MAYO CLINIC

General Study Information

Principal Investigator: Meegan Van Straaten, PT and colleagues

Study Title: Natural History of Shoulder Pathology in Manual Wheelchair Users

Protocol version number and date: Version 24 (05/29/2024)

Purpose

Hypothesis: Our *central hypothesis* is that the progression of rotator cuff pathology, such as tendinopathy and partial thickness tears in manual wheelchair (MWC) users, will be strongly associated with the cumulative exposure to risk-related arm use metrics (more time in risk-related arm postures, less time in tendon recovery arm postures, and increased rates of repetitive movement).

Aims, purpose, or objectives:

Specific Aim 1: Track the progression of rotator cuff tendinopathy, partial tears, and pain worsening and quantify the effect of sex, SCI lesion level, and time since SCI.

Ha: The rate of rotator cuff pathology/pain progression will be higher in MWC users compared to age- and sex-matched able-bodied individuals across multiple years of follow-up. Additionally, when controlling for age, factors such as female sex, higher SCI lesion level, and greater time since SCI will be associated with an increased rate of rotator cuff pathology/pain progression. The MWC users and matched able-bodied participants will have shoulder MRI assessments at baseline and longitudinally. Attempts will be made to collect MRI data at least once per year (not exceeding three times total per year, and not exceeding two scans per shoulder per year). MRI images will be graded based on changes in the rotator cuff and biceps tendon as well as assessing the supporting musculature.

Specific Aim 2: Determine the association between daily arm use (arm posture, repetitive motion and recovery) and progression of rotator cuff pathology and pain.

Ha: Rotator cuff pathology/pain progression will be associated with greater exposure to risk-related arm use metrics. During daily life, the MWC cohort will exhibit greater exposure to risk-related arm use metrics compared to the able-bodied cohort. Risk-related arm use metrics in MWC users (Group 1, n=95) and an age-/sex- (1:1) matched able-bodied cohort (Group 2, n=75) will be assessed by measurement of real-world arm use with commercially available wearable sensors. Field collections may occur multiple times during the year. Field data collections will not exceed 4 field collections per year. Each field collection will collect data for multiple days (max 7 days) that are representative of a subject's daily routine. For example, if a subject participates in wheelchair athletics twice a week then data will be collected to capture both a day without athletic participation and a day with athletic participation. Field collections will continue to occur until this study is closed.

Additional analysis will be done with the data from currently participating female participants. Additional female participants with SCI who use MWCs and who may also be part of racially underrepresented groups will be recruited at the Kessler Foundation (KF). This will allow more in-depth study of sex- and gender-specific

factors that contribute to pain and shoulder health decline in women. Study activities will be nearly identical to the original protocol (MRI, surveys, wearing of sensors) as well as an additional structured interview. Additional male and female participants with SCIs will be recruited at UTMB and will follow the same protocols as the Mayo Clinic participants (including structured interviews for female participants, no additional control participants will be recruited). We will not recruit additional participants at Mayo Clinic or age-matched able-bodied controls for this aspect of the study.

Background: (*Include relevant experience, gaps in current knowledge, preliminary data, etc.*):
Of the 1.6 million wheelchair (WC) users in the United States (US), nearly 90 percent, or ***1.5 million persons use manual wheelchairs***[2] (MWCs). People with traumatic and non-traumatic spinal cord injuries (SCI) make up approximately 20% of the MWC users, and 12,000 new traumatic SCIs occur every year[1]. People who have sustained a traumatic SCI are typically young and active and will propel a MWC for a large portion of their lives[1, 13-16], making the preservation of their upper body function crucial to their independence, quality of life (QOL), and general health.

Pain, including upper extremity (UE) pain, is one of the most frequent secondary medical complications following SCI[17]. Shoulder pain is the most common site of musculoskeletal pain in MWC users[17] and can significantly limit function. The incidence of shoulder pain in MWC users ranges from 31-73% [18, 19], compared to 2.9% in the general population[20]. ***Of those MWC users who have pain, up to 93% have pathological signs on MRI***[3, 21]. Costs associated with the diagnosis, surgery, and rehabilitation of shoulder pain and pathology are components of the estimated $67K yearly and $2.3M lifetime medical expenses for individuals with a paraplegic-level SCI[1].

Current knowledge about the natural history of shoulder pathology in MWC users point to a “wear and tear” etiology from overuse of an inherently unstable shoulder joint which is poorly designed for weight bearing, ambulation, and performing tasks overhead from a seated position[7]. Patient reports[24, 25] revealed that MWC propulsion up a ramp, propulsion for durations longer than 10 minutes, and performing body transfers to/from the WC are prominent sources of daily pain[26]. High mechanical loads on the shoulder and potentially risky UE kinematics have been documented during MWC propulsion over level and ramp surfaces[6, 27-39] and during transfers[40]. MR Imaging findings revealed that experienced MWC users who propel with a greater force directed towards the axle are at a higher risk of progressive abnormal shoulder MRI findings over a two year period[41]. Associations between shoulder kinetics and clinical pathology on MRI were also reported in a cross-sectional study of experienced MWC users with a low incidence of pain[42]. ***These results highlight the knowledge to be gained from linking risk-related arm use metrics and MRI findings; however, a critical barrier to understanding the mechanistic link exists in the lack of longitudinal and cumulative exposure data.***

Non-traumatic tendon tears are thought to be preceded by tendinopathy[43]; however, the mechanism of the pathogenic pathway remains largely undefined. The specific location of tendon tears has provided some mechanistic insight. Partial thickness tears on the bursal side imply external impingement and articular side tears imply internal impingement and posterior capsule tightness[10-12]. Intrasubstance tears imply a mechanism of tensile overload when the tendon is in traction. In general, non-traumatic tendon tears in the shoulder have been associated with overuse (shoulder elevation and loading) in animal[44] and human studies[43, 45]. In rats, significant

changes were observed in the supraspinatus tendon after only 4 weeks of over-use[44]. Occupational ergonomic research exposure-response analyses have revealed that supraspinatus tendinopathy was significantly related to lifetime upper arm elevation[43], and shoulder elevation above 90° for greater than 10% of the day more than doubles the risk of tendon pathology[45]. ***MRI results from this work will identify the location of incident disease and determine the exposure-response relationship to aid in a mechanistic understanding of shoulder pathology.***

There exists an opportunity for study findings to lead to insight about shoulder pathology in other populations. Adult MWC users with SCI are a unique group that experiences an abrupt change in exposure to altered shoulder function. This gives us the rare ability to measure the disease process from the onset of the new exposure. Additionally, the high incidence of shoulder pathology in this population provides for an efficient use of resources to follow the exposure and disease response long-term. In able-bodied adults with musculoskeletal pain, only low back has a higher prevalence over shoulder complaints[46]. ***This work may have important implications for translation into the general population to address shoulder pathology.***

We expect the overall impact to be significant in our understanding of the altered daily life of MWC users. Potential identification of unsafe exposure levels of risk-related arm use metrics may also be applied to new rehabilitation techniques, activity performance modifications, human factors design, and justification in insurance requests for coverage of wheelchairs made from lighter materials to preserve shoulder health. ***The detailed longitudinal data to be gained from this project is explicitly necessary to define prevention measures for shoulder dysfunction in MWC users and will inform appropriate follow-up work to establish causality.***

Subject Information – charts, records, images, or specimens are considered 'subjects'

Target accrual: 173 (Group 1 n=98, Group 2 n=75)

Subject population:
Group 1: Adults who use a manual wheelchair

Group 2: Age- and sex-matched able-bodied adults; matched to the participants in Group 1

Inclusion Criteria:
Group 1:

- 18 – 70 years of age at the time of consent
- Use of a manual wheelchair as the primary mode of mobility
- Functional upper extremity range of motion
- Willingness to participate in study
- Ability to return to receive shoulder MRI 1-3 times/year, and once per year receive physical exam.

Group 2:

- 18-70 years of age at time of consent
- Able to walk independently with no reliance on an orthotic, prosthetic, or gait aid
- Functional upper extremity range of motion
- Willingness to participate in study

- Ability to receive shoulder MRI 1-3 times/year, and once per year receive physical exam.

Exclusion Criteria:
Group 1:

- Previous diagnosis of bilateral complete supraspinatus tendon tears prior to spinal cord injury or suspected complete bilateral supraspinatus tendon tears with physical exam
- They have a known history of any condition or factor judged by the investigator to preclude participation in the study or which might hinder adherence.

Group 2:

- Any documented musculoskeletal or neurological disorders that would be expected to impact shoulder health or change ability to walk independently
- Previous diagnosis of unilateral or bilateral complete supraspinatus tendon tear(s) prior to enrollment or suspected complete supraspinatus tendon tear with physical exam
- They have a known history of any condition or factor judged by the investigator to preclude participation in the study or which might hinder adherence.

☐ Yes ☒ No Will a Certificate of Confidentiality (COC) be obtained from NIH? If yes,
Who is obtaining the COC: Mayo Clinic investigator, study sponsor, other:
Explain why a COC is needed:

Study Design

Overview. Study participation will last for 3 to 11 years (Note: The study period for participants recruited at KF will be 1 year, and for those recruited at UTMB will be 3 years), and includes the collection of MRI, activity monitor, and survey data collected at baseline and longitudinally. This protocol was originally written and approved for a NIH R01, which was recently approved for renewal. We will attempt to follow study participants who were enrolled under the original application, provided that they are willing to continue and still meet eligibility requirements.

Research Participant Recruitment. Following Institutional Review Board (IRB) and HIPAA guidelines, participants currently enrolled in the original study will be asked if they would like to continue to participate in the next phase of study. The **original study** was approved for recruitment and consent of 65 MWC users (which may include up to 5 MWC users without SCIs) for the study (Group 1) and 65 age- and sex-matched able-bodied participants (Group 2). During **this phase** (renewal) of the study, an additional 10 individuals who are female, have an SCI, use a MWC, and who may also be part of an underrepresented racial/socioeconomic group will be recruited for Group 1, and will be recruited at the KF site. An additional 13 individuals who are male/female, have an SCI, use a MWC, and who may also be part of an underrepresented racial/socioeconomic group will be recruited for Group 1 at the UTMB site. Group 1 subjects will be recruited at sites that treat and rehabilitate people with disabilities that require manual wheelchair use. Recruitment sources will include the Spinal Cord Injury Rehabilitation Center at the Mayo Clinic, Rochester, MN, the Mayo Clinic EMR, and provider referral. For recruitment sites that are not part of Mayo Clinic, the study team will get formal approval from these institutions for actions such as contacting healthcare providers, hanging flyers or using approved phone scripts. The recruitment sources at UTMB will include the UTMB electronic medical record and a

recruitment flyer with a brief intake form. The electronic medical record will be used to screen potential participants in the local Houston and Galveston area, as well as the local area around UTMB. Then, approval will be received from the potential study subject's physician prior to recruitment. The recruitment flyer will include a QR code that leads to the intake form for potential participants to indicate their interest. Study staff will use responses from the intake form to contact those who may be eligible to participate. The inclusion and exclusion criteria were chosen to include a sample of the population of people with SCIs who will use MWCs as their primary mode of mobility inside and outside the home. For most participants in Group 1, an age and sex able-bodied matched participant will be recruited from a sample of convenience (Group 2). For new participants recruited at UTMB and KF, we will not recruit additional matched control subjects.

The recruitment in cooperation with these non-Mayo Clinic sites will not require non-Mayo Clinic staff to be study personnel, and Mayo Clinic study personnel will not be engaging in research at the non-Mayo Clinic site locations. Additionally, a second study site at University of Illinois Urbana-Champaign (site PI: Jacob Sosnoff) will participate for all study activities under their own IRB review. **NOTE:** *This paragraph applied only to Phase 1 of the study/the original application, but will* ***not*** *apply in the next phase of the study (study renewal).*

Informed Consent. Documentation of informed consent will involve the use of the On-Site Electronic Consent technology. The study team may print a copy of the signed form for the subject. If re-consent is required and the participant is not scheduled for an in-person visit, documentation of informed consent may involve the use of the Remote Electronic Consent technology. The subject may print or electronically save the form through AdobeSign or may contact the study team to provide a copy of the form.

Note: If the subject prefers not to use the On-Site or Remote Electronic Consent technology, the study team will provide a paper consent form for signature.

Participant Retention. Participants will receive remuneration for their participation in study activities, as indicated below. They will be paid throughout the duration of the study after each activity is completed:

- For each MRI and study visit, participants will be remunerated $150.
- For activity monitor data collections, participants will be paid $25 per day of wear, up to 7 days per data collection, and an additional $25 if they complete all 7 days for a maximum total of $200.
- Participants in the MWC group (Mayo Clinic site) may be reimbursed up to $350 for eligible travel/lodging/food expenses associated with their MRI visit.
    - Participants in the MWC group at UTMB only needing to travel 300 miles or more to the study visit site may be reimbursed up to $600 for eligible travel/lodging/food expenses.
- The subset of MWC (Group 1) participants who collect additional data as described below (Aim 2) will be remunerated a minimum of $125 for 1.5 hours of time, and $25 for every 30 minutes of data collection beyond the first 1.5 hours (up to 6 hours/$350).
- The subset of Control (Group 2) participants who collect additional data as described below (Aim 2) will be remunerated an additional $50 for the visit.
- Participants will receive a $100 payment for completion of the first phase of the study that was part of the initial application (Baseline-Year 3 MRI). To qualify for this study phase completion payment, participants must still be enrolled during this time frame, and should complete all annual MRIs/data

collections unless health concerns prevent an MRI/data collection, as determined/approved by the PI. Those who missed MRIs for health concerns are still able to receive this remuneration and are eligible for future MRIs if the health concern is resolved and they are still enrolled in the study.
- For in-person study visits/MRIs, participants will receive a parking voucher or be reimbursed for parking for up to 4 hours.

Physical Examination. A screening physical exam of the shoulders will be performed on all MWC users and able-bodied participants by a licensed physical therapist or similarly qualified clinical staff to confirm inclusion/exclusion criteria. Follow-up exams of the shoulders will occur longitudinally approximately annually. Due to limited availability of exam room space and to reduce burden on study participants, study staff may conduct follow-up study visits via video visit.

Specific Aim 1 Track the progression of rotator cuff tendinopathy, partial tears, and pain worsening and quantify the effect of sex, SCI lesion level, and time since SCI.
The objective of this aim is to measure changes in shoulder health on MRI in MWC users over 3 to 11 years, to compare observed changes against a matched cohort to determine MWC user-specific patterns of disease. Shoulder MRIs will be collected yearly (not to exceed 3 times per year*) and graded at baseline and longitudinally for the duration of the study. This aim will define patterns of shoulder MRI changes differentiated from the able-bodied population. Additionally, potential confounders and shoulder pain will be assessed in both the MWC user and able-bodied cohort.

*MRIs may need to be performed more than once per year if the participant reports new shoulder pain or if the participant prefers to have each shoulder done at separate study visits.
**For participants recruited through the KF, they will have 1 bilateral MRI during their 1-year participation in the study.
***For participants recruited through UTMB, they will have up to 3 MRIs during their 3-year participation in the study.

Magnetic Resonance Imaging (MRI) of the Shoulder. Shoulders of both cohorts will be imaged using standard clinical imaging protocol at Mayo Clinic (including MCHS) or external site. Participants who live out-of-state/far from Rochester may choose to have the clinical MRI done at an external, non-Mayo facility that is closer to their location. Research staff will need to check with the non-Mayo MRI facility to ensure that the MRI will provide the appropriate data for this study. MRIs performed at external locations will be billed to research in the same manner as those performed at Mayo Clinic, and will not be billed to the participant. Study staff will work closely with Dr. Naveen Murthy, M.D., a board-certified, fellowship-trained, musculoskeletal radiologist, prior to getting imaging studies to make sure that the scans will be sufficient to make comparisons across time and between subjects. For example, some research participants may have spasticity and certain scanners have available hardware and software to reduce motion artifact. Dr. Murthy will assess all images for the presence or absence of shoulder and rotator cuff pathology.

MR Scanner and Imaging Protocol. All participants will be imaged on a conventional MRI scanner at 1.5 or 3 Tesla using a dedicated, commercially available, shoulder coil. The participants will be imaged in a supine position with the arm and wrist in a neutral position. A combination of axial, oblique sagittal and oblique

coronal T1 FSE, proton density, and T2 FSE FS image sequences will be obtained following the Mayo Clinic, Division of Musculoskeletal Radiology shoulder MRI protocol as closely as possible.

Assessment of MR Images. The musculoskeletal radiologist will be blinded to the study cohorts but not to the prior MRI examinations of each participant in order to assess for subtle changes over time as is done in routine clinical care. The radiologist will assess the images for rotator cuff and biceps tendon abnormalities as well as assessing the supporting musculature for any changes including bulk and strain. Tears will be classified as partial, full, or complete with designation of location. Tendinopathy will be classified as mild, mild/moderate, moderate, moderate/severe or severe. The musculature will be as assessed for atrophy and any associated injuries including signs of strain. The following pathologies will be graded: rotator cuff tendinopathy, biceps tendinopathy, acromioclavicular degenerative arthrosis, osseous edema involving the AC joint, subacromial spur formation, coracoacromial ligament thickening, and muscular atrophy and strain. Following assessment by the radiologist, the scores for each subject will be summed such that a pathology index is obtained.

Specific Aim 2: Determine the association between daily arm use (arm posture, repetitive motion and recovery) and progression of rotator cuff pathology and pain.

***In-person Data Collections*.** While participants are on site for their MRI, they may also be asked don the activity monitors and perform a series of tasks to collect reference values including overhead reaching and lifting tasks. MWC users may also perform level propulsion over carpet, propulsion up a ramp, lifting their wheelchair, and a sit-and-pivot transfer. In addition to donning sensors, the participant's quick release wheelchair wheels may be temporarily (only for the duration of the session) replaced with Smart Wheels. This does not alter their wheelchair in any way. Alternatively, and if appropriate, the participant may use a similar wheelchair that the study staff provides that is equipped with Smart Wheels. These data would serve as a reference for the shoulder motion that will be collected in the real-world.

Photographs and/or video may be taken of the subjects while sitting and during other daily activities that are observed during the physical exam/study visit, such as wheelchair propulsion, reaching, and car transfers. When taking video of car transfers, the license plate will not appear in the image. Photography and/or video will improve documentation and categorization of sitting postures and techniques that are known to correlate to kinematics that put the shoulder at risk. These photos/videos will also be used to verify activity monitor data during these sessions. Statements regarding verification/validation of activity monitor data are required for any manuscript submission.

In-person Data Collections: Subset of Participants. A small subset of participants (chosen from a sample of convenience) may be asked to perform other activities in order to collect pilot data to inform future related studies. Data may be collected in the lab or in the participant's home/community environment (with their permission) and may include any combination of video/photo, activity monitor, surface-based electromyography (EMG), spinal posture and center of seated pressure data. These participants will be asked to wear external sensors on their trunk, arms, and wheelchair and perform typical daily tasks (such as preparing a meal or transferring from a wheelchair to couch) and structured tasks (such as an arm raise) while wearing the sensors. Prior to this data collection, participants will be interviewed one-on-one via Zoom to gather

information about their daily routine. These interviews may be recorded for transcription purposes. The recordings will be destroyed once the transcription is complete.

Community (Free-Living) Data Collections using Wearable Activity Monitors: All Participants. Up to four times per year for the duration of the study, arm, trunk, and wheelchair motion will be collected for multiple days using commercially available wearable activity monitors (7 days per data collection) to characterize the cumulative exposure to arm use patterns in both cohorts. Participants will be instructed on proper use and wearing of the activity monitors and instructions on how to return them to the study team either in-person or via mail. Collections may be managed either in-person (on-site or at the participant's home, with permission) or by shipping the activity monitors (shipping materials will be provided by the study team) and the study team may make a video-conference or phone call to confirm understanding of instructions. Participants may be asked to participate in a short interview where they will be asked questions about their experiences wearing the sensors.

All activity monitors can be worn comfortably under or over clothing. Activity monitors are attached with Velcro straps or elastic sleeves worn on the upper arms bilaterally, on the trunk (with an elastic chest harness, a lanyard/necklace, or hypoallergenic medical-grade skin adhesive), on the wrist (with a watch band or elastic strap), and on the participant's wheelchair/wheel (Group 1) which will not interfere with the wheelchair's function. The activity monitors are worn during the participants' waking hours, but will not be worn while bathing or swimming. After donning the activity monitors each morning, the participant will perform a series of calibration tasks such as: (1) move the upper arms above shoulder level, (2) sit still with the arms at their side (thumb facing forward) for 60 seconds, and (3) move upper arms below chest level. They will be provided with video/written instructions for the calibration sequence. This will allow for determination of orientation of the activity monitors. If the activity monitors are removed in the middle of the day, participants will be asked to perform the calibration tasks again once the activity monitors are put back on. To account for seasonal variation, we may attempt to make data collections during both winter months and summer months.

Survey Data Collection. In combination with the activity monitor data collections and/or MRI, participants may be asked to complete surveys in-person, via phone/videoconference, via email, or via REDCap survey related to musculoskeletal and shoulder pain and their comfort and satisfaction with the study (ie. MRI and activity monitors)to be returned when the data collection is done.

Additional Variables. Updated demographic information will be collected for each study cohort participant yearly including but not limited to weight, chair type (for MWC users), health status, medication use, and job type.

Structured Interviews (female participants only). Female participants that are part of the current study and those recruited at KF and UTMB will complete an additional structured interview in-person or via HIPAA compliant videoconferencing software. The interviews will focus on the health of the participants' shoulders and the importance of their shoulders in performing their activities of daily living.

Resources: The resources necessary to conduct this research are being provided by the NICHD within the NIH. This is a funded R01 study. On-site study visits will utilize exam room space at the Clinical Research and Trials Unit (CRTU) at the Charlton Building. This is a multi-site study where Mayo Clinic will serve as the primary

site/IRB, and University of Texas Medical Branch at Galveston (UTMB), West Virginia University (WVU), and Kessler Foundation (KF) will be relying sites. No participant interactions or data collection will occur at WVU; only data analysis and development of data collection procedures will occur at this site. Dr. Melissa Morrow is a Co-PI at UTMB and will oversee data collection and analysis at UTMB. Dr. Stephen Cain is a Co-PI at WVU and will oversee data analysis at WVU. Dr. Nathan Hogaboom is a Co-PI at KF and will oversee data collection and analysis at KF.

Check all that apply. If none apply, leave blank:

☒ This is a multisite study involving Mayo Clinic and non-Mayo Clinic sites.
When checked, describe the research procedures/activities being conducted **only** at Mayo Clinic:

☐ Mayo Clinic staff will be engaged in research activity at a non-Mayo Clinic site. *When checked, provide the location and a detailed description of the Mayo Clinic research staff involvement.*

☐ This study is to establish and/or maintain an ongoing database or registry for research purposes only.

☒ The research involves contact or interaction with subjects, for example, surveys, questionnaires, observation, blood draw.

☒ The study involves photographing, audiotaping or videotaping subjects (and guests).

Review of Chart, Images, Specimens

Provide the date range for collection of data and/or specimens that will be included in your research dataset. *Example: 01/01/2000 to 12/31/2013* or all records through mm/dd/yyyy.

For a retrospective chart review, enter the date range:

Check all that apply:

☐ This study involves only data and/or specimens that exist at the time this application is submitted to the IRB (IRB submission date). No data or specimens will be collected beyond this date.

☐ This study involves only data and/or specimens that will be collected after submission to the IRB.

☐ The study involves data and/or specimens that exist at the time of submission to the IRB **and** data and/or specimens that will be collected after submission to the IRB, for example a study that includes collection of existing data and prospective collection of specimens.

☐ Data and/or specimens used in this study are collected under another IRB protocol. *When checked, provide the IRB number(s) from which the research material will be obtained. When appropriate, check the box below*

to attest that subjects have provided consent for future use of their data and/or specimens, as described in this protocol.

IRB Number/s - Data Only: _____

IRB Number/s - Specimens Only: _____

IRB Number/s - Data and Specimens: _____

Note: When subjects provided consent for use of their data and/or specimens, as described in this protocol.

☐ Other data sources will be utilized in this study, e.g. receiving data/specimens from an external party. When checked, provide all data sources:

Data Confidentiality, HIPAA Subject Identifiers

Review the list of subject identifiers below and, if applicable, check the box next to each subject identifier being recorded at the time you are collecting/abstracting data/specimens for use in this study.

Subject Identifiers: Individually identifiable information, including demographic data, that identifies the individual or for which there is reasonable basis to believe it can be used to identify the individual. NOTE: Identifiers apply to subjects enrolled in your study and to the subject's relatives, household members, employers, etc.

Internal refers to subject identifiers that will be included in the dataset maintained by the study team.
External refers to subject identifiers that will be shared with persons outside of the immediate study team, for example, sent to an external collaborator or shared with a national registry.

SUBJECT IDENTIFIERS **Check all that apply**	INTERNAL IDENTIFIER	EXTERNAL IDENTIFIER
Name	X	X
Social Security number	X	X
Medical record/patient registration number, lab accession, specimen or radiologic image number	X	X
Study number, subject ID, or any other unique identifying number, characteristic or code that can be used to link the identity of the subject to the data	X	X
Dates: All elements of dates [month, day, and year] directly related to an individual. Their birth date, date of death, date of diagnosis, etc. **Note:** Recording a year only is not a unique identifier.	X	X
Medical device identifiers and serial numbers		
Biometric identifiers, including finger and voice prints, full face photographic images and any comparable images	X	X

Web Universal Resource Locators (URLs), Internet Protocol (IP) address numbers, email address	X	X
Street address, city, county, precinct, zip code, and their equivalent geocodes	X	X
Phone or fax numbers	X	X
Account, member, certificate or professional license numbers, health beneficiary numbers		
Vehicle identifiers and serial numbers, including license plate numbers		
If None of the above identifiers will be recorded or maintained in the dataset and/or sent outside of the study team, please check "None".	☐ None	☐ None

Statistical Information

Power Statement:

Aim 1: The MRI findings from baseline and year 1 visits indicated that a sample size of 22 (MWC users) will provide 80% power to detect an effect size of 0.6 (progression of RC tendon pathology, total score, in one year) at an alpha level 0.05 (two tails). Testing 40 participants will provide 95% power for aim 1. Further, a sample size of 16 SCI MWC users and 16 matched able-bodied adults will provide 81% power to detect an effect size of 0.79 (change in total score in one year) at an alpha level 0.05 (two tails). Testing 20 participants (each cohort) will provide 90% power and 40 participants (each cohort) will provide 99% power.

Aim 2: Primary outcome measures are the risky postures and recovery metrics. The primary analyses will test the association of these variables with pathology/pain progression, and between-cohort differences being tested in the secondary analysis. Based on the preliminary correlation of the recovery metric with pathology progression (correlation coefficient = -0.477), a sample size of 32 MWC users will provide 81% power to detect a significant correlation. Based on the preliminary correlation of the risk metric with pathology progression (correlation coefficient=0.681), a sample size of 14 MWC users will provide 81% power to detect a significant correlation. For cohort differences, a minimum sample size of 34 participants per group is necessary based on a two-sided, paired t-test analysis (α=0.05) for 80% power. Forty participants (current retention goal) per group provide 89% and 99% power for recovery and risk metrics, respectively.

Note: Current participants (after participants lost to follow-up were removed) are 33 matched pairs. Adding recruitment of participants (from N=65 to N=75) in both groups will allow for expected loss of participants (to follow-up and other reasons) in phase 2 of this study.

Data Analysis Plan:

Statistical Analysis of Aim 1. *(**H1**) The rate of rotator cuff pathology/pain progression will be higher in MWC users compared to age- and sex-matched able-bodied individuals.* Repeated measures analysis using mixed models will be implemented in SPSS 25 (IBM Corp., Armonk, NY) to test for between group (MWC users vs. age- and sex-matched able-bodied participants) differences in (1) tendon pathology score progression in the shoulders over the follow-up period (α=.05) and (2) pain worsening during follow-up. The primary outcome (dependent) variables are the yearly repeated measures of MRI grading for the shoulder and the visual analog scale pain measures. The primary predictor is the binary participant designation of MWC user or able-bodied. Potential confounders/covariates that will be accounted for include demographic variables (age, sex, weight,

chair type, time since injury, injury level, arm dominance, etc.). ***(H2)*** *When controlling for age, factors such as female sex, higher SCI lesion level, and greater time since SCI will be associated with an increase in rotator cuff pathology/pain progression.* To test the association between the demographic factors (predictors) and pathology progression or pain worsening (outcomes), Generalized Estimating Equations (GEE) will be used to determine the regression coefficients and odds ratio of pathology and pain progression.

Statistical Analysis of Aim 2 Hypotheses.
(H1) *Rotator cuff pathology/pain progression will be associated with greater exposure to risk-related arm use metrics (more time in risk-related arm postures, less time in tendon recovery arm postures, and increased rates of repetitive movement).* The association of metrics of arm use with tendon pathology/pain progression will be investigated for each cohort and across sub-groups of SCI injury level, time since injury, and sex while accounting for age and use of pain medication. The regression coefficients will be determined utilizing Generalized Estimating Equations (GEE). Independent samples T-test or Mann-Whitney U test will be used to compare the exposure to risk-related arm use metrics between the individuals with rotator cuff tendon pathology progression and without tendon pathology progression in each cohort. The sensitivity and specificity of metrics will be determined for correctly classifying participants as having or not having rotator cuff tendon pathology progression. ***(H2)*** *During daily life, the MWC cohort will exhibit greater exposure to risk-related arm use metrics compared to the able-bodied cohort.* Paired sample T-test or Wilcoxon signed-rank test will be used to test for differences in arm use metrics between cohorts at each time point (cross-sectional). Separate general linear models will be utilized to assess and compare associations between the covariates (age, time since injury, and sex) and arm use metrics in MWC users and matched participant cohorts. Normalization methods for skewed data will be used if needed. Repeated measures analysis using mixed models will be used for longitudinal analysis. All analysis will be performed two-sided with significance set at α=0.05, and missing data will be managed with multiple imputation[100]. *Sex as a biological variable for Aim 1 and 2.* Data will be reported disaggregated by sex. Variables will be explored for sex differences and sex-interaction effects will be included in linear models. There is mixed evidence on whether females or males incur a greater risk for shoulder pathology, but there is little to no evidence available for whether arm use patterns differ by sex.

Statistical Analysis of MRI, Arm use, and Demographic Factors: To test the association between the demographic factors including sex and gender (predictors), arm use, and pathology or pain (outcomes), Generalized Estimating Equations (GEE) will be used to determine the regression coefficients and odds ratio of pathology and pain prevalence. Additional analyses will be performed to test the effect of AIS score, wheelchair setup metrics, comorbidities and medications and other demographic and anthropometric factors on the full shoulder pathology and pain measures and sex and gender. Interviews: Interview data will be recorded, transcribed, and anonymized. Transcripts and fieldnotes will be entered into specialized qualitative software (NVivo12, QRS International, 2018) for data management and analyzed using the framework method. Following the framework method our qualitative researchers will categorize and code transcripts and fieldnotes.

Endpoints:
Primary: Participant completion of MRI and Field (activity monitor) measurements after 3 to 11 years follow-up.