AWARD NUMBER: W81XWH-17-1-0335

TITLE: Assessing Rehabilitation Outcomes after Severe Neuromusculoskeletal Injury: Development of Patient Reported Outcomes Assessment Instruments

PRINCIPAL INVESTIGATOR: David S. Tulsky, PhD

CONTRACTING ORGANIZATION: University of Delaware
Newark DE 19716-0099

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6. AUTHOR(S)
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5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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14. ABSTRACT

Currently, there is a paucity of patient reported outcomes (PRO) measures of secondary health effects and complications that result from neuromusculoskeletal injuries, which greatly limits the clinical care and successful rehabilitation, reintegration, and return to duty/work of injured individuals. This study will create valid, standardized, psychometrically robust, and clinically useful PRO measures for traits and symptoms relevant to understanding quality of life and the health and rehabilitation outcomes of Wounded Warriors and civilians with neuromusculoskeletal trauma. Furthermore, this study will develop clinical score reports in an actionable format to improve the clinical workflow and standard of care for individuals with traumatic limb injuries. During year three, we successfully prepared for and launched large-scale field testing. To date, 159 participants have begun baseline and 154 have completed the baseline interviews. Work to plan for data analyses is underway. We have also worked this year amid challenges from the COVID-19 pandemic, which affected our daily operations and caused the pace of recruitment to slow. However, we have established processes for remote recruitment, consenting, and data collection. We have identified several additional sites that have eligible participants and are willing to recruit them, to help increase recruitment throughput.

15. SUBJECT TERMS
Traumatic Limb Injuries, PRO Measures, Neuromusculoskeletal Trauma, Upper/Lower Extremity Amputation, Psychosocial Functioning, Outcomes Measurement

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1. INTRODUCTION

Currently, there is a paucity of patient reported outcomes (PRO) measures of secondary health effects and complications that result from neuromusculoskeletal injuries, which greatly limits the clinical care and successful rehabilitation, reintegration, and return to duty/work of injured individuals. This study will create valid, standardized, psychometrically robust, and clinically useful PRO measures for traits and symptoms relevant to understanding quality of life and the health and rehabilitation outcomes of Wounded Warriors and civilians with neuromusculoskeletal trauma. Furthermore, this study will develop clinical score reports in an actionable format to improve the clinical workflow and standard of care for individuals with traumatic limb injuries.

2. KEYWORDS

Traumatic Limb Injuries, PRO Measures, Neuromusculoskeletal Trauma, Upper/Lower Extremity Amputation, Psychosocial Functioning, Outcomes Measurement

3. ACCOMPLISHMENTS

What were the major goals of the project?

The major goals of this project are: (1) to develop pools of items that measure secondary physical and psychosocial health effects and rehabilitation outcomes. which includes several major steps, including expert reviews, cognitive debriefing interviews, baseline and longitudinal field testing; (2) to create, using Item Response Theory, computer adaptive test (CAT) forms and fixed-length “short forms” for each content domain, based on rigorous statistical analyses; (3) to develop scientifically based clinical score reports for these measures, to be used in clinical care; and (4) to integrate tests and reports into a “package” for applied use. A precursor to a majority of these activities was obtaining human subjects regulatory approval at University of Delaware (UD) and at each of the participating partner sites (which includes IRB and approval from the Human Research Protection Office [HRPO]). The sites also required administrative approvals prior to study initiation, including Cooperative Research and Development Agreements (CRADA) for three sites and data use agreements (DUAs) for all sites.

What was accomplished under these goals?

During year 1, major accomplishments were achieved on three essential initial components of this project: (1) preparing initial item pools for cognitive interviewing, (2) developing a research infrastructure to carry out data collection activities, and 3) obtaining regulatory and administrative approvals. The details of these accomplishments were described in the 2018 annual report.

During year 2, major accomplishments were achieved on four essential components of this project: (1) All cognitive interviews were completed, (2) Item pools were revised and finalized based on feedback gathered during cognitive interviews, (3) A data collection plan was developed and finalized for the large-scale field testing, and (4) Regulatory and administrative approvals were secured at the remaining sites. The details of these accomplishments were described in the 2019 annual report.

During year 3, our efforts were focused in four main areas: (1) Preparing for large-scale field testing, which included reviewing the feedback from cognitive interviews, finalizing the data collection system for baseline interviews, standardizing procedures, and training staff; (2)

Launching large-scale field testing baseline data collection; (3) Working to continue data collection and meet our sample targets amid challenges from the COVID-19 pandemic; and (4) Developing detailed data analytic specifications and beginning to write program syntax and code to speed up the analytic process once the sample has been collected.

The PRO items were refined based on cognitive interview feedback. The reviews began with 579 items total. Based on our review of the cognitive interview data, 115 items were removed, 33 were revised, and 32 were added. Twelve pools of new items (496) were brought forward to be administered for calibration in baseline testing. The baseline interview protocol also includes items from 25 existing PRO scales that are relevant to measuring quality of life. These existing PRO measures include 136 items, for a total of 632 items to be administered. Given the large number of items, baseline interviews were designed to be completed over two sessions (each about 90 minutes in length).

An investigator meeting was held in September 2019 to review these item decisions and discuss plans for recruitment and data collection. Investigators from all sites were represented at the meeting and important discussions included application and interpretation of the inclusion criteria in practice and plans for the rollout of data collection interviews. The measurement system name was also discussed, and a name change was proposed and agreed upon: Limb Injury Measurement Battery for Quality of Life, or LIMB-QOL. Following this investigator meeting, the 632 items for baseline interviews were programmed into REDCap. Standardized procedures were developed to cover the processes involved in secure storage of research information, procedures for communicating with participants throughout the data collection process, and documentation. Two research assistants were trained in the standardized telephone interview procedures. The training included several practice calls with research staff, as well as calling live participants with observation. Both research assistants satisfactorily completed the training.

Large-scale data collection for field testing began in the last week of November 2019, by first calling participants who had previously taken part in the Cognitive Interview portion of the study earlier in 2019. Then, newly recruited participants were contacted and interviewed. Teleconferences have been held on a biweekly basis with all of the recruiting sites to track progress on recruitment and medical record abstraction, to discuss relevant study or data collection questions, and to follow up as needed about participants (e.g., when there is difficulty scheduling). These routine meetings will continue throughout the course of data collection. By the end of year 3, 159 individuals began baseline and 154 have completed the interviews.

Beginning in March 2020 there was a significant impact of the COVID-19 pandemic on study recruitment, as study personnel at the University of Delaware and partnering sites were required to telework. This limited the opportunities to recruit from clinics and other venues and necessitated changes to the project's daily operations, some of which required additional regulatory approvals for remote consenting. These obstacles caused the pace of data collection to slow. UD worked with sites to minimize barriers to recruitment, which has included submitting regulatory document changes that will more easily permit remote recruitment and consenting. Moreover, UD identified and contacted several additional sites that have eligible participants, and is engaging with them to recruit additional participants that will help meet targets in a timelier manner. These sites (TIRR Memorial Hermann, Kessler Foundation, University of Pennsylvania-Penn Medicine, and McGill University) have all verbally agreed to recruit participants for this study. Regulatory and administrative documentation has been drafted in all cases, and IRB approval has been obtained for TIRR and Kessler. These changes and additions have been communicated to HRPO, and we will continue to do so as additional site regulatory documents are approved.

Also in response to the pandemic, we have added to our data collection protocol selected questions for participants about COVID-19 (e.g., whether they have been diagnosed, extent of illness), as well as standardized PRO assessments of social isolation, loneliness, and stress, so that we can have additional information about our sample during the pandemic that may be relevant when conducting analyses and developing interpretation guidelines. These additions have been approved by the UD and site IRBs as appropriate and have been submitted to and acknowledged by HRPO.

We have also begun developing the analysis plan. This has involved writing the requisite programming code and conducting quality assurance testing to eventually conduct item response theory (IRT) calibration analyses. The statistical team has begun meeting regularly to plan these analyses, conduct initial runs, and generate report architecture. By beginning this process now, we will be prepared to run the analyses more efficiently once the final dataset is collected, allowing for improved efficiency.

Finally, during year 3, lingering administrative approvals were obtained at one remaining site (i.e., BAMC data sharing agreement). The only outstanding administrative document is a CRADA between UD, WRNMMC, and the Henry Jackson Foundation, which provides support to WRNMMC. This negotiation is still in process and will likely be executed early in year 4.

What opportunities for training and professional development has the project provided?

Nothing to Report

How were the results disseminated to communities of interest?

See information on dissemination of results below in Section 6 (Products).

What do you plan to do during the next reporting period to accomplish the goals?

During the next reporting period, we will continue baseline data collection. Our goal is to complete the remaining 496 baseline interviews by end of year 4, with the addition of several sites as noted above. We will continue to have biweekly meetings with recruiting sites to monitor progress and discuss any barriers that may arise. We will initiate one-year follow-up assessments in November 2020. Our sampling target is to recruit and complete data collection with 650 individuals for the baseline interviews, 400 individuals for the 1- and 2-year follow-up, and 200 individuals for the 1-week retest (which will occur 1-2 weeks after the 1-year follow-up assessment).

Plans for future face-to-face investigator meetings are on hold, due to travel restrictions from the COVID-19 pandemic.

4. IMPACT

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

5. CHANGES/PROBLEMS

Changes in approach and reasons for change

There have been no changes in objective or scope of this project. However, as described in previous reports, regulatory and administrative approvals took far longer than the 6 months allocated to them in our project plan.

During the past several months, data collection proceeded at a slower-than-expected pace. There has been a negative effect of the COVID-19 pandemic on recruitment. We are working with sites to identify challenges and to help them make changes to recruitment plans to ensure completion of data collection. We are adding several new sites to increase recruitment throughput. We anticipate that the problems with recruitment will be overcome within the next year and that we will meet targets for conducting all planned analyses.

Actual or anticipated problems or delays and actions or plans to resolve them

As noted above, while we have initiated data collection, with 154 individuals who have been recruited and tested, we will need to increase data throughput to meet targets. We have had problem-solving meetings with our recruitment sites and have alerted them that we will need to reallocate funding if recruitment does not proceed at a brisker pace. We are also bringing on several additional recruitment sites to address our recruitment shortfall. We will continue to actively manage recruitment and data collection challenges by meeting with sites biweekly, reviewing the available pool of participants and collaboratively discussing strategies to successfully recruit as many of these eligible participants. Our ultimate goal is to assure we have collected a large, well-defined research data sample to effectuate the creation of valid, reliable rehabilitation outcome measures. Our adjustments and increased communication should allow us to accomplish that goal.

Changes that had a significant impact on expenditures

The delays described in our data collection efforts and implementation have caused some delays in spending for data collection. However, we anticipate that the effect of this will be neutral on the budget over the life of the project.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects.

Nothing to Report

Significant changes in use or care of vertebrate animals.

Nothing to Report

Significant changes in use of biohazards and/or select agents.

Nothing to Report

6. PRODUCTS

Publications, conference papers, and presentations

Journal publications. Nothing to Report

Books or other non-periodical, one-time publications. Nothing to Report

Other publications, conference papers, and presentations. Two conference presentation abstracts were presented during the reporting period.

1. Tyner, C.E., Slotkin, J., Kisala, P.A., Zafonte, R., Kalpakjian, C., Kingsbury, T., Cancio, J.M., Dearth, C.L., Griffith, A.M., Ma, M.L., Boulton, A.J., & Tulsky, D.S. (2019, August). *Developing new items for the Extremity Trauma and Amputation Quality of Life Measurement System: Cognitive debriefing interviews.* Poster presented at the Military Health System Research Symposium, Kissimmee, Florida.

2. Tulsky, D., Tyner, C.E., Slotkin, J., Cancio, J.M., Dearth, C.L., Kingsbury, T., Kalpakjian, C., Zafonte, R., Pruziner, A., Kisala, P.A., & Boulton, A.J. (2019, August). *The Extremity Trauma and Amputation Quality of Life Assessments: Developing a new measurement system for neuromusculoskeletal trauma.* Poster presented at the Military Health System Research Symposium, Kissimmee, Florida.

Website(s) or other Internet site(s)

Nothing to Report

Technologies or techniques

Nothing to Report

Inventions, patent applications, and/or licenses

Nothing to Report

Other Products

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Note: Values for nearest person month worked listed below are for the current reporting period.

Name:	**David Tulsky, PhD**
Project Role:	Project PI
Researcher Identifier (e.g. ORCID ID):	None
Nearest person month worked:	1
Contribution to Project:	No change

Name:	**Jerry Slotkin, PhD**
Project Role:	Co-I
Researcher Identifier:	None
Nearest person month worked:	2
Contribution to Project:	No change

Name:	**Callie Tyner, PhD**
Project Role:	Co-I
Researcher Identifier:	0000-0003-2945-392X
Nearest person month worked:	2
Contribution to Project:	No change

Name:	**Pamela Kisala, MA**
Project Role:	Co-I
Researcher Identifier:	0000-0003-3234-795X
Nearest person month worked:	1
Contribution to Project:	No change

Name:	**Aaron Boulton, PhD**
Project Role:	Biostatistician
Researcher Identifier:	0000-0001-7349-162X
Nearest person month worked:	1
Contribution to Project:	No change

Name:	**Ratna Nandakumar, PhD**
Project Role:	Biostatistician
Researcher Identifier:	None
Nearest person month worked:	1
Contribution to Project:	Dr. Nandakumar has begun planning the psychometric analyses and programming for item calibration.

Name:	**Emily Forth, BA**
Project Role:	Research Assistant
Researcher Identifier:	None
Nearest person month worked:	9
Contribution to Project:	No change

Name:	**Alexis Silverman, MA**
Project Role:	Graduate Student Research Assistant
Researcher Identifier:	None
Nearest person month worked:	6
Contribution to Project:	No change

Name:	Trevor Kingsbury, MA
Project Role:	Site PI, NMCSD
Researcher Identifier:	0000-0001-5298-8725
Nearest person month worked:	1
Contribution to Project:	No change

Name:	Josef Butkus, MS, OTR/L
Project Role:	Site PI, WRNMMC
Researcher Identifier:	None
Nearest person month worked:	1
Contribution to Project:	No change.

Name:	Christopher Dearth, PhD
Project Role:	Co-I, WRNMMC
Researcher Identifier:	None
Nearest person month worked:	1
Contribution to Project:	No change.

Name:	W. Lee Childers, PhD, CP
Project Role:	Site PI, CFI/BAMC
Researcher Identifier:	0000-0002-6119-983X
Nearest person month worked:	1
Contribution to Project:	No change.

Name:	Ross Zafonte, DO
Project Role:	Site PI, SRH
Researcher Identifier:	None
Nearest person month worked:	1
Contribution to Project:	No change

Name:	Claire Kalpakjian, PhD
Project Role:	Site PI, UM
Researcher Identifier:	0000-0001-6652-1245
Nearest person month worked:	1
Contribution to Project:	No change

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

All PIs and key personnel are listed below, along with any changes in the active support of each (if applicable).

David Tulsky, PhD

New funding:

1. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities
   Funding Agency: NIH
   Project dates: 9/5/2019 - 6/30/2024

Effort: 1.20 academic months, 1.00 summer months
Description: This project's broad, long-term objective is to understand the complex patterns of symptoms displayed after acquired injuries to the brain, spine, or limb, so that clinical care can be improved.
Overlap: none

2. Title: Stakeholder Determination of Patient-Reported Outcomes for Adults with Communication Disorders
Funding Agency: NIH/NIGMS
Project dates: 12/1/2019 - 11/30/2020
Effort: 0.13 academic
Description: Goal is to develop and disseminate the COMM-PRO measurement system—a set of feasibly administered and psychometrically robust measures (COMMPROMs) for adults in speech-language therapy.
Overlap: none
3. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities (Supplement)
Funding Agency: NIH
Project dates: 7/22/2020 - 6/30/2021
Effort: 1.20 academic months, 1.00 summer months
Description: The work proposed with this administrative supplement is needed to evaluate the generalizability of the symptom clusters identified in parent grant Aim 1 to a mild cognitive impairment (MCI)/Alzheimer's disease (AD) population. Additionally, this will allow us to develop resources and collect pilot data to support an application for funding to study symptom clusters in MCI and AD.
Overlap: none

Previous funding:

- Clinical Adaptation of the SCI-QOL Psychosocial Measures (Craig H. Neilsen Foundation); Ended 4/29/2019
- Community Reintegration, Functional Outcomes and QOL after Upper and Lower Extremity Trauma (DoD W81XWH-11-0222); Ended 9/29/2019

Jerry Slotkin, PhD

New funding:

1. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities
Funding Agency: NIH
Project dates: 9/5/2019 - 6/30/2024
Effort: 0.60 calendar months
Description: This project's broad, long-term objective is to understand the complex patterns of symptoms displayed after acquired injuries to the brain, spine, or limb, so that clinical care can be improved.
Overlap: none
2. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities (Supplement)
Funding Agency: NIH
Project dates: 7/22/2020 - 6/30/2021
Effort: 0.68 calendar months
Description: The work proposed with this administrative supplement is needed to evaluate the generalizability of the symptom clusters identified in parent grant Aim 1 to a mild cognitive impairment (MCI)/Alzheimer's disease (AD) population. Additionally, this

will allow us to develop resources and collect pilot data to support an application for funding to study symptom clusters in MCI and AD.
Overlap: none

Previous funding:

- Community Reintegration, Functional Outcomes and QOL after Upper and Lower Extremity Trauma (DoD W81XWH-11-0222); Ended 9/29/2019

Callie Tyner, PhD

New funding:

1. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities
   Funding Agency: NIH
   Project dates: 9/5/2019 - 6/30/2024
   Effort: 1.20 calendar months
   Description: This project's broad, long-term objective is to understand the complex patterns of symptoms displayed after acquired injuries to the brain, spine, or limb, so that clinical care can be improved.
   Overlap: none
2. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities (Supplement)
   Funding Agency: NIH
   Project dates: 7/22/2020 - 6/30/2021
   Effort: 1.8 calendar months
   Description: The work proposed with this administrative supplement is needed to evaluate the generalizability of the symptom clusters identified in parent grant Aim 1 to a mild cognitive impairment (MCI)/Alzheimer's disease (AD) population. Additionally, this will allow us to develop resources and collect pilot data to support an application for funding to study symptom clusters in MCI and AD.
   Overlap: none

Previous funding:

- Development of a Psychosocial Symptom Monitoring and Self-Management System for Individuals with SCI (Craig H. Neilsen Foundation); Ended 4/29/2019
- Community Reintegration, Functional Outcomes and QOL after Upper and Lower Extremity Trauma (DoD W81XWH-11-0222); Ended 9/29/2019

Pamela Kisala, MA

New funding:

1. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities
   Funding Agency: NIH
   Project dates: 9/5/2019 - 6/30/2024
   Effort: 3.0 calendar months
   Description: This project's broad, long-term objective is to understand the complex patterns of symptoms displayed after acquired injuries to the brain, spine, or limb, so that clinical care can be improved.
   Overlap: none
2. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities (Supplement)
   Funding Agency: NIH

Project dates: 7/22/2020 - 6/30/2021
Effort: 3.0 calendar months
Description: The work proposed with this administrative supplement is needed to evaluate the generalizability of the symptom clusters identified in parent grant Aim 1 to a mild cognitive impairment (MCI)/Alzheimer's disease (AD) population. Additionally, this will allow us to develop resources and collect pilot data to support an application for funding to study symptom clusters in MCI and AD.
Overlap: none

Previous funding:

- Clinical Adaptation of the SCI-QOL Psychosocial Measures (Craig H. Neilsen Foundation); Ended 4/29/2019
- Community Reintegration, Functional Outcomes and QOL after Upper and Lower Extremity Trauma (DoD W81XWH-11-0222); Ended 9/29/2019

Aaron Boulton, PhD

New funding:

1. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities
   Funding Agency: NIH
   Project dates: 9/5/2019 - 6/30/2024
   Effort: 4.8 calendar months
   Description: This project's broad, long-term objective is to understand the complex patterns of symptoms displayed after acquired injuries to the brain, spine, or limb, so that clinical care can be improved.
   Overlap: none
2. Title: Dynamic Stability in the ACL Injured Knee
   Funding Agency: NIH/NICHD
   Project dates: 3/1/2020 – 2/28/2022
   Effort: 1.2 calendar months
   Description: This international cohort proposed studies will begin to elucidate the particular clinical markers that contribute to the success or failure following ACL rupture and reconstruction and/or return to full activity and provide clinicians with practical, useful and evidence-based treatment options that may improve function after ACL injury or reconstruction.
   Overlap: none
3. Title: Measuring Symptom Clusters in People with Sudden-Onset Disabilities (Supplement)
   Funding Agency: NIH
   Project dates: 7/22/2020 - 6/30/2021
   Effort: 2.4 calendar months
   Description: The work proposed with this administrative supplement is needed to evaluate the generalizability of the symptom clusters identified in parent grant Aim 1 to a mild cognitive impairment (MCI)/Alzheimer's disease (AD) population. Additionally, this will allow us to develop resources and collect pilot data to support an application for funding to study symptom clusters in MCI and AD.
   Overlap: none

Previous funding:

- Clinical Adaptation of the SCI-QOL Psychosocial Measures (Craig H. Neilsen Foundation); Ended 4/29/2019

- Community Reintegration, Functional Outcomes and QOL after Upper and Lower Extremity Trauma (DoD W81XWH-11-0222); Ended 9/29/2019

Trevor Kingsbury, MA

Nothing to report

Josef Butkus, MS OTR/L

Nothing to report

W. Lee Childers, PhD, CP

Nothing to report

Ross Zafonte, DO

New funding:

1. Title: Acquired Brain Injury Resilience and Recovery
   Funding Agency: Heinz Family Foundation
   Project Dates: 01/01/2020-12/31/2024
   Effort: 0.00 calendar months ($275,000 cumulative total costs)
   Description: This funding from the Heinz Family Foundation supplements funding received from the SameYou Foundation for the research project on resilience and recovery after moderate to severe acquired brain injury (see below).
   Overlap: none
2. Title: Resiliency After Acquired Brain Injury: Defining and Enhancing Biopsychosocial Function
   Funding Agency: SameYou Foundation
   Project Dates: 10/01/2019-09/30/2022
   Effort: 0.12 calendar months ($1,057,186 cumulative total costs)
   Description: The major goal of this study is to explore the psychological, neurobiological, and neural-systems features of resilience that influence recovery in persons who have experienced moderate to severe acquired brain injury.
   Overlap: none
3. Title: The Spectrum of Concussion: Predictors of Clinical Recovery, Treatment and Rehabilitation, and Possible Long-Term Effects
   Funding Agency: National Football League
   Project dates: 09/11/2018-09/10/2022
   Effort: 0.12 calendar months ($1,584,588 cumulative total costs)
   Description: The major goals of this project are to examine acute effects, functional recovery, treatment and rehabilitation after concussion for youth who are slow to recover, possible long-term effects on brain health, and rehabilitation of retired amateur athletes.
   Overlap: none

4. Title: Multimodal Intervention to Improve Function and Metabolism in Spinal Cord Injury
   Funding Agency: NIH/NICHD
   Project dates: 08/21/2018-04/30/2023
   Effort: 0.47 calendar months ($465,541 cumulative total costs)
   Description: This is a randomized trial involving persons with spinal cord injury to determine whether a Home-Based Multimodality Functional Recovery and Metabolic Health Enhancement Program combined with an androgen (19-nortestosterone decanoate, 19ND) is more efficacious than arm ergometry alone in improving aerobic capacity, muscle mass and strength, metabolic health, self-reported function and mobility, and wellbeing.
   Overlap: none
5. Funding Agency: Foundation for PM&R
   Project dates: 01/01/2018-12/31/2020
   Effort: 0.0 calendar months ($30,000 cumulative total costs)
   Description: Identifying key non-traditional risk factors for cardiovascular disease following spinal cord injury. The major goal of this project is to identify non-traditional risk factors for cardiovascular disease following SCI.
   Overlap: none

Previous funding:

- Regeneration and Enhanced Recovery of Injured Skeletal Muscles using External, Non-invasive, Passive Mechanical Stimulation, ended 05/31/2019
- Multimodal Assessment of Sensorimotor Activity Following Mild Traumatic Brain Injury, ended 09/30/2019

Claire Kalpakjian, PhD

Nothing to report

What other organizations were involved as partners?

- **Organization Name:** Walter Reed National Military Medical Center
- **Location of Organization:** Bethesda, MD
- **Partner's contribution to the project:**
  - In-kind support
  - Collaboration

- **Organization Name:** Center for the Intrepid/Brooke Army Medical Center
- **Location of Organization:** San Antonio, TX
- **Partner's contribution to the project:**
  - In-kind support
  - Collaboration

- **Organization Name:** Naval Medical Center San Diego
- **Location of Organization:** San Diego, CA
- **Partner's contribution to the project:**
  - In-kind support
  - Collaboration

- **Organization Name:** Spaulding Rehabilitation Hospital
- **Location of Organization:** Charlestown, MA
- **Partner's contribution to the project:**
    - Collaboration

- **Organization Name:** University of Michigan
- **Location of Organization:** Ann Arbor, MI
- **Partner's contribution to the project:**
    - Collaboration

8. SPECIAL REPORTING REQUIREMENTS

Collaborative Awards:

n/a

Quad Charts:

Please see Appendix A for the most current quad chart.

9. APPENDICES

See Appendix A for Quad Chart.

See Appendix B for attached abstracts from research presentations described in question 6.

APPENDIX A – Quad Chart. Assessing Rehabilitation Outcomes after Severe Neuromusculoskeletal Injury: Development of Patient Reported Outcomes Assessment Instruments

Log Number BA160178

Award Number: W81XWH-17-1-0335

PI: David Tulsky, Ph.D. **Organization:** University of Delaware **Award Amount:** $4,126,339

Specific Aims

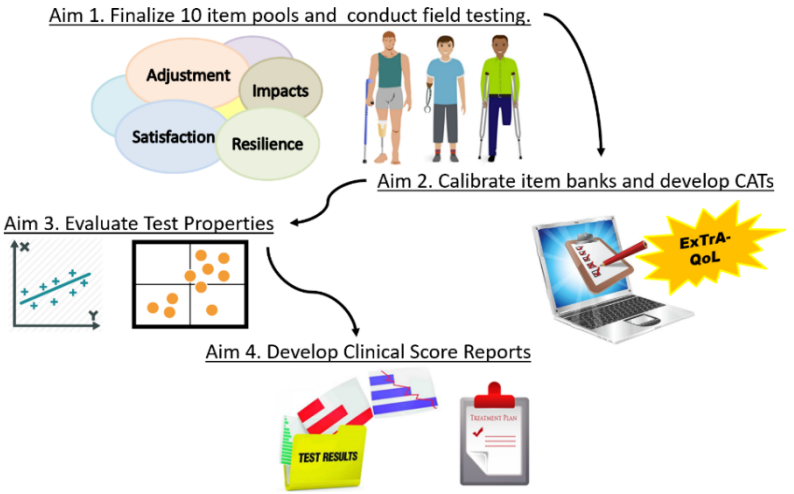
1: Finalize 10 item pools which measure secondary physical and psychosocial health effects and rehabilitation outcomes and field test the item pools in a large sample of Wounded Warriors and civilians with severe neuromusculoskeletal injuries.

2: Calibrate item banks using IRT analysis and develop computer adaptive tests (CATs) for each item bank.

3: Evaluate the psychometric properties (e.g., reliability, validity, and responsiveness) of the newly developed CATs.

4: Develop scientifically based clinical score reports that will allow the scales to be used in orthopedic research and clinical practice.

Approach: This study will create valid, standardized, psychometrically robust, and clinically useful PRO measures for traits and symptoms that are of critical importance to understanding the health and rehabilitation outcomes of Wounded Warriors and civilians with neuromusculoskeletal trauma. Furthermore, this study will develop clinical score reports in an actionable format to improve the clinical workflow and standard of care for individuals with traumatic limb injuries. We will first conduct expert item reviews and cognitive debriefing interviews to refine the 10 preliminary item pools into clear and comprehensive sets of items that are ready for large-scale calibration testing. Then, we will conduct large-scale field testing, administering the newly developed item pools to individuals with a history of major extremity trauma (upper- and lower-limb amputation and limb preservation) recruited from 5 data collection sites. Data will be analyzed to calibrate the items and develop computer adaptive tests (CATs). Last, clinical score reports will be designed based on needs identified in clinician focus groups and revised based on expert feedback from cognitive debriefing.



Accomplishments: In year 3, quarter 4 of this project, we continued large-scale field testing. By the end of this quarter, **159** participants had begun the baseline interview and **154** had completed the baseline interview. Regulatory and administrative paperwork is underway to add several additional recruitment sites, to help overcome recruitment obstacles from the COVID-19 pandemic. Plans for data analyses for the item response theory (IRT) calibrations are underway. These data analyses will be finalized once the baseline interview data collection is complete.

Revised Timeline and Cost

Activities	Year 1	Year 2	Year 3	Year 4	Year 5
IRB & HRPO Approval	■				
Expert Item Review	■				
Data Collection: Cognitive Interviewing		■			
Data Collection: Field Testing (Baseline)		■	■		
Data Collection: Medical Record Abstraction		■	■		
Data Collection: Field Testing (1 year Follow-Up)			■	■	
Data Analyses: IRT Calibrations			■	■	
CAT programming				■	
Data Collection: Field Testing (2 year Follow-Up)				■	■
Data Analyses: Longitudinal Data					■
Clinician Focus Groups					■
Score Report Development and Refinement					■
Cognitive Debriefing Interviews with Clinicians					■
Implementation of Scales & Reports					■
Estimated Budget ($K)	*$884*	*$867*	*$875*	*$820*	*$680*

Updated: 31-Aug-2020

Revised Goals/Milestones

Year 1
- ☑ Obtain regulatory approval (IRB & HRPO; complete at 5 of 6 sites)
- ☑ Conduct expert item review (internal scientific reviews & external expert reviews complete)

Year 2
- ☑ Conduct data collection: Cognitive Interviewing
- ☑ Begin data collection: Field Testing

Year 3
- ☑ Continue data collection: Field Testing
- ☑ Begin data analyses: IRT calibrations

Year 4
- ☐ Continue data collection: Field Testing
- ☐ Complete data analyses: IRT calibrations
- ☐ Conduct CAT programming

Year 5
- ☐ Complete data collection: Field Testing
- ☐ Conduct Longitudinal Data Analyses
- ☐ Conduct clinician focus groups
- ☐ Develop clinical score reports
- ☐ Implement scales and reports

Comments/Challenges/Issues/Concerns. Data collection is proceeding at a slower-than-expected pace, primarily due to the negative effects of the COVID-19 pandemic on recruitment. We are working with sites to address these new challenges and making changes to recruitment plans to ensure completion of data collection. We are also adding several new sites to increase recruitment throughput.

Budget Expenditure to Date:
Projected Expenditure: **$2,536,065**
Actual Expenditure: **$1,303,216**

(Note: differences are primarily due to timing and delayed start of data collection)

APPENDIX B – Presentation Abstracts

Abstracts for research presentations described in question 6 above.

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1. Poster Presentation Abstract

Tyner, C.E., Slotkin, J., Kisala, P.A., Zafonte, R., Kalpakjian, C., Kingsbury, T., Cancio, J.M., Dearth, C.L., Griffith, A.M., Ma, M.L., Boulton, A.J., & Tulsky, D.S. (2019, August). *Developing new items for the Extremity Trauma and Amputation Quality of Life Measurement System: Cognitive debriefing interviews.* Poster presented at the Military Health System Research Symposium, Kissimmee, Florida.

Background: Major extremity trauma is a considerable cause of disability for military service members. Individuals with limb trauma often experience a variety of secondary physical symptoms, mental health challenges, and social participation side effects. These physical and psychosocial difficulties may remain persistent after returning to work and/or the community. Over 2 million Americans are living with amputations, with more than 20,000 new traumatic limb injuries occurring each year. Health-related quality of life (HRQOL) following a traumatic limb injury is not solely based upon injury severity. Rather, a variety of physical, mental and social factors interact to produce disability. It can be difficult to predict who will return to duty and/or the community following these injuries. Currently, no population-specific measurement tools exist to measure HRQOL following traumatic limb injury. Existing tools validated for other populations do not fully capture the experiences of these individuals. The present study seeks to integrate and build upon existing high-quality measurement systems to develop a reliable, valid and comprehensive patient-reported outcome measurement tool, specific to the needs of individuals with major extremity trauma. This presentation reports on the results from the completed first phase of this study's data collection: Cognitive Debriefing Interviews. The primary purpose of including cognitive interviewing in the development of a new patient-reported outcome measure is to help refine the items with feedback from those in the population who have been affected by the given disability, to ensure all important concepts are included and clearly communicated. This report describes the process and results of gathering cognitive interview feedback from service members and civilian patients on the salience and clarity of items from 12 new content domains.

Methods: Items were developed following focus groups with military service members who sustained a traumatic limb injury (n = 56) as well as their clinicians (n = 34). Twelve new item pools based on common, unidimensional constructs were developed and specific items (n = 582) were generated around the 12 central themes. In addition to newly generated items, an extensive literature review of existing measurement systems was conducted. Relevant items from high-quality measurement systems were adopted and/or modified for inclusion (n = 256). Extremity trauma experts in the field further evaluated the items to ensure proper grammar, clarity, relevance, and translatability. A subset of items from each of the item pools (n = 412) was selected for cognitive interviewing. Participants included in cognitive interviews were recruited from three Military Treatment Facilities and two civilian healthcare facilities from across the country. Participation criteria included a history of upper or lower major extremity trauma with corresponding amputation and/or a history of limb preservation surgery. Participants were contacted by University of Delaware researchers via telephone. Cognitive interviewing procedures followed the methods recommended by Willis et al. (1999). After providing informed consent, participants were asked to review a subset of the survey questions from the 12 conceptual content domains (approximately 40-80 items). This included listening to the items as

they were read aloud by a trained interviewer, responding to the items, and providing feedback on their thought processes as well as any general opinions of the items. Participants were asked to critique the wording, context, timeframe, and response choices of items, as well as to provide feedback on any important components of a particular topic that were not covered. Responses were recorded in notes taken by the interviewer through a secure REDCap database.

Results: Forty-one cognitive interviews were completed. The sample was comprised of 10 active-duty service members, 12 veterans, and 19 civilians. Consistent with the limb trauma population as a whole, more men (n = 35) than women (n = 6) participated. Participants included 31 individuals who sustained lower limb trauma, seven participants with upper limb trauma, and three individuals with trauma to both upper and lower limbs. A total of 30 participants have had injuries that resulted in an amputation only, two participants have undergone limb preservation only, and an additional nine participants have experienced both limb preservation and amputation. For participants with a history of amputation, average time since amputation was 8 years, 9 months. Time since initial injury ranged from two months to 45 years (mean = 9 years, 10 months). All of the 412 items subjected to cognitive interviewing were reviewed by at least five participants, meeting the generally accepted methodological target for saturation. Feedback on the items has primarily been positive, indicating a high relevance of the topics covered and appropriateness of the wording for affected participants. Important feedback was received on the wording of items relevant to experiences of social and personal role/identity changes for military service members, given that not all who experience these injuries leave their military careers. Some items about physical functioning and mobility were found to be primarily applicable to individuals who experienced lower-limb injuries. In contrast, items regarding body image appeared to resonate most strongly with more-recently injured individuals and those who had experienced upper-limb amputation. Of note, participants who were married at the time of the interview responded differently to items concerning their sense of security in their romantic relationships, as compared to participants who were single who faced more fear of stigma in dating relationships. Certain words, such as “job,” were found to have distinct interpretations for participants depending on their circumstances (e.g., working at a place of employment, going to rehabilitation appointments, or managing a home). Items in some banks, in particular future outlook, were found to be primarily related to participants’ personal philosophies, and were not heavily influenced by current symptoms or ongoing post-injury physical difficulties. Work is ongoing to incorporate these and other salient results from cognitive interviewing to revise items and devise new items in topic areas where insufficient content was detected, as well as to remove items to which participants raised relevant concerns.

Conclusion: This ongoing work represents an initial but vital step in the development of a new, empirically tested system of patient-reported outcome (PRO) measures focused on major extremity trauma. The methods used for cognitive interviewing are aligned with the PROMIS® initiative. The PROMIS® initiative was developed in concert with the National Institutes of Health as a set of high standards for item development, and specifies the process in qualitative research for using item response theory to construct PROs that are both reliable and valid. Based upon the cognitive interviewing feedback and in accordance with the PROMIS® initiative, items are being further refined for clarity and relevance. Results of the cognitive interviews indicate overall that this sample of individuals with major extremity trauma and amputation, representing current service members, veterans and civilians, responded positively to the vast majority of items developed for ExTrA-QoL. In each domain, select items elicited feedback from multiple participants that indicated a need for revision or removal from the bank. Feedback on specific factors that influence interpretation of items—such as injury characteristics, personality factors, and life circumstances—will be used to refine wording and content of the item banks.

Large-scale field-testing will then be used to calibrate items, analyze differential item functioning, and evaluate responsiveness.

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2. Poster Presentation Abstract

Tulsky, D.S., Tyner, C.E., Slotkin, J., Cancio, J.M., Dearth, C.L., Kingsbury, T., Kalpakjian, C., Zafonte, R., Pruziner, A., Kisala, P.A., & Boulton, A.J. (2019, August). *The Extremity Trauma and Amputation Quality of Life Assessments: Developing a new measurement system for neuromusculoskeletal trauma.* Poster presented at the Military Health System Research Symposium, Kissimmee, Florida.

Background: Disability caused by major extremity trauma is prominent in both military and civilian populations. In the United States, more than 20,000 new major extremity traumas occur annually. Traumatic limb injuries are both diverse and complex. Among military Service Members, the physical and psychosocial consequences following limb injury often continue after individuals return to duty or reintegrate into civilian life. Importantly, long-term disability and reintegration into military service and the community are predicted by factors outside of injury severity alone. Emotional functioning, coping and adjustment, health status and physical symptoms, adoption of and adjustment to the use of assistive technology, and psychosocial factors that influence participation and integration in the community all influence health-related quality of life (HRQOL). A lack of patient reported outcome (PRO) measures currently exists to quantify HRQOL following major extremity trauma. The experiences of individuals following major extremity trauma are not fully captured by existing measurement tools designed for other populations, because they often focus on only a handful of symptom topics in each measure. The present research intends to address this deficiency. This will be achieved by building upon previous comprehensive measurement systems for rehabilitation populations, such as the Spinal Cord Injury Quality of Life Measurement System (SCI-QOL) and the Traumatic Brain Injury Quality of Life Measurement System (TBI-QOL). Specifically, the researchers have developed a comprehensive plan for a set of measurement tools (i.e., item banks) that can be utilized to measure salient aspects of HRQOL in both military and civilian populations following major extremity trauma. Therefore, the primary aim of this project was to adopt, modify, and construct items in approximately 10 content domains specific to this clinical population that can be used in conjunction with measures of more general domains of HRQOL that are relevant across rehabilitation populations (e.g., fatigue, self-care, anxiety). This work constitutes a major development in the advancement of a patient-reported quality of life measurement system following major extremity trauma.

Methods: New items for this planned measurement system were developed based on focus group feedback from military service members who sustained a major extremity trauma, as well as their clinicians and members of their multi-disciplinary care teams. Focus groups met at three DoD Military Treatment Facilities and one Veterans hospital. Fifty-six service members and veterans with a history of limb trauma and/or amputation and thirty-four clinical providers participated in the focus groups. Participation criteria included individuals who had sustained an upper and/or lower traumatic limb injury and who either experienced limb amputation or limb preservation procedures following their injury(ies). Clinician participants included occupational and physical therapists, physiatrists, and other mental health care professionals. The focus group meetings were audio recorded and transcripts were then examined for content. The International Classification of Functioning, Disability, and Health (ICF) criteria were used to categorically group statements. The frequency of conceptual statements was used to define new item pools (e.g., future outlook, body image). Transcripts were then analyzed to generate new, population-specific items. The researchers generated definitions for each item pool to

assist in developing content of new items around central themes. Each item pool was hypothesized to be comprised of a single unidimensional construct. An extensive review of existing measurement tools was undertaken during the item writing process. In addition to newly generated items, relevant items from existing measurement systems were adopted and/or modified for the new measure. Items were further evaluated to ensure proper grammar and clarity, relevance to construct, and translatability.

Results: Twelve new conceptual content domains were defined relevant to this population: Self-Esteem, Body Image, Weight Management Difficulties, Health-Related Self Efficacy, Satisfaction with Physical Abilities/Fitness/Athleticism, Satisfaction with Social Function & Participation, Grief & Loss, Adjustment to Military Identity/Role Change, Satisfaction with Orthosis/Prosthesis, Arthrosis Impact, Resilience, and Future Outlook. A total of 582 new items were developed for each of the concept domains. Additionally, 256 relevant items from existing measurement systems were adopted. Existing items were drawn from the Patient-Reported Outcomes Measurement Information System (PROMIS®), the Quality of Life in Neurological Disorders Measurement System (Neuro-QoL), the Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me®), the SCI-QOL, and TBI-QOL, due to their pertinence to the limb trauma population. Existing relevant, high-quality items were not available for certain domains specific to the major extremity trauma population (e.g., Weight Management, Adjustment to Military Identity/Role Change, and Satisfaction with Orthosis/Prosthesis). To pair with these new domains, 19 existing measures/item banks from PROMIS®, Neuro-QoL, SCI-QOL, and TBI-QOL were selected for calibration testing with this sample of major extremity trauma across 4 domains: 1) Physical Functioning (Fatigue, Physical Function, Mobility, Upper Extremity Function, Self-Care, Fine Motor Function); 2) Physical Symptoms (Pain Interference, Pain Intensity); 3) Mental Health (Anger, Anxiety, Depression, Positive Affect & Well-Being, PTSD/Trauma, Stigma, Cognition); 4) Social Participation (Ability to Participate in Social Roles and Activities [SRA], Satisfaction with SRA, Independence, Economic Quality of Life). Together, these selected measures will be tested and calibrated to form a new, comprehensive measure system for HRQOL after major extremity trauma.

Conclusion: This work constitutes an essential initial step in the development of a new patient reported outcome measurement system designed specifically for clinicians and researchers measuring HRQOL for military service members, veterans, and civilians following major extremity trauma. The methods used in development are aligned with the National Institutes of Health PROMIS® initiative following guidelines for developing new measures for medical rehabilitation populations. The PROMIS® initiative provides a set of high standards for item development and outlines the specific process for using item response theory in qualitative research to generate reliable and valid PROs. Currently, work is underway to further test and refine items using additional qualitative methods, including feedback from experts in the field and cognitive interviews with civilians, military service members, and veterans who have experienced traumatic limb injuries. In future work, large-scale field-testing will be used to calibrate items, analyze item bias and differential item functioning, and evaluate responsiveness.