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TITLE: Impact of Evidence-Based Nonsurgical Management Guidelines on Outcomes for Disabling Knee Injuries: Long-Term Health Deficits, Disability, and Economic Analysis

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CONTRACTING ORGANIZATION: The Geneva Foundation

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Background: Service members are at an increased risk for development of arthritic conditions, such as OA of the knee, and therefore continued research into optimal intervention strategies is needed.
Design: Comparative effectiveness parallel-group randomized controlled clinical trial
Methods: Subjects with a diagnosis of knee OA will be recruited through the primary care clinics across 3 military hospitals (MAMC, WHASC, and BAMC). Patients that consent and enroll will be randomized to receive usual care defined as the core management strategies defined by the DoD/VA Guidelines for the Management of Knee Osteoarthritis or this same usual care in addition to physical therapy. Patients will follow up at 6 weeks, 6 months, 1 year and 2 years after enrollment.
Summary: The results of this study will help inform and develop best practices for those with a diagnosis of Knee OA.

15. SUBJECT TERMS
Pain Management

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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1. INTRODUCTION:

Our overall objective is to improve the non-surgical management of TRICARE beneficiaries who have been recently diagnosed with knee OA. We hypothesize that more effective early management following diagnosis affords the greatest opportunity to improve clinical outcomes and reduce costs by delaying or avoiding the need for costly, invasive procedures. Specifically, we hypothesize that consistent delivery of evidence-based PT early in the care process for individuals recently diagnosed with knee OA will be more effective than providing only the core set of management strategies currently advocated in the VA/DoD Guidelines, and while providing PT will increase initial health care costs, the reduction in subsequent procedures will make the addition of PT a cost-effective early management strategy.

2. KEYWORDS:

Knee osteoarthritis, guidelines, usual care, service members, physical therapy

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Our overall objective is to improve the non-surgical management of military beneficiaries who have been recently diagnosed with knee OA.

1. Compare the effectiveness of two early management strategies (Core Set vs. Core Set + PT) for Tricare beneficiaries recently diagnosed with knee OA by a primary care provider in the MHS for the primary outcome of knee function collected over the 2-year follow-up period.
2. Compare the effectiveness of the two early management strategies for secondary outcomes including knee pain, sleep disturbance, psychological distress (anxiety and depression), activity profile status, knee-related health care costs and utilization of invasive OA-related health care procedures (injections, arthroscopy, TKA) collected over the 2-year follow-up period.
3. Explore primary and secondary outcomes of the two early management strategies for sub-groups of patients recently diagnosed with knee OA based on OA etiology (post-traumatic vs. degenerative) and age at diagnosis (< 50 vs. > 50).
4. Compare the cost-effectiveness of two early management strategies collected over the 2-year follow-up

What was accomplished under these goals?

ACCOMPLISHMENTS

1. Project was approved by the primary site IRB at Brooke Army Medical Center 11 October 2018
2. Site Specific Addendum of Protocol submitted to each sub-site IRB and approved at all sites.
    a. Madigan Army Medical Center (IRB, May 2019; HRPO, June 2019)
    b. CLOSED // Carl R. Darnall Army Medical Center (IRB, February 2019; HRPO, March 2019)
    c. Wilford Hall Ambulatory Surgical Center (IRB, November 2018; HRPO, Dec. 2018)
3. Enrollment across all sites: 49 subjects (as of 29 September 2020)

FUTURE PLANS

We just began slowly enrolling at one site just a few weeks before this current period ended, after a hiatus due to due to COVID-19. We have been subsequently cleared to start recruitment at all of our sites. Currently, we are problem solving ways to maximize recruitment as the face to face appointments are not as common now compared to pre-COVID-19, which means fewer patients are coming into seek care.

Statement of Work Completed Tasks

	Timeline Months	**Site 1** (MAJ Pickens/ Dr. Rhon)	**Site 2** (Dr. Hatler)	***Site 3** (MAJ Samson)	**STATUS**
Initial Task IRB submission, personnel hiring, and study-related training					
Subtask IT1. Hiring of research assistant(s) (months 1-3) and physical therapists (months 3-5)	0-3	Dr. R			COMPLETE
Subtask IT2: Submission of protocol at primary **IRB (BAMC – months 0-2) and then sub-site IRBs (after approval at primary site)	0-6	Dr. R	Dr. H	MAJ S	COMPLETE
Subtask IT3: Submit IRB approval and necessary documents for ***HRPO review.	6-9	Dr. R			COMPLETE
Subtask IT4: Establish administrative support for enrolling subjects. - A. Research Assistants/Project Manager will create all subject packets - B. Provide the appropriate documentation to all relevant clinicians - C. Establish databases for data collection and follow-up tracking (setup and test REDCap) - D. Manual of Procedures (MOPs) and training guidelines will be created.	6-9	Dr. R			COMPLETE

Statement of Work Future Tasks

	Timeline Months	**Site 1** (MAJ Pickens/ Dr. Rhon)	**Site 2** (Dr. Hatler)	***Site 3** (Maj Samson)	**STATUS**
Milestone 1: IRB approval and HRPO Approval	6-9				COMPLETE
Specific Aim 1: Compare effectiveness of two early management strategies (core set vs. core set + PT) over the 2-year	**9-46**				

follow-up period					
Task 1a: Enrollment of 300 subjects between 2 sites					
Subtask 1: Subjects are consented and study measures, that include self-report and physical performance tests, are taken	13-28	Dr. R (N = 150)	TBD *(N = 150)	TBD *(Alternate)	
Milestone 2: Target enrollment met	28				
Task 1b: Follow-up occurs for a 2-year period, with follow-ups at 3 months, 6 months, 1 year, and 2 years.	16-42	Dr. R	TBD	TBD	
Subtask 1: REDCap surveys sent at each time point Subtask 2: Track compliance with follow-ups	16-42	Dr. R			
Milestone 3: 2-year follow-up period complete	*42*				
Task 1c: Prepare data for analysis	42-43	Dr. R			
Subtask 1: Extract data from REDcap Subtask 2: Organize database for analysis	44	Dr. R			
Task 1d: Analyze data for AIM 1	44-46	Dr. R			
Specific Aim 2: Compare the two early management strategies for secondary outcomes collected over the 2-year follow-up period.	42-48	Dr. R			
Task 2a: Analyze data for AIM 2. (This is a data-analysis task and requires no additional subject testing beyond Aim 1.)	44-48	Dr. R			
Task 2b: Perform sensitivity analysis, and account for specific populations (PTOA, age variations, etc)	44-48	Dr. R			
Specific Aim 3: Evaluate outcomes for sub-groups of patients recently diagnosed with knee OA based on OA etiology (post-traumatic vs. degenerative) and age at diagnosis ($\leq$ 35 vs. > 35)	44-48	Dr. R			
Task 3a: Analyze data for AIM 3. (This is a data-analysis task and	44-48	Dr. R			

requires no additional subject testing beyond Aim 1.)					
Task 3b: Perform sensitivity analysis, and account for specific populations (PTOA, age variations, etc)	44-48	Dr. R			
Specific Aim 4: Compare the cost-effectiveness of two early management strategies collected over the 2-year follow-up period.	40-48	Dr. R			
Task 4a: DSA with DHA	38-45	Dr. R			
Subtask 1: Submit DSA Application to DHA for permission to collect healthcare utilization data from MDR database	38	Dr. R			
Subtask 2: Approved DSA submitted to PASBA for extraction of healthcare utilization data	40-45	Dr. R			
Task 4b: Consolidate and organize healthcare utilization data. (This is a data-analysis task and requires no additional subject testing beyond Aim 1.)	45-46	Dr. R			
Subtask 1: Match MDR data with appropriate subject ID numbers	45-46	Dr. R			
Subtask 2: Consolidate data from both sources (REDCap and MDR), and organize by individual subject ID to obtain master spreadsheet for analysis	45-46	Dr. R			
Task 4c: Compare healthcare utilization costs between groups. (This is a data-analysis task and requires no additional subject testing beyond Aim 1.)	46-48	Dr. R			
Specific Aim 5: Evaluate the mediating effects of co-morbidities and activity self-efficacy on the primary outcome.	45-48	Dr. R			
Task 5a: Conduct mediation analysis (This is a data-analysis task and requires no additional subject testing beyond Aim 1.)					

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

Nothing to Report

How were the results disseminated to communities of interest?

Nothing to Report

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

We were forced to take a COVID-related pause in recruitment at all of our sites, which put is substantially behind schedule. We have been cleared to begin enrolling again at all sites, and we hope to get that started back up again at all sites very soon (before the end of October 2020). Currently, we are problem solving ways to maximize recruitment as the face to face appointments are not as common now compared to pre-COVID-19.

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.

CURRENT PROBLEMS/ISSUES:

As of 9/29/2020, 2 of the 3 sites had been cleared to start recruitment again, but this happened just recently and so the systems are being put into place to allow this to happen. However, many of the challenges we faced Q3 of this year during suspension of recruitment are still present. Face-to-face treatments in primary care and physical therapy are limited and reserved for more acute injuries and conditions. Knee OA is not as urgent of a case leading to barriers with recruitment. The clinics are slowly starting to bring in more face-to-face visits and with this transition we hope to see an increase in Knee OA visits. We have now had 7 full months with no new enrollments due to COVID.

PREVIOUSLY REPORTED PROBLEMS:

As of 6/29/2020, enrollment is still suspended at all sites due to COVID-19. Family medicine clinics are still operating as we reported in the last report, but at reduced capacity and patients with knee OA are usually not urgent cases which are prioritized to come in for face-to-face visits, making recruitment very challenging. Physical therapy clinics are primarily treating patients via telehealth and providers are alternating days in the clinic to meet distancing requirements. We continue to monitor patients currently enrolled in the trial, and we continue to monitor current guidance for re-opening of care at each site. At our 2 San Antonio hospitals, there has been a regression in progress and returning back to normal care has been postponed even longer due to the resurgence of cases locally. We've had barely 2 full quarters of recruitment so far, and those quarters yielded almost 50 subjects enrolled, which would have had us on pace to meet our original targets. At this point completing the study within the expected POP is unlikely and we will need to request a no-cost extension.

As of 3/09/2020, we have suspended enrollment of patients at all sites based on circumstances to activities due to COVID-19). Family medicine clinics have restricted patient care to essential only for in person appointment which minimizes traffic in the clinics to keep immunocompromised patients safe who must come in for care. As of Monday, 3/23/2020 the IRBs restricted all non-essential study's to suspend recruitment to keep patients safe. Across all sites, a total of 12 patients randomized to physical therapy have either had appointments cancelled, transitioned to virtual telehealth in alignment with clinic policies, or care has been suspended until further notice due to COVID-19. We continue to monitor these patients and assess their care.

As of 7/15/2019: We are about 1 quarter behind right now in terms of enrollment. We are recruiting at all 3 sites, but have only enrolled at 1 site. We are currently working through hurdles of improving recruitment at each site. Madigan begin recruitment on July 25th.

As of 4/15/2019: The IRB has had some slow-downs with the transition to the new Common Rule. Part of this was due to their rollout of new protocol templates which we had to use (and subsequently transfer documentation from old templates to the new ones). There were some CRADA delays with US Army and the University of Utah, which prevented us from stopping at the 1 site that is approved by HRPO, however it appears that those have been taken care and we should be able to start recruitment soon. Those issues are not the current rate limiting step as we are still waiting on HRPO to provide approval at the other sites.

Changes that had a significant impact on expenditures

A large proportion of our budget goes to personnel, and therefore we have had personnel expenditures over the last 7-8 months, without being able to conduct much work on this project. That will likely impact our bottom line on the backend, as we get nearer to the end of the period of performance.

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

N/A

Significant changes in use or care of vertebrate animals

N/A

Significant changes in use of biohazards and/or select agents

N/A

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.

Nothing to Report

- **Website(s) or other Internet site(s)**

Nothing to Report

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

N/A

- **Other Products**

N/A

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Dr. Daniel Rhon
Project Role:	Primary Investigator
Researcher Identifier (e.g. ORCID ID):	0000-0002-4320-990X
Nearest person month worked:	0.3
Contribution to Project:	Grant PI – coordinate studies across all sites
Funding Support:	Partially from this grant
Name:	Dr. Julie Fritz
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	0
Contribution to Project:	Manages subaward to U. of Utah, helps coordinate study, and provides input into study design

Name:	Maria Olvera-Munoz
Project Role:	Research Coordinator- WA
Researcher Identifier (e.g. ORCID ID):	N/A

Nearest person month worked:	2.9
Contribution to Project:	Coordinates execution of project – recruitment, enrollment, follow-ups.
Funding Support:	N/A

Name:	Rachel Mayhew
Project Role:	Research Coordinator at MAMC location/PT
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	3.9
Contribution to Project:	Coordinates execution of project at MAMC – recruitment, enrollment, follow-ups.
Funding Support:	Partially from this grant

Name:	Mary Laugesen
Project Role:	Research coordinator at BAMC/WHASC location/PT
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	2.6
Contribution to Project:	Coordinates execution of project at BAMC – recruitment, enrollment, follow-ups.
Funding Support:	Partially from this grant
Name:	Jeremy Steiner
Project Role:	Research Physical Therapist
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	3.7
Contribution to Project:	Coordinates execution of project – recruitment, enrollment, follow-ups.
Funding Support:	Partially from this grant
Name:	Athena Farias
Project Role:	Research Physical Therapist
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1.8
Contribution to Project:	Coordinates execution of project – recruitment, enrollment, follow-ups.
Funding Support:	Partially from this grant

Name:	Gregory Weaver
Project Role:	Research Physical Therapist
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	2
Contribution to Project:	Coordinates execution of project – recruitment, enrollment, follow-ups.
Funding Support:	Partially from this grant

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

Nothing to Report

What other organizations were involved as partners?

We continue to work in collaboration with the University of Utah, who has received a subaward for this project

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:
QUAD CHARTS:

9. APPENDICES: N/A