EXAMINING THE ASSOCIATION BETWEEN LOCATION-SPECIFIC CHRONIC PAIN AND OBJECTIVELY MEASURED PHYSICAL ACTIVITY

by

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Abstract

Background Chronic pain (CP) is an important public health problem because of its high prevalence and its effects on the physical and psychological well-being of individuals. The association between CP and physical activity (PA) has been discussed in previous literature. However, in most studies, the assessments of PA is done via self report, which can be affected by substantial bias and measurement error. In recent years, the use of wearable technology allowed the objective quantification of the frequency, duration, and intensity of PA. The current study is focused on assessing the associations between objectively measured PA chronic upper limb pain, chronic spinal pain, and chronic lower limb pain in U.S. adults.

Methods The sample was comprised of U.S. adults aged between 25 and 85 years from the 2003-2004 National Health and Nutritional Examination Survey data (NHANES, $N = 2,516$), and was stratified into age- and gender-specific groups. PA data obtained via hip-worn accelerometry were summarized into

ABSTRACT

6 objective measures of volume and 2 measures of fragmentation. Survey-weighted regression models were conducted which regressed each PA measure on location-specific pain indicator, with and without adjustment for potential confounders, including age, race/ethnicity, behaviors, and medical conditions.

Results Chronic upper limb pain, chronic spinal pain, and chronic lower limb pain showed higher prevalence among females and middle-aged study participants. All three types of CP were strongly associated with lower levels of physical activity in 45-65 years old females. Males aged 25-45 or 65-85 years old with either CP in spine or leg also engaged in less physical activity than those without pain. The statistical significance of the associations remained, even after adjusting for relevant covariates.

Conclusion This study identified statistically significant associations between objectively measured PA and self-reported CP. The magnitude of the signal varies with the reported location of CP, gender, and age category. These findings may inform that clinical management could be targeted by the CP location. Moreover, results emphasized the importance of wearable technology for providing objective and reproducible measurements in health-related research.

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Chapter 1

Introduction

1.1 Background of Chronic Pain

1.1.1 Definition & Impacts

Chronic pain (CP) is a highly prevalent health problem that is associated with high costs for the individual and the health system. According to the International Association for the Study of Pain (IASP), CP is defined as pain that persists beyond the normal tissue healing time [1]. Even after the illness or injury that caused pain has gone, the pain signals can still be sent and perceived for a prolonged period of time. Chronic pain is not always attributed to a specific cause; some people report it even if they have not suffered an injury or apparent body damage. Although it has become a health crisis due to its high prevalence, there is no universally accepted standard definition for

chronic pain. A common definition identifies chronic pain as pain lasting for at least three months. Other definitions include information about pain frequency and intensity [2, 3].

CP may be linked to conditions occurring in different painful regions. In the IASP criteria, CP has been categorized according to the body location: (i) head, face, and mouth; (ii) cervical region; (iii) upper shoulder and upper limbs; (iv) thoracic region; (v) abdominal region; (vi) lower back, lumbar spine, sacrum, and coccyx; (vii) lower limbs; (viii) pelvic region; and (ix) anal, perineal, and genital region [4]. In an internet-based survey studying the prevalence of chronic pain in the U.S. adults, the most common locations for CP were lower back, knee, neck, shoulder, and legs or feet [2].

CP is currently a major public health issue. The estimates of chronic pain prevalence vary from 10.1% to 55.2% according to 13 studies conducted in various countries including the U.K., Australia, Canada, and France [5]. Heterogeneity in these findings might be caused by factors including study samples, survey methodology, and CP definition [2]. In a multi-center study carried out in 1998 by the World Health Organization (WHO), chronic pain affected 22% of the world population [6]. In the U.S., from a study analyzing National Health Interview Survey data, an estimated 20.4% of U.S. adults (≈ 50.0 million) had chronic pain and 8.0% of adults (19.6 million) had high-impact chronic pain that limited at least one major life activity in 2016 [7].

CP may contribute to functional impairment, disability, depression and anxiety, and it is often difficult to treat [8]. Recently, lumbar and cervical pain has been identified as one of the 10 leading causes of incapacity worldwide [6]. In the U.S., 13% of the people who suffered pain in previous 2 weeks reported a reduced ability to work. Approximately 61 billion dollars of lost productivity

each year is estimated to be associated with CP [8].

In addition to the effects on the individual, CP increases the economic burden on health care services around the world. It has been reported that CP is associated with a two-fold increase in medical consultations and hospitalizations and five times higher utilization of emergency services. The estimated cost for CP in the United States is ranging from \$560 to \$635 billion annually [9]. In summary, CP has become a severe public health problem due to its effects on the individual well-being and health care services.

1.1.2 Risk Factors

Although the prevalence estimates of chronic pain differ in epidemiologic studies, the potential factors related to CP have been generally consistent [2]. For example, there is a higher prevalence of CP among females and the elderly population [10]. A two-fold increase has been reported in the odds of incidence of pain among the age group older than 75 years compared to the group between 18 and 25 years, which might be attributed to the aging of musculoskeletal system aging [6]. Moreover, non-Hispanic white adults have a higher prevalence of reported CP [7].

Furthermore, indicators of lower socioeconomic status, including lower education level, manual occupations, unemployment, and residence in public housing, are associated with an increased prevalence of CP [2]. CP is less prevalent among adults with a bachelor's degree or higher compared to all other education levels. A recent study showed that, among unemployed individuals the prevalence of CP was 78.9% compared to 39.8% among individuals with paid em-

ployment [11]. In addition cigarette use, alcohol use, marriage status, veteran identity, body mass index (BMI), mental health, genetics, and some medical conditions also have a close association with CP [10].

1.2 Chronic Pain and Physical Activity

In this section we focus on the association between CP and physical activity (PA). It is well known that regular physical activity is closely related to the improvement and maintenance of health [12, 13]. Several large population studies have shown that individuals with CP have lower levels of PA than healthy controls, and those who are more physically active have a lower risk of developing CP and reduce ongoing pain symptoms. For example, a 14-year prospective longitudinal study investigated whether exercise was associated with a substantial reduction in musculoskeletal pain after controlling for gender and BMI [14]. The epidemiological research from the Nord-Trondelag Health Study (HUNT 3) identified a linear association between CP and the frequency, duration, and intensity of recreational exercise for the older individuals. It found that the prevalence of CP was 21% to 38% lower among older women who have higher levels of physical activity [15]. Another cross-sectional study found a U-shaped relationship between PA and lower back pain (LBP), concluding that both the extremes of low and high PA levels are associated with a high risk of LBP [16].

PA and CP could be connected bidirectionally, although the direction of causality has not yet been inferred. Some evidence supports the idea that individuals with pain may reduce their activity and PA reduces CP by counteracting the

decline in pain modulatory capacity [17]. Several studies have focused on the association between PA and CP, especially on how PA is associated with chronic widespread pain (CWP). CWP is defined by the American College of Rheumatology (ACR) as the pain in the left and right sides of the body, above and below the waistline, together with axial skeletal pain [18]. A study showed that individuals with CWP tended to have lower activity counts per minute and less time spent in moderate-to-vigorous PA than people without CWP. However, sedentary behavior, light, and lifestyle PA were not found to be associated with CWP status [19]. The study also identified gender differences in the prevalence of CWP and PA among U.S. adults [20]. Our research focus is CP in several specific body sites, including chronic spinal pain, which is the biggest cause of years of life with disability worldwide [21]. Our overall goal is to examine the association between location-specific CP and PA.

An important aspect of our analysis is to use the objectively measure PA data. Most traditional investigations characterizing PA in adults with CP were based on questionnaires and surveys. However, self-reported assessments of PA are highly subjective and imprecise, leading to potential measurement errors as well as substantial recall, cognitive and social desirability bias [22–24]. Participants may also have different perceptions of PA intensity, timing, and volume and their answers can be affected by cognitive impairment, which is related to their health status, age, mood, and psychosocial factors [25]. Wearable devices that include accelerometers provide detailed, objective measurements of daily PA which can complement the self-reported PA. Accelerometers typically measure the acceleration of a particular part of the body (e.g., thigh, hip, wrist) in three orthogonal axes and is measured in m/s^2. The raw data are typically summarized at the minute level using proprietary algorithms (e.g., activity counts) or open source algorithms (e.g., Euclidian Norm Minus One [26],

Activity Index [27, 28], Mean Amplitude Deviation [29]). The advantage of accelerometers is that they can be used to track continuous activities of daily living at high resolution, and then provide the duration, intensity, and patterns of PA data within and across days [30].

As the associations between self-reported and objective measures of PA tend to be weak in general and weaker within populations with CP [25, 31], characterizing PA with accelerometers becomes an exciting alternative to subjectively measured PA. Unfortunately, there is a very limited literature on the association between CP and objectively measured PA. To address this problem, we focus on the National Health and Nutrition Examination Survey (NHANES), which contains measures of free-living PA behaviors using hip-worn accelerometers in a population-based sample in the US. We will focus on quantifying and comparing PA intensity, volume and patterns among adults with or without CP at different body locations [32].

Chapter 2

Methodology

2.1 Data

2.1.1 NHANES Datasets

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative, cross-sectional survey conducted by the Centers for Disease Control (CDC) to provide information on the health and nutritional status of the U.S. population. It began in the early 1960s and became continuously implemented since 1999 [32]. It combines interviews collecting person-level demographic, health-related, and socioeconomic information, combined with medical, dental, and physiological examinations as well as clinical laboratory tests [33]. Therefore, "NHANES data could help monitor trends in the prevalence, awareness, treatment, and control of specific diseases and provide

information for medical and public health studies" [34].

NHANES datasets are released in 2-year cycles [33]. Our analysis uses the NHANES 2003-2004 dataset, which sampled the noninstitutionalized civilian population living in the 50 United States and the District of Columbia. In the sampling procedure, NHANES conducts a stratified, multistage probability sampling design, which over-samples the certain groups, such as African Americans, Mexican Americans, low-income persons, and those aged 12-19 years and 60 years or older [35]. The NHANES 2003-2004 survey contains data for 10,122 individuals of all ages, and standardized data-collection methods have been used to minimize site-specific error and inter-examiner bias [34, 36].

In the 2003-2004 cycle, NHANES added a PA monitor (PAM), which was used to collect objective information on PA for the U.S. population. All ambulatory participants aged 6 years and over were asked to wear PAMs on the right hip for 7 consecutive days except during sleeping, swimming, or bathing. The PAM used in NHANES was the uniaxial ActiGraph AM-7164 accelerometer (ActiGraph, Ft. Walton Beach, FL), which could summarize acceleration data as activity counts over each 1-minute time interval [37]. In the following analysis, we use this dataset to assess the intensity and duration of PA.

For the purpose of our analysis, we are also interested in the following NHANES datasets to derive the traditional risk factors of chronic pain: (i) "Sample person demographics" file, which includes demographic variables such as gender, age, race/ethnicity, and education status; (ii) "Clinical laboratory testing" files, which provide information on body measurements, including the body mass index (BMI); and (iii) "Medical condition" file, which provides self-reported history of cancer, stroke, congestive heart failure, diabetes, etc.; (iv) Questionnaire files, which provide information on current employment, alcohol con-

sumption, and cigarette/tobacco use information. These NHANES datasets are all publicly available from the CDC website at https://www.cdc.gov/nchs/nhanes/index.htm.

2.1.2 Pain Classification

CP was defined based on individual's responses to the "Miscellaneous pain" questionnaire collected during the household interview. Study participants reported whether they had a problem with pain that lasted more than 24 hours during the past month. Study participants who answered "no" were identified as part of the no pain group. Study participants who answered "yes", were further asked for how long they have experienced the pain. According to the American College of Rheumatology (ACR) criteria [18], individuals reporting pain for more than 3 months were identified as part of the chronic pain group, and those with pain for less than 3 months were identified as part of the acute pain group. Based on this definition and the NHANES data, we have created a three level variable to indicating no pain, chronic pain, and acute pain. As the focus of this document is primarily on current, chronic, non-minor pain, individuals who report acute pain at the time of examination are excluded from all analyses.

Additionally, the NHANES questionnaire also asked about the pain status on 32 body regions (such as right/left shoulder, right/left elbow, head, low back, etc.), which are shown on a pictorial manikin displaying the front and back of a human figure. Participants with CP need to indicate whether they are experiencing pain at each potential pain location. Considering the practical value for clinical applications and the requirement of a large enough sample

size, in this study, we analyze the following three specific pain locations: (i) pain in upper limbs (shoulder/girdle, upper arm, mid-arm, lower arm, hand); (ii) spinal pain (upper back, lower back, neck, spine); and (iii) pain in the lower limbs (buttock, upper leg, mid-leg, lower leg, foot). The three location-specific pain indicators were coded as binary variables (presence/absence) [19, 38].

2.1.3 Study Population

The NHANES 2003-2004 accelerometry data were downloaded, processed, and combined with demography, clinical laboratory tests, miscellaneous pain, and employment variables as well as survey weights [39]. For the purpose of our analysis, we limit our sample population to the participants aged 25 to 85 years old in the no pain group or chronic pain group. The sample size for these data is $3,347$. For accelerometry, we define a "valid day" as a day when accelerometry data were collected for a minimum of 10 hours. Study participants who had fewer than three valid days were excluded from the analysis ($N = 544$). Additional study participants were excluded for having missing covariates: body mass index (BMI) ($N = 29$); education status ($N = 3$); alcohol consumption information ($N = 181$); cigarette/tobacco use ($N = 1$); diabetes mellitus ($N = 47$); congestive heart failure (CHF) ($N = 11$); asthma ($N = 6$); emphysema ($N = 3$); bronchitis ($N = 6$); cancer ($N = 6$); myocardial infarction ($N = 6$); and stroke ($N = 3$). The final data set includes $2,516$ individuals, among which $1,263$ are females and $1,253$ are males. Among the $2,516$ study participants, $2,060$ reported no pain, and 407 reported chronic pain in at least one body location (upper limbs, spine, or lower limbs). Among the ones suffering chronic pain, 175 of them had pain in upper limbs, 270 had pain in spine, and 244 had pain in

the lower limbs.

In this analysis, we compare PA summaries between individuals who report location-specific chronic pain and individuals who report neither chronic nor acute pain at the time of examination. As a result, individuals may be represented in multiple chronic pain groups if they have chronic pain in more than one location, however the no pain group is consistent across all comparisons.

2.2 Variables and Measures

2.2.1 Accelerometer-assessed Physical Activity Variables

Physical activity measurements are assessed objectively using an accelerometer (Actigraph AM-7164), which produced data expressed as activity counts in 1-minute epochs, where more intense activity is associated with higher activity counts. Because such minute-level accelerometer-derived PA data are large, it is common to transform the raw activity counts to a number of indicators of PA. In this analysis, we derive the following PA measurements to capture different aspects of an individual's physical activity profile:

Measures of PA volume:

a) Total activity counts (TAC): the sum of all activity counts accumulated on a valid accelerometer wear day, being used to measure the volume of total

activity.

b) Total log-transformed activity counts (TLAC), or total log (1 + activity count): similar to TAC but reduces the strong right skewness of the TAC. TLAC is calculated by transforming minute-level activity count to log (1 + activity count) and then adding over all minutes of the day.

c) Mean activity counts per minute (CPM): calculated via dividing TAC for a valid day by the number of minutes of wear time.

d) Sedentary activity (ST): the total number of minutes during the day when the individual was sedentary, where a sedentary minute is defined as having an activity count < 100. ST contains sitting or lying down while awake, and it is characterized by an energy expenditure < 1.5 metabolic equivalents (METs). 1 MET is defined as the energy expenditure when resting.

e) Light-intensity physical activity (LIPA): defined as the number of minutes during the valid wear day with an activity count ≥ 100 and $< 2,020$, and it could be considered as the combination of light activity and lifestyle activity. Its energy expenditure of LIPA ≥ 1.5 METs and < 3.0 METs.

f) Moderate-to-vigorous activity (MVPA): defined as the number of minutes during the valid wear day with an activity count $\geq 2,020$. It is a combination of moderate-intensity PA ($2,020$ - $5,998$ counts per minute) and vigorous-intensity PA ($\geq 5,999$ counts per minute), and includes fast walking, jogging, bicycling uphill. The energy expenditure of MVPA ≥ 3.0 METs. [40, 41]

Measures of PA fragmentation:

a) Active to sedentary transition probability ($\text{ASTP}_{sl/nw}$): denotes the probability of transitioning from an active to a sedentary state. It is calculated as the reciprocal of the average active bout duration, where the active bout length is defined as the number of consecutive minutes spent in an active state (activity counts ≥ 100 counts per minute). Since functional decline is usually characterized by the progressive shortening of the active bout duration, ASTP is highly related to clinical measures of physical function in adults [42].

b) Sedentary to active transition probability ($\text{SATP}_{sl/nw}$): denotes the probability of transitioning from a sedentary to an active state. It is calculated as the reciprocal of the average sedentary bout duration, where the sedentary bout length is defined as the number of consecutive minutes spent in a sedentary state (activity counts < 100 counts per minute). SATP and ASTP measures could capture the PA fragmentation of participants.

The above PA summaries are all obtained for one day and are subsequently averaged over the valid days. Although participants in NHANES were instructed to wear the device for the full 7-day period, not all of them completed the requirements. Therefore, the means of PA measurements for each participant are calculated on the basis of his or her number of days with good quality PA data (valid days) [19].

2.2.2 Confounding Variables

For quantifying the association between location-specific CP and PA measurements, the following CP risk factors were discussed as potential confounding

variables: gender, age, race/ethnicity, body mass index (BMI), education status, current employment status, cigarette/tobacco use, alcohol consumption, diabetes mellitus, congestive heart failure (CHF), asthma, emphysema, bronchitis, cancer (nonskin), myocardial infarction, stroke. The selection of the above variables is based on previous publications.

Demographic variables in NHANES such as gender, race/ethnicity, age (years), and the highest degree received were recorded during the home interview. In this analysis, race/ethnicity is categorized as white, (non-Hispanic) white, (non-Hispanic) black, Mexican-American, other Hispanic, and other. Education status is classified as three levels including less than high school, high school or equivalent, and college graduate or above. Participants' height and weight were measured and used to calculate BMI (kg/m^2) during the body measurement component [43]. We categorize BMI into four levels: underweight (BMI ≤ 18.5), normal ($18.5 <$ BMI ≤ 25), overweight ($25 <$ BMI ≤ 30), and obese (BMI > 30).

For lifestyle condition covariates, some require additional data processing, which includes merging information from multiple questions. For example, when creating the current employment variable, we consider the following two questions: 1) whether worked at a job or business last week, and 2) whether usually works 35 or more hours per week. We use this information to categorize individuals into full-time employed, part-time employed, and unemployed. Similarly, current alcohol consumption is categorized into three levels as non-drinker, moderate drinker, and heavy drinker, and the self-reported history of smoking is grouped into never smoker, former smoker, and current smoker. More details about the covariate building process could be found in the *rnhanesdata* package [39].

For each medical condition covariate of interest, participants were asked whether a doctor ever told them that they have that particular disease. According to their responses, we created binary indicator variables to denote individual status of diabetes mellitus, CHF, asthma, emphysema, bronchitis, cancer, myocardial infarction, and stroke.

2.3 Statistical Analysis

2.3.1 Exploratory Analysis

First, we conduct descriptive analyses to describe the basic features of demographic and clinical characteristics for the NHANES population, stratified by pain location and gender. Since all the covariates are binary or categorical variables, we provide the sample size of study participants in each category and the corresponding percentage (in parentheses).

Next, in order to examine how the PA levels change by age for each pain status, we display the average daily value of PA measures across the whole age range for the CP groups, respectively.

In addition, we investigate and compare the daily PA level within each location-specific CP group. We plot the average minute-specific activity counts across all valid 24-hour periods for various age groups and three age categories.

2.3.2 Statistical Models

We establish three groups of multiple linear regression models to examine the association between chronic pain and objectively measured physical activity, sequentially adjusting for sociodemographic characteristics and various medical conditions that might confound the relationship. All regression models were estimated separately for the 8 PA outcome measurements: TAC, TLAC, CPM, ST, LIPA, MVPA, ASTP, and SATP.

Considering the complex survey design in sampling, NHANES assigns a sample weight to each participant, indicating the number of individuals in the U.S. population who are represented by that particular participant. In this analysis, all models incorporate the participants' 2-year full sample examination weights, so that results are generalizable to the U.S. population. We normalize the survey weights in the 2003-2004 wave to increase numerical stability for the estimation procedures using the *reweight_accel()* function from *rnhanesdata* package in R [8, 44]. The survey-weighted regression models are implemented using the *svyglm()* function from the *survey* package.

To compute standard errors of survey estimates from the NHANES stratified multistage sampling design, we created a replicate-weights survey design using the Balanced Repeated Replicates (BBR) technique. It is a resampling method that builds a set of "balanced" pseudoreplicated datasets from the original dataset. We apply the *as.svrepdesign()* function in the R package *survey* and specify the *type* argument as *"BRR"*. The R code of the statistical model fitting has been provided in the Appendix: R Code for Model Fitting.

i) Non-stratified Models

First, we conduct non-stratified analyses. Study participants with CP in each pain location of interest (upper limbs, spine, lower limbs) as well as people with CP in at least one of the three locations were compared with study participants with no pain. This was implemented by fitting three models that sequentially adjust for an increasing number of potential confounders as follows:

- **Model 1:** The first model considers the marginal association between PA and location-specific CP, where a binary indicator has been used to denote the pain status (presence/absence) at the specific location. The no pain group serves as the reference group.
- **Model 2:** The second model includes the status of location-specific CP and, in addition, adjusts for gender (male/female), age, BMI (underweight, normal, overweight, obese), race/ethnicity (White, Mexican-American, Black, other Hispanic, other), education status (less than high school, high school equivalent, more than high school), current employment (unemployed, part-time employed, full-time employed), history of smoking (current, former, never), and alcohol consumption (non-drinker, moderate, heavy).
- **Model 3:** The third model includes all variables present in Model 2 and additionally adjusts for indicator variables (yes/no) of a variety of medical conditions, including diabetes, CHF, stroke, cancer, asthma, emphysema, bronchitis, and myocardial.

ii) Stratified Models

Next, we fit the models stratified by gender. In addition, we present results across the entire age range as well as stratified by 20-year age categories: 25-45, 45-65, and 65-85, based on the consideration that the asso-

ciation between CP and PA measurements might not be consistent across the entire age range.

For each pain location of interest (upper limbs, spine, lower limbs), we fit similar three group of models. The only difference compared with the above models is that we do not include age as a potential confounder in Models 2 and 3 anymore:

- **Model 1:** The first model considers the marginal association between PA and location-specific chronic pain, where a binary indicator has been used to denote the pain status (presence/absence) on the specific location. The no pain group serves as the reference group.
- **Model 2:** The second model includes the status of location-specific chronic pain and, in addition, adjusts for age, BMI, race/ethnicity, education status, current employment, history of smoking, and alcohol consumption.
- **Model 3:** The third model includes all variables present in Model 2 and additionally adjusts for diabetes, CHF, stroke, cancer, asthma, emphysema, bronchitis, and myocardial.

All estimates of the pain indicator variable are presented as point estimates with 95% confidence intervals (CIs). We considered type I error rates of 0.05 and 0.01 as the thresholds for statistical significance.

Chapter 3

Results

3.1 Exploratory Analysis

In this section, we provide data visualizations to summarize the population prevalence of CP and display the characteristics of potential confounders and PA measures within different subgroups.

3.1.1 Prevalence of Chronic Pain

Figure 3.1 displays the sample size for the entire data set and three age subgroups. In this figure, the above panel is for females and the one below one is for males. Different color bars indicate pain locations: arm (violet), spine (blue), leg (green), and any of the three body locations (yellow).

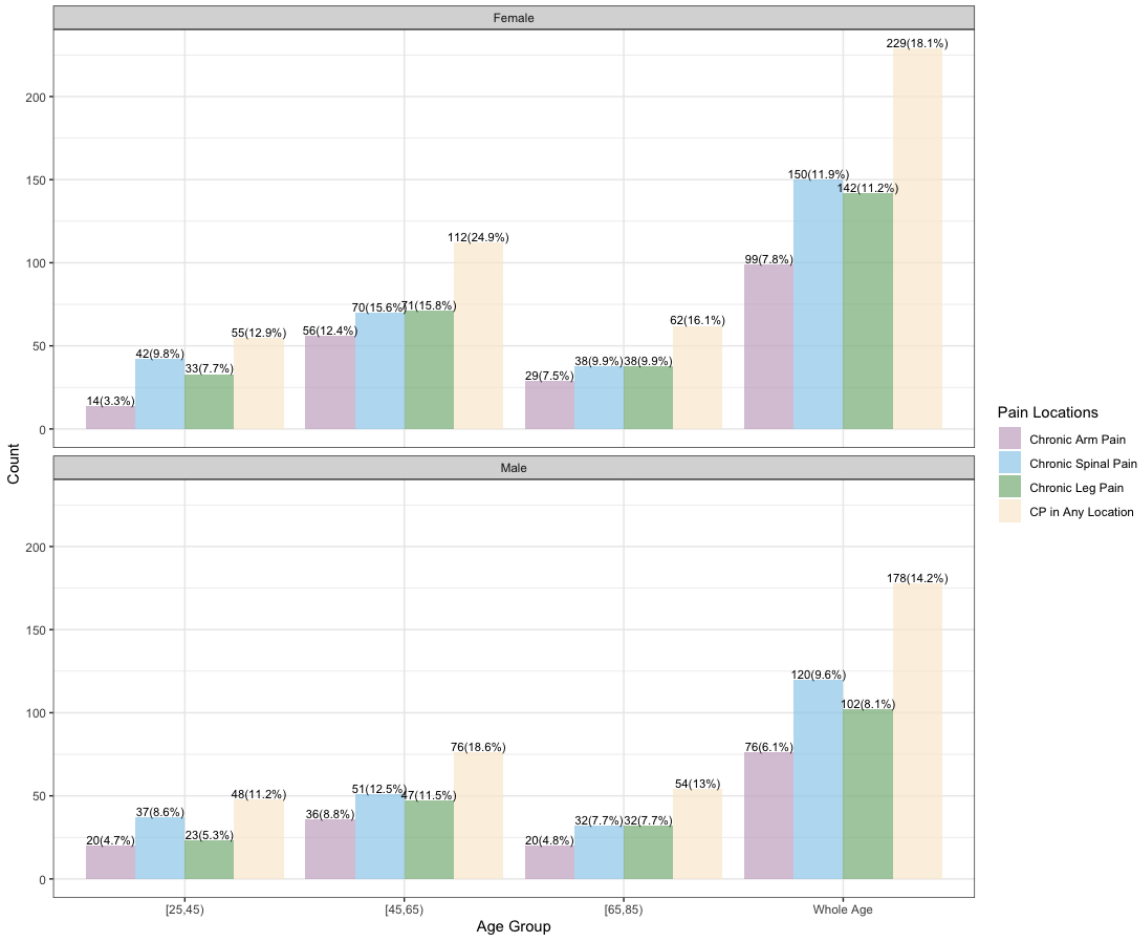

Figure 3.1: Number of people reporting chronic pain at various body locations(arm: violet, spine: blue, leg: green, any body locations: yellow) stratified by gender (top plot corresponds to females) and age (x-axis).

Figure 3.1 indicates that in the entire group there are 229 females and 178 males who reported CP in at least one body location (upper limbs, spine, or lower limbs). The sex ratio is around $1:1$ in our complete dataset ($1,263$ are females and $1,253$ males) and the percent of reporting CP for females (18.1%) is larger than for males (14.2%), which holds even for the re-weighted prevalence (19.8% for females and 16.1% for males). However, the difference in the unweighted and weighted means is smaller than what was previously reported in the literature. The ratio of reporting CP for females is higher for all three age groups (12.9% for females vs. 11.2% for males in the 25-45 age group, 24.9%

vs. 18.6% in the 45-65 age group, and 16.1% vs. 13% in the 65-85 age group).

We also investigate how age is associated with the reported CP status. Study participants between 45-65 have the largest percentage (23.1%) of reporting CP in at least one location (arm, spine, or leg) compared to the 25-45 and 65-85 age groups, which are 15.3% and 15.9%, respectively. This finding holds for both females and males. Indeed, 24.9% of females and 18.6% of males aged 45-65 years old reported CP, both of which are higher than the prevalence of CP both in the 25-45 (12.9% for females and 11.2% for males) and 65-85 (16.1% for females and 13% for males) age groups.

Third, we inspect the sample size of different location-specific CP. For the 25-45 years old age group, chronic spinal pain is most common in both males and females (9.8% in females and 8.6% in males). For people aged 45-65 and 65-85, the prevalence of CP in spine and lower limbs become almost equal (In 45-65 females: 15.6% for spine and 15.8% for leg; In 45-65 males: 12.5% for spine and 11.5% for leg; In 65-85 females: 9.9% for both spine and leg; In 65-85 males: 7.7% for both spine and leg), which are higher than the reported prevalence in the upper limbs (12.4% in 45-65 females, 8.8% in 45-65 males, 7.5% in 65-85 females, 4.8% in 65-85 males)

3.1.2 Demographic and Clinical Characteristics

Table 3.1 provides mean and standard deviations for continuous variables and counts and percentages for categorical variables (by rows) stratified by sex and location of CP (by columns). The covariates considered include age, race, sociodemographic status, life behaviors, and medical conditions. In all

		Male					Female				
		CP in Arm	CP in Spine	CP in Leg	CP in Any Location	No Pain	CP in Arm	CP in Spine	CP in Leg	CP in Any Location	No Pain
Total		76	120	102	178	1059	99	150	142	229	1001
Age	25-45	20 (26.3%)	37 (30.8%)	23 (22.5%)	48 (27%)	375 (35.4%)	14 (14.1%)	42 (28%)	33 (23.2%)	55 (24%)	352 (35.2%)
	45-65	36 (47.4%)	51 (42.5%)	47 (46.1%)	76 (42.7%)	328 (31%)	56 (56.6%)	70 (46.7%)	71 (50%)	112 (48.9%)	333 (33.3%)
	65-85	20 (26.3%)	32 (26.7%)	32 (31.4%)	54 (30.3%)	356 (33.6%)	29 (29.3%)	38 (25.3%)	38 (26.8%)	62 (27.1%)	316 (31.6%)
Race	White	54 (71.1%)	86 (71.7%)	70 (68.6%)	127 (71.3%)	572 (54%)	58 (58.6%)	89 (59.3%)	98 (69%)	145 (63.3%)	534 (53.3%)
	Black	6 (7.9%)	15 (12.5%)	12 (11.8%)	21 (11.8%)	171 (16.1%)	17 (17.2%)	24 (16%)	22 (15.5%)	34 (14.8%)	184 (18.4%)
	Mexican	10 (13.2%)	12 (10%)	13 (12.7%)	21 (11.8%)	251 (23.7%)	17 (17.2%)	26 (17.3%)	14 (9.9%)	35 (15.3%)	223 (22.3%)
	Other Hispanic	2 (2.6%)	1 (0.8%)	1 (1%)	2 (1.1%)	24 (2.3%)	3 (3%)	2 (1.3%)	3 (2.1%)	3 (1.3%)	26 (2.6%)
	Other	4 (5.3%)	6 (5%)	6 (5.9%)	7 (3.9%)	41 (3.9%)	4 (4%)	9 (6%)	5 (3.5%)	12 (5.2%)	34 (3.4%)
BMI	Underweight	1 (1.3%)	2 (1.7%)	1 (1%)	2 (1.1%)	6 (0.6%)	1 (1%)	1 (0.7%)	2 (1.4%)	2 (0.9%)	13 (1.3%)
	Normal	19 (25%)	28 (23.3%)	28 (27.5%)	43 (24.2%)	277 (26.2%)	24 (24.2%)	33 (22%)	31 (21.8%)	51 (22.3%)	308 (30.8%)
	Overweight	27 (35.5%)	52 (43.3%)	33 (32.4%)	73 (41%)	456 (43.1%)	33 (33.3%)	49 (32.7%)	44 (31%)	76 (33.2%)	323 (32.3%)
	Obese	29 (38.2%)	38 (31.7%)	40 (39.2%)	60 (33.7%)	320 (30.2%)	41 (41.4%)	67 (44.7%)	65 (45.8%)	100 (43.7%)	357 (35.7%)
Education	Below High School	19 (25%)	31 (25.8%)	28 (27.5%)	46 (25.8%)	300 (28.3%)	32 (32.3%)	51 (34%)	41 (28.9%)	73 (31.9%)	261 (26.1%)
	High School	21 (27.6%)	35 (29.2%)	25 (24.5%)	50 (28.1%)	257 (24.3%)	21 (21.2%)	38 (25.3%)	34 (23.9%)	55 (24%)	243 (24.3%)
	Above High School	36 (47.4%)	54 (45%)	49 (48%)	82 (46.1%)	502 (47.4%)	46 (46.5%)	61 (40.7%)	67 (47.2%)	101 (44.1%)	497 (49.7%)
Employment	Full-Time	30 (39.5%)	49 (40.8%)	34 (33.3%)	71 (39.9%)	596 (56.3%)	26 (26.3%)	41 (27.3%)	39 (27.5%)	67 (29.3%)	397 (39.7%)
	Part-Time	3 (3.9%)	9 (7.5%)	10 (9.8%)	13 (7.3%)	64 (6%)	7 (7.1%)	17 (11.3%)	16 (11.3%)	24 (10.5%)	110 (11%)
	Unemployed	43 (56.6%)	62 (51.7%)	58 (56.9%)	94 (52.8%)	399 (37.7%)	66 (66.7%)	92 (61.3%)	87 (61.3%)	138 (60.3%)	494 (49.4%)
Smoker	Current	30 (39.5%)	44 (36.7%)	35 (34.3%)	62 (34.8%)	260 (24.6%)	26 (26.3%)	46 (30.7%)	34 (23.9%)	61 (26.6%)	139 (13.9%)
	Former	24 (31.6%)	44 (36.7%)	38 (37.3%)	65 (36.5%)	366 (34.6%)	24 (24.2%)	39 (26%)	41 (28.9%)	61 (26.6%)	236 (23.6%)
	Never	22 (28.9%)	32 (26.7%)	29 (28.4%)	51 (28.7%)	433 (40.9%)	49 (49.5%)	65 (43.3%)	67 (47.2%)	107 (46.7%)	626 (62.5%)
Drinker	Heavy	6 (7.9%)	11 (9.2%)	10 (9.8%)	15 (8.4%)	92 (8.7%)	8 (8.1%)	8 (5.3%)	9 (6.3%)	12 (5.2%)	41 (4.1%)
	Moderate	46 (60.5%)	63 (52.5%)	58 (56.9%)	100 (56.2%)	644 (60.8%)	45 (45.5%)	71 (47.3%)	65 (45.8%)	111 (48.5%)	515 (51.4%)
	Never	24 (31.6%)	46 (38.3%)	34 (33.3%)	63 (35.4%)	323 (30.5%)	46 (46.5%)	71 (47.3%)	68 (47.9%)	106 (46.3%)	445 (44.5%)
Diabetes		15 (19.7%)	14 (11.7%)	19 (18.6%)	27 (15.2%)	134 (12.7%)	19 (19.2%)	23 (15.3%)	27 (19%)	41 (17.9%)	99 (9.9%)
CHF		4 (5.3%)	12 (10%)	6 (5.9%)	14 (7.9%)	39 (3.7%)	10 (10.1%)	10 (6.7%)	12 (8.5%)	16 (7%)	18 (1.8%)
Asthma		11 (14.5%)	22 (18.3%)	15 (14.7%)	26 (14.6%)	72 (6.8%)	19 (19.2%)	28 (18.7%)	23 (16.2%)	36 (15.7%)	127 (12.7%)
Emphysema		0 (0%)	6 (5%)	2 (2%)	6 (3.4%)	30 (2.8%)	3 (3%)	5 (3.3%)	4 (2.8%)	5 (2.2%)	13 (1.3%)
Bronchitis		11 (14.5%)	13 (10.8%)	10 (9.8%)	17 (9.6%)	35 (3.3%)	19 (19.2%)	27 (18%)	21 (14.8%)	37 (16.2%)	70 (7%)
Cancer		10 (13.2%)	16 (13.3%)	10 (9.8%)	25 (14%)	106 (10%)	9 (9.1%)	19 (12.7%)	23 (16.2%)	32 (14%)	94 (9.4%)
Myocardial		12 (15.8%)	17 (14.2%)	12 (11.8%)	38 (21.3%)	73 (6.9%)	13 (13.1%)	14 (9.3%)	13 (9.2%)	57 (24.9%)	25 (2.5%)
Stroke		3 (3.9%)	8 (6.7%)	3 (2.9%)	24 (13.5%)	42 (4%)	6 (6.1%)	8 (5.3%)	7 (4.9%)	17 (7.4%)	27 (2.7%)

Table 3.1: Summaries of demographic and medical characteristics, organized by location-specific CP groups, CP in any location (arm, spine, or leg) group, and no pain group. For the binary and categorical variables, the sample size of study participants in each category and the corresponding percentage (in parentheses) are provided.

CP groups, nearly half of the individuals who report CP are aged 45-65. Study participants who do not report pain are evenly distributed in the three age categories. Among males without pain there are 35.4% aged 25-45, 31% aged 45-65, and 33.6% aged 65-85. Among females without pain there are 35.2% aged 25-45, 33.3% aged 45-65, and 31.6% aged 65-85). Moreover, for both males and females, the proportions of white, obese, unemployed and current smoker are substantially higher in the CP groups compared to the no pain group. For instance, 71.3% males and 63.3% females with CP in any location (arm, spine, or leg) are white, and the corresponding percentages in the no pain group are 54% and 53.3%. Comorbidities seem to be associated to CP. For example, the preva-

lence of asthma in males ranges from 14.5% to 18.3% across CP groups and is 6.8% in the no pain group. Similar differences can be observed for diabetes, bronchitis, and myocardial disease. We conclude that these demographic and medical characteristics need to be considered as potential confounders in the association between objectively measured PA and CP.

3.1.3 PA Characteristics

i) PA measures across age

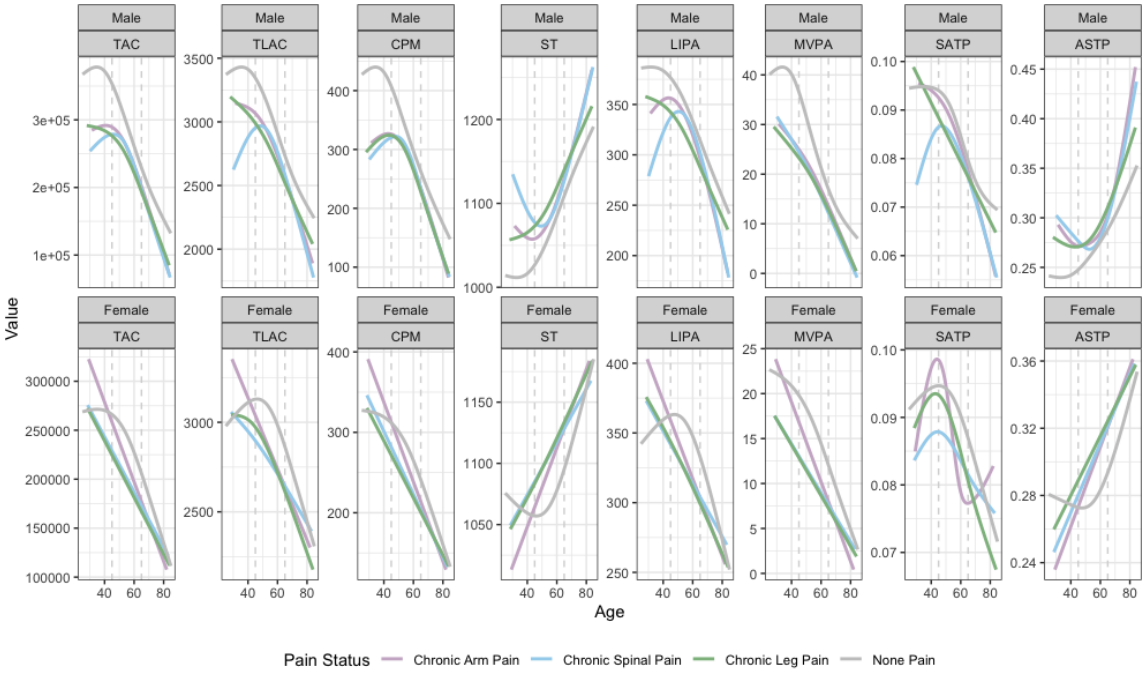

Figure 3.2: Average daily value of eight PA measures as functions of age (x-axis) stratified by gender (male: top panels) and pain locations (colors of different lines). The y-axis denotes the value of each PA measure.

Figure 3.2 displays the average daily value of eight PA measures as functions of age. The x-axes in all subplots span the entire age range considered in this analysis, 25-85 years old. Subplots are stratified by sex (male:

top panels) and pain locations (colors of different lines). Curves are not adjusted for any other covariates other than sex and CP location. **Figure 3.2** indicates that most PA measures for males have a non-linear relationship with age within each CP group. Consider, for example, all four curves of the CPM variable for males (first row, third column) increase with age until 40-45 years of age and then start declining for the rest of the age span. The curve corresponding to the no pain group (gray) is always above the other three curves that correspond to the various CP groups (purple, blue, and green). Such discrepancy is largest among the 25 to 45 year old group, though some large differences can be observed for the 65 to 85 year old group.

However, for females, we observe different patterns. Note that for CPM measurements (second row, third column): (i) the curve for the no pain group and the three curves of CP groups are closer over the age range; (ii) curves are linear and decline with age; (iii) the average CPM (counts er minute) curve for CP (chronic pain) in the arm is higher than the CPM curve for the no pain group.

Other PA outcomes, including TAC, TLAC, LIPA, and MVPA, have similar decreasing patterns, while ST and ASTP increase with age. This is expected, as ST is a measure of time spend sedentary and ASTP is a measure of the probability of transitioning from active to sedentary during the day. This exploratory analysis provides a general description of how various PA measurements change with age for males and females.

ii) Minute-level activity counts during the day

Figure 3.3 provides the average daily pattern of minute-level PA for the entire age group for males (left) and females (right) for different pain loca-

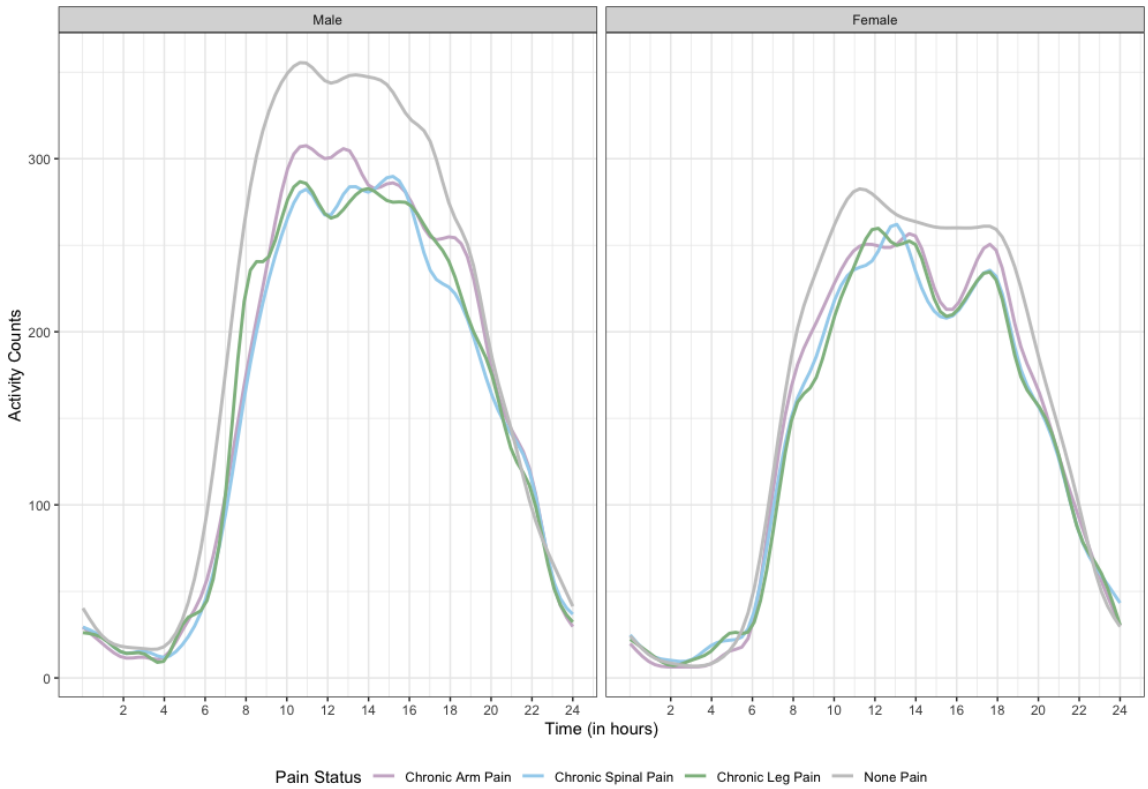

Figure 3.3: Average daily pattern of minute-level PA for the entire age group for males (left) and females (right) for different pain locations (no pain: gray; arm pain: violet; spinal pain: blue; leg pain: green). The x-axis is the time from 0 AM to 0 AM. The y-axis is the average activity count at a particular minute of the day.

tions (no pain: gray; arm pain: violet; spinal pain: blue; leg pain: green). Both males and females who do not report pain (gray curve) have higher activity counts than the corresponding groups that reported CP in arm, spine or leg. The only exception is for females who reported chronic pain in their arms, where differences are not that clear. In general the differences between the average curves for males are much more pronounced than for females.

Figure 3.4 provides additional insight into the effect of age on the average daily activity counts. As panels are compared from left to right (younger to older), the average activity counts decreases for both males

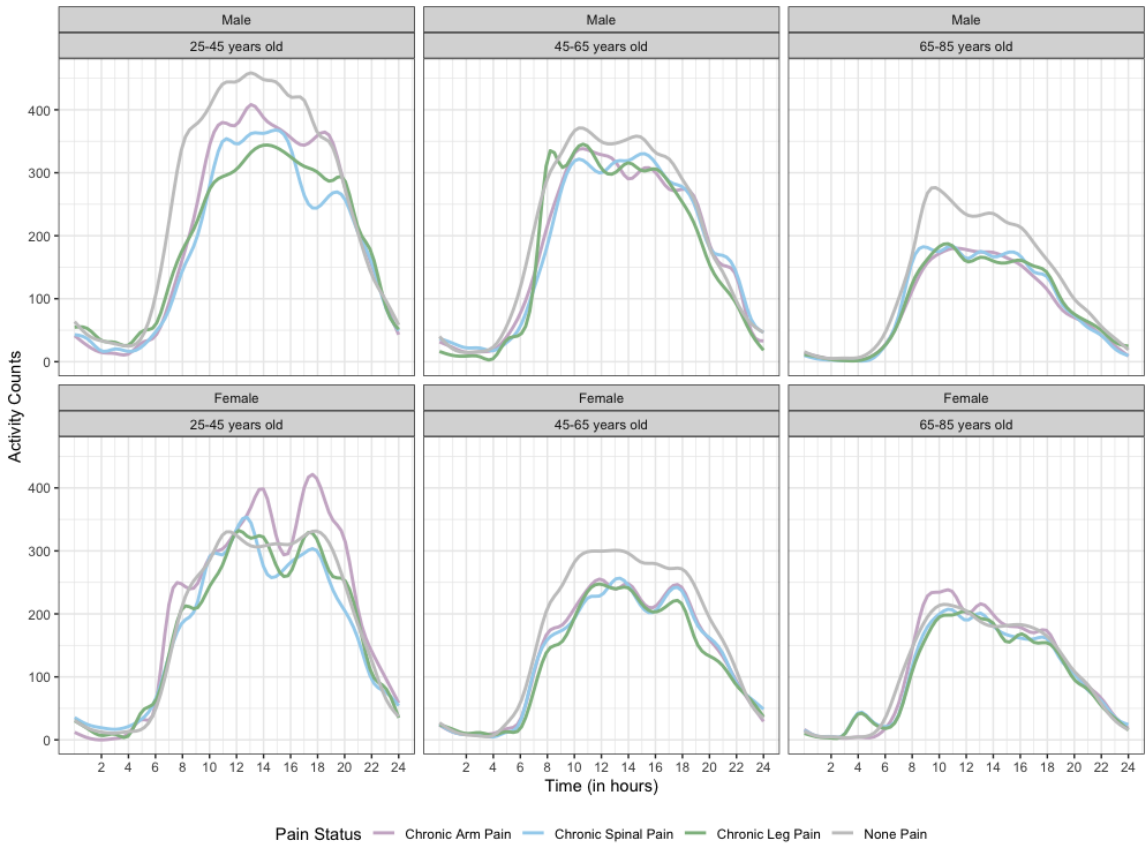

Figure 3.4: Average daily pattern of minute-level PA group for males (top panels) and females (bottom panels) for the age groups 25-45 (left), 45-65 (middle), and 65-85 (right). Different pain locations are indicated by the color of the lines (no pain: gray; arm pain: violet; spinal pain: blue; leg pain: green). The x-axis is the time from 0 AM to 0 AM. The y-axis is the average activity count at a particular minute of the day.

and females across pain groups. The largest differences between PA intensity profiles can be observed for females aged 45-65 and males aged 25-45 and 65-85. In the age group 25-45 the average PA level for male and female study participants with chronic arm pain is higher than for chronic spinal or leg pain. This phenomenon is not observed in other age groups. These visualizations of the minute-level PA data suggest potential relationships between location-specific CP and PA.

3.2 Non-stratified Models for Association between PA and Pain Status

		Age Group: 25-85 years old			
		Arm	Spine	Leg	Any
TAC	Model 1	-38852.9	-51326	-52056.8	-44505
		(-65790.6, -11915.2) **	(-74096.6, -28555.3) **	(-74828.5, -29285.2) **	(-66244.9, -22765.2) **
	Model 2	-7308.4	-26224.8	-16707.4	-16421
		(-28444.1, 13827.3)	(-43214.7, -9234.9) **	(-32827.7, -587) *	(-33123.4, 281.5)
	Model 3	-1297	-22042.7	-12379.1	-12636.4
		(-21661.9, 19067.8)	(-39169.3, -4916.1) *	(-28300, 3541.8)	(-28661.3, 3388.4)
TLAC	Model 1	-191.4 (-341.5, -41.3) *	-230.9 (-332.6, -129.2) **	-246.8 (-351.3, -142.3) **	-198.5 (-286.7, -110.3) **
	Model 2	-46.2 (-160.2, 67.8)	-119 (-212.1, -26) *	-93.9 (-201.3, 13.5)	-76.3 (-161.1, 8.5)
	Model 3	-9.3 (-109.8, 91.2)	-84.4 (-168.4, -0.4) *	-63.1 (-169, 42.8)	-48 (-125.3, 29.3)
CPM	Model 1	-44.5 (-74.6, -14.4) **	-56.8 (-83.4, -30.1) **	-55.9 (-81, -30.9) **	-50.2 (-75.8, -24.5) **
	Model 2	-10.5 (-35.6, 14.6)	-30.5 (-51.1, -9.8) **	-17.7 (-36.1, 0.7)	-19.7 (-40.2, 0.8)
	Model 3	-3.8 (-29, 21.5)	-25.9 (-46.5, -5.4) *	-12.9 (-31.2, 5.5)	-15.5 (-35.3, 4.3)
ST	Model 1	24.1 (2.7, 45.5) *	32.2 (17.4, 47) **	31.9 (16.3, 47.5) **	25.9 (12.6, 39.1) **
	Model 2	3.5 (-13.3, 20.3)	17.2 (3.6, 30.7) *	10.3 (-5.8, 26.5)	8.7 (-4.1, 21.5)
	Model 3	-2.2 (-17.1, 12.6)	12.1 (0.2, 24.1) *	5.5 (-10.2, 21.1)	4.4 (-6.8, 15.7)
LIPA	Model 1	-17.1 (-36.5, 2.2)	-23.7 (-36.8, -10.5) **	-22.7 (-37.6, -7.9) **	-18.2 (-29.8, -6.7) **
	Model 2	-1.1 (-16.8, 14.6)	-12.5 (-25.6, 0.5)	-6.6 (-22.6, 9.4)	-5.4 (-17.2, 6.4)
	Model 3	4 (-10.1, 18.1)	-7.9 (-19, 3.3)	-2.1 (-17.9, 13.6)	-1.5 (-11.7, 8.8)
MVPA	Model 1	-6.9 (-10.5, -3.4) **	-8.5 (-12.3, -4.7) **	-9.2 (-13.5, -4.8) **	-7.6 (-11.5, -3.8) **
	Model 2	-2.4 (-5.7, 0.9)	-4.6 (-7.3, -1.9) **	-3.7 (-7.2, -0.2) *	-3.3 (-6.4, -0.2) *
	Model 3	-1.8 (-5.1, 1.5)	-4.3 (-7, -1.5) **	-3.3 (-6.7, 0.1)	-3 (-6, 0)
SATP	Model 1	-0.003 (-0.007, 0.001)	-0.004 (-0.008, 0) *	-0.006 (-0.008, -0.003) **	-0.003 (-0.006, -0.001) **
	Model 2	0 (-0.004, 0.004)	-0.002 (-0.005, 0.001)	-0.003 (-0.006, 0)	-0.001 (-0.004, 0.002)
	Model 3	0.001 (-0.003, 0.004)	-0.001 (-0.004, 0.002)	-0.002 (-0.005, 0.001)	0 (-0.003, 0.002)
ASTP	Model 1	0.019 (0.003, 0.036) *	0.02 (0.007, 0.034) **	0.017 (0.004, 0.03) **	0.017 (0.005, 0.03) **
	Model 2	0.006 (-0.007, 0.019)	0.011 (-0.001, 0.023)	0.004 (-0.008, 0.016)	0.007 (-0.004, 0.017)
	Model 3	0.001 (-0.01, 0.012)	0.007 (-0.004, 0.018)	0 (-0.011, 0.01)	0.003 (-0.006, 0.012)

Table 3.2: Associations of PA and location-specific chronic pain for the whole age group. Each cell shows the coefficient estimates, 95% CIs, and corresponding p values of Models 1, 2, and 3. The p-values ≤ 0.05 and p-values ≤ 0.01 are marked as * and **. Model 1: marginal model; Model 2: adjusted for gender, age, BMI, race, education status, current employment, history of smoking, and alcohol consumption; Model 3: adjusted for gender, age, BMI, race, education status, current employment, history of smoking, and alcohol consumption, diabetes, CHF, stroke, cancer, asthma, emphysema, bronchitis, and myocardial.

Table 3.2 provides the results of the non-stratified survey-weighted regression models in the 25-85 years old age group (entire group). For the association between each PA outcome and pain indicator (CP in upper limbs, spine, lower limbs, or at least one of the three locations), we provide the corresponding coefficient estimates, 95% CIs, and p-values of Models 1, 2, and 3. We use * to denote a p-value ≤ 0.05 and ** to denote a p-value ≤ 0.01.

First, we provide results for Model 1, which includes only the pain indicator in the regression model. We provide a discussion of results by for measures of PA volume first (TAC, TLAC, CPM, ST, LIPA, MVPA) and then for measures of PA fragmentation (SATP and ASTP).

i) Measures of PA volume

For people with CP in arm, spine, leg or any location, they all tend to have significantly *lower* levels of volume of total/average activity, including TAC ($\beta_{arm} = -38852.9$, $p_{arm} = 0.005$; $\beta_{spine} = -51326$, $p_{spine} < 0.001$; $\beta_{leg} = -52056.8$, $p_{leg} < 0.001$; $\beta_{anywhere} = -44505$, $p_{anywhere} < 0.001$), $TLAC$($\beta_{arm} = -191.4$, $p_{arm} = 0.012$; $\beta_{spine} = -230.9$, $p_{spine} < 0.001$; $\beta_{leg} = -246.8$, $p_{leg} < 0.001$; $\beta_{anywhere} = -198.5$, $p_{anywhere} < 0.001$); and CPM ($\beta_{arm} = -44.5$, $p_{arm} = 0.004$; $\beta_{spine} = -56.8$, $p_{spine} < 0.001$; $\beta_{leg} = -55.9$, $p_{leg} < 0.001$; $\beta_{anywhere} = -50.2$, $p_{anywhere} < 0.001$). Furthermore, they also have *lower* light (LIPA: $\beta_{spine} = -23.7$, $p_{spine} < 0.001$; $\beta_{leg} = -22.7$, $p_{leg} = 0.003$; $\beta_{anywhere} = -18.2$, $p_{anywhere} = 0.002$) and moderate and vigorous PA (MVPA: $\beta_{arm} = -6.9$, $p_{arm} < 0.001$; $\beta_{spine} = -8.5$, $p_{spine} < 0.001$; $\beta_{leg} = -9.2$, $p_{leg} < 0.001$; $\beta_{anywhere} = -7.6$, $p_{anywhere} < 0.001$), as well as *higher* sedentary time (ST: $\beta_{arm} = 24.1$, $p_{arm} = 0.027$; $\beta_{spine} = 32.2$, $p_{spine} < 0.001$; $\beta_{leg} = 31.9$, $p_{leg} < 0.001$; $\beta_{anywhere} = 25.9$, $p_{anywhere} < 0.001$). The only exception is LIPA for study participants with arm pain.

ii) Measures of PA fragmentation

Compared with people with no pain, people within the location-specific CP groups (arm, spine, and leg) and within the CP in any location group have significantly *higher* ASTP ($\beta_{arm} = 0.019$, $p_{arm} = 0.02$; $\beta_{spine} = 0.02$, $p_{spine} = 0.003$; $\beta_{leg} = 0.017$, $p_{leg} = 0.009$; $\beta_{anywhere} = 0.017$, $p_{anywhere} = 0.007$) and *lower* SATP ($\beta_{spine} = -0.004$, $p_{spine} = 0.034$; $\beta_{leg} = -0.006$, $p_{leg} < 0.001$;

$\beta_{anywhere} = -0.003$, $p_{anywhere} = 0.008$). The only exception is SATP in people with arm pain.

Next, we consider the effects of potential confounders and establish adjusted models (Models 2 and 3):

i) Measures of PA volume

For participants with chronic spinal pain, in both Models 2 and 3, their pain status are significantly associated with TAC ($Model\,2 : \beta = -26224.8$, $p = 0.002$; $Model\,3 : \beta = -22042.7$, $p = 0.012$), TLAC ($Model\,2 : \beta = -119$, $p = 0.012$; $Model\,3 : \beta = -84.4$, $p = 0.049$), CPM ($Model\,2 : \beta = -30.5$, $p = 0.004$; $Model\,3 : \beta = -25.9$, $p = 0.013$), ST ($Model\,2 : \beta = 17.2$, $p = 0.013$; $Model\,3 : \beta = 12.1$, $p = 0.047$), MVPA ($Model\,2 : \beta = -4.6$, $p = 0.001$; $Model\,3 : \beta = -4.3$, $p = 0.003$). In addition, in Model 2, CP in leg is significantly related to TAC ($\beta = -16707.4$, $p = 0.042$) and MVPA ($\beta = -3.7$, $p = 0.036$), and CP in any location is related to MVPA ($\beta = -3.3$, $p = 0.035$).

ii) Measures of PA fragmentation

In adjusted analyses, there are no significant differences between the either CP group and the no pain group.

In summary, in the entire group (25-85 years old), study participants with CP in any location have less PA in the marginal models. However, the statistical significance is present only in the spinal CP group after adjusting for demographic and medical conditions.

3.3 Stratified Models for Association between PA and Pain Status

Tables 3.3, 3.4, 3.5 and 3.6 provide results similar with **Table 3.2**. However, they display the results of stratified models in different age groups (whole age range, 25-45 years old, 45-65 years old, and 65-85 years old) separately. The outputs within each table are organized by pain locations (upper limbs, spine, and lower limbs) and gender (male/female). In this section, we will describe the association results by age group, starting with the entire group and then from the youngest to the oldest groups.

3.3.1 Associations in the entire age group

Table 3.3 displays the estimated associations between the 8 daily PA summaries and location-specific CP for the 25-85 years old age group (entire group). We first investigate the results obtained from the marginal models (Model 1) to discuss the PA volume (TAC, TLAC, CPM, ST, LIPA, MVPA) and the measures of PA fragmentation (SATP and ASTP).

i) Measures of PA volume

In unadjusted analyses, people with either spinal or leg CP, both males and females tend to have significantly *lower* levels of TAC ($males: \beta_{spine} = -57405.5$, $p_{spine} < 0.001$; $\beta_{leg} = -61876.7$, $p_{leg} < 0.001$; $females: \beta_{spine} = -39534.5$, $p_{spine} = 0.001$; $\beta_{leg} = -33563.2$, $p_{leg} = 0.014$), TLAC ($males: \beta_{spine} = -270.3$, $p_{spine} < 0.001$; $\beta_{leg} = -322.7$, $p_{leg} < 0.001$; $females: \beta_{spine} =$

		Age Group: 25-85 years old					
		Arm		Spine		Leg	
		Male	Female	Male	Female	Male	Female
TAC	Model 1	-44208.9	-27385.4	-57405.5	-39534.5	-61876.7	-33563.2
		(-75475.2, -12942.6) **	(-63936.3, 9165.4)	(-87728.6, -27082.5) **	(-62228.6, -16840.4) **	(-88116.8, -35636.6) **	(-60282, -6844.4) *
	Model 2	-12192.9	-5672.6	-30093.6	-23339.7	-22281.9	-13124.8
		(-36154.4, 11768.6)	(-30668.9, 19323.6)	(-62982.4, 2795.3)	(-38068.3, -8611.1) **	(-45488.7, 924.8)	(-29841.8, 3592.2)
	Model 3	-6949	361.1	-25657.2	-19748	-19336.1	-8996.5
		(-29424.3, 15526.3)	(-27272.5, 27994.7)	(-56741.8, 5427.3)	(-37938.1, -1557.8) *	(-41848.1, 3175.8)	(-27220.7, 9227.6)
TLAC	Model 1	-195.1 (-366, -24.2) *	-177.2 (-384.1, 29.6)	-270.3 (-421.1, -119.5) **	-187.2 (-331, -43.4) *	-322.7 (-471.5, -173.9) **	-176.6 (-326.2, -26.9) *
	Model 2	-22.4 (-186.3, 141.5)	-70.5 (-239.6, 98.6)	-133.7 (-312.3, 44.9)	-102.5 (-219.5, 14.6)	-118.6 (-281.7, 44.6)	-75.8 (-218.3, 66.8)
	Model 3	-8.1 (-160, 143.9)	-25.6 (-185.7, 134.4)	-107.5 (-271.1, 56.1)	-69.5 (-173.8, 34.8)	-104.8 (-266.6, 56.9)	-43.3 (-178.6, 91.9)
CPM	Model 1	-56.4 (-94.1, -18.7) **	-27.1 (-67, 12.9)	-66.3 (-101.8, -30.8) **	-41.6 (-66.4, -16.8) **	-69.4 (-95.9, -42.9) **	-34.1 (-64.9, -3.2) *
	Model 2	-22.7 (-51.6, 6.1)	-3.4 (-31.1, 24.3)	-36.7 (-74, 0.6)	-25.1 (-43, -7.3) **	-26.3 (-47.5, -5) *	-12 (-33.3, 9.3)
	Model 3	-17.1 (-43.7, 9.5)	4.1 (-28.2, 36.3)	-31.4 (-66.2, 3.4)	-21.1 (-43.5, 1.4)	-22.7 (-43.5, -1.8) *	-6.7 (-30.3, 16.9)
ST	Model 1	23.8 (-2.5, 50)	22.4 (-7.9, 52.7)	38 (14, 62) **	25.4 (5.5, 45.4) *	44.8 (24, 65.6) **	20 (-3.1, 43.1)
	Model 2	0.4 (-26.2, 26.9)	6.8 (-18.8, 32.4)	19.6 (-9.1, 48.4)	14.4 (-2.3, 31.1)	16.9 (-6.7, 40.5)	5.3 (-15.9, 26.5)
	Model 3	-1.2 (-25.3, 23)	-1.1 (-26.6, 24.5)	16.4 (-10.9, 43.7)	9 (-5.6, 23.6)	15.3 (-8.4, 39)	-0.8 (-20.1, 18.4)
LIPA	Model 1	-16.4 (-42.1, 9.4)	-17.2 (-45.5, 11.2)	-28.9 (-50.8, -6.9) **	-18.8 (-38.4, 0.9)	-35.5 (-56.6, -14.3) **	-13.2 (-34.9, 8.6)
	Model 2	2.7 (-24.5, 29.9)	-4.3 (-29.2, 20.5)	-14.4 (-40.6, 11.7)	-10.1 (-27.7, 7.5)	-13.3 (-37.4, 10.7)	-1.2 (-22.2, 19.7)
	Model 3	3 (-22.3, 28.3)	3.3 (-21.4, 27.9)	-12.1 (-37.2, 13)	-4.8 (-19.8, 10.2)	-12.3 (-36.6, 12)	4.7 (-13.9, 23.4)
MVPA	Model 1	-7.4 (-13.7, -1.1) *	-5.2 (-9.3, -1.1) *	-9.2 (-14, -4.3) **	-6.7 (-10.3, -3) **	-9.3 (-16.3, -2.3) **	-6.8 (-10.3, -3.3) **
	Model 2	-3 (-8.2, 2.1)	-2.5 (-5.3, 0.2)	-5.2 (-9.7, -0.7) *	-4.3 (-7.1, -1.5) **	-3.6 (-10, 2.8)	-4 (-6.1, -2) **
	Model 3	-1.8 (-7.3, 3.6)	-2.2 (-5.2, 0.9)	-4.3 (-8.8, 0.2)	-4.2 (-7.5, -1) *	-3 (-9.4, 3.5)	-3.9 (-6.2, -1.6) **
SATP	Model 1	0 (-0.005, 0.005)	-0.006 (-0.011, 0) *	-0.004 (-0.009, 0) *	-0.004 (-0.01, 0.002)	-0.007 (-0.012, -0.002) *	-0.006 (-0.01, -0.002) **
	Model 2	0.003 (-0.002, 0.009)	-0.003 (-0.007, 0.002)	-0.002 (-0.006, 0.002)	-0.002 (-0.007, 0.004)	-0.003 (-0.009, 0.003)	-0.003 (-0.007, 0.002)
	Model 3	0.003 (-0.002, 0.009)	-0.002 (-0.006, 0.002)	-0.002 (-0.006, 0.003)	-0.001 (-0.006, 0.004)	-0.003 (-0.009, 0.003)	-0.002 (-0.006, 0.002)
ASTP	Model 1	0.023 (0.003, 0.042) *	0.014 (-0.008, 0.036)	0.021 (0.002, 0.041) *	0.017 (0.001, 0.034) *	0.027 (0.016, 0.037) **	0.007 (-0.013, 0.027)
	Model 2	0.008 (-0.011, 0.026)	0.005 (-0.013, 0.023)	0.01 (-0.011, 0.032)	0.011 (-0.003, 0.024)	0.01 (0, 0.02)	-0.001 (-0.02, 0.017)
	Model 3	0.006 (-0.011, 0.024)	-0.004 (-0.022, 0.013)	0.007 (-0.013, 0.028)	0.005 (-0.005, 0.016)	0.008 (-0.002, 0.019)	-0.008 (-0.024, 0.008)

Table 3.3: Associations of PA and location-specific chronic pain for the whole age group. Each cell shows the coefficient estimates, 95% CIs, and corresponding p-values for Models 1, 2, and 3. The p-values ≤ 0.05 and p-values ≤ 0.01 are marked as * and **, respectively. Model 1: marginal model; Model 2: adjusted for age, BMI, race, education status, current employment, history of smoking, and alcohol consumption; Model 3: additional adjustments for diabetes, CHF, stroke, cancer, asthma, emphysema, bronchitis, and myocardial disease.

-187.2, $p_{spine} = 0.011$; $\beta_{leg} = -176.6$, $p_{leg} = 0.021$), CPM ($males$: $\beta_{spine} = -66.3$, $p_{spine} < 0.001$; $\beta_{leg} = -69.4$, $p_{leg} < 0.001$; $females$: $\beta_{spine} = -41.6$, $p_{spine} = 0.001$; $\beta_{leg} = -34.1$, $p_{leg} = 0.031$), when comparing with those without pain. In addition, males with CP in spine or leg have *lower* LIPA ($\beta_{spine} = -28.9$, $p_{spine} = 0.01$; $\beta_{leg} = -35.5$, $p_{leg} = 0.001$), *lower* MVPA ($\beta_{spine} = -9.2$, $p_{spine} < 0.001$; $\beta_{leg} = -9.3$, $p_{leg} = 0.009$), and *higher* ST ($\beta_{spine} = 38$, $p_{spine} = 0.002$; $\beta_{leg} = 44.8$, $p_{leg} < 0.001$). Females with spinal or leg pain have *lower* MVPA ($\beta_{spine} = -6.7$, $p_{spine} < 0.001$; $\beta_{leg} = -6.8$, $p_{leg} < 0.001$), while females with spinal pain have *higher* ST ($\beta = 25.4$, $p = 0.012$).

Males with chronic arm pain have *lower* TAC ($\beta = -44208.9$, $p = 0.006$), TLAC ($\beta = -195.1$, $p = 0.025$), CPM ($\beta = -56.4$, $p = 0.003$), and MVPA

($\beta = -7.4$, $p = 0.021$) when compared to the no-pain group. For females, only MVPA is significantly different ($\beta = -5.2$, $p = 0.012$). In general, the estimated differences in PA measurements between pain groups tend to be lower in females compared to males.

ii) Measures of PA fragmentation

In unadjusted analyses, ASTP tends to be significantly *higher* for males with CP at any body location ($\beta_{arm} = 0.023$, $p_{arm} = 0.022$; $\beta_{spine} = 0.021$, $p_{spine} = 0.035$; $\beta_{leg} = 0.027$, $p_{leg} < 0.001$) and females with spinal CP ($\beta = 0.017$, $p = 0.036$). SATP tends to be *lower* for males with leg or spinal CP ($\beta_{spine} = -0.004$, $p_{spine} = 0.031$; $\beta_{leg} = -0.007$, $p_{leg} = 0.011$) and females with arm or leg pain ($\beta_{arm} = -0.006$, $p_{arm} = 0.043$; $\beta_{leg} = -0.006$, $p_{leg} = 0.003$).

Next, we consider the effects of potential confounders and summarize the results in adjusted models (Models 2 and 3):

i) Measures of PA volume

In adjusted models, the females in the spinal CP have significantly *lower* levels of TAC ($Model\,2 : \beta = -23339.7$, $p = 0.002$; $Model\,3 : \beta = -19748$, $p = 0.033$) and MVPA ($Model\,2 : \beta = -4.3$, $p = 0.002$; $Model\,3 : \beta = -4.2$, $p = 0.011$) in Models 2 and 3, and *lower* CPM ($\beta = -25.1$, $p = 0.006$) in Model 2. For males with spinal pain, the only significant difference was observed for MVPA ($\beta = -5.2$, $p = 0.024$) in Model 2. In the leg CP group males tend to have significantly *lower* CPM ($\beta = -26.3$, $p = 0.015$) and females have *lower* MVPA ($\beta = -4$, $p < 0.001$) compared to the no-pain group. After adjusting for confounders, in the arm CP group there are no PA outcomes that are significantly associated with pain status.

ii) Measures of PA fragmentation

After adjusting for confounders, there are no significant differences for either sex when comparing CP groups with the no pain group.

Results suggest that marginally, in the 25-85 years old age sample, individuals with any type of CP engage in less physical activity in both males and females, and have increased activity fragmentation. Differences between CP groups are less pronounced in females compared to males, and the differences appear to vary based on the CP location. For many locations, except those discussed above, the statistical significance of the association disappears when adjusting for potential confounders. This could be due to the small sample sizes used once data are stratified by sex and CP location.

3.3.2 Associations in the 25-45 years old age group

Table 3.4 provides results similar with **Table 3.3**, but focused on the 25-45 age group instead of the entire group. We first investigate the results obtained from the marginal models (Model 1):

i) Measures of PA volume

For males having spinal and leg CP, have significantly *lower* TAC ($\beta_{spine} = -86911.2$, $p_{spine} < 0.001$; $\beta_{leg} = -87056.1$, $p_{leg} = 0.025$), TLAC ($\beta_{spine} = -357.3$, $p_{spine} < 0.001$; $\beta_{leg} = -530.1$, $p_{leg} = 0.004$), CPM ($\beta_{spine} = -115.1$, $p_{spine} < 0.001$; $\beta_{leg} = -112.6$, $p_{leg} = 0.006$), LIPA ($\beta_{spine} = -39.8$, $p_{spine} < 0.001$; $\beta_{leg} = -74.1$, $p_{leg} = 0.002$), and *higher* ST ($\beta_{spine} = 53.9$, $p_{spine} < 0.001$; $\beta_{leg} =$

		Age Group: 25-45 years old					
		Arm		Spine		Leg	
		Male	Female	Male	Female	Male	Female
TAC	Model 1	-33143.8	30704.6	-86911.2	-15256.9	-87056.1	-21658.8
		(-116027.1, 49739.4)	(-32872.2, 94281.3)	(-127519.2, -46303.1) **	(-59837.2, 29323.4)	(-163021.1, -11091) *	(-59244.3, 15926.8)
	Model 2	14593.4	41729.8	-62041.4	1325.4	-47921.4	-259.7
		(-61316, 90502.8)	(-33850.7, 117310.3)	(-88412, -35670.8) **	(-48930.8, 51581.7)	(-122035.3, 26192.5)	(-47405.4, 46886)
	Model 3	24332.9	44560.1	-56516.7	-1794.9	-45797	-5657.6
		(-37926.2, 86592.1)	(17812.5, 71307.7) **	(-73171.8, -39861.7) **	(-19971.8, 16382)	(-83823.9, -7770.2) *	(-25434.2, 14119)
TLAC	Model 1	-106.9 (-397.9, 184.2)	141.1 (-332.9, 615.2)	-357.3 (-497.5, -217.1) **	-56.8 (-262.6, 149)	-530.1 (-889.4, -170.9) **	-81 (-315.3, 153.3)
	Model 2	140.4 (-194, 474.7)	215.8 (-289.4, 721)	-223 (-343, -102.9) **	-4.6 (-256, 246.7)	-322 (-659.9, 15.9)	-5.9 (-261.8, 250)
	Model 3	194.6 (-75.2, 464.3)	221.8 (69.4, 374.3) **	-184.3 (-328.6, -40) *	-6.7 (-81.4, 68)	-308.6 (-485.1, -132.1) **	-27.5 (-97.3, 42.3)
CPM	Model 1	-61.3 (-148.5, 25.9)	40.2 (-30.5, 110.9)	-115.1 (-170.8, -59.4) **	-12.1 (-67.1, 42.9)	-112.6 (-192.5, -32.6) **	-10.2 (-48.8, 28.4)
	Model 2	-10.1 (-89.1, 68.9)	50.7 (-35.9, 137.3)	-87.7 (-133.1, -42.3) **	5.5 (-56.6, 67.7)	-69.7 (-144.7, 5.3)	12.4 (-42.8, 67.7)
	Model 3	1.2 (-58.9, 61.4)	50.9 (17.8, 84) **	-80.9 (-103.1, -58.6) **	0.6 (-19.8, 21)	-65.3 (-104.1, -26.5) **	5.4 (-18.7, 29.6)
ST	Model 1	15.9 (-27.1, 58.8)	-39.2 (-109, 30.5)	53.9 (32.8, 75.1) **	1.5 (-32.1, 35)	83.4 (31.8, 135.1) **	-6.4 (-36, 23.1)
	Model 2	-20.3 (-71, 30.3)	-52 (-128.6, 24.6)	35.4 (14.2, 56.7) **	-6.8 (-47.9, 34.2)	53.7 (11.4, 95.9) *	-17 (-51.5, 17.5)
	Model 3	-27.3 (-67.4, 12.8)	-51.8 (-78, -25.6) **	30.6 (8.6, 52.7) **	-4.9 (-13.8, 3.9)	51.5 (23.2, 79.8) **	-11.7 (-21.3, -2) *
LIPA	Model 1	-9.8 (-41.1, 21.5)	40 (-26.5, 106.5)	-39.8 (-58.7, -20.9) **	3.8 (-26.5, 34.2)	-74.1 (-120.6, -27.7) **	14.4 (-13.2, 41.9)
	Model 2	19.3 (-20.8, 59.4)	51.3 (-20.6, 123.2)	-24.8 (-46.8, -2.8) *	9.2 (-28.5, 46.8)	-50.2 (-87.2, -13.3) **	20.8 (-9.2, 50.8)
	Model 3	24.1 (-6.9, 55.1)	50.6 (26, 75.1) **	-21.3 (-43.6, 1)	7.9 (1, 14.9) *	-48.6 (-80.6, -16.7) **	16.1 (8.7, 23.6) **
MVPA	Model 1	-6 (-23.4, 11.4)	-0.8 (-6.4, 4.8)	-14.1 (-22.5, -5.7) **	-5.3 (-11.4, 0.9)	-9.3 (-27.9, 9.3)	-8 (-14.5, -1.4) *
	Model 2	1 (-13.6, 15.7)	0.7 (-6.7, 8)	-10.6 (-16.5, -4.7) **	-2.4 (-8.9, 4.2)	-3.4 (-23.9, 17.1)	-3.9 (-11.6, 3.9)
	Model 3	3.2 (-9.2, 15.6)	1.3 (-1.5, 4.1)	-9.3 (-12.3, -6.3) **	-3 (-6.5, 0.6)	-2.9 (-14.4, 8.7)	-4.5 (-7.4, -1.5) **
SATP	Model 1	0.003 (-0.004, 0.009)	-0.004 (-0.02, 0.013)	-0.003 (-0.012, 0.006)	-0.004 (-0.012, 0.004)	-0.012 (-0.023, 0)	-0.009 (-0.016, -0.001) *
	Model 2	0.008 (-0.001, 0.016)	-0.003 (-0.018, 0.012)	-0.001 (-0.01, 0.009)	-0.003 (-0.012, 0.007)	-0.008 (-0.018, 0.002)	-0.006 (-0.014, 0.002)
	Model 3	0.009 (0.001, 0.016) *	-0.003 (-0.009, 0.004)	-0.001 (-0.009, 0.008)	-0.002 (-0.005, 0)	-0.008 (-0.017, 0.001)	-0.006 (-0.009, -0.004) **
ASTP	Model 1	0.016 (-0.007, 0.04)	-0.043 (-0.079, -0.007) *	0.035 (0.009, 0.061) **	-0.013 (-0.041, 0.016)	0.047 (0.015, 0.078) **	-0.032 (-0.055, -0.008) **
	Model 2	-0.004 (-0.036, 0.028)	-0.05 (-0.093, -0.007) *	0.022 (-0.002, 0.047)	-0.017 (-0.042, 0.008)	0.028 (0.005, 0.051) *	-0.034 (-0.057, -0.012) **
	Model 3	-0.007 (-0.03, 0.017)	-0.05 (-0.074, -0.026) **	0.02 (0.006, 0.033) **	-0.013 (-0.02, -0.007) **	0.026 (0.012, 0.041) **	-0.029 (-0.038, -0.021) **

Table 3.4: Associations of PA and location-specific chronic pain for the 25-45 age group. Each cell shows the coefficient estimates, 95% CIs, and corresponding p values of Models 1, 2, and 3. The p-values ≤ 0.05 and p-values ≤ 0.01 are marked as * and **.

83.4, $p_{leg} = 0.002$), which is consistent with *lower* levels of volume of activity compared to study participants who did not report CP. In addition, MVPA is significantly *lower* for males with spinal CP compared to the no CP group ($\beta = -14.1$, $p = 0.001$), though not for those with leg CP.

ii) Measures of PA fragmentation

Compared with the no CP group, ASTP is significantly *higher* for males having chronic spinal or leg pain ($\beta_{spine} = 0.035$, $p_{spine} = 0.009$; $\beta_{leg} = 0.047$, $p_{leg} = 0.004$), but it is *lower* for females having chronic arm or leg pain ($\beta_{arm} = -0.043$, $p_{arm} = 0.019$; $\beta_{leg} = -0.032$, $p_{leg} = 0.008$). For SATP, only females with leg CP have a significantly *lower* value compared to the no CP group ($\beta = -0.009$, $p = 0.008$).

Next, we consider the effects of potential confounders and establish adjusted

models (Models 2 and 3) for the 25-45 age group:

i) Measures of PA volume

For males with CP in spine, in both adjusted Models 2 and 3, the pain status is significantly associated with all measures of PA volume including TAC ($Model\,2: \beta = -62041.4,\ p < 0.001;\ Model\,3: \beta = -56516.7,\ p < 0.001$), TLAC ($Model\,2: \beta = -223,\ p < 0.001;\ Model\,3: \beta = -184.3,\ p = 0.012$), CPM ($Model\,2: \beta = -87.7,\ p < 0.001;\ Model\,3: \beta = -80.9,\ p < 0.001$), ST ($Model\,2: \beta = 35.4,\ p = 0.001;\ Model\,3: \beta = 30.6,\ p = 0.006$), LIPA ($Model\,2: \beta = -24.8,\ p = 0.027$), and MVPA ($Model\,2: \beta = -10.6,\ p < 0.001$; $Model\,3: \beta = -9.3,\ p < 0.001$). The only exception was LIPA in Model 3. For males with CP in leg, the CP indicator is significantly associated with ST ($Model\,2: \beta = 53.7,\ p = 0.013;\ Model\,3: \beta = 51.5,\ p < 0.001$) and LIPA ($Model\,2: \beta = -50.2,\ p = 0.013;\ Model\,3: \beta = -48.6,\ p = 0.003$) in both Model 2 and Model 3, and it is significantly associated with TAC ($\beta = -45797,\ p = 0.018$), TLAC ($\beta = -308.6,\ p = 0.001$), and CPM ($\beta = -65.3,\ p = 0.001$) only in Model 3.

We also observe some counter-intuitive results for females with chronic arm pain. Compared to females who did not report pain, they tend to have statistically significant and *higher* TAC ($\beta = 44560.1,\ p = 0.001$), TLAC ($\beta = 221.8,\ p = 0.004$), CPM ($\beta = 50.9,\ p = 0.003$), LIPA ($\beta = 50.6,\ p < 0.001$), and *lower* ST ($\beta = -51.8,\ p < 0.001$) in Model 3. This finding is consistent with Figure 2.

ii) Measures of PA fragmentation

In both Models 2 and 3, ASTP is significantly *lower* for females with CP in arm or leg ($Model\,2: \beta_{arm} = -0.05,\ p_{arm} = 0.023;\ \beta_{leg} = -0.034,\ p_{leg} =$

0.003; $Model\,3 : \beta_{arm} = -0.05$, $p_{arm} < 0.001$; $\beta_{leg} = -0.029$, $p_{leg} < 0.001$), and it is *higher* for males with CP in leg ($Model\,2 : \beta = 0.028$, $p = 0.017$; $Model\,3 : \beta = 0.026$, $p < 0.001$). In the spinal pain group, ASTP is *lower* for females but *higher* for males in Model 3 compared to the corresponding no pain group ($males : \beta = 0.02, p = 0.005$; $females : \beta = -0.013, p < 0.001$). In addition, in Model 3, males with CP in arm have *higher* SATP ($\beta = 0.009$, $p < 0.001$), while females with CP in leg have *lower* SATP ($\beta = -0.006$, $p = 0.018$) compared to the corresponding no pain group.

In summary, among the group 25-45 age group, males with either spinal or leg CP are less physically active even after adjusting for confounding. In addition, females with arm CP tend to have higher levels of total PA as well as light, moderate, and vigorous intensity PA, even after adjusting for demographic and medical covariates.

3.3.3 Associations in the 45-65 years old age group

Table 3.5 provides results similar with **Tables 3.3 and 3.4**, but focused on the 45-65 age group. We first investigate the results obtained from the marginal models (Model 1):

i) Measures of PA volume

In unadjusted analyses, females with any type of chronic pain (arm, spine, or leg) engage in significantly less physical activity as indicated by their *lower* TAC ($\beta_{arm} = -51933.5$, $p_{arm} = 0.004$; $\beta_{spine} = -69354.6$, $p_{spine} < 0.001$; $\beta_{leg} = -47579$, $p_{leg} = 0.001$), TLAC ($\beta_{arm} = -358.5$, $p_{arm} = 0.004$; $\beta_{spine} =$

		Age Group: 45-65 years old					
		Arm		Spine		Leg	
		Male	Female	Male	Female	Male	Female
TAC	Model 1	-44017.2	-51933.5	-36419.7	-69354.6	-39401.3	-47579
		(-93714.1, 5679.6)	(-86818.7, -17048.4) **	(-76235.6, 3396.2)	(-95331.6, -43377.5) **	(-68712.5, -10090.1) **	(-76169.7, -18988.4) **
	Model 2	-27520.1	-31401.5	-9413.6	-57894.4	-7209	-33182.9
		(-75987.2, 20947.1)	(-60320.3, -2482.6) *	(-47225.7, 28398.4)	(-87353.4, -28435.4) **	(-37044, 22626)	(-59282.9, -7083) *
	Model 3	-25851.3	-24675.7	-13187	-50793.2	-9244.7	-25033.2
		(-67761.2, 16058.6)	(-52503.1, 3151.7)	(-55521.8, 29147.8)	(-83221.8, -18364.6) **	(-39500.6, 21011.2)	(-51121.1, 1054.7)
TLAC	Model 1	-209.6 (-458.1, 39)	-358.5 (-603.6, -113.3) **	-213.2 (-465.6, 39.2)	-328.6 (-600.9, -56.3) *	-193.2 (-494, 107.7)	-305.8 (-499.8, -111.9) **
	Model 2	-99.7 (-373.2, 173.8)	-233.4 (-447.2, -19.7) *	-58.1 (-263.1, 146.9)	-224.8 (-517.1, 67.4)	0.4 (-285.7, 286.5)	-211.8 (-414.4, -9.1) *
	Model 3	-94.2 (-406.1, 217.8)	-160.1 (-324.3, 4.1)	-77.6 (-311.2, 156)	-123.5 (-354.3, 107.3)	0.9 (-299.3, 301.1)	-131.4 (-253.2, -9.6) *
CPM	Model 1	-45.5 (-102, 10.9)	-52.8 (-90.7, -14.8) **	-30.8 (-75.1, 13.6)	-76.2 (-105.7, -46.8) **	-35.3 (-59.5, -11.1) **	-51.5 (-84.6, -18.5) **
	Model 2	-35.2 (-90.6, 20.1)	-32 (-65.9, 1.9)	-4.2 (-46.8, 38.4)	-66.8 (-103.1, -30.6) **	-5.6 (-30.7, 19.6)	-37.8 (-70.5, -5.1) *
	Model 3	-34.5 (-81.1, 12.1)	-23.9 (-61, 13.2)	-8.1 (-54.9, 38.7)	-60.2 (-102.7, -17.6) **	-9.5 (-41.5, 22.6)	-28 (-61.4, 5.3)
ST	Model 1	21.5 (-14.3, 57.3)	55.4 (22.2, 88.5) **	27.4 (-11.3, 66.1)	51.2 (13.7, 88.7) **	20.7 (-20.8, 62.3)	44.4 (12.6, 76.2) **
	Model 2	8.6 (-33.1, 50.3)	38.7 (6.8, 70.6) *	7.9 (-26.2, 42.1)	40.2 (-1.3, 81.8)	-4.7 (-46.9, 37.5)	32 (-1.8, 65.9)
	Model 3	9.4 (-37.5, 56.3)	27.8 (5.7, 49.8) *	12.1 (-23.3, 47.5)	25.7 (-9.2, 60.6)	-3.2 (-46.3, 39.9)	19 (-2.5, 40.5)
LIPA	Model 1	-14.6 (-49.4, 20.2)	-48.1 (-80, -16.2) **	-22.1 (-60.5, 16.2)	-41 (-78.9, -3.2) *	-13.7 (-55.8, 28.4)	-36.7 (-67.8, -5.6) *
	Model 2	-2.9 (-45.7, 39.8)	-33.6 (-64.3, -2.8) *	-6.4 (-42.5, 29.7)	-31.2 (-73.2, 10.8)	8 (-36.8, 52.8)	-25.8 (-59.6, 8)
	Model 3	-4.7 (-52.8, 43.3)	-23 (-43.8, -2.1) *	-10.7 (-48, 26.5)	-16.6 (-50.5, 17.3)	6.4 (-39.4, 52.1)	-13.1 (-34.6, 8.4)
MVPA	Model 1	-6.9 (-16.7, 2.9)	-7.3 (-11.2, -3.3) **	-5.3 (-12.6, 2)	-10.1 (-13.7, -6.6) **	-7 (-13.2, -0.9) *	-7.7 (-11.4, -4) **
	Model 2	-5.6 (-15.4, 4.2)	-5.1 (-9.1, -1.2) *	-1.5 (-9.2, 6.1)	-9 (-14.8, -3.3) **	-3.3 (-10.8, 4.2)	-6.2 (-9.8, -2.7) **
	Model 3	-4.7 (-12.5, 3.2)	-4.8 (-9.6, -0.1) *	-1.4 (-9.9, 7.1)	-9.1 (-15.2, -3) **	-3.2 (-11.3, 4.9)	-5.9 (-10.2, -1.5) **
SATP	Model 1	-0.001 (-0.008, 0.006)	-0.008 (-0.015, -0.001) *	-0.006 (-0.014, 0.002)	-0.005 (-0.014, 0.004)	-0.004 (-0.015, 0.006)	-0.007 (-0.013, -0.001) *
	Model 2	0 (-0.008, 0.008)	-0.004 (-0.011, 0.002)	-0.004 (-0.011, 0.004)	-0.001 (-0.01, 0.008)	-0.002 (-0.012, 0.009)	-0.003 (-0.01, 0.003)
	Model 3	0.001 (-0.008, 0.01)	-0.002 (-0.008, 0.004)	-0.004 (-0.012, 0.004)	0.002 (-0.004, 0.009)	0 (-0.012, 0.011)	-0.001 (-0.005, 0.003)
ASTP	Model 1	0.021 (-0.01, 0.051)	0.043 (0.014, 0.072) **	0.009 (-0.014, 0.031)	0.046 (0.017, 0.075) **	0.01 (-0.004, 0.023)	0.033 (0.004, 0.062) *
	Model 2	0.009 (-0.022, 0.041)	0.035 (0.001, 0.068) *	-0.002 (-0.024, 0.02)	0.043 (0.008, 0.079) *	-0.007 (-0.026, 0.012)	0.028 (-0.004, 0.06)
	Model 3	0.008 (-0.023, 0.04)	0.022 (-0.01, 0.053)	-0.002 (-0.024, 0.021)	0.032 (-0.001, 0.064)	-0.005 (-0.024, 0.014)	0.013 (-0.005, 0.031)

Table 3.5: Associations of PA and location-specific chronic pain for the 45-65 age group. Each cell shows the coefficient estimates, 95% CIs, and corresponding p values of Models 1, 2, and 3. The p-values ≤ 0.05 and p-values ≤ 0.01 are marked as * and **.

-328.6, $p_{spine} = 0.018$; $\beta_{leg} = -305.8$, $p_{leg} = 0.002$), CPM ($\beta_{arm} = -52.8$, $p_{arm} = 0.006$; $\beta_{spine} = -76.2$, $p_{spine} < 0.001$; $\beta_{leg} = -51.5$, $p_{leg} = 0.002$), LIPA ($\beta_{arm} = -48.1$, $p_{arm} = 0.003$; $\beta_{spine} = -41$, $p_{spine} = 0.034$; $\beta_{leg} = -36.7$, $p_{leg} = 0.021$), MVPA ($\beta_{arm} = -7.3$, $p_{arm} < 0.001$; $\beta_{spine} = -10.1$, $p_{spine} < 0.001$; $\beta_{leg} = -7.7$, $p_{leg} < 0.001$), and *higher* ST ($\beta_{arm} = 55.4$, $p_{arm} = 0.001$; $\beta_{spine} = 51.2$, $p_{spine} = 0.008$; $\beta_{leg} = 44.4$, $p_{leg} = 0.006$). For males, only the ones with CP in leg have *lower* values of TAC ($\beta = -39401.3$, $p = 0.008$), CPM ($\beta = -35.3$, $p = 0.004$), and MVPA ($\beta = -7$, $p = 0.024$).

ii) Measures of PA fragmentation

In unadjusted analyses, ASTP is significantly *higher* for females with with any type of CP ($\beta_{arm} = 0.043$, $p_{arm} = 0.004$; $\beta_{spine} = 0.046$, $p_{spine} = 0.002$; $\beta_{leg} = 0.033$, $p_{leg} = 0.025$), and SATP is *lower* for those with CP in

arm or leg ($\beta_{arm} = -0.008$, $p_{arm} = 0.023$; $\beta_{leg} = -0.007$, $p_{leg} = 0.013$). However, there are no differences in either ASTP or SATP for males.

Second, we focus on the the adjusted models (Models 2 and 3):

i) Measures of PA volume

After adjusting for confounders, there is no significant difference between CP and no pain groups in males. For females, measures of PA volume (TAC, TLAC, CPM) are significantly associated with pain status in Model 2 (TAC: $\beta_{arm} = -31401.5$, $p_{arm} = 0.033$; $\beta_{spine} = -57894.4$, $p_{spine} < 0.001$; $\beta_{leg} = -33182.9$, $p_{leg} = 0.013$; TLAC: $\beta_{arm} = -233.4$, $p_{arm} = 0.032$; $\beta_{leg} = -211.8$, $p_{leg} = 0.041$; CPM: $\beta_{spine} = -66.8$, $p_{spine} < 0.001$). Some exceptions are CPM for the arm and leg pain group and TLAC for the spinal pain group. In the fully adjusted Model 3, only TAC ($\beta = -50793.2$, $p = 0.002$) and CPM ($\beta = -60.2$, $p = 0.006$) are significantly associated with spinal pain, and TLAC ($\beta = -131.4$, $p = 0.034$) is associated with leg pain.

For PA volume estimators for time spent in specific activity intensity (ST, LIPA, MVPA), the significance levels appear to differ by the locations of CP. In adjusted Models 2 and 3, ST ($Model\,2 : \beta = 38.7$, $p = 0.017$; $Model\,3 : \beta = 27.8$, $p = 0.014$), LIPA ($Model\,2 : \beta = -33.6$, $p = 0.032$; $Model\,3 : \beta = -23$, $p = 0.031$), and MVPA ($Model\,2 : \beta = -5.1$, $p = 0.011$; $Model\,3 : \beta = -4.8$, $p = 0.048$) are all associated with arm pain, and MVPA is also associated with spinal and leg pain ($Model\,2 : \beta_{spine} = -9$, $p_{spine} = 0.002$; $\beta_{leg} = -6.2$, $p_{leg} = 0.001$; $Model\,3 : \beta_{spine} = -9.1$, $p_{spine} = 0.004$; $\beta_{leg} = -5.9$, $p_{leg} = 0.008$).

ii) Measures of PA fragmentation

In adjusted models, only ASTP in Model 2 is significantly *higher* for females with CP in arm or spine ($\beta_{arm} = 0.035$, $p_{arm} = 0.044$; $\beta_{spine} = 0.043$, $p_{spine} = 0.017$).

In summary, for the 45-65 years old age group, the estimated differences for measurements of both volume and fragmentation tend to be stronger in females than males. Females with any type of chronic pain engage in less physical activity, and the statistical significance of some measures of association hold even after adjusting for confounders.

3.3.4 Associations in the 65-85 years old age group

		Age Group: 65-85 years old					
		Arm		Spine		Leg	
		Male	Female	Male	Female	Male	Female
TAC	Model 1	-45078.2	2395.8	-50490.5	-13973.2	-45985.2	-1640.8
		(-71599.6, -18556.9) **	(-37861.6, 42653.2)	(-73262.4, -27718.7) **	(-43505.1, 15558.7)	(-73893.4, -18077) **	(-32070.5, 28788.9)
	Model 2	-34555.7	-8618.6	-51780.5	-15964.9	-42618.1	-12837.8
		(-69103.8, -7.6) *	(-43039.6, 25802.3)	(-77352.4, -26208.6) **	(-47885.6, 15955.8)	(-67694.1, -17542.1) **	(-46147.4, 20471.8)
	Model 3	-27234.4	-8660.7	-39404.9	-16270.6	-42463.8	-11332.1
		(-55060.4, 591.7)	(-52796.4, 35475.1)	(-60972.1, -17837.7) **	(-56135.8, 23594.6)	(-66893.6, -18034) **	(-49209.2, 26545)
TLAC	Model 1	-245.4 (-585.9, 95.1)	-26 (-377.2, 325.1)	-246.8 (-468.7, -24.9) *	-170.5 (-387.3, 46.3)	-191.5 (-466.9, 83.8)	-5.6 (-258, 246.7)
	Model 2	-155.1 (-465.1, 154.8)	-84 (-392.3, 224.3)	-243.7 (-562.6, 75.2)	-175.7 (-400.6, 49.2)	-208.5 (-411.3, -5.6) *	-60.2 (-324.1, 203.7)
	Model 3	-141.7 (-384.4, 101)	-81 (-437.4, 275.4)	-165.4 (-473.3, 142.5)	-181.1 (-453.3, 91.1)	-241 (-447.7, -34.3) *	-53.6 (-340.5, 233.3)
CPM	Model 1	-49.7 (-83.5, -15.9) **	7 (-45, 59.1)	-52.7 (-79.7, -25.6) **	-10.8 (-46.7, 25.1)	-43.7 (-84.5, -2.9) *	-1.7 (-33.3, 29.8)
	Model 2	-37.9 (-82.2, 6.4)	-6.5 (-53.2, 40.3)	-54.5 (-85.7, -23.4) **	-13.7 (-49.4, 22.1)	-38.5 (-75.4, -1.7) *	-14.8 (-47.2, 17.6)
	Model 3	-31.8 (-72.9, 9.3)	-5 (-61, 51)	-44.1 (-68.7, -19.5) **	-13.4 (-56.8, 30)	-38.9 (-74.6, -3.2) *	-12.9 (-51.2, 25.5)
ST	Model 1	36.4 (-9.3, 82.2)	-3.9 (-52.2, 44.5)	33.4 (1.7, 65.1) *	17.3 (-13.9, 48.6)	28.2 (-16.4, 72.9)	-3.7 (-42.6, 35.1)
	Model 2	23.2 (-20.3, 66.6)	5.5 (-32.4, 43.4)	33.7 (-8.5, 75.8)	17.8 (-13.4, 48.9)	29.6 (-5.9, 65.1)	5.6 (-33.5, 44.8)
	Model 3	18.8 (-13.6, 51.1)	5.5 (-38, 49)	23.5 (-15.9, 62.9)	18.9 (-22, 59.8)	31.7 (-1.7, 65.2)	4 (-39.1, 47.1)
LIPA	Model 1	-30.2 (-77, 16.5)	4.1 (-42.6, 50.7)	-25.7 (-56.8, 5.3)	-17 (-45.4, 11.5)	-20.6 (-65.2, 24)	4.3 (-32.3, 41)
	Model 2	-17.7 (-60.7, 25.3)	-4 (-40.7, 32.6)	-25.9 (-67.7, 15.8)	-17.1 (-45.7, 11.6)	-23 (-57.4, 11.5)	-3.6 (-39.9, 32.7)
	Model 3	-14.6 (-47.5, 18.3)	-3.2 (-43.5, 37.2)	-17.9 (-57.9, 22.2)	-17.8 (-55.1, 19.5)	-25.4 (-58.3, 7.5)	-1.8 (-41.6, 37.9)
MVPA	Model 1	-6.2 (-10.3, -2.2) **	-0.2 (-5.2, 4.7)	-7.6 (-9.6, -5.6) **	-0.4 (-4.2, 3.5)	-7.6 (-9.1, -6.1) **	-0.6 (-4.3, 3.1)
	Model 2	-5.5 (-11.5, 0.5)	-1.5 (-6.1, 3.1)	-7.7 (-9.2, -6.2) **	-0.7 (-5, 3.6)	-6.6 (-9, -4.3) **	-2 (-6.2, 2.2)
	Model 3	-4.2 (-10.3, 2)	-2.3 (-7.7, 3)	-5.6 (-7.8, -3.5) **	-1.1 (-5.7, 3.6)	-6.3 (-9.3, -3.4) **	-2.2 (-6.4, 2.1)
SATP	Model 1	-0.006 (-0.015, 0.003)	-0.001 (-0.011, 0.009)	-0.004 (-0.011, 0.004)	-0.005 (-0.011, 0)	-0.004 (-0.012, 0.003)	0 (-0.009, 0.009)
	Model 2	-0.003 (-0.011, 0.006)	-0.002 (-0.01, 0.007)	-0.002 (-0.012, 0.007)	-0.005 (-0.011, 0.002)	-0.005 (-0.01, 0)	-0.001 (-0.01, 0.008)
	Model 3	-0.002 (-0.01, 0.007)	-0.003 (-0.011, 0.005)	0 (-0.01, 0.01)	-0.006 (-0.013, 0.001)	-0.005 (-0.011, 0.001)	-0.001 (-0.009, 0.007)
ASTP	Model 1	0.037 (-0.003, 0.078)	-0.006 (-0.053, 0.04)	0.031 (0.001, 0.061) *	0.005 (-0.034, 0.045)	0.032 (-0.016, 0.081)	-0.007 (-0.039, 0.024)
	Model 2	0.036 (-0.002, 0.073)	0.002 (-0.039, 0.043)	0.039 (0.006, 0.072) *	0.007 (-0.026, 0.04)	0.037 (-0.005, 0.078)	0.002 (-0.03, 0.033)
	Model 3	0.033 (0, 0.066) *	-0.004 (-0.046, 0.038)	0.034 (0.006, 0.063) *	0.005 (-0.029, 0.039)	0.039 (0.002, 0.077) *	-0.003 (-0.038, 0.033)

Table 3.6: Associations of PA and location-specific chronic pain for the 65-85 age group. Each cell shows the coefficient estimates, 95% CIs, and corresponding p values of Models 1, 2, and 3. The p-values ≤ 0.05 and p-values ≤ 0.01 are marked as * and **.

Table 3.6 provides results similar with **Tables 3.3, 3.4, and 3.5**, but focused on the 65-85 age group. We first investigate the results obtained from the marginal models (Model 1):

i) Measures of PA volume

In unadjusted analyses, for females there are no significant differences in PA levels between the CP groups and no pain group. For males with CP, irrespective to pain location, they all tend to have *lower* levels of TAC ($\beta_{arm} = -45078.2$, $p_{arm} = 0.001$; $\beta_{spine} = -50490.5$, $p_{spine} < 0.001$; $\beta_{leg} = -45985.2$, $p_{leg} = 0.001$), CPM ($\beta_{arm} = -49.7$, $p_{arm} = 0.004$; $\beta_{spine} = -52.7$, $p_{spine} < 0.001$; $\beta_{leg} = -43.7$, $p_{leg} = 0.036$), and MVPA ($\beta_{arm} = -6.2$, $p_{arm} = 0.003$; $\beta_{spine} = -7.6$, $p_{spine} < 0.001$; $\beta_{leg} = -7.6$, $p_{leg} < 0.001$). In addition, males with spinal pain have *lower* TLAC ($\beta = -246.8$, $p = 0.029$) and *higher* ST ($\beta = 33.4$, $p = 0.039$) .

ii) Measures of PA fragmentation

In unadjusted analyses, only males with CP in spine tend to have *higher* ASTP ($\beta = 0.031$, $p = 0.045$).

Further, the adjusted models (Models 2 and 3) suggest that:

i) Measures of PA volume

In adjusted models, the differences in PA outcomes comparing individuals with and without pain remains significant for males. In Models 2 and 3, both spinal and leg pain indicators are significantly associated with TAC ($Model\,2$: $\beta_{spine} = -51780.5$, $p_{spine} < 0.001$; $\beta_{leg} = -42618.1$, $p_{leg} = 0.001$; $Model\,3$: $\beta_{spine} = -39404.9$, $p_{spine} < 0.001$; $\beta_{leg} = -42463.8$, $p_{leg} =$

0.001), CPM ($Model\,2 : \beta_{spine} = -54.5,\ p_{spine} = 0.001;\ \beta_{leg} = -38.5,\ p_{leg} = 0.04;\ Model\,3 : \beta_{spine} = -44.1,\ p_{spine} < 0.001;\ \beta_{leg} = -38.9,\ p_{leg} = 0.032$), and MVPA ($Model\,2 : \beta_{spine} = -7.7,\ p_{spine} < 0.001;\ \beta_{leg} = -6.6,\ p_{leg} < 0.001;\ Model\,3 : \beta_{spine} = -5.6,\ p_{spine} < 0.001;\ \beta_{leg} = -6.3,\ p_{leg} < 0.001$), and leg pain is significantly associated with TLAC ($Model\,2 : \beta = -208.5,\ p = 0.044;\ Model\,3 : \beta = -241,\ p = 0.022$). Arm pain is associated with TAC ($\beta = -34555.7,\ p = 0.05$) in Model 2 but not in Model 3.

ii) Measures of PA fragmentation

In fully adjusted models (Model 3), ASTP is significantly *higher* for males with any type ofCP ($\beta_{arm} = 0.033,\ p_{arm} = 0.047;\ \beta_{spine} = 0.034,\ p_{spine} = 0.017;\ \beta_{leg} = 0.039,\ p_{leg} = 0.038$). In models adjusted only for demographic variables (Model 2), ASTP was only *higher* for males with CP in spine ($\beta = 0.039,\ p = 0.022$).

In summary, among the 65-85 years old males, participants with CP have significantly lower PA levels than those with no pain. In general, the differences are larger in measures of total PA volume and intensity compared to PA fragmentation measures.

Chapter 4

Discussion

We have assessed the associations between PA measures and CP in different body locations, and have shown that the magnitude of the associations may vary by gender and age strata. To the best of our knowledge, this is the first population-based research studying the association between location-specific CP and objective measures of PA. Our results provide evidence indicating that: (i) individuals with CP tend to engage in less PA compared to the ones with no pain; and (ii) these differences are more pronounced in males than females especially in the 25-45 and 65-85 age groups. The present study shows that 25-45 and 65-85 years old males with CP in spine or lower limbs, and 45-65 years old females with CP in upper limbs, spine, or lower limbs tend to have lower values of TAC, a measure that is strongly correlated with maximum intensity activity. Furthermore, 45-65 year old females with any type of CP and young males with CP in spine have higher ST, lower LIPA and MVPA compared to those without pain. They also have higher ASTP, a measure of PA fragmentation. Finally, for 65-85 year old males, spinal and leg CP is significantly associated

with MVPA but not LIPA. Although adjusting for relevant covariates typically reduces the magnitude of estimated associations between CP and PA outcomes, most differences discussed above remain statistically significant (as shown in **Table 3.3**, Models 2 and 3).

These findings add to the current understanding of CP at various body locations, which could potentially be used to gain additional insights into CP pain management. Previous evidence indicates that regular PA may be beneficial for treating and even preventing chronic pain [16, 45, 46]. Therefore, wearable technology could be used to continuously monitor individuals' PA volume, intensity, and fragmentation. Coupled with information about pain intensity and timing, this information could potentially be used to further explore the association and causal direction of the association between PA and pain. PA interventions could potentially reduce CP and improve pain at the individual level and help improve CP management systems [19, 20].

Our study extends previous investigations of the association of CP with PA measures and has several strengths. First, we make use of the data collected by the NHANES, which is a large, US representative survey that contains detailed information about CP, PA, and potential confounders. Second, NHANES provides information about the specific body regions that are experiencing CP. We have used this information to explore the potential of differential associations between CP and PA by location of CP. Third, our study used objective, accelerometer-assessed PA data, which is less prone to bias and measurement error compared to self-reported PA. Moreover, we have considered several PA measurement summaries of volume (TAC, TLAC, SPM), intensity duration (ST, LIPA, MVPA), and fragmentation (SATP and ASTP). The normality of the distribution for each PA measure distribution has been checked. Fourth, we

have conducted age-stratified analyses, as the prevalence of CP varies with age groups and associations between PA and CP may vary non-linearly with age. Fifth, we have conducted both unadjusted and adjusted analysis by taking into account potential demographic and medical history confounders.

Our study has several weakness. First, the pain symptoms are self-reported by participants instead of being examined by clinical diagnosis. This may affect the definition of CP as the duration of pain may not be accurately estimated. Some individuals who were classified as part of the pain group in NHANES may not meet the clinical criterion for CP, while some study participants who met the clinical criteria might have been missed in NHANES due to self report. Second, our study is designed to quantify the association between CP and PA, but was not designed to study the causal pathways. Third, NHANES does not contain information about pain intensity, which did not allow us to investigate the association between objective and self-reported pain intensity [19]. Fourth, NHANES did not use the "Miscellaneous Pain" questionnaire after the 2003-2004 cycle, which made it impossible to use the 2005-2006 NHANES PA data in this study. Fifth, the generalization of current results to the 2021 US population given that data are now 17 to 18 years old. Sixth, the sample sizes in the three CP groups are relatively small compared with the no pain group, which could have effects on the stability and reproducibility of results.

In conclusion, our study supports and enriches past publications assessing the relationship between CP and PA. Using the best available public data for the U.S. population, we conduct a study of association between location-specific CP and objective PA summary measurements. The results suggest that the association of PA measures with CP varies by the patients' CP location, gender, and age category. Our findings further emphasize the importance of wearable

technology in health-related research. More research is needed to explore the underlying mechanisms of the PA effect on chronic pain in different body locations.

Appendix A

R Code for Model Fitting

A.1 Non-stratified Models

The R code of the non-stratified model fitting has been provided as the following:

```
> # Apply the survey weights in the 2003-2004 wave,
    using the normalized 2-year full sample examination weights
> # Use the complete dataset
> data_svy <- svydesign(id = ~SDMVPSU,
                        strata = ~SDMVSTRA,
                        weights = ~wtmec2yr_unadj_norm,
                        data = data, nest = TRUE)
> # Creates a replicate-weights survey design object,
    using the balanced repeated replicates (BBR) technique
> data_brr <- as.svrepdesign(data_svy, type = "BRR")
> # Model 1: Marginal model
> model1 = svyglm(PA outcome ~ CP indicator, design = data_brr)
> # Model 2: Adjusted for demographic confounders
> model2 = svyglm(PA outcome ~ CP indicator + Gender +
                  Age + BMI + Race + Education + Employment +
                  Smoking + Drinking, design = data_brr)
> # Model 3: Adjusted for demographic and medical
```

```
    condition confounders
> model3 = svyglm(PA outcome ~ CP indicator + Gender +
                  Age + BMI + Race + Education + Employment +
                  Smoking + Drinking + Diabetes + CHF +
                  Stroke + Cancer + Asthma + Emphysema +
                  Bronchitis + Myocardial, design = data_brr)
```

A.2 Stratified Models

The R code of the stratified model fitting has been provided as the following:

```
> # Apply the survey weights in the 2003-2004 wave,
    using the normalized 2-year full sample examination weights
> # Use the data with samples in specific gender and age group
    of which association we are examining
> data_svy <- svydesign(id = ~SDMVPSU,
                        strata = ~SDMVSTRA,
                        weights = ~wtmec2yr_unadj_norm,
                        data = data, nest = TRUE)
> # Creates a replicate-weights survey design object,
    using the balanced repeated replicates (BBR) technique
> data_brr <- as.svrepdesign(data_svy, type = "BRR")
> # Model 1: Marginal model
> model1 = svyglm(PA outcome ~ CP indicator, design = data_brr)
> # Model 2: Adjusted for demographic confounders
> model2 = svyglm(PA outcome ~ CP indicator + Age +
                  BMI + Race + Education + Employment +
                  Smoking + Drinking, design = data_brr)
> # Model 3: Adjusted for demographic and medical
    condition confounders
> model3 = svyglm(PA outcome ~ CP indicator + Age +
                  BMI + Race + Education + Employment +
                  Smoking + Drinking + Diabetes + CHF +
                  Stroke + Cancer + Asthma + Emphysema +
                  Bronchitis + Myocardial, design = data_brr)
```

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