies have found an association.[21,32] 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.[7,12,33-38] For LEPI, there is some evidence to suggest that forceful exertions or a combination of high force and high repetition,[39-41] combinations of extreme posture with either high force or high repetition,[38] forearm supination with forceful lifting [41], forceful arm rotation,[42] and longer duration of employment in strenuous jobs [42] are associated with occurrence of LEPI. Regardless, in the absence of robust estimates of exposure-responses, preventive measures are unclear and have been defined vaguely (e.g., "avoid highly repetitive activities").[43]

#### 2.1.1.1 *Biomechanical Risk Assessment Tools*

The difficulty of measuring multiple risk factors simultaneously and combining them into a summary measure of risk is a major challenge for research on DUE MSDs. Two of the most widely used tools to measure DUE job physical exposures are: (i) the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) for Hand Activity Level (HAL) [44] and the (ii) 1995 Strain Index (SI).[10] Both tools offer summary measures of risk (by combining two or more risk factors) and can be applied by safety professionals at workplaces.[45]

The TLV for HAL includes two risk factors: normalized PF and repetition;[44] it is simple to use but ignores hand/wrist posture and duration of physical exposure per day. Studies using TLV for HAL have shown mixed results for risk of CTS and DUE MSDs.[19,36-38,46-49] Recent studies of the TLV for HAL and CTS have suggested that at least the Action Limit (AL) — medium risk exposure cut point — places workers at arguable too high a risk of CTS.[38,49] This suggests that the AL and TLV for the TLV for HAL need to be re-examined. However, it is unclear how cut-point revisions might affect risk prediction for other MSDs such as LEPI and MEPI due to a dearth of studies on MSDs other than CTS.

The 1995 SI includes six risk factors (force, repetition, % duration of exertion (duty cycle), posture, speed of work, duration of exposure/day).[10] The 1995 SI incorporates interactions between the risk factors and weights the effect of force more heavily. While several studies have shown a relationship between the 1995 SI and risk of DUE MSDs,[10,34,50-52] only one is prospective.[53]

A few studies have simultaneously used both the 1995 SI and the TLV for HAL to determine exposure-response relationships for: (i) CTS,[33] (ii) LEPI,[54] (iii) trigger digit,[55] and (iv) hand/wrist tendonopathies.[56] For each of these outcomes, the 1995 SI and TLV for HAL have performed comparably insofar as both suggest an association between increased physical exposure and increased risk of prevalence and incidence of DUE MSDs. However, in general, these studies rely on small sample sizes, and none of them has performed a detailed examination of how the scores and exposure-response relationships for 1995 SI and TLV for HAL compare to one another. Thus, it remains unclear how practitioners should best use these tools for surveillance and intervention.

#### 2.1.1.2 *Job Organizational Factors*

Many believe job rotation to be an effective strategy for preventing, or at least managing MSDs; however, it is not well studied. Roquelaure et al. [57] reported that both: (i) a lack of job rotation and (ii) a change in tasks or breaks of less than 15% of the daily duty cycle were associated with increased risk of CTS.[57]

### 2.1.2 DUE MSDs and Non-Occupational Factors

A number of non-occupational factors have been reported, primarily for CTS. The most prominent include: age, female gender, obesity, diabetes mellitus, rheumatoid/inflammatory arthritides, pregnancy, and presence of other DUE MSDs.[12,19,29,32,33,46,57-63] Associations between smoking, hand dominance, birth control pills, use of hormone replacement therapy, prevalence of other DUE MSDs and gout, and CTS are less well established.[64] Associations between age and gender,[40,41,65-68] obesity,[40] smoking,[40,41,65,66,69] other DUE MSDs,[69] and risk of LEPI are unclear. High quality studies of MEPI in occupational studies are lacking. Adjustments for non-occupational risk factors are required, yet many studies have not included these factors.

### 2.1.3 DUE MSDs and Psychosocial and Other Factors

Relatively few studies have assessed associations between psychosocial factors and CTS.[12,31,33,36,38,51,57,70-72] Social distress, lack of job security, marital status, depression, and work organizational factors have been suggested as risk factors.[18,33,73-76] Associations between psychosocial factors and risk of LEPI and MEPI are unclear.[39,41]

### 2.1.4 Effect Modification of Risk Factors

Epidemiological studies suggest that interactions exist between force and repetition.[12,31,33,36,38,51,57,70,71] Interactions may also exist between non-physical factors and job physical factors. Very few studies have examined interactions between individual risk factors and job physical factors, or psychosocial factors and job physical factors.[12,23,35,77]

## *2.2 Hypothesis and Specific Aims*

The alternative hypothesis for this study was:

H1: There are associations between biomechanical stressors and CTS, LEPI, and MEPI, while accounting for relevant medical history and demographic, psychosocial, and non-occupational factors.

Specific Aims were to:

1. Develop a pooled dataset with worker specific information on: (i) CTS, LEPI, and MEPI, (ii) detailed biomechanical stressors measured at the job, task, and sub-task levels for each worker and each hand, (iii) personal factors (demographics, medical history, activities outside of work), and (iv) psychosocial factors.

2. Calculate pooled baseline prevalence and average annual incidence rates for CTS, LEPI, and MEPI.

3. Estimate associations between prevalent cases of CTS, LEPI, and MEPI, and measures of biomechanical stressors adjusted for effect modifiers and confounders (using primary and secondary analyses as noted in Aim 4).

4. Perform primary analyses to estimate associations between incident cases of CTS, LEPI, and MEPI, and four measures of biomechanical stressors adjusted for effect modifiers and confounders. These measures are: (i) ACGIH Threshold Limit Value for Hand Activity Level (TLV for HAL), (ii) 1995 Strain Index (SI), (iii) Composite Strain Index (COSI), and (iv) Cumulative Strain Index (CUSI). Perform secondary analyses to examine relationships between the three health outcomes and: (i) force, (ii) repetition, (iii) posture, (iv) hand/arm vibration, and (v) combination of high force-high repetition.

5. Recommend revised cut-points for TLV for HAL and SI scores to better estimate risk of CTS, LEPI, and MEPI.

### 2.2.1 Summary of Specific Aims Progress and Completion

Specific Aim #1
Raw data were pooled between the sites after establishing compatible definitions for each variable. At each site, physical exposure data for each exertion were already summarized and organized into tasks. Tasks were similarly organized into jobs. Jobs were studied over time and changes were documented using similar methods between sites. Scales used to quantify force for exertions differed between sites, so LNI data were re-analyzed for compatibility.

Psychosocial data had more limited compatibility. Nevertheless 10 questions were deemed compatible and merged. Outcomes data were merged based where variable definitions matched. These definitions are described in Section 2.3.2.3.

All work for Specific Aim #1 was fully completed as proposed.

Specific Aim #2
Using merged data, prevalence and incidence rates for CTS, LEPI and MEPI were calculated and are provided in Section 2.4.1. Prevalence rates have been published. Incidence rates are included in draft publications slated for submission in 2018.

Analyses for Specific Aim #2 were fully completed as proposed. Publications are ongoing.

Specific Aim #3
Work for Aim #3 began by determining which factors should be considered as covariates and/or effect modifiers in exposure-response relationship analyses of prevalence (and later incidence) data. Analyses began by testing for associations between job physical exposures and psychosocial factors. Surprisingly, we found strong associations between physical exposures and nearly all psychosocial measures (see Section 2.4.5)

Raw personal risk factor data were available to create a Framingham CVD risk score on a subset of workers and we tested the CVD risk score against prevalence of CTS, LEPI, and MEPI. Again, to our surprise, we found persistent associations between CVD score and prevalence of MSDs (see Section 2.4.2.4)

Lastly, we studied associations between work organizational, biomechanical, and psychosocial factors. We found significant associations between these measures. Further, we found that work organization factors were themselves associated with prevalence of MSDs (see Section 2.4.2.1)

Based on these findings we concluded that we had too little information about underlying complexities of how the various secondary factors such as work organization and psychosocial factors were contributing to risk of MSDs. Thus, we moved to publish our findings on psychosocial, work organizational, psychosocial factors, and CVD risk and proceed with prevalence (and incidence) analyses adjusting only for the traditional risk factors of age, gender, and BMI.

Analyses for a restricted version of Aim #3 are complete. Secondary results have been published. Primary results for CTS have recently been published. Prevalence results for LEPI and MEPI are currently being drafted for publication.

Specific Aim #4

As described above, adjusting for secondary factors was deemed imprudent given the strong evidence of association between primary and secondary factors, and the somewhat limited forms of secondary information in this study. Thus, Aim #4 was restricted to primary analyses of quantifying exposure-response relationships between the TLV for HAL, and the 1995 SI and incidence of CTS, LEPI and MEPI. In addition, we quantified exposure-response relationships between the newly developed RSI (see Aim #5 below) and incidence of these MSDs.

Analyses for Aim #4 are complete. Publications are being drafted and will be submitted in 2018.

Specific Aim #5

Analyses for Aim #5 began by exhaustively comparing the TLV for HAL and the 1995 SI to one another, as well as comparing their exposure-response relationships with prevalence of CTS. We found that the two models disagreed with one another on about half of task exposure classifications and that the two models were somewhat poorly correlated. Nonetheless, they exhibited near identical exposure-response relationships with prevalence of CTS. This led us to suspect that neither model was adequately describing risk.

These analyses, combined with natural data limitations and potential biases associated with the facilities from which data were collected, strongly implied that deriving risk thresholds empirically using our data would be imprudent. Rather, we deemed that the correct approach would be to use laboratory (e.g. psychophysical) and other data to develop revised thresholds where they are warranted. In this regard, the AL within the TLV for HAL appears to be too high and not sufficiently protective of workers. Unfortunately, analyses of laboratory and other sources of data to develop new thresholds is beyond the scope of work directed by Aim #5 (see Section 2.4.4 for details).

As an alternative, we chose to invest our time into developing a new model, the Revised Strain Index, capable of resolving the common problems of complex tasks (i.e., tasks that consist of multiple sub-tasks with varying levels of force, duration of force, and posture), and multiple task jobs. When developing the model we set an a-priori high-exposure threshold of RSI = 10.0. During analyses for Aim #4 we concluded that 10.0 was too low. By comparing RSI exposure percentiles to those of the 1995 SI and the TLV for HAL, we concluded that a cut-point of RSI = 15.0 was more appropriate. This threshold also provided stronger exposure-response relationships between RSI and incidence of MSDs (see Sections 2.4.3.1 and 2.4.3.2).

Aim #5 was mostly unsuccessful as originally proposed. However, modifying the purpose of the Aim resulted in the Revised Strain Index which has been published and will likely be a valuable tool for job design. Results from Aim #5 have been published.

Project Accomplishments not Otherwise Specified in Aims

To estimate robust exposure-response relationships (Aim #4) we implemented and expanded continuous analyses of incidence data using penalized and linear splines.

This approach was first applied to occupational physical exposure data by Garg et al.[33] For this project we further developed the technique and fully describe it as well as provide a tutorial in an open access journal publication.[78]

## *2.3 Methodology*

This study pooled data from three large prospective epidemiologic research studies conducted by: (i) the Washington State Department of Labor & Industries (LNI), (ii) the University of Utah (UU), and (iii) the University of Wisconsin-Milwaukee (UWM). Workers in these studies were employed across a wide variety of manufacturing and service industries (Table 1).

**Table 1: Summary of types of industries studied by the three sites**

| Industry | UWM | UU | LNI | Industry | UWM | UU | LNI |
|---|---|---|---|---|---|---|---|
| Automotive parts mfg. | X | X | X | Glass/Window assembly | X | | X |
| Billboard sign mfg. | X | | | Hospital laundry | | | X |
| Book printing/binding | | X | | Lawn equipment mfg. | X | | |
| Cabinet making | | X | X | Medical equipment mfg. | | | X |
| Commercial lighting mfg. | X | | | Medical lab equipment mfg. | X | X | |
| Distribution warehouse | | X | | Office work | | X | X |
| Electronics assembly | X | | X | Pharmacy | | | X |
| Electric motor mfg. | X | | | Plastic bag mfg. | X | | |
| Electric sensors mfg. | X | | | Poultry processing | X | | |
| Exercise equipment mfg. | | | X | Red meat processing | | X | |
| Garage door mfg. | | X | | Small engine mfg. | X | | |
| Garment mfg. | | X | | Wood processing | | | X |
| Generator mfg. | X | | | | | | |

### 2.3.1 History of the NIOSH MSD Consortium

Between 2000 and 2003, NIOSH funded seven research groups (including LNI, UU, and UWM) to perform prospective cohort studies and examine associations between biomechanical stressors and DUE MSDs (RFA OH-2000-003 and OH-2002-010 and U01s/R01s). These studies were able to collect a large volume of data in the field (videos of tasks in particular) that can be used to generate comprehensive sub-task level data. However, methods to perform sub-task analyses were not readily available at that time and therefore these studies did not include comprehensive sub-task data extraction in their proposals.

The seven research groups created a MSD Consortium to foster collaboration and possible post-hoc data pooling. In 2010, NIOSH funded an R01 proposal for pooled CTS consortia data (NIOSH CTS Consortium, project ending August 2013). The consortium used pre-existing data from the seven members. No resources were requested for additional extraction of sub-task data from video and subsequent analyses of sub-task level biomechanical stressors. While the consortium recognized the importance of sub-task analyses, extraction of sub-task data from video is very resource intensive. Therefore, the CTS consortium was not able to obtain these data and analyze them as part of the original consortium project.

The NIOSH CTS Consortium has several strengths including: (i) large sample size, (ii) NCS, (iii) common CTS case definition, (iv) data on most individual and psychosocial factors, and (v) individual job exposure measurements. The primary limitation of the consortium is that it is limited to analysis of pre-existing physical exposure data. Because most sites used differing methods to collect, quantify, and analyze job physical exposure data, quantification of job physical exposure is limited to relatively simple analyses of: (i) force, (ii) repetition, (iii) posture, and (iv) TLV for HAL.

Three of the seven consortium members (LNI, UU, UWM) recognized the importance of sub-task analyses relatively early in their original studies. Thus, these sites began extracting highly detailed sub-task physical exposure data from video and did so using very similar methods for assessments and analyses. This current research project allowed these three members to complete sub-task data extraction from video, create a pooled dataset to provide a large sample size, and perform sub-task level analyses. These analyses have helped to: (i) more precisely model risk, especially for complex physical exposures and job rotation, (ii) improve existing biomechanical risk assessment tools, and (iii) provide guidance for better design of safe and productive jobs.

### 2.3.2 Developing a Pooled Dataset with Worker Specific Information

This study uses previously collected data on workers from 35 facilities representing 25 industries in the U.S. states of Illinois, Utah, Washington and Wisconsin. These data were collected by three research teams: LNI, UU, and UWM. Raw data on job physical exposures, DUE MSDs, and individual and psychosocial covariates from LNI, UU, and UWM were combined into several datasets. Combined data were then exhaustively data-checked for integrity. Two types of data checks were performed: (i) a check for logical and data-entry/processing errors, and (ii) analytical checks to challenge the validity of common variable definitions between the sites. Combined data were de-identified and protected health information were removed to greatest extend feasible. De-identified “gold master” datasets were created and provided to each of the three sites (and American University, AU) for analyses.

#### *2.3.2.1 Physical Exposure Measurements*

Hand physical exposures were quantified for each task performed by each worker. Both left and right hands were quantified separately and dominant hand exposures were used for most analyses. Peak (PF) [44] and overall hand forces [10,33,79] were rated by trained ergonomists using the Borg CR-10 scale.[80] Hand forces for LNI data were re-analyzed to provide Borg CR-10 ratings (for compatibility with UU and UWM data). Hand activity level (HAL) was rated by trained analysts using the HAL verbal anchor scale.[81] Frequency of exertion, duty cycle (% duration of exertion), hand/wrist posture, and speed of work were quantified from video recordings using time-study techniques. For cyclic tasks with cycle times of 2 minutes or less, a minimum of 10 task cycles were randomly analyzed. If cycles times were very short (i.e., < 30 s), a minimum of 5 minutes of cycles were randomly analyzed. For longer duration tasks, a minimum of three representative task cycles were analyzed (5). Time-study results produced continuous measures of frequency and duration of exertions stratified by Borg CR-10 force level.

TLV for HAL scores for each task were calculated using the equation: Score = (Analyst Peak Force Rating on Borg CR–10 Scale/(10 - HAL Rating)). Subsequently, these scores were classified into the ACGIH TLV for HAL exposure categories of: (i) below Action Limit (AL, score < 0.56), between AL and TLV (0.56 ≤ score ≤ 0.78), and above TLV (score > 0.78). These categories were considered “low”, “medium”, and “high” exposure, respectively.

1995 SI scores for each task were calculated using: (i) overall force, (ii) frequency of exertion, (iii) duty cycle, (iv) hand/wrist posture, (v) speed of work, and (vi) hours of exposure per day as described by Moore and Garg [10] and Garg et al.[33] Frequency of exertion and duty cycle were categorized using their respective 1995 SI rating scales. Final 1995 SI scores were based upon only those exertions that occurred at an analyst estimated force level of one or more on the Borg CR-10 scale (i.e., Force rating ≥ 1, “very light” or harder).[82] Removal of exertions below Borg CR-10 of one was in response to the findings of Garg et al.[33,54] and Kapellusch et al.[55] who noted that including all exertions likely resulted in many task’s physical exposure being over-estimated due to the rating scales lacking ability to handle the very high number of exertions that occurred at very low force levels. 1995 SI scores were classified into exposure categories of ‘low’ (SI ≤ 3.0), ‘medium’ (3.0 < SI ≤ 6.1), and ‘high’ (SI > 6.1) using the recommended limits of Moore et al.[52]

Revised Strain Index (RSI, see also Section 2.3.3) [83,84] were calculated from detailed time-study data and, unlike the 1995 SI, included exertions performed at all Borg CR-10 force levels. RSI scores were based upon: (i) Borg CR-10 force rating, (ii) duration per exertion, (iii) frequency of exertion, (iv) posture, and (v) hours of exposure per day. RSI scores were calculated for each sub-task (i.e., for each exertion separately), and then combined into task and job physical exposures scores using the Composite (COSI) and Cumulative (CUSI) SI algorithms.[83] COSI-, and CUSI-based RSI scores were categorized into low- and high-risk groups using the a-priori cut-point of 10.0.[84]

Nearly half of workers performed multi-task jobs (i.e., performed two or more tasks during their work shift — commonly referred to as job rotation in industry). For those workers with multi-task jobs, TLV for HAL, and 1995 SI were summarized at the job-level (i.e., daily exposure) using three previously reported techniques: (i) Time-Weighted Average (TWA) of tasks based on task hours per day,[37,41,85,86] (ii) TYPICAL exposure defined as the task performed for the largest proportion of the work shift,[33,87] and (ii) PEAK exposure defined as the task with the highest (i.e., worst) physical exposure.[37,38] Multi-task job physical exposures were classified into each model’s low-, medium-, and high-exposure categories in the same manner as described above. For RSI scores, the COSI and CUSI algorithms were used to describe physical exposures at the task and job levels, respectively. TWA, TYPICAL, and PEAK techniques were not used for RSI scores.

Work organizational data were collected by interviewing workers and their immediate supervisors. Raw data were combined into variables for: job rotation (working two or more tasks in a work-shift — yes/no); working overtime (working more than 40 hours in a week — yes/no); working a second job (working for two or more employers — yes/no); and work pace (analyst determined and classified trichotomously into line-paced, self-paced, and piece rate). Work pace was assigned at the task level. For workers with multiple-tasks, work-pace for the longest duration task was assigned.[88]

#### 2.3.2.2 Individual and Psychosocial Measurements

Questionnaire data included age, gender, hobbies, exercise habits, job satisfaction, depression symptoms, diabetes mellitus, and hypertension. Body Mass Indices (BMIs) were calculated from measured heights and weights. Blood pressure was measured using automatic cuffs after being seated for at least five minutes.[53,89]

Psychosocial measures were assessed via baseline questionnaires. Ten psychosocial measures were deemed compatible and pooled between the three research sites. Responses to each measure were categorized into three or four levels depending on the number of potential responses.[90]

Compatible questions used in this study were:

1. How is your general health compared with people your own age? (Much better/excellent; Somewhat better/good; The same/fair; Worse/poor)
2. How often do you feel down, blue, or depressed? (Never; Seldom; Often; Always)
3. How often are you physically exhausted after work? (Never; Seldom; Often; Always)
4. How often are you mentally exhausted after work? (Never; Seldom; Often; Always)
5. How often do you get along with your coworkers? (Hardly ever/never; Some of the time/occasionally; Always/often)
6. How satisfied are you with your job? (Satisfied; Neither satisfied nor dissatisfied; Dissatisfied)
7. How often do you have supervisor support? (Always; Occasionally; Hardly ever/never)
8. How likely are you to recommend your job to someone else? (Strongly recommend; Recommend; Neither recommend nor discourage; Not recommend)
9. How likely are you to take this job again? (Very likely; Likely; Neither likely nor unlikely; Unlikely)
10. My employer cares about my health and safety on the job. (Strongly agree; Agree; Disagree; Strongly disagree)

Three questions (numbers 1, 2, and 10) were adapted from the NIOSH Generic Job Stress Questionnaire,[91] and three others (questions 6, 8, and 9) were adapted from the Job Content Questionnaire.[92] The remaining questions (questions 3, 4, 5, and 7) were developed by the research teams for these studies.[53] Not all of these questions have been validated.

For participants in the UU and UWM studies, wrist ratio was measured using a digitized caliper.[53,93] Measured WR categories were stratified into WR of 0.681 or less (rectangular), WR between 0.681 and 0.700 (middle), and WR above 0.700 (square).[93]

### *2.3.2.3 Health Outcomes Measurements*

All sites conducted surveys, interviews, and physical examinations at baseline and regularly throughout the original studies using substantially similar methods. Nerve conduction studies (NCS) were performed at baseline and throughout the studies to determine CTS. Physical examination maneuvers and measurements were consistent among the three research sites. However, LEPI and MEPI symptoms were defined slightly differently. UWM and UU defined the LEPI symptom as pain in the lateral elbow [53] while LNI included pain, aching, stiffness, burning, numbness, or tingling in the elbow or forearm for either four or more episodes in the past year, one episode of at least 7 days duration in the past year, or an episode of at least 1 day duration in the past 7 days.[94] Similar, minor differences existed for the MEPI symptoms between UWM, UU, and LNI. Compatible case definitions are provided in Table 2.

**Table 2. Case definitions for CTS, LEPI and MEPI**

| | | |
|---|---|---|
| **Carpal Tunnel Syndrome (CTS):** | Tingling, numbness, or burning in one or more of the first three digits (thumb, index, and long finger) for ≥ 7 days | NCS criteria (for sensory measures at the peak):<br>1) Paired transcarpal sensory delta of > 0.55 ms (at 8 cm). (Paired transcarpal delta is the difference in sensory latencies across the wrist segment.) OR<br>2) Sensory latency >3.5 ms (at 12 cm) OR<br>3) Motor latency >4.5 ms (at 6cm) |
| **Lateral Epicondylitis (LEPI):** | Pain in the lateral elbow for ≥ 7 days | Tenderness upon palpation + Pain in the lateral elbow on resisted wrist extension. |
| **Medial Epicondylitis (MEPI):** | Pain in the medial elbow for ≥ 7 days | Tenderness upon palpation + Pain in the medial elbow on resisted wrist flexion. |

<u>Carpal Tunnel Syndrome</u>

Symptoms consistent with CTS included pain, numbness, tingling, and/or burning with no acute or traumatic onset, in two or more of the first four digits of the hand for greater than one week, or three or more times in the prior year.[95] Workers had abnormal nerve conduction if the following combined criteria were met for the dominant hand: (i) median motor latency > 4.5 ms at 8 cm, or median sensory latency > 3.5 ms at 14 cm, or mid-palmer latency > 2.2 ms at 8 cm; AND (ii) ulnar sensory latency < 3.7 ms at 14 cm, or medium-ulnar sensory latency difference > 0.5 ms, or mid-palmer median-ulnar difference > 0.3 ms (20). Workers were determined to be cases for CTS if they had both (i) symptoms consistent with CTS and (ii) abnormal median nerve conduction in either their right or left hand (i.e., hand-specific analyses). Workers were CTS prevalent if they met the case definition at baseline. Workers were CTS incident cases on the date they first were recorded as meeting the above case definition. Prevalent workers were not eligible to incident cases.

<u>Lateral Epicondylitis</u>

Structured interviews were administered and included symptoms diagrams for anatomically localizing pain. The presence and distribution of pain was captured by location. Data collected for this study's health outcomes on all subjects regardless of symptoms were: (i) lateral elbow pain, (ii) resisted wrist extension and/or (iii) resisted middle finger extension. The LEPI case definition was lateral epicondylar pain, tenderness on palpation, and at least one positive physical maneuver, either resisted wrist extension or resisted middle finger extension, evoking lateral epicondylar pain.

Medial Epicondylitis

The MEPI case definition was medial epicondylar pain and medial epicondylar pain with resisted wrist flexion.

Framingham Heart Study Risk Model

During preliminary analyses a question was raised as to whether or not cardiovascular risk was associated with DUE MSDs. Thus a subset of the cohort data were adapted into the Framingham heart disease risk model.[89] For the Framingham model, gender stratified point values were assigned for variables of age, treated and untreated hypertension, tobacco use and diabetes mellitus. Blood pressure was scored for participants in Illinois, Utah and Wisconsin where measured blood pressures were available. LNI did not measure blood pressure resulting in n = 749 missing measurements. Those workers without a blood pressure measurement but with a history of hypertension were conservatively assigned a blood pressure value of 1 point. Cholesterol was excluded from the scoring as it was not measured. Each worker's CVD risk score was calculated by summing the individual CVD variable point values. Individualized CVD risk scores ranged from 0 to 29. Scores above 16 were too infrequent to provide adequate statistical power and thus an a priori decision was made (without knowledge of relationships to MSD outcomes) to collapse scores ≥ 16 into one category. Additional analyses of the risk from the Framingham risk model on the Illinois, Utah and Wisconsin data were performed that included blood pressure measurements, hypertensive history and cholesterol history.

### 2.3.3 Development of the Revised Strain Index (RSI)

Analyses associated with Aim #5 (potential risk classification cut-point revisions) suggested that the 1995 SI was indeed in need of revision. Thus, the Revised Strain Index was developed.[84]

Despite it's large size, we felt that the pooled dataset lacked sufficiently robust distributions of physical exposures to empirically derive the RSI model's multipliers. Thus, the RSI was developed using: (i) published psychophysical data, (ii) unpublished psychophysical data collected by Drs. Garg, Moore, Kapellusch, and their students, and (iii) the collective professional judgment of Drs. Garg, Moore and Kapellusch. The precise development process and rationale are described in Garg et al. 2017a.[84]

As a part of RSI development, the Composite Strain Index (COSI), and Cumulative Strain Index (CUSI) algorithms were also fully developed in a manner consistent with the proposal for this project.[83]

### 2.3.4 Calculating Pooled Baseline Prevalence and Average Annual Incidence Rates for CTS, LEPI, and MEPI

Baseline prevalence and crude average annual incidence rates (i.e., new cases per 100 person-years (P-Y)) were calculated for CTS, LEPI, and MEPI using this study's a-priori case definitions. For incidence rate calculations, prevalent cases were excluded. Gender-, hand-, and age-specific incidence rates were calculated. Average follow-up time and follow up time range were calculated for the combined dataset and for each individual research site (UU, UWM, LNI).

### 2.3.5 Associations Between Job Organizational, Biomechanical, and Psychosocial Factors

Early in Aim #3, we hypothesized that: (i) work organization and technology determine biomechanical stressors on the workers and influence their psychosocial factors, (ii) biomechanical and psychosocial exposures may result in or be associated with different musculoskeletal health consequences, and (iii) biomechanical exposures and musculoskeletal health status influence changes in work organization and technology.[96] We tested these hypotheses using the following methods:

Initial analyses used ordered logistic regression to assess the associations between biomechanical exposures and psychosocial factors.[90] Later, we employed bivariate analyses to assess the association between work organizational and biomechanical exposure variables, and between work organizational and psychosocial variables.[96] For the continuous biomechanical exposure variables, the median values of the corresponding biomechanical exposure variables for the different work organization variable categories were calculated. Kruskal–Wallis tests were used to assess differences in the mean ranks of the respective biomechanical exposure variables in the different work organizational variable categories. For the categorical psychosocial variables, frequencies and proportions of occurrences of the different categories were calculated. Odds ratios were calculated to evaluate responses to the different psychosocial questions for different work organizational variable categories.

For the analysis of work pace at the task level, median values of the task level biomechanical variables were calculated. Kruskal – Wallist tests were used to assess differences in the mean ranks of the respective biomechanical exposure variables in the three categories of work pace variable. Pairwise comparisons were performed in the post hoc analyses using Dwass, Steel, Critchlow-Fligner (DSCF) multiple comparison analysis.

### 2.3.6 Estimating Associations Between Prevalent Cases of CTS, LEPI, and MEPI, and Measures of Biomechanical Stressors

Mixed effects logistic regression was used to determine odds ratios and 95% confidence intervals for the TLV for HAL and the 1995 SI, and prevalent cases of CTS,[97] LEPI and MEPI. All models were a-priori adjusted for age, gender, and BMI, and included research site (UT, WA, WI) as a random effect. Separate models including only the a-priori adjustment factors (i.e., no physical exposure) were built to estimate the associations between age, gender and BMI, and prevalence of CTS, LEPI, and MEPI.

### 2.3.7 Estimate Associations Between Incident Cases of CTS, LEPI, and MEPI, and Measures of Biomechanical Stressors

Workers were analyzed for incidence of CTS, LEPI, MEPI and combined LEPI or MEPI (i.e., EPI). Workers were incident eligible if they did not have the MSD at baseline.

For incident eligible workers, time from study enrollment to first occurrence of the MSD was modeled using Cox proportional hazard (PH) regression [98]. Workers lost to follow-up prior to developing an incident case of CTS were censored as non-cases on the last date they contributed data. Hazard ratios (HR) and corresponding 95% confidence intervals (95% CI) were calculated.

Cox frailty models with research site as a random effect were used to account for any variation in the outcome that was unexplained by the individual exposure variables and covariates.[99]

Physical exposures were treated as time-varying covariates and all variables were treated as continuous wherever possible.[78]

The functional form of each continuous variable was examined using Martingale residual plots.[100] The null PH model was fit and the resulting Martingale residuals were plotted against each of the continuous variables. Smoothed plots of the residuals provided approximate shapes of the association between the log HR and a given covariate.[100] Both loess and cubic smoothing splines were used as exible means of estimating distribution shapes, as different smoothing methods may suggest different functional forms.[101]

Where non-linearities were apparent, linear splines with a single knot were used to model them in a manner consistent with that described in.[78] When no transformations were suggested, continuous variables were treated as linear within the Cox regression models.

The 1995 SI, TLV for HAL, and RSI were also modeled as categorical variables using either a-priori, or empirical cut-points.

#### 2.3.8 Statistical Power

Power calculations were based on the prospective analysis of incident cases in a Cox model. The power for testing an elevated HR is presented for a 1 standard deviation unit change of a continuous exposure variable. The basis for the calculation is the total of 1,698 subjects with available follow-up and the 101, 128, and 67 incident cases of dominant hand CTS, LEPI, and MEPI, respectively. The calculations further assume 80% power, two-sided tests at the $p<0.05$ significance level and that the exposure variable has R-squared = 0.2 when regressed on the covariates. With these assumptions, incident analyses presented in this report had minimum detectable HRs for CTS, LEPI, and MEPI are 1.37, 1.32 and 1.47, respectively, per 1 standard deviation change in the exposure. The power to detect hazard ratios of 2.0 or larger was essentially 100% for all three outcomes. (Power analyses performed using the PASS statistical software).[102]

### *2.4 Results and Discussion*

The three studies had combined, total enrollment of 2,020 workers. Of those 2,020 workers, 1,834 (90.8%) completed both health and physical exposure baseline assessments. Multi-task jobs were performed by 710 of the workers (i.e., workers had job rotation), while the remaining 1,124 worked mono-task jobs (i.e., performed only one task for their entire work shift). The 710 workers with multi-task jobs performed a total of

3,647 tasks, i.e., they rotated to an average of 5.1 tasks/worker (median = 4, range: 2–12) during their work day, with a large majority (81%) rotating to between two and six tasks per day.[97]

### 2.4.1 Pooled Prevalence and Incidence Rates for CTS, LEPI, and MEPI

Carpal Tunnel Syndrome

Total prevalence of CTS for the entire eligible cohort was 18.4% (347 participants with CTS in the right, left, or both hands). Right hand, left hand, and bilateral prevalence were 16.9%, 6.5%, and 4.4%, respectively. The point prevalence of dominant hand CTS was 16.3%. Females, older workers and obese workers had higher prevalence of CTS. Dominant hand prevalence for females was 20.1% as compared to 10.7% for males, 22.7% for those classified as obese (i.e., BMI ≥ 30 kg/m2) as compared to 13.0% for non-obese, and 21.4% for those older than 42 years of age (median age) versus 11.7% for younger workers.[82]

There were 157 incident cases of dominant hand CTS over 3,327.8 person-years (P-Y) of follow-up for a total incidence rate of 4.72 per 100 P-Y. Females, older workers, and workers with higher BMI were at increased risk of CTS with incident rate ratios (IRR) of 1.26, 1.39, and 1.35, respectively. Incident rate for the 798 eligible females was 5.13 as compared to 4.06 for the 527 eligible males. The 682 workers above the median age of 41 years had incident rate of 5.42 as compared to 3.90 for 643 workers below. Similarly, the 668 workers above median BMI of 27.3 had incidence rate of 5.40 compared to 4.01 for the 657 below.

Lateral Epicondylitis

A total of 273 workers (15.0%) had lateral elbow symptoms at baseline. A positive examination finding of either resisted wrist extension or resisted middle finger extension was present in 264 (14.5%). LEPI, defined by both lateral elbow symptoms and a resisted examination maneuver, was present in 121 workers for a point prevalence of 6.6%. [89]. Dominant hand LEPI prevalence was 3.6% (65 cases). The mean age was greater among those with symptoms (OR per year = 1.02, $p < 0.0004$. The population had more females than males (n = 1088, 59.6%), and modestly higher risk of LE with female sex OR = 1.72, 95% CI 1.15, 2.58 ($p = 0.008$).[89]

There were 114 incident cases of dominant arm LEPI over 4,017.4 person-years (P-Y) of follow-up for a total incidence rate of 2.84 per 100 P-Y. Females, and older workers were at increased risk of LEPI with incident rate ratios (IRR) of 1.21 and 1.65, respectively. Workers with elevated BMI were at least risk for LEPI wit IRR of 0.87. Incident rate for the 973 eligible females was 3.03 as compared to 2.50 for the 616 eligible males. The 847 workers above the median age of 41 years had incident rate of 3.44 as compared to 2.08 for the 742 workers below. Conversely, the 816 workers above median BMI of 27.3 had incidence rate of 2.66 compared to 3.05 for the 773 below.

Medial Epicondylitis

There were only 14 workers with prevalence of MEPI (0.8%).

There were 53 incident cases of MEPI over 4,267.1 person-years (P-Y) of follow-up for a total incidence rate of 1.31 per 100 P-Y. Females were at modestly more risk for MEPI than males (IRR=1.14). Older workers were at increased risk of MEPI with IRR=1.38. Similar to LEPI, workers with elevated BMI were at modestly less risk for MEPI with

IRR=0.88. Incident rate for the 1007 eligible females was 1.30 as compared to 1.14 for the 629 eligible males. The 875 workers above the median age of 41 years had incident rate of 1.41 as compared to 1.02 for the 761 workers below. Conversely, the 884 workers above median BMI of 27.3 had incidence rate of 1.17 compared to 1.33 for the 792 below.

<u>Summary</u>
With the exception of MEPI, both prevalence and incidence rates were high in this cohort, perhaps reflecting the cohorts relatively older age (median=41 years), and the hand-intensive work industries they represented.

CTS and LEPI showed similar prevalence rates whereas MEPI was far less common (less than one tenth the prevalence of LEPI and CTS). CTS had the highest incidence rate. Incidence of LEPI was about 75% of the rate for CTS. Similar to prevalence, MEPI occurred far less often, though more frequently than prevalence would suggest (CTS occurred nearly 3 times more often, and LEPI about twice as often). It is unclear whether the diagnostic sensitivity of these case definitions are comparable and thus direct comparisons of rates should be made with care. Female gender and higher age were consistent risk factors for all three MSDs, whereas elevated BMI was a risk factor for CTS and protective for both LEPI and MEPI.

### 2.4.2 Prevalence Analyses

#### *2.4.2.1 Biomechanical Exposures and Prevalence of CTS*

After adjusting for age, gender, and BMI, both the TLV for HAL and the 1995 SI showed evidence of exposure-response relationships with prevalence of CTS when using the TWA, PEAK, and TYPICAL multi-task exposure methods. The 1995 SI using the TWA technique to account for multi-task exposures, showed a relatively stronger association than the TLV for HAL. ORs for 1995 SI with TWA technique were 1.34 (95% CI: 0.95-2.01) and 1.65 (95% CI: 1.19-2.30) for medium- and high-risk, respectively whereas ORs for TLV for HAL with TWA technique were 1.39 (95% CI: 0.93-2.08) and 1.33 (95% CI: 0.88-1.99) for medium- and high-risk, respectively. For both the TLV for HAL and the 1995 SI, TYPICAL exposure showed the strongest association between high-risk classifications and prevalence of CTS (ORs: 1.48 (95% CI: 1.03-2.12) and 1.66 (95% CI: 1.19-2.30), respectively). However, the ORs for medium-risk classifications were somewhat attenuated relative to those of the TWA technique [82]. Among the TWA, TYPICAL, and PEAK multi-task exposure techniques, PEAK performed relatively poorly with fewer statistically significant risk-classifications and relatively lower ORs, regardless of whether the 1995 SI or TLV for HAL was used.[82] The RSI model was not finalized in time for prevalence analyses and was thus excluded from these analyses.

When risk classifications from the 1995 SI and TLV for HAL were combined into a single measure of exposure (i.e., high-risk: both models classify as high, low-risk: both models classify as low, and medium-risk: all other model combinations), exposure-response relationships improved. Using the TWA multi-task exposure technique, this hybrid model had ORs of 1.57 (95% CI: 1.16-2.13) and 1.84 (95% CI: 1.14-2.95) for medium- and high-risk classifications, respectively. For this hybrid model, the TYPICAL and PEAK techniques also performed well.[82]

These findings suggest that neither the 1995 SI, nor the TLV for HAL reflect the true physical demands of hand-intensive work. However, the models' combined information might be useful for surveillance of DUE MSDs. None of the three generally accepted techniques for aggregating physical exposure from multi-task jobs into a single measure of physical exposure (i.e., TWA, TYPICAL, and PEAK) appear to be truly adequate. With the exception of the combined exposures approach, PEAK worked relatively poorly. TYPICAL works comparably to TWA, however TYPICAL (like PEAK) ignores all but one task being performed. TWA includes information from all tasks, but systematically under-estimates physical exposures due to the averaging process within the technique.[97] Nevertheless, precisely because it does include all available information, the TWA technique is likely best among the three for epidemiological studies. Conversely, TYPICAL is likely best for surveillance strategies as it focuses attention on a single task for targeted intervention.[97] TWA was used for all subsequent 1995 SI and TLV for HAL analyses.

Workers with job rotation (i.e., multi-task jobs) generally had higher job biomechanical risk levels as evaluated by the 1995 SI and the TLV for HAL [97] and higher exposure levels in terms of measurements of forceful exertions, repetition, and duration of exertions.[96] Thus, job rotation was associated with increased risk of CTS (OR=1.23, 95% CI: 1.00-1.50). However, neither working overtime nor work pace showed association with CTS.[88]

*2.4.2.2 Biomechanical Exposures and Prevalence of LEPI and MEPI*

There were very few prevalent cases of MEPI (0.8% prevalence, 14 cases) and that limited our ability to study that outcome separately. Based on the findings from Section 2.4.2.1, only TWA was used to aggregate multiple tasks into daily physical exposure.

For LEPI, the TLV for HAL suggested increased risk above the AL (OR=1.66, 95%CI: 0.77 to 3.55), but not above the TLV (OR=1.10, 95%CI: 0.45 to 2.68). The 1995 SI showed a statistically significant trend for increased risk ($p < 0.05$) but neither the medium risk ($3.0 < SI \leq 6.1$, OR=1.17, 95% CI: 0.56 to 2.41) nor the high risk ($SI > 6.1$, OR=1.36, 95% CI 0.71 to 2.63) categories were statistically significant.

For combined LEPI and MEPI analyses, confidence intervals narrowed for both the TLV for HAL and 1995 SI, but not enough to achieve statistical significance for any of the risk categories.

Job rotation trended towards significant association with LEPI (OR=1.69, 95% CI: 0.96-2.97); but showed no association with MEPI. Working overtime was protective for LEPI (OR=0.48, 95% CI: 0.28-0.84) and suggested protective for MEPI (OR=0.59, 95% CI: 0.24-3.12) albeit with a wide confidence interval due to the small case count. Work pace showed no association with LEPI and there were too few cases to study association with MEPI.[88]

In this cohort, workers who worked overtime usually had lower peak forces than those without overtime work, even though they had higher job physical exposure as measured by the 1995 SI. This paradox was primarily due to relatively higher repetition and duration of exertion.[96] This might suggest that force is a relatively more influential risk factor for LEPI, at least when physical exposures are over longer working hours.

Workers with job rotations also reported lower job satisfaction—they were more likely not to recommend their jobs to others, more likely to report dissatisfaction with their jobs, more unlikely to take the same jobs again, more likely to disagree that their employer cared about their health and safety, and more likely to report hardly ever getting along with their supervisors.[96]

*2.4.2.3 Non-Physical Factors and Prevalence of CTS*

Females (OR = 1.74, 95% CI =1.30-2.31), older workers (OR = 1.03/year, 95% CI =1.02-1.04) and obese workers (OR = 1.06/unit BMI, 95% CI =1.04-1.08) were more likely to be prevalent CTS cases.[82]

Framingham CVD risk factor scores showed a trend of increasing risk for CTS, across CVD score categories with a peak OR of 4.94 (95% CI 2.51, 9.71). Association with abnormal NCS were generally stronger with a peak OR of 8.06 (95% CI 3.43, 18.90). After adjusting the models for BMI, 1995 SI, and job satisfaction, ORs generally rose with adjusted peak OR for CTS 4.16 (95% CI 2.28, 7.61) and adjusted peak OR for NCS of 7.35 (95% CI 3.09, 17.53).[103]

Multifactorial etiologies for CTS have long been suspected and these results suggest that CVD risk may play a role in underlying mechanism(s).

Wrist Ratio (WR), and in particular "square wrist" was associated with prevalence of CTS. As compared to "rectangular" wrist, those with "square" wrists had a prevalence ratio (PR) of 2.27 (95% CI: 1.33-3.86). WR appeared to be interacted with BMI with PR decreasing from a peak of 8.2 (95% CI: 1.63-40.96) for BMI < 25.33, to PR=4.3 (95% CI: 1.19-15.36) for BMI between 25.33 and 30, to a non-statistically-significant PR=1.4 (95% CI: 0.74-2.76 for BMI greater than 30.[93]

*2.4.2.4 Non-Physical Factors and Prevalence of LEPI, and MEPI*

The mean age was greater among those with symptoms, examination findings or having LEPI (OR per year = 1.02, p < 0.0004, 1.02 p < 0.0001, and 1.03, p < 0.001 respectively). The population had more females than males (n = 1088, 59.6%), and modestly higher risk of LEPI with female sex OR = 1.72, 95% CI 1.15, 2.58 (p = 0.008).[89]

Framingham CVD score was associated with prevalence of LEPI with a suggested trend of increasing prevalence as CVD score increased [89] with a peak OR of 6.2 (95% CI: 2.05 - 18.8) for CVD score of 16 or more. 1995 SI score was included in the logistic regression model as a linear factor and a modestly protective association between linear 1995 SI score and LEPI was found (OR = 0.97, 95% CI: 0.95 - 1.0). The apparent effect modification of CVD risk on association between the 1995 SI and LEPI requires further analyses that are beyond the capabilities of this cohort's data.

After adjusting for age, gender, BMI, and 1995 SI score, trends for association were found between most measures psychosocial factors and prevalence of LEPI and MEPI.[104] Exceptions were supervisor support for LEPI, and perception of general health and supervisor support for MEPI. The highest ORs were observed for physically exhausted after work (trend of increasing ORs: 1.00, 3.90, 6.73, and 7.04 for LEPI, and 1.00 1.63, 2.50, 3.47 for MEPI; individual ORs significant at p<0.05 for LEPI); mentally exhausted after work (trend of increasing ORs: 1.00, 3.50, 6.24, 4.74 for LEPI, and 1.00, 2.01, 3.52, 6.51 for MEPI; individual ORs significant at p<0.05 for LEPI and MEPI with the exception of 2.01 for MEPI); and willingness to take job again (trend of increasing ORs: 1.00, 2.19, 2.42, 4.20 for LEPI, and 1.00, 1.26, 1.41, 3.20 for MEPI, individual ORs significant at p<0.05 for LEPI, and 3.20 for MEPI).[104]

### 2.4.3 Incidence Analyses

#### *2.4.3.1 Biomechanical Exposures and Incidence of CTS*

All models were adjusted for age, gender, BMI, and study site as a random effect.

When treated as simple linear variables, the 1995 SI and the RSI showed statistical association with CTS whereas the TLV for HAL (as a score), showed non-significant increased risk. Confidence intervals (95%) for per-unit increases in HR were: 0.92-2.16, 1.00-1.03, and 1.00-1.04 for TLV for HAL, 1995 SI, and RSI respectively. HRs at the 95th percentile of exposure were: HR=1.42 for TLV for HAL, HR=1.31 for 1995 SI, and HR=1.58 for RSI.

An examination of Martingale residual plots suggested strong attenuations in risk above the 90th percentile of exposure. Linear splines with single knots placed at either the 90th or 95th percentile of cases were used to model this attenuation (90th percentile for TLV for HAL, and 95th percentile for both 1995 SI and RSI). Below the knots in the linear splines,[78] all three models showed strong exposure-response relationships with incidence of CTS, followed by a statistical leveling of risk above the knot. Below the knots, confidence intervals (95%) for per-unit increases in HR were: 1.38-5.26, 1.01-1.07, and 1.01-1.05 for TLV for HAL, 1995 SI, and RSI respectively. HRs at the 95th percentile of exposure were: HR=2.89 for TLV for HAL, HR=1.89 for 1995 SI, and HR=2.18 for RSI.

Using the a-prior cut-points of below AL, and below TLV for the TLV for HAL, below 6.1 for the 1995 SI,[52] and below 10.0 for the RSI,[84] none of the three models showed statistically significant increased risk for CTS. HRs for TLV for HAL were 1.46 (95% CI: 0.92-2.31), and 1.34 (95% CI: 0.84-2.11) for medium- and high-risk, respectively. The HR for 1995 SI was 1.30 (95% CI: 0.92-1.82), and the HR for RSI was 1.28 (95% CI: 0.93-1.76).

The relatively poor performance of the RSI a-priori cut-point, combined with analyses associated with Aim #5 (see section 2.4.4) suggested that the RSI a-prior cut-point was too low. A revised cut-point of 15.0 was determined by comparing 1995 SI and TLV for HAL exposure distributions to that of the RSI. After applying that cut-point, the exposure response relationship improved dramatically to a statistically significant HR=1.47 (95% CI: 1.04-2.07).

Table 3: Exposure-Response Relationship with Incidence of CTS

| Model | Simple Linear | | Linear Spline | | Categorical | |
|---|---|---|---|---|---|---|
| | 95% CI | 95th %ile[1] HR | 95% CI | 95th %ile[1] HR | Exposure Level | HR (95% CI) |
| TLV for HAL[2] | 0.92-2.16 | 1.42 | ***1.38-5.26*** | ***2.89*** | AL–TLV | 1.46 (0.92-2.31) |
| | | | | | > TLV | 1.34 (0.84-2.11) |
| 1995 SI[2] | **1.00-1.03** | **1.31** | **1.01-1.07** | **1.89** | > 6.1 | 1.30 (0.92-1.82) |
| RSI[3] | ***1.00-1.04*** | ***1.58*** | **1.01-1.05** | **2.18** | > 10.0 | 1.28 (0.93-1.76) |
| | | | | | > 15.0 | ***1.47 (1.04-2.07)*** |

[1] HR at 95th percentile of measured physical exposure
[2] TWA of multi-task physical exposure, where applicable
[3] RSI score from CUSI of multi-task physical exposure, where applicable
**Bold:** statistically significant at p=0.05
***Bold-Italic*:** strongest exposure-response relationship with outcome

Table 3 summarizes the exposure-response models for incidence of CTS. None of the three models appears to be particularly good for CTS surveillance (consistent with prevalence findings, see Section 2.4.2.1 and Kapellusch et al.[82,97]). It is unclear whether this tendency is due to model inadequacy, or simply non-occupational factor influences on incidence of CTS. The revised RSI cut-point of 15.0 yielded statistically significant and relatively high HR, but the RSI model is labor intensive to use as a surveillance tool. However, the RSI should be effective as a design tool to systematically reduce risk of CTS from jobs.

#### *2.4.3.2 Biomechanical Exposures and Incidence of LEPI and MEPI*

All models were adjusted for age, gender, BMI, and study site as a random effect.

Simple Linear Models
When treated as simple linear variables, the 1995 SI and the RSI showed statistical association with LEPI whereas the TLV for HAL (as a score), showed or suggested increased risk. Confidence intervals (95%) for per-unit increases in HR were: 0.93-2.51, 1.00-1.04, and 1.00-1.04 for TLV for HAL, 1995 SI, and RSI respectively. HRs at the 95th percentile of exposure were: HR=1.6 for TLV for HAL, HR=1.35 for 1995 SI, and HR=1.62 for RSI.

The opposite statistical pattern was observed for MEPI. The TLV for HAL showed statistical association whereas the 1995 SI and the RSI narrowly did not. Confidence intervals (95%) for per-unit increases in HR were: 1.26-4.30, 0.99-1.05, and 0.99-1.05 for TLV for HAL, 1995 SI, and RSI respectively. HRs at the 95th percentile of exposure were: HR=2.49 for TLV for HAL, HR=1.40 for 1995 SI, and HR=1.71 for RSI.

When combined into simply EPI (i.e., developing either LEPI or MEPI), all three models were statistically associated with increased risk. Confidence intervals (95%) for per-unit increases in HR were: 1.07-2.56, 1.00-1.04, and 1.00-1.04 for TLV for HAL, 1995 SI, and RSI respectively. HRs at the 95th percentile of exposure were: HR=1.72 for TLV for HAL, HR=1.38 for 1995 SI, and HR=1.71 for RSI.

On the whole, the RSI and the TLV for HAL appeared to perform the best, with the RSI more strongly associated with LEPI and the TLV for HAL more strongly associated with MEPI. Both suggested similar levels of risk for EPI. In all cases, the 1995 SI showed relatively lower effect size, albeit with similar statistical significance.

Modeling Non-Linearity with Linear Splines

Similar to CTS, Martingale residual plots suggested strong attenuations in risk above the 75th, 90th, or 95th percentile of cases. For LEPI and EPI, knots were placed at 90th percentile for TLV for HAL, and 95th percentile for 1995 SI and RSI. For MEPI, knots were placed at the 90th percentile for TLV for HAL, 95th percentile for 1995 SI, and 75th percentile for RSI.

After applying the linear splines, all three models exhibited the same basic trend, regardless of outcome — risk increased steadily to the knot and then statistically leveled. Depending on the model, the HR point estimates above the knot varied from model to model and outcome to outcome, sometimes suggesting a modest decrease and other times a modest continued increase in risk. Second leg confidence intervals never approached statistical significance (which is unsurprising given the small number of cases above the knot).

For LEPI, effect size improved for all three models after applying the linear splines. Statistical significance improved for the TLV for HAL and 1995 SI and become nominally worse for the RSI. Below the knots, confidence intervals (95%) for per-unit increases in HR were: 1.18-5.60, 1.01-1.09, and 0.99-1.05 for TLV for HAL, 1995 SI, and RSI respectively. HRs at the 95th percentile of exposure were: HR=2.74 for TLV for HAL, HR=2.21 for 1995 SI, and HR=1.76 for RSI.

For MEPI, both effect size and statistical association improved for all three models, and in particular the TLV for HAL. Below the knots, confidence intervals (95%) for per-unit increases in HR were: 3.53-37.41, 1.01-1.12, and 1.01-1.16 for TLV for HAL, 1995 SI, and RSI respectively. HRs at the 95th percentile of exposure were: HR=13.6 for TLV for HAL, HR=2.90 for 1995 SI, and HR=7.91 for RSI.

Combined EPI was similar to LEPI in effect size but with all three models showing statistical association. Below the knots, confidence intervals (95%) for per-unit increases in HR were: 1.48-5.92, 1.02-1.09, and 1.00-1.05 for TLV for HAL, 1995 SI, and RSI respectively. HRs at the 95th percentile of exposure were: HR=3.19 for TLV for HAL, HR=2.49 for 1995 SI, and HR=1.96 for RSI.

Analyses using a-priori threshold limits

Using their respective a-prior cut-points for high-, medium- (where applicable), and low-risk, the TLV for HAL showed consistent and statistically significant associations with LEPI, MEPI, and EPI. The 1995 SI showed association with LEPI and EPI, but was not statistically associated with MEPI. The RSI showed poor association when using the a-priori cut-point of RSI=10.0.

For LEPI, HRs for TLV for HAL were 2.35 (95% CI: 1.47-3.78), and 1.71 (95% CI: 1.00-2.90) for medium- and high-risk, respectively. The HR for 1995 SI was 1.57 (95% CI: 1.04-2.37), and the HR for RSI was 1.12 (95% CI: 0.75-1.66).

For MEPI, HRs for TLV for HAL were 3.07 (95% CI: 1.56-6.05), and 3.35 (95% CI: 1.69-6.63) for medium- and high-risk, respectively. The HR for 1995 SI was 1.62 (95% CI: 0.92-2.84), and the HR for RSI was 1.21 (95% CI: 0.70-2.09).

For combined EPI, HRs for TLV for HAL were 2.27 (95% CI: 1.46-3.53), and 1.93 (95% CI: 1.22-3.06) for medium- and high-risk, respectively. The HR for 1995 SI was 1.52 (95% CI: 1.04-2.21), and the HR for RSI was 1.12 (95% CI: 0.78-1.61).

Using the revised RSI cut-point of 15.0 (see Sections 2.4.3.1 and 2.4.4) improved exposure-response relationships dramatically to: HR=1.67 (95% CI: 1.10-2.52), HR=1.52 (95% CI: 0.85-2.71), and HR=1.59 (95% CI: 1.09-2.35) for LEPI, MEPI, and EPI, respectively. However, the revised cut-point failed to reach statistical significance for MEPI.

Table 4: Exposure-Response Relationship with Incidence of LEPI

| | Simple Linear | | Linear Spline | | Categorical | |
|---|---|---|---|---|---|---|
| Model | 95% CI | 95th %ile[1] HR | 95% CI | 95th %ile[1] HR | Exposure Level | HR (95% CI) |
| TLV for HAL[2] | 0.93-2.51 | 1.60 | ***1.18-5.60*** | ***2.74*** | ***AL–TLV*** | ***2.35 (1.47-3.78)*** |
| | | | | | ***> TLV*** | ***1.71 (1.00-2.90)*** |
| 1995 SI[2] | **1.00-1.04** | **1.35** | **1.01-1.09** | **2.21** | **> 6.1** | **1.57 (1.04-2.37)** |
| RSI[3] | ***1.00-1.04*** | ***1.62*** | 0.99-1.05 | 1.76 | > 10.0 | 1.12 (0.75-1.66) |
| | | | | | **> 15.0** | **1.67 (1.10-2.52)** |

[1] HR at 95th percentile of measured physical exposure
[2] TWA of multi-task physical exposure, where applicable
[3] RSI score from CUSI of multi-task physical exposure, where applicable
**Bold:** statistically significant at p=0.05
***Bold-Italic***: strongest exposure-response relationship with outcome

Table 5: Exposure-Response Relationship with Incidence of MEPI

| | Simple Linear | | Linear Spline | | Categorical | |
|---|---|---|---|---|---|---|
| Model | 95% CI | 95th %ile[1] HR | 95% CI | 95th %ile[1] HR | Exposure Level | HR (95% CI) |
| TLV for HAL[2] | ***1.26-4.30*** | ***2.49*** | ***3.53-37.4*** | ***13.6*** | ***AL–TLV*** | ***3.07 (1.56-6.05)*** |
| | | | | | ***> TLV*** | ***3.35 (1.69-6.63)*** |
| 1995 SI[2] | 0.99-1.05 | 1.40 | **1.01-1.12** | **2.90** | **> 6.1** | **1.62 (0.92-2.84)** |
| RSI[3] | 0.99-1.05 | 1.71 | **1.01-1.16** | **7.91** | > 10.0 | 1.21 (0.70-2.09) |
| | | | | | > 15.0 | 1.52 (0.85-2.71) |

[1] HR at 95th percentile of measured physical exposure
[2] TWA of multi-task physical exposure, where applicable
[3] RSI score from CUSI of multi-task physical exposure, where applicable
**Bold:** statistically significant at p=0.05
***Bold-Italic***: strongest exposure-response relationship with outcome

Table 5: Exposure-Response Relationship with Incidence of EPI

| | Simple Linear | | Linear Spline | | Categorical | |
|---|---|---|---|---|---|---|
| Model | 95% CI | 95th %ile[1] HR | 95% CI | 95th %ile[1] HR | Exposure Level | HR (95% CI) |
| TLV for HAL[2] | ***1.07-2.56*** | ***1.72*** | ***1.48-5.92*** | ***3.19*** | ***AL–TLV*** | ***2.27 (1.46-3.53)*** |
| | | | | | ***> TLV*** | ***1.93 (1.22-3.06)*** |
| 1995 SI[2] | **1.00-1.04** | **1.38** | **1.02-1.09** | **2.49** | **> 6.1** | **1.52 (1.04-2.21)** |
| RSI[3] | **1.00-1.04** | **1.71** | **1.00-1.05** | **1.96** | > 10.0 | 1.12 (0.78-1.61) |
| | | | | | **> 15.0** | **1.59 (1.09-2.35)** |

[1] HR at 95th percentile of measured physical exposure
[2] TWA of multi-task physical exposure, where applicable
[3] RSI score from CUSI of multi-task physical exposure, where applicable
**Bold:** statistically significant at p=0.05
***Bold-Italic***: strongest exposure-response relationship with outcome

Summary of Incidence analyses of EPI

Tables 4-7 summarize the exposure-response relationships for incidence of LEPI, MEPI, and EPI, respectively. In general, all models showed good to strong association with LEPI, MEPI, and EPI. Statistical significance at the p=0.05 was mostly achieved and

HRs were generally high. For simple linear models, high-exposure HRs for TLV for HAL ranged from 1.6 to 2.5 for TLV for HAL, were about 1.4 for the 1995 SI, and ranged from 1.6 to 1.7 for the RSI. As expected,[78] these HRs improved after linear splines were applied (thus accounting for likely HR biases due to healthy worker survivor effect and occasional very high exposures that fall outside the normal distribution). For linear spline models, high-exposure HRs for TLV for HAL ranged from 2.7 to 13.6, from 2.2 to 2.9 for the 1995 SI, and from 1.8 to 7.9 for the RSI. Using risk threshold cut-points, HRs ranged from 1.7 to 3.4 for TLV for HAL, from 1.5 to 1.6 for the 1995 SI, and from 1.5 to 1.7 for the RSI.

These results suggest that the TLV for HAL is a good tool for surveillance of EPI — showing good association and being fast and easy to use. The RSI is superior as a design tool since the model accounts for all exertions and all tasks, explicitly.

#### 2.4.4 Recommending Revised Cut-Points for the TLV for HAL, 1995 SI, and RSI

Within this cohort of workers, physical exposures (as measured by the 1995 SI and the TLV for HAL) ranged from very low to very high. However, most individual tasks exposed workers to relatively low force (median peak force rating = 2.0), moderate repetition (median HAL = 5, median exertions/min = 15, median duty cycle = 49%), and good to very good hand/wrist posture (83.5% tasks).[97] While the cohort represents a wide range of physical exposures, the relative distributions of those exposures are unbalanced and might not be sufficiently representative of the totality of exposures in industry. Thus, using these data to empirically derive "optimal" cut-points for the 1995 SI, TLV for HAL, or RSI is not feasible in the manner we had originally intended.

With regard to the TLV for HAL and the 1995 SI, between model risk-assessment agreement was fair (kappa = 0.28) with the two models agreeing on about half of classifications (49%).[97] A near majority (48%) of this disagreement occurred between low- and medium-risk classifications, suggesting that revising the low-risk cut-points of one or both models is justified. However, an evaluation of the two models' raw scores showed wide variation (Spearman's Rho = 0.50) [97] and a careful examination of those scores revealed that simply raising (or lowering) the cut-points of one or both models would not resolve between model disagreement. Similarly, plotting the models' scores against cases and non-cases of CTS, LEPI, and MEPI, suggests that simple upward or downward adjustments to the thresholds of these models would likely not substantially improve their exposure-response relationships outside of this specific cohort.

The TLV for HAL tends to classify many more tasks as low-risk than does the 1995 SI.[87,97,105] Further, it has been suggested that the current AL places too many workers at risk for CTS.[38,49] Our own prevalence and incidence analyses for both CTS and EPI suggest this as well. However, our analyses have not revealed a cut-point that would materially improve exposure-response relationships. There is some evidence that *non-linear* thresholds for the AL and TLV might improve the predictive ability of the TLV for HAL model.[49] However, it is not immediately clear how such non-linear thresholds would be derived given the data limitations of this cohort. It might be possible to develop non-linear cutpoints using other sources of information (e.g., psychophysical data) but this would require substantial research and analyses that are beyond the scope of this current project.

The RSI was developed with an a-priori cut-point of 10.0 for “high-risk”. By comparing the RSI score distribution to distributions of the 1995 SI and TLV for HAL scores using this cohort’s exposure data, it appeared that a threshold score of 15.0 would be more consistent with the 1995 SI and TLV for HAL risk classifications, and better describe risk of CTS, LEPI, and MEPI. Using the revised high-exposure threshold, the RSI showed about 50% increased risk of CTS (HR=1.47, 95% CI: 1.04 to 2.07), about 70% increased risk of LEPI (HR=1.67, 95% CI: 1.10 to 2.52), about 50% increased risk of MEPI, albeit non-statistically significant (HR=1.52, 95% CI: 0.85 to 2.71), and about 60% increased risk of combined EPI (HR=1.60, 95% CI: 1.09 to 2.33).

### 2.4.5 Associations Between Job Organizational, Biomechanical, and Psychosocial Factors

Initial analyses showed several associations between quantified biomechanical exposures and psychosocial factors.[90] Similarly, there were strong associations between age, gender, and BMI, and all psychosocial measures except willingness to take the job again and recommending the job to others. Both the TLV for HAL and the 1995 SI were associated with job satisfaction, supervisor support, whether a worker would recommend the job to someone else and how likely the worker would be to take the job again ($p \leq 0.05$). The TLV for HAL was also associated with physical exhaustion after work and whether the employer was thought to care about the worker’s health and safety on the job ($p \leq 0.01$). The only psychosocial factor associated with the 1995 SI but not the TLV for HAL was mental exhaustion after work ($p \leq 0.01$). Neither the TLV fo HAL nor the 1995 SI showed association with general health status, feelings of depression, or supervisor support ($p > 0.17$). Consistent with our hypotheses, as physical exposure increased, psychosocial responses worsened. Constituent biomechanical factors, such as frequency of exertion, were also tested and showed similar associations with worsening psychosocial responses.

In subsequent analyses we explored the associations between job organization, biomechanical exposure, and psychosocial factors.[96]

Workers with job rotation were consistently exposed to statistically higher biomechanical stressors, regardless of whether the 1995 SI, TLV for HAL, or constituent variables such as frequency of exertion were used to describe those stressors. Job rotation was also statistically associated with several psychosocial measures. Those with job rotation generally reported that they were: (i) unlikely to ‘recommend their jobs to others’ (odds ratio (OR): 1.31), (ii) likely to report ‘dissatisfaction with their jobs’ (OR: 1.65), (iii) unlikely to ‘take the same jobs again’ (OR: 1.63), (iv) likely to disagree that their ‘employer cared about their health and safety’ (OR: 1.39) and (v) likely to report hardly ever ‘getting along with their supervisors’ (OR: 1.36).

Those exposed to more than 40 hours of work per week from their primary job tended to also be exposed to higher biomechanical stressors as measured by the 1995 SI. However, when biomechanical stressors were evaluated using the TLV for HAL, this relationship disappeared. Overtime work had statistically lower peak forces compared to non-overtime but the force differences were small (median value of 2.0 vs. 3.0 on the Borg CR-10 scale). Conversely, overtime work usually had higher repetition (measured by either HAL and efforts per minute of typical forces).

Those performing overtime work were more likely to: (i) strongly agree that their 'employers cared about their health and safety' (OR=0.61), (ii) report almost always 'getting along with their co-workers' (OR=0.71), and (iii) strongly 'recommend their jobs to others' (OR=0.77). However, these same workers appeared more likely to report feeling always 'physically exhausted' than those without overtime work (OR=1.20), although this was not statistically significant.

Having a second job showed no statistical association with any of the biomechanical measures or psychosocial measures in this study.

Work pace showed strong statistical associations with all biomechanical measures ($p<0.0001$). Machine-paced tasks had higher mean repetition compared to self-paced tasks. Piece rate tasks had lower forceful repetition compared machine-paced and self-paced tasks. When all exertions were considered, piece rate tasks had longer durations of exertion compared to machine-paced and self-paced tasks; however, when constrained to only forceful exertions (i.e., those with Borg CR-10 ≥ 2), the relationship reversed and machine-paced tasks had the longest durations of exertion followed by self-paced and then piece rate tasks.

Work pace also showed statistical association with certain psychosocial variables. For example, more workers with piece rate jobs strongly agreed that their 'employers cared about their health and safety' compared to self-paced (OR=0.60); however, fewer workers with machine-paced jobs shared those beliefs (OR=1.07). More workers with piece rate jobs felt that they 'always get along with their supervisors or co-workers' compared to self-paced (OR=0.35/0.50), but fewer workers with machine-paced jobs felt that way. Workers with machine-paced jobs felt that they could 'hardly ever get along with their-co-workers' (OR=1.55), but could 'almost always get along with their supervisors' compared to self-paced (OR=0.76). More workers with piece rate jobs reported being satisfied with their jobs and might strongly 'recommend their jobs to others' compared to self-paced (OR=0.41), but fewer workers in the machine-paced jobs felt satisfied and were more likely not to 'recommend their jobs to others' compared to the self-paced (OR=1.55). Both piece rate and machine-paced groups reported being always 'physically exhausted' than the self-paced group (OR=3.28 and 1.23 respectively). The piece rate group was also more likely to report being 'depressed' than the self-paced group (OR=1.06).

These analyses are cross-sectional and based upon somewhat limited pre-existing parent data. Nevertheless, the number and strength of mutual relationships between job organizational, biomechanical, and psychosocial factors is unexpectedly large. The association between physical exposure and psychosocial factors appears to contradict the findings of Harris-Adamson et al. [106] who found psychosocial and biomechanical exposures were independent risk factors for CTS. Thus, further research is needed to clarify these complicated and likely important relationships. In this regard, more detailed operational variable definitions of the work pace may be necessary so that one can better understand how the work pace influence biomechanical exposures. Understanding of the nature of tasks within different work pace categories may also be of interest to understand their psychosocial effects on workers. This study lacks high quality longitudinal information about work organizational and psychosocial factors and as such, prospective analyses have not yet performed. Nevertheless, these preliminary results provide a strong caution with regard to using any of these factors as covariates in regression models of association between any of these factors and prevalence of incidence of MSDs. Further, they suggest a strong need for specialized longitudinal studies that could test causal associations between these factors.

### *2.5 Conclusion*

The 1995 SI, the TLV for HAL, and the RSI exhibited strong exposure-response relationships with incidence of CTS, LEPI, MEPI, and EPI (i.e., combined LEPI or MEPI). The TLV for HAL is relatively quick and easy use and therefore may be the preferred tool for DUE MSD surveillance. The RSI provides a robust tool for detailed job design and evaluation. It should prove valuable to engineers and job designers and would be particularly valuable in support of continuous-improvement strategies.

In this cohort, job rotation increased risk for the MSDs studied. This was likely due to relatively higher physical exposures to those workers with rotation. This suggests that workers should not simply rotate from one high exposure task to another, but rather rotate to tasks with differing levels of exposure or at least tasks that require different muscle groups.

Workers with higher physical exposures provided less positive psychosocial responses than those with lower exposures (e.g., reported having lower job satisfaction). This might explain why some studies of DUE MSDs have reported associations with psychosocial factors. Prospective studies that simultaneously measure physical exposure and psychosocial responses are needed in order to better understand this potentially important association.

A noteworthy finding of this study was the association between cardiovascular disease (CVD) risk factors and prevalence of CTS, LEPI, and MEPI — providing further evidence of the complex pathologies of these occupational MSDs. Future studies should consider incorporating regular assessments of CVD risk factors so that robust prospective analyses of CVD and MSD association can be performed.

The findings of this study should help inform comprehensive MSD intervention strategies. Continuous exposure-response relationships provide a basis for companies to develop exposure policies. The RSI model provides a foundation for detailed design-level evaluation and decision making. Evidence of association between job organizational, biomechanical, and psychosocial factors provide insight into comprehensive workplace interventions. Proven association between CVD risk factors and occupational MSDs provides a basis and possible strategy for workplace wellness initiatives.

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## 2.7 *Project Publications*

### 2.7.1 Publications in Calendar Year 2017

Kapellusch JM, Silverstein BA, Bao SS, Thiese MS, Merryweather AS, Hegmann KT, & Garg A (2017). Risk assessments using the Strain Index and the TLV for HAL, part II: Multi-task jobs and prevalence of CTS. Journal of Occupational and Environmental Hygiene, in-press.

Kapellusch, JM, Bao SS, Silverstein BA, Merryweather AS, Thiese MS, Hegmann KT, & Garg A (2017). Risk Assessments Using the Strain Index and the TLV for HAL, Part I: Task and Multi-Task-Job Exposure Classifications. Journal of Occupational and Environmental Hygiene, 14(12): 1011-1019.

Malloy EJ, Kapellusch JM, & Garg A (2017). Estimating and Interpreting Effects from Nonlinear Exposure-Response Curves in Occupational Cohorts Using Truncated Power Basis Expansions and Penalized Splines. Computational and Mathematical Methods in Medicine, 2017(7518035): 1-16.

Hegmann KT, Thiese MS, Kapellusch JM, Merryweather AS, Bao SS, Silverstein BA, Wood EM, Kendall R, Foster J, Drury DL & Garg, A (2017). Association between Epicondylitis and Cardiovascular Risk Factors in Pooled Occupational Cohorts. BMC musculoskeletal disorders, 18(1), 227.

Thiese MS, Merryweather AS, Koric A, Ott U, Wood EM, Kapellusch JM, Foster J, Garg A, Deckow-Schaefer G, Tomich S, Kendall R, Drury DL, Wertsch JJ, & Hegmann, KT (2017). The Association Between Wrist Ratio and Carpal Tunnel Syndrome: Effect Modification by Body Mass Index. Muscle & Nerve 56(6): 1047-1053.

Garg A, Moore JS, & Kapellusch JM (2017). The Composite Strain Index (COSI) and Cumulative Strain Index (CUSI): methodologies for quantifying biomechanical stressors for complex tasks and job rotation using the Revised Strain Index. Ergonomics 60(8): 1033-1041.

Garg A, Moore JS, & Kapellusch JM (2017). The Revised Strain Index: an improved upper extremity exposure assessment model. Ergonomics 60(7): 912-922.

### 2.7.2 Publications in Calendar Year 2016

Bao SS, Kapellusch JM, Merryweather AS, Thiese MS, Garg A, Hegmann KT, Silverstein BA, Marcum JL & Tang, R (2016). Impact of work organizational factors on carpal tunnel syndrome and epicondylitis. Journal of occupational and environmental medicine 58(8): 760-764.

Thiese MS, Hegmann KT, Kapellusch JM, Merryweather AS, Bao SS, Silverstein BA, Tang R & Garg, A (2016). Psychosocial factors related to lateral and medial epicondylitis: results from pooled study analyses. Journal of occupational and environmental medicine 58(6): 588-593.

Bao SS, Kapellusch JM, Merryweather AS, Thiese MS, Garg A, Hegmann KT, & Silverstein BA (2016). Relationships between job organisational factors, biomechanical and psychosocial exposures. Ergonomics 59(2): 179-194.

Hegmann KT, Thiese MS, Kapellusch JM, Merryweather AS, Bao SS, Silverstein BA, Wood EM, Kendall R, Wertsch J, Foster J, Drury D & Garg A. (2016). Association between cardiovascular risk factors and carpal tunnel syndrome in pooled occupational cohorts. Journal of occupational and environmental medicine 58(1): 87-93.

### 2.7.3 Publications in Calendar Year 2015

Thiese MS, Hegmann KT, Kapellusch JM, Merryweather AS, Bao SS, Silverstein BA, & Garg, A (2015). Associations between distal upper extremity job physical factors and psychosocial measures in a pooled study. BioMed research international 2015(643192): 1-9.

## *2.8 Conference Proceedings and Presentations*

### 2.8.1 Presentations in Calendar Year 2017

Kapellusch JM, Garg A, "Using the New Cumulative Lifting Index and Cumulative Strain Index," American Industrial Hygiene Conference & Exposition, Seattle, WA. (June 6, 2017).

### 2.8.2 Presentations in Calendar Year 2016

Bao SS, Kapellusch JM, Merryweather AS, Thiese MS, Garg A, Hegmann KT, Silverstein BA, "Relationships between work organization factors and carpal tunnel syndrome and epicondylitis", 25th Epidemiology in Occupational Health Conference (EPICOH). (September 5, 2016).

Kapellusch JM, Dembinsky K, O'Donnell C, "A comparison of three techniques for quantifying HAL and their impact on the ACGIH TLV for HAL risk predictions", 9th International Scientific Conference on the Prevention of Work-Related Musculoskeletal Disorders (PREMUS), Toronto, Canada. (June 21, 2016).

Kapellusch JM, Garg A, "The Strain Index and Risk of Upper Limb Musculoskeletal Disorders: Results from the WISTAH Hand Study," 25th Epidemiology in Occupational Health Conference (EPICOH), Barcelona, Spain. (September 5, 2016).

Kapellusch JM, Harris-Adamson C, Rempel D, "Associations between force, repetition, posture, duty cycle, Threshold Limit Value for Hand Activity Level (TLV for HAL) and risk of carpal tunnel syndrome," 25th Epidemiology in Occupational Health Conference (EPICOH), Barcelona, Spain. (September 5, 2016).

### 2.8.3 Presentations in Calendar Year 2015

Bao SS, Kapellusch JM, Merryweather AS, Garg A, Silverstein SS, Thiese MS, Hegmann KT, "Pooling sub-task physical exposure data to study work-related carpal tunnel syndrome and epicondylitis", 19th Triennial Congress of the International Ergonomics Association Melbourne, Australia. (August 2015).

Hegmann, KT, “Impacts of Varying Epidemiological Case Definitions on Apparent Risk Factors for Musculoskeletal Disorders,” panel on “Physical Risk Factors and Musculoskeletal Disorders: A Review of Findings from the NIOSH Field-Based Studies.” American Industrial Hygiene Conference and Exposition, Salt Lake City, UT. (June 3. 2015).

Merryweather AS, Kapellusch JM, Bao SS, Thiese MS, Silverstein BA, Hegmann KT, Garg A, "Are work pace, overtime, job rotation or secondary employment associated with CTS and epicondylitis?", 19th Triennial Congress of the International Ergonomics Association, Melbourne, Australia. (August 2015).

Muthe PA, Knudson AJ**,** Ott U, Effiong A, Thiese M, Wood E, Hegmann KT, Association between Cardiovascular Risk Factors and Carpal Tunnel Syndrome. Presented at the 13th Annual National Occupational Research Agenda (NORA) Young/New Investigators Symposium, Salt Lake City, UT. (April 16, 2015)

#### 2.8.4 Presentations in Calendar Year 2014

Farokhi A, Thiese MS, Wood E, Hegmann KT, Psychosocial Factors and Carpal Tunnel Syndrome a Cross Sectional Analyses of the RMCOEH WISTAH Hand Study. Presented at the Western Occupational Health Conference, San Diego, CA (Sept. 18-20, 2014).

# PHS Inclusion Enrollment Report

**This report format should NOT be used for collecting data from study participants.**

OMB Number: 0925-0001 and 0925-0002
Expiration Date: 10/31/2018

***Study Title (must be unique):** Exposure Response Relationships for CTS and Epicondylitis from Pooled Data

* Delayed Onset Study? ☐ Yes ☒ No

***If study is not delayed onset, the following selections are required:***

**Enrollment Type** ☐ Planned ☒ Cumulative (Actual)

**Using an Existing Dataset or Resource** ☒ Yes ☐ No

**Enrollment Location** ☒ Domestic ☐ Foreign

**Clinical Trial** ☐ Yes ☒ No **NIH-Defined Phase III Clinical Trial** ☐ Yes ☐ No

**Comments:**

| Racial Categories | Ethnic Categories | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Not Hispanic or Latino | | | Hispanic or Latino | | | Unknown/Not Reported Ethnicity | | | **Total** |
| | **Female** | **Male** | **Unknown/ Not Reported** | **Female** | **Male** | **Unknown/ Not Reported** | **Female** | **Male** | **Unknown/ Not Reported** | |
| American Indian/ Alaska Native | 11 | 18 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 29 |
| Asian | 115 | 77 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 192 |
| Native Hawaiian or Other Pacific Islander | 31 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 34 |
| Black or African American | 56 | 38 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 94 |
| White | 778 | 533 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1,311 |
| More than One Race | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Unknown or Not Reported | 21 | 19 | 0 | 158 | 115 | 0 | 0 | 0 | 47 | 360 |
| **Total** | 1,012 | 688 | 0 | 158 | 115 | 0 | 0 | 0 | 47 | 2,020 |

**Report 1 of 1**

**To ensure proper performance, please save frequently.**

### 2.10 Inclusion of Children Document

Data were collected at places of employment. Children 18 years and older were not excluded from enrollment in the original studies. A total of 47 children were enrolled (2.4% of participants). Because the children were legally adults, there were no differences in how they were treated by their employers. Similarly, the original investigators treated participants between 18-21 years identically to those 21 years of age or older.

### 2.11 Materials Available for Other Investigators

Data for this study are voluminous and intrinsically complex. Analyses are ongoing. Currently, data are not in formats suitable to share without restriction (dataset(s) for each analysis must be generated from raw information using scripts – assumptions that require detailed knowledge of the underlying data and methods are required to build these scripts). Investigators interested in using these data may contact the project PI (A. Garg). The PI and co-Investigators are willing to partner with other investigators to further analyze and explore these data.