Longitudinal Data Collection of Neurotoxicant Exposures and Health Symptoms in Gulf War Veterans

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BACKGROUND

- 1990-1991 Gulf War (GW) veterans were exposed to numerous neurotoxicants during the war including, chemical warfare agents (sarin/cyclosarin), pesticide sprays and creams, pyridostigmine bromide (PB) prophylactic anti-nerve gas pills, smoke from oilwell fires, and tent heater exhausts.
- Exposures have been associated with a multitude of health symptoms, collectively known as Gulf War Illness (GWI).
- The two most widely used case criteria for GWI are the Center for Disease Control (CDC)'s criteria for Chronic Multisymptom Illness (CMI)[2] and the Kansas GWI criteria[3].
  - Both case criteria were developed over 20 years and only capture symptoms over a finite period of time.
- Our cohort, the Ft. Devens Cohort (FDC), is the longest running population-based cohort of GW veterans, which has been surveyed multiple times over the past 30 years. **Figure 1** shows the survey timeline. Exposure and health symptom data have been collected and analyzed at each time period.
- Prior analyses have not included change in health status over the multiple time points with each person serving as their own control[1].

METHODS

- The current longitudinal study utilized a subset of FDC participants (N = 293) who completed the Health Symptom Checklist (HSC)[4] at all 3 follow-up time points.
- Variations of the HSC were administered at each follow-up with 15 total symptoms consistently assessed at all 3 timepoints.
- Based on health symptoms and CMI case status, veterans were categorized into 5 a priori symptom trajectory groups:
  - never reported symptom
  - develops symptom
  - mixed reporting of symptom
  - remitting symptom
  - consistent reporting of symptom

Fig. 1 Ft. Devens cohort reunion survey timeline

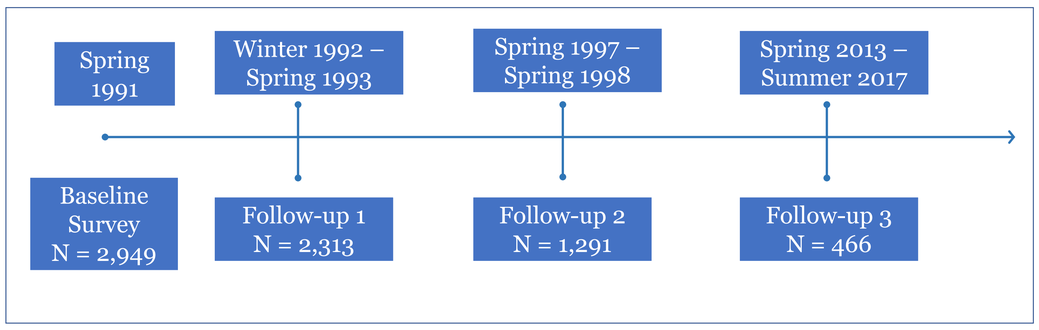

Table 1. Demographics and Characteristics

Demographics/Characteristics	Full Devens Cohort (N = 2949)	Study Sample (N = 293)
Age at baseline survey, years	30.2 + 8.3	32.3 + 8.5
Age at follow-up 3, years		54.28 + 8.56
Male, n (%)*	2702 (91.6)	256 (87.4)
White, n (%)*	2443 (82.8)	272 (92.8)
Active Duty at time of Gulf War, n (%)* (versus Reserve, National Guard)	823 (27.9)	48 (16.4)
Mississippi PTSD scale-score	61.9 + 13.4	62.0 + 14.2
Clinical cutoff on Mississippi scale-score, n (%)	116 (3.9)	16 (5.5)
GW-Specific Neurotoxicant Exposures, n (%) Time 4 (*N* = 1291)		
Took more than 21 Pyridostigmine Bromide (PB) Pills	210 (16.3)	50 (17.1)
20 or More Times on "Formal Alert" for a Chemical Attack	263 (20.4)	70 (23.9)
Received the 2000 DoD Notification for Possible Sarin Exposure from the Khamisiyah Weapons Demolition*	1024 (34.7)	121 (41.3)
Tent Heater or Stove in the Area Where you Slept	788 (61.0)	200 (68.3)

***p* < 0.05**

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DATA ANALYSES

- A multinomial logistic regression was run with health symptom trajectory group as the dependent variable, and specific GW-exposures as the independent variable.
- Covariates taken from baseline survey data (1991) included age, sex and post-traumatic stress disorder (PTSD) status.
  - Baseline PTSD status was used as a covariate to control from cognitive, mood, and somatic symptoms that may have been a result of trauma rather than neurotoxicant exposures.[5, 6] Individual exposure models included all other neurotoxicant exposures as covariates to control for effects on symptoms due to other exposures.

RESULTS

These findings showed significant (p's < 0.05) associations between individual symptom trajectories and neurotoxicant exposures in Veterans who reported exposure to:

PB Pills (more than 21)
- Associated with fluctuating symptom reporting of nervous or tense, hands sweating, and depressed mood.
- Those who reported this exposure were more than 2x as likely to develop difficulty concentrating, nervous or tense, shortness of breath, depressed mood, and skin rash over the three follow-ups.
- Those who reported this exposure were more than 2x as likely to consistently report dizziness, fatigue, nervous or tense, trouble sleeping, upset stomach/nausea, and depressed mood over the three follow-ups.
- **Figure 2** displays the symptom trajectory groups for meeting CMI case criteria over time. by exposure status.

Chemical Alert (20 or more)
- Those who reported this exposure were more than 4x as likely to have fluctuated reporting of headaches over time.
- Those who reported this exposure were *less likely* to develop skin rash over time.

Tent Heaters
- Those who reported this exposure were more than 3x as likely to develop upset stomach/nausea and shortness of breath over time .
- Those who reported this exposure were more than 3x as likely to consistently report muscle twitching over time.

- **Over 30% of this cohort consistently endorsed symptoms of fatigue, general aches, pain and joint pain, at all 3 timepoints over the span of 25+ years.**

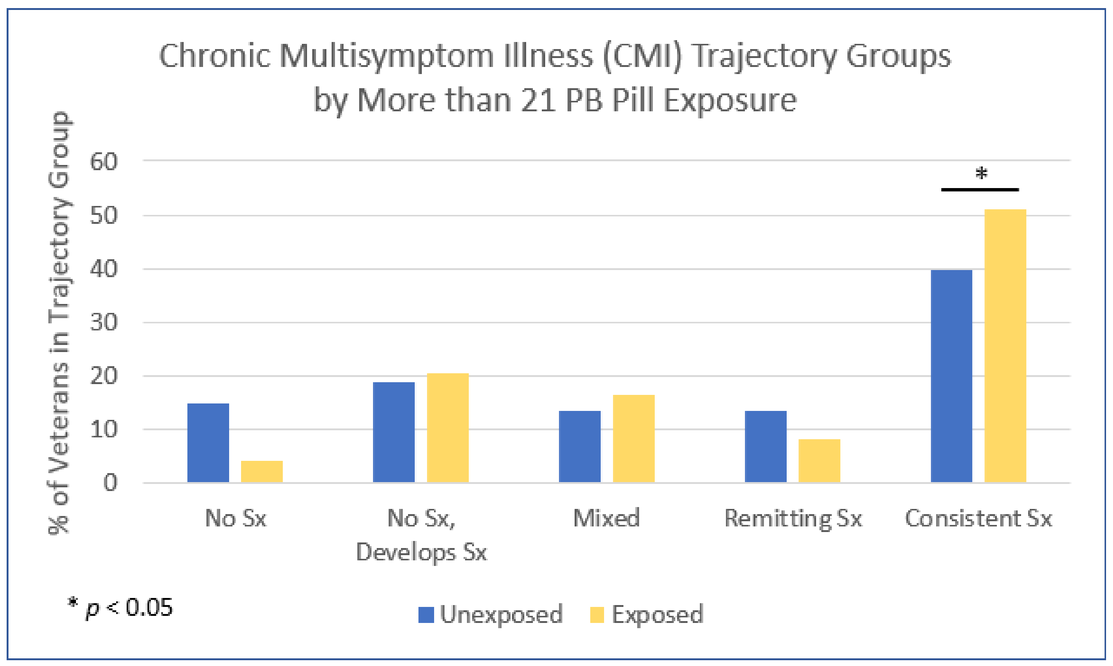

Fig. 2. Percentage of veterans in chronic multisymptom illness (CMI) trajectory group by more than 21 pyridostigmine bromide (PB) pill exposure

CONCLUSION

- To our knowledge, this study is the first of its kind that has longitudinally examined (25+ years) individual health symptom trajectories and their associations with GW-specific neurotoxicants.
- The current analysis was limited to our study sample which was majority male and White, and less likely to have been Active Duty during the GW, and was limited to self-report measures of GW-specific neurotoxicants.
- This study highlights the importance of exposure-outcome relationships and the necessity of continued health symptom documentation of GW veterans.
- While the current recommend case criteria (CDC, Kansas) remain relevant based on this longitudinal analysis, the exclusionary criteria may in fact be too strict and should further refine symptom inclusionary criteria based on our reported exposure-outcome relationships.
- Future studies need to assess the impact of normal aging on these exposure-based health outcomes.

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