Final Progress Report

Developing a general population job exposure matrix for studies of work-related Musculoskeletal Disorders

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LIST OF TERMS AND ABBREVIATIONS

ACGIH = American Conference of Governmental Industrial Hygienists
CI=Confidence Interval
CONSTANCES = “Cohorte des consultants des Centres d’examens de santé” (a large French general population cohort study)
CTS = Carpal Tunnel Syndrome
EDS = electrodiagnostic studies (for measuring nerve conduction)
EKG = electrocardiogram
HR= Hazard Ratio
HEGs = homogenous exposure groups
ISCO = International Standard Codes of Occupations
JEM = Job Exposure Matrix
JEMs = Job Exposure Matrices
O*NET= Occupational Information Network
PCS = “Profession et Catégorie Sociale” (the French 4-digit national job coding System)
SOC = Standardized Occupational Categories (the American national job coding system)
TLV=Threshold Limit Value
UE = upper extremity

ABSTRACT

Project title: Developing a general population job exposure matrix for studies of work-related Musculoskeletal Disorders.
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Exposure assessment is a major methodological challenge for studies of work-related musculoskeletal disorders (MSDs) and other conditions affected by workplace physical exposures. Job-Exposure Matrices (JEMs) can provide efficient estimation of current and past exposures, particularly in large-scale general population studies where it is often infeasible to perform detailed individual level data collection. While the use of JEMs to study associations between health outcomes and workplace physical exposures is increasing, their use is relatively uncommon, the number of studied exposure variables is limited, and little work has examined the validity or comparability of existing JEMs. This project used data from a large French prospective cohort study (CONSTANCES) to create a new general population JEM based on self-reported data from >35,000 adults working in more than 400 different jobs, representative of the French working population. This JEM created homogenous exposure groups that could differentiate exposures between different jobs and provide unbiased exposure estimates. This created new possibilities to study the effects of current and past workplace physical exposures on a variety of health conditions within a large general population study.

After creating the new JEM, we conducted analyses to validate its exposure estimates and to compare exposure estimates between different JEMs and with directly observed exposures of individual workers. We found moderate to substantial agreement between the exposure estimates given by our new French JEM and an existing American JEM. These findings inform cross-national comparisons of study results and may support use of general population JEMs outside their countries of origin. We compared agreement between exposure estimates provided by both JEMs to observed exposure measures from individual workers from a large American cohort, and found good agreement at the level of the job. We then tested the ability of the JEMs to replicate known disease-exposure associations. We found that JEM derived exposures predicted current pain at the wrist, low back, shoulder, and knee in the French cohort. We also studied incident Carpal Tunnel Syndrome (CTS) and found that exposures estimated with the American JEM provided similar exposure-disease associations for CTS compared with associations obtained using the more labor intensive 'gold standard' method of individual worker observations. While JEMs have a number of limitations, our results show that they provide useful and valid exposure estimates, and are particularly useful in situations where exposure data could not otherwise be obtained, such as large existing datasets and in studies of past exposures. Our new JEM has been used to study cumulative physical exposures in published or ongoing studies of musculoskeletal disorders. In related publications, we have also described how JEMs can improve risk factor surveillance and other public health and occupational disease care by providing a basic assessment of exposures relevant to different health conditions.

SECTION 1 OF THE FINAL PROGRESS REPORT

Significant or Key Findings: Our overall study goal was to advance exposure assessment methods used in large epidemiology studies of work-related musculoskeletal disorders. To our knowledge, the proposed study was the first to compare agreement between estimates of biomechanical exposures provided by general population JEMs from different countries, was the first study to directly compare agreement between JEMs and multiple observed biomechanical exposures, and to test the validity of JEMs by studying associations between musculoskeletal disorders and exposure estimates made using the gold standard of individually observed exposures.

In our first study aim, we built a general population Job Exposure Matrix to enable large-scale studies of associations between workplace physical exposures and chronic diseases including MSD. In a large French General Population study (CONSTANCES), we pooled at the job level 27 different self-reported physical exposures from participants' current jobs. Our results demonstrated the ability of this new JEM to create unbiased homogenous exposure groups of physical risk factors that discriminated between different jobs. We found that useful JEMs can be constructed using self-reported data; this method uses workers' knowledge of their jobs, while reducing information bias by pooling at the job level. This JEM provides a potentially robust assessment method for assigning current or cumulative past workplace physical exposures in general population studies. (Evanoff, 2019b).

Our second aim conducted a cross-national comparison between physical exposure estimates from the new general population French JEM created in Aim 1, and an existing general population American JEM (O*NET). We demonstrated that these JEMs were strongly related to each other, sharing high correlations and moderate agreement between the majority of variable pairs that measured similar exposures. Our results suggest that these French and American JEMs may be suitable for use in other populations without available general population workplace physical exposure data, and could complement existing JEMs that lack particular exposures. (Evanoff, 2019a)

Our third aim compared upper extremity exposure estimates from the French and American JEMs to individually observed exposure data on 2474 workers from a large, multi-center American cohort study (the NIOSH Upper Limb Consortium study. We compared these detailed observed data to exposure estimates from the American and French JEMs, and quantified misclassification of exposures. We found that strength of agreement between JEM and other exposure estimates is influenced by the distribution of the worker population and the number of jobs under study; both of these factors may influence the within-job versus between-job variation in JEM-based exposure estimates. Importantly, these findings indicate that that a larger variability of jobs within a studied cohort will improve the ability of general population JEM to demonstrate exposure–disease associations. (Yung, 2020b)

Our fourth aim tested the ability of the new French JEM to demonstrate known exposure-response associations for MSD in cohorts of both French and American workers. In the French CONSTANCES cohort, we showed strong associations between workplace physical exposures estimated by the French JEM and *current pain* in the hand-wrist, shoulder, low back and knee. (Yung, 2020a) We also showed that both the O*NET and CONSTANCES JEMs demonstrated meaningful exposure–disease associations with incident Carpal Tunnel Syndrome (CTS). In exploratory models, adding exposure data from the JEMs to individual level measures improved the prediction of incident CTS. Methods and results for this aim are described in our study publication “Applying two general population job exposure matrices to predict incident carpal tunnel syndrome: A cross-national approach to improve estimation of workplace physical exposures.” (Yung, 2020b)

JEMs are simple, cost-effective, and useful tools that provide a source of workplace exposure data, particularly for epidemiological studies that lack individual-level exposure data. Our results suggest that the CONSTANCES JEM based on self-reported physical exposures from asymptomatic workers replicates known associations between physical risk factors and prevalent MSD symptoms. Physical exposure JEMs, such as the CONSTANCES JEM, open avenues of research in the prevention of MSDs and other health conditions related to workplace physical activities.

Translation of Findings: Overall, our results suggest that job-level physical exposure estimates were similar between the French JEM American JEMs. Further cross-national comparisons with other available physical exposure JEMs will further inform this rapidly expanding area of occupational disease epidemiology. Comparisons of exposure estimates from different countries can improve our understanding of exposure–outcome relationships and explain variation in their findings. Future work will also evaluate the ability of different JEMs to reproduce known exposure– response associations obtained with other exposure assessment methods. JEMs that can be applied cross-nationally may also enable multinational studies of associations between workplace exposures and diseases, and inform region-specific or cohort-specific JEMs. Cross-national comparisons of JEMs could also provide additional exposure data to complement existing national JEMs that might lack particular exposures. These data suggest potential for combining exposure methods to improve the estimation of workplace physical exposures for surveillance and epidemiology studies. Our new JEM has been used in several published studies (Fadel, 2019; Ngabirano 2020b & 2020a), in multiple ongoing studies, and has helped to spark increased interest in use of JEMs as a research and public health tool. (Descatha, 2019b; Fadel, 2020)

Research Outcomes/Impact: The results of this project can be immediately applied to facilitate important research that is currently infeasible. General population JEMs provide the ability to assign improved work exposure data to the many general population data sets that include health outcomes and job titles, but no other work exposure data. JEMs provide an attractive tool for exposure assessment because of their relatively low cost and their ability to assign both past and current exposures; our study findings demonstrated their validity and applicability.

In addition to research applications, our study has pointed to applications of JEMs in risk factor surveillance and public health. With our French colleagues, our group has recently described how JEM could assist in the clinical care of workers, and in the workers’ compensation process, by providing a basic assessment of exposures relevant to different health conditions. Because occupational diseases are often under-recognized, another practical application is using a JEM to screen for occupational exposures as part of health surveillance. By summarizing multiple exposures at a job level, JEM may also assist policy-makers in setting priorities for hazards and controls at work, and assist occupational practitioners to target prevention efforts and direct the conduct of more precise exposure measures to particular jobs. (Fadel, 2020)

SECTION 2 OF THE FINAL PROGRESS REPORT: SCIENTIFIC REPORT

Background:

Assessment of workplace physical exposures is a critical aspect of research into work-related musculoskeletal disorders and other conditions that may be affected by workplace physical exposures, including vascular disease, pregnancy outcomes, cancers, hernias, and work disability. Existing methods for biomechanical exposure assessment all suffer from various limitations. Direct measurement of worker exposures and detailed observational assessments are precise, but may misclassify exposures in jobs where exposures vary over a longer time than the period of job observation. Direct measurement and observation are expensive and time-consuming, potentially limiting their application to large groups of workers. Exposure questionnaires are easier to administer to large populations, but self-reported exposures are probably less precise than observation or direct measurement; importantly, responses by individuals to exposure questionnaires are potentially subject to recall bias or other information biases, particularly if perceptions of exposures may be altered by health status. Although prospectively obtained individual level data are considered the best estimates of exposure, these methods are difficult to apply in large cohort studies, and usually cannot be applied to studies of existing data. The ability to add exposure information to the health outcomes contained in large population data sets would greatly improve our knowledge of the health effects of workplace physical exposures, particularly for relatively uncommon disorders such as ulnar neuropathy, and for disorders such as osteoarthritis, where relevant exposures may be cumulative or have occurred years before disease recognition. This study proposed to develop and test a JEM that would add such work exposure data to general population datasets containing job titles.

In the absence of individual level exposure data or historical data, job exposure matrices (JEMs) are commonly used in occupational epidemiology research to estimate respondents' exposures to chemical and physical risk factors based on job titles, industry information, and population exposure data. A JEM provides a means to convert coded job titles into exposure estimates for epidemiological studies. Although this technique has frequently been used in studies of occupational cancers, using a job-exposure matrix to assign exposures to physical exposures such as posture, repetition, or force has been less common. Recognition that JEMs estimating physical exposures have been underutilized has prompted their use in recent studies. In addition to their efficiency, JEMs have two additional advantages: they can decrease information bias between cases and non-cases, and they allow the estimation of exposure data when no such data are otherwise available. This latter advantage is particularly relevant for estimating historical exposures.

Obtaining unbiased exposure estimates is an important goal for all epidemiology studies. It has long been recognized that persons with a disease may differentially report exposures compared to those without the disease, and that persons with existing conditions may behave differently in ways that alter their current exposures. These issues are of concern for studies of musculoskeletal disorders and workplace exposures, as self-reported exposures may be biased by symptoms of MSD, leading to perceptions of exposure that are higher among symptomatic workers; also, workers with symptoms may alter their work behaviors in a way that changes their exposures when assessed by objective measures. Both of these sources of information bias can lead to errors in measured associations, particularly in cross-sectional studies. Because JEMs make no distinction between diseased and non-diseased subjects, and assign exposures at the group level, the potential for differential information bias is markedly decreased by the use of a JEM.

While detailed individual level exposure information is lacking from many health outcomes databases, collection of basic information on occupation (such as job title and employer or industry) is more common. General population JEMs provide a means of assigning more detailed work exposure information when only these rudimentary data are available. This can be useful to studies of current or recent exposures, and is even more valuable to the study of past exposures. The evaluation of retrospective exposures in general population studies is particularly difficult, and poses a significant obstacle to studying the associations between long-term or past occupational exposures and the development of chronic diseases later in life. It is often difficult and complicated to evaluate exposures over a wide range of occupations and industries for long periods of time (perhaps decades) to assess exposures that may be relevant to chronic diseases. Few data systems in the USA and other countries contain both long-term health outcomes data and workplace exposure data; the ability to evaluate the health effects of long-term exposures is thus severely limited.

JEMs constructed to measure physical exposures have usually derived estimates of exposure from one of two sources: the assessments of experienced experts assigning exposures to job groups, or the self-reported exposures of individual workers in different jobs. Some sources, such as O*NET, use a combination of these methods. Each of these methods has advantages. Expert assessments are often used in the construction of JEMs for industry-specific studies of chemical exposures, and rely on assessors with accurate knowledge of rated jobs. For general population studies, knowledge of many different jobs is required, and individual assessors may or may not have direct knowledge of the very broad range of rated jobs. Inter-rater agreement has been reported as fair to moderate with regard to rankings of job categories in a general population JEM for lower extremity exposures; other studies have found substantial variation between raters in assigning exposures. Use of self-reported exposures is less common in constructing JEMs, though this method offers some advantages.
JEMs based on self-reported exposures make use of workers' knowledge of their usual job exposures, thus pooling data from many respondents for each job. By pooling information and assigning exposures based on group level rather than individual level responses, JEMs reduce information biases due to individual variation in reporting.

This approach has been used in a few prior studies of work-related psychosocial exposures and physical exposures, where use of a JEM provided abundant and inexpensive exposure data while eliminating the information bias that may result from symptomatic workers reporting higher exposures than non-symptomatic workers in the same job. Our project proposed to extend these methods to produce a JEM developed based on responses from a large general population cohort, in order to estimate physical exposures specific to multiple body regions including the upper and lower extremities, back, and neck. We created a JEM within the rich dataset of the French CONSTANCES study, which contains self-reported exposure information on multiple physical exposures not contained in O*NET, and contains health outcome data on a large and representative sample of the French general population. Our study used data from this large, newly implemented French cohort to build and test a JEM of workplace physical exposures relevant to MSD and other conditions. Our primary goals were to create an exposure tool useful for studying chronic MSD and other disorders related to physical activity in a large and rich French cohort, to test agreement between the new French

JEM and the existing American JEM based on O*NET, and to conduct large scale validation studies comparing the ability of JEMs to reproduce known exposure-response associations in large French and American worker cohorts. Ultimately, we hoped that these novel cross-national comparisons and between-method comparisons of both exposures and exposure-response associations would inform and encourage future studies using JEMs to study the effects of physical exposures on a variety of chronic diseases. Creation of the French JEM would also enable future studies within the large longitudinal CONSTANCES cohort of many conditions that may be related to current and past workplace physical exposures, including vascular diseases and chronic MSD such as knee osteoarthritis.

The questions posed by our study were innovative in several ways. We sought to create and test the most complete general population JEM assessing physical exposures, based on detailed questionnaire data on multiple exposures from >35,000 active workers. Construction of a JEM based on this detailed occupational exposure allowed assignment of exposure estimates that were *unbiased by variation in individual self-report,* which may be influenced by symptoms and other factors. These exposure estimates could be assigned to both current and past jobs, allowing estimation of lifetime physical exposures in studies of chronic MSD and other health conditions. The French CONSTANCES study is a unique general population cohort of 200,000 working-aged people in France, who will be followed longitudinally for multiple health and disability outcomes through repeated questionnaires, physical examination, and national administrative data. Developing and then applying the JEM to this remarkable cohort will allow many future studies of associations between workplace physical exposures and a wide variety of diseases and health outcomes.

Our study was also meant to advance exposure assessment methods used in occupational research. There are few comparisons between different multi-occupation sources of exposure information; to our knowledge, the proposed study was the first to compare agreement between estimates of physical exposures provided by two general population JEMs, was the first study to directly compare agreement between two different JEMs to observed exposures, and to test the validity of these JEMs by studying exposure disease associations established using different exposure methods. Study results inform the application of JEMs to improve exposure estimates in large general population studies in the USA and in other countries in order to address questions important to American workers.

Specific Aims:

<u>Specific Aim 1: Build a general population Job Exposure Matrix to enable large-scale studies of associations between workplace physical exposures and chronic diseases including MSD.</u> *Objective: This aim grouped self-reported physical exposures at the level of job titles in order to provide unbiased homogenous exposure groups appropriate for epidemiological studies.* We constructed a JEM based on exposures reported by CONSTANCES participants for their current jobs, compared within- and between-job variance of different physical exposure factors, and compared job-level to individual-level exposure estimates. Methods and results from this aim are described in our study publication “The CONSTANCES job exposure matrix based on self reported exposure to physical risk factors: development and evaluation” (Evanoff, 2019b).

<u>Specific Aim 2: Compare exposure estimates from the new French JEM to exposure</u>

estimates from an American JEM. *Hypothesis: Moderate to good agreement will be found between exposure estimates from the French JEM and an existing American JEM based on data from the Occupational Information Network (O*NET).* We transcoded French job titles into the American Standard Occupational Classification (SOC), then compared physical exposure values made by the French JEM to those contained in the American JEM. Methods and results for this aim are described in our study publication "Cross-national comparison of two general population job exposure matrices for physical work exposures." (Evanoff, 2019a)

Specific Aim 3: Compare upper extremity exposure estimates from the French and American JEMs to observed exposures from a large American cohort. *Hypothesis: Moderate agreement will be found between exposure estimates made by the two JEMs and observed exposures from the NIOSH Upper Extremity Consortium Study.* The NIOSH consortium study pooled exposure and outcomes data from six prospective studies; observed exposure data were available for 2474 workers in 140 separate SOC codes. We compared these detailed observed data to exposure estimates from the American and French JEMs, and quantified misclassification of exposures. Methods and results for this aim are described in our study publication "Applying two general population job exposure matrices to predict incident carpal tunnel syndrome: A cross-national approach to improve estimation of workplace physical exposures" (Yung, 2020b)

Specific Aim 4: Test the ability of the French JEM to demonstrate known exposure-response associations for MSD in cohorts of both French and American workers. *Hypothesis: Current physical exposures defined by the JEM will be associated with current MSD symptoms at multiple body parts, and with incident carpal tunnel syndrome (CTS).*
Aim 4a: Using the CONSTANCES cohort, we examined associations between the French JEM and *current pain* in the hand-wrist, shoulder, low back and knee. Methods and results for this aim are described in our study publication "Musculoskeletal Symptoms Associated with Workplace Physical Exposures Estimated by a Job Exposure Matrix and by Self-Report." (Yung, 2020a)
Aim 4b: We examined associations between the French and American JEMs and incident CTS in the NIOSH Upper Extremity Consortium cohort. We compared the performance of the two JEMs to detect known exposure-response relationships in this cohort, including the possibility of improved prediction of outcomes from inclusion of the additional exposure variables contained in the French data. Methods and results for this aim are described in our study publication "Applying two general population job exposure matrices to predict incident carpal tunnel syndrome: A cross-national approach to improve estimation of workplace physical exposures" (Yung, 2020b)

Methods:

Overview of Approach: The overall aims of this study were to use the extensive individual-level exposure data from the large new French CONSTANCES study to create and validate a general population JEM applicable to studies of current and past work exposures among this general population cohort of 200,000 people. The study took advantage of existing collaborations between our American and French research teams, and was based on prior work using self-reported exposures and JEMs in both American and French cohorts. In Aim 1, we built a general population JEM based on self-reported physical work exposures relevant to chronic diseases including MSDs, using individual-level data from more than 30,000 active workers in CONSTANCES. In Aim 2, we compared exposure estimates from this French JEM to exposure estimates from an existing American JEM based on data from the Occupational Information Network (O*NET). In Aim 3 we compared upper extremity exposure estimates from the French and American JEMs to observed exposures from the NIOSH Upper Extremity Consortium Study, which has pooled exposure and outcomes data from six prospective studies with a total of 4,321 subjects. In Aim 4 we tested the ability of the French JEM to demonstrate known exposure-response associations for MSD in both the French and American cohorts. The sections below describe the international study team, the CONSTANCES study, the NIOSH UE Consortium study, and our approach to each aim.

Study Personnel: This project brought together French and American teams with significant expertise and experience in exposure and outcomes assessment in epidemiological studies of work related MSD. Our combined American and French study team has worked together since 2005, with 46 joint research publications to date. American researchers Evanoff and Dale worked together with French researchers Descatha and Roquelaure to obtain permission from the International Scientific Committee of CONSTANCES to access study data on workplace physical exposures and MSD. Drs. Evanoff and Dale led one of the six studies comprising the NIOSH Upper Extremity Consortium study of upper extremity musculoskeletal disorders, and worked with leaders of these other NIOSH studies to incorporate the NIOSH UE consortium data into this project.

The CONSTANCES cohort: CONSTANCES (“Cohorte des consultants des Centres d’examens de santé”) is a large (final n = 200,000) prospective population-based longitudinal cohort designed as an "open epidemiological laboratory" accessible to the international epidemiologic research community, with the aims of contributing to the development of epidemiologic research and providing useful public health information. The major objectives of CONSTANCES are to study the occupational and social determinants of health, chronic diseases, and aging in the general population. CONSTANCES is conducted in partnership with the French Ministry of Health, National Institute of Health and Medical Research (INSERM), and National Health Insurance Fund. Applications to use the CONSTANCES data are invited from the international research community.

Overall design of CONSTANCES: This cohort was designed to provide a representative sample of the French salaried worker population in terms of age, sex, and socioeconomic status. The cohort is composed of a random sample of adults aged 18 - 69 at inception, with recruitment taking place in a national network of Health Screening Centers. Study recruitment was ongoing at the time our study started. Participants in CONSTANCES complete a baseline questionnaire, donate blood and urine, and complete a clinical examination that includes height, weight, blood pressure, EKG, vision, audiogram, spirometry, cognitive testing, and other testing. Participants receive annual follow-up by questionnaire, and will receive future examinations. The comprehensive CONSTANCES study questionnaire assesses multiple domains of interest using standard scales with established psychometric properties. Detailed information on CONSTANCES is available at: www.constances.fr. To our knowledge, there is no comparable study representative of the American working age population with a similar wealth of longitudinal health outcome measures and occupational data.

Exposures: For participants who were working at the time of the baseline survey, current occupational exposures to physical and chemical agents were collected as part of the CONSTANCES study questionnaire. 27 workplace physical exposure measures included overall physical workload, kneeling, twisting and bending the trunk, overhead work, hand vibration, repetitive work, and lifting/moving objects of varying weights. Past and current job titles and dates of employment were collected at baseline for all participants. These job titles were coded using the French 4-digit PCS (Profession et Catégorie Sociale) system, which contains 486 distinct job codes that our team subsequently mapped to the International Standard Classification of Occupations (ISCO-88).

Outcomes: Multiple self-reported health scales were collected on the questionnaire, including perceived general health and health-related quality of life. MSD symptoms were assessed via a modified Nordic questionnaire that assessed the location, duration, and severity of pain in different body regions. Self-reported medical history included questions on a number of co-morbidities and past surgery. These self-reported medical history data can be linked to medical procedure data from the French National Health Insurance Information System.

NIOSH UE Consortium Data:
The NIOSH UE cohort consisted of pooled data from six prospective studies of workplace risk factors for upper extremity musculoskeletal disorders. Details of the pooled cohort have been described in several studies. (Kapellusch, 2014, Dale, 2013) Briefly, study participants were full-time employees, 18 years of age or older, who performed hand-intensive activities, and were employed in industries such as manufacturing, production, service, and construction. In total, 4321 workers were recruited across the six study sites and followed between 2001 and 2010. At enrollment, all study participants completed baseline questionnaires and underwent physical examinations that included median and ulnar electrodiagnostic studies (EDS) across the wrist. Individual workplace exposure assessments included interviews to identify primary work tasks, videotaped recordings of workers performing their usual work tasks, and measurements of hand forces used to complete each task. Video analysis of work tasks provided estimates of hand force, repetitiveness in tasks, and temporal exertion patterns for repetition, hand exertions, duty cycle and posture. The Institutional Review Board at each study site approved relevant study protocols, and all participants provided written informed consent.

Approach to Specific Aim 1: Build a general population Job Exposure Matrix to enable large-scale studies of associations between workplace physical exposures and chronic diseases including MSD.

Overview: The objective of this aim was to group self-reported physical exposures at the level of job titles in order to provide unbiased homogenous exposure groups appropriate for epidemiological studies. We used individual respondents' self-reported physical exposures experienced in their current jobs, and pooled their reported exposures at the level of the French job title (PCS).

Questionnaire data: The CONSTANCES questionnaire contains information on social, demographic, health, and work characteristics. CONSTANCES participants answered questions estimating 27 different physical risk factors in each participant's current job. Overall intensity of physical workload was assessed with the Borg Rating of Perceived

Exertion Scale, ranging from 6 (no effort at all) to 20 (exhausting). Questions pertaining to the duration or frequency of performing specific actions, including postures, repetitive motion and the use of vibrating tools, were evaluated on a 4-point Likert Scale. Generally, the Likert Scale was formatted with the following anchor points: 'Never or nearly never', 'Rarely (<2 hours per day)", 'Often (2 to 4 hours per day)" and 'Always or nearly always'. Questions pertaining to regular handling, moving or carrying loads asked participants to report whether they handle objects greater than 1 kg (yes/no), and if yes, asked the frequency of handling objects based on different ranges of weights, following the 4-point Likert Scale above.

JEM development: We used data from the first 81,425 CONSTANCES participants. Reported job titles were assigned a French 4-digit Profession et Catégorie Sociale (PCS) job code using the "SiCore" automated coding system. The PCS classification system involves three nested levels of classification, from broad 1-digit socioprofessional job categories to the specific 4-digit PCS job code. This assignment of job titles resulted in participants with 418 different PCS job codes. Participants who were not currently working (n=35,466), those who did not report a job title, those who were not assigned a PCS job code through automatic coding (n=10,396), and those who had missing exposure data (n=30), were excluded from analysis. To produce reliable estimates within each exposure category, we required a minimum of 10 valid responses for each risk factor within each PCS job code. PCS jobs with fewer than 10 responses were grouped with other similar PCS jobs to create adequately sized groups (a minimum of 10 valid responses for each exposure for each PCS code). This method has been previously applied in grouping American standard occupational classification (SOC) codes. To create groups of similar jobs, we first used a PCS to ISCO-88 (International Standard Classification of Occupations) crosswalk (Codage Assisté des Professions et Secteurs d'activité) and an existing French autocoding system tool. Many PCS codes with few respondents shared a single ISCO-88 code, thus creating natural groupings. To group the remaining PCS job codes with few respondents, we used an ISCO-88 to ISCO-08 crosswalk, and an ISCO-08 to SOC crosswalk. All such groupings were reviewed, and PCS job codes that were not successfully grouped via crosswalks were grouped manually based on consensus opinions from three of the investigators (Evanoff, Dale, Descatha). PCS codes with a small sample size that could not be meaningfully merged with other jobs were excluded (n=7 participants). After all exclusions and job code grouping, the JEM comprised 27 physical exposures assigned to 407 PCS codes from 35,526 eligible participants.

Analysis for Aim 1: We first conducted preliminary analyses to determine whether exposure data from both symptomatic and asymptomatic workers should be included in the JEM. Since workers with symptoms of MSD may overestimate physical exposures compared with asymptomatic workers, reporting bias is a potential concern. Symptomatic workers were defined as those reporting a pain level of 6 or more (on a scale from 0 to 10) in one or more of six body regions in the previous 7 days at the time of the baseline exam (and reporting of work exposures). We first used linear mixed models to compare self-reported exposure levels between symptomatic and asymptomatic individuals. Separate models were produced for each of 26 risk factors (the variable work outdoors was not analyzed, as we expected this risk factor was unrelated to physical pain). A second analysis examined whether a JEM consisting of only asymptomatic workers led to more favorable Homgenous Exposure Groups (HEGs) than a JEM with both symptomatic and asymptomatic participants (full cohort); for this analysis, the within-job pooled variance was compared between the full cohort and the asymptomatic cohort for each risk factor. All statistical analyses were carried out with R statistical software (R Foundation for Statistical Computing, Vienna, Austria). The significant main effect was set at an α level of 0.05.

To evaluate the JEM we computed descriptive statistics to assess the demographics of the cohort, the overall distributions of each of the 27 risk factors, and proportion of symptomatic and asymptomatic participants. To better enable interpretation of JEM-assigned exposure estimates and comparison with exposures based on other methods, the ordinal questionnaire responses were recoded to time based variables (ie, minutes of activity per day). We selected the median value of the questionnaire time interval: 0 min (rating of 0 on the 5-point ordinal scale), 5 min (rating of 1 = 'Never or nearly never'), 60 min (rating of 2 = 'Rarely (<2 hours per day)'), 180 min (rating of 3 = 'Often (2 to 4 hours per day') and 360 min (rating of 4 = 'Always or nearly always'). We tested the validity of JEM classification by assessing the homogeneity of exposures classified by PCS codes by calculating within-job and between-job variance, to determine if the JEM base exposures separated workers into HEGs (variation of exposures between jobs should be larger than variation within workers in the same job). We performed non-parametric multivariate analysis of variance (NPMANOVA) to compare within-job and between-job exposure variance for all 27 exposures. NPMANOVA is a robust alternative to multivariate analysis of variance, and computes the sums of squares using metric distance matrices. Since there was a relatively large number of dependent variables (27 risk factors), we selected Manhattan distances, which is the sum of the absolute value of the differences among vector coordinates. Manhattan distances are particularly appropriate for high-dimensional data, providing significantly higher relative contrast between different points and a more meaningful indication of proximity than Euclidean distance metrics.

Because the process of merging jobs with fewer than 10 workers resulted in overlapping job groups, we first combined overlapping PCS codes to create 229 mutually exclusive job groupings. Each exposure was then scaled by rank transformation; the Manhattan distance between two groups was then the sum of the absolute differences between ranks among the 27 exposures. Univariate Kruskal-Wallis tests were performed for each of the 27 exposure variables to evaluate between-job and within-job variance for each exposure variable. To help visualize within-PCS and between-PCS job code groupings, we created a multidimensional scaling (MDS) plots with confidence ellipses to depict the Manhattan distances between exposure vectors.

When reporting JEM-assigned exposure values, studies have used different exposure metrics. MSD-focused JEMs have typically reported arithmetic means and medians of exposures; therefore we reported both metrics. We also corrected the JEM mean value using empirical quantile mapping (EQM) methods to adjust the group-level data to better reflect the distributions of individual- level exposure estimates. Using EQM, JEM mean values falling within every 1% quantile range were adjusted to reflect respective 1% quantiles of the individual-level self-reported values; this adjusted JEM mean is referred to as bias-corrected mean. To compare exposure metrics, we calculated the within-job variance, between-job variance and r2 values for these three exposure metrics for all 27 physical exposures. Within-job variance was defined as the average of the squared deviation from group metric values; between-job variance was the average of the squared deviation of metric values from the global mean.

We also compared JEM exposure estimates to individually reported exposures. For each physical risk factor, we created residual plots of the differences between individually reported exposures and exposures estimated by each of the three JEM metrics, which assigned exposure based on job title. We calculated the average of differences, the average absolute difference, and difference in variance between individually reported and JEM-estimated exposure values.

Approach to Specific aim 2. Compare exposure estimates from the CONSTANCES JEM to exposure estimates from an American JEM.

Overview: We compared the French JEM exposures to physical job demands from a JEM based on the Occupational Information Network (O*NET), a publicly available data set describing the physical and mental requirements of more than 800 occupations, defined based on SOC codes. We used a crosswalk to match French Profession et Catégorie Sociale job codes with American Standard Occupational Classification job codes, and defined a priori 50 matched French and American JEM variable pairs that measured similar exposures. We then calculated Spearman's correlations and Cohen's kappa values for exposure variable pairs between these French and American JEMs.

Crosswalk to compare French with American JEM: We created a new crosswalk to match French PCS codes with American SOC codes based on similarity of work physical exposures (available from the authors on request). We first matched PCS codes with the International Standard Classification of Occupations (ISCO-88) codes. During this step, French job titles were searched using Codage Assisté des Professions et Secteurs d'activité, which provided multiple ISCO-88 code options for each PCS code. We also used an existing French autocoding system tool to convert PCS codes into three-digit ISCO-88 codes. Guided by the output from these two French coding systems, three investigators with experience in job coding systems and knowledge of multiple job types (Dale, Descatha, and Evanoff) independently assigned a unique ISCO-88 code to each PCS code, with differences resolved by consensus. We then matched ISCO-88 codes to ISCO-08 codes using an existing cross-walk from the International Labor Organization. Finally, ISCO-08 codes were then matched to American SOC codes, using an existing cross-walk from the US Bureau of Labour Statistics (www.bls.gov/ soc/). In each of these stages, the investigators selected the best matches based on job tasks if multiple options were available for a single job code, and selected the SOC code that best matched the PCS job title in cases where PCS codes were not successfully assigned an ISCO code. This cross-walk process resulted in 239 SOC codes paired with 367 PCS codes. In a final stage, the investigators reviewed all PCS to SOC assignments to ensure comparability of the French and American job titles.

Analysis for Aim 2: In order to highlight differences and similarities between French and American JEM exposures, we selected O*NET variables a priori that seemed to assess similar exposures to the 27 French CONSTANCES JEM variables. We found matches between one or more of 21 O*NET items and 21 CONSTANCES items, for a total of 50 matched exposure pairs comparing the French with the American JEM-derived exposure estimates (Table 1 below). Six CONSTANCES items could not be matched with an O*NET variable, including four exposures relevant to the upper extremity. In Table 1, we list all 27 French JEM physical exposures contained in CONSTANCES (n=367 PCS job codes) and the 21 matching American JEM physical exposures from O*NET (n=239 SOC job codes). Descriptions of each exposure variable, scale and assigned exposure estimates (mean, SD min and max) are shown in online supplementary material for our publication. (Evanoff,2019a) We carried out two comparison analyses: Spearman's rank correlation coefficient to measure correlation, and Cohen's kappa to measure the degree of agreement. We calculated Cohen's kappa values by dichotomizing physical exposure estimates for both French and American JEMs at the median physical exposure level; our Cohen's kappa calculation therefore indicates the level of agreement in assignment of jobs to high and low exposure groups between French and American JEM exposures. We grouped both Spearman's rank correlation and Cohen's kappa values using conventional interpretations: Kappa values $\kappa \leq 0.2$ represent slight/no agreement, $\kappa=0.21–0.40$ is fair agreement, $\kappa=0.41–0.60$ is moderate, $\kappa=0.61–0.80$ is substantial and $\kappa \geq 0.81$ is almost perfect agreement.

Table 1 A priori matches of American O*NET JEM exposure variables (n=239 SOC codes) to French CONSTANCES JEM exposure variables (n=367 PCS codes)

French CONSTANCES JEM	American O*NET JEM
Physical intensity.	Performing general physical activities. Dynamic strength. Static strength. Trunk strength.
Stand.	Spend time standing. Spend time walking and running.
Repetition.	Spend time making repetitive motions. Spend time using your hands. Handling and moving objects. Wrist finger speed.
Changes tasks.	No exposure match.
Rest eyes.	No exposure match.
Kneel or squat.	Spend time kneeling, crouching, stooping or crawling.
Bend trunk.	Spend time bending or twisting body. Cramped work space and awkward positions.
Drive machinery.	Operating vehicles mechanised devices or equipment.
Drive car or truck.	Operating vehicles mechanised devices or equipment.
†Handle object: 1–4 kg and >4 kg. †Carry loads: <10 kg, 10–25 kg and >25 kg.	Spend time using your hands (only for handle object 1–4 kg). Dynamic strength (all handle/carry variables). Static strength (all handle/carry variables). Handling and moving objects (all handle/carry variables). Trunk strength (only for carry loads 10–25 kg and >25 kg).
Use vibrating tools.	Exposed to whole body vibration.
Use computer screen.	Interacting with computers.
Use keyboard or scanner.	Interacting with computers. Importance of repeating same tasks.
Bend neck.	No exposure match.
Arms above shoulder.	No exposure match.
Reach behind.	Cramped work space and awkward positions. Spend time bending or twisting body.
Arms abducted.	No exposure match.
Bend elbow.	Handling and moving objects.
Rotate forearm.	Spend time using your hands. Handling and moving objects.
Bend wrist.	Spend time using your hands. Handling and moving objects. Wrist finger speed.
Press base of hand.	No exposure match.
Finger pinch.	Finger dexterity. Manual dexterity. Wrist finger speed.
Work outdoors.	Outdoors exposed to weather. Outdoors under cover.

†There are two separate questions under 'handle object' and three questions under 'carry loads', representing different weights handled. We indicate in parentheses the matches between O*NET variables and CONSTANCES 'handle object' and 'carry loads' variables, comprising a total of 18 matched pairs.
CONSTANCES, *Cohorte des consultants des Centres d'examens de santé* ; JEM, job exposure matrix; O*NET, Occupational Information Network; PCS, Profession et Catégorie Sociale.

Approach to Specific Aim 3: Compare upper extremity exposure estimates from the French and American JEMs to observed exposures from a large American cohort.

<u>Overview:</u> In Aim 2, we described agreement between multiple exposure estimates from the American and French JEMs relevant to many anatomic regions. In this aim, we compared hand/wrist exposures from the two JEMs to a referent standard of individually observed exposures from the NIOSH UE Consortium studies. The consortium studies collected detailed, individual level exposure measures of the hand and wrist, including hand force, repetition, duty cycle (duration of hand activity), and posture. Most exposure data were collected by the time intensive process of videotaping workers' tasks and later analysing the video to measure postures, repetitions, and duty cycles. Exposures measured in different work tasks were combined using time-weighted averaging to estimate work exposures for each individual.

Comparison of exposure estimates made from JEM vs. individual measures: To compare exposure estimates between JEMs and individual-level exposure measures from the NIOSH UE Consortium we calculated Spearman's rank correlation coefficient and Cohen's kappa. We matched *a priori* similar exposure variables in order to compare exposure estimates between JEM and observation. Matched exposure variables assessed similar ergonomic risk factors (i.e. force, repetition, posture, duration). For the O*NET JEM, we matched ≥1 of 8 O*NET variables to 11 consortium variables, resulting in 41 matched pairs. For the CONSTANCES JEM, we matched ≥1 of 9 CONSTANCES variables to 11 consortium variables, resulting in 54 matched pairs. We assigned exposure values from both JEMs to each of 2393 workers with individual-level measurement from the NIOSH UE Consortium studies, and calculated Spearman correlations and Cohen's kappa at the worker level between: (i) O*NET JEM and individual consortium exposures, (ii) CONSTANCES JEM and individual consortium exposures, and (iii) CONSTANCES and O*NET JEM. We also performed the same comparisons at the level of the job within the 130 job codes contained in the consortium data. When calculating Cohen's kappa, we dichotomized physical exposure estimates from the CONSTANCES JEM, O*NET JEM, and consortium individual-level measure exposure data at their respective median physical exposure levels. We interpreted our Cohen's kappa calculation as the level of agreement in categorizing high and low exposure groups between exposure methods for each paired exposure variable.

Approach to Specific Aim 4: Test the ability of the French JEM to demonstrate known exposure-response associations for MSD in cohorts of both French and American workers.

Aim 4a: Within the French data, this aim tested the hypothesis that past and current physical exposures defined by a JEM would be associated with current MSD symptoms. We used the job title based exposures derived from Aim 1 and studied their association with *current musculoskeletal pain* in the hand-wrist, shoulder, low back and knee reported on the CONSTANCES questionnaire. The JEM created in Aim 1 used responses from the first wave of participants recruited to the CONSTANCES study. The second wave of 69,782 CONSTANCES participants, recruited to the study from 2015 to 2017, formed the *validation sample* to evaluate whether the CONSTANCES JEM could replicate known exposure-outcome associations in a worker group whose data were not used in the creation of the JEM. From this cohort of new participants, we excluded individuals who were not currently employed, or whose reported job titles were not assigned one of the 407 4-digit PCS codes used in the JEM, leaving 38,730 participants as the "Validation cohort."

Exposures: Tested exposures for the hand/wrist included use of vibrating tools; bending or rotation of the wrist; use of pinch grip; pressing or tapping with the base of the hand; repeating the same actions more than 2-4 times per minute; ability to take work breaks; regularly handling or moving a load, part or object weighing 4 kg or more; and overall physical exertion. For other body areas, exposures included handling and moving heavier loads, as well as specific postures relevant to the shoulder, back, and knee: use of arms overhead, bending the trunk forward or to the side, and kneeling.

Case definitions: *Current pain* in the hand-wrist, shoulder, low back and knee were reported on the Nordic Questionnaire, which asks about the presence and duration of pain or discomfort over the past 7 days and over the past 12 months in multiple body parts, and also asks about symptom severity for each body part on a 0-10 scale from "no pain or discomfort” to “the most pain imaginable.” We examined current pain (pain in the past week) as well as pain occurring for $\geq$30 days during the past 12 months. Within these time intervals, we defined pain as symptoms of more than 5 on the 0-10 scale.

Analysis for Aim 4a:
We first compared the level of agreement between self-reported exposures and JEM-assigned exposure estimates. For each of the 27 physical exposure variables, we calculated weighted kappa and 95% upper and lower limits between individual self-reported exposure values and JEM-assigned bias-corrected mean exposure estimates. This analysis was performed across all PCS codes for the validation sample cohort (n = 38,730).

We next calculated associations between self-reported exposures, JEM-assigned exposure estimates, and musculoskeletal pain. From the 27 JEM physical exposure variables, we selected *a priori* those exposures thought to be most relevant to MSD pain specific to each of six body locations: hand, elbow, shoulder, low back, knee, and neck. For each body location, we graded the *a priori* selected exposures based on the expected strength of their association with MSD pain: strong association, some association, and possible association. This analysis was performed for the outcomes of current pain (definition: >5 rating on a 0-10 self-reported ordinal scale in the previous 7 days) and/or chronic musculoskeletal pain (pain occurring 30 or more days within the previous year) at the six body locations. We computed prevalence ratios (PR) and 95% confidence intervals using Poisson regression models with robust sandwich estimators adjusted for age and sex for both individual self-reported exposures and JEM-assigned exposures. We analyzed two models for all exposures: a continuous model using the full scale of the exposure values and a dichotomous model where exposures were split at the median exposure value. For two of the variables (“Use computer screen” and “Use keyboard or scanner”), the median value was at the maximum scale rating, and therefore high exposure reflects the maximum value whereas low exposure reflects exposures less than the maximum. We did not adjust for multiple comparisons.

Aim 4b: We examined associations between incident CTS in the NIOSH UE Consortium and biomechanical exposures estimated using three different exposure methods: exposures estimated by the French and American JEMs, and by the detailed individual observed exposures described in Aim 3. This aim tested the validity of the JEMs by studying their ability to replicate exposure disease associations established using an established exposure method.

Outcome data in the NIOSH UE Consortium studies came from questionnaires and physical examinations that included nerve conduction studies (NCS) performed at the wrist. Questionnaires gathered information on demographics, medical history, work history, and musculoskeletal symptoms. Workers’ current and prior job titles, industry, dates of employment, and job task descriptions were available for each worker. The primary outcome was an epidemiological case definition of prevalent CTS that required both hand symptoms typical of CTS and median nerve conduction abnormality. Workers having hand symptoms and abnormal nerve studies in the dominant hand were considered cases of CTS.

Analysis for Aim 4b: In this aim we studied the incident cases of CTS in the NIOSH UE Consortium, and computed Cox proportional hazard models to evaluate relationships between baseline physical work exposure and incident CTS. We determined hazard ratios (HR) and 95% confidence intervals (CI) adjusted for age, gender, body mass index (BMI), and study site. Each model included a single physical work exposure from the CONSTANCES JEM, O*NET JEM, or individual-level measurement. Since exposure data from all sources were expressed on different scales, we examined a dichotomous exposure model where values were split at the median value (high versus low), in addition to continuous exposure models (per 1-unit increase). We applied robust sandwich estimators to account for intra-cluster dependence within each model.

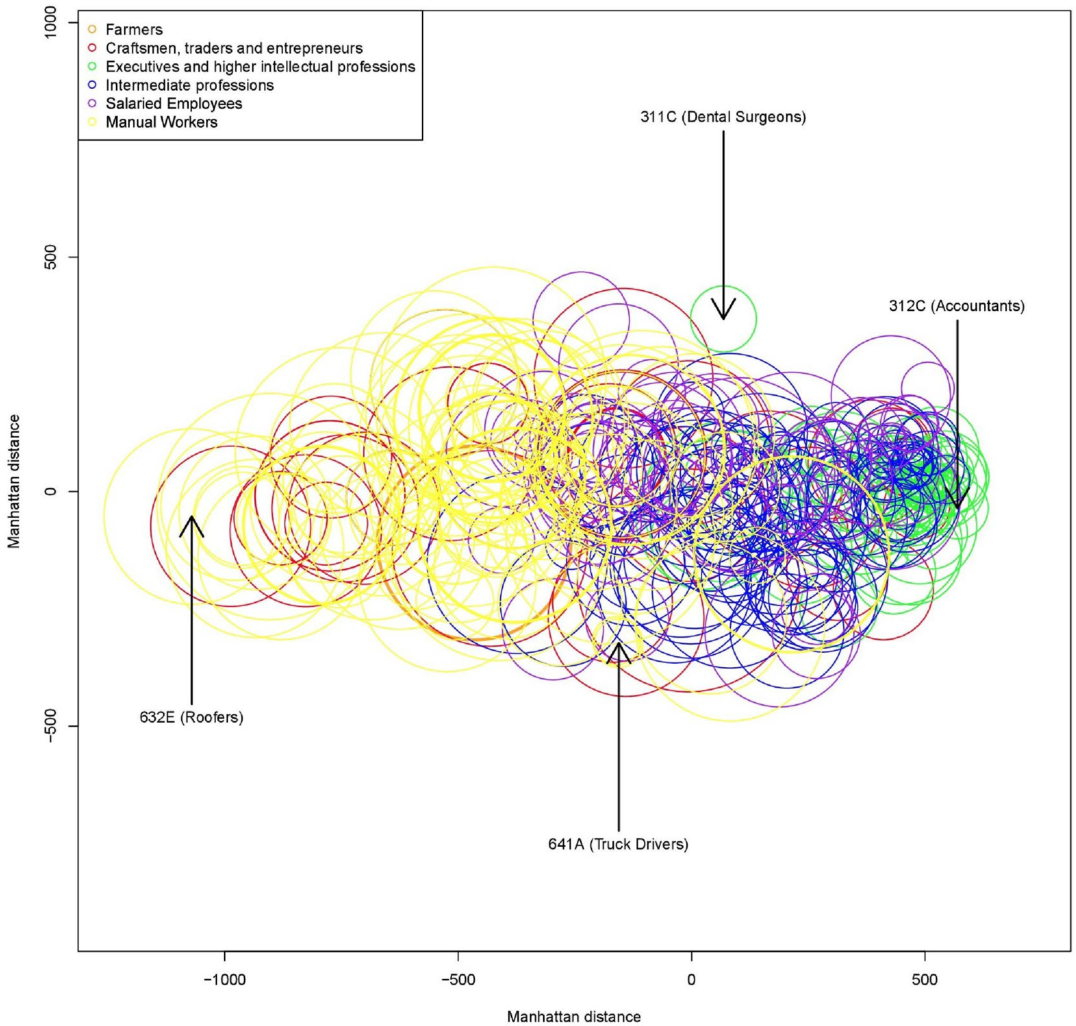
Results and Discussion:

Aim 1: Build a general population Job Exposure Matrix to enable large-scale studies of associations between workplace physical exposures and chronic diseases including MSD.

JEM development: Eligible participants represented 407 French PCS job titles nested within six broad socioprofessional categories. We first assessed the effect of symptoms on pain reporting, and whether a model excluding symptomatic workers would result in more favorable Heterogenous Exposure Groupings (HEG) at the level of the job title. Twenty-three per cent of the cohort reported musculoskeletal pain in one or more body regions. A linear mixed model compared exposure values between symptomatic and asymptomatic participants and found that 23 of 26 risk factors demonstrated statistically significant differences in reported exposures. Positive β coefficients from these models indicated that symptomatic individuals reported higher exposure values than asymptomatic individuals within the same PCS job code. Of the 26 linear mixed models, 21 exposure variables had statistically significant positive β estimates. Eleven exposure variables had β estimates greater than 0.2. Using responses only from the asymptomatic workers we found lower within-job variance than when using responses from the full cohort, resulting in more favorable HEGs and thus better ability to separate different jobs based on exposures. As a result, only exposure estimates from asymptomatic workers were included in the JEM.

JEM evaluation: As expected for the general population in an industrialized country, the individual risk factors with the highest mean and median duration of daily activity were related to computer or office work, with much lower daily durations of heavy lifting or hand exertion. Examining individually reported exposures at the level of the job, NPMANOVA analysis showed significantly higher between-job variance than within-job variance among the 27 exposures (229 PCS groupings; $F(228,21989)=67.18$, $p<0.0001$). PCS job codes explained 41.4% of the variance in individual self-reported exposures in the overall model. Univariate analysis for each risk factor variable revealed r2 values ranging from 5% (reaching for items behind back) to 55% (standing). This indicates that the amount of variance explained by PCS job codes was different between risk factor variables; of the 27 risk factors, 12 variables achieved r2 greater than 30%, while three variables resulted in explained variance less than 10%. Despite the large range of explained variance, all univariate models were statistically significant (all $p<0.0001$) indicating a relationship between exposures estimated by PCS code and self-reported exposure variables among asymptomatic workers. Taking all reported risk factors into account, we observed non-overlapping relationships between individual PCS codes (shown by ellipses in Figure 1 below), indicating separation between different jobs. We also noted clustering of PCS codes within the same socioprofessional categories (represented by color), as expected.

Figure 1 Multidimensional scaling plots of exposure vectors for all PCS codes with 95% confidence ellipses based on Monte Carlo simulations. Colour coded by PCS subgroup (first digit of PCS). PCS, Profession et Catégorie Sociale.



JEM exposure metrics: To create Heterogenous Exposure Groupings, it is important to minimize within-job exposure estimates and maximize between-job variance. We compared three three different exposure metrics expressing the central tendency of exposures in each job title (mean, median, bias-corrected mean). We observed comparable within-job variance using the means (variance=0.15 to 6.13), medians (variance=0.18 to 6.73) and bias-corrected means (variance=0.22 to 7.62). In contrast, the bias-corrected mean (variance=25.60 to 1193.55) showed markedly higher between-job variance than means (variance=2.35 to 492.03) or medians (variance=5.93 to 764.15). R2 values of the 27 physical risk factors ranged from 0.06 to 0.57 (JEM mean), 0.17 to 0.64 (JEM median) and 0.38 to 0.65 (JEM bias-corrected mean). Thus, use of bias-corrected means resulted in more favorable HEGs at the job level (greater contrast of within-job and between-job variance), and allowed job title level exposures to explain more of the variance in individually reported exposures. Use of the bias-corrected mean also led to smaller differences between individually reported and job title level exposures at all exposure levels compared with the JEM mean and median plots.

Discussion: Assessment of workplace physical exposures is critical for the prevention of MSD and other conditions that may be affected by workplace physical activity. This study developed and evaluated a JEM using individual-level self-reported physical exposure data from a prospective general population cohort study in France. After clustering the PCS codes into 229 groups, we found significantly higher between-job variance than within-job variance among all 27 exposures tested. Our data showed that the CONSTANCES JEM created HEGs, with distinct separation of exposures between jobs and some clustering of exposures within broad job categories. We also found that using a bias-corrected mean exposure for each job title level led to the most favorable HEGs, while best approximating individual-level exposure reports at the level of the job. The CONSTANCES JEM was constructed using self-reported data from asymptomatic workers. Symptomatic study participants reported higher workplace physical exposures than asymptomatic participants; previous studies have shown differential reporting of exposures by symptomatic workers due to higher perception of exposures or altered work behaviors. It is also possible that higher exposures were accurately reported by those with MSD symptoms, because of actual exposure differences between individuals within the same jobs. While using only the exposures reported by asymptomatic workers created more HEGs, this approach somewhat reduced the overall mean exposures estimated for each job.

Several metrics have been used to express the central tendency in JEMs. In this study, we compared bias-corrected mean to the arithmetic mean and median exposure values. We observed that bias-corrected mean values led to comparable within-job variance but larger between-job variance and therefore more homogeneous exposure measures at the job level. These methodological differences show a need to further investigate the ability of different exposure metrics to approximate individual-level exposures. Our results suggest that use of EQM methods may correct biases and better reflect the shape of the underlying exposure distribution.

Although we demonstrated that the CONSTANCES JEM, based on self-reported physical exposure data, may be an effective tool to estimate individual workers' job exposures, there are several potential limitations to this JEM relating to the source population, the coding of job titles and the ordinal nature of the self-reported exposure estimates. The CONSTANCES study does not include self-employed workers, who are affiliated with other health insurance funds in France. This raises the question of the generalizability of the JEM. However, the source population represents more than 85% of the general population, including individuals living and working in diverse settings, individuals from different regions and different population density areas, and individuals that represent a broad range of socioeconomic status and occupations. We developed this JEM using a traditional non-gendered approach. Given evidence that sex and gender influence the reported frequency and magnitude of awkward postures and physical workload within the same job title and task, future work should evaluate the differences in individual-level reports within each PCS group, and consider sex-specific/gender-specific stratification.

Reported job titles in our study were assigned a standardized PCS job code using the automated SiCore coding system. This process coded 87% of provided job titles, consistent with coding results in previous surveys. Manual coding of the currently uncoded jobs will allow future adjustments to the CONSTANCES JEM in case these uncoded jobs were substantively different from those automatically coded.

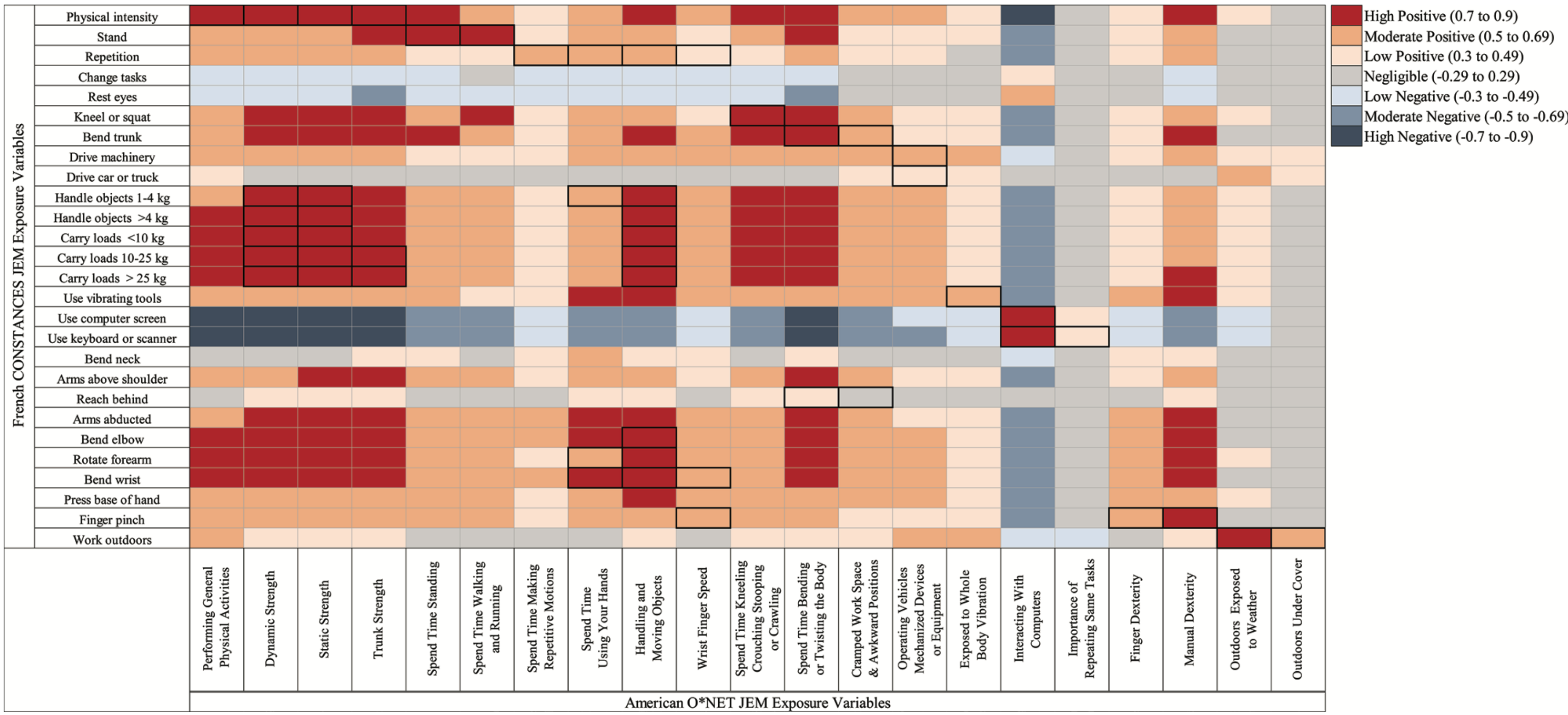
Conclusion: JEMs can be constructed using self-reported data; this method of obtaining data uses workers' knowledge of their jobs, while pooling this information at the level of the job reduces information bias. We developed a JEM using self-reported data for 27 physical risk factors. Our results demonstrated the ability of this novel JEM to create HEGs of physical risk factors that discriminated between different jobs. This JEM provides a potentially robust assessment method for assigning current or cumulative workplace physical exposures in general population studies.

Aim 2: Compare exposure estimates from the new French JEM to exposure estimates from an American JEM.

Correlations between French and American exposure measures: Strength and direction of correlation coefficients between 27 French JEM and 21 American JEM exposure variables were represented by a heat map (Figure 2). The heat map consists of a matrix of elements with different hues and intensity of colors representing ranges of Spearman correlations. Positive correlations are represented by warm (red) colors, while negative correlations are represented by cool (blue) colors. Correlations closer to zero are represented by neutral shading. Of 567 total variable pairs, 269 had correlations $\rho \geq 0.50$ (moderate positive correlation); 103 pairs had correlations $\rho \geq 0.70$ (high positive correlation). There were 11 physical exposure pairs that had correlations less than −0.70 (high negative correlation). Among these pairs were use keyboard or scanner (French JEM) or use computer screen (French JEM) versus performing general physical activities (American JEM). As expected, these strong but negatively correlated pairs consisted of variables that measured mutually exclusive exposures (e.g. manual physical work vs. office work).

In Figure 2, we emphasized a priori matched exposure variable groups with bold outlined boxes. Of the matched pairs, all matched physical exposures were positively correlated, ranging from $\rho=0.27$ (reach behind [French JEM] vs cramped work space and awkward position [American JEM]) to $\rho=0.83$ (physical intensity [French JEM] vs trunk strength [American JEM]).

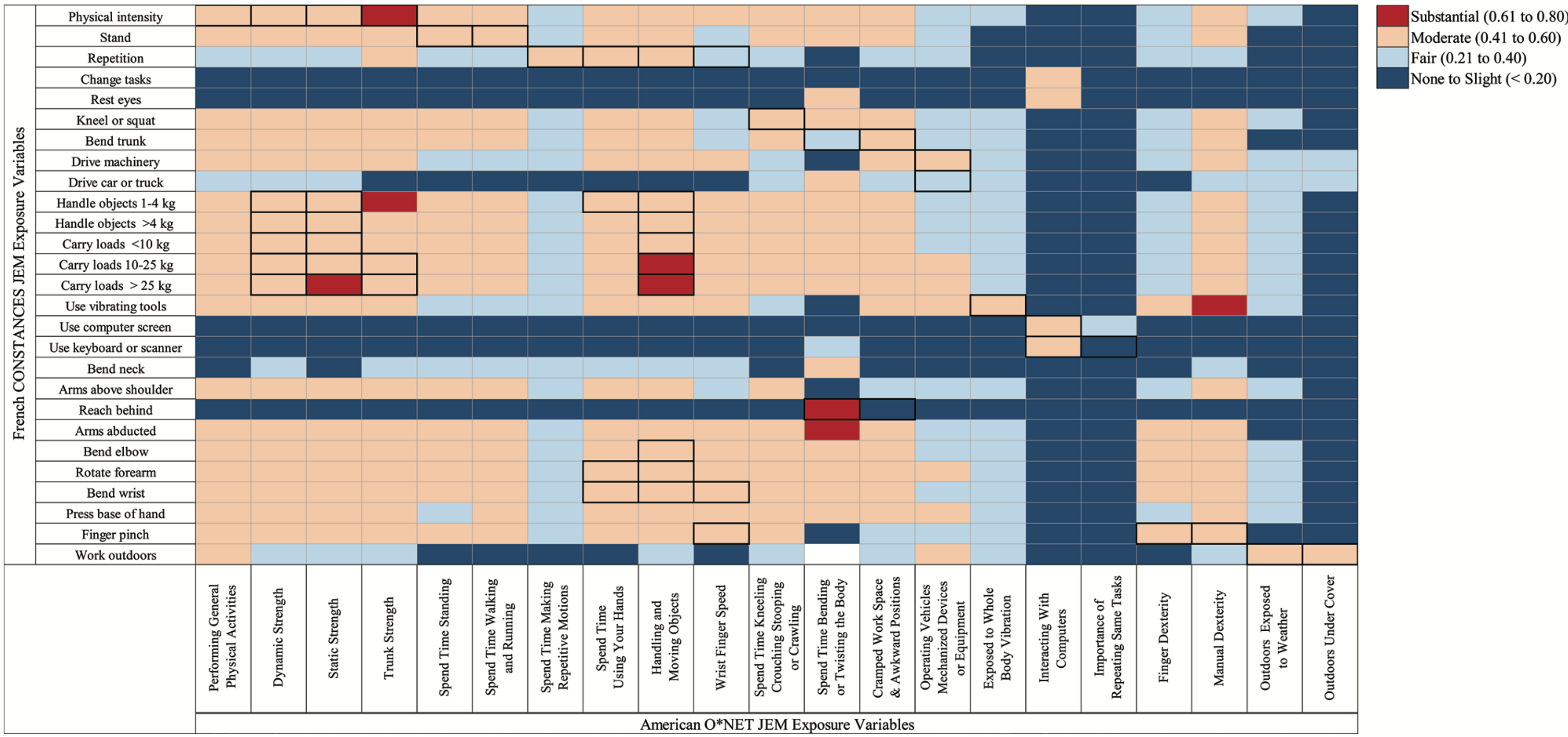
Figure 2: Heat map of Spearman's correlations between French JEM and American JEM exposures. Similar exposure matches highlighted with black outline. correlation ranges grouped by conventional Spearman's correlation interpretations. n=367 PcS codes. Matched exposure variable pairs are outlined with black boxes.



Thirty-three of 50 matched pairs had correlations ρ ≥0.70 (high correlation). The exposure pairs that led to the highest correlations were related to physical intensity (French JEM) and various strength exposure categories in the American JEM (dynamic strength, static strength and trunk strength). Several variable pairs that were not explicitly matched a priori had correlations greater than 0.70. For instance, handle objects (1–4 kg and >4 kg) and carry loads (<10 kg) had correlations greater than 0.70 with trunk strength. Overall, these results indicate that the most similar type of exposures from variables in the French and American JEMs showed strong positive correlations, dissimilar exposure variables showed weak relationships, and exposures expected to be mutually exclusive showed strong negative correlations.

Agreement between French and American exposure measures: We created a heat map to represent the kappa values between 27 French JEM physical exposure variables and 21 American JEM variables (Figure 3 below). Cohen's kappa (κ) indicates the level of agreement in high and low exposure groups between French JEM exposures and American JEM exposures after dichotomizing exposure estimates at the median exposure level. In Figure 3, different colors represent the strength of the paired relationships, where darker shades indicate stronger agreement. There were no kappa values that exceeded κ=0.62. Of the 567 pairs, 246 pairs had kappa agreements greater than moderate agreement, while 194 pairs showed slight/no agreement. Kappa values for all exposure variable pairs are shown in online supplementary material for our publication (Evanoff, 2019a). Similar to Spearman's correlations, we outlined the 50 matched variable pairs in Figure 3. Among all matched variable pairs, the kappa values ranged between κ=0.13 (reach behind [French JEM] and cramped work space and awkward positions [American JEM]) and κ=0.62 (physical intensity [French JEM] and trunk strength [American JEM]). We observed that 46 of 50 *a priori* matched exposure pairs showed moderate to substantial agreement in assignment of high versus low exposure level. Exposure pairs that indicated no agreement were observed with variable pairs that measured dissimilar exposures, including reach behind (French JEM) and outdoors exposed to weather (American JEM) (κ=0.02), as well as drive car or truck (French JEM) and spend time standing (American JEM) (κ=−0.02).

Figure 3: Heat map of cohen's kappa agreement values between French and American JEM exposures. Similar exposures are matched and highlighted with a black outline. Kappa ranges based on conventional Cohen's kappa interpretations. n=367 PCS codes. Matched exposure variable pairs are outlined with black boxes.



Discussion: This study found moderate to high positive correlations and moderate to substantial agreement between similar exposure variables when comparing two general population JEMs for workplace physical exposures. Generally, we found the strongest correlations and agreement between French and American JEM exposures related to force, particularly whole body high forceful exertions (eg, carrying/handling various loads [French JEM] vs static strength [American JEM]: $0.75 \leq \rho \leq 0.82$, $0.59 \leq \kappa \leq 0.61$). Several explanations exist for these stronger associations. The exposure estimates in both JEMs may be similarly distributed; both general population JEMs were created from jobs within industrialized countries where exposures related to heavy lifting and forceful exertions are relatively uncommon at the population level. Stronger correlation and agreement have been observed between self-reported and expert observations for maximum force compared with posture, repetition and movement velocity in other studies.

Along with the strengths of this study, there were several limitations. Our cross-walk involved a multistep process (PCS→ISCO-88→ISCO- 08→SOC) in order to match French PCS codes with American SOC codes. Although existing software programs and tools assisted in the assignment of job codes, selections included some level of subjective opinion, possibly leading to differential or non-differential misclassification that may have affected the observed levels of correlation and agreement. If the cross-walk process was performed by another research group, different matches between PCS and SOC codes might occur. Our analyses were performed at the level of the job title; each of 367 PCS codes was weighted equally in the analysis. The levels of correlation and agreement may be different from those observed in this study if they are applied to different working populations with varying distributions of workers in each job.

Questions within CONSTANCES and O*NET measured similar but not identical constructs and used different ordinal scales with different ranges and anchors. Most CONSTANCES scales measure the duration of exposures defined by frequency or intensity, while O*NET scales represent the magnitude of exposure or the frequency of an exposure. As expected, we did not observe perfect correlations, but when French and American JEM variables were matched and grouped based on similar exposures, the majority of matched pairs were highly correlated. The levels of correlation and agreement were quite high given the differences in scales and questions between the two JEMs. We used Cohen's kappa statistic to calculate the level of agreement in high and low exposure groups between French JEM and American JEM variables. Exposures were dichotomized at the median exposure estimate, a common practice to define high and low exposed in JEMs. However, dichotomization may have led to lower measured agreement than using the full range of data. Also, the selection of the cut-off point remains arbitrary and may not equally optimize the specificity and sensitivity of all exposures. Raising or lowering the cut-off point may lead to differential effects on uncommon and common exposures. Further analysis to determine optimal cut-off points in the French and American exposure estimates will aid the interpretation of exposure–outcome associations obtained using JEM exposures.

The majority of the 50 variable pairs matched a priori based on common exposures showed high correlation and at least moderate agreement. We also saw high correlation or agreement between a number of unmatched variable pairs. These exposures are likely to covary, as they occur in highly physically demanding jobs. For instance, we observed high correlation and agreement between handle objects 1–4 kg and trunk strength. Handling objects and carrying loads are complex multi-joint dynamic activities that require trunk strength; these demands would co-occur in jobs requiring manual material handling. As expected, exposure variables that were mutually exclusive (e.g. use computer screen/ use keyboard or scanner vs. performing general physical activities) showed high negative correlation and low agreement.

Overall, our results suggest that job-level physical exposure estimates were similar between the French JEM American JEMs. Further cross-national comparisons with other available physical exposure JEMs will further inform this rapidly expanding area of occupational disease epidemiology. Comparisons of exposure estimates from different countries can improve our understanding of exposure–outcome relationships and explain variation in their findings. Future work will also evaluate the ability of different JEMs to reproduce known exposure– response associations obtained with other exposure assessment methods. JEMs that can be applied cross-nationally may also enable multinational studies of associations between workplace exposures and diseases, and inform region-specific or cohort-specific JEMs. Cross-national comparisons of JEMs could also provide additional exposure data to complement existing national JEMs that might lack particular exposures.

Conclusion: We conducted a cross-national comparison between physical exposure estimates of a general population French JEM, based on individual self-reported data, and a general population American JEM (O*NET), based on expert opinion and worker self-reports. We demonstrated that these JEMs were strongly related to each other, sharing high correlations and moderate agreement between the majority of variable pairs that measured similar exposures. Our results suggest that French and American JEMs may be suitable for use in other populations without available general population workplace physical exposure data, and may complement existing JEMs that might lack particular exposures of interest.

Aim3: Compare upper extremity exposure estimates from the French and American JEMs to observed exposures from a large American cohort.

In this aim we compared the individually observed exposures from the NIOSH UE Consortium to the exposures estimated from the French CONSTANCES JEM and the American O*NET JEMs. Among the 54 *a priori* matched pairs of exposures, correlation coefficients between CONSTANCES JEM assigned exposures and consortium individual-level observed exposure variables ranged from -0.01 to 0.36. 9 pairs demonstrated low positive correlations while the remaining 45 pairs were negligibly correlated. Between CONSTANCES JEM and consortium observed variables, Cohen's kappa values ranged between -0.07 and 0.37. Of the 54 matched pairs between CONSTANCES and individual-level measures, 17 pairs demonstrated fair agreement. Unmatched exposure variable pairs showed low correlation and low-to-fair agreement.

We also compared O*NET and CONSTANCES JEM exposure variables with consortium observed measures at the level of the job (rather than the individual worker) for 130 SOC job codes. Between CONSTANCES and consortium estimates, correlations ranged between 0.06 (negligible) and 0.59 (moderate). Of 54 matched exposure pairs, 27 were moderately correlated. Cohen's kappa values ranged between -0.02 and 0.51. 23 matched pairs demonstrated moderate agreement.

We also found mostly low correlations and slight agreement between matched variables from the O*NET JEM and consortium individual-level measures when assigned to workers. Comparing CONSTANCES and O*NET JEM exposure estimates assigned to workers, the correlations between matched variables were minimal but agreement was fair to moderate. When comparing exposure estimates at the job level, correlation and agreement between CONSTANCES JEM, O*NET JEM, and individual-level measure variables were substantially higher. Full tables and results can be found in published and supplementary materials from our publication “Applying two general population job exposure matrices to predict incident carpal tunnel syndrome: A cross-national approach to improve estimation of workplace physical exposures” (Yung, 2020b)

Discussion: Although we observed meaningful exposure–disease associations with incident CTS using the CONSTANCES and O*NET JEMs (see Aim 4b below), we observed negligible-to-low correlations and low-to-fair agreement between individual level exposure measures comparing the observed exposures from the consortium study and exposures estimated by both JEMs. In part, these results likely reflected the different scales and methods used to obtain exposure data from CONSTANCES, O*NET, and the NIOSH UE consortium study. These results also reflect analysis at the individual worker level rather than at the job title level. In Aim 2, we found moderate-to-high positive correlations and moderate-to-substantial agreement between CONSTANCES and O*NET exposure variables at the job level for 367 job codes; in that analysis, each job code was weighted equally. In the current study, we observed higher correlations and agreement between JEM exposure estimates when comparing agreement at the job level than when comparing agreement at the individual worker level; when assigning exposure estimates at the worker level, correlations and agreement are dependent on the distribution of workers in different jobs within the population. The comparison of JEM exposures with the NIOSH UE Consortium data also examined a smaller number of job codes (130 SOC codes and 77 PCS codes) than the previous CONSTANCES to O*NET comparison (367 job codes). The strength of agreement between JEM and other exposure estimates may be influenced by the distribution of the worker population and the number of jobs under study; both of these factors may influence the within-job versus between-job variation in JEM-based exposure estimates.

Aim 4a: Examine associations between the French JEM and *current pain* in the hand-wrist, shoulder, low back and knee among participants in the CONSTANCES cohort.

Worker characteristics: The validation sample cohort shared similar demographics as the cohort used for the creation of the JEM, with striking similarities in the distribution of workers by broad socio-professional job categories (i.e., the first digit PCS code) and nearly identical distribution by sex. In both cohorts, the largest number of workers represented civil servants, managerial staff, and higher intellectual professions, as well as workers representing associate professionals in teaching, health, and administration. We found that in both the JEM cohort and validation sample cohort, there was a higher distribution of female (55%) than male workers (45%). Workers in the validation sample were somewhat younger than the JEM creation cohort, with a lower proportion of workers who were 65 years or older. Mean and median exposure ratings were generally consistent between the two cohorts.

In the validation sample cohort, 14.7% of the 38,730 participants reported current low back pain, followed by neck pain (9.9%) and knee pain (8.6%). Overall, 26.5% of the validation sample cohort reported current pain at one or more body locations, while 45.4% reported chronic pain at one or more body locations (occurring 30 days or more in the previous year). 23.9% reported chronic low back pain.

Comparison of Level of Agreement between self-reported exposures and JEM-assigned exposure estimates: Overall, agreement between individually self-reported and JEM-assigned exposures was fair to good. Weighted kappa values ranged from $\kappa = 0.16$ (variable: “Reach Behind”) to 0.71 (variable: “Use Computer Screen”). Six exposure variables demonstrated good agreement (variables: “Physical Intensity”, “Stand”, “Handle Objects 1-4 kg”, “Handle Objects >4kg”, “Use Computer Screen”, and “Use Keyboard or Scanner”), fifteen exposure variables demonstrated moderate agreement, five variables demonstrated fair agreement, and one variable demonstrated poor agreement, consistent with the differences in individual level exposure variance explained by job codes seen in Aim 1.

Associations between self-reported exposures, JEM-assigned exposure estimates, and musculoskeletal pain: We calculated prevalence ratios of musculoskeletal pain at six body locations (hand, elbow, shoulder, low back, knee, and neck) using self-reported and JEM-assigned exposure estimates. We observed consistent and significant exposure-outcome relationships for both self-reported and JEM-assigned exposure estimates in both continuous and dichotomous models for all six body locations. Effect sizes from JEM estimates were marginally attenuated compared to effect sizes from self-report. Generally, we observed that longer exposure durations were associated with higher prevalence of musculoskeletal pain. Consistent with previous studies, two variables (“Use Computer Screen” and “Use Keyboard or Scanner”) were significantly *protective* of hand and neck pain using both self-reported and JEM-assigned estimates for continuous and dichotomous models.

Discussion: After assigning CONSTANCES JEM exposure estimates to a large validation sample of CONSTANCES participants, we first evaluated the agreement between exposure values obtained from individual self-report and from JEM-assigned estimates. Of the 27 physical exposure variables, 21 variables demonstrated moderate to good agreement. Second, we evaluated associations of self-reported and JEM-assigned exposure estimates with current musculoskeletal pain at six body locations; both exposure estimation methods demonstrated significant exposure-outcome associations with musculoskeletal symptoms, with generally similar results. These findings support the conclusion that a general population JEM for physical exposures, including this CONSTANCES JEM, can be an effective method to estimate workplace exposures.

In this study, we compared the CONSTANCES JEM to individual self-report between similar population samples and identical exposure variables. The point estimates of JEM-assigned estimates were marginally attenuated compared to individual self-report; JEMs usually do not take into account variability of exposures between workers within the same job codes, since the same value is assigned to all workers each job code. Using a JEM to assign a single exposure estimate for each code may then result in non-differential misclassification of exposures and may consequently attenuate risk estimates towards the null. However, in both continuous and dichotomous Poisson regression models, we observed substantially similar, statistically significant associations for the same variables in all body locations using both exposure methods. Generally, our *a priori* selected variables demonstrated meaningful positive associations with musculoskeletal pain, with the exception of variables estimating computer use and the outcomes of hand pain and neck pain. Our results indicated that computer use was significantly protective for hand and neck pain. In this general population study, office workers were compared to workers in other job sectors, who were more highly exposed to other physical factors such as forceful exertions, heavy lifting and carrying, vibration, and awkward postures.

We observed consistent exposure-outcome associations using JEM-assigned exposure estimates with self-reported exposure data, indicating that a JEM is a reasonable exposure assessment method to predict prevalent MSD symptoms in a general population cohort. Self-reported data are susceptible to information biases due to individual variation in reporting, and to potentially biased reporting when symptoms and exposures are reported at the same time in cross-sectional studies. A JEM based on self-report minimizes these potential information biases as it consists of pooled exposure data from all workers, and assigns exposures at the job level. A JEM constructed from self-reported exposures makes use of workers' knowledge and provides a method to estimate cumulative exposure. Unlike self-reported data, a JEM can also be applied retroactively to assign past exposures based on job titles that can then be used to study current or future chronic diseases.

JEMs are simple, cost-effective, and useful tools that provide a source of workplace exposure data, particularly for epidemiological studies that lack individual-level exposure data. Our results suggest that the CONSTANCES JEM based on self-reported physical exposures from asymptomatic workers replicates known associations between physical risk factors and prevalent MSD symptoms. Physical exposure JEMs, such as the CONSTANCES JEM, open avenues of research in the prevention of MSDs and other health conditions related to workplace physical activities.

<u>Aim 4b: Examine associations between the French and American JEMs and incident CTS in the NIOSH Upper Extremity Consortium cohort.</u>

This aim examined associations of workplace exposures with incident Carpal Tunnel Syndrome, using the French and American JEM exposure in addition to the individual observed exposures used in the prior UE consortium studies. As shown in Table 2 below, Hazard Ratios (HR) for consortium individual-level observed measures ranged from 1.00–1.42 for continuous exposure models. Of 11 consortium exposure variables, 9 were statistically meaningful, with the highest HR value observed with composite exposure measure provided by the ACGIH TLV. In analyzing the dichotomous models, 5 exposure variables were statistically meaningful.

All 8 O*NET variables were statistically meaningful in their relationship to incident CTS. HR ranged from 1.31 (95% CI 1.01–1.70) (wrist finger speed) to 2.01 (95% CI 1.55–2.59) (spend time using your hands) in the continuous models. We observed HR ranging from 0.99–1.64 in the dichotomous models where 4 variables were statistically significant.

HR for CTS from continuous models were in the range of 1.08–2.05 for CONSTANCES exposure variables. Of 11 variables, only 2 were statistically meaningful. "Finger pinch" demonstrated the highest HR of 2.05 (95% CI 1.38–3.06), followed by "rotate forearm" (HR 1.44, 95% CI 1.10–1.89). Dichotomous models showed HR between 0.81–1.46, only "repetition" was statistically significant.

In summary, we observed significant exposure–disease associations using O*NET JEM exposure variables to predict CTS in a US worker population; these associations were broadly similar to variables assessed by individual-level measures. We also observed some, but fewer, significant exposure–disease associations using the CONSTANCES JEM to predict CTS in a US worker population.

Table 2: Hazard ratios (HR) and 95% CI calculated from Cox proportional hazard models to evaluate relationship between baseline physical exposure and incident CTS. Adjusted for age, gender, body mass index (BMI), and research site. Applied with robust sandwich estimates (Lin & Wei, 1989). N=2393. [JEM=job exposure matrix]

Exposure variable	Continuous exposure (per 1-unit increase)		Dichotomous exposure (at median)	
	HR	95% CI	HR	95% CI
CONSTANCES JEM				
Physical intensity	1.08	0.99–1.18	1.21	0.83–1.76
Repetition	1.27	0.91–1.77	1.46	1.08–1.99
Handle objects 1–4kg	1.15	0.95–1.39	1.10	0.74–1.66
Handle objects >4kg	1.12	0.91–1.37	1.16	0.74–1.83
Carry loads <10kg	1.14	0.92–1.41	1.24	0.80–1.92
Carry loads 10–25kg	1.08	0.87–1.35	0.81	0.55–1.17
Carry loads >25kg	1.13	0.87–1.47	1.33	0.89–1.99
Rotate forearm	1.44	1.10–1.89	1.40	0.97–2.00
Bend wrist	1.39	0.92–2.09	1.13	0.75–1.69
Finger pinch	2.05	1.38–3.06	1.35	0.91–2.02
Use vibrating tools	1.31	0.97–1.77	1.37	0.90–2.07
O*NET JEM				
Performing general physical Activities	1.34	1.12–1.60	1.49	1.06–2.09
Trunk strength	1.53	1.23–1.90	1.39	0.90–2.14
Static strength	1.43	1.20–1.71	1.31	0.89–1.95
Dynamic strength	1.61	1.29–2.00	1.64	1.14–2.38
Handling & moving objects	1.33	1.16–1.52	1.49	1.04–2.14
Spend time making repetitive motions	1.41	1.11–1.78	1.26	0.89–1.77
Wrist finger speed	1.31	1.01–1.70	0.99	0.66–1.49
Spend time using your hands	2.01	1.55–2.59	1.51	1.09–2.09
Consortium (individual-level measures)				
Peak hand force (worker rated)	1.10	1.04–1.16	1.91	1.39–2.61
Peak hand force (analyst rated)	1.16	1.09–1.25	1.38	1.08–1.76
Hand activity level (analyst rated)	1.08	0.96–1.22	1.28	0.90–1.83
ACGIH TLV (worker rated)	1.21	1.07–1.37	1.52	1.14–2.03
ACGIH TLV (analyst rated)	1.42	1.25–1.63	1.73	1.18–2.54
Repetition per minute for all exertions	1.01	1.00–1.02	1.24	0.92–1.69
Repetition per minute for forceful exertions	1.02	1.01–1.02	1.38	0.98–1.95
Duty cycle of all exertions	1.00	1.00–1.01	1.05	0.74–1.49
Duty cycle of forceful exertions	1.01	1.01–1.02	1.74	1.38–2.20
%Time ≥50 ° wrist extension	1.00	0.99–1.00	0.77	0.57–1.05
%Time ≥30 ° wrist flexion	1.02	1.00–1.04	1.15	0.87–1.51

We also explored models combining CONSTANCES, O*NET, and individual-level measures to predict incident CTS. In short, combining exposure variables from two sources of exposure information improved model performance compared to a single source of exposure information. Combining CONSTANCES JEM variables with O*NET JEM variables better predicted CTS than a model of only O*NET variables. Combining either CONSTANCES JEM or O*NET JEM exposure variables with individual-level measures also improved model performance, as assessed by higher c-indices (P=0.01 to P=0.02) and lower AICs (Δ=-16.6 to Δ=-10.30).

Table 2 Hazard ratios (HR) and 95% CI calculated from Cox proportional hazard models to evaluate relationship between baseline physical exposure and incident CTS. Adjusted for age, gender, body mass index (BMI), and research site. N=2393. [JEM=job exposure matrix]

Discussion Aim 4b: We observed meaningful exposure-disease associations with incident CTS in a US worker population using job-title based exposure estimates from both the American O*NET JEM and the French CONSTANCES JEM. In this American worker cohort, more significant exposure-disease associations were found using the American JEM than the French JEM. Combining exposures from two JEM or combining exposures from a JEM with individual-level measures improved the prediction of CTS in exploratory models. We previously evaluated a subset of O*NET exposure variables and their relationship with incident CTS (Dale, 2018) and found that O*NET JEM exposure estimates predicted CTS with similar effect sizes as exposure values obtained from individual-level measurement. In this study, we extended this evaluation by including three additional O*NET variables and found similar, significant exposure–disease associations using O*NET JEM exposure estimates, particularly with variables related to strength and job demands requiring hand motions. We also evaluated the French CONSTANCES JEM, which includes physical exposures not available through O*NET, including pinch grip, hand or wrist posture, and hand vibration. CONSTANCES exposure variables pertaining to repetition were statistically meaningful in both continuous and dichotomous survival analysis models, while “rotate forearm” and “use vibrating tools” were statistically meaningful predictors in log binomial analyses. Differences between O*NET and CONSTANCES questions and scales might help explain contrasts in the exposure–disease associations between seemingly similar exposure variables. Most of the O*NET variables we tested address the *magnitude or intensity* of exposure, whereas CONSTANCES variables pertain to *duration* of exposure at a given intensity or frequency.

Differences in constructs between general population JEMs provide an opportunity to combine complementary variables into a single multivariable model. Hybrid exposure assessment methods have been used in studies of prostate cancer risk and shoulder disorders. Since the development of MSD is multifactorial, relying on a single source of exposure information may not provide the optimal breadth of physical exposure data, and hybrid exposure methods may offer the opportunity to improve precision while maintaining the efficiency of a JEM. Our exploratory comparison of multivariable exposure models supports the use of combining data obtained from individual-level measures with JEM data, and combining data from different JEM. These findings warrant further research in combining exposure data from different methods to better predict risks of work-related MSD.

Overall, our results suggest that O*NET JEM and to some degree CONSTANCES JEM can reproduce known exposure–disease associations obtained from individual level measures. Combining exposure estimates between two JEMs and between JEM and individual-level measures improved the prediction of CTS when compared to single source models. Exposure information from a JEM could potentially enrich existing individual-level datasets or complement an existing JEM that might lack particular exposures.

Conclusion Aim 4b: Both O*NET and CONSTANCES JEM demonstrated meaningful exposure–disease associations with incident CTS. The O*NET general population JEM demonstrated generally similar results as individual-level measures when calculating exposure–disease associations for CTS in the same worker cohort while the CONSTANCES JEM demonstrated fewer associations for CTS. This suggests that these JEM are useful tools for estimating workplace physical exposures in population studies. In exploratory models, adding exposure data from JEM to individual level measures improved the prediction of incident CTS in our study, as did combining data from JEM from two different countries. These data suggest potential for combining exposure methods to improve the estimation of workplace physical exposures for surveillance and epidemiology studies. The performance of a general population JEM is influenced on the distribution of jobs within the studied worker population; in most cases it is likely that a larger variability of jobs within a studied cohort will improve the ability of general population JEM to demonstrate exposure–disease associations.

Additional work outside the original study aims:
This project was also responsible for a number of additional findings and publications beyond the original four study aims described above. These studies included additional exposure assessment comparisons and applications of the JEM in collaboration with our French colleagues, methods studies, application of the JEM to epidemiology studies, and a translational study demonstrating the theoretical effectiveness of new exposure limits on forceful hand exertion.

Exposure assessment studies: The aims of our grant focused on current work exposures. Working with our French colleagues, we have used the CONSTANCES JEM in conjunction with lifetime job histories to construct cumulative physical exposure assessments across the working lifetime, in order to better study chronic musculoskeletal disorders, as well as other chronic diseases such as cardiovascular disease that may be moderated by physical activity.

In “Comparison Between a Job-Exposure Matrix (JEM) Score and Self-Reported Exposures for Carrying Heavy Loads Over the Working Lifetime in the CONSTANCES Cohort,” (Ngabirano, 2020b) we used lifetime job histories to construct cumulative measures of lifting and carrying heavy loads over the working lifetime. We also found that cumulative exposures based on the JEM were predictive of current knee and low back pain.

In another study with French colleagues, we compared a JEM that was created based on expert estimates of exposure with the CONSTANCES JEM (based on workers’ self reported exposures). Comparison Between a Self-Reported Job Exposure Matrix (JEM CONSTANCES) to an Expertise-Based Job Exposure Matrix (MADE) for Biomechanical Exposures. (Descatha, 2019a)

Methods development: In order to code jobs using a JEM, the job titles and industries must first be coded into standard occupational classifications. Another spin-off paper from this grant tested the “Efficiency of autocoding programs for converting job descriptors into standard occupational classification (SOC) codes.” (Buckner-Petty 2019) This was the first paper to directly compare two publicly available job coding programs (NIOCCS and SOCCER). We entered industry and occupation descriptions from two existing cohort studies into two publicly available SOC autocoding programs. SOC codes were also assigned manually by experienced coders. These SOC codes were then linked to exposures from the Occupational Information Network (O*NET). Agreement between the SOC codes produced by autocoding programs and those produced manually was modest at the 6-digit level, and strong at the 2-digit level. Importantly, O*NET exposure values based on SOC code assignment showed strong agreement between manual and autocoded methods. We showed that both available autocoding programs can be useful tools for assigning SOC codes, allowing linkage of occupational exposures to data containing free-text occupation descriptors. Importantly, the assigned exposure values showed stronger agreement than the job codes, as closely related jobs with different SOC codes tend to have similar physical exposures. These data suggest that autocoding job and industry information and linking the resulting SOC codes to a JEM can provide an efficient and useful means for assigning workplace exposures in large cohort studies based on reported job titles.

<u>Epidemiology studies:</u> Two published studies, and several more studies underway have used the new JEM to analyze data from the large CONSTANCES study. One study (Fadel, 2019) examined associations between occupational exposure and Dupuytren's contracture in the CONSTANCES cohort using hand exposure values from our JEM. Importantly, this study used the JEM to assign cumulative exposures across the working life. Using the JEM we assessed exposure to vibration and/or forearm rotation for participants whose work history was available. Surgery for Dupuytren's contracture was determined by linkage to national health insurance records. Work history was retrieved for 23 795 subjects among whom 98 underwent surgery for Dupuytren's contracture. Adjusted OR (aOR) was 2.08 (1.03-4.2) for being ever exposed to vibration and/or forearm rotation for subjects <60 years and 1.20 (0.69-2.08) for subjects ≥60 years. These data showed that manual work is associated with surgery for Dupuytren's contracture among younger workers, and showed the utility of a JEM for estimating exposures across multiple past jobs.

Another study (Ngabirano, 2020a) studied the association between lifetime exposure to carrying heavy loads and limitations in climbing stairs in the French CONSTANCES study. We again combined our Job-Exposure Matrix (JEM) with lifetime job histories to build a cumulative exposure score, and compared lifetime work exposures to reported limitations in climbing stairs. Reported difficulties in climbing stairs was associated with cumulative exposure to carrying heavy loads: adjusted PR= 2.17 (1.75-2.73) for men, 1.50 (1.30-1.74) for women. Use of our JEM allowed the demonstration that cumulative work exposure to carrying heavy loads across the working life was associated with physical limitations in climbing stairs.

<u>Translational studies:</u> Based on the success of our grant aims, we have also published on future use of JEMs to facilitate research in occupational health, and to use JEMs as a tool in occupational medicine practice and in public health.

One paper arising from our cross-national comparison aims was a proposal to extend cross national JEM research and investigate the creation of a common JEM that could be used internationally. “JEMINI (Job Exposure Matrix InterNatIonal) Initiative: a Utopian Possibility for Helping Occupational Exposure Assessment All Around the World?” (Descatha, 2019b). In 2021, the EU started an initiative to create a common JEM for musculoskeltal exposures, to faciliatate cross-national data pooling and “megacohort” studies, which our research group is engaged in. Another paper suggested that JEMs could be used for clinical medicine and public health. “Not just a research method: If used with caution, can job-exposure matrices be a useful tool in the practice of occupational medicine and public health?” (Fadel, 2020)

Another study output modeled the effects of the 2018 revised ACGIH(®) Hand Activity Threshold Limit Value(®) (TLV) at reducing risk for carpal tunnel syndrome. (Yung 2019) Though not directly related to JEMs, this study analyzed the NIOSH UE consortium data used in our validation aims to test how many cases of CTS would have been prevented if our cohort were exposed at or below the revised 2018 standard rather than at or below the 2001 TLV. We compared the effect of applying the 2018 TLV vs. the 2001 TLV to predict incident CTS within a large occupational pooled cohort study (n = 4,321 workers). We found that eliminating exposures above the 2001 TLV might have prevented 11.2% of all cases of CTS seen in our pooled cohort, vs. 25.1% of cases potentially prevented by elimnating exposures above the 2018 value. We concluded that the 2018 revision of the TLV better protects workers from CTS, a recognized occupational health indicator important to public health. We also found that a significant number of workers in the NIOSH UE cohort were exposed to forceful repetitive hand activity above these national guidelines. We concluded that public health professionals should work to increase awareness of these new guidelines and encourage employers to reduce hand intensive exposures to prevent CTS and other musculoskeletal disorders.

Publications:

Publications directly supported by the NIOSH grant:

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