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TITLE: Examining the Risk of Alzheimer's Disease and Related Dementia Among People with Spinal Cord Injury: A Mixed-Methods Study Comparing Veterans and Civilians

PRINCIPAL INVESTIGATOR: Elham Mahmoudi, PhD

CONTRACTING ORGANIZATION: University of Michigan

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Fort Detrick, Maryland 21702-5012

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The Regents of the University of Michigan
Department of Family Medicine
1018 Fuller Street
Ann Arbor, Michigan
48104-1213

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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13. SUPPLEMENTARY NOTES The complex disease etiologies faced by people with TSCI require careful examination of the types of screening, preventative, and rehabilitative services that may reduce their risk of cognitive decline.

14. ABSTRACT : Traumatic spinal cord injury (TSCI) is often associated with life-long debilitating consequences that negatively impact quality of life. With advances in healthcare, life expectancy for people afflicted with TSCI has increased substantially. While aging is the main risk factor for Alzheimer's Disease and Related Dementia (ADRD), new evidence on higher likelihood for developing ADRD after TSCI is emerging. In particular, during our recent study of commercially insured individuals with TSCI in the United States, we found that people with TSCI had an elevated risk for ADRD compared to a matched cohort of the general population without disability. Yet there is a scarcity of epidemiological studies examining associations between TSCI and ADRD and use of services that may ameliorate this risk. Given that the Veterans Health Administration (VA) is known as the largest and most comprehensive system of care in the U.S., it is imperative to examine the composite of protective effects conferred by therapeutics and lifestyle on incident ADRD.

15. SUBJECT TERMS
Spinal cord injury, Alzheimer's Disease

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1. INTRODUCTION: *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Traumatic spinal cord injury (TSCI) is often associated with life-long debilitating consequences that negatively impact quality of life. With advances in healthcare, life expectancy for people afflicted with TSCI has increased substantially. While aging is the main risk factor for Alzheimer's Disease and Related Dementia (ADRD), new evidence on higher likelihood for developing ADRD after TSCI is emerging. In particular, during our recent study of commercially insured individuals with TSCI in the United States, we found that people with TSCI had an elevated risk for ADRD compared to a matched cohort of the general population without disability. Yet there is a scarcity of epidemiological studies examining associations between TSCI and ADRD and use of services that may ameliorate this risk. Given that the Veterans Health Administration (VA) is known as the largest and most comprehensive system of care in the U.S., it is imperative to examine the composite of protective effects conferred by therapeutics and lifestyle on incident ADRD. The complex disease etiologies faced by people with TSCI require careful examination of the types of screening, preventative, and rehabilitative services that may reduce their risk of cognitive decline.

Hypothesis and Objectives: The overarching goal of this study is to examine the risk of ADRD among people with TSCI, comparing Veterans and commercially insured individuals. As a secondary aim, we will examine the potential mitigating effects for regular use of specific preventative, therapeutic, and rehabilitative services after TSCI on risk of ADRD. Use of these services may improve neurological recovery, management of daily activities, quality of life, and possibly delay incident ADRD. Finally, our tertiary aim will underscore an urgent need to understand barriers and facilitators in use of services (e.g., preventative, therapeutics) or lifestyle choices (e.g., exercise, leisure cognitive activities that have shown promising results in reducing risk of ADRD.

Study Design: This study will use a sequential explanatory mixed methods approach (quantitative and qualitative). For quantitative analyses (Aims 1 and 2), we will use 2012-2019 nationally representative private health insurance claims and VA electronic medical records, respectively, to carefully assess: (1) the association between TSCI and ADRD; and (2) the potential ameliorating association between use of preventative, therapeutic, and rehabilitative services after TSCI on risk of incident ADRD. In Aim 3, using semi-structured interviews, we will qualitatively explore the barriers and facilitators in access to and use of the aforementioned services among Veterans and civilians with TSCI.

Impact: This novel proposal will foster a new direction in the field of TSCI research by focusing on heightened risk of incident ADRD among people with TSCI. Our proposed research addresses two of the FY20 SCIRP focus areas: (1) psychosocial issues relevant to people with SCI, their families, and/or their care partners, and (2) rehabilitation and regeneration – maximizing the function of the residual neural circuitry, including harnessing neuroplasticity and recovery to improve function after TSCI. Information from this study will begin to fill a research gap and influence clinical care for persons with TSCI. The outcome of this proposed study will be an evidence-based recommended bundle of care to promote healthy brain aging in persons with TSCI.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Traumatic Spinal Cord Injury; Alzheimer's Disease and Related Dementia; Claims Data Analysis; Mixed Methods Analysis; HCCI; VA.

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

	Timeline	**Completion Status**
Major Task 1: Maintain regular contact with Funding agency and Steering Committee	Months	
Contacted Project Officer, Completed Technical Report..	1-3	100% Completed
Milestones:		

	Timeline	**Completion Status**
Major Task 2: Complete all necessary regulatory review and approval processes for research involving human subjects and data user agreeements	Months	
Finalize IRB, Consent form……	1-3	100% completed
Milestones:		

	Timeline	**Completion Status**
Major Task 3: Data Management and Analysis of the HCCI and VA data – Aim 1 (months 3 to 15)	Months	
	3-15	100% completed

	Timeline	**Completion Status**
Task 4: Compare the results of Aim 1 between the VA and civilians (months 15-16; Study Site: UM)	Months	
	15-16	30% completed

	Timeline	**Completion Status**
Task 5: Conduct a set of three analyses related to Aim 2 using VA and HCCI data (months 15-16; Study Site UM)	Months	
	15-16	40% completed

	Timeline	Completion Status
Task 6: Compare the results of Aim 2 between the VA and civilians (months 24-25); Study Site UM	Months	
	24-25	0% completed

	Timeline	Completion Status
Task 7: Develop screening survey to recruit potential participants for the semi-structured interviews forAim 3 - qualitative interviews with persons with TSCI (VA and civilians) (months 12 to 14; Study Site: UM)	Months	
	12-14	100% completed

	Timeline	Completion Status
Task 8: Select participants for semi-structured interviews (months 14 to 18; Study Site: UM)	Months	
	14-18	30% completed

	Timeline	Completion Status
Task 9: Conduct in-depth interviews with 50 VA and non-VA individuals with TSCI (months 18 to 24;Study Site: UM (virtual interviews)	Months	
	18-24	20% completed

Task 10: Transcribe, "clean" data from interviews and enter into qualitative software (months 24 to 25;Study Site: UM)	Months	
	24-25	10% completed

Describe the Regulatory Protocol and Activity Status (if applicable).

Task 11: Code and analyze interviews (months 25 to 33; Study Site: UM)	Months	
	25-33	0% completed

Task 12: Finalize conclusions, disseminate and begin utilization of results (months 12 to 36; Study Site:UM)	Months	
	12-36	0% completed

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

1) major activities;

Qualitative Interviews have begun in support of Aim 3.

2) specific objectives;

- Initial IRB approval for the University of Michigan and the VA has been obtained.
- HCCI – We defined our patient cohort (Adults 45 years and older with an incident of TSCI) in HCCI data (2012-2019):
    - We had a total of 14,731,374 unique in HCCI. We identified 5,222 people with at least one TSCI diagnosis in inpatient services. Our final cohort of people with TSCI included 573 people with at least 5 years of continuous enrollment (one year lookback period and 4 years of follow-up).
    - Schematic flow diagram is prepared
    - We are in the process of defining time varying chronic conditions and logical grouping of these conditions for our regression models.
    - We are in the process of defining time varying medications that people with incidence of traumatic spinal cord used overtime.
    - VA TSCI cohort was derived similar to concurrent HCCI work, but tailored to VA data infrastructure. Cases were defined as patients with a diagnosis code indicating traumatic spinal cord injury (TSCI) associated with an inpatient stay, within either a VA Hospital or the larger community. Dates of inclusion were limited to the ten-year period from 2005 to 2015. In order to determine "incident"/index TSCI, all available outpatient records from patients with an inpatient TSCI were queried for any diagnoses codes indicating TSCI, and any with a prior TSCI were excluded. And so, 12,608 Patients w/ index TSCI between 2005-2015, without any prior TSCI diagnoses, age ≥ 45, and without Prior ADRD/TBI/Plegia were considered as cases. Dissimilarly, controls were defined as any VA patient without any TSCI diagnoses code, from any source, between 2000 and 2015, and without any indication of ADRD or Plegia. Thus, 4,483,965 controls were identified in this manner. For analytic purposes each case was matched to three controls on exact age, sex, and presence of comorbid conditions (broad categories of cardiometabolic, respiratory, and psychological comorbidities). From each patient, a comprehensive list of medications were collected based on 6 broad categories (Anticholinergics, Antidepressants/Sleep, Antispasmodics, Benzodiazepines, Neuropathic Pain Medication, Opiates/Narcotics for Pain). In comparing trends in medication fills between our sample (VA), and HCCI data sources, we have become concerned that we may not be collecting the actual date of an individual index TSCI. As we feel it is important to more precisely identify "index" TSCI, current efforts are aimed at redesigning the case cohort to indicate the first TSCI diagnosis code in the record, from any source, as the index TSCI. Concurrently, a TSCI specialist associated with the VA is helping to develop an algorithm based on primary admission diagnosis codes to more clearly identify "index" TSCI.
    - TSCI cohort cases were derived as patients with a principal ICD-9 diagnosis codes(HCCI has 3 measures of ICD-9 codes) indicating traumatic spinal cord injury (TSCI) associated with an inpatient stay (i.e. facility visit).
    - Similar procedure was followed to derive cases with outpatient and physician visits(i.e. non-facility visits), but an additional criterion of overlapping emergency room visits was included for final inclusion of the non-facility cases.

- All individuals who were ages 45+ between 01/01/2012 and 09/30/2019, had four years of continuous insurance enrollment , with 1 year of look back information and without Prior ADRD/TBI/Plegia were included. Records before October 1st 2015 were used to identify TSCI criteria to ensure cases with ICD-9 classification were only analyzed.
- After identification of the cases, a TSCI specialist of our group further classified the cases as 'likely' and 'least likely' and the least likely cases were dropped from the final sample.
- Our final case count was 251 (220 from facility and 31from non-facility)
- Control group was derived for adults without TSCI using same inclusion criteria as above. Index date for the controls was generated using a random uniform distribution. Total, 7,294,031 controls were identified in this manner. For analytic purposes each case was matched to ten controls on exact age, sex, and presence of comorbid conditions (broad categories of cardiometabolic, respiratory, and psychological comorbidities) using propensity score matching. Total matched cohort came to 2461 (instead of 2510) as we did not find a perfect match for some of our cases.
- The National Neighborhood (NANDA) data were merged to generate affluence rank and disadvantage rank (Rank1,Rank2,Rank3 and unknown) for our cases and matched control based on member zip codes.
- From each patient, a comprehensive list of medications use was developed based on 6 broad categories (Anticholinergics, Antidepressants/Sleep, Antispasmodics, Benzodiazepines, Neuropathic Pain Medication, Opiates/Narcotics for Pain) using NDC codes (both 9digit and 11digit codes) from pharmacy claims dataset of HCCI.
- Monthly medication fills for patients on each of these categories were used to derive trends in medication usage over 48 follow-up months for each of these categories respectively. Spikes in opiates usage was observed in the first two months.

- *Recruitment has begun for qualitative interviews. We have received 345 eligibility questionnaires from which we will choose the participants who we will invite for an interview.*
- *Qualitative Interviews in support of Aim 3 have begun*
  - *To date we have completed 13 interviews.*

3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or
None to date

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Dr. Adit Doza is a postdoctoral fellow at the University of Michigan. He works directly with the PI (Dr. Mahmoudi) and is responsible for analyzing the HCCI data, conducting analytic modeling, and writing manuscripts. As part of his professional development, he has learned how to efficiently work with claims data using SAS software for programming. He will be presenting the work at national conferences.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We anticipate finishing writing our first paper using HCCI data and send out abstract to present the work at national conferences. We will start conducting regression decomposition (Aim 2) using HCCI data. We also anticipate our analytic work using the VA data to be completed to start writing the first manuscript out of the VA data.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report.

5. CHANGES/PROBLEMS: *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to report.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

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

Nothing to report.

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  No publication yet. We anticipate having several manuscripts under review in the next few months.

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.

Nothing to report.

- **Website(s) or other Internet site(s)**
List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**
Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report.

- *Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.*

Nothing to report.

- **Other Products**

  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name:	Elham Mahmoudi
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	0000-0002-9746-8165
Nearest person month worked:	1.2
Contribution to Project:	Research Design and responsible for all aspects of the proposal
Name:	Martha Boggs
Project Role:	Project coordinator/project manager
Nearest person month worked:	.60 calendar months
Contribution to Project:	Regulatory Management
Name:	Adit Doza
Project Role:	Postdoctoral Trainee - Data analyst - HCCI
Nearest person month worked	12 calendar months

Contribution to Project	Dr. Adit cleans, manages, and analyzes the data from large claim datasets, implements and evaluates appropriate econometrics and modeling techniques for the study
Name:	Neil Kamdar
Project Role:	Co-investigator
Nearest Person Month Worked	.60 cal months
Contribution to Project	Supervises the analysis of the HCCI data
Name:	Gianna Rodriguez
Project Role:	SCI physician and collaborator
Nearest Person Month Worked	.12 cal months
Contribution to Project	SCI physician and collaborator
Name:	Chris Cigolle
Project Role:	SCI physician and collaborator
Nearest Person Month Worked	.30 cal months
Contribution to Project	Interpretation of the results, particularly differences in access and use of services between the VA and private healthcare systems
Name:	Michelle Meade
Project Role:	Co-Investigator
Nearest Person Month Worked	.24 cal months
Contribution to Project	Supervises the qualitative analysis and assists with the interpretation of the results and dissemination of the data. Including data analysis, supervision of project staff, preparation of reports and manuscripts
Name:	Richard Evans
Project Role:	Data Analyst - VA
Nearest person month worked	.60 calendar months
Contribution to the Project	Data Analyst - VA
Name:	Wyndi Wiitala
Project Role:	Data Analyst
Nearest person month worked:	.60 calendar months
Contribution to Project:	Dr. Wiitala will lead project activities including the obtaining of data and analysis planning that will serve as the basis for quantifying the effects associated with differences in preventative

	services.
Name:	James Tyler Glenn
Project Role:	Post Doctoral Fellow
Nearest person month worked:	1.2 calendar months
Contribution to Project:	Postdoctoral Trainee – Qualitative and mixed Method Analyst

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)
- *Financial support;*

- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ebrap.org/eBRAP/public/index.htm*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil/Pages/Resources.aspx) should be updated and submitted with attachments.*

Quad Chart

Examining the Risk of Alzheimer's Disease and Related Dementia among People with Traumatic Spinal Cord Injury: A Mixed Methods Study Comparing Veterans and Civilians *Grant #: W81XWH2110751 Log #: SC200247*

PI: Elham Mahmoudi **Org:** The Regents of the University of Michigan **Direct Award Amount:** $500,000

Study Aims

Aim 1 (Quantitative): Examine the risk of incident ADRD among Veterans and civilians with TSCI, respectively.

Aim 2 (Quantitative): Examine the use of preventative, therapeutic, and rehabilitative services.

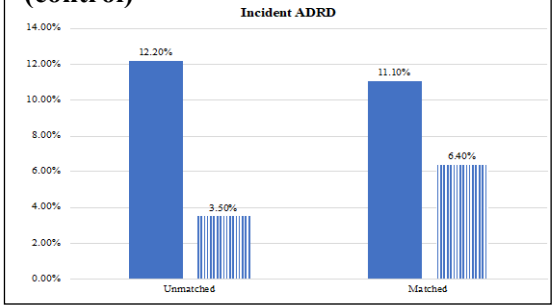
a) Examine the risk of incident ADRD associated with time-varying use of preventative, therapeutic, and rehabilitative services for Veterans and civilians with TSCI, respectively.
b) Quantify the direct and indirect effects associated with differences in utilization of preventative, therapeutic, and rehabilitative services comparing the VA and civilians with TSCI.
c) Quantify the direct and indirect effects associated with differences in utilization of preventative, therapeutic, and rehabilitative services comparing TSCI patients with and without ADRD among the VA and civilian population, respectively.

Aim 3 (Qualitative): Explore the barriers and facilitators in use of preventative, therapeutic, and rehabilitative services between Veterans and civilians with TSCI that may reduce risk of ADRD onset/progression.

Approach

The objective of the proposed mixed methods investigation is to assess the influence of fixed and time-varying injury characteristics and health conditions on incident ADRD, comparing the matched cohort of adults with TSCI and those without disability among privately insured and Veterans, respectively. Furthermore, we will examine whether using preventative, therapeutic, and rehabilitative services and their level of use after TSCI could ameliorate the risk of incident ADRD, and if yes, to what extent. The objective is to propose a bundle of care that has shown evidence of protection against incident ADRD. Finally, we will qualitatively explore barriers and facilitators in access and use of services that have been shown to be effective in promoting healthy brain aging among persons with TSCI.

Unadjusted Incident ADRD among Privately Insured Adults with TSCI (case) and Those without Disability (control)



Our preliminary work using the private administrative Clinformatics™ Data Mart Database (OptumInsight, Eden Prairie, MN), comparing adults aged 45 and older with TSCIs with their unmatched and matched cohort of adults without disability (control) indicate higher incident ADRD among adults with TSCI.

Timeline and Cost

Activities CY	**9/21 to 1/22**	**1/22 to 1/23**	**1/23 to 1/24**	**1/24 to 9/24**
IRB and data user agreement (DUA) approval				
Gain access to data				
Data management				
Data analysis – Aim 1				
Data analysis – Aim 2				
Recruitment process for Aim 3 (qualitative data)				
Defining the final participants for Aim 3				
Conducting the interviews				
Conducting the analysis for Aim 3				
Writing/Revising/Presenting the results				
Estimated Budget ($K)	**$83K**	**$166K**	**$167K**	**$84K**

Goals/Milestones

CY21 Goal – Process IRB and DUA
Gain access to VA and HCCI data
Start the data management – Identify our case and control groups (those with TSCI and non-TSCI) using VA and HCCI data, respectively.
Match the case and control group

CY22 Goal – Analyze data for Aims 1-2
Complete the analyses required for Aims 1-2
Develop Tables/Figures for publication purposes
Start the patient recruitment process for Aim 3
Mail the consent/survey forms to potential participants for Aim 3

CY23 Goal – Conduct the qualitative analyses (Aim 3)
Complete the analyses, interpret the results, write the manuscripts related to Aims 1 & 2.
Complete the qualitative data collection for Aim 3
Analyze the qualitative data/Write manuscripts

CY24 Goal –Disseminate the results
Write manuscripts/Revise/Present/Disseminate

9. APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*

None