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TITLE: Redefining Gulf War Illness Using Longitudinal Health Data: The Fort Devens Cohort

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Approved for public release; distribution is unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Current estimates suggest that 25 percent of Gulf War (GW) veterans (nearly 170,000) have reported some type of persisting multi-symptom illness. Currently used GW Illness (GWI) case definitions have been found to be lacking in sensitivity and specificity with many veterans falling in the false positive and false negative ranges. These GWI definitions, based on cross-sectional studies, allow for reporting of health symptoms only once, and do not consider that symptoms can emerge over time (or remit); thus they likely provide inaccurate representations of veterans' health. Reliance solely on cross-sectional studies or on follow-ups with different methodologies results in the lack of a consensual definition of GWI, and has limited the ability to determine appropriate treatment options or to compare results among studies. Only through the use of longitudinal data, where health symptoms were first measured shortly after deployment and then repeatedly over the following 20 years, would consideration of symptom trajectories (patterns of change over time) be possible. We believe that the use of longitudinal data, which allows consideration of relapsing, remitting and late emerging symptoms, is necessary to refine the case definition of GWI. This will allow for comparison of competing existing case definitions by considering symptom change, and can lead to a consensual definition. The Ft. Devens, MA cohort was designed as a longitudinal cohort and as such will be useful in ameliorating the existing problems with case definition. The ultimate goal for this study is to provide a consistent case definition of GWI, which can serve future studies and treatment trials as a valid outcome.

15. SUBJECT TERMS
Nothing Listed

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

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

Gulf War Illness case definitions have been found to be lacking in sensitivity and specificity with many veterans falling outside the range for diagnostic accuracy. The prior definitions were based on cross-sectional cohorts and did not allow for symptoms that emerge or change over time. The Ft. Devens cohort was designed as a longitudinal study allowing for consideration of symptom change to refine case definition. This study was designed to ameliorate the problems with current case definition.

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

Gulf War, Gulf War Illness, Neurotoxicant exposures, health symptoms, pyridostigmine bromide, pesticides, Case Definition, Longitudinal design

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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.

Task 1: **Months 1-6 Finalize plan for participant recruitment: All Tasks completed** in 1st year of the project
- Task 1a. **Submit human use documents for IRB approvals** to VA Boston, BUSPH, and HRPO
- Task 1b. **Receive health symptom comparison data** from Ft Devens Cohort study participants Time 1, 2, 3, and 4
- Task 1c. **Identify current address and contact** information from Time 1 cohort of 2, 949

Task 2. **Months 4-9: Finalize methods for web survey design**: **All Tasks completed in** 1st year of the project
- Task 2a. Design teleform and website for collection of current health symptom status
- Task 2b. Develop dataset for health symptom survey including all time periods

Task 3: **Months 9-36: Recontact the Devens Cohort and Data Collection: All tasks except 3d completed**
- Task 3a. **Send out pre-survey letter** to original cohort participants with opt-out postcards for those not wishing to participate
- Task 3b. **Obtain demographic information and information pertaining to current health status** and changes in medical or psychiatric diagnoses by use of we-survey and mail questionnaire for those who do not have access to a computer
- Task 3c. **Follow-up calls** made to individuals who have not responded.
- Task 3d. Contact a **subsample of 150** participants to complete blood study*
- Task 3e. **Data cleaning** will be ongoing

Task 4: **Months 30 until the end of the study: Collection, cleaning and dissemination of data**: **Tasks completed July, 2020**
- Task 4a. **Double key** data from paper surveys
- Task 4b. Continue to **recruit blood stud**y participants from Devens cohort
- Task 4c. **Present results** at local and national conferences
- Task 4d. **Draft manuscripts** pertaining to symptom patterns and trajectories
- Task 4e. **Make recommendations** for updated case definition

*Task 3d remains ongoing.

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**
    a. Recontact the Ft Devens Cohort participants
        i. We sent opt-out post-cards to the approximately 2600 of the 2949 original participants. We received post-cards for opt out 118 original Ft Devens Participants
        ii. We learned of 130 deceased
        iii. We sent out 1600 letters with links to surveys for completion of online survey
        iv. We sent out follow-up letters with paper surveys at 2 time points and received 520 surveys
        v. We compiled demographic data for the Time 5 participants and compared against the original cohort (**see Yee et al, 2019; Zundel et al, 2020)**
2. **Specific Objectives**
    a. Objective 1 was to document current health symptoms of returning survey participants to compare with prior survey results using longitudinal analyses
        i. We sought to document symptoms that persisted overtime
        ii. We sought to document symptoms that diminished overtime
        iii. We sought to document symptoms that emerged years after deployment
    b. Objective 2 was to document specific neurotoxicant exposures that were related to health symptoms: **See Tables Below**

    c. Objective 2 was to document biomarkers of Gulf War Ill veterans relative to Gulf War non-ill using PON1 blood markers

3. **Significant Results/Key Outcomes**
    a. Results of current health symptoms (T 5) were first compared relative to demographic variables, including mild Traumatic Brain Injury
        i. These analyses resulted in 2 poster presentation (Seichepine 2/2014, Yee 2/2016)
        ii. These analyses resulted in 2 manuscripts (Yee et al, 2016; Yee et al, 2017)
    b. Results of current health symptoms were compared to prior Time 4 health symptoms
        i. These analyses resulted in 3 poster presentations (Seichepine, Yee, Abigail 2/2015) and 2 oral presentations (Krengel 6/2015, Krengel 7/2016)
    c. Results of current health symptoms were compared with Time 3 and Time 2 relative to demographic variables, including sex
        i. These analyses resulted in 1 dissertation study (unpublished dissertation; Maule)
    d. Results of current health symptoms and rates of current case definition criteria were analyzed relative to neurotoxicant exposures
        i. These analyses resulted in 6 poster presentations (Yee, Krengel, Zundel, Cohen, Zundel, Grasso)
        ii. These analyses resulted in 3 published manuscripts (Zundel et al, 2019, Yee et al, 2017, Zundel et al, 2020)
    e. Results of current health symptoms were compared with a civilian cohort (NHANES) to document symptoms of deployed veterans relative to same age and sex medical symptoms
        i. These analyses resulted in 1 published manuscript (Zundel et al, 2020)
    f. Longitudinal trajectories of health symptoms were analyzed relative to neurotoxicant exposures
        i. Analyses were conducted examining rates of Post-Traumatic Stress disorder (PTSD) over time relative to toxicant exposures resulting in 1 submitted manuscript (Zundel in press)
        ii. Analyses were conducted examining rates of health symptoms over time for participants who had at least 2 prior time points. This analysis resulted in 1 submitted manuscript (Krengel submitted)
    g. PON1 data were collected on Ft Devens Cohort participants
        i. The following results were found
        ii. Data were combined with 3 other cohorts for final analyses to increase power. To be published as a combined cohort.

Specific Aims 1 and 2. To describe the health symptoms and trajectories in this large GW veteran cohort over time as compared with prior case definitions (CMI). (Yee et al, 2017; Yee et al, 2018, Zundel et al, 2019, Zundel et al, 2020) See attached Publications for case definitions and health symptoms.
Below are tabulated results for 3f above.

Table #1a. Significant associations between **Khamisiyah Exposure** and Symptom Trajectory Groups		
Outcome	Comparison	OR 95% CI
Difficulty Concentrating	No dx	Ref
	No dx, develops dx	1.082 [0.495-2.364]
	Mixed	1.592 [0.680-3.284]
	dx, loses dx	1.494 [0.680-3.284]
	Consistent dx	**2.457 [1.158-5.212]**
Dizziness	No dx	Ref
	No dx, develops dx	0.649 [0.301-1.402]
	Mixed	0.968 [0.459-2.043]
	dx, loses dx	0.990 [0.484-2.027]
	Consistent dx	**2.938 [1.012-8.529]**

All analyses included age, gender, and baseline PTSD status as covariates.

Table #1b. Significant associations between **Tent Heater Exposure** and Symptom Trajectory Groups		
Outcome	Comparison	OR 95% CI
Fatigue	No dx	Ref
	No dx, develops dx	1.519 [0.649-3.556]
	Mixed	1.277 [0.470-3.471]
	dx, loses dx	**3.369 [1.247-9.100]**
	Consistent dx	1.369 [0.628-2.987]
Crying Easily	No dx	Ref
	No dx, develops dx	2.461 [0.945-6.405]
	Mixed	2.151 [0.636-7.276]
	dx, loses dx	**2.795 [1.068-7.312]**
	Consistent dx	**11.408 [1.140-114.131]**
Nervous or Tense	No dx	Ref
	No dx, develops dx	1.082 [0.517-2.265]
	Mixed	**2.346 [1.024-5.374]**
	dx, loses dx	1.791 [0.735-4.365]
	Consistent dx	1.662 [0.733-3.771]
Upset Stomach/Nausea	No dx	Ref
	No dx, develops dx	**3.218 [1.139-9.091]**
	Mixed	1.023 [0.474-2.212]
	dx, loses dx	1.365 [0.687-2.712]
	Consistent dx	1.706 [0.715-4.072]
Shortness of Breath	No dx	Ref
	No dx, develops dx	**2.297 [1.089-4.943]**
	Mixed	1.771 [0.662-4.733]
	dx, loses dx	1.482 [0.501-4.381]
	Consistent dx	0.365 [0.136-0.975]

All analyses included age, gender, and baseline PTSD status as covariates.

Table #1c. Associations between **PB Pill (21 or more) Exposure** and Symptom Trajectory Groups		
Symptom	Trajectory Grouping	OR 95% CI
Fatigue	No dx	Ref
	No dx, develops dx	**4.199 [1.084-16.263]**
	Mixed	3.760 [0.812-17.404]
	dx, loses dx	1.783 [0.400-7.941]
	Consistent dx	**3.767 [1.052-13.487]**
Depressed Mood	No dx	Ref
	No dx, develops dx	**3.611 [1.150-11.335]**
	Mixed	**3.619 [1.069-12.256]**
	dx, loses dx	2.601 [0.784-.8626]
	Consistent dx	**5.468 [1.548-19.312**
Nervous or Tense	No dx	Ref
	No dx, develops dx	**3.708 [1.026-13.397]**
	Mixed	**4.077 [1.112-14.938]**
	dx, loses dx	3.464 [0.862-13.912]
	Consistent dx	**7.276 [1.953-27.105]**
Headaches	No dx	Ref
	No dx, develops dx	0.776 [0.169-3.557]
	Mixed	1.008 [0.216-4.700]
	dx, loses dx	2.285 [0.810-6.446]
	Consistent dx	**3.362 [1.132-9.989]**
Muscle Twitching	No dx	Ref
	No dx, develops dx	1.639 [0.634-4.240]
	Mixed	1.358 [0.385-4.784]
	dx, loses dx	1.138 [0.372-3.484]
	Consistent dx	**2.950 [1.059-8.213]**
Skin Rash	No dx	Ref
	No dx, develops dx	**2.936 [1.139-7.572]**
	Mixed	2.289 [0.770-6.800]
	dx, loses dx	1.521 [0.458-5.047]
	Consistent dx	2.039 [0.540-7.704]
Dizziness	No dx	Ref
	No dx, develops dx	**6.034 [2.309-15.767]**
	Mixed	0.432 [0.086-2.181]
	dx, loses dx	2.461 [0.899-6.737]
	Consistent dx	**6.388 [1.718-23.752]**

All analyses included age, gender, and baseline PTSD status as covariates.

Table #1d. Associations between **PB Pill (21 or more) Exposure** and Symptom Trajectory Groups		
Symptom	Trajectory Grouping	OR 95% CI
Hands Sweating	No dx	Ref
	No dx, develops dx	4.006 [0.999-16.061]
	Mixed	**4.578 [1.173-17.867]**
	dx, loses dx	2.383 [0.920-6.171]
	Consistent dx	3.085 [0.317-30.067]
Upset Stomach/Nausea	No dx	Ref
	No dx, develops dx	0.717 [0.182-2.825]
	Mixed	0.772 [0.201-2.968]
	dx, loses dx	1.582 [0.661-3.786]
	Consistent dx	**3.745 [1.257-11.156]**
Trouble Sleeping	No dx	Ref
	No dx, develops dx	1.591 [0.459-5.512]
	Mixed	3.412 [0.890-13.085]
	dx, loses dx	2.381 [0.606-9.365]
	Consistent dx	**4.399 [1.388-13.935]**
Shortness of Breath	No dx	Ref
	No dx, develops dx	**3.133 [1.315-7.459]**
	Mixed	2.772 [0.742-10.357]
	dx, loses dx	1.857 [0.524-6.582]
	Consistent dx	2.274 [0.543-9.520]

All analyses included age, gender, and baseline PTSD status as covariates.

Table #1e. Associations between **Chemical Alert Exposure (20 or more)** and Symptom Trajectory Groups		
Outcome	Comparison	OR 95% CI
Crying Easily	No dx	Ref
	No dx, develops dx	1.384 [0.560-3.420]
	Mixed	0.734 [0.183-2.946]
	dx, loses dx	1.485 [0.628-3.513]
	Consistent dx	**3.969 [1.079-14.602]**
Headaches	No dx	Ref
	No dx, develops dx	2.376 [0.778-7.254]
	Mixed	**4.334 [1.554-12.084]**
	dx, loses dx	1.367 [0.523-3.572]
	Consistent dx	**3.237 [1.286-8.143]**
Dizziness	No dx	Ref
	No dx, develops dx	**2.441 [1.100-5.415]**
	Mixed	1.732 [0.743-4.035]
	dx, loses dx	1.506 [0.654-3.470]
	Consistent dx	1.762 [0.579-5.359]
Shortness of Breath	No dx	Ref
	No dx, develops dx	**2.107 [1.038-4.278]**
	Mixed	1.510 [0.561-4.070]
	dx, loses dx	0.548 [0.142-2.122]
	Consistent dx	2.628 [0.947-7.297]

All analyses included age, gender, and baseline PTSD status as covariates.

Specific Aim 3. Consider pre-deployment characteristics that distinguish among health symptoms (including genetic moderation by PON1 status). (we analyzed pre-deployment characteristics of age at exposure, type of exposure and mild traumatic brain injury and PTSD status. Blood markers are ongoing). **We did not end up with enough power for these analyses in total so we combined our efforts with Dr. Linda Chao and Dr. Patricia Janulewicz. These results are forthcoming.**

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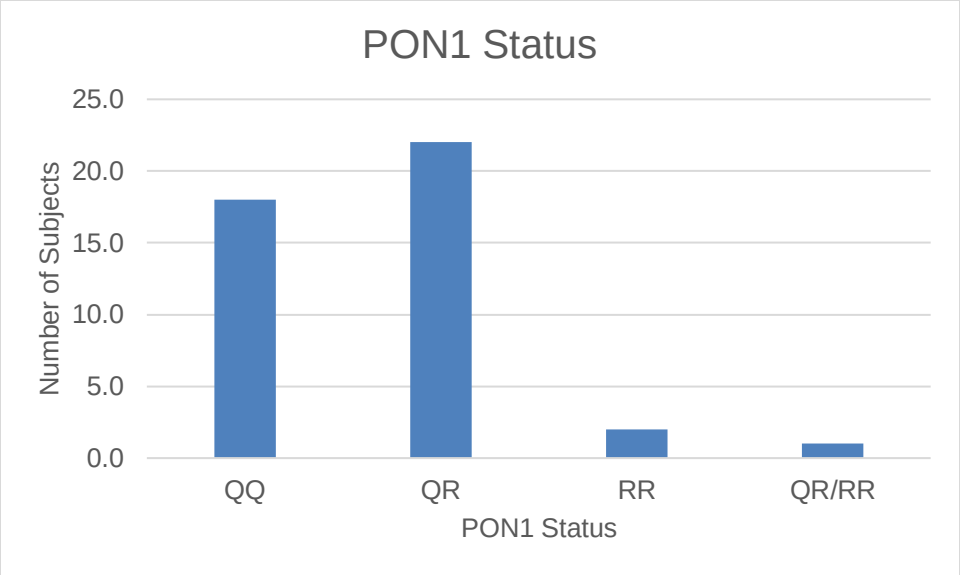
Table #2. Demographics of PON1 FDC Sample (N=43)	
Demographic	Mean ± SD N (%)
Age	57.80 ± 9.32
Ethnicity	
White/Caucasian	40 (93%)
Hispanic	1 (2%)
Missing	2 (5%)
Years of Education	14.92 ± 2.31
Status at time of GW	
Active Duty	9 (21%)
Reserves	12 (28%)
National Guard	22 (51%)
Meet Inclusionary Symptom Criteria for Kansas GWI	
Yes	26 (60%)
No	15 (35%)
Missing	2 (5)
Met Criteria for CMI	
Yes	34 (79%)
No	7 (16%)
Missing	2 (5%)
Reported Exposure to:	
Agent Orange	2 (5%)
Chemical/Biological Warfare	16 (37%)
Anthrax Vaccine	31 (72%)
PB Pills	26 (60%)

N=43	Paraoxonase Units/Liter	Diazoxonase Units/Liter	Arylesterase Units/mL
Mean ± SD	740.27 ± 499.45	12475.62 ± 4068.31	131.83 ± 42.23
Range	148.16 - 2429.51	6437.35 - 23071.05	241.04



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.

1. Megan Yee, MPH entered and completed her program while employed on this project
2. Clara Zundel, ABD, has been designing studies and working on manuscripts, including her dissertation
3. Alexis Maule completed her dissertation with FDC data analyzing exposures and health symptoms over time and now works for DOD as a post-doctoral fellow

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.

Results were presented to the following communities

1. The Massachusetts Neuropsychological Society
2. The Research Advisory Committee on Gulf War Veterans Illnesses
3. The Behavioral Sciences Department at the Graduate School of Medicine at BU
4. The Department of Environmental Health at the BU School of Public Health
5. The International Neuropsychological Society- North American and International Conferences
6. State of the Science Conference/ Joint program of DoD and VA
7. Neurology Department of BU School of Medicine, Grand Rounds

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.

Nothing to report

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice orbehavior 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).

1. GW veterans are showing increased rates of aging related disorders (Zundel et al, 2019). This will have an impact on medical care for GWI veterans with screening for high blood pressure, heart attack, stroke, diabetes, which could lead to earlier neurodegenerative disorders including dementia.
2. mTBIs are associated with increased rates of GWI cases. This suggests that all GW veterans should also be screened for mTBI with multiple mTBIs resulting in increased rates of symptomatology
3. Exposures overall are related to health outcomes, including variability of symptoms depending on type of exposure. Chemical weapons exposure is related to higher rates of GWI.
4. Longitudinal analyses of exposures during the war showed increased symptoms in those exposed to chemical weapons, tent heaters and PB pills suggesting that these exposures should be queried during VA health care visits.
5. In this longitudinally followed cohort, there were changes overtime in health symptom reporting. We are recommending that some of the case definition criteria change in their importance.
6. After 19 years veterans are still reporting symptoms related to their time in the Gulf. Some of the original symptoms have become less pronounced, whereas others have maintained or increased in prevalence. Therefore, case criteria such as the Kansas criteria remains warranted, perhaps in addition to other symptoms that are likely to have emerged later.

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.

The results from this project will be used to inform current practitioners working in the field of GWI to initiate new treatment methodologies and current case definition. Our goal is to use these findings for VA and non-VA training modules on neurotoxicant exposures and longitudinal health symptoms as part of our newly funded study that builds upon these results.

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.*

1. Results from this project will help to provide information to the community at large regarding the impact of neurotoxicant exposures and longitudinal health symptoms
2. Results validate the self-report from veterans that they have longitudinal symptoms and are developing age related disorders at an earlier age that should be monitored with hopes of prevention
3. We are informing the GW veteran treatment providers and researchers about the importance of continued care and ways in which to study health symptoms over time.

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

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

N/A

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).*

*Yee, M. K., Seichepine, D. R., Janulewicz, P. A., Sullivan, K. A., Proctor, S. P., & **Krengel, M. (**2016). Self-Reported Traumatic Brain Injury, Health and Rate of Chronic Multisymptom Illness in Veterans From the 1990-1991 Gulf War. *Journal of Head Trauma Rehabilitation*, *31*(5), 320-328. Acknowledgement of support: Yes

*Yee, M., Janulewicz, P., Seichepine, D., Sullivan, K., Proctor, S., & **Krengel, M.** (2017). Multiple Mild Traumatic Brain Injuries Are Associated with Increased Rates of Health Symptoms and Gulf War Illness in a Cohort of 1990–1991 Gulf War Veterans. *Brain Sciences*, *7*(7), 79. Acknowledgement of support: Yes

*Maule, A. L., Janulewicz, P. A., Sullivan, K. A., Krengel, M. H., Yee, M. K., McClean, M., & White, R. F. (2018). Meta-analysis of self-reported health symptoms in 1990–1991 Gulf War and Gulf War-era veterans. *BMJ Open*, *8*(2), e016086 Acknowledgement of support: Yes

Zundel, C., **Krengel, M.H.,** Heeren, T., Yee, M…..Sullivan, K. (2019). Rates of chronic medical conditions in 1991 GW Veterans compared to the general population. *International Journal of Environmental Research and Public Health*, 16 (6), 949 Acknowledgement of support: Yes

Yee, M., Zundel, C., Maule, A, Proctor, S., Sullivan, K, **Krengel, MH.** (2020). A longitudinal assessment of GW exposures and health symptoms in 1990-1991 GW veterans in the Ft. Devens Cohort. *Journal of Occupational and Environmental Medicine, online ahead of print.* Acknowledgement of support: Yes

Zundel, C., Heeren, T; Grasso, C……Krengel, MH (2020). Changes in health status in the Ft. Devens Gulf War Cohort: 1997-2017. *Neuroscience Insights*. *Epub ahead of print*. Acknowledgement of support: Yes

Krengel, M; Zundel, C; Heeren, T; Spiro, A; Proctor, S; Grasso, C; Sullivan, K. (under review Brain Sciences). Redefining GW veterans illness using longitudinal health data over 25 years.

Zundel, C.; Price, K., Spiro, A; Grasso, C.; Proctor, S.; Sullivan, K., Krengel, M. (under review *IJERPH*).

Other publications, conference papers, and presentations. *Identify any other 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.*

Maule, Alexis unpublished doctoral dissertation; Boston University School of Public Health, Department of Environmental Health

Seichepine, D.R., Yee, M., Fineman, A., Janulewicz-Lloyd, P., Sullivan, K., & **Krengel, M.** (2014). Gulf War Illness: Chronicity of Health Symptoms in the Ft. Devens Cohort. International Neuropsychological Society Annual Meeting Seattle, WA

*Yee, M.K., Seichepine, D.R., Patten, C., & **Krengel, M.H.** (2014). Pre-surgical Neuropsychological Tests Predict Post-deep Brain Stimulations Surgery Functional Status in Parkinson's Disease. International Neuropsychological Society Annual Meeting Seattle, WA

Lemons, A., Seichepine, D.R., Yee, M.K., Janulewicz, P.A., Sullivan, K., & **Krengel, M.** (2014). Post-War Traumatice Brain Injuries are Influenced by Number of Pre-War, but not Deployment-Related Brain Injuries in Gulf War Veterans. International Neuropsychological Society Annual Meeting Seattle, WA

Seichepine, D.R., Yee, M.K., Lemons, A., Janulewicz, P.A., Sullivan, K., & **Krengel, M.** (2015). Frequency of Traumatic Brain Injuries in a Cohort of 1990-1991 Gulf War Veterans. International Neuropsychological Society Annual Meeting Denver, CO

*Maule, A.L., Janulewicz, P.A., **Krengel, M.**, White, R.F., Cirillo, J., Judd, S., & Sullivan, K. (2016). A Meta-anaylsis of Self-reported Neurological and Neuropsychological Symptoms in Gulf War Veterans. International Neuropsychological Society Annual Meeting Boston, MA

***Krengel MH**, Yee M, Nolan T, Janulewicz Lloyd PA, Sullivan K & Seichepine DR. (2016). Multiple Self-reported Exposures to Mild Traumatic Brain Injury and Neurotoxicants Predict Current Total Health Symptoms in a Cohort of 1990-1991 Gulf War Veterans. International Neuropsychological Society Annual meeting. Boston, MA

*Zundel, C.G., Lad, S.S., Yee, M.K., Grasso, C.M., Janulewicz Lloyd, P.A., Sullivan, K.A., **Krengel, M.H.** (2017) Rates of medical conditions: Do Gulf War veterans differ from the general population? International Neuropsychological Society 2018 Conference, Washington D.C.

*Zundel, C.G., Grasso, C.M., **Krengel, M.H**. (2019). Exposures, Health, and Neuropsychological Outcomes in Gulf War Veterans 25+ Years Post War. Poster presentation at Massachusetts Neuropsychological Society Science Symposium Boston, MA**.**

*Zundel, C.G., Killiany, R., Koo., B., **Krengel, M.,** Toomey, R., Ajama, J., Januelwicz-Lloyd P., Abreu, M., Heeren, T., Sisson, E., Little, D., Steele, L., Klimas, N., Sullivan, K. (2019). Objective Biomarkers of Gulf War Illness: White Matter Microstructural Integrity, Cognition and Blood Biomarkers in Gulf War Veterans. International Neuropsychological Society Annual Meeting, New York, NY

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

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. 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.

N/A

- **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;*
  - *biospecimen 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.*

1. Databases- VA Boston Healthcare System, Gulf War Veterans Illness Data repository

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."

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*

Researcher Identifier (e.g. ORCID ID): *1234567*
Nearest person month worked: *5*

Contribution to Project: *Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support: *The Ford Foundation (Complete only if the funding support is provided from other than this award).*

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?
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.

No Change

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. 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.