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TITLE: Predeployment, Perideployment, and Postdeployment Trajectories and Mechanisms of Psychopathology, Psychological Health, and Resilience Over 9 Years of Prospective Followup in the Reserves

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14. ABSTRACT The general objective of the Ohio Army National Guard Mental Health Initiative is to evaluate the relationships between resilience and risk factors, both cross-sectionally and longitudinally, before, during, and after deployment in the Ohio Army National Guard. The primary project collects long-term data on a random representative sample of N=3578 service members per year in the OANG, both treatment seeking and non-treatment seeking. Since 2006, the primary objective of the OHARNG MHI was designed to function as the template upon which other projects, including but not limited to those of a translational research nature, will be superimposed. Over the past year, nine manuscripts have been published, with 4 others currently under peer review. The OHARNG MHI has an established track record and solid infrastructure in place to address substantive questions in both basic and applied science. Most importantly, this project has provided the military with novel, long-term, prospective data on the National Guard, traditionally an understudied military population. This project has in the past and will continue in the future to provide the TAG, aTAG, and commanders of the Ohio Guard with useful, pragmatic information immediately relevant to the training of men and women in the Ohio Reserve Component.					
15. SUBJECT TERMS Pre-, Peri-, and post-deployment, Ohio Army National Guard, longitudinal study, resilience, PTSD, depression, psychopathology					
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1. INTRODUCTION:

The main platform project is a comprehensive yearly survey of a large sample of Ohio Army National Guard members that assesses a wide range of psychological, social and biological variables, and flexibly expands and modifies the factors studied in response to early findings. We work to delineate the relative importance of military and civilian experiences, in an attempt to identify potentially modifiable risk factors. Importantly, using our existing DNA samples, we are investigating genetic factors associated with trajectories of risk and resilience, leveraging data obtained with our custom 3700 SNP Illumina chip to examine trajectories as phenotypic markers. Building upon our prior work we plan to study alcohol misuse and its relationship to resilience and posttraumatic psychopathology and their trajectories. Understanding trajectories of psychological health among these troops is of great importance to their long-term health and resilience. It will also inform planning for their health care delivery.

SPECIFIC AIM 1: To complete our longitudinal examination of the roles of pre-, peri-, and post-deployment experiences, both military and civilian, in jointly contributing to trajectories of psychopathology, psychological adjustment and resilience over nine years of follow-up.

- H1 – Pre-, Peri-, and post-deployment factors will jointly predict distinct trajectories of posttraumatic psychopathology, psychological adjustment and resilience.
- H2 – Genetic, interpersonal, intrapersonal, and contextual factors will jointly predict distinct trajectories of posttraumatic psychopathology, psychological adjustment and resilience.
- H3 – Military and civilian experiences co-equally shape longitudinal risk for psychopathology, psychological adjustment and resilience among Ohio National Guard soldiers.

SPECIFIC AIM 2: To examine the role of hazardous alcohol use and alcohol use disorders in the multimorbidity of PTSD, depression, TBI and other psychopathology and psychological adjustment and resilience, and their chronicity over nine years of follow-up.

- H1 – Hazardous alcohol use and alcohol use disorders will be associated with new onset of psychiatric disorders, psychological adjustment and resilience.
- H2 – Hazardous alcohol use and alcohol use disorders will strongly predict chronicity of comorbid psychiatric disorders and psychological adjustment and resilience.

SPECIFIC AIM 3: To examine the bidirectional, longitudinal relationships among hazardous and risky health behaviors, and psychopathology over nine years of follow-up.

- H1 – Individuals with psychopathology or trajectories of chronic dysfunction are more likely to exhibit hazardous and risky health behaviors.
- H2 – Hazardous and risky health behaviors are associated with the onset of posttraumatic psychopathology.
- H3 – Hazardous and risky health behaviors persist in the long-term after resolution of psychopathology.

2. KEYWORDS:

Pre-, Peri-, and post-deployment, Ohio Army National Guard, longitudinal study, resilience, PTSD, depression, psychopathology

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Task 1 - Data Collection – 100%

- 1.1 All instruments are reviewed by investigators and study staff to ensure relevance and feasibility and survey is submitted to the IRB for approval.
- 1.2 Work collaboratively with the ONG and Abt SRBI to update contact information for current participants in the survey and send “alert letter” and “opt out letter” as outlined in the study protocol.
- 1.3 The survey is administered by Abt SRBI, Inc.’s staff at baseline and each successive year. After the completion of each wave of interviewing, Abt. SRBI, Inc. provides a de-identified data set.

Task 2 - Data Dissemination – 100%

- 2.1 Performance of analysis of the data collected from the platform including, but not limited to, pre, peri, and post deployment experiences and traits, and their impact on psychological health and resilience including the trajectories of psychopathology, hazardous alcohol use and co-morbid illnesses and risky behaviors and suicidal ideation.
- 2.2 At least 3 submissions to peer-reviewed journals derived from study data and at least 3 academic presentations per year.
- 2.3 Data syntheses and presentations, including pragmatic recommendations for possible applications of the data for fostering resilience and psychological health, targeted to NG leadership, health providers, and psychological health officers at the national level and within Ohio.

Task 3 - Oversight Meetings – 100%

- 3.1 Administrative Advisory Board, consisting of ONG senior leadership, local leaders, administrators, and stakeholders providing guidance on issues and pragmatic applications of the data for each year of the survey.
- 3.2 Scientific Advisory Board, consisting of nationally and internationally renowned individuals with established scientific credibility, and a strong record of scientific productivity and scholarship, provide feedback to the investigators.
- 3.3 Sponsor Review Meeting to update the leadership of MOMRP and DHP

Task 4 – Reporting – 100%

- 4.1 Quarterly financial reporting to USAMRAA, as required; Annual progress report to USAMRMC
- 4.2 Progress reports to sponsoring agency, as required; Local Institutional Review Board submissions, etc.
- 4.3 Continuing Review, and applicable submissions to DoD Office of Research Protections

Task 5 - Provision of Platform Support for Projects Developing Interventions to Improve Psychological Health and Expanding the Understanding of Biological Mechanisms – 100%

- 5.1 Maintenance of saliva DNA samples collected in waves 1-4 and collection and maintenance of saliva DNA samples collected in waves 6-9
- 5.2 Tamburrino and Liberzon: fMRI project studying the relationship between childhood adversity and PTSD
- 5.3 Fred Blow et al: “OHARNG MHI: Alcohol Intervention”, an early intervention study to reduce alcohol misuse and abuse.

What was accomplished under these goals?

Task 1 - Data Collection

Wave 6 Data Collection

The Wave 6 surveys were finalized and submitted to the UHCMC IRB on July 20, 2015 and approved August 8, 2015. After pre-testing of the Wave 6 follow-up survey, it was determined that updates and changes needed to be made to the survey. These changes were submitted to the UHCMC IRB on October 16, 2015 and approved on November 7, 2015. Wave 6 data collection began November 18, 2015 and ended November 10, 2016. Abt. Associates completed 1,650 follow-up surveys during this wave of data collection, exceeding our goal of 1,500 surveys completed from the main cohort.

Wave 6 Dynamic Cohort Data Collection

Due to changes in the ONG’s privacy policy, the recruitment method for the Dynamic Cohort had to be changed from opt-out procedures to opt-in procedures to adhere to the new policy. The coordinating site, Abt. Associates and the ONG worked together to determine the new opt-in procedures. These changes were submitted to the UHCMC IRB on March 17, 2016 and approved on March 29, 2016. Wave 6 Dynamic Cohort data collection began May 18, 2016 and ended December 20, 2016. Abt. Associates, Inc. completed 73 DC baseline surveys, well below our target of 500 surveys. This was due to the changes in ONG privacy policy, which had required us to change our DC recruitment method from opt-out to opt-in.

Wave 7 Data Collection

The Wave 7 follow-up survey was finalized submitted to the UHCMC IRB on December 12, 2016 was approved December 19, 2016. After pre-testing of the Wave 7 follow-up survey, it was determined that updates and changes needed to be made to the survey. In addition, after ongoing discussions with CPT David Kirker, Director of Psychological Health, Behavioral Health Science Officer, Ohio Army National Guard and Colin B. Fowler, MS, LPCC-S, Psychological Health Coordinator, Ohio Army National Guard it was decided to include additional questions that address barriers to seeking care.. These changes were submitted to the UHCMC IRB in January and approved shortly thereafter. The Wave 7 survey was fully launched February 23, 2017 and ended March 4, 2018. Abt. Associates completed 1,429 follow-up surveys during this wave of data collection.

Wave 7 Dynamic Cohort Data Collection

After discussions with ONG leadership regarding our low enrollment in to the Wave 6 Dynamic Cohort due to the change in recruitment methodology, we were given permission to return to our

previous opt-out procedures, with the provision that we would only be given telephone numbers for new ONG soldiers who were recruited since January 2016 and did not opt-out. The coordinating center revised the IRB protocol to revert back to opt-out procedures with the new stipulations. In addition, Abt. Associates, Inc. and Boston University updated the Wave 7 DC survey based on feedback from the ONG and to add questions that will ensure that the person the interviewer is talking to is an ONG soldier. Wave 7 Dynamic Cohort data collection began May 16, 2018 and ended September 13, 2018. Abt Associates, Inc. completed 156 Wave 7 DC surveys.

Wave 8 Data Collection

The coordinating center worked with Abt. Associates, Inc. and the epidemiologic team at Boston University to develop the Wave 8 follow-up telephone survey. The Wave 8 survey was been finalized and submitted to the UH IRB for approval. Approval was received on December 22, 2017. Just prior to Wave 8 data collection beginning, it was discovered that some minor edits needed to be made to the Wave 8 survey before dialing could begin. Due to updates being made to the UHCMC IRB system, we were not able to submit these changes until April 12, 2018. These changes were approved on April 26, 2018. Wave 8 data collection began May 16, 2018 and ended August 8, 2019. Abt. Associates completed 1,140 follow-up surveys during this wave of data collection.

Wave 8 Dynamic Cohort Data Collection

No changes were made to the survey for this year. Wave 8 DC data collection began February 26, 2019 and ended August 8, 2019. Abt Associates, Inc. completed 34 Wave 8 DC surveys. Recruitment in to this DC wave was lower than expected, Abt. Associates found that the contact information they had for these service members was not up-to-date. We worked with the ONG to get updated contact information, but were unable to access this data.

Wave 9 Data Collection

Preparations for Wave 9 data collection started March 2019, which will be the final wave of data collection for the project. No changes were made to the survey for the following year. Wave 9 data collection began June 12, 2019 and ended May 7, 2020. Abt. Associates completed 1,095 follow-up surveys during this final wave of data collection.

There was no Wave 9 Dynamic Cohort data collection.

Table 1 below shows enrollment in to the Dynamic Cohort during each wave, as well as the number of main cohort follow up surveys that were completed during each wave. Table 2 at the end of the document shows enrollment in to the Dynamic Cohort by quarter.

Table 1

Project Year	Dynamic Cohort (DC) Enrollment	Main Cohort Follow-Up Surveys	Total Telephone Surveys Completed
Wave 6	73	1,650	1,723
Wave 7	156	1,429	1,585
Wave 8	34	1,140	1,174

Wave 9	0	1,095	1,095
Total	263	5,314	5,557

Task 2 - Data Dissemination

The following manuscripts were published or accepted for publication since the start of this award:

1. Biehn, TL, Contractor, AA, Elhai, JD, Tamburrino, M, Fine, TH, Cohen, G, Shirley, E, Chan, PK, Liberzon, I, Calabrese, JR, Galea, S. Latent dimensions of posttraumatic stress disorder and their relations with alcohol use disorder. *Soc Psychiatry Psychiatr Epidemiol.* 2016 Mar;51(3):421-429. PMID: 26520448
2. Sampson L, Cohen GH, Calabrese JR, Fink DS, Tamburrino M, Liberzon I, Chan P, Galea S. Mental health over time in a military population: the impact of alcohol use disorder on trajectories of psychopathology after deployment. *J Trauma Stress.* 2015 Dec;28(6):547-55. PMID: 26625353
3. Fink DS, Gallaway MS, Tamburrino MB, Liberzon I, Chan P, Cohen GH, Sampson L, Shirley E, Goto T, D'Arcangelo N, Fine T, Reed PL, Calabrese JR, Galea S. Onset of alcohol use disorders and comorbid psychiatric disorders in a military cohort: Are there critical periods for prevention of alcohol use disorders? *Prev Sci.* 2016 Apr;17(3):347-56. PMID: 26687202
4. Ganocy SJ, Goto T, Chan PK, Cohen GH, Sampson L, Galea S, Liberzon I, Fine T, Shirley E, Sizemore J, Calabrese JR, Tamburrino MB. Association of Spirituality with Mental Health Conditions in Ohio National Guard Soldiers. *J Nerv Ment Dis.* 2016 Jul;204(7):524-9. PMID: 27065107
5. Fink DS, Chen Q, Liu Y, Tamburrino MB, Liberzon I, Shirley E, Fine T, Cohen GH, Galea S, Calabrese JR. Incidence and Risk for Mood and Anxiety Disorders in a Representative Sample of Ohio Army National Guard Members. *Public Health Reports.* 2016 Jul-Aug; 131:614-22. PMID: PMC4937124
6. Fink DS, Calabrese JR, Liberzon I, Tamburrino MB, Chan P, Cohen GH, Sampson L, Reed PL, Shirley E, Goto T, D'Arcangelo N, Fine T, Galea S. Retrospective age-of-onset and projected lifetime prevalence of psychiatric disorders among U.S. Army National Guard soldiers. *J Affect Disord.* 2016 Sep 15; 202:171-177. PMID: 27262639.
7. Byllesby BM, Elhai JD, Tamburrino M, Fine T, Cohen G, Sampson, L, Shirley, E, Chan P, Liberzon I, Galea S, Calabrese J. General distress is more important than PTSD's cognition and mood alterations factor in accounting for PTSD and depression's comorbidity. *J Affect Disord.* 2017 Mar 15;211:118-123. PMID: 28110158
8. Cohen GH, Fink DS, Sampson L, Tamburrino. M, Liberzon I, Calabrese JR, Galea S. Coincident alcohol dependence and depression increases risk of suicidal ideation among Army National Guard soldiers. *Ann Epidemiol.* 2017 Mar;27(3):157-163. PMID: 28139369
9. Fink DS, Keyes KM, Calabrese JR, Liberzon I, Tamburrino MB, Cohen GH, Sampson L, Galea S. Deployment and Alcohol Use in a Military Cohort: Use of Combined Methods to Account for Exposure-Related Covariates and Heterogeneous Response to Exposure. *Am J Epidemiol.* 2017 Aug 15;186(4):411-419. PMID: PMC5860008
10. Fink DS, Gradus JL, Keyes KM, Calabrese JR, Liberzon I, Tamburrino MB, Cohen GH, Sampson L, Galea S. Subthreshold PTSD and PTSD in a prospective-longitudinal cohort of

military personnel: Potential targets for preventive interventions. *Depress Anxiety*. 2018 Nov; 35(11):1048-1055. PMID: 30099820

11. Bergman HE, Chan P, Cooper AA, Shirley E, Goto T, Fine T, Cohen GH, Sampson L, Ganocy S, Tamburrino M, Liberzon I, Calabrese J, Galea S, Feeny NC. Examining the impact of PTSD symptomatology on cigarette smoking among Ohio Army National Guard soldiers. *Military Behavioral Health*. 2019;7(1): 46-56.
12. Gallaway MS, Fink DS, Sampson L, Cohen GH, Tamburrino M, Liberzon I, Calabrese J, Galea S. Prevalence and covariates of problematic gambling among a US military cohort. *Addict Behav*. 2019 Aug; 95:166-171. PMID: PMC6574081
13. Sampson L, Jiang T, Gradus JL, Cabral HJ, Rosellini AJ, Calabrese JR, Cohen GH, Fink DS, King AP, Liberzon I, Galea S. A machine learning approach to predicting new-onset depression in a military population. *Psychiatric Research and Clinical Practice*. *In press*.

The Fink D, et al. manuscript titled “Deployment and Alcohol Use in a Military Cohort: Use of Combined Methods to Account for Exposure-Related Covariates and Heterogeneous Response to Exposure” was selected as one of the 2017 Articles of the Year the *American Journal of Epidemiology*.

In addition to the above manuscripts, the following short articles were published in ISTSS online publications:

1. Laura Sampson, PhD wrote an article titled “Alcohol use disorder influences trajectories of posttraumatic stress and depression in National Guard members after deployment”, which was included in the Journal of Traumatic Stress Highlights, Trauma Blog in December 2015.
2. Greg Cohen, PhD and Laura Sampson, PhD wrote a short article titled “The Ohio Army National Guard Mental Health Initiative: Cohort summary and key findings”, which was included in the Military Matters section of ISTSS Stress Points newsletter on September 1, 2018.

Copies of the published manuscripts were emailed to USAMRAA and are included with this report.

The following posters have been presented since the start of this award:

1. Wang X. Rostral anterior cingulate cortex may relate to PTSD symptoms in gene FKBP5 SNP rs1360780 T-carriers. Society of Biological Psychiatry Annual Meeting. May 14, 2016
2. Fink D et al. Deployment and Alcohol Trajectories in a Military Cohort: Use of Propensity Score Techniques to Account for Exposure-related Covariates. 49th Annual Meeting of the Society for Epidemiologic Research (SER). June 21, 2016.
3. Ganocy S et al. Association of Spirituality with Mental Health Conditions in Ohio National Guard Soldiers. Poster. Military Health System Research Symposium (MHSRS). August 16, 2016.
4. Fink D et al. On the Assessment of Subthreshold PTSD: Convergent, Discriminant, and Concurrent Validity according to various definitions. International Society for Traumatic Stress Studies (ISTSS) 32nd Annual Meeting. November 10, 2016.
5. Sampson et al. Is the relationship between lifetime stressful events and past-year depression

mediated by unit social support during deployment among National Guard members? International Society for Traumatic Stress Studies (ISTSS) 32nd Annual Meeting. November 11, 2016.

6. Fink D et al. First test of a harm reduction model of e-cigarette and combustible cigarette use in a high-risk longitudinal cohort. College on Problems of Drug Dependence (CPDD) 79th Annual Scientific Meeting. June 19, 2017.
7. Sampson L et al. New Onset of Mental Health Disorders across Six Years of Follow-up in a Sample of National Guard Members. International Society for Traumatic Stress Studies 33rd Annual Meeting. November 9, 2017.
8. Fink D et al. Proportion of subsequent psychopathology conferred by subthreshold PTSD in a military cohort. Society for Epidemiologic Research 51st Annual Meeting. June 19, 2018.
9. Sampson, L et al. Childhood Adversity and Trajectories of Depression Symptoms in Adulthood across Six Years in a U.S. Army National Guard Cohort. International Society for Traumatic Stress Studies 34th Annual Meeting. November 8, 2018.
10. Sampson, L et al. A machine learning approach to predicting incident depression. Society for Epidemiologic Research 52nd Annual Meeting. June 19, 2019.

All posters are included with this report.

The following oral presentations took place since the start of this award:

1. Elhai J. “Structural Relations Between DSM-5 PTSD and Major Depression Symptoms in Military Soldiers” 14th Meeting of the European Society for Traumatic Stress Studies. June 24, 2015
2. Calabrese J. Panel on the future of veterans’ health care. Association of Health Care Journalists’ Annual Conference. April 6, 2016
3. Fink, D. “Proportion of subsequent psychopathology conferred by subthreshold PTSD in a military cohort” International Society for Traumatic Stress Studies (ISTSS) Annual Meeting. November 10, 2018.

The following abstracts were submitted for presentation since the start of this award:

1. Wang X. Rostral anterior cingulate cortex may relate to PTSD symptoms in gene FKBP5 SNP rs1360780 T-carriers. Poster. Society of Biological Psychiatry Annual Meeting. Accepted.
2. Ganocy S. Association of Spirituality with Mental Health Conditions in Ohio National Guard Soldiers. Poster. Military Health System Research Symposium (MHSRS). Accepted.
3. Sampson L. Is the relationship between lifetime stressful events and past-year depression mediated by unit social support during deployment among National Guard members? Poster. International Society for Traumatic Stress Studies (ISTSS) Annual Meeting. Accepted.
4. Fink D. On the Assessment of Subthreshold PTSD: Convergent, Discriminant, and Concurrent Validity according to various definitions. Accepted.
5. Fink D et al. Harm reduction or tool for initiation: Testing two models of e-cigarette and cigarette use in a high-risk longitudinal cohort. College on Problems of Drug Dependence (CPDD) 2017 Annual Meeting. Accepted.
6. Sampson L et al. New onset of mental disorders across six years of follow-up in a sample

- of National Guard members. 2017 International Society for Traumatic Stress Studies (ISTSS). Accepted.
7. Gallaway et al. Prevalence and covariates of problematic gambling among a military cohort. Association of Military Surgeons of the United States 2017 Annual Meeting. Rejected.
 8. Fink et al. Proportion of subsequent psychopathology conferred by subthreshold PTSD in a military cohort. Society for Epidemiologic Research 51st Annual Meeting. Accepted.
 9. Sampson L et al. Childhood adversity and trajectories of depression symptoms in adulthood across six years in a U.S. Army National Guard cohort. 2018 International Society for Traumatic Stress Studies (ISTSS). Accepted.
 10. Fink et al. Proportion of subsequent psychopathology conferred by subthreshold PTSD in a military cohort. 2018 International Society for Traumatic Stress Studies (ISTSS). Accepted.
 11. Sampson L et al. A machine learning approach to predicting incident depression. Society for Epidemiologic Research 52nd Annual Meeting. Accepted.
 12. Walsh K et al. Longitudinal Reciprocal Associations between Sexual Assault, Posttraumatic Stress Disorder, and Alcohol Use Disorder in Ohio Army National Guard Soldiers. International Society for Traumatic Stress Studies (ISTSS) 2019 Annual Meeting. Rejected.
 13. Sampson et al. Stressful life events outside of deployment are associated with incident depression in a U.S. Army National Guard cohort. Society for Epidemiologic Research 53rd Annual Meeting. Accepted. (Note: This poster was accepted, but due to COVID-19, the meeting was rescheduled to December 2020. Ms. Sampson is unable to attend the rescheduled date, so the abstract was withdrawn).

Study Website

The University of Toledo developed a website for this project. This website includes information that will be useful to Ohio National Guard Members, their families and friends, the academic community and the lay audience. Once the design, layout and content of the website were finished, UT worked with the ONG to get their feedback on the website. In addition, UT worked with the Public Information Officer in The Adjutant General's Department to get a quote from the ONG was included on the website and in the press release that went out the website went live. The quote spoke to the importance of our studying risk and resilience and/or how the website might be helpful or of interest to the Guard/family members/lay audience who visit the website. The University of Toledo completed a rebuild the dissemination website in the 4th quarter 2019 on a new platform to make it more user friendly for both those maintaining the site and those who visit the website. The website can be found at <http://www.militarybehavioralhealth.org/>

Task 3 - Oversight Meetings

PTSD Biomarker In Progress Review (IPR)

Dr. Calabrese and Dr. Liberzon attended the MOMRP PTSD Biomarker meeting at Fort Detrick on June 24 – 25, 2015. Presentation details can be found in the 2016 annual report.

Dr. Calabrese and Gregory Cohen attended the MOMRP PTSD Biomarker meeting at Fort Detrick on June 22 – 23, 2016. Presentation details can be found in the 2017 annual report.

Dr. Calabrese and Gregory Cohen attended the MOMRP PTSD Biomarker meeting at Fort Detrick on June 18 – 29, 2017. Presentation details can be found in the 2018 annual report.

Dr. Sandro Galea and Gregory Cohen attended the MOMRP PTSD Biomarker meeting at Fort Detrick in person on June 27 – 28, 2018. Presentation details can be found in the 2019 annual report.

Gregory Cohen attended the MOMRP PTSD Biomarker meeting at Fort Detrick in person on June 20 – 21, 2019. Presentation details can be found in the Year 5 Quarter 1 quarterly report.

Scientific Advisory Board (SAB) Meetings

The 2015/2016 External Scientific Advisory Board (SAB) meeting took place on November 7, 2016. Attendee and presentation details can be found in the 2017 annual report.

The 2017/2018 External Scientific Advisory Board (SAB) meeting took place on July 16, 2018 via teleconference. Attendee and presentation details can be found in the 2019 annual report.

The 2019/2020 External Scientific Advisory Board (SAB) meeting took place on May 14, 2020 via teleconference. Attendees included:

- **Lori Davis, M.D.** - Chief of the Research and Development Service, Tuscaloosa VA Medical Center
- **Matthew J. Friedman, M.D., Ph.D.** - Senior Advisor, National Center for PTSD; Geisel School of Medicine at Dartmouth, Professor of Psychiatry and Pharmacology & Toxicology
- **Joel Gelernter, M.D.** - Professor, Psychiatry, Genetics & Neurobiology, Yale University School of Medicine
- **Robert K. Gifford, Ph.D.** - Senior Project Director, Study to Assess Risk & Resilience Among Service Members (STARRS); Executive Officer, Center for the Study of Traumatic Stress, Department of Psychiatry, USUHS
- **Richard A. McCormick, Ph.D.** - Senior Scholar, Center for Healthcare Research & Policy, MetroHealth Medical Center, Case Western Reserve University
- **Thomas A. Mellman, M.D.** - Prof Psychiatry, Director, Clinical and Translational Research and Stress and Sleep Studies, Howard University College of Medicine
- **Colin Fowler, LPCC-S** - Psychological Health Coordinator, Ohio Army National Guard

Please see the attached 2019/2020 SAB slides for an overview of the presentations.

Administrative Advisory Board (AAB) Meetings

The 2016/2017 Administrative Advisory Board (AAB) meeting took place on March 9, 2017. Presentation details can be found in the 2017 annual report.

The 2018 AAB meeting was held on Thursday, March 29, 2018 in Cleveland, OH. Please see the attached slides for an overview of the presentation. Presentation details can be found in the 2018 annual report.

The 2019/2020 AAB meeting took place on May 14, 2020 in conjunction with the 2020 SAB

meeting. Presentation details can be found above.

Task 4 – Reporting

Quarterly financial and technical reporting to USAMRAA, and continuing review reports to local IRBs and USAMRMC HRPO were submitted as required.

Task 5 - Provision of Platform Support for Projects Developing Interventions to Improve Psychological Health and Expanding the Understanding of Biological Mechanisms

- 5.1 Maintenance of saliva DNA samples collected in waves 1-4 and collection and maintenance of saliva DNA samples collected in waves 6-9

Enrollment in to the genetics repository was on hold during Wave 5 (previous award) but began again with the start of Wave 6 in November 2015. Since this start of this award, 173 Guard members have consented to the genetics repository and provided a saliva sample, bringing our total enrollment in the repository to 1,283 since the beginning of the project.

Staff at VERAM maintained the genetic (DNA) repository for the OHARNG project by obtaining, purifying, QC, and archival of new genomic specimens into our repository, and necessary routine maintenance of our repository.

Efforts with genetic analyses (beyond the crucially necessary DNA archival that is supported) has focused upon “candidate gene” genotyping, using a small Illumina microarray (~3800 SNPs). We will repeat these analyses using our genome-wide data when we have these data (i.e. will repeat the analyses of the longitudinal dependent variables using GWAS format). We received approvals in 2018 from VA ORD and legal teams from all collaborators for performing genome-wide genotyping on ~1000 of our samples, using the Psychiatric Genetics Consortium Infinium “PsychArray-24” beadassay (Illumina, Inc.). This 24 sample bead array includes 265,000 validated tag SNPs from Infinium Core-24 BeadChip, 245,000 markers from Infinium Exome-24 BeadChip, and 50,000 additional markers associated with common psychiatric disorders (schizophrenia, bipolar disorder, ASD, ADHD, MDD, OCD, and Tourette’s syndrome) from GWAS findings from Psychiatric Genomics Consortium studies.

- 5.2 Liberzon: fMRI project studying the relationship between childhood adversity and PTSD

Enrollment for this project ended in December 2014 but data analysis for the project was ongoing during this award. This study concluded that early mild traumatic brain injury (mTBI) effects on visual and emotion pathways may contribute to development of PTSD symptoms in trauma survivors. In addition, there appears to be an interaction between PTSD diagnosis and a risk genotype (FKBP5 SNP rs1360780 T-carrier), such that right anterior cingulate cortex (rACC) volume reduction was associated with PTSD development in FKBP5 rs1360780 T-carriers, but not in non-T-carriers.

Results from this study were used as preliminary data in an R01 application submitted by

Dr. Xin Wang from the University of Toledo, who collaborated with Dr. Tamburrino and Dr. Liberzon on this project. Dr. Wang was awarded this grant in September 2016 (1R01MH110483).

- 5.3 Fred Blow et al: “OHARNG MHI: Alcohol Intervention”, an early intervention study to reduce alcohol misuse and abuse.

The development of the smartphone app was completed in early 2017, as was testing of the app. Study staff worked to complete study manuals to assist with recruitment and data management and the database was created and finalized. Based on feedback at the 2016 Substance Abuse IPR and after a conference call with the Science officers and study team, it was decided that the contingency management portion of the app would be discarded. Because of this, changes needed to be made to the protocol at all sites before enrollment could begin. In addition, updates had to be made to the app to remove references to contingency management.

The study was IRB and HRPO approved for all 3 sites and recruitment began March, 2017. Due to lower than expected enrollment, study staff began attending Periodic Health Assessment events and recruiting subjects in person. In late 2019, it was decided that due to low rates of subjects randomized to the app group actually using the app, as well as low follow-up rates, that we would increase our N to 850 subjects randomized. This change was approved by site IRBs in early 2020. On February 5, 2020, we randomized our 850th subject in to the study so enrollment is now closed. More detailed enrollment information can be found in the quarterly report for this project (W81XWH-14-2-0007 Log #13277015).

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

This project has afforded the opportunity for the professional development and directed mentorship of several masters’ level and doctoral students. These opportunities have been fostered and maintained at the “academic homes” of each of the study investigators. In particular, students are given mentorship in manuscript writing, academic presentations, and administrative regulatory/reporting duties and data from this project was used in Dr. Laura Sampson’s dissertation.

How were the results disseminated to communities of interest?

Manuscripts have been published in peer-reviewed journals and abstracts and posters have been presented at scientific conferences, as means to disseminate study results to the academic community. In addition, now that the study website is available to the public, service members, their families, the public and professionals have access to summaries of study results.

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

Nothing to Report

4. IMPACT:

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

We continue to impact the fields of psychiatry and epidemiology with our study, and note some highlights:

- As whole, the data has helped add to the current literature on how pre-, peri- and post-deployment experiences shape the mental health of service members over the deployment lifecycle (Sampson et al., 2015).
- Our manuscript on the impact of deployment on problem drinking (Fink et al., 2017), which used novel methods to control for the “healthy warrior effect,” was recognized as one of the 2017 articles of the year in American Journal of Epidemiology.
- We have examined the prevalence and predictors of problem gambling (Gallaway et al., 2018) and e-cigarette use among service members (Fink et al., 2017, both emerging areas of interest in the study of addictive behaviors.
- We examined sub-threshold PTSD, and its substantial contribution to later burden of diagnosable PTSD (Fink et al., 2018).
- Our work has shed light on the understudied relationship between spirituality and mental health among service members (Ganocy et al., 2016).
- We have also explored and illuminated the psychometric relationships between the constructs of depression and PTSD (Byllesby et al., 2017), generalized anxiety disorder and PTSD (Contractor et al., 2015), and alcohol misuse and PTSD (Biehn et al., 2016).
- We previously identified novel SNPs within the ADRB2 gene that confer risk of PTSD in combination with adverse childhood trauma (Liberzon et al., 2014), and recently identified a SNP within the GRIN2B gene that was associated with depression trajectory group membership, in interaction with childhood trauma (Manuscript Under Preparation).

In addition, we have been able to evaluate the majority of our study hypotheses. We provide below, a summary of our findings from the current performance period, organized by aims and hypotheses:

SPECIFIC AIM 1: To complete our longitudinal examination of the roles of pre-, peri-, and post-deployment experiences, both military and civilian, in jointly contributing to trajectories of psychopathology, psychological adjustment and resilience over nine years of follow-up.

Aim 1 Hypothesis 1: Pre-, Peri-, and post-deployment factors will jointly predict distinct trajectories of posttraumatic psychopathology, psychological adjustment and resilience.

- ***Supported.*** Findings from Sampson (2015, Journal of Traumatic Stress) support this hypothesis that factors across the deployment cycle jointly predict trajectories of posttraumatic psychopathology, including symptom patterns of both depression and posttraumatic stress. In particular, we found that peri-deployment factors (area of conflict deployment), post-deployment factors (alcohol use disorder and PTSD measured after deployment), and factors that span across pre-, peri-, and post-deployment periods (marital status and number of lifetime stressors) were each associated with distinct *depression symptom trajectories* after deployment. For

example, having four or more types of lifetime stressors at baseline (e.g., job loss, divorce) was associated with belonging to either the increasing depression symptom trajectory group or the chronically high depression symptom group, compared to the resistant and resilient trajectory groups over time. Similarly, we found that peri-deployment factors (area of conflict deployment), post-deployment factors (alcohol use disorder, depression and post-deployment traumatic events), and factors that span across pre-, peri-, and post-deployment periods (education level and number of lifetime traumatic events at baseline) were each associated with distinct *posttraumatic stress symptom (PTS) trajectories*. For example, being deployed to an area of conflict (Iraq or Afghanistan) within two years of baseline was associated with having a constant pattern of moderate symptoms of PTS at all follow-up time points, compared to being deployed to a non-conflict area. We have also updated these trajectories with newer data from more recent follow-up surveys, as presented at the International Society for Traumatic Stress Studies 34th Annual Meeting in 2018 (appended as a poster and as part of the Scientific Advisory Board meeting slides). In that updated analyses which will also be submitted as a manuscript, we found similar patterns of trajectories of depression symptoms over time as in the earlier paper, and a strong association between pre-deployment childhood adversity and membership in higher-symptom trajectory groups.

Aim 1 Hypothesis 2: Genetic, interpersonal, intrapersonal, and contextual factors will jointly predict distinct trajectories of posttraumatic psychopathology, psychological adjustment and resilience.

- ***Supported.*** Findings from an analysis in progress suggest that genetic and interpersonal factors jointly predict trajectories of depression across six years of follow up. We identified a single-nucleotide polymorphism within the GRIN2B gene (rs220590), in interaction with childhood trauma, which was associated with depression trajectory group membership. Specifically, we first used latent class growth analysis to find a 4-group model that best fit our cohort, with the following symptom pattern groups: resistant (consistently no symptoms over time; 54.1%), decreasing symptoms over time (15.7%), increasing symptoms (18.5%), and chronic (consistently high-level symptoms; 11.7%). These groups were then collapsed into a binary variable (chronic/increasing vs. resistant/decreasing groups) for use as an outcome in models among the sample that provided genetic data (n=660). Controlling for ancestry, sex, and traumatic events during adult life, we identified a single-nucleotide polymorphism within the GRIN2B gene (rs220590), in interaction with childhood trauma, which was associated with depression trajectory group membership ($P=2.09 \times 10^{-4}$). Soldiers with the risk variant (AA and AG genotypes) and childhood trauma had 2.07 times the odds of being in the increasing or chronic trajectory groups compared to the decreasing or resistant groups, relative to those with neither the high-risk variant nor childhood trauma. These findings have important implications for etiology of depression symptoms and their course over time.

Aim 1 Hypothesis 3: Military and civilian experiences co-equally shape longitudinal risk

for psychopathology, psychological adjustment and resilience among Ohio National Guard soldiers.

- **Supported.** A study by Fink (2016, Journal of Affective Disorders) showed that at a population level, military and civilian experience both play key roles in longitudinal risk for psychopathology among service members. In particular, we found that the majority (64%) of lifetime psychiatric disorders onset prior to military enlistment, suggesting that the influence of civilian experiences play a key role in driving longitudinal risk for psychopathology. On the other hand, 36% of disorders onset after engagement with military service, suggesting that for this 36%, longitudinal risk for psychopathology is driven by a mix of military and civilian experiences. This study confirms our prior findings that experiences, civilian and military, occurring across the deployment cycle, shape longitudinal risk for psychopathology (Sampson, 2015, Journal of Traumatic Stress). Another study we published in 2016 (Fink, Public Health Reports) provided evidence to support this hypothesis, showing that both military and civilian events were predictive of anxiety or mood disorder onset. In particular, soldiers with a deployment in the past year had a 29% greater risk of anxiety or mood disorder onset, and those who experienced a potentially traumatic event outside of deployment (e.g., unexpected death of a loved one) had a 32% greater risk of anxiety or mood disorder onset. Finally, a machine learning paper currently in press (Sampson, 2020, Psychiatric Research and Clinical Practice) found that a combination of many different risk factors across the lifecourse, including both civilian experiences (e.g., financial problems, divorce) and military experiences (e.g., years of service, traumatic combat events), all measured at baseline, jointly predicted new-onset depression across five years of follow-up.

SPECIFIC AIM 2: To examine the role of hazardous alcohol use and alcohol use disorders in the multimorbidity of PTSD, depression, TBI and other psychopathology and psychological adjustment and resilience, and their chronicity over nine years of follow-up.

Aim 2 Hypothesis 1: Hazardous alcohol use and alcohol use disorders will be associated with new onset of psychiatric disorders, psychological adjustment and resilience.

- **Supported.** Several studies we published supported this hypothesis across a variety of psychopathologies, including anxiety disorders, mood disorders, and suicidal ideation. First, we found support that alcohol use disorders confer risk for new-onset mood and anxiety disorders in a longitudinal study (Fink, 2016, Prevention Science) that examined the sequencing of initial and co-occurring disorders for those with a history of comorbid alcohol and mood or anxiety disorders. We found that an approximately equal proportion of individuals had anxiety disorders onset first as had alcohol use disorders onset first. The same was true for those with a presentation of comorbid mood and alcohol use disorders. Another study we published (Cohen, 2017, Annals of Epidemiology) showed that alcohol dependence confers risk of new-onset suicidal ideation, in concert with depression. Finally, a machine learning study we conducted (Sampson, 2020, Psychiatric Research and Clinical Practice) found that alcohol abuse was predictive of new onset depression across five years of follow-up,

particularly for women.

Aim 2 Hypothesis 2: Hazardous alcohol use and alcohol use disorders will strongly predict chronicity of comorbid psychiatric disorders and psychological adjustment and resilience.

- ***Supported.*** We found that alcohol use disorder, including past year alcohol abuse or alcohol dependence, contributed substantially to trajectories of both depression and posttraumatic stress symptoms over about 4 years of follow-up (Sampson, 2015, Journal of Traumatic Stress). Alcohol use disorder was associated with an exacerbation of symptoms in all trajectory groups, altering their shapes over time, but exacerbations were highest among the 2 groups with the greatest number of symptoms, both for depression and posttraumatic stress.

SPECIFIC AIM 3: To examine the bidirectional, longitudinal relationships among hazardous and risky health behaviors, and psychopathology over nine years of follow-up.

Aim 3 Hypothesis 1: Individuals with psychopathology or trajectories of chronic dysfunction are more likely to exhibit hazardous and risky health behaviors.

- ***Supported.*** We found that depression and alcohol dependence were associated with problematic gambling (Galloway, 2019, Addictive Behaviors). Past-year frequent gambling (at least once per week) and lifetime potential problematic gambling were reported by 13% and 8% of respondents, respectively, and were also associated with being male, currently unmarried, having left the Guard or retired, legal problems, and pain.

Aim 3 Hypothesis 2: Hazardous and risky health behaviors are associated with the onset of posttraumatic psychopathology.

- ***Untested.*** We plan to test this hypothesis, but have not yet had the opportunity.

Aim 3 Hypothesis 3: Hazardous and risky health behaviors persist in the long-term after resolution of psychopathology.

- ***Untested.*** We plan to test this hypothesis, but have not yet had the opportunity.

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?

As whole, the data has helped add to the current literature in how pre-, peri- and post-deployment experiences affect soldiers in the short term and in the long term. In addition, data from the

project has been used by the ONG to develop tools to assess for suicide risk, make additions to PTSD stigma reduction training and aid in designing programs to improve unit cohesion. The ONG feels these changes will help soldiers be more “mission ready”, as well as be better equipped to deal with stress in their civilian life.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Due to changes in ONG policy, we had to change our recruitment methods from opt-out procedures to opt-in procedures for Wave 6. Instead of the ONG sending out an alert letter and Abt. Associates contacting those who do not specifically opt-out, the ONG sent out alert letters which required potential participants to respond indicating either yes, they wish to participate or no, they do not wish to participate. Because the change to opt-in procedures had such a negative impact on recruitment in to the Dynamic Cohort in Wave 6, after consulting with ONG leadership and obtaining their approval, we were able to change back to opt-out procedures, which helped improve recruitment numbers in to the Dynamic Cohort in Wave 7.

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

Having to change from an opt-out recruitment methodology to opt-in recruitment methodology delayed the start up for Wave 6 Dynamic Cohort recruitment.

Changes that had a significant impact on expenditures

Due to low enrollment in to the dynamic cohort through this award, Abt. Associates expenditures were lower than anticipated due to a decrease in personnel time and stipend costs.

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

Nothing to Report

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals.

No activities involving the use or care of vertebrate animals were performed to complete this project.

Significant changes in use of biohazards and/or select agents

No activities involving the use biohazards and/or select agents were performed to complete this project.

6. PRODUCTS

- **Publications, conference papers, and presentations**

The following publications and presentations have come from work under this award.

Publications

1. Biehn, TL, Contractor, AA, Elhai, JD, Tamburrino, M, Fine, TH, Cohen, G, Shirley, E, Chan, PK, Liberzon, I, Calabrese, JR, Galea, S. Latent dimensions of posttraumatic stress disorder and their relations with alcohol use disorder. *Soc Psychiatry Psychiatr Epidemiol.* 2016 Mar;51(3):421-429. PMID: 26520448
2. Sampson L, Cohen GH, Calabrese JR, Fink DS, Tamburrino M, Liberzon I, Chan P, Galea S. Mental health over time in a military population: the impact of alcohol use disorder on trajectories of psychopathology after deployment. *J Trauma Stress.* 2015 Dec;28(6):547-55. PMID: 26625353
3. Fink DS, Gallaway MS, Tamburrino MB, Liberzon I, Chan P, Cohen GH, Sampson L, Shirley E, Goto T, D'Arcangelo N, Fine T, Reed PL, Calabrese JR, Galea S. Onset of alcohol use disorders and comorbid psychiatric disorders in a military cohort: Are there critical periods for prevention of alcohol use disorders? *Prev Sci. Prev Sci.* 2016 Apr;17(3):347-56. PMID: 26687202
4. Ganocy SJ, Goto T, Chan PK, Cohen GH, Sampson L, Galea S, Liberzon I, Fine T, Shirley E, Sizemore J, Calabrese JR, Tamburrino MB. Association of Spirituality with Mental Health Conditions in Ohio National Guard Soldiers. *J Nerv Ment Dis.* 2016 Jul;204(7):524-9. PMID: 27065107
5. Fink DS, Chen Q, Liu Y, Tamburrino MB, Liberzon I, Shirley E, Fine T, Cohen GH, Galea S, Calabrese JR. Incidence and Risk for Mood and Anxiety Disorders in a Representative Sample of Ohio Army National Guard Members. *Public Health Reports.* 2016 Jul-Aug; 131:614-22. PMCID: PMC4937124
6. Fink DS, Calabrese JR, Liberzon I, Tamburrino MB, Chan P, Cohen GH, Sampson L, Reed PL, Shirley E, Goto T, D'Arcangelo N, Fine T, Galea S. Retrospective age-of-onset and projected lifetime prevalence of psychiatric disorders among U.S. Army National Guard soldiers. *J Affect Disord.* 2016 Sep 15; 202:171-177. PMID: 27262639.
7. Byllesby BM, Elhai JD, Tamburrino M, Fine T, Cohen G, Sampson, L, Shirley, E, Chan P, Liberzon I, Galea S, Calabrese J. General distress is more important than PTSD's cognition and mood alterations factor in accounting for PTSD and depression's comorbidity. *J Affect Disord.* 2017 Mar 15;211:118-123. PMID: 28110158
8. Cohen GH, Fink DS, Sampson L, Tamburrino. M, Liberzon I, Calabrese JR, Galea S. Coincident alcohol dependence and depression increases risk of suicidal ideation among Army National Guard soldiers. *Ann Epidemiol.* 2017 Mar;27(3):157-163. PMID: 28139369
9. Fink DS, Keyes KM, Calabrese JR, Liberzon I, Tamburrino MB, Cohen GH, Sampson L, Galea S. Deployment and Alcohol Use in a Military Cohort: Use of Combined Methods to Account for Exposure-Related Covariates and Heterogeneous Response to Exposure. *Am J Epidemiol.* 2017 Aug 15;186(4):411-419. PMCID: PMC5860008
10. Fink DS, Gradus JL, Keyes KM, Calabrese JR, Liberzon I, Tamburrino MB, Cohen GH, Sampson L, Galea S. Subthreshold PTSD and PTSD in a prospective-longitudinal cohort of military personnel: Potential targets for preventive interventions. *Depress Anxiety.* 2018 Nov; 35(11):1048-1055. PMID: 30099820
11. Bergman HE, Chan P, Cooper AA, Shirley E, Goto T, Fine T, Cohen GH, Sampson

- L, Ganocy S, Tamburrino M, Liberzon I, Calabrese J, Galea S, Feeny NC. Examining the impact of PTSD symptomatology on cigarette smoking among Ohio Army National Guard soldiers. *Military Behavioral Health*. 2019;7(1): 46-56.
12. Gallaway MS, Fink DS, Sampson L, Cohen GH, Tamburrino M, Liberzon I, Calabrese J, Galea S. Prevalence and covariates of problematic gambling among a US military cohort. *Addict Behav*. 2019 Aug; 95:166-171. PMID: PMC6574081
 13. Sampson L, Jiang T, Gradus JL, Cabral HJ, Rosellini AJ, Calabrese JR, Cohen GH, Fink DS, King AP, Liberzon I, Galea S. (In press.) A machine learning approach to predicting new-onset depression in a military population. *Psychiatric Research and Clinical Practice*. *In press*.

Conference Presentations - Poster

1. Wang X. Rostral anterior cingulate cortex may relate to PTSD symptoms in gene FKBP5 SNP rs1360780 T-carriers. Society of Biological Psychiatry Annual Meeting. May 14, 2016
2. Fink D et al. Deployment and Alcohol Trajectories in a Military Cohort: Use of Propensity Score Techniques to Account for Exposure-related Covariates. 49th Annual Meeting of the Society for Epidemiologic Research (SER). June 21, 2016.
3. Ganocy S et al. Association of Spirituality with Mental Health Conditions in Ohio National Guard Soldiers. Poster. Military Health System Research Symposium (MHSRS). August 16, 2016.
4. Fink D et al. On the Assessment of Subthreshold PTSD: Convergent, Discriminant, and Concurrent Validity according to various definitions. International Society for Traumatic Stress Studies (ISTSS) 32nd Annual Meeting. November 10, 2016.
5. Sampson et al. Is the relationship between lifetime stressful events and past-year depression mediated by unit social support during deployment among National Guard members? International Society for Traumatic Stress Studies (ISTSS) 32nd Annual Meeting. November 11, 2016.
6. Fink D et al. First test of a harm reduction model of e-cigarette and combustible cigarette use in a high-risk longitudinal cohort. College on Problems of Drug Dependence (CPDD) 79th Annual Scientific Meeting. June 19, 2017.
7. Sampson L et al. New Onset of Mental Health Disorders across Six Years of Follow-up in a Sample of National Guard Members. International Society for Traumatic Stress Studies 33rd Annual Meeting. November 9, 2017.
8. Fink D et al. Proportion of subsequent psychopathology conferred by subthreshold PTSD in a military cohort. Society for Epidemiologic Research 51st Annual Meeting. June 19, 2018.
9. Sampson, L et al. Childhood Adversity and Trajectories of Depression Symptoms in Adulthood across Six Years in a U.S. Army National Guard Cohort. International Society for Traumatic Stress Studies 34th Annual Meeting. November 8, 2018.
10. Sampson, L et al. A machine learning approach to predicting incident depression. Society for Epidemiologic Research 52nd Annual Meeting. June 19, 2019.

Conference Presentations – Oral Presentation

1. Elhai J. “Structural Relations Between DSM-5 PTSD and Major Depression Symptoms in Military Soldiers” 14th Meeting of the European Society for Traumatic

- Stress Studies. June 24, 2015
2. Calabrese J. Panel on the future of veterans' health care. Association of Health Care Journalists' Annual Conference. April 6, 2016
 3. Fink, D. "Proportion of subsequent psychopathology conferred by subthreshold PTSD in a military cohort" International Society for Traumatic Stress Studies (ISTSS) Annual Meeting. November 10, 2018.
- **Books or other non-periodical, one-time publications.**
Nothing to Report
 - **Other publications, conference papers, and presentations.**
 1. Laura Sampson. Alcohol use disorder influences trajectories of posttraumatic stress and depression in National Guard members after deployment. *Journal of Traumatic Stress Highlights, Trauma Blog* December 2015 <http://www.istss.org/education-research/traumatic-stresspoints/2015-december/alcohol-use-disorder-influences-trajectories-of-po.aspx>
 2. Laura Sampson and Gregory H. Cohen. The Ohio National Guard Mental Health Initiative: Cohort Summary and Key Findings. *StressPoints: An award-winning e-newsletter for the International Society for Traumatic Stress Studies* October 2018
 - **Website(s) or other Internet site(s)**
The study website went live in September 2017. Updates to the website have been made as needed. The website can be found at <http://www.militarybehavioralhealth.org/>
 - **Technologies or techniques**
Nothing to Report
 - **Inventions, patent applications, and/or licenses**
Nothing to Report
 - **Other Products**
Per the ONG Director of Psychological Health, Behavioral Health Science Officer, CPT David Kirker, the following products have developed partially based on this project's findings:
 - "Suicide Stand-Down" trainings, which aim to reduce suicide risk and focus on targeting comorbid and dual diagnosis populations
 - Stigma reduction training to reduce stigma and barriers to care, and encourage broader adoption of treatment seeking.
 - Delivered among leadership and at the unit level.
 - National Guard Bureau considering of use these trainings for all National Guard service members.
 - Utilized in a PTSD stigma reduction video produced with the VA and Governor's Office Mental Health and Addiction Services.
 - Creation of risk formularies for those with identified suicidal or homicidal ideation
 - Programming designed to improve unit cohesion, which has the potential to reduce

- sexual harassment and assault during deployment as well as mental health outcomes.
- Provision of opportunities to strengthen pre-deployment preparedness, peri-deployment unit support, and especially post-deployment social support.
 - Creation of Unit Risk Inventories that help identify and triage units in need of greater support.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Joseph R. Calabrese, MD

Project Role: Principal Investigator

Researcher Identifier (e.g. ORCID ID): ERA Commons - jcalabrese

Nearest person month worked: 3.6 calendar months

Contribution to Project: Dr. Calabrese is responsible for the ongoing administration and oversight of all aspects of the Ohio Army National Guard Mental Health Initiative. Dr. Calabrese serves as the primary liaison with the Ohio Army National Guard, which includes the annual Administrative Advisory Board meetings with the TAG, aTAG, and commanders in Columbus. He ensures study and data collected are done with fidelity to the protocol and provides oversight of manuscript writing, data presentations and working with the research team on developing new proposals.

Name: Carla Conroy, MPH

Project Role: Coordinating Center Administrator

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 7.2 calendar months

Contribution to Project: Ms. Conroy provides administrative support including maintaining compliance with DoD OHRP policies, local IRBs of record policies, as well as coordinating monthly Steering Committee teleconferences and quarterly Data Safety and Monitoring Board (DSMB) meetings. Ms. Conroy is also responsible for fiscal and project management of the Coordinating Center and all subsequent funded projects that fall under the platform. She provides ongoing administrative support including working with sites to execute sub-contracts, overseeing all budgets and contracts/subcontracts administration and award monitoring. Ms. Conroy interacts regularly with the subcontracted sites to ensure ongoing progress with the primary platform.

Name: Mary Beth Serrano, MA

Project Role: Coordinating Center Fiscal Administrator

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 4.8 calendar months

Contribution to Project: Ms Serrano provided administrative support during this reporting period including working with sites to execute sub-contracts, overseeing all budgets and contracts/subcontracts administration and award monitoring. Ms Serrano worked on the project until May 2018.

Name: Nicole D’Arcangelo

Project Role: Administrative Assistant

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 1.6 calendar months

Contribution to Project: Ms. D’Arcangelo provided administrative assistance to Dr. Calabrese and other project staff arranging logistics for successful completion of the project. Ms. D’Arcangelo worked on the project until September 2019.

Name: Toyomi Goto

Project Role: Triage Clinician

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 0.6 calendar months

Contribution to Project: Ms. Goto provided the clinical triage of participants who, during their annual Telephone Survey, present with psychiatric symptoms and are at risk of harming themselves or others, or who desire to talk with a mental health clinician. Ms. Goto worked on the project until August 2018.

Name: Leslie Estremera

Project Role: Administrative Assistant

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 6.0 calendar months

Contribution to Project: Ms. Estremera provided administrative assistance to Dr. Calabrese and other project staff, including but not limited to, scheduling regular conference calls for the primary platform and secondary projects, interacting with the Ohio National Guard Leadership and other sites involved with the project, and arranging other logistics for successful completion of the project. Ms. Estremera worked on the project until November 2016.

Name: Brittany Brownrigg

Project Role: Coordinating Center Administrator

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 3.6 calendar months

Contribution to Project: Ms. Brownrigg assists Ms. Conroy in providing administrative support including overseeing committee (i.e. Steering Committee, Data Safety and Monitoring Board) meetings, maintaining compliance with DoD OHRP policies, local IRBs of record policies, and applicable federal guidelines for conducting research. She also coordinates the project’s Data Safety and Monitoring Board (DSMB), facilitating real-time review of any Serious Adverse Events with the medical monitor (Dr. Segraves) as well as scheduling and leading the agenda for the quarterly DSMB meetings. She is also be involved with the implementation of the funded secondary projects. Ms. Brownrigg began working on the project in June 2019.

Name: Nicole Jones

Project Role: Administrative Assistant

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 2.4 calendar months

Contribution to Project: Ms. Jones assists in providing administrative assistance to Dr. Calabrese and other project staff arranging logistics for successful completion of the project. Ms. Jones worked on the project from June 2019 - March 2020.

Name: Israel Liberzon, MD

Project Role: Director of the Genetics Repository

Researcher Identifier (e.g. ORCID ID): ERA Commons - iliberzon

Nearest person month worked: 1 calendar month

Contribution to Project: Dr. Israel Liberzon is Professor of Psychiatry, Neuroscience, and Psychology, and is the Director of the Genetics Repository. He assumes primary scientific oversight and responsibility for all aspects of this effort, and serves on the Steering Committee of the OHARNG MHI. Dr. Liberzon served as the PI of the Ann Arbor VA site until early 2019, At that time, he became no-cost effort on this project, but remained the Director of the Genetics Repository

Name: Nirmala Rajaram

Project Role: Site PI

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 6.5 calendar months

Contribution to Project: Dr. Nirmala Rajaram became the site PI of the Ann Arbor VA site early 2019. She is responsible for all regulatory requirements, specimen tracking / logistics, database management and oversight of the genetic repository established by this project. She is also involved in scientific analyses and manuscript preparation. Prior to that, she worked in the Genetics Repository processing samples and overseeing the lab.

Name: Anthony King, PhD

Project Role: Co-Investigator

Researcher Identifier (e.g. ORCID ID): orcid.org/0000-0002-0764-9625

Nearest person month worked: 1 calendar months

Contribution to Project: Dr. King is an Assistant Professor of Psychiatry and a scientific collaborator on this project in the Translational Science site, and is involved in analyses scientific analysis, and interpretation and communication of genetic, neuroimaging, and gene x environment analyses. He also contributes to research administrative / human subjects issues as necessary. Dr. King is at a no-cost effort on this project effective May 2019.

Name: Hedieh Briggs

Project Role: Project Manager

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 1

Contribution to Project: Administrative and oversight.

Name: Sandro Galea, MD, DrPH

Project Role: Scientific Principal Investigator

Researcher Identifier (e.g. ORCID ID): ERA Commons – sgalea

Nearest person month worked: 0.6 calendar months

Contribution to Project: Dr. Galea continues to lead the Research Methods Core team, ensuring the integrity of our study survey, data collection procedures, data analysis, and manuscript development.

Name: Gregory H Cohen, MSW, MS

Project Role: Data Analyst

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 3.6 calendar months

Contribution to Project: Mr. Cohen has worked on survey design survey implementation, data analysis, and manuscript development.

Name: Laura Sampson, BA

Project Role: Research Analyst

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 4.6 calendar months

Contribution to Project: Ms. Sampson has worked on survey design survey implementation, data analysis, and manuscript development.

Name: Steven Lehar, PhD

Project Role: Programmer

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 7.2

Contribution to Project: Mr. Lehar worked on statistical analysis, programming, and simulation modeling. Mr. Lehar worked until June 2016.

Name: Shailesh Tamrakar, MS

Project Role: Research Programmer

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 4.1 calendar months

Contribution to Project: Mr. Tamrakar assisted with data analysis and preparation of study findings for manuscripts and presentations. Mr. Tamrakar began working on the project in November 2016.

Name: Chia-Ying Lin, BA

Project Role: Research Analyst

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 1.40

Contribution to Project: Miss Lin assisted with literature review and preparation of study findings for manuscripts and presentations. Miss Lin worked on the project from November 2016 – May 2017.

Name: Shui Yu

Project Role: Research Analyst

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 4.1 calendar months

Contribution to Project: Ms. Yu assisted with data analysis and preparation of study findings for manuscripts and presentations. Ms. Yu began working on the project in January 2017.

Name: Salma Abdalla

Project Role: Research Analyst

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 6.8 calendar months

Contribution to Project: Ms. Abdalla assisted with data analysis and preparation of study findings for manuscripts and presentations. Ms. Abdalla began working on the project in January 2017.

Name: Marijo Tamburrino, MD

Project Role: Co-investigator, Site Principal Investigator

Researcher Identifier (e.g. ORCID ID): ERA Commons – mtamburrino

Nearest Person Month: 1.2 calendar months

Contribution to Project: Dr. Tamburrino was responsible for the oversight of the efforts committed by the University of Toledo. More specifically, she worked on the dissemination initiative. Dr. Tamburrino was PI of the UT site until her retirement in June 2017.

Name: John Wryobeck, PhD

Project Role: Site Principal Investigator

Researcher Identifier (e.g. ORCID ID):

Nearest Person Month: 0.36 calendar months

Contribution to Project: Dr. Wryobeck was responsible for the oversight of the efforts committed by the University of Toledo. He worked with Dr. Elhai to explore new methods of dissemination which included modifying the current website and developing methods of sharing information and engaging guard leadership in how they might use the OHARNG outcome data. Dr. Wryobeck became the PI of the UT site when Dr. Tamburrino retired in June 2017. Dr. Wryobeck was on medical leave from June 2019 – January 2020.

Name: Cheryl McCullumsmith, MD PhD

Project Role: Interim Site Principal Investigator

Researcher Identifier (e.g. ORCID ID):

Nearest Person Month: 0.36 calendar months

Contribution to Project: Dr. McCullumsmith assumed responsibility as interim site PI when Dr. Wryobeck went on medical leave in June 2019. She was responsible for the oversight of the efforts committed by the University of Toledo and was at a no-cost effort on this project.

Name: Jon Elhai, PhD

Project Role: Co-investigator

Researcher Identifier (e.g. ORCID ID):

Nearest Person Month: 1.68 calendar months

Contribution to Project: Dr. Elhai coordinated and implemented the dissemination initiative of the grant. More specifically, Dr. Elhai launched and maintained the ONG website.

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?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

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

Updated Quad Chart attached

Table 2

	Year 1				Year 2				Year 3				Year 4				Year 5			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Telephone Survey New Enrollment	0	0	0	0	11	29	33	0	0	0	0	140	11	5	0	34	0	0	0	0
Cumulative total	0	0	0	0	11	40	73	73	73	73	73	213	224	229	229	263	263	263	263	263

Pre-, Peri-, and Post-deployment Trajectories and Mechanisms of Psychopathology, Psychological Health and Resilience over Nine Years of Follow-up in a Reserve Population

Log Number: JW148412

Award Number: W81XWH-15-1-0080

PI: Joseph R. Calabrese, M.D

Org: University Hospitals Cleveland Medical Center

Award Amount: \$6,398,612



Study Aims

- To complete our longitudinal examination of the roles of pre-, peri-, and post-deployment experiences, both military and civilian, in jointly contributing to trajectories of psychopathology over nine years of follow-up.
- To examine the role of hazardous alcohol use and alcohol use disorders in the multimorbidity of PTSD, depression, TBI and other psychopathology, and their chronicity over nine years of follow-up.
- To examine the bidirectional, longitudinal relationships among hazardous and risky health behaviors, and psychopathology over nine years of follow-up.

Approach

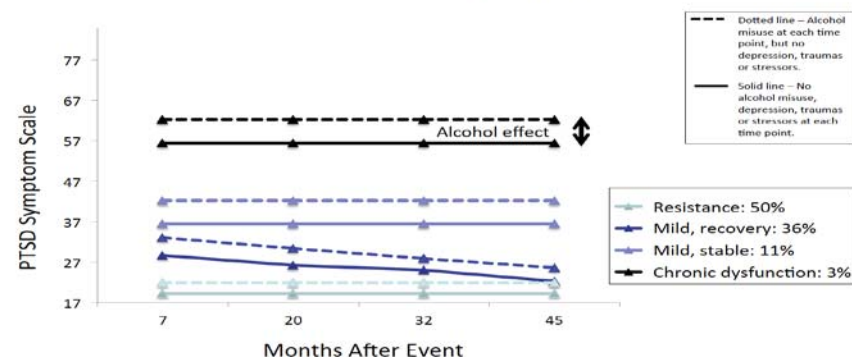
- PTSD symptomatology measured with PCL-C (PTSD Checklist – Civilian; Weathers & Ford, 1996).
- Alcohol misuse, including DSM IV Abuse or Dependence measured with the MINI (Mini-International Neuropsychiatric Interview; Sheehan et al., 1998).
- Group-based trajectories of PTSD symptomatology and the impact of alcohol misuse on those identified trajectories were modeled with SAS-callable Proc Traj (Jones et al., 2001).

Timeline and Cost

Activities	CY	15-16	16-17	17-18	18-19	19-20
Descriptive Analyses/ Publications		[Green bar spanning 15-16 to 19-20]				
Wave 5 Primary Platform Data Collection		[Green bar]				
Wave 6-9 Primary Platform Data Collection			[Green bar spanning 16-17 to 19-20]			
Genetics Repository		[Green bar spanning 15-16 to 19-20]				
fMRI Pilot Project		[Green bar]				
Alcohol Prevention and Intervention Project		[Green bar spanning 15-16 to 19-20]				
Estimated Budget		\$1.7mil	\$1.6mil	\$1.6mil	\$1.6mil	NCE

Updated: 8/19/2020

Alcohol Misuse Modifies Longitudinal Trajectories of PTSD Symptoms Among Deployed Soldiers



Four distinct trajectories of PTSD symptomatology emerged, with most demonstrating resistance (50%), and mild symptomatology with recovery (36%). Only a small proportion of individuals (3%) had trajectories of chronic dysfunction. Alcohol misuse at each wave predicted an increase in PTSD symptomatology across each of the trajectory groups.

Goals/Milestones

- CY15-16 Goals:** Descriptive analyses/publications Wave 5 Data collection
 Preparations for Wave 6 Data collection Genetics repository
 Provision of Support for Secondary Translational Projects
- CY16-17 Goals:** Descriptive analyses/publications Wave 6 Data collection
 Preparations for Wave 7 Data collection Genetics repository
 Provision of Support for Secondary Translational Projects
- CY17-18 Goals:** Descriptive analyses/publications Wave 7 Data collection
 Preparations for Wave 8 Data collection Genetics repository
 Provision of Support for Secondary Translational Projects
- CY18-19 Goals:** Descriptive analyses/publications Wave 8 Data collection
 Preparations for Wave 9 Data collection Genetics repository
 Provision of Support for Secondary Translational Projects
- CY19-20 Goals:** Descriptive analyses/publications Wave 9 Data collection
 Genetics repository Provision of Support for Secondary Translational Projects

Comments/Challenges/Issues/Concerns

- Due to delays in changing back to our former opt-out recruitment methodology, enrollment in to the Wave 7 and Wave 8 DC was lower than expected, impacting enrollment and expenditures.

Budget Expenditure to Date (Expenditures below include expenses through May 2020)

Projected Expenditure: \$6,398,612

Actual Expenditure: \$5,674,615

9. APPENDICES:

Reprints of all published articles that resulted from this award, as well as all posters that were presented at scientific conferences, are included with this report. We have also included a short summary of findings from each publication.

In addition, slides from the 2020 SAB are included.

Latent dimensions of posttraumatic stress disorder and their relations with alcohol use disorder

Tracey L. Biehn^{1,2} · Ateka A. Contractor^{2,9} · Jon D. Elhai^{2,3} · Marijo Tamburrino⁴ · Thomas H. Fine⁴ · Gregory Cohen⁵ · Edwin Shirley⁶ · Philip K. Chan⁶ · Israel Liberzon⁷ · Joseph R. Calabrese⁸ · Sandro Galea⁵

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Abstract

Purpose The objective of this study was to evaluate the relationship between factors of posttraumatic stress disorder (PTSD) and alcohol use disorder (AUD) using confirmatory factor analysis (CFA) in order to further our understanding of the substantial comorbidity between these two disorders.

Methods CFA was used to examine which factors of PTSD's dysphoria model were most related to AUD in a military sample. Ohio National Guard soldiers with a history of overseas deployment participated in the survey ($n = 1215$). Participants completed the PTSD Checklist and a 12-item survey from the National Survey on Drug Use used to diagnosis AUD.

Results The results of the CFA indicated that a combined model of PTSD's four factors and a single AUD factor fit the data very well. Correlations between PTSD's factors and a latent AUD factor ranged from correlation coefficients of 0.258–0.285, with PTSD's dysphoria factor demonstrating the strongest correlation. However, Wald tests of parameter constraints revealed that AUD was not

more correlated with PTSD's dysphoria than other PTSD factors.

Conclusions All four factors of PTSD's dysphoria model demonstrate comparable correlations with AUD. The role of dysphoria to the construct of PTSD is discussed.

Keywords Posttraumatic stress disorder · Alcohol use disorder · Comorbidity · Confirmatory factor analysis

Introduction

There is substantial comorbidity between posttraumatic stress disorder (PTSD) and alcohol use disorder (AUD) among military personnel and veterans [1]. A review article by Debell and colleagues documented that the comorbidity rate of alcohol misuse among individuals with PTSD ranged from 9.8 to 61.3 % [2]. Alcohol abuse/dependence was the most common comorbid disorder among men with PTSD in the National Comorbidity study [3]. McCauley et al. [3] noted that comorbid PTSD and substance use are

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often associated with a more complex and costly clinical course when compared with either disorder alone, and alcohol misuse among veterans has been shown to be associated with greater rates of spousal abuse [4], job performance problems, and legal problems [5]. Given the high rates of comorbid PTSD and lifetime AUD and its associated cost and dysfunction, we sought to examine which factors of PTSD are most related to AUD at the latent level to further our understanding of their comorbidity. The dysphoria model [6], a model based on the PTSD symptoms from the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)* [7] was used in the present study.

Relationship between PTSD and AUD

The self-medicating theory of substance use disorders is often used to explain the high PTSD–AUD comorbidity rates [8]. This theory proposes that some individuals use alcohol to cope with distressing symptoms of PTSD. There is a great deal of support for this theory as applied to PTSD and AUD, which is reviewed by Stewart [9] and McCauley et al. [4]. Stewart [9] notes that the majority of studies find that PTSD symptoms tend to precede alcohol abuse problems and that individuals with comorbid PTSD–AUD report perceiving a causal relationship between PTSD symptoms and their later development of alcohol problems. A treatment study by Hien et al. [10] supports the self-medicating theory. In this study participants who saw an improvement in their PTSD symptoms also had improvements in their substance use, but participants who had improvements in their substance use did not have a corresponding improvement in their PTSD symptoms.

Studies examining the comorbidity between AUD and PTSD often conceptualize the effect of alcohol use on different PTSD symptoms clusters. For instance, McFall et al. [11] found that Vietnam combat veterans' alcohol problems had a significantly positive correlation with the severity of PTSD's hyperarousal symptoms ($r = 0.34$). A review article by Stewart [9] suggests that alcohol may be used to self-medicate to cope with negative affectivity and guilt associated with PTSD. The study by McFall and colleagues [11] found that cognitive reexperiencing was significantly correlated with drinking behavior ($r = 0.25$), but Saladin et al. [12] found that there was no significant difference in the number of reexperiencing symptoms reported by individuals with comorbid PTSD and alcohol abuse compared to individuals presenting with PTSD only. Given the discrepant findings between the relationship between PTSD's factors and alcohol misuse/abuse, further study is necessary to understand the relation between the components of PTSD and drinking behavior.

PTSD's factor structure

PTSD's dysphoria model [6] was used in the current study to conceptualize PTSD's structure rather than PTSD's emotional numbing model [13]. This model of PTSD has garnered substantial theoretical and empirical support [14, 15] and is consistent with theory indicating a general negative affectivity component underlying most affective disorders [16]. A recent meta-analysis of PTSD models found that the dysphoria model fits somewhat better than other models [15] and this model of PTSD was also demonstrated superior fit in a military sample [17]. Therefore, this study focused solely on the dysphoria model since the dysphoria factor is more distress related and is thus more amenable to exploring relations within psychopathology.

The four-factor dysphoria model is identical to the *DSM-IV* [7] model of PTSD, with the exception of two important distinctions: (1) the avoidance and numbing symptom clusters are split into separate symptom clusters and (2) three hyperarousal symptoms (difficulty sleeping, difficulty concentrating, and irritability) are combined with the five numbing symptoms forming the dysphoria symptom cluster (see Table 1). It is important to note that this study assessed subjects for the symptoms of PTSD from the fourth edition of the *DSM* and that significant changes were made to PTSD's diagnostic criteria in the fifth and most recent edition of the *DSM* [18]. In the *DSM-5* there are 20 PTSD symptoms that are placed into four different symptom clusters that more closely resemble the emotional numbing model [13].

There has been an ongoing debate about whether PTSD's dysphoria factor captures PTSD's non-specific distress, possibly explaining its comorbidity with other distress-based internalizing disorders [6, 16, 19, 20]. We extended the aforementioned line of inquiry to assess if PTSD's dysphoria would possibly explain comorbidity with an externalizing behavior such as AUD; this has been rarely researched in the literature to our knowledge [19].

Current study

The purpose of this study was to analyze a combined confirmatory factor analysis (CFA) model of PTSD and AUD to further examine the correlations between the AUD and PTSD factors. We were particularly interested if PTSD's dysphoria factor demonstrated a significantly greater correlation with AUD compared to other PTSD factors, which would be consistent with previous research highlighting dysphoria's strong correlation with other measures of psychopathology [6, 19–21] or if PTSD's specific factors correlate more strongly with AUD which would be consistent with previous literature examining the relationship between PTSD and AUD [11, 12]. Due to the

Table 1 Item mappings for *DSM-IV* and the dysphoria PTSD models; and the dysphoria factor loadings

PTSD symptom	DSM-IV	Dysphoria	Dysphoria factor loadings
B1: Intrusive thoughts	R	R	0.825
B2: Nightmares	R	R	0.824
B3: Reliving trauma	R	R	0.797
B4: Emotional cue reactivity	R	R	0.821
B5: Physiological cue reactivity	R	R	0.825
C1: Avoidance of thoughts	A/N	A	0.827
C2: Avoidance of reminders	A/N	A	0.818
C3: Trauma-related amnesia	A/N	D	0.518
C4: Loss of interest	A/N	D	0.768
C5: Feeling detached	A/N	D	0.810
C6: Feeling numb	A/N	D	0.763
C7: Hopelessness	A/N	D	0.588
D1: Difficulty sleeping	H	D	0.792
D2: Irritable/angry	H	D	0.814
D3: Difficulty concentrating	H	D	0.810
D4: Overly alert	H	H	0.838
D5: Easily startled	H	H	0.884

R Reexperiencing, A Avoidance, N Numbing, H Hyperarousal, D Dysphoria

scant and mixed findings regarding the relationship between AUD and PTSD's factors, no specific hypotheses are made regarding which PTSD factors (if any) will show the strongest correlation with AUD.

This study further investigated a mediation model in which AUD was a mediator of relations between (1) PTSD's hyperarousal and dysphoria factors, and (2) PTSD's reexperiencing and dysphoria factors. Research highlights a strong relation between AUD and PTSD's re-experiencing symptoms [22, 23]. A study by Maguen et al. [24] found that PTSD's re-experiencing symptoms were the only significant predictor of post-deployment problematic drinking. Research also highlights a strong relation between problematic alcohol use and PTSD's hyperarousal symptoms [11, 12]. People may consume alcohol to reduce physiological reactivity associated with PTSD's hyperarousal symptoms [9, 22, 23, 25–28], to dampen symptoms such as exaggerated startle [26, 29], and to reduce negative affect related to sleep difficulties which are a part of PTSD's hyperarousal symptoms [30].

Thus, individuals may consume alcohol to cope with PTSD's re-experiencing [9, 26, 31] or hyperarousal symptoms [9, 22, 25–28]; this may in turn influence PTSD's dysphoria symptoms [9, 14]. Thus, we hypothesized that AUD would mediate the relationship between hyperarousal and dysphoria and between reexperiencing and dysphoria. We did not focus on PTSD's avoidance symptoms when assessing mediation models based on research indicating that PTSD's avoidance symptoms do not significantly relate with problematic alcohol use [11,

12]. In fact, the study by Simons et al. [26] found the weakest correlation between hazardous drinking and PTSD's avoidance symptoms.

Methods

Participants and procedures

The present study was part of the Ohio Army National Guard Mental Health Initiative, a large-scale epidemiological study of mental health among National Guard soldiers in Ohio. All members of the Ohio National Guard who were active between July 2008 and February 2009 were invited to participate in the telephone interview portion of the study. There were 12,225 Guard members with a valid mailing address who were invited to participate (345 individuals were excluded for having no mailing address). Among the pool of potential subjects, 1013 (8.3 %) declined to participate, 1130 (10.1 %) did not have a telephone number listed with the Guard, and 3568 (31.8 %) did not have a correct or working phone number. Among the remaining 6514 Guard members (58.1 %), the following individuals were excluded: 187 (2.8 %) based on age eligibility restrictions, 1364 (20.9 %) declined to participate, 31 (0.4 %) for having English language or hearing difficulties, and 2316 (35.5 %) for not being contacted before the cohort was closed to new recruitment. There were 1243 trauma-exposed subjects with a history of overseas deployment. Twenty-eight subjects were excluded for not completing

Table 2 Demographic information

Total number of participants	<i>n</i> = 1215
<i>Demographic variables</i>	
Age	<i>M</i> = 33.1 years (SD = 8.7)
Male	1103 (90.8 %)
Caucasian	1084 (89.2 %)
Hispanic	16 (1.3 %)
Working full-time	840 (69.1 %)
Working part-time	98 (8.1 %)
Unemployed	177 (14.6 %)
Student	77 (6.3 %)
Household income >\$80,000	324 (26.7 %)
<i>Military variables</i>	
Time served in military	<i>M</i> = 12.6 years (SD = 7.7)
Number of deployments	<i>M</i> = 2 (SD = 1.8)
Most recent deployment was to Iraq or Afghanistan	716 (58.9 %)
Most recent deployment was to an area of non-conflict	480 (39.5 %)
<i>Trauma variables</i>	
Exposed to combat	963 (79.3 %)
Experiencing the sudden unexpected death of a loved one or close friend	837 (68.9 %)
Witnessing someone killed/injured	672 (55.3 %)
Witnessing severe human suffering	572 (47.1 %)
Being in a fire or explosion	542 (44.6 %)
<i>Index trauma</i>	
Combat exposure	618 (50.9 %)
Experiencing the sudden unexpected death of a loved one or close friend	68 (5.6 %)
Witnessing someone killed/injured	62 (5.1 %)

the AUD items leaving an effective dataset of 1215. See Table 2 for demographic information.

The National Guard Bureau, Office of Human Research Protections of the U.S. Army Medical Research and Materiel Command, along with several affiliated hospital and university institutional review boards (University Hospitals Case Medical Center, University of Toledo, Columbia University, and University of Michigan), approved the study, with written informed consent waived in lieu of verbal consent by telephone.

Instrumentation

A computer-assisted telephone interview was conducted for all participants by trained professionals. Demographic characteristics and mental health functioning were assessed using standardized questionnaires.

PTSD checklist (PCL)

Participants completed the PCL based on their most distressing military trauma. The PCL was adapted so that participants were asked to anchor their PTSD ratings to one's self nominated worst deployment trauma. The PCL is a self-report measure that maps onto the 17 *DSM-IV* [7]

PTSD symptom criteria. Respondents indicate how distressed they were by each symptom over the past month using a five-point Likert-type scale; however, in our study we assessed lifetime symptoms. The PCL has demonstrated adequate reliability ($\alpha = 0.94$; test-retest $r = 0.88$) in various trauma-exposed populations [32] and total scores were found to highly correlate with those from structured PTSD diagnostic interviews ($r_s = 0.8$ – 0.9) in military veterans [33]. In the current sample, the PCL was found to be very reliable ($\alpha = 0.95$). Cronbach's alpha for subscale scores ranged from 0.80 (avoidance) to 0.91 (reexperiencing). The average PCL score in the present sample was 28.30 (SD = 13.78). There were 123 participants (10.1 %) with PCL scores greater than 50, indicating probable PTSD diagnosis [34].

Alcohol use disorder

The AUD behaviors were measured from modules used in studies from the National Survey on Drug Use and Health [35]. The items inquired about lifetime use, age of first use, and use since last deployment. There were 12 items that directly assessed AUD according to *DSM-IV* criteria and were used in the CFA analyses. Respondents answered yes/

no to these 12 questions. Each of the 12 items mapped onto the one factor AUD factor. Cronbach's alpha for this measure was 0.80.

Analysis

There were nominal amounts of missing data from the PCL and AUD items. Missing data were estimated with Mplus 6.1 software [36] to derive parameter estimates using full information maximum likelihood (ML) procedures with a pairwise present estimation [37]. Results of univariate and multivariate non-normality assessment indicated several PCL and AUD items with skewness values greater than 2 and kurtosis values greater than 7; this indicated a non-normal univariate distribution. Further, Mardia's multivariate skewness and kurtosis tests indicated a non-normal multivariate distribution ($p < 0.001$). The primary analyses consisted of the following three steps.

Confirmatory factor analysis (CFA)

CFA analyses were conducted using Mplus 6.1 software. Error covariances were fixed to zero, and factor variances were fixed to 1 to scale the factors within a model. All tests were two-tailed. Goodness of fit indices are reported below, including the comparative fit index (CFI), Tucker Lewis Index (TLI), and root mean square error of approximation (RMSEA). Models fitting very well (or adequately) are indicated by CFI and TLI ≥ 0.95 (0.90–0.94), and RMSEA ≤ 0.06 (0.07–0.08) [38].

CFA analyses for the PCL were conducted using maximum likelihood estimation with a mean-adjusted Chi square (MLM) (the Satorra-Bentler Chi square value), which is robust to non-normality [39]. In the first CFA, we examined PTSD's dysphoria model (see Table 1). The PCL items were treated as continuously scaled items. Next, the items of the AUD measure were all specified to load onto a one-factor AUD factor. The AUD items were dichotomous; so weighted least squares estimation with a mean-and variance-adjusted Chi square (WLSMV) was used for estimation as this is the preferred method of estimation for dichotomous data [40, 41]. WLSMV uses a tetrachoric covariance matrix and probit coefficients. A CFA was then conducted to examine the combined PTSD dysphoria and AUD model also using WLSMV for estimation, with all factors allowed to correlate.

Wald tests

Wald tests were used to test the latent-level relations between alcohol usage and PTSD's factors. They assess the null

hypothesis that the difference between two correlation paths is zero.

Mediation

Finally, regression analyses were computed in Mplus in which AUD was tested as a mediator of hyperarousal and dysphoria and of reexperiencing and dysphoria. Mediation analyses used the product of path coefficients approach, which is a recommended alternative to the Baron and Kenny [42] approach. The indirect effect test statistic is divided by its standard error (estimated using the delta method) to compare the obtained value to a standard normal distribution [43]. Additionally, the current study used the bootstrap method to estimate standard errors, which computed indirect effects and their standard errors in 5000 bootstrapped samples. The indirect effect is represented as the effect of PTSD's dysphoria on PTSD's hyperarousal/intrusion factor taking into account the effect of the AUD factor. Direct effects were analyzed between all factors as well.

Results

The results from the CFA of the PTSD dysphoria model indicate that the data fit the model well, $\chi^2(113) = 564.22$, RMSEA = 0.06, CFI = 0.94, TLI = 0.93. Table 1 provides the standardized factor loading for the dysphoria model and Table 3 provides the factor correlations.

The one-factor AUD model also fits the data well, $\chi^2(54) = 216.07$, RMSEA = 0.06, CFI = 0.97, TLI = 0.96. Standardized factor loadings for the one-factor AUD model ranged from 0.66 to 0.87 with the exception of one item with a factor loading of 0.46. The five factor PTSD–AUD model demonstrated excellent fit, $\chi^2(367) = 606.05$, RMSEA = 0.02, CFI = 0.97, TLI = 0.97.

The correlations between the PTSD factors and AUD factor were examined. All PTSD factors showed correlations between 0.258 and 0.285 and all correlations were significant at the $p \leq .001$ level. The AUD factor correlated most strongly with PTSD's dysphoria factor

Table 3 Correlations among PTSDs factors

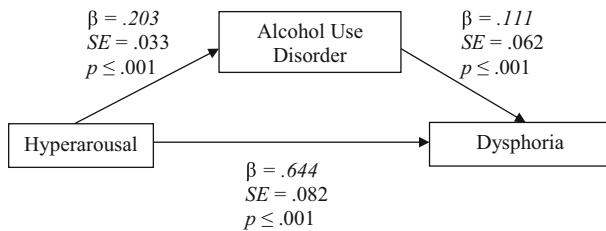
	R	A	D	H
R	–	0.908	0.864	0.803
A		–	.863	0.761
D			–	0.792
H				–

R Reexperiencing, A Avoidance, D Dysphoria, H Hyperarousal

Table 4 Wald's chi-square test results

Correlation between factors	<i>r</i> value	Wald's Chi-square
Alcohol use disorder with reexperiencing	$r = 0.276^*$	$\chi^2 (1) = 0.224, p = .636$
Alcohol use disorder with dysphoria	$r = 0.285^*$	
Alcohol use disorder with avoidance	$r = 0.277^*$	$\chi^2 (1) = 0.099, p = .753$
Alcohol use disorder with dysphoria	$r = 0.285^*$	
Alcohol use disorder with hyperarousal	$r = 0.258^*$	$\chi^2 (1) = 0.990, p = .320$
Alcohol use disorder with dysphoria	$r = 0.285^*$	

* $p \leq .001$



Model Indirect Effect: $\beta = .023$, 95% CI = .010 - .038, $p \leq .001$

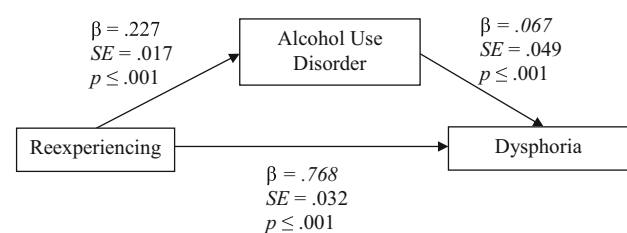
Fig. 1 Mediation results of alcohol use disorder as a mediator between hyperarousal and dysphoria. Model indirect effect: $\beta = 0.023$, 95 % CI = 0.010–0.038, $p \leq .001$

($r = 0.285$) and the hyperarousal factor showed the weakest correlation with AUD ($r = 0.258$). However, in terms of statistical tests Wald's Chi square tests indicated AUD was no more correlated with PTSD's dysphoria than other PTSD factors (see Table 4). In other words, despite the larger correlation between AUD and dysphoria, this correlation is not statistically greater compared to other PTSD factors with AUD.

Results of mediation analyses indicated that the AUD factor significantly mediated the relation between PTSD's hyperarousal and dysphoria factors ($\beta = 0.023$, $SE = 0.006$, $p \leq .001$). All direct effects between hyperarousal, AUD, and dysphoria were significant at the $p \leq .001$ level (Fig. 1). Similar results were obtained for the mediation model in which AUD was tested as a mediator between PTSD's reexperiencing and dysphoria factors. Specifically, the model was significant ($\beta = 0.015$, $SE = 0.005$, $p = .002$). All direct effects between hyperarousal, AUD, and dysphoria were significant at the $p \leq .001$ level (see Fig. 2).

Discussion

Using data from a sample of 1215 military veterans we found excellent fit for the five-factor PTSD–AUD model. Wald test results showed no significant differences between AUD and PTSD's dysphoria factor compared to AUD's



Model Indirect Effect: $\beta = .015$, 95%: CI = .006 - .025, $p = .002$

Fig. 2 Mediation results of alcohol use disorder as a mediator between reexperiencing and dysphoria. Model indirect effect: $\beta = 0.015$, 95 %: CI = 0.006–0.025, $p = .002$

relation with other PTSD dysphoria model factors; all PTSD dysphoria model factors significantly and positively correlated with AUD. Noteworthy is that the AUD factor significantly mediated the relation between PTSD's hyperarousal/re-experiencing factors and PTSD's dysphoria factor.

PTSD's dysphoria factor

Results of the current study did not support dysphoria as having a significantly stronger relation with AUD compared to other PTSD factors, contradictory to some prior findings in the literature [11, 19]. Findings, however, are consistent with studies indicating that dysphoria symptoms may not represent PTSD's non-specific symptoms and may not account for PTSD's comorbidity with other disorders [44, 45].

There could be some explanations for differences between the current study's findings compared to prior studies. First, our study focused on alcohol usage rather than a broader substance usage variable in prior studies [19]. Second, our sample included a veteran cohort, which is different than prior studies [12]. Third, prior studies did not assess alcohol as a latent factor and instead used item level measurements for their calculations.

Comorbidity between alcohol usage and PTSD may actually be better captured by several PTSD factors functioning concurrently, rather than primarily by one PTSD

factor [19]. An avenue for future research could be to look at additive effects of the PTSD factors as they relate to AUD. It could be speculated that dysphoria may explain PTSD's comorbidity with more internalizing conditions such as depression [46–48] rather than externalizing conditions such as AUD. Understanding what PTSD factor may drive the PTSD-externalizing behavior relation is another avenue for future research.

Previous studies have documented strong support for a 5-factor model of PTSD that separates the dysphoria factor into two separate factors (numbing and dysphoric arousal) [49]. Several studies have found that separating the dysphoria factor into two separate factors results in a better fit [50, 51] and suggests that the general distress component of PTSD may actually be comprised of distinct factors. Future research examining the relations between PTSD's dysphoria factor and AUD should further examine the dysphoric arousal and anxious arousal components of PTSD in an effort to determine what role these factors may play in the relationship between PTSD and AUD. Additionally, newer models of PTSD based on the 20 PTSD symptoms from the *DSM-5* should also be examined including 6-factor models proposed by Liu and colleagues [52] Tsai et al. [53] and a hybrid 7-factor model proposed by Armour et al. [54]. Research examining these models have the potential of further elucidating the role of dysphoria with regards to the onset and maintenance of AUD as these models break dysphoria down into various factors such as anhedonia, negative affect, and dysphoric arousal.

Role of alcohol usage in PTSD symptomatology

The self-medication theory [9] has long highlighted the role of substance use in PTSD's symptomatology; the current study added to the theory by highlighting the specific role of AUD in relation to PTSD's latent factors (corresponding to PTSD's symptom dimensions) using statistically superior methods. In fact, past research with the self-medication theory has mainly looked at the alcohol use-PTSD relation with distress as an external construct. We have considered PTSD's inherent distress as represented by PTSD's dysphoria factor which is unique in the existing literature.

Findings indicate that veterans may resort to alcohol to cope with PTSD's hyperarousal and re-experiencing symptoms [9, 11, 55]. Our study further indicates that increase in dysphoria severity (representing PTSD's distress) may relate to alcohol use. It is possible that alcohol use may relate to decreases in dysphoria symptom severity in the short-run [28], but may then relate to increases in dysphoria symptom severity in the long-run [9]. Such temporal sequencing and time-related differences were not

captured in the current study; this is an important avenue for future research.

Noteworthy is the possibility that alcohol use may have an impulsive quality, highlighting its "emotional dysregulation" tendency in PTSD symptomatology [56]. Given impulsivity's well-established relation with PTSD [56] and alcohol usage [57], one could hypothesize that alcohol use may possibly represent an *impulsive* strategy to cope with PTSD's re-experiencing and hyperarousal symptoms, mainly reducing negative emotional states immediately [58, 59].

Implications and future research

The results of the current study have several clinical and theoretical implications. First, it highlights the importance of addressing alcohol use as a component of trauma-based treatment [10, 60]. Second, alcohol use with its significant correlation with all PTSD latent factors and its functional role in PTSD symptomatology supports existing literature on treatment of comorbid PTSD-substance usage [61]. Third, alcohol use may relate to increased distress, although the intention to drink alcohol may be to reduce negative affect. Analyzing such a question with longitudinal data and assessing for factors that explain this particular mechanism are important areas of further research.

Lastly, PTSD's dysphoria, although not accounting for PTSD's comorbidity with alcohol usage compared to other PTSD dysphoria model factors, may capture PTSD's non-specific distress when conceptualizing alcohol's function of coping with PTSD's re-experiencing and hyperarousal symptoms. Future studies could extend this path analyses framework with additional variables of coping styles and other substances of use.

Limitations

The current study is not without limitations. First, use of cross-sectional data for mediation analyses does not indicate any causal mechanisms [42]. The current study's significant results justify further time and effort to pursue similar mediation analyses longitudinally [62]. Second, use of self-report measures may reflect social desirability effects; future research could additionally use clinician-administered measures. Third, the alcohol use measure was not a standardized instrument, possibly reducing the validity of findings. Finally, it is unclear how well these results will generalize to a civilian trauma sample.

Despite these limitations, the current study has several strengths such as a representative sample of the Ohio Army National Guard with a relatively high prevalence of PTSD and AUD; [63] use of a statistically superior method of

factor-level analyses; [16] and results highlighting possible functional role of AUD in PTSD symptomatology.

Compliance with ethical standards

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Mental Health Over Time in a Military Sample: The Impact of Alcohol Use Disorder on Trajectories of Psychopathology After Deployment

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To identify trajectories of depression and posttraumatic stress (PTS) symptom groups after deployment and determine the effect of alcohol use disorder on these trajectories, depression symptoms were modeled using the 9-item Patient Health Questionnaire in 727 Ohio National Guard members, and PTS symptoms were modeled using the PTSD Checklist in 472 Ohio National Guard members. There were 55.8% who were resistant to depression symptoms across the 4 years of study, and 41.5% who were resistant to PTS symptoms. There were 18.7% and 42.2% of participants who showed resilience (experiencing slightly elevated symptoms followed by a decline, according to Bonanno et al., 2002) to depression and PTS symptoms, respectively. Mild and chronic dysfunction constituted the smallest trajectory groups across disorders. Marital status, deployment to an area of conflict, and number of lifetime stressors were associated with membership into different latent groups for depression (unstandardized β estimates range = 0.69 to 1.37). Deployment to an area of conflict, number of lifetime traumatic events and education predicted membership into different latent groups for PTS (significant unstandardized β estimate range = 0.83 to 3.17). AUD was associated with an increase in both symptom outcomes (significant unstandardized β estimate range = 0.20 to 9.45). These results suggested that alcohol use disorder may have contributed substantially to trajectories of psychopathology in this population.

It is well established that posttraumatic stress (PTS) and depression are more prevalent in military (Thomas et al., 2010) compared to civilian (Kessler et al., 2005) populations. Posttraumatic stress disorder (PTSD) prevalence estimates among Operation Enduring Freedom (OEF) and Operation Iraqi

Freedom (OIF) veterans range from about 5% to 20% (Kok, Herrell, Thomas, & Hoge, 2012; Ramchand et al., 2010; Smith et al., 2008); depression prevalence estimates range from about 2% to 16% (Tanielian & Jaycox, 2008; Wells et al., 2010). The experiences of OEF/OIF veterans suggest that the trajectories, or paths followed over time, of these disorders may reflect life-course civilian and combat experiences that depart from those of previous generations (Bonanno et al., 2012). Trajectories of mental health over time, however, have been predominately studied in civilian populations following specific traumatic event (TE) experiences (Lowe, Galea, Uddin, & Koenen, 2014; Nandi, Tracy, Beard, Vlahov, & Galea, 2009; Pietrzak, Van Ness, Fried, Galea, & Norris, 2013). Generally these trajectory groups include resilient (initial symptomology followed by a decline), resistant (consistently low or no symptomology), chronic dysfunction (consistently high symptomology), and typically one or two other groups of either increasing or stable mild symptoms (Bonanno et al., 2012; Norris, Tracy, & Galea, 2009).

We also know that alcohol use disorder (AUD) is prevalent among military personnel (Bray et al., 2010; Cohen, Fink,

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Sampson, & Galea, 2015), possibly due to efforts to self-medicate existing mental illness symptoms (Schumm & Chard, 2012). Although AUD frequently coexists with psychopathology in military populations (Thomas et al., 2010), we do not know how it interacts with trajectories of depression and PTS over time. There is a lack of longitudinal follow-up research among OEF/OIF veterans in general (Hoge, Auchterlonie, & Milliken, 2006), with few exceptions (Duma, Reger, Canning, McNeil, & Gahm, 2010; Milliken, Auchterlonie, & Hoge, 2007; Schaller et al., 2014; Seal et al., 2009; Thomas et al., 2010). Further, we are not aware of any published work that has documented trajectories of both depression and PTS in OEF/OIF personnel in a single U.S. study. We aimed to document trajectories of symptoms after deployment among OEF/OIF personnel, and to estimate how time-stable risk factors and time-varying covariates, including AUD, affected these trajectories across four waves of cohort data.

Method

Participants and Procedure

Participants were drawn from the Ohio Army National Guard using a simple random sample as part of the Ohio Army National Guard Mental Health Initiative (OHARNG MHI), drawn from all serving members between 2008 and 2009. After eliminating members who declined to participate, who did not have a valid telephone number, or who were deemed ineligible due to age, retirement status, or language, the official enrollment at baseline was 2,616, with a cooperation rate of 67.5% and a response rate of 43.2%. Detailed information on sampling methods are described elsewhere (Calabrese et al., 2011).

Respondents were interviewed from 2008–2012, with approximately 12 months between interviews for all subjects. A second round of baseline interviews for new participants ($n = 578$) was also initiated in 2010–2011 to replenish the sample after loss to follow-up. Every respondent included in this analysis participated in at least two waves. The final analytic samples consisted of 727 respondents for depression (those who completed two or more study waves, were deployed in the past 2 years from baseline assessment, and were nonmissing on all risk factors), and 472 respondents for PTS (those who completed two or more study waves, were nonmissing on all risk factors, had a TE during a deployment within 2 years of baseline assessment, and chose that same event as their “worst” event throughout all follow-up interviews, in order to consistently follow symptoms from the same event).

Table 1 presents the prevalence of risk factors for both analytical samples, as well as the percentage of respondents who completed each wave. The demographics of the analytical samples largely matched those of the entire OHARNG MHI sample, with the exception of a lower prevalence of female respondents in both of the analytical samples (not shown), which reflected the fact that our samples included only those who had been deployed within

2 years, and women tend to be deployed less frequently (Tanielian & Jaycox, 2008).

We ran additional analyses comparing respondents who completed all four waves with those who were lost to follow-up on risk factors, covariates, and outcomes. For the depression analytic sample, we found that married soldiers were more likely to have completed all waves ($p = .016$). The mean number of depression symptoms at baseline, however, was not associated with follow-up completion, so we were not concerned about potential respondent bias. For the PTS analytic sample, complete follow-up was not associated with any risk factors, time-varying covariates, or PTS symptoms at baseline (results not shown).

An alert letter with an opt-out was sent to all listed participants, and verbal informed consent was obtained from all participants prior to participation. Interviews (about 60 min in length) were administered via a computer-assisted telephone survey.

The Ohio National Guard and the institutional review boards of University Hospitals Case Medical Center, University of Toledo, University of Michigan, Ann Arbor Veterans Administration Medical Center, Columbia University, Boston University, and the Office of Human Research Protections of the U.S. Army Medical Research and Materiel Command approved this study protocol.

Measures

Depression symptoms were scored using a symptom count (0–9) from the Patient Health Questionnaire (PHQ; Kroenke, Spitzer, & Williams, 2001); symptoms present at all (in a yes/no format) during the last 30 days for at least 2 weeks were counted as positive. PTS symptoms were scored using the PTSD Checklist-Civilian Version (PCL), which includes 17 items, each scored from 1 = *not at all* to 5 = *extremely*, resulting in a range of 17 to 85 (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996). PTS symptoms had a Cronbach's α of .94 at baseline in our analytic sample.

Time-stable risk factors (assessed only at baseline) and time-varying covariates (collected at each time point) were selected for inclusion based on theoretical considerations, significance of terms when entered into models, and model convergence.

TEs were assessed with the Life Events Checklist-Civilian Version (Gray, Litz, Hsu, & Lombardo, 2004), the Deployment Risk and Resilience Inventory items (King, King, Vogt, Knight, & Samper, 2006), and events used by Breslau et al. (1998). Events could have occurred either during or outside of the most recent deployment. These were all events that met Criterion A1 for the definition of a TE according to the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.; *DSM-IV-TR*; American Psychiatric Association [APA], 2000); the full list of which are presented in the first part of Supplemental Table 1. A binary variable for a high level of TEs was created

Table 1
Baseline Prevalence of Risk Factors and follow-up completion by Subsample

Variable	Depression subsample (<i>n</i> = 727)		PTS subsample (<i>n</i> = 472)	
	<i>n</i>	%	<i>n</i>	%
Completed wave 2	628	86.4	412	87.3
Completed wave 3	478	65.8	304	64.4
Completed wave 4	395	54.3	252	53.4
Not married	332	45.7	212	44.9
High school/GED or less	173	23.8	109	23.1
10+ lifetime TEs	335	46.1	284	60.2
4+ lifetime stressful events	345	47.5	235	49.8

Note. PTS = posttraumatic stress; GED = general education development (degree); TEs = traumatic events.

using the median (10) of the count of total TEs in the sample. Stressors were events from the above-stated instruments that did not qualify for Criterion A1, and are presented in the second half of Supplemental Table 1. A binary variable for high level of stressors was also created using the median (4) of the count in the sample.

Being deployed to an area of conflict (AOC) was defined as deployment to either Iraq or Afghanistan during the most recent deployment at baseline. Considering everyone in this sample was deployed within 2 years of baseline, these deployments were to OEF/OIF. Low education was defined as having a high school diploma, general education development diploma, or less.

AUD was defined as having either past-year abuse or dependence according to the *DSM-IV-TR* (APA, 2000), as assessed by the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998). Alcohol abuse and dependence were both validated among a random sample of 500 soldiers from the original baseline sample assessed by trained clinicians (Calabrese et al., 2011).

PTSD as a time-varying covariate (for TEs that occurred both in and outside of deployment) was defined as meeting criteria for past-year PTSD, according to the *DSM-IV-TR* using the PCL (Blanchard et al., 1996), which was validated using the Clinician-Administered PTSD Scale in the clinical sample described above and found to have high sensitivity (.92) and moderate specificity (.54; Prescott et al., 2014).

Past-year depression as a time-varying covariate was defined as reporting a period of at least 2 weeks with two or more co-occurring symptoms on the PHQ-9 (Kroenke et al., 2001), with one symptom being depressed mood or anhedonia. This definition included, but was not limited to, the *DSM-IV-TR* diagnosis of major depressive disorder. This inclusive definition was chosen due to higher sensitivity relative to major depressive disorder by itself (.51 compared to .35; both had specificity greater than .82) when validated against the Structured Clinical Interview for DSM-IV-TR (SCID; First, Spitzer, Gibbon, & Williams, 2002) in the clinical sample (Prescott et al., 2014).

Cumulative TEs were defined as reporting at least one TE (from deployment or not) since last study wave. For all participants, cumulative TEs at baseline were coded as zero to avoid colinearity with the time-stable measure of baseline TE count.

Data Analysis

Proc Traj, a SAS-callable add-on package that estimates discrete mixture models for longitudinal data (Jones, Nagin, & Roeder, 2001; Jung & Wickrama, 2008), was used to estimate trajectories in SAS version 9.4. Proc Traj is used for group-based latent class growth analysis, which fixes within-group variance to zero to more clearly identify latent classes (existing but not yet manifested) and therefore serves as a more hypothesis-generating method compared to more conventional growth modeling approaches (Jung & Wickrama, 2008). Proc Traj drops respondents who are missing any baseline risk factors from the analysis; consequently, our analytic samples only included participants with nonmissing risk factors (*n* = 727 for depression and *n* = 472 for PTS). Respondents missing time-varying variables, including outcomes and covariates, are kept in the model, and are estimated using other data points under the assumption that they are missing at random (Nagin, 2009). Because we had loss to follow-up across the four waves (see Table 1), these missing data points were estimated under this assumption.

Past-year depression symptoms were modeled assuming a zero-inflated Poisson distribution (ideal for a highly skewed outcome), and PTS symptoms were modeled assuming a censored normal distribution (considered appropriate for psychiatric scale data; Jones et al., 2001; Nagin & Tremblay, 1999).

Our first step in the analysis was to determine the ideal number of latent groups for each outcome using the Bayesian information criterion (BIC; an approximation of the Bayes factor) and mean posterior probability ($\geq .80$ on average for each group; Andruff, Thompson, Gaudreau, & Louvet, 2009). BIC indices suggested that a model with four groups was most appropriate for both outcomes, and all probabilities for these

models were $\geq .79$ for depression (Supplemental Table 2) and $.84$ for PTS (Supplemental Table 4), showing a high predictive probability. The order and shape of each trajectory was then determined by iteratively assessing the significance of each term. Covariates and risk factors were added to each model one at a time. Finally, predicted symptoms were graphed to specify the difference in predicted trajectory paths based on fixed values of each time-varying covariate (Jones et al., 2001).

Results

Most participants had low levels of depression symptoms throughout the study period. The means of the number of symptoms at each wave were as follows: $M = 1.04$ ($SD = 1.88$), $M = 1.07$ ($SD = 2.02$), $M = 0.92$ ($SD = 1.77$), and $M = 1.02$ ($SD = 2.09$). There were 406 respondents (55.8% of the depression sample) who were resistant to symptoms; 136 (18.7%) were resilient; 93 (12.8%) had a steady increase in symptoms throughout the study period; and 92 (12.7%) had a fairly stable high level of symptomatology throughout (referred to as the chronic dysfunction group). Figure 1 shows a graph of predicted symptoms across the four time points (Supplemental Table 2 presents data points).

Tables 2 and 3 present risk factors and time-varying covariates, respectively, that were significant in the final models, along with their corresponding unstandardized β estimates. For depression, baseline risk factors associated with group membership included marital status, AOC deployment, and lifetime stressors (Table 2). Having four or more lifetime stressors made respondents more likely to fall into the chronic dysfunction (unstandardized $\beta = 1.37$, $p < .001$) and increasing (unstandardized $\beta = 0.69$, $p = .018$) groups. AOC deployment was significantly associated with membership in the chronic dysfunction (unstandardized $\beta = 1.02$, $p < .001$) and resilient

(unstandardized $\beta = 0.92$, $p < .001$) groups. Being unmarried was significantly associated with membership in the resilient group ($\beta = 0.80$, $p = .004$). All of these comparisons are with reference to the resistant group.

For depression, past-year AUD and PTSD both significantly contributed to a change in shape for all four trajectory groups (Table 3). Figure 2 shows the potential effect of AUD on each trajectory (data points presented in Supplemental Table 3). The solid lines represent predicted trajectories of symptoms as they are in Figure 1. The dotted lines represent predicted trajectories of symptoms where past-year PTSD was set to a constant 0 but past-year AUD was set to 1 at every time point. AUD at each point resulted in an increase of the number of symptoms of depression overall. The group affected most by AUD was the mild increasing group (unstandardized $\beta = 0.92$, $p < .001$). The gap between the predicted trajectories of the increasing group widened with time, whereas the resilient group showed a smaller gap between the two potential shapes as more time since deployment passed. The chronic dysfunction and resistant groups both showed the same general shape across time, with a small increase in symptoms.

The means of the PCL at each wave were as follows: $M = 28.92$ ($SD = 13.68$), $M = 25.35$ ($SD = 12.11$), $M = 24.44$ ($SD = 12.42$), and $M = 24.93$ ($SD = 13.93$). We observed a resistant group ($n = 196$; 41.5%), a resilient group ($n = 199$; 42.2%), a mild constant group ($n = 55$; 11.7%), and a chronic dysfunction group ($n = 22$; 4.7%) for PTS. Figure 3 shows a graph of these predicted symptoms across the four time points (data points specified in Supplemental Table 4).

Risk factors at baseline that were associated with group membership for PTS included education, TEs, and AOC deployment (Table 2). Reporting high lifetime TEs was significantly associated with membership in the chronic dysfunction (unstandardized $\beta = 3.17$, $p = .003$) and constant mild (unstandardized

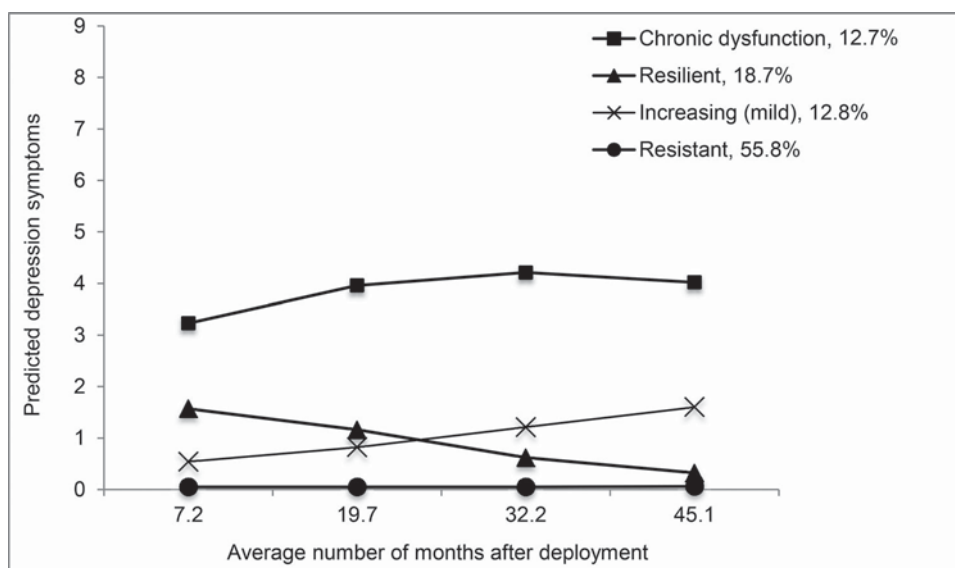


Figure 1. $n = 727$. Predicted trajectories of depression symptoms from the 9-item Patient Health Questionnaire in the depression subsample.

Table 2
Unstandardized β Estimates of Risk Factors by Subsample

Depression subsample ($n = 727$)			PTS subsample ($n = 472$)		
Latent group	Risk factor	Estimate	Latent group	Risk factor	Estimate
Resistant group ($n = 406$)	Referent		Resistant group ($n = 196$)	Referent	
Resilient group ($n = 136$)	Unmarried	0.80*	Resilient group ($n = 199$)	Deployed to AOC	0.52
	Deployed to AOC	0.92*		10+ lifetime TEs	1.54*
	4+ lifetime stressors	0.51		Low education	0.83*
Increasing group ($n = 93$)	Unmarried	-0.16	Constant group ($n = 55$)	Deployed to AOC	1.59*
	Deployed to AOC	0.13		10+ lifetime TEs	2.04*
	4+ lifetime stressors	0.69*		Low education	0.78
Chronic dysfunction group ($n = 92$)	Unmarried	-0.15	Chronic dysfunction ($n = 22$)	Deployed to AOC	1.24
	Deployed to AOC	1.02*		10+ lifetime TEs	3.17*
	4+ lifetime stressors	1.37*		Low education	1.01

Note. AOC = area of conflict; TEs = traumatic events.

* $p < .05$.

$\beta = 2.04, p < .001$) groups. AOC deployment was significantly associated with membership in the mild constant group (unstandardized $\beta = 1.59, p = .001$). Having low education was associated with membership in the resilient group (unstandardized $\beta = 0.83, p = .032$). All of these comparisons are with reference to the resistant group.

AUD, cumulative TEs, and past-year depression were all significantly associated with trajectory shape (Table 3). Figure 4 shows the potential effect of AUD on PTS trajectories (data points are specified in Supplemental Table 5). Holding other

time-varying covariates constant and setting AUD as positive at each time point flattened out the slope of all trajectory groups and produced elevated symptoms for all groups. The mild constant group showed the largest increase (unstandardized $\beta = 9.45, p < .001$ for AUD).

Discussion

Using data from a sample of National Guard service members followed across 4 years after deployment, discrete mixture

Table 3
Unstandardized β Estimates of Parameters and Time-Varying Covariates by Subsample

Depression subsample ($n = 727$)			PTS subsample ($n = 472$)			
Latent group	Parameter	Estimate	Latent group	Parameter	Estimate	
Resistant group ($n = 406$)	Linear	-0.03	Resistant group ($n = 196$)	Alcohol use disorder	6.11*	
	Quadratic	0.00*		Depression	3.57*	
	Alcohol use disorder	0.75*		Cumulative TEs	-1.86	
	PTSD	3.74*				
Resilient group ($n = 136$)	Linear	0.01	Resilient group ($n = 199$)	Linear	-0.15*	
	Quadratic	0.00*		Alcohol use disorder	5.28*	
	Alcohol use disorder	0.51*		Depression	8.32*	
	PTSD	1.41*		Cumulative TEs	-1.30	
Increasing group ($n = 93$)	Linear	0.03*	Constant group ($n = 55$)	Alcohol use disorder	9.45*	
	Alcohol use disorder	0.92*		Depression	14.02*	
	PTSD	-1.99*		Cumulative TEs	1.30	
Chronic dysfunction group ($n = 92$)	Linear	0.03	Chronic dysfunction ($n = 22$)	Alcohol use disorder	5.72	
	Quadratic	0.00		Depression	9.65*	
	Cubic	0.00		Cumulative TEs	4.17*	
	Alcohol use disorder	0.20*				
	PTSD	0.40*				

Note. PTSD = posttraumatic stress disorder; TEs = traumatic events.

* $p < .05$.

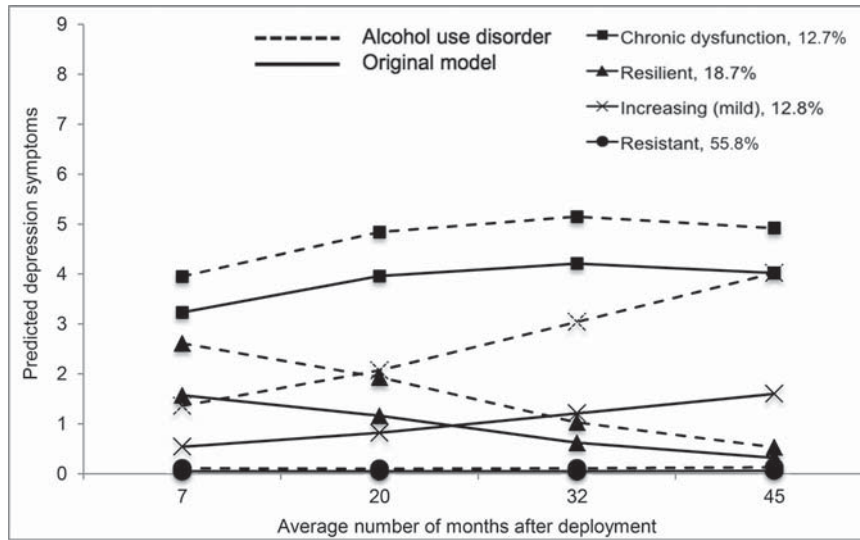


Figure 2. *n* = 727. Potential effect of alcohol use disorder on depression symptoms from the 9-item Patient Health Questionnaire in the depression subsample.

modeling documented four trajectory groups of both depression and PTSD. For both outcomes, the majority of respondents fell into one of the two lowest-symptom groups, supporting previous studies that people are modally resistant to trauma (Bonanno, 2004; Bonanno et al., 2012; Lowe et al., 2014; Nandi et al., 2009). Both Lowe et al. (2014) and Bonanno et al. (2012), using samples exposed to TE experiences, estimated four groups for PTSD as well, including a consistently low-level symptom group and a chronically high group with similar proportions of respondents in each group compared with our findings. Our study is the first, as far as we are aware,

to have shown similar findings in a sample of U.S. military personnel.

We found that a high number of lifetime stressful events was associated with higher-symptom trajectory group membership for depression. Stressful events have been widely known to contribute to poor mental health symptoms in the military (Nash et al., 2010). Our finding that being unmarried was associated with resilience might be explained by a lack of relationship/family stress, which has been shown to contribute to depression outcomes, particularly in military populations (Gibbs, Clinton-Sherrod, & Johnson, 2012; Martin et al., 2013).

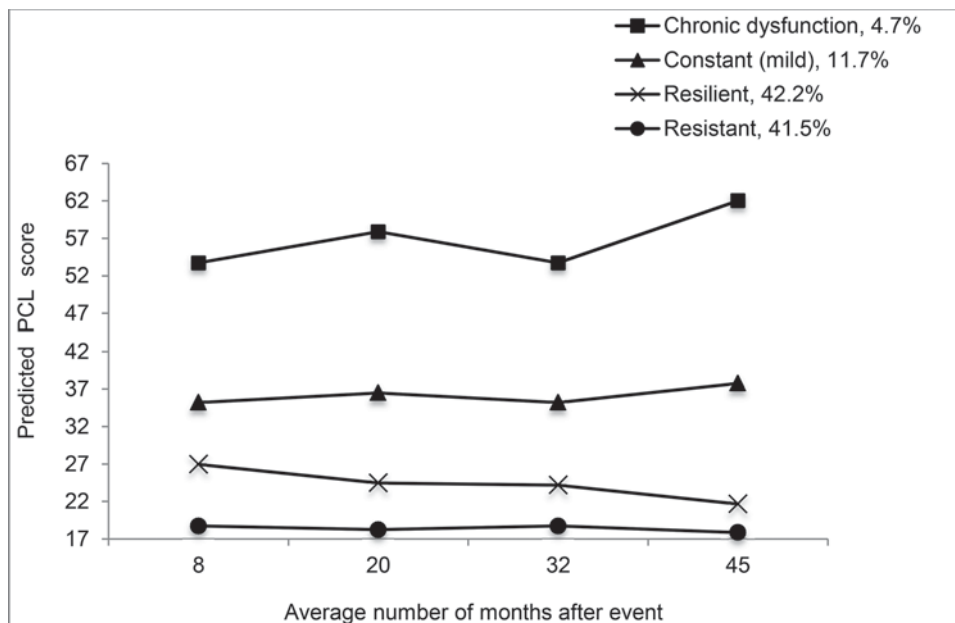


Figure 3. Predicted trajectories of posttraumatic stress symptoms using the Posttraumatic Stress Checklist (PCL) score.

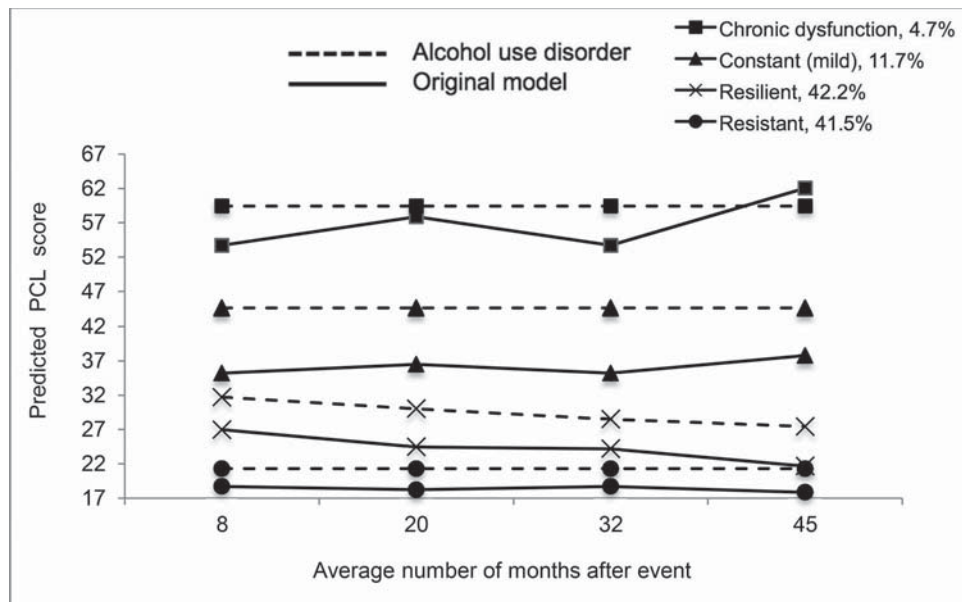


Figure 4. Potential effect of alcohol use disorder on posttraumatic stress symptoms using the Posttraumatic Stress Checklist (PCL) score.

For both trajectory outcomes, we found that soldiers deployed to an AOC were more likely to be in the higher-symptom groups. This is consistent with Hoge et al.'s (2006) findings that service members returning from Iraq or Afghanistan were more likely to have mental health problems compared to those deployed to other locations.

For PTS, we found that experiencing more lifetime TEs was associated with membership in higher-symptom trajectory groups, which agrees with civilian trajectories research (Lowe et al., 2014; Nandi et al., 2009).

AUD at all time points was associated with an increase in both depression and PTS symptoms, with the largest effect seen on the already higher-symptom trajectory groups. For the increasing depression symptom group, the gap between the original predicted trajectory and that with AUD present increased over time, suggesting that the addition of AUD contributed to a steeper increase in symptoms among those with increasing symptoms as more time passed since their initial deployment. In contrast, the depression-resilient group actually showed a smaller gap between the two potential shapes as more time from their deployment passed, suggesting that resilience toward depression symptoms after a deployment experience may put individuals in a better position to be resilient to the effect of AUD on depression as well. Similarly, AUD had the smallest effect on the resistant group for PTS, suggesting that if a respondent reported consistently low PTS symptoms after a traumatic event, the addition of AUD is not likely to change this outcome. In contrast, respondents who are already affected by PTS symptoms were more likely to worsen even more with co-occurring AUD.

These findings that AUD exacerbated both depression and PTS symptom trajectories build on previous literature that comorbidity can substantially, adversely affect outcomes in al-

ready vulnerable populations (Campbell et al., 2007; Guadiano & Zimmerman, 2010; Smith, 2012). Our findings also illustrated how the cumulative effect of AUD may manifest in a higher burden of psychopathology at multiple time points across the study period. This is especially important considering that AUD has been documented as a modifiable risk factor in U.S. service members (Pemberton et al., 2011).

A few limitations must be considered in interpreting our findings. First, we used median scores as cutoffs for some dichotomous risk factors, which means our conclusions for these variables may not be able to extend past our sample. Second, although this was a longitudinal study and we had estimates of AUD, depression, and PTS at every time point, we could not make any statements about direction or causation; it is possible that high depression/PTS symptoms lead to AUD, not the reverse.

Third, there was loss to follow-up across the 4 years of our study, requiring additional recruitment. This concern, however, is mitigated by a few observations: (a) attrition is a problem in most large-scale military cohorts like ours (Littman et al., 2010), including in another trajectory study (Boasso, Steenkamp, Nash, Larson, & Litz, 2015), particularly due to the fact that the military is a young and mobile population (Bush, Sheppard, Fantelli, Bell, & Reger, 2013); (b) the Proc Traj SAS procedure estimates missing data points using available data (Jones et al., 2001; Nagin, 2009); and (c) loss to follow-up in our samples was not associated with PTS or depression at baseline. Future longitudinal studies should aim to minimize attrition, as there are so few long-term military studies that keep participation rates constant across time. Additionally, longitudinal military studies should employ latent class analysis to allow for more comparison between studies. One direction could be to model AUD as an outcome or to investigate other

outcomes such as generalized anxiety. If a study has a large enough sample, it may be illuminating to observe the differences between male and female service members' trajectories.


Despite limitations, our findings suggested a longitudinal perspective is important when investigating psychopathology in service members. This is particularly so currently given that a greater proportion of service members are returning home with mental health burdens compared with past conflicts (Institute of Medicine Committee on the Initial Assessment of Readjustment Needs of Military Personnel, 2010). Finally, the role of AUD is key in understanding longer-term psychopathology as it modifies trajectories of depression and PTS.

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Onset of Alcohol Use Disorders and Comorbid Psychiatric Disorders in a Military Cohort: Are there Critical Periods for Prevention of Alcohol Use Disorders?

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Abstract Alcohol use disorders (AUD) are commonly comorbid with anxiety and mood disorders; however, a strategy for AUD prevention remains unclear in the presence of three competing etiological models that each recommends different high-risk groups. Therefore, the investigation of the three hypotheses in a characteristically unique cohort is critical to identifying pervasive characteristics of AUD that can inform a universal prevention strategy. The current study evaluated the temporality and onset of comorbid AUD and psychiatric disorders in a representative sample of 528 Ohio Army National Guard soldiers using structured clinical interviews from 2009 to 2012. We examined temporality both statistically and graphically to identify patterns that could inform prevention. General estimating equations with dichotomous predictor variables were used to estimate odds ratios between comorbid psychiatric disorders and AUDs. An annualized rate

of 13.5 % persons per year was diagnosed with any AUD between 2010 and 2012. About an equal proportion of participants with comorbid psychiatric disorders and AUD initiated the psychiatric disorder prior to the AUD and half initiated the psychiatric disorder after the AUD. Regardless of onset, however, the majority (80 %) AUD initiated during a short interval between the ages of 16 and 23. Focused primary prevention during this narrow age range (16–23 years) may have the greatest potential to reduce population mental health burden of AUD, irrespective of the sequencing of comorbid psychiatric disorder.

Keywords Prevention · Alcohol-related disorders · Mental disorder · Age of onset · Military personnel

Models of disease etiology that progress from the identification of risk factors to explanation of mechanisms inform interventions to mitigate disease states. In psychiatric epidemiology, decades of research have documented that alcohol use disorders (AUD), including both alcohol abuse and dependence, are commonly comorbid with anxiety and mood disorders in the US population (Hasin et al. 2005; Marshall et al. 2012) and there is substantial evidence for a bidirectional relationship between these disorders. Indeed, nearly 1 in 5 individuals diagnosed with a past-year AUD has a comorbid anxiety or mood disorder (Grant et al. 2004; Kenneson et al. 2013) and those with a primary anxiety or mood disorder are 2–3 times more likely to develop a secondary AUD (Martins and Gorelick 2011). However, three competing models, each suggesting a unique prevention strategy, have all been shown robust in accounting for a range of observed data.

Some studies have found that in those with comorbid AUD and anxiety or mood disorders that the anxiety or mood

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disorder was primary to the AUD (Bell and Britton 2014; Crum et al. 2013; Wilk et al. 2010), proposing that AUDs may result as a consequence of self-medicating existing psychiatric disorders. In contrast, other studies have documented that respondents with incident psychiatric disorders also have AUDs, suggesting that problematic alcohol consumption increases psychogenesis through both adverse physiological and contextual changes to the person's life (downward spiral hypothesis) (Falk et al. 2008; Marquenie et al. 2007). Finally, a third model posits that an exogenous common risk factor can simultaneously increase the risk of both an AUD and anxiety or mood disorder. For example, several studies have shown that individuals who experience childhood adversities (e.g., family violence, family disruption, parental mental illness) are at an increase risk of developing both major depression and alcohol misuse in adulthood (Green et al. 2010; McLaughlin et al. 2010).

Each of the three hypotheses suggests that prevention priorities be focused on different groups at different time periods. First, the self-medicating model would suggest that psychiatric disorders predominantly onset prior to AUD, presupposing that secondary prevention focused on the treatment of psychiatric disorders will offer the greatest reduction in AUD burden to individuals with psychiatric disorders and the population in general. Second, the "downward spiral" model implies that alcohol consumption can initiate chains-of-risk whereby depression is the consequent of a series of negative effects that all began with problematic alcohol consumption. Thus, primary prevention aiming to change social norms about alcohol consumption would have the greatest effect on the population burden of AUD. Third, a shared exogenous factor model calls for a prevention of the primary drivers that increase the risk of subsequent comorbidity—such as, childhood maltreatment that is shown to increase latent liabilities to develop psychopathology (Keyes et al. 2012).

Decades of research in general populations and treatment samples continue to confirm each of these three models. Hence, replication studies that continue to focus on risk estimates in a general population are unlikely to provide a more general prevention strategy. Therefore, assessing comorbid disorder etiology in a unique cohort of individuals who are adequately different from extant samples, but have enough in common to expect many shared influences throughout the life course, can help explicate the critical drivers of AUD across the life course that both groups share.

We posit that investigating AUD and comorbid anxiety or mood disorder in a representative military sample will inform similarities and differences between populations that may identify more universal characteristics of AUD. Given the US military force is screened for mental illness vulnerability at enlistment (Jones et al. 2003), experience traumatic events not germane to the general civilian population (e.g., combat), and reside and work in a social environment that treats alcohol

use with widespread indifference (Ames and Cunradi 2004; Ames et al. 2008), they have different risk factors for comorbid AUD and psychiatric disorders—such that, we would anticipate disorders onset after both the screening for vulnerability at enlistment and subsequent exposure to military-specific traumatic events. These population characteristics are likely to both increase the burden of comorbid AUD and psychiatric disorders and provide new insight into the temporal relationship between disorder onsets in both the general US population and military force. However, to our knowledge, no prior studies have examined the temporality of clinically diagnosed comorbid alcohol and psychiatric disorders in a representative military sample.

Alcohol use represents a substantial public health concern in the US military that is exacerbated in the presence of psychiatric disorders. Each year, nearly 35,000 arrests per year result from excessive drinking among service members (Harwood et al. 2009) and AUDs have been associated with increased soldier misconduct (Hoge et al. 2005) and absenteeism from duty (Armed Forces Health Surveillance Center 2012). Moreover, alcohol abuse has been documented to increase risk of suicidal behaviors among those with a comorbid psychiatric disorder (Calabrese et al. 2011; Oquendo et al. 2010). Because of the excess risk for morbidity (Blanco et al. 2012) and mortality (Calabrese et al. 2011; Oquendo et al. 2010) that is conferred by a comorbid psychiatric disorder, studies are needed to provide novel insight into the etiology of comorbidity that can inform prevention and treatment priorities in military personnel. Therefore, we used both longitudinal data and retrospectively assessed symptom reports in a representative sample in a US military cohort to respectively investigate (1) the temporal relationship between alcohol use disorders and anxiety or mood disorders and (2) whether alcohol use disorders were more likely to be diagnosed in the presence of a current anxiety or mood disorder.

Methods

Study Sample

Data are based on the in-depth clinical cohort study, nested within the Ohio Army National Guard (OHARNG) Mental Health Initiative (MHI). The OHARNG MHI design has been described in detail elsewhere (Calabrese et al. 2011). The baseline clinical validation subsample ($n = 500$) was randomly chosen from the OHARNG MHI telephone survey. In addition, we enrolled 105 recently enlisted OHARNG to the clinical validation subsample in 2011 (year 3) to increase both the analytical power and provide data on the most recent cohort of enlisted soldiers. Of the 605 total participants enrolled in the validation subsample ($n = 500$ in 2009, plus $n = 105$ in 2011), we excluded 77 (12.7 %) respondents who were assessed only

at baseline, retaining a final analytical sample of 528 respondents who contributed a total of 1210 person-years (2.4 ± 0.9 years per person on average). Among these 528 respondents, 374 (70.8 %) had complete data, 96 (18.2 %) missed one interview, and 58 (11.0 %) missed two interviews. The subjects lost to follow up did not differ significantly from those retained in the study on several baseline characteristics that included current psychiatric diagnoses (e.g., major depression, PTSD), demographic characteristics (e.g., age, sex, education), and military characteristics (i.e., rank, prior lifetime deployment). The Institutional Review Boards at both the University Hospital Case Medical Center (UHCMC) and University of Toledo (UT) approved the study protocol.

Procedures

Across four 1-year intervals from 2008 to 2012, study-trained clinicians completed face-to-face diagnostic interviews with each respondent in non-military private locations (e.g., private library room, participant's home). At time 1 (June 2008 to December 2009), study-trained clinicians explained the study, received informed consent, and administered the clinical interview, time 2 interviews were conducted from January to December 2010, time 3 interviews from January to December 2011, and time 4 interviews from January 2012 to February 2013. The interview consisted of questions that assessed soldiers' military experiences, psychiatric health history, treatment history, and socioeconomic circumstances; interviews lasted on average 2.12 h. The five study-trained clinicians performed monthly inter-rater reliability for the Structured Clinical Interview for DSM-IV (SCID) and Clinician-Administered PTSD Scale (CAPS) to assure that the interviewers were standardized in their diagnostic assessment methods and interviewing techniques (Free-marginal Multirater Kappa >0.85) (Brennan and Prediger 1981).

Measures

At the first assessment, the SCID (First et al. 2002) was administered to assess DSM-IV (American Psychiatric Association 2000) criteria for a lifetime or current AUD, which consist of alcohol dependence or alcohol abuse. Diagnosis of alcohol abuse was determined if s/he experienced one or more problems with functioning in a 12-month period (i.e., failure in obligations, alcohol use in hazardous situations, recurrent legal problems, or continued use despite social or interpersonal problems) that led to "Clinically significant impairment or distress." Alcohol dependence was diagnosed if s/he exhibited three or more dependence symptoms (e.g., tolerance, withdrawal) within a 12-month period. Participants diagnosed with alcohol abuse without dependence (AAWOD) or alcohol dependence (AD) were

determined to have any AUD. Retrospective age-of-onset was assessed as part of the interview in a method that has been shown reliable through this form of assessment (Farrer et al. 1989; Prusoff et al. 1988).

Similar to the methods for assessing lifetime and past-year AUD outlined above, psychiatric disorders were assessed using a diagnostic interview that included the CAPS (Blake et al. 2000) and the SCID (First et al. 2002). At the first assessment, the CAPS was administered twice to assess lifetime and current PTSD symptoms based on the individuals' self-selected "worst" event during their most recent deployment and then again for the "worst" event outside of their most recent deployment (Breslau et al. 1998). We defined a case of PTSD by using the frequency ≥ 1 and intensity ≥ 2 method (Blake et al. 2000). Participant meeting diagnostic criteria on either CAPS were classified as having PTSD. Next, the SCID was administered to assess Axis-I disorders (First et al. 2002). The mental disorders examined included anxiety disorders (panic disorder, agoraphobia without panic disorder, specific phobia, social phobia) and mood disorders (major depressive disorder and bipolar I/II disorders). All diagnoses were based on DSM-IV criteria and a decision tree approach was used to record the presence or absence of each disorder for current and lifetime occurrences. Retrospective age-of-onset was assessed as part of the baseline interview, which has been shown reliable through this form of assessment (Farrer et al. 1989; Prusoff et al. 1988).

Following administration of the CAPS and SCID at the first assessment, study interviewers annually reassessed DSM-IV criteria for psychiatric disorders since the last interview. All psychiatric diagnoses were determined in methods identical to those outlined for the first assessment.

Standard individual characteristics were assessed, including age at baseline, sex, ethnicity (white, black, or other), education ($<$ HS, HS/GED, some college/AA, college \leq), marital status (single/never married, married, separated/divorced/widowed), rank (enlisted, officer), and lifetime deployment (yes/no).

Statistical Analysis

The temporal relationship between AUD and anxiety or mood disorders was investigated in two steps. First, bivariate analyses (two-sided α level ≤ 0.05) were conducted comparing baseline lifetime prevalence of alcohol abuse without dependence, alcohol dependence, and any AUD with relevant sociodemographic and military characteristics. χ^2 tests or Fisher exact tests were performed for categorical characteristics and student *t* test for continuous variables. Second, age-of-onset distributions and temporality were examined graphically by plotting cumulative age-of-onset distributions.

Next, we examined the 1210 person-years of follow-up data and investigated whether an AUD was more likely to

be diagnosed in the presence of a current anxiety or mood disorder. As respondents contributed data from multiple time points, we used the generalized estimating equation (GEE) method to estimate adjusted odds-ratios (AOR) and 95 % confidence intervals (CI) between past-year comorbid AUD and psychiatric disorders using the `proc genmod` procedure in SAS v. 9.3 (SAS, Cary, NC). All GEE models were adjusted for sociodemographic and military characteristics.

Results

Table 1 displays the baseline demographic and military characteristics of the 528 participants stratified by AAWOD, AD, and any AUD. Participants were predominately male (88 %), white (89 %), enlisted (89 %), had deployed at least once (61 %), and had a mean age (\pm SD) of 31 ± 10 years. At baseline, about a third of participants had a lifetime diagnosis of anxiety (19 %) or mood disorder (29 %). Of participants who received a lifetime AUD (46 %) at baseline, 59 % were diagnosed with AAWOD and 41 % were diagnosed with AD. In the bivariate analysis, older age, ethnicity, prior deployment, lifetime mood disorder, and lifetime psychotherapy and pharmacotherapy were significantly ($p < 0.05$) associated with any baseline lifetime AUD diagnosis. Further, lifetime anxiety and mood disorders were significantly associated with AD, but not AAWOD. The period prevalence of any AUD in the sample was 13.5 % of persons per year, which included 8.8 and 4.7 % per year who were diagnosed with AAWOD and AD, respectively.

Figure 1 shows temporality between age-of-onset of co-occurrence for participants with lifetime comorbid AUD and mood ($n = 116$) or anxiety ($n = 97$) disorders. Three categories were created to examine temporality of comorbid disorders: (i) mood or anxiety disorder onset the same year as the AUD, (ii) anxiety or mood disorder started at an earlier age than the AUD, or (iii) AUD started at an earlier age than the anxiety or mood disorder. Among participants with comorbid mood and AUD, about 42 % reported AUD onset first, 39 % reported mood disorder onset first, while 19 % reported both disorders onset during the same year. Further, among participants with comorbid anxiety disorder, 43 % reported AUD onset first, 46 % anxiety disorder onset first, and about 10 % reported both disorders onset during the same year. Overall, the two distributions were not significantly different ($p = 0.18$).

Figures 2, 3, and 4 show the cumulative age-of-onset distribution of the three groups described in Fig. 1. Figure 2 shows the cumulative age-of-onset distribution of the 39 % of participants who reported that mood disorder onset prior to AUD (solid black colored line) and 42 % of participants who reported that AUD onset prior to mood disorder (solid gray colored line). Figure 3 shows the same information for anxiety disorder. Both figures show that about 80 % of AUD, regardless of whether they onset prior to mood or after mood

disorder, initiated during a small interval from about 16–23 years. However, the distributions of the anxiety and mood disorders occurred during different age intervals based on their temporality with AUD. Lastly, Fig. 4 shows that age-of-onset distributions were similar for participants reporting comorbid AUD and anxiety or mood disorders initiated in the same year.

Table 2 shows that after adjusting for sociodemographic and military characteristics that a significantly higher odds of past-year AAWOD, AD, and AUD was observed in respondents with anxiety disorder, mood disorder, or both than those without such disorder, with only comorbid mood disorder and AAWOD not being significant ($p = 0.45$). In this model, past-year mood disorder increased the odds of comorbid AD by a factor of 4 (AOR = 3.9, 95 % CI 2.4–10.2), while past-year mood or anxiety disorder increased the odds of any comorbid past-year AUD by a factor of 3 (AOR = 3.1, 95 % CI 2.0–4.7).

Discussion

In data from a representative sample assessing reservists' comorbid alcohol and mood or anxiety disorders, we found that AUDs start during a narrow age interval (16–23 years) irrespective of a lifetime comorbid mood or anxiety disorder. Although this finding is unable to resolve the stalemate among the three competing etiological models that aim to explain comorbid AUD and psychiatric disorders, we have identified a critical period for AUD onset in persons with comorbidity, robust across diverse samples, which nonetheless can inform prevention priorities. Substance use disorders, unlike all other psychiatric disorders except PTSD, have a *necessary* exposure (i.e., alcohol consumption) required for a diagnosis. In other words, the presence of an AUD implies alcohol consumption, whereas alcohol consumption does not imply that an AUD will develop. In this context, interventions aimed at persons in this critical window are likely to reach the greatest proportion of high-risk persons.

Our results emphasize the need to focus on methods to intervene with alcohol use among adolescents with and without comorbid mood or anxiety disorder. In particular, since an equal proportion of the participants in our sample reported AUD before the onset of a comorbid psychiatric disorder, and vice versa in the other half of the sample, a high-risk intervention strategy, exclusively targeting adolescents with preexisting psychiatric disorders, will likely neglect half of the population at risk to develop comorbid disorders. Although our findings are derived from a military sample, these conclusions have similar implications for the college drinking population and general population. Although the military and universities are unable to mitigate existing risk contributed by genetics (Kendler et al. 2012) or adverse childhood events (Keyes et al. 2012), the widespread and permissive use

Table 1 Baseline characteristics of respondents with alcohol abuse without dependence, alcohol dependence, or alcohol use disorder ($N=528$)

Characteristic at baseline	Total ($n=528$)	AAWOD		<i>P</i> value	AD		<i>P</i> value	Any AUD		<i>P</i> value
		Absent ($n=384$)	Present ($n=144$)		Absent ($n=427$)	Present ($n=101$)		Absent ($n=283$)	Present ($n=245$)	
Age, mean (SD), y	31 (10.0)	29.9 (9.7)	31.6 (10.1)	0.09	30.3 (10.1)	30.9 (8.8)	0.52	29.6 (10.0)	31.3 (9.6)	0.04
Age joining military, mean (SD), y	21 (4.5)	21.3 (4.8)	20.5 (3.6)	0.03	20.9 (4.3)	21.9 (5.2)	0.07	21.1 (4.6)	21.1 (4.4)	0.90
Sex, no. (%)				0.33			0.01 ^d			0.27
Male	463 (87.7)	340 (88.5)	123 (85.4)		367 (86.0)	96 (95.1)		244 (86.2)	219 (89.4)	
Female	65 (12.3)	44 (11.5)	21 (14.6)		60 (14.1)	5 (5.0)		39 (13.8)	26 (10.6)	
Ethnicity, no. (%)				0.74			0.03 ^d			0.02
White	467 (88.6)	337 (88.0)	130 (90.3)		370 (86.9)	97 (96.0)		240 (85.1)	227 (92.7)	
Black	36 (6.8)	28 (7.3)	8 (5.6)		34 (8.0)	2 (2.0)		26 (9.2)	10 (4.1)	
Other	24 (4.6)	18 (4.7)	6 (4.2)		22 (5.2)	2 (2.0)		16 (5.7)	8 (3.3)	
Education, (y), no. (%)				0.24 ^d			0.09 ^d			0.11 ^d
<12	5 (1.0)	5 (1.3)	0 (0.0)		5 (1.2)	0 (0.0)		5 (1.8)	0 (0.0)	
12 or GED	93 (17.6)	72 (18.8)	21 (14.6)		68 (15.9)	25 (24.8)		47 (16.6)	46 (18.8)	
>12	430 (81.4)	307 (80.0)	123 (85.4)		354 (82.9)	76 (75.3)		231 (81.6)	199 (81.2)	
Marital status, no. (%)				0.51			0.08			0.18
Single, never married	237 (44.9)	177 (46.1)	60 (41.7)		196 (45.9)	41 (40.6)		136 (48.1)	101 (41.2)	
Married	235 (44.5)	165 (43.0)	70 (48.6)		192 (45.0)	43 (42.6)		122 (43.1)	113 (46.1)	
Separated/divorced/widowed	56 (10.6)	42 (10.9)	14 (9.7)		39 (9.1)	17 (16.8)		25 (8.8)	31 (12.7)	
Rank, no. (%)				0.15			0.02 ^d			0.61
Enlisted	468 (88.6)	345 (89.8)	123 (85.4)		372 (88.1)	96 (95.1)		249 (88.0)	219 (89.4)	
Officer	60 (11.4)	43 (10.2)	21 (14.6)		55 (12.9)	5 (5.0)		34 (12.0)	26 (10.6)	
Prior deployment (yes), no. (%)	320 (60.6)	219 (57.0)	101 (70.1)	0.006	252 (59.0)	68 (67.3)	0.12	151 (53.4)	169 (69.0)	0.0002
Lifetime psychiatric diagnoses ^a										
Anxiety disorder ^b	102 (19.3)	81 (21.1)	21 (14.6)	0.09	67 (15.7)	35 (34.7)	<0.0001	46 (16.3)	56 (22.9)	0.06
Mood disorder ^c	155 (29.4)	114 (29.7)	41 (28.5)	0.78	106 (24.8)	49 (48.5)	<0.0001	65 (23.0)	90 (36.7)	0.0005
Either mood or anxiety disorder ^{bc}	195 (36.9)	143 (37.2)	52 (36.1)	0.81	138 (32.3)	57 (56.4)	<0.0001	86 (30.4)	109 (44.5)	0.0008
Treatment										
Psychotherapy	223 (42.2)	159 (41.4)	64 (44.4)	0.53	165 (38.6)	58 (57.4)	0.0006	101 (35.7)	122 (49.8)	0.001
Pharmacotherapy	157 (29.7)	101 (26.3)	56 (38.9)	0.005	117 (27.4)	40 (39.6)	0.02	61 (21.6)	96 (39.2)	<0.0001

AAWOD alcohol abuse without dependence, AD alcohol abuse, AUD alcohol use disorder, GED general equivalency diploma

^a Diagnostic categories are not mutually exclusive

^b Includes lifetime history of panic disorder, agoraphobia, social phobia, specific phobia, generalized anxiety, obsessive-compulsive, and posttraumatic stress disorders

^c Includes lifetime history of bipolar I/II, major depression, mania/hypomania, and dysthymia disorders

^d Fisher's exact test

of alcohol in these institutions (Ames and Cunradi 2004; Ames et al. 2008) may increase exposure to alcohol, exacerbating other early life risk factors for AUD. The Institute of Medicine recommended that the Department of Defense (DoD) should adopt “consistent enforcement of regulations on underage drinking, a reduced number of alcohol outlets, and limited hours of operation of such outlets” to combat the current lenient environment towards alcohol consumption (Institute of Medicine 2013). Whereas, in the last decade, US universities have effectively confronted problem drinking

among students through social advertising and interventions aimed at changing the social norms on university campuses away from excess drinking (Lewis and Neighbors 2006; Wechsler and Nelson 2008). The shift on university campuses from a punitive focus to a “social norms approach” could provide insight to the DoD and secondary education on future directions to reduce the burden of alcohol use disorders in the force and general community, respectively.

In the context of the military, our study reported that about half of the participants with lifetime comorbid disorders had

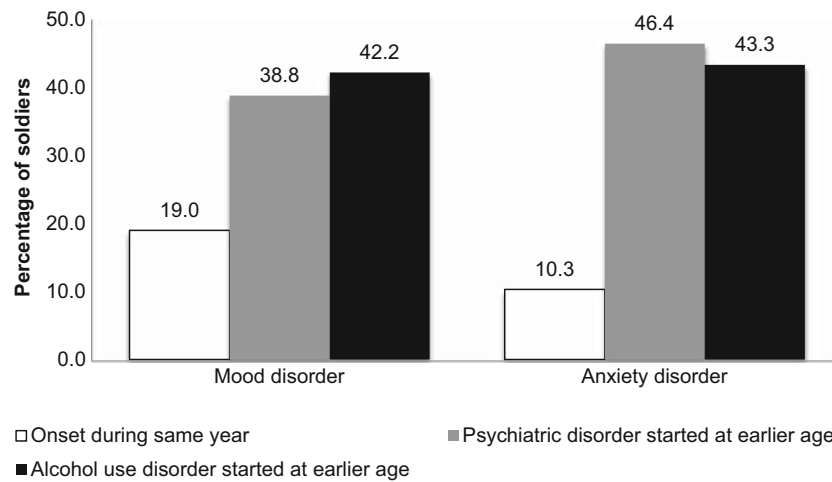


Fig. 1 Temporality between age of onset of lifetime co-occurrence for respondents with co-occurrence of alcohol use and mood or anxiety disorders. NS difference between mood or alcohol onset first ($p=0.76$). Significant difference between either mood ($p=0.007$) or alcohol

($p=0.002$) first versus same time. NS difference between anxiety or alcohol onset first ($p=0.83$). Significant difference between either anxiety ($p<0.0001$) or alcohol ($p<0.0001$) first versus same time. Overall, NS difference between two mood and anxiety disorder distributions ($p=0.18$)

developed their AUD by the mean age our sample joined the military (21 years), consistent with previous literature (Kessler et al. 2014), and combat deployment was significantly associated with AAWOD and AUD. This is consistent with extant evidence that about two times as many cases of post-deployment AUD represent a pre-deployment disorder compared to first incident disorder (Kehle et al. 2012). Although deployment may not represent the primary driver of military AUD burden, substantial evidence suggests that combat deployment experiences are associated with screening positive for alcohol misuse (Wilk et al. 2010), psychopathology, and readjustment stress (Hoge et al. 2004). Furthermore, individuals with mental health issues, particularly undiagnosed

issues, are likely to exhibit increased alcohol consumption (Bell and Britton 2014; Cohen et al. 2015). To mitigate chronic psychopathology, these findings emphasize the importance of a continuous systematic monitoring of military personnel serving in high stress positions for early signs of both alcohol use and psychiatric disorders.

We found an equal balance of cases where AUD was primary to the psychiatric disorder and vice versa. Irrespective of the direction of causation, these findings suggest that multiple processes, rather than a single underlying mechanism, are likely to drive this association between AUD and psychiatric disorder. Two processes, in particular, require further investigation. First, temporality is being affected by a third factor not

Fig. 2 Cumulative age of onset distribution of primary and secondary disorders in respondents with co-occurring mood and alcohol use disorders (AUD). Note: The solid line shows the cumulative age-of-onset distribution of the first onset disorder (i.e., black solid line for mood disorder onset first and solid gray line for AUD onset first), while the dotted line shows the cumulative age-of-onset distribution of the second onset disorder (i.e., gray dotted line for AUD onset second and black dotted line for mood disorder onset second). Shaded area represents ages 16–23

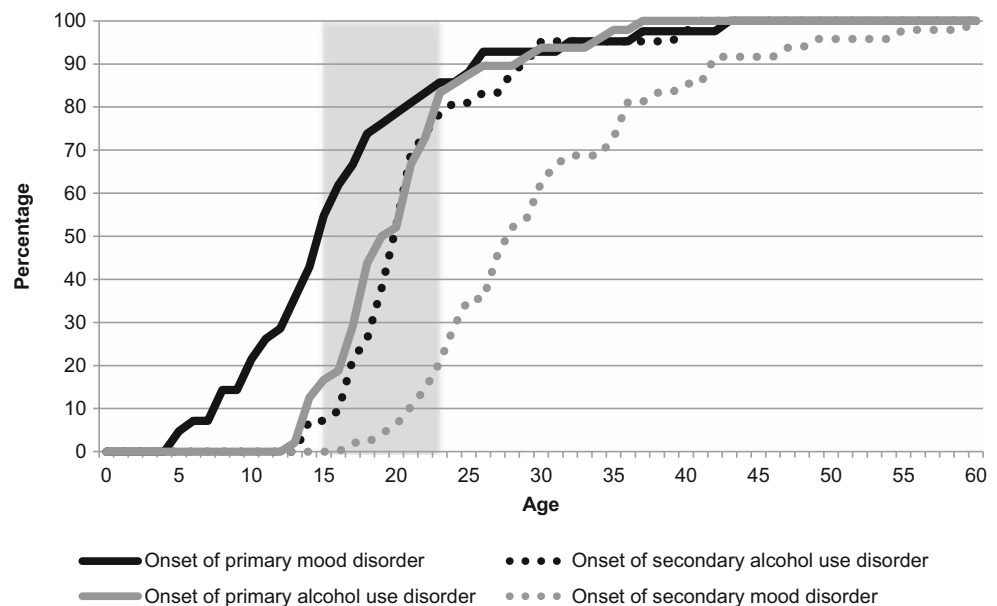
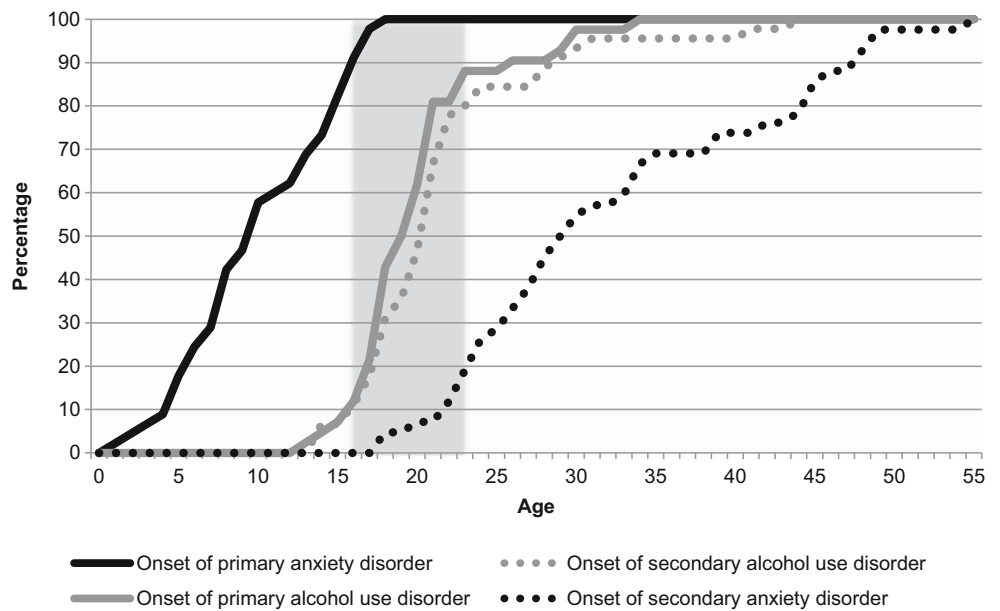


Fig. 3 Cumulative age of onset distribution of primary and secondary disorders in respondents with co-occurring anxiety and alcohol use disorders (AUD). Note: The *solid line* shows the cumulative age-of-onset distribution of the first onset disorder (i.e., *black solid line* for anxiety disorder onset first and *solid gray line* for AUD onset first), while the *dotted line* shows the cumulative age-of-onset distribution of the second onset disorder (i.e., *gray dotted line* for AUD onset second and *black dotted line* for anxiety disorder onset second). *Shaded area* represents ages 16–23



considered in previous studies. This hypothesis suggests a need for a life course framework to explain the complex interplay between genetics and environment in the development of comorbid alcohol use and psychiatric disorders. A recent literature has begun to elucidate the influence of premilitary experiences on military psychopathology, including a study that documented a higher probability of childhood adversity in military personnel than comparable civilians (Blosnich et al. 2014) and two papers documenting a majority of military psychiatric diagnoses initiate prior to military service (Kessler et al. 2014; Rosellini et al. 2014). The second hypothesis is that temporality may be disorder specific. Extant literature has documented that an AUD is more likely to onset in the presence of certain primary anxiety (Falk et al. 2008) and mood disorders (Falk et al. 2008; Kenneson et al. 2013) compared to other disorders. Kenneson et al. (2013), for example, showed

that compared to those without a current mood disorder, respondents aged 12–17 years with bipolar disorder (aOR = 3.7; 95 % CI = 2.6–5.5) were more likely than those with major depressive disorders (aOR = 1.8; 95 % CI = 1.3–2.4) to develop a subsequent substance use disorder. While our sample size did not provide sufficient power to stratify by psychiatric disorder, future large cohort studies should consider examining disorder-specific temporality.

This study is not without limitations. First, age-of-onset was self-reported, which may introduce some variance with regard to exact age-of-onset. Reassuring in this regard, while longitudinal investigations have documented that persons may fail to remember previously reported disorders (Takayanagi et al. 2014), two longitudinal studies have documented moderate test-retest reliability for age-of-onset questions (Johnson and Mott 2001; Parra et al. 2003). Further, the interviewers’ utilized

Fig. 4 Cumulative age of onset distribution of first onset psychiatric and alcohol use disorder in respondents with psychiatric and alcohol use disorders occurring in the same year

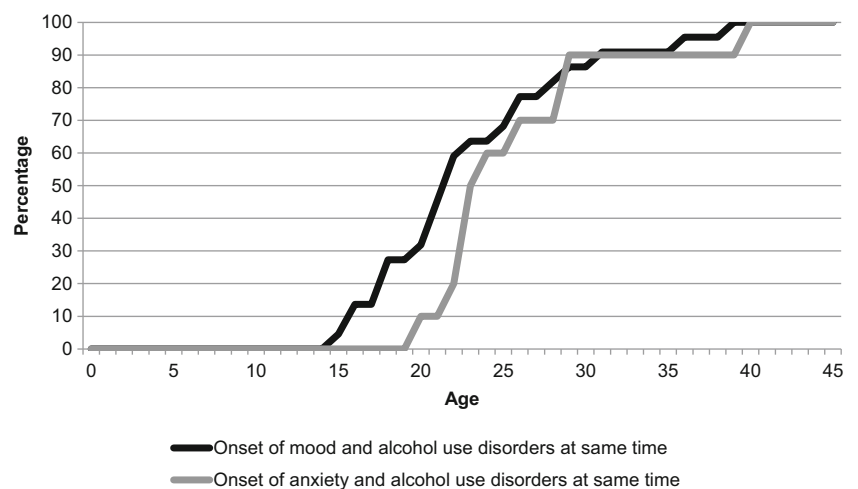


Table 2 12-month period prevalence of co-occurring DSM-IV diagnosed alcohol use disorders with anxiety and mood disorders adjusting for sociodemographic and military characteristics

Mental disorders	12-Month co-occurrence						
	AAWOD (n = 106)		Bivariate GEE regression analysis, AOR (95 % CI) ^a	AD (n = 57)	Bivariate GEE regression analysis, AOR (95 % CI) ^a	Any AUD (n = 163)	Bivariate GEE regression analysis, AOR (95 % CI) ^a
	χ^2	P value		χ^2	P value	χ^2	P value
Mood disorder	0.6	0.45	1.3 (0.7, 2.6)	19.1	<0.0001	5.0 (2.4, 10.2)	11.7 <0.0001 2.4 (1.5, 4.1)
Anxiety disorder	14.1	<0.0001	2.9 (1.7, 5.0)	4.9	0.03	2.2 (1.1, 4.4)	20.0 <0.0001 2.9 (1.8, 4.5)
Any disorder	11.6	<0.0001	2.4 (1.5, 4.1)	15.7	<0.0001	3.6 (1.9, 6.7)	27.0 <0.0001 3.1 (2.0, 4.7)

Total person-time = 1210 person years

AAWOD alcohol abuse without dependence, AD alcohol dependence, AUD alcohol use disorder, GEE generalized estimating equation, AOR adjusted odds ration, CI confidence interval

^a Adjusted for age, sex, race/ethnicity, marital status, rank, and lifetime deployment

a method that included probes about symptoms during particular time periods that was previously shown reliable in assessing disorder age-of-onset (Farrer et al. 1989; Prusoff et al. 1988). Second, while military personnel are likely to provide truthful answers if they believe a survey will be used for legitimate purposes and individual answers will remain confidential (Warner et al. 2011), the presence or perception of mental illness stigma (Kim et al. 2010) and a bias against reporting embarrassing behaviors (Tourangeau and Yan 2007) remain prevalent in the military. Thus, participants were assured that individual answers will remain confidential, both verbally and in writing, prior their volunteering for the study to compensate for this concern. Additionally, confidentiality was improved by having civilian clinicians conduct all assessments in neutral locations without the presence of military personnel.

Our observation that the age-of-onset for most AUD occurred within a narrow period of time (16–23 years), and the knowledge that AUD development can only occur in the presence of an external environmental factor (alcohol), suggests that universal primary prevention strategies (e.g., enforcement of minimum drinking age laws across the military) focused during this age range (i.e., during and after military enlistment) may have the greatest potential to reduce the population mental health burden. In addition, identifying the appropriate treatment is important for those with comorbid disorders. Given the high rates of comorbid alcohol use and psychiatric disorders, clinicians treating either AUDs or psychiatric disorders should routinely assess potential comorbid conditions to inform prescribed treatment. Recognition of family history for AUD and psychiatric disorders is likely the first step to understanding whether a person may be predisposed, and require further education related to early signs, symptoms, and risk factors. In the military setting, this suggests a need for selective prevention towards personnel at elevated risk driven by personal or family history of mental illness.

Compliance with Ethical Standards “All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.”

Conflict of Interest The authors declare that they have no conflict of interest.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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Association of Spirituality With Mental Health Conditions in Ohio National Guard Soldiers

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Abstract: Research exploring spirituality in military populations is a relatively new field with limited published reports. This study used the Spiritual Well-Being Scale to examine the association of spiritual well-being with suicidal ideation/behavior, posttraumatic stress disorder (PTSD), and depression and alcohol use disorders in a randomized sample of Ohio Army National Guard soldiers. The participants were 418 soldiers, mostly white and male, with nearly three-quarters indicating that they had been deployed at least once during their careers. Higher spirituality, especially in the existential well-being subscale, was associated with significantly less lifetime PTSD, depression, and alcohol use disorders and with less suicidal ideation over the past year. Future research in this area may benefit from a longitudinal design that can assess spirituality and mental health behaviors in addition to diagnoses at different time points, to begin to explore spirituality in a larger context.

Key Words: Spirituality, mental health, suicidal ideation, military, logistic regression

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Emerging literature suggests that religiosity and/or spirituality is associated with positive mental health outcomes in military personnel (Barlas et al., 2011; Benda, 2004; Wester, 2009). Religiosity generally refers to one's practice of an institutionalized religion, such as attending church or temple services, whereas spirituality is much more broadly defined to include existential qualities such as self-awareness and a sense of meaning or purpose in life (Hufford et al., 2010; Koenig, 2012).

Research in spirituality/religiosity and mental health in military populations is a relatively new field with limited published reports. However, some studies have reported associations between spirituality/religiosity and depression and posttraumatic stress disorder (PTSD). Berg (2011) studied Vietnam combat veterans with PTSD and found that high spiritual distress was significantly associated with both PTSD diagnosis and higher depression level as measured by the Zung Self-Rating Depression Scale. Chang et al. (2001) reported that among female outpatient veterans with military sexual trauma history, frequently attending religious services served as a buffer against depressive symptoms. Witvliet et al. (2004) used the Brief Religious Coping Scale in a Veterans Affairs (VA) outpatient clinic and found that negative religious coping was associated with higher severity of depressive and PTSD symptoms. In a sample of 1250 Army soldiers based in an Iraqi combat

zone, Wester (2009) reported strong correlations between high spirituality and positive affectivity, with positive affectivity believed to protect against depression. In Wester's study, spirituality was assessed with 15 questions, encompassing three subscales of connection to others, religious identification, and hopeful outlooks.

There have also been reports of higher spirituality associated with significantly lower alcohol use and suicide risk. In 2011, the Department of Defense (DoD) Health Related Behaviors Survey of Active Duty Military Personnel (Barlas et al., 2011) assessed spirituality with two questions and found that low spirituality was more often associated with heavy drinking and higher levels of depression and suicidal ideation. In a small pilot study of Croatian war veterans with PTSD, the relationship between suicidality, blood cortisol levels, and spirituality was examined using the Spiritual Well-Being Scale (SWBS) and the Beck Hopelessness Scale; higher spiritual well-being (SWB) scores correlated with lower cortisol levels and with lower suicide risk (Mihaljevic et al., 2011). Other authors (Tsuang et al., 2002) also used the SWBS, investigating 100 twin pairs from the Vietnam Era Twin Registry, and found that both the existential well-being (EWB) and the religious well-being (RWB) subscales of SWBS were significantly inversely associated with alcohol abuse or alcohol dependence.

With the exceptions of the studies of Tsuang et al. (2002, 2007), Hourani et al. (2012), Wester (2009), and Barlas (2011), most evidence on spirituality and mental health in the military is based on patient populations. The study samples of Tsuang et al. (2002, 2007) of twin veterans were randomly drawn and used a well-validated clinical structured interview. The study of Wester (2009) of deployed soldiers and Hourani et al. (2012) both studied a large representative sample whose results for mental health variables were based on self-report items. Barlas et al. (2011) had the largest sample size ($N = 39,877$), which represented the DOD and Coast Guard. Their self-report survey was extensive and comprehensive using mental health questions that were not standardized measures. Our sample includes nonpatient, nondeployed soldiers. Our mental health variables are based on standardized clinician-rated interviews, which could aid in knowledge gaps and provide more balanced perspectives on the relationship between spirituality and mental health.

The aim of the current study was to explore whether spiritual well-being in a National Guard sample would be associated with better mental health outcomes; the reserve population has been relatively understudied regarding spirituality/religiosity.

METHODS

As detailed elsewhere (Prescott et al., 2014), the Ohio Army National Guard (OHARNG) Mental Health Initiative is a longitudinal cohort study of a sample of members who enrolled in the guard beginning June 2008. Of the 6514 possible subjects with working phone numbers, 1364 (20.9%) declined to participate. A total of 187 (2.8%) were retired and were thus ineligible; 31 (0.4%) were disqualified for other reasons, such as did not speak English or had hearing problems; and 2316 (35.6%) potentially eligible participants were not included because they were not enrolled before the baseline cohort closed 12 months after November 2008. Thus, we obtained a sample of 2616 (43.2%

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participation rate), which comprised the baseline, platform study for the telephone survey. This sample was slightly older, included more married participants (38.5% in OHARNG and 47% in the telephone sample) and officers (9.5% in OHARNG and 13.1% in phone sample) than the OHARNG population, but the proportion of race and sex did not differ significantly (Calabrese et al., 2011). To form the cohort group reported in this article, 40% of individuals completing the telephone survey were randomly invited to participate in a re-appraisal subsample (91% agreed; $n = 952$), that used self-report methodology and face-to-face interviews with trained master's- and doctoral-level clinicians. Of the 952 individuals who were initially interested, 25 (2.7%) later declined, 21 (2.3%) did not attend the scheduled interview, and the goal of enrolling 500 participants in the baseline year was reached in December 2009 with 406 (43.7%) individuals who either were still waiting to be called or scheduled but were not contacted. There were no differences between the characteristics of the baseline telephone cohort and the reappraisal samples (Prescott et al., 2014). In the following year (wave 2), 418 (83.6%) guard members participated in the current study. Of the 500 original in-person participants, we identified that 10 participants (2%) were deployed when wave 2 interview was conducted, 6 withdrew consent, 1 was deceased, 6 declined or delayed this wave but remained in the cohort, and 59 (11.8%) were lost upon follow-up. In-person participants were compensated at the rate of \$50 per hour (15-minute increments), and mean (SD) period between baseline and wave 2 interview was 360.98 (55.09) days (range, 231–635 days). Every effort was made to schedule the same interviewer in the following year, and of 418 participants, 368 (88%) were scheduled with the same in-person interviewers, and the remaining were scheduled with different interviewers because of scheduling conflicts. Contact was made by using telephone and e-mail (only if participants could not be reached by multiple calls), and the average number of telephone contacts for baseline and wave 2 was 4.16 and 3.22 per participant, respectively. Interviews averaged 2.12 hours in length and occurred in neutral, private settings such as a private library room during hours in which the participants were not on duty. This study protocol was approved by the National Guard Bureau and the institutional review boards of University Hospitals Case Medical Center, University of Toledo, University of Michigan, Ann Arbor Veterans Administration Medical Center, Columbia University, and the Office of Human Research Protections of the US Army Medical Research and Materiel Command. The data used in the analyses presented in this article were obtained in the second year survey (wave 2), which occurred 1 year after the initial, baseline assessment of the soldiers. Among the assessments given to the subjects was the self-administered 20-item SWBS (Paloutzian and Ellison, 1982) and a 15-item Columbia-Suicide Severity Rating Scale (C-SSRS) (Posner et al., 2009). The soldiers were presented with the opportunity to participate in the SWBS only during the wave 2 interview; hence, there is only a cross-sectional look at this measure.

The SWBS is a self-administered scale used to assess spiritual well-being as measured by religious and existential factors. The SWBS consists of 20 items rated on a 6-point Likert scale ranging from 6 (strongly agree) to 1 (strongly disagree). The SWBS also yields two subscales: RWB is based on the 10 questions pertaining to one's relationship with "a higher power" (i.e., "I believe that a higher power is concerned about my problems" and "My relation with a higher power contributes to my sense of well-being"), and the EWB is derived from the 10 items pertaining to life satisfaction and purpose/meaning (i.e., "I feel a sense of well-being about the direction my life is headed in" and "I feel good about my future"). Nearly half of the items are phrased in the negative direction to avoid any possible response bias. The overall SWBS score is then defined as the sum of the Religious and Existential scores and ranges from 20 to 120, whereas the RWB and EWB score each ranges from 10 to 60. The psychometric properties of the SWBS, including good face validity and subscale internal consistency,

have been described by others (Bufford et al., 1991; Ellison, 1983; Taliaferro et al., 2009; You and Yoo, 2016).

From the C-SSRS, both suicidal ideation and suicidal behavior were determined as dichotomous response (absence/presence) variables. Assessment for lifetime PTSD explored both civilian- and deployment-related trauma, using the Clinician-Administered PTSD Scale for *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV)* (Blake et al., 1995). Depression and alcohol use disorder (AUD) diagnoses were assessed with the Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders (nonpatient version) (First et al., 1997).

To examine the association of spiritual well-being with suicidal ideation/behavior, PTSD, depression and alcohol use while adjusting for other covariates, logistic regression models were used. SAS version 9.3 was used to conduct all logistic regression analyses. Adjustment was made for age, sex, race, and deployment status. Age was treated as continuous, whereas sex, race, and deployment status were categorical. Because continuous variables provide greater information content (entropy) than do categorical variables, continuous spiritual well-being scores were used in the modeling process instead of spiritual well-being categories. Total scores of RWB and EWB were entered into logistic regression models separately. Both unadjusted and adjusted logistic regression models were examined. Statistical significance was set at 0.05.

RESULTS

The general demographic characteristics of the 418 soldiers indicated that wave 2 participants were predominately white (89.2%) and male (88.0%). Two-thirds of the soldiers were younger than 35 years and most had at least some college education (84.0%). Nearly three-fourths (73.0%) indicated that they had been deployed at least once during their military careers. A little more than half (53.5%) were married and less than half had middle income (39.2%).

Comparison of wave 2 participants with those at baseline (wave 1) showed that the demographic characteristics did not change between the two interview times, although there was a decrease in total number (Table 1). The comparison with the general make-up of the OHARNG in 2008 did reveal significant differences in racial, age, and marital status characteristics. The 2008 cohort had more blacks, more young members, and more single individuals. Note that combining blacks and other race would result in a similar proportion between the two groups (10.8% vs. 11.7%; $p = 0.54$).

Of the 418 soldiers, 414 had sufficient data on demographic information, spirituality, suicidal ideation/behavior, and lifetime PTSD to provide modeling using multiple logistic regression. Because of randomly missing data, not all 414 soldiers were included in each analysis.

Confirmatory factor analysis on 398 soldiers who had complete information for the SWBS indicated that a two-factor solution (religious and existential) did indeed adequately describe the spirituality results. Analysis with IBM SPSS AMOS 22 yielded a chi-square of 568.8, 167 degrees of freedom with associated p value < 0.001 . Other goodness-of-fit values were Tucker-Lewis Index of 0.923, comparative fit index of 0.932, and root mean square error of approximation of 0.078. In addition, Cronbach's alpha for the three spirituality scores were 0.57 for overall SWB, 0.86 for RWB, and 0.95 for EWB. Means (SD) values were 87.2 (18.3) for overall SWB, 40.6 (13.0) for RWB, and 46.6 (8.7) for EWB. The correlation between RWB and EWB was 0.40 ($p < 0.01$). Pairwise correlations among the primary independent and dependent variables are given in Table 2.

Path analysis to determine if EWB acted as a mediator for RWB on current suicidal ideation, lifetime suicidal behavior, lifetime PTSD, lifetime depression, and lifetime AUD indicated no evidence of any indirect effect of RWB through EWB on any of these outcomes. Analysis using Mplus 7 revealed that the indirect effect for each of the five outcomes was equal to 0.

TABLE 1. Demographic Comparison of the 418 OHARNG Soldiers Who Participated in The Spiritual Well-Being Study (Wave 2) With Wave 1 Participants and OHARNG Membership in 2008

Characteristic	Wave 2 (N = 418)		Wave 1 (N = 500)		χ^2	P ^a	OHARNG (N = 10,778)		χ^2	P ^a
	n	%	n	%			n	%		
Sex					0.00	0.99			1.12	0.29
Male	368	88.0	440	88.0			9,293	86.2		
Female	50	12.0	60	12.0			1,485	13.8		
Race					0.04	0.98			17.2	<0.01
White	373	89.2	444	88.8			9,512	88.3		
Black	28	6.7	35	7.0			1,083	10.0		
Other	17	4.1	20	4.0			183	1.7		
Age, yrs					0.53	0.91			14.9	<0.01
17–24	125	29.9	160	32.0			4043	37.5		
25–34	154	36.8	182	36.4			3746	34.8		
35–44	90	21.5	103	20.6			2143	19.9		
≥45	49	11.7	55	11.0			846	7.8		
Marital status					4.24	0.12			70.0	<0.01
Married	222	53.1	238	47.6			4154	38.5		
Divorced/separated/widowed	47	11.2	53	10.6			657	6.1		
Single	146	34.9	209	41.8			5967	55.4		
Income					0.47	0.49		N/A		
≤\$60,000	227	54.3	279	55.8						
>\$60,000	183	43.8	205	38.0						
Education					0.15	0.93		N/A		
HS grad/GED	79	18.9	97	19.4						
Some college/tech	234	56.0	282	56.4						
College/grad degree	105	25.1	120	24.0						
Rank					0.02	0.89			1.75	0.19
Officer	48	11.5	56	11.2			1028	9.5		
Enlisted/cadet/civilian employee	370	88.5	444	88.8			9750	90.5		

^aComparison with wave 2.

GED indicates General Educational Development; HS, high school; N/A, not available.

The number of the 414 soldiers demonstrating suicidal ideation according to the C-SSRS was 32 (7.7%), with 37 (8.9%) expressing suicidal behavior by this scale. Suicidal ideation was referenced only over the time from the soldier's baseline assessment until the wave 2 assessment, whereas suicidal behavior referred to any such behavior that had

occurred during the soldier's lifetime. PTSD, AUDs, and depression were also referenced over lifetime. There were 28 (6.8%) soldiers with a lifetime diagnosis of PTSD, 100 (24.2%) soldiers with lifetime depression, and 21 (5.1%) soldiers diagnosed with both lifetime PTSD and depression.

TABLE 2. Correlations Among Dependent and Independent Variables

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Suicidal ideation	1										
2. Suicidal behavior	0.26**	1									
3. PTSD lifetime	0.24**	0.18**	1								
4. Depression lifetime	0.32**	0.28**	0.32**	1							
5. SWB	-0.15**	-0.03	-0.15**	-0.04	1						
6. RWB	-0.07	0.04	-0.07	0.06	0.90**	1					
7. EWB	-0.18**	-0.09	-0.18**	-0.16**	0.75**	0.45**	1				
8. Age	0.03	-0.03	0.05	0.09	0.07	0.14**	-0.08	1			
9. Sex	-0.01	-0.00	-0.07	0.02	0.06	0.07	-0.01	0.03	1		
10. Race	-0.10	-0.11*	-0.13*	-0.06	0.03	-0.01	0.07	0.02	0.23**	1	
11. Ever deployed	0.03	-0.07	0.10	-0.04	-0.06	-0.02	-0.13*	0.42**	-0.03	0.01	1

*p < 0.05.

**p < 0.01.

Suicidal Ideation/Behavior and Spirituality

As can be seen from Table 3, overall spiritual well-being and existential well-being were significantly associated with past-year suicidal ideation, whereas religious well-being was not. The odds ratio (OR) for overall spiritual well-being (OR, 0.97; 95% confidence interval, 0.95–0.99) indicated a 3% decrease in risk of current suicidal ideation for every 1-point increase in SWB score. This translates to a 15% decrease in risk of current suicidal ideation for every 5-point increase in score. Similarly, the OR for existential well-being (0.92; 0.88–0.96) showed an 8% decrease in risk of current suicidal ideation for every 1-point increase in score, thus a 34% decrease for every 5-point increase. Of the demographic variables in the overall spirituality model, white soldiers (OR, 0.39; 0.16–0.99) had a 61% decreased risk of suicidal ideation compared with nonwhite soldiers, and male soldiers (OR, 0.36; 0.13–0.97) had a 64% decrease compared with female soldiers. Although RWB was not significant, both male (OR, 0.36; 0.14–0.93) and white (OR, 0.39; 0.16–0.97) soldiers had significantly decreased risk of suicidal ideation in the adjusted RWB model.

With respect to lifetime suicidal behavior, none of the spirituality scores was related to the outcome. However, white soldiers were associated with decreased risk (59%) in both the overall SWB (OR, 0.41; 0.17–0.97) and RWB (OR, 0.41; 0.17–0.96) models.

PTSD and Spirituality

Higher overall spiritual well-being (OR, 0.96; 0.94–0.99) and existential well-being (OR, 0.92; 0.87–0.96) were associated with less lifetime PTSD (Table 4). A 1-point improvement in overall spiritual well-being score indicated a 3% decrease in risk for lifetime PTSD in both the unadjusted and adjusted logistic regression models. For existential well-being, a 1-point increase in score translated to an 8% decrease in risk for lifetime PTSD. There was no statistically significant relationship between religious well-being and PTSD.

White soldiers showed a significantly decreased risk to lifetime PTSD in all three models—SWB: OR, 0.30; 0.11–0.77; RWB: OR, 0.30; 0.11–0.77; and EWB: OR, 0.36; 0.13–0.96. Furthermore, having ever been deployed indicated increased risk for lifetime PTSD in the religious well-being model (OR, 3.92; 1.04–14.72), that is, a nearly 4:1 risk.

Depression, Alcohol Use and Spirituality

Overall spiritual well-being and religious well-being were not significantly associated with less lifetime depression (Table 4). However,

TABLE 4. Relationship Between Spirituality and Both the Occurrence of Lifetime PTSD and Depression Among OHARNG Soldiers

Effect	Unadjusted Model			Adjusted Model ^a		
	OR	95% LCL	95% UCL	OR	95% LCL	95% UCL
Lifetime PTSD						
Overall spiritual well-being	0.97	0.94	0.99	0.96	0.94	0.99
Religious well-being	0.98	0.95	1.01	0.98	0.95	1.01
Existential well-being	0.91	0.87	0.96	0.92	0.87	0.96
Lifetime depression						
Overall spiritual well-being	1.00	0.98	1.01	0.99	0.98	1.01
Religious well-being	1.01	0.99	1.03	1.01	0.99	1.03
Existential well-being	0.96	0.93	0.98	0.95	0.93	0.98

^aAdjusted for age, sex, race and deployment status.
LCL indicates lower confidence limit; UCL, upper confidence limit.

the relationship between age in the overall spiritual well-being model was statistically significant (OR, 1.03; 1.01–1.06). On the EWB, decreased risk of lifetime depression was statistically significant (OR, 0.95; 0.93–0.98). Male soldiers had significantly decreased risk of lifetime depression in all three models—SWB: OR, 0.28; 0.15–0.53; RWB: OR, 0.28; 0.15–0.53; and EWB: OR, 0.27; 0.14–0.53.

Lifetime AUD was found to be negatively correlated with overall SWB ($r = -0.11, p = 0.03$) and EWB ($r = -0.11, p = 0.02$). Although significant, these correlations explain only a small amount of the total variation between the two variables. The correlation with RWB was not statistically significant but did show a trend ($r = -0.08, p = 0.09$).

DISCUSSION

In this sample of OHARNG members, we found that higher spirituality measured by SWBS was associated with lower levels of mental health problems of lifetime PTSD, depression, and AUDs. Similarly, higher spirituality was associated with less suicidal ideation over the past year. Our findings are consistent with other military studies that report an association between spirituality and better mental health outcomes and also with the more robust civilian literature in this field (Bonelli and Koenig, 2013). Our findings on the subscales of the SWBS suggest that the EWB may be the more determining influence, rather than the RWB. However, some argue that “existential well-being” may be merely measuring positive mental health traits (e.g., feeling that life is a positive experience, feeling fulfilled and satisfied with life, and feeling good about their future (Koenig, 2008; Tsuang et al., 2007). Koenig (2008) states that “by including indicators of mental health in the definition of spirituality, this assures a positive correlation between spirituality and mental health.” Conversely, others, such as Taliaferro et al. (2009), present evidence that supports existential well-being as a distinct dimension that “adds unique explanatory power to the prediction of mental health.” In the Taliaferro et al. study, existential well-being, after controlling for other demographic and psychosocial factors, remained a significant predictor of lower levels of suicidal thoughts. Tick (2005) believes that PTSD and depression are strongly associated with spiritual distress and that finding meaning in one’s suffering is essential to the healing process. Our finding that when other variables are adjusted, existential well-being relates more to one’s mental health state than religious well-being, as measured on the SWBS, is consistent with other reports in the literature, including the research of Nad et al. (2008) on Croatian war veterans with PTSD, the Vietnam Era Twin Registry study by Tsuang et al. (2007),

TABLE 3. Relationship Between Spirituality and Both Current Suicidal Ideation and Lifetime Suicidal Behavior Among OHARNG Soldiers

Effect	Unadjusted Model			Adjusted Model ^a		
	OR	95% LCL	95% UCL	OR	95% LCL	95% UCL
Current suicidal ideation						
Overall spiritual well-being	0.97	0.95	0.99	0.97	0.95	0.99
Religious well-being	0.98	0.95	1.01	0.98	0.95	1.00
Existential well-being	0.92	0.88	0.96	0.92	0.88	0.96
Lifetime suicidal behavior						
Overall spiritual well-being	0.99	0.98	1.01	0.99	0.98	1.01
Religious well-being	1.01	0.98	1.03	1.01	0.98	1.04
Existential well-being	0.96	0.92	1.00	0.96	0.92	1.00

^aAdjusted for age, sex, race and deployment status.

LCL indicates lower confidence limit; UCL, upper confidence limit.

and also with a college sample surveyed with the SWBS (Taliaferro et al., 2009).

Although it is out of the scope of this article, when interpreting our results, two issues emerged that invite further investigation. First, how should we define “spirituality”? Second, how do we interpret existential well-being in the context of spirituality research? Koenig (2008) argues that in the research field, the definition of spirituality should be limited to the religious domain and should not use measures “contaminated” with positive psychological characteristics. Even though the SWBS has been a widely used tool to measure religious and spirituality beliefs, there are other dimensions in assessing spirituality that provide further understanding of the relationship between spirituality and mental health. For example, spiritual behavior (e.g., frequency of prayer, rituals, and attendance at religious services) (e.g., Bonelli and Koenig, 2013) and experiences (e.g., perception of a higher power, coping strategies, and religious struggle) (e.g., Witvliet et al., 2004) have also been found to be significantly related to mental health outcomes. Our results indicate that religious well-being was not a determining factor when compared with existential well-being, and there was no evidence of any indirect effect of religious well-being through existential well-being on the mental health outcomes we assessed in this article. The effect of existential well-being was independent of that of religious well-being in our sample. This should not undermine the effect of religiosity on mental health because we should remind readers that the SWBS assesses only one dimension of spirituality. Peterman et al. (2002) also commented that the RWB may not be an ideal fit for religions that do not emphasize having a “personal relationship with” one’s God or higher power. Future studies could explore use of the SWBS and particularly the fit of the RWB in military populations.

In the present study, the lack of any association with spirituality and lifetime suicidal behavior was unanticipated and contrasts with the findings from the 2011 DoD Health Related Behaviors Survey (HRBS) of Active Duty Military Personnel (Barlas et al., 2011). However, the 2011 HRBS limited suicidal behavior to the past year. In another self-report study on past year and lifetime suicidal ideation, Klimes-Dougan (1998) found that lifetime suicidal ideation was underreported compared with past year recall; perhaps reporting suicidal behavior is perceived as even more stigmatizing than reporting suicidal ideation and could contribute to more recall bias, affecting our suicidal behavior and spirituality findings.

This study has a number of limitations, including an overall limited response rate. Also, because of its cross-sectional design, our data could not examine whether one’s spirituality can change after significant life events like deployment, suicide attempt, and other traumatic experiences such as the death of loved ones. As mentioned earlier, there can also be recall bias when subjects are asked to remember events over a lifetime. The OHARNG is primarily male and white in composition, and although our sample appears to be representative of the percentage of females and minorities (when combining blacks with other races) in the overall OHARNG composition, the numbers of women and minorities in this study were relatively low, making sex and race comparisons difficult. Literature suggests that there are sex and cultural differences in spirituality (Randolph-Seng et al., 2008; Wink and Dillon, 2002). Therefore, even though our sample is a nonpatient population and partially representative of Ohio National Guard, the results may not be generalizable to other populations.

CONCLUSIONS

In this military sample, higher spirituality, as assessed by the SWBS, was associated with better mental health outcomes in lifetime PTSD, depression, and AUDs and less suicidal ideation over the past year. The EWB appeared to account for the major findings, as opposed to the RWB. Future research directions include exploring whether spirituality and existential well-being can be strengthened or enhanced by

training or other interventions and identifying effective ways for mental health providers and clergy leaders to incorporate spirituality into clinical practice.

Although religious well-being appeared to be less associated with mental health outcomes, it could be very relevant to other aspects of mental health behaviors. Fontana and Rosenheck (2004) examined VA data from 1300 outpatient and inpatient visits for PTSD diagnosis and identified guilt feelings and “weakened faith,” not PTSD symptom severity, as the main factors determining use of mental health treatment. Adding other dimensions of religious measurements, such as involvement and coping strategies, may enhance understanding of the relationship between spirituality and mental health outcomes. With Spiritual Fitness recently added to the Total Force Fitness initiative of the DoD to promote the health and resiliency of US troops (US DoD, Task Force on the Prevention of Suicide by Members of the Armed Forces, 2010), more research in the area of spirituality is expected.

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DISCLOSURE

The authors declare no conflict of interest.

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Incidence and Risk for Mood and Anxiety Disorders in a Representative Sample of Ohio Army National Guard Members, 2008–2012

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ABSTRACT

Objective. We investigated the incidence of first-onset psychiatric disorders among Ohio Army National Guard members and the sociodemographic and military factors associated with these incident disorders. We aimed to identify potential risk factors and mitigating factors for a range of psychiatric disorders in a representative military sample.

Methods. We analyzed data on a representative sample of 528 Ohio Army National Guard members who were assessed in person annually for first-onset psychiatric disorders from 2008 through 2012 using structured clinical interviews. We used a multivariable discrete-time Cox proportional hazard model to determine risk factors of first-onset anxiety or mood disorders.

Results. The annualized incidence rate of any first-onset psychiatric disorder was 9.8 per 100 person-years at risk. Alcohol use disorder and major depressive disorder had the highest incidence rates among the unique disorders under study (5.0 and 4.2 per 100 person-years at risk, respectively). We found an association between respondents endorsing past-year deployment and a 29% increase in the risk of incident anxiety or mood disorder, whereas the past-year experience of any non-deployment traumatic event was associated with a 32% increase in risk of incident anxiety or mood disorder.

Conclusion. Soldiers experience a substantial burden of first-onset alcohol use disorder and major depressive disorder annually; the experience of non-deployment-related traumatic events contributes substantially to increasing risk, suggesting that any effort aimed at mitigating mood and anxiety disorders in this population must consider the soldier's life experience and military experience.

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Since 2001, the U.S. military has deployed more than 2.6 million service members to support the longest sustained ground combat operation in the nation's history. These operations require lengthy, often repetitive, and demanding deployments by both active-duty and National Guard and Reserve (reserve component) forces.¹ As the military increased occupational and personal demands on soldiers, the percentage of service members diagnosed with psychiatric disorders increased by 65% between 2001 and 2011 (2001: 5,387.1 cases per 100,000 person-years; 2011: 8,900.5 cases per 100,000 person-years),² the hospital rate and number of ambulatory visits caused by mental disorders doubled between 2006 and 2010,³ and the civilian-adjusted suicide incidence rate was surpassed for the first time in 2008 (active-duty Army personnel rate in 2008: 20.2 suicides per 100,000 population; civilian-adjusted rate in 2005: 19.5 suicides per 100,000 population).⁴ The simultaneous increase in military demands and psychiatric burden led to a scientific and public discourse on aspects of military service (e.g., deployment) and health policy changes (e.g., increased awareness of psychiatric disorder) that caused the increase in psychopathology among service members.^{5,6} However, much of the research that supports this association between aspects of military service and psychiatric disorders is based on prevalence studies; these studies assess disease burden but not disease risk.⁷⁻⁹

Historically, the burden of mental illness has been lower for military and veteran populations than for civilians; however, recent evidence suggests this difference has reversed.⁴ In 2014, Kessler and colleagues¹⁰ showed that the prevalence of 30-day psychiatric disorders is higher among U.S. service members than among sociodemographically matched civilians. This finding fits with the contemporary understanding that military experiences may lead to an increased psychiatric burden. However, this same report indicated that most service members with disorders reported that their symptoms began before enlistment.¹⁰ Furthermore, a population-based study published in 2014 documented that service members are more likely than non-military civilians to report adverse childhood experiences.¹¹ These two studies suggest an alternative mechanism for the military's psychiatric burden that is driven by chronic, cyclical, or re-aggravated pre-military psychiatric symptomatology.

Although prior research provides insight into the burden of mental illness in the military, at least three gaps in the literature limit our knowledge about its risk. First, although one in three service members has never been deployed,¹² most studies restrict analysis to deploying populations, limiting inferences about the

risk associated with the more general military experience.¹³ Second, previous military studies have reported either the cross-sectional prevalence or proportion of "new-onset" psychiatric disorder cases. New-onset cases are qualified only by the absence of a disorder at the baseline interview and disorder diagnosis at a later interview, rather than the absence of a lifetime history of disorder at baseline. Because a substantial proportion of psychiatric disorders begin before military service,¹⁰ analyses of first-onset disorders is likely to overestimate the incidence rate of first-onset psychiatric disorders during service. Third, previous studies have focused on only three disorders (alcohol use disorder [AUD], major depressive disorder [MDD], and posttraumatic stress disorder [PTSD]), leading to a deficiency of data on the risk and burden of several less prevalent psychiatric disorders (e.g., phobias, dysthymia).

To address these limitations, we investigated sociodemographic and military predictors of first incidence of psychiatric disorders in a representative sample of military personnel followed during four annual study waves. We describe the first incidence estimates of the rates of psychiatric disorders in a reservist population and investigate sociodemographic and military factors that may increase the risk of anxiety or mood disorders.

METHODS

Participants

The Ohio Army National Guard (OHARNG) Mental Health Initiative is an ongoing, population-based, open, prospective study that has enrolled OHARNG service members annually since 2008. We chose the OHARNG for this study because of its similarities in several key demographic and social factors to U.S. populations (e.g., proportion of high school graduates, per-capita income) and National Guard populations (e.g., age, sex, rank).^{14,15} We conducted this analysis among respondents completing the in-person interview component of the larger prospective telephone survey¹⁶ that assessed resilience and risk factors for psychiatric disorders. The validity of the data collected by telephone was assessed by comparing them with data collected through clinical psychiatric interviews, which are considered the gold standard for psychiatric assessment.¹⁷

We used data collected from 2008 through February 2012. Sample selection occurred in three phases. First, as described elsewhere,¹⁶ the telephone survey randomly selected currently serving OHARNG members aged ≥ 17 years ($n=2,616$). Using American Association for Public Opinion Research definitions,¹⁸ the overall

cooperation rate (defined as number of OHARNG members who consented [$n=2,834$] divided by number of successfully contacted people with working telephone numbers [$n=4,198$]) was 67.5%, and the response rate (defined as OHARNG members who completed the survey [$n=2,616$] plus those who consented but were ineligible [$n=187$] divided by the number of working telephone numbers [$n=6,154$] minus those disqualified [$n=31$]) was 43.2%; both rates were similar to other population-based military cohort studies, such as Army Study to Assess Risk and Resilience in Servicemembers (65.1% cooperation rate and 49.8% response rate). Second, we randomly invited 1,046 (40%) individuals completing the telephone survey to receive more information by postal mail and participate in the clinical interview; 952 (91%) agreed to the clinical interview. Of these 952 service members, 452 (47.5%) were not contacted before the targeted number of OHARNG service members ($n=500$) provided written informed consent and were enrolled in the study. Third, in 2010, 105 new service members were added to the sample using the same protocols used for the baseline sample ($n=605$). We excluded 77 respondents who were assessed only at baseline, leaving a final analytical sample of 528 respondents.

Measures

Diagnostic assessment. Trained doctoral- or masters-level clinicians administered the *Structured Clinical Interview for DSM-IV* (SCID)¹⁹ and *Clinician-Administered PTSD Scale* (CAPS)²⁰ annually from June 2008 through February 2012 in a neutral, private location (e.g., private library room, participant's home) to assess first incidence of *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV) psychiatric disorders.²¹ The baseline interview assessed respondents' military, mental health, and treatment history, and social and economic circumstances, while annual follow-up assessments focused on interim mental health risk factors and diagnostic symptomology.

The SCID assesses Axis I disorders,¹⁹ which we categorized into three classes: anxiety disorder (panic disorder, agoraphobia without panic disorder, specific phobia, social phobia, and PTSD), mood disorders (MDD, dysthymia, and bipolar disorder I/II), and substance use disorders (alcohol and/or drug abuse and/or dependence). All diagnoses were based on DSM-IV criteria, and a decision tree approach was used to record the presence or absence of each disorder for current and lifetime occurrences. We did not include sub-threshold disorders.

The CAPS was administered twice during each assessment to assess PTSD symptoms: once to assess

symptoms caused by an event described by the participant as the worst event (hereinafter referred to as "potentially traumatic event") to occur during his or her most recent deployment and a second time to assess symptoms caused by an event described by the participant as the worst event to occur outside his or her most recent deployment.²² We defined a case of PTSD by using the frequency ≥ 1 and intensity ≥ 2 method, which is the most sensitive and the original scoring rule.^{20,23} Frequency ratings of symptoms are made on a five-point scale, from 0 (never or none of the time) to 5 (daily or almost every day), and intensity symptoms are also made on a five-point scale, from 0 (none or no problem with symptom) to 5 (extreme, incapacitating). Thus, symptoms with frequency ≥ 1 and intensity ≥ 2 suggest that the person is experiencing the symptom with at least mild intensity some of the time. Participants meeting diagnostic criteria for PTSD on either CAPS were classified as having PTSD. We found monthly interrater reliability for the SCID and CAPS showed good concordance between interviewers and diagnostic assessment methods for our study (free-marginal multirater $\kappa > 0.85$).²⁴

Potentially traumatic events. We assessed potentially traumatic events using the 16-item Life Events Checklist. The Life Events Checklist and CAPS were developed concurrently with the intent that the Life Events Checklist would screen for potentially traumatic events for the CAPS. We selected the original 16 Life Events Checklist items because of their association with PTSD symptomology.²⁵ In our study, participants were asked about lifetime potentially traumatic events at the baseline interview and past-year potentially traumatic events during follow-up interviews.

Sociodemographic and military characteristics. Baseline sociodemographic risk factors included cohort (baseline, dynamic cohort [i.e., the 105 people who were added after the baseline cohort, during wave 3]), age at enrollment, race (non-Hispanic white, non-Hispanic black, other), and sex. Additional baseline military risk factors included age at joining the military and lifetime deployment (yes/no). Potential time-varying risk factors included marital status (single/never married, married, previously married [separated, divorced, widowed]), education (\leq high school, some college, \geq college degree), pay grade (enlisted [E1–E9], officer [warrant officer 1–5, officer 1–10]), and deployment (yes/no) since the respondent's last interview. We also adjusted the model of mood and anxiety disorder for AUD (never, ever but not last year, last year) and drug use disorder (never/ever).

Statistical analyses

We used sequential regression multiple imputation to impute the interval censoring of disorder symptoms and missing covariates.²⁶ We generated five imputations. Interval censoring occurred after baseline when a respondent reported the onset of disorder symptoms at a follow-up interview but did not participate in one or more intermediate interviews. With interval censoring, it is unclear if the respondent developed the disorder at the time of interview or at an earlier time point. The timing of disorder onset mattered when we calculated the person-years at risk to estimate incident rates and the time to event in survival data analysis.

We calculated the number of service members at risk, new cases, and person-years at risk of developing each psychiatric disorder. We calculated number of service members at risk as the number of respondents who were disorder-free during their lifetime at baseline (i.e., who did not ever have a diagnosis of a disorder). New cases were respondents who did not have a diagnosis of a disorder at baseline and who received a diagnosis of the disorder during follow-up. We calculated person-years at risk of developing each psychiatric disorder from the baseline survey date to either the date of disorder onset, loss to follow-up, or end of the study period. We estimated the incidence rate of each disorder by using intercept-only Poisson regression, in which the number of new cases was the outcome and the person-years at risk was the offset. We calculated the incidence rate for an aggregate category as the first onset of any unique disorder among formerly disorder-free respondents for all unique disorders in the category at baseline. We calculated incidence rates for each unique disorder irrespective of the other disorders in the category.

We estimated the odds ratios of risk factors associated with the prevalence of mood or anxiety disorder at baseline using logistic regression. We conducted bivariate and multivariable logistic regression estimates with 95% confidence intervals (CIs) of the prevalence of mood or anxiety disorder at baseline. Among the respondents who were disorder-free at baseline and had at least one follow-up interview, we estimated hazard ratios of incidence using unadjusted and adjusted discrete-time Cox proportional hazard models. We obtained estimates and standard errors by fitting the models separately in each of the imputed datasets first and then combining the results across the five imputed datasets using Rubin's rule.^{27,28} We conducted all statistical analyses using R.²⁹

RESULTS

Of the 528 study participants, most were aged 17–34 years (70.9%), male (87.7%), non-Hispanic white (88.4%), enlisted personnel (88.6%), and previously deployed (57.5%). The demographic and military characteristics of study participants and the OHARNG population were similar, except for marital status: 44.8% of study participants were single and 44.6% were married, whereas 55.4% of the OHARNG population were single and 38.5% were married (Table 1).

At baseline, 336 respondents met diagnostic criteria for one or more psychiatric disorders. The unadjusted and adjusted models for baseline disorders were similar for most characteristics, with the exception of education and marital status, where the bivariate association was significant and the multivariable association was

Table 1. Characteristics of Ohio Army National Guard (OHARNG) members and a sample of the OHARNG population, United States, 2008 through 2012

Characteristic	Study participants	OHARNG
	(sample n=528) N (percent) ^a	2008 profile (n=10,778) N (percent) ^a
Total	528 (100.0)	10,778 (100.0)
Age, in years		
17–24	193 (36.6)	6,430 (39.1)
25–34	181 (34.3)	5,477 (33.3)
35–44	99 (18.8)	3,361 (20.5)
≥45	55 (10.4)	1,166 (7.1)
Sex		
Male	462 (87.7)	14,239 (86.6)
Female	65 (12.3)	2,195 (13.4)
Race/ethnicity		
Non-Hispanic white	466 (88.4)	9,512 (88.3)
Non-Hispanic black	36 (6.8)	1,083 (10.0)
Other ^b	25 (4.7)	183 (1.7)
Marital status		
Single, never married	236 (44.8)	5,967 (55.4)
Married	235 (44.6)	4,154 (38.5)
Divorced/separated/widowed	56 (10.6)	657 (6.1)
Rank		
Enlisted (E1–E9)	467 (88.6)	9,750 (90.5)
Officer (W1–5/O1–10)	60 (11.4)	1,028 (9.5)
Ever deployed		
Yes	303 (57.5)	5,863 (54.4)
No	224 (42.5)	4,915 (45.6)

^aNot all percentages total to 100 because of rounding.

^bIncludes American Indian/Alaska Native, Asian American/Pacific Islander, or Hispanic

E = enlisted

W = warrant officer

O = officer

not. Respondents with an anxiety or mood disorder at baseline were more likely to be female than male (adjusted odds ratio [AOR] = 1.91, 95% CI 1.12, 3.25), to have more potentially traumatic events (AOR=1.56, 95% CI 1.12, 2.16), and to meet diagnostic criteria for lifetime AUD (AOR=1.71, 95% CI 1.18, 2.49) or drug use disorder (AOR=1.65, 95% CI 1.00, 2.73). We found no association between lifetime deployment and baseline disorder (Table 2).

Among the 192 respondents who were disorder-free at baseline, 41 respondents were diagnosed with a first-onset psychiatric disorder during the 417 person-years of follow-up, for an incidence rate of 9.8 individuals per 100 person-years, or 9.8% per year (Figure). Although average incidence rates across the aggregate categories (i.e., anxiety disorders, mood disorders, substance use disorders) differed by <1 percentage point (range: 3.8%–4.6%), the incidence rates across component categories of mood disorders and substance use disorders were heterogeneous. The two highest incident rates for any category were for AUD (5.0%, 95% CI 3.5, 7.0) and MDD (4.2%, 95% CI 3.0, 5.7) and the two lowest rates were for drug use disorder (0.6%, 95% CI 0.3, 1.3) and bipolar II (0.5%, 95% CI 0.2, 1.1). In contrast, the incidence rates for anxiety disorders were homogenous, ranging from 0.7% (obsessive-compulsive disorder) to 1.8% (specific phobia).

Incident anxiety or mood disorder was modestly associated with past-year deployment (adjusted hazard ratio [AHR] = 1.29, 95% CI 1.00, 1.66), non-deployment-related traumatic event in past year (AHR=1.32, 95% CI 1.10, 1.59), and lifetime potentially traumatic events (AHR=2.25, 95% CI 1.11, 4.55). Although lifetime AUD was not associated with incident risk of anxiety or mood disorder, past-year AUD was associated with a moderate increase in risk (AHR=1.68, 95% CI 1.35, 2.08). Finally, previously married respondents were 3.73 (95% CI 1.47, 9.48) times more likely than those who were single or never married to be diagnosed with an incident anxiety or mood disorder during follow-up (Table 3).

DISCUSSION

In a representative sample of OHARNG members, we documented 9.8 new cases of any first incidence of DSM-IV disorder per 100 person-years at risk. Our analyses produced four major findings. First, we found that the incidence rates for disorders in this study were considerably higher than the U.S. civilian rates for AUD (5.0% vs. 1.7%)³⁰ and MDD (4.2% vs. 1.5%).^{30,31} The higher rates reported for these two disorders could be attributed to sociodemographic differences between

Table 2. Bivariable and multivariable logistic regression models for lifetime prevalence of anxiety or mood disorders at baseline in a sample of Ohio Army National Guard members (n=528), United States, 2008 through 2012

Characteristic	Anxiety or mood disorder	
	Bivariable analysis OR (95% CI)	Multivariable analysis AOR ^a (95% CI)
Age at baseline	1.01 (0.99, 1.03)	1.00 (0.97, 1.03)
Age joining military	1.04 (1.00, 1.08)	1.03 (0.98, 1.08)
Cohort ^b		
2008 sample (baseline)	Ref.	Ref.
2010 sample	0.98 (0.63, 1.52)	1.46 (0.85, 2.50)
Sex		
Male	Ref.	Ref.
Female	1.63 (1.00, 2.64)	1.91 (1.12, 3.25)
Race/ethnicity		
Non-Hispanic white	Ref.	Ref.
Non-Hispanic black	0.96 (0.50, 1.85)	1.01 (0.50, 2.05)
Other ^c	0.94 (0.42, 2.08)	0.88 (0.38, 2.04)
Education		
≤High school	Ref.	Ref.
Some college	0.78 (0.51, 1.20)	0.72 (0.54, 1.13)
≥College degree	0.56 (0.33, 0.95)	0.68 (0.37, 1.25)
Marital status		
Single/never married	Ref.	Ref.
Married	1.22 (0.86, 1.74)	1.44 (0.89, 2.34)
Divorced/separated/ widowed	2.12 (1.21, 3.72)	1.91 (0.97, 3.78)
Rank		
Enlisted (E1–E9)	Ref.	Ref.
Officer (W1–5/O1–10)	0.51 (0.22, 0.77)	0.41 (0.20, 0.87)
Ever deployed		
No	Ref.	Ref.
Yes	0.97 (0.69, 1.35)	0.79 (0.51, 1.24)
Potentially traumatic events	1.51 (1.15, 1.98)	1.56 (1.12, 2.16)
Alcohol use disorder		
Never	Ref.	Ref.
Ever	1.90 (1.36, 2.66)	1.71 (1.18, 2.49)
Drug use disorder		
Never	Ref.	Ref.
Ever	2.20 (1.39, 3.48)	1.65 (1.00, 2.73)

^aAdjusted for all other variables in the table

^bThe study sample comprised 500 people who were recruited in 2008 and 105 people who were recruited in 2010.

^cIncludes American Indian/Alaska Native, Asian American/Pacific Islander, or Hispanic

OR = odds ratio

CI = confidence interval

AOR = adjusted odds ratio

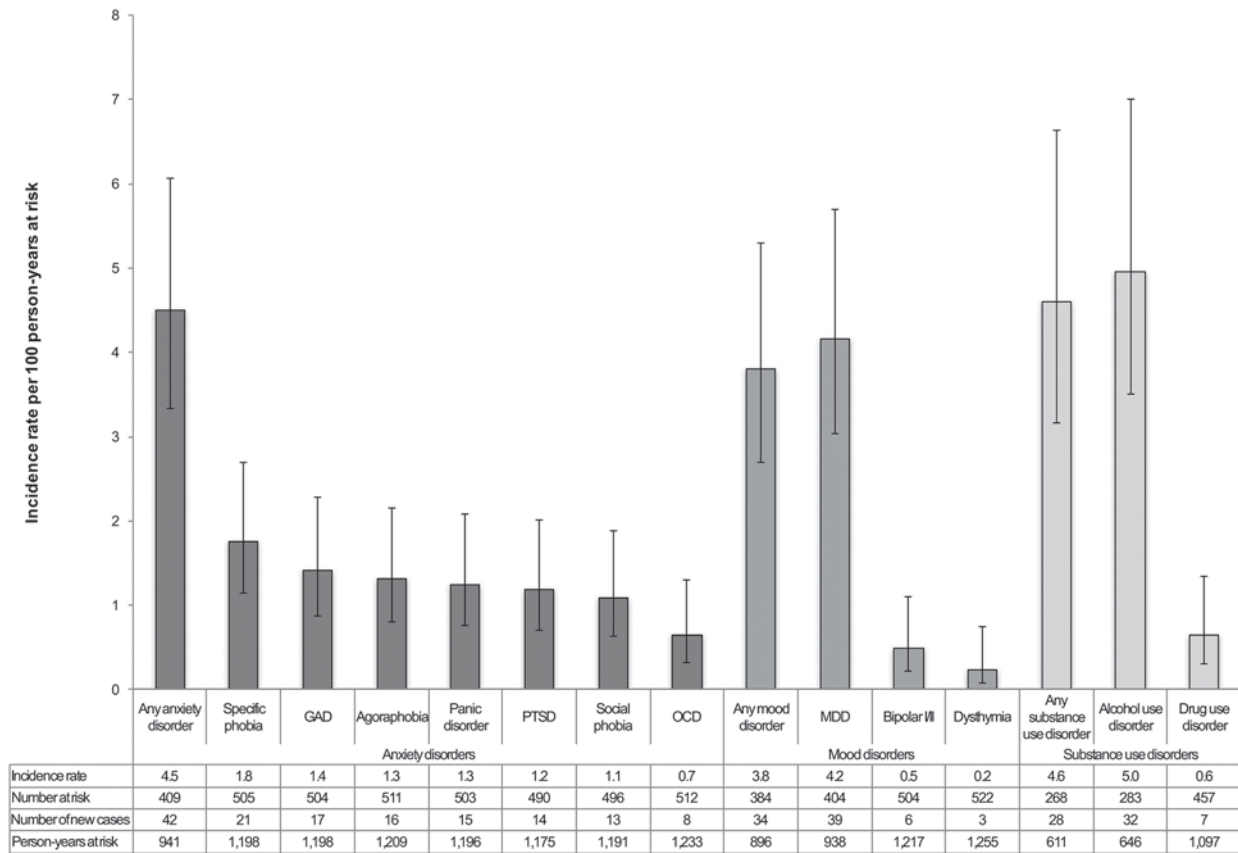
Ref. = reference group

E = enlisted

W = warrant officer

O = officer

Figure. Incidence rates and 95% confidence intervals of anxiety, mood, and substance use disorders per 100 person-years at risk, Ohio Army National Guard (n=528), 2008 through 2012^a



^aError bars indicate 95% confidence intervals.

GAD = generalized anxiety disorder

PTSD = posttraumatic stress disorder

OCD = obsessive-compulsive disorder

MDD = major depressive disorder

the military and civilian samples; military populations are predominantly younger (75% are ≤ 35 years of age) and male (>80%) compared with the U.S. population, which is on average 35 years of age and 51% female. Both disorders are commonly associated with younger age,³⁰⁻³² and male sex is commonly associated with AUD.^{32,33} Discrepancies in incidence rates among studies may also reflect differential exposure to predictors of mental illness. Military personnel are twice as likely as civilians to have adverse childhood experiences, including household substance abuse, physical abuse, and sexual abuse,¹¹ which have been documented to increase the risk of AUD and MDD.³⁴⁻³⁶

Second, the incidence rates for AUD, MDD, and PTSD in our study were consistent with previously published military rates. Two previous studies, the Millennium Cohort Study and the Readiness and Resil-

ience in National Guard Soldiers study, documented first-onset psychiatric disorders in the reserve component and provide a useful comparison. Consistent with previous studies, 58% of our sample had ever deployed.¹² Insofar as deployment is a risk factor for psychiatric disorders, the incidence of AUD (5.0%) and MDD (4.2%) in our study was similar to the incidence in a non-deployed subsample of the Millennium Cohort Study but lower than the incidence in a deployed subsample reporting combat exposure in the Millennium Cohort Study^{37,38} and Readiness and Resilience in National Guard Soldiers study.³⁹ That our incidence estimates were between those of deployed personnel with combat exposure (6.0% for AUD and 8.2% for MDD) and without combat exposure (2.8% for AUD and 2.8% for MDD)^{37,38} could be attributed, in part, to the healthy warrior effect, which proposes

Table 3. Bivariable and multivariable Cox proportional hazard models for incident anxiety or mood disorders in a sample of Ohio Army National Guard members (n=528), United States, 2008 through 2012

Characteristic	Anxiety or mood disorder ^a	
	Bivariable analysis	Multivariable analysis
	HR (95% CI)	AHR ^b (95% CI)
Age at baseline	0.98 (0.96, 1.01)	0.98 (0.93, 1.02)
Age joining military	1.00 (0.93, 1.06)	1.01 (0.93, 1.09)
Cohort ^c		
2008 sample (baseline)	Ref.	Ref.
2010 sample	1.53 (0.69, 3.40)	1.84 (0.72, 4.74)
Sex		
Male	Ref.	Ref.
Female	0.90 (0.32, 2.49)	0.99 (0.33, 2.99)
Race/ethnicity		
Non-Hispanic white	Ref.	Ref.
Non-Hispanic black	0.84 (0.26, 2.71)	0.90 (0.26, 3.17)
Other ^d	0.61 (0.09, 4.33)	0.41 (0.06, 3.10)
Education		
≤High school	Ref.	Ref.
Some college	0.86 (0.42, 1.76)	0.83 (0.40, 1.76)
≥College degree	0.58 (0.24, 1.40)	0.86 (0.30, 2.48)
Marital status		
Single/never married	Ref.	Ref.
Married	0.89 (0.49, 1.64)	1.28 (0.59, 2.78)
Divorced/separated/ widowed	2.45 (1.07, 5.59)	3.73 (1.47, 9.48)
Rank		
Enlisted (E1–E9)	Ref.	Ref.
Officer (W1–5/O1–10)	0.48 (0.17, 1.32)	0.61 (0.17, 2.11)
Ever deployed		
No	Ref.	Ref.
Yes	0.77 (0.44, 1.35)	0.65 (0.32, 1.32)
Potentially traumatic events	1.70 (1.02, 2.86)	2.25 (1.11, 4.55)
Time-dependent covariates		
Deployed, past year	2.14 (1.07, 4.29)	1.29 (1.00, 1.66)
Traumatic event, past year	1.46 (1.01, 2.11)	1.32 (1.10, 1.59)
Alcohol use disorder		
Never	Ref.	Ref.
Ever, but not past year	1.17 (0.58, 2.36)	1.09 (0.86, 1.38)
Past year	1.91 (1.00, 3.66)	1.68 (1.35, 2.08)
Drug use disorder		
Never	Ref.	Ref.
Ever, but not past year	1.12 (0.47, 2.63)	0.91 (0.65, 1.29)

^aA total of 89 episodes; 889 person-years at risk

^bAdjusted for all other variables in the table

^cThe study sample comprised 500 people who were recruited in 2008 and 105 people who were recruited in 2010.

^dIncludes American Indian/Alaska Native, Asian American/Pacific Islander, or Hispanic

HR = hazard ratio

CI = confidence interval

AHR = adjusted hazard ratio

Ref. = reference group

E = enlisted

W = warrant officer

that the military is more likely to deploy healthier personnel.^{40,41} Furthermore, differences may also be associated with the increased risk of mental illness after stressful combat experiences.^{42,43}

Third, our observation that the incidence rate of first-onset PTSD was 1.2% per year was substantially lower than previously documented rates of first-onset PTSD among soldiers (2.9%–11.3%).^{44–46} The lower rates reported for PTSD could be attributed to the different case definitions used by studies. Among the reserve component, all previous prospective studies assessed first-onset disorder, which is a measure combining data on disorders that were not present at baseline but were re-aggravated during a follow-up interval with data on first-incidence disorders. Because about one in three PTSD cases begin before military service,¹⁰ and because PTSD has been documented to be cyclical in more than 25% of cases,^{47,48} the higher rates documented in previous studies could be due to re-aggravated disorders.

Fourth, our finding that previously married respondents and respondents reporting exposure to a traumatic lifetime event or past-year event had the highest incidence of anxiety or mood disorder is consistent with existing literature.^{49–52} Relationship issues are common among military personnel.^{53,54} Although literature examining the association among military stressors, mental health, and relationship issues⁵⁵ exists, the association between these stressors and the rising rates of divorce in military marriages is unclear.^{56,57} Recent studies proposed a mediation model whereby the association between combat deployment and relationship/marital satisfaction is mediated by screening positive for PTSD.^{39,58} Other studies provided evidence on the interactive effect of PTSD, alcohol misuse, intimate partner violence, and relationship issues among civilians and combat veterans.^{59,60} Future analyses are needed to investigate these two hypotheses explaining the interrelationships among trauma, marital disruption, and mental illness in military personnel.

Limitations

This study had several limitations. First, the data were susceptible to information bias. Although a bias against reporting embarrassing behaviors⁶¹ and the perception of psychiatric illness stigma are prevalent in the military,⁶² we compensated for this concern by assuring participants' confidentiality, both verbally and in writing, before volunteering for this study and by conducting all assessments in neutral locations using civilian clinicians and no military personnel. Second, these findings may not be generalizable to other reservists (e.g., Navy Reserve) from other states or active-duty

military personnel. Although the OHARNG population is similar in several key demographic and social factors to the U.S. population (e.g., proportion of high school graduates, per-capita income)¹⁴ and National Guard population (e.g., age, sex, rank),¹⁵ our study sample had a higher proportion of respondents who were divorced, separated, or widowed, a group shown to be at increased risk for mood or anxiety disorder. The higher number of divorced, separated, and widowed respondents may have resulted in increased incidence rates. Future replication of findings in other states and components would improve confidence in our findings.

CONCLUSION

This study is the first to prospectively estimate first incidence of several psychiatric disorders using gold-standard clinical interviews in a representative sample of U.S. armed services members, OHARNG members. Our study advances the literature on military psychiatric epidemiology by overcoming limitations of previous studies that examined disorder prevalence or first-onset disorders or restricted analyses to deployed service members. The greater incidence of anxiety and mood disorders among previously married respondents and people experiencing lifetime and past-year potentially traumatic events underscores the need for heightened vigilance in identifying and monitoring service members who are experiencing marital disruptions, particularly in relation to other potentially traumatic experiences. The marginal association between past-year deployment and first incidence of anxiety or mood disorder suggests that studies selecting respondents on deployment status limit knowledge about the causal mechanisms that contribute to mental illness burden in the military. Therefore, future studies should consider deployment experiences as part of a broader set of life-course risk factors that can affect the psychopathology of mental illness among service members.

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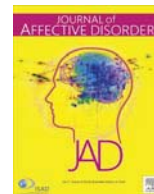
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Research paper

Retrospective age-of-onset and projected lifetime prevalence of psychiatric disorders among U.S. Army National Guard soldiers



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ABSTRACT

Background: The study of military-related mental health has been disproportionately focused on current symptomology rather than potentially more informative life course mental health. Indeed, no study has assessed age-of-onset and projected lifetime prevalence of disorders among reservists.

Methods: Age-of-onset and projected lifetime DSM-IV anxiety, mood, and substance use disorders were assessed in 671 Ohio Army National Guard soldiers aged 17–60 years. Between 2008 and 2012, face-to-face clinical assessments and surveys were conducted using the Structured Clinical Interview for DSM-IV and Clinician-Administered PTSD Scale.

Results: Lifetime prevalence of psychiatric disorders was 61%. Alcohol abuse/dependence (44%) and major depressive disorder (23%) were the most common disorders. The majority (64%) of participants reported disorders antedating enlistment. Median age-of-onset varied with anxiety disorders – particularly phobias and OCD – having the earliest (median = 15 years) and mood disorders the latest median age-of-onset (median = 21 years).

Limitations: The study was limited by both the retrospective investigation of age-of-onset and the location of our sample. As our sample may not represent the general military population, our findings need to be confirmed in additional samples.

Conclusions: Each psychiatric disorder exhibited a distinct age-of-onset pattern, such that phobias and OCD onset earliest, substance use disorders onset during a short interval from late-adolescence to early-adulthood, and mood disorders onset the latest. Our finding that the majority of participants reported disorders antedating enlistment suggests that an assessment of lifetime psychopathology is essential to understanding the mental health burden of both current and former military personnel.

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1. Introduction

It is estimated that nearly one in five United States (US) military service members are experiencing a psychiatric disorder at any given time (Riddle et al., 2007). While nearly all military studies ask questions of service members about their military experiences and beyond, much of the scientific writing in this area has omitted

discussion of pre-military experiences and how they might shape “military mental health”. This potential set of omitted variables that might be of consequence here emerges readily from a life course perspective on the production of mental health.

Psychiatric epidemiology has been revolutionized by the development of a life course approach for examining physical and social exposure across the life span on adult disease risk (Koenen et al., 2014; Kuh et al., 2003). Just 4 decades ago psychiatric disorder age-of-onset was a controversial and uncertain topic (Rutter, 1972), while now we understand that the majority of psychiatric disorders first onset prior to age 15 (Kessler et al., 2007; Kim-Cohen et al., 2003). The importance of employing a life course

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perspective when examining psychiatric disorders among service members is hinted at in examples from recent literature. For example, Gallaway et al. (2013) documented that soldiers granted enlistment waivers for pre-military concerns (e.g., alcohol or drugs problems,) from 2003 to 2008 were significantly more likely to test positive for an illicit substance, be screened for admission to an alcohol/drug abuse program, and attrite from the Army for behavioral misconduct. Further, several studies have documented that about half of military suicides are among service members that have never deployed (LeardMann et al., 2013; Schoenbaum et al., 2014), that most of the suicidal behaviors during military service have had pre-enlistment onset (Nock et al., 2014), and that exposure to child abuse prior to military service is associated with suicidal behaviors during military service (Afifi et al., 2016). Nonetheless, military studies continue to primarily examine recent exposures, lending to the paucity of literature into life course factors among military personnel.

The focus on deployment experiences as the cause of psychiatric disorders among service members, rather than on the life course patterns of psychiatric disorders (e.g., pre-military psychiatric disorders, age-of-onset) that might be more central to the production of the health indicators of interest, has limited our understanding about the course of psychiatric disorders both prior to and during military service. Furthermore, understanding the life course patterns of mental illness among service members can change the narrative about the etiology of psychiatric disorders during military service, such that military experiences might be exacerbating earlier symptomology, rather than first incident disorders. However, our understanding of early life, pre-military, mental illness remains limited.

Mental illness is a major health concern in the US armed forces, particularly among the Reserves and National Guard (reserve component) (Cohen et al., 2015). Investigations to date have indicated that the reserve component suffers a greater burden of psychiatric disorders compared to the active component (Cohen et al., 2015; Iowa Persian Gulf Study Group, 1997; Milliken et al., 2007; Thomas et al., 2010). Prior to 2001, the National Guard had largely supported individual states during times of emergency; however, in the aftermath of the Vietnam War, the Total Force Policy was adopted to treat the 2 components (i.e., active-duty and reserve component) as a single operational force. As a result, during the height of mobilization in Operation Enduring Freedom and Operation Iraqi Freedom and (OEF/OIF) the reserve component forces constituted about 40% of deployed service members in combat operations. This reliance on the reserve component is not idiosyncratic to OEF/OIF; it is part of the Department of Defense's long-term strategic vision to increase the size, roles, and responsibilities of the reserve component moving forward (Department of Defense, 2011; Department of Defense, 2008). Nonetheless, there is a paucity of research addressing the mental health of reservists (Cohen et al., 2015).

In this study we used face-to-face clinical assessment using gold-standard instruments to document the age-of-onset and projected lifetime prevalence of psychiatric disorders in a representative sample of Ohio Army National Guard soldiers. Thus the first aim of this study was to investigate the lifetime prevalence and age-of-onset of DSM-IV psychiatric disorders using the Structured Clinical Interview for DSM-IV (SCID) and Clinician-Administered PTSD Scale (CAPS). The second aim was to use the lifetime prevalence of psychiatric disorders, and their respective age-of-onset, to determine the probability of disorder onset at each year of life from age 0–50 years. The third aim was to compare the psychiatric disorder age-of-onset to respondents' date of enlistment to determine the prevalence of disorders that onset prior to initiating military service. We hypothesized that substance use disorders and PTSD would be the most prevalent psychiatric

disorders. Secondly, we expected substance use disorders to onset prior to military service, particularly during late-adolescents to early-adulthood (e.g., 16–24). Third, we expected PTSD, the sentinel trauma-related psychiatric disorder, to onset primarily after respondents enlisted into military service.

2. Methods

2.1. Participants

We used data from an in-depth clinical cohort study, nested within the Ohio Army National Guard (OHARNG) Mental Health Initiative (MHI). The OHARNG MHI is a representative longitudinal cohort study examining risk and resilience factors among OHARNG members (Calabrese et al., 2011). To examine the validity of the telephone survey mental health screening tools, we randomly selected 500 respondents from the baseline OHARNG MHI telephone survey sample. In addition, we randomly selected an additional 171 recently enlisted OHARNG to the clinical validation subsample in 2011 ($n=105$) and 2012 ($n=171$) to increase both the analytical power and provide data on the most recent cohort of OHARNG.

For the purpose of the current study, we used baseline data from the in-depth clinical cohort of the OHARNG MHI study. The clinical cohort was predominantly white (87%), male (87%), and single-never married (51%) (Table 1). The median age of the sample was 26 years (standard deviation: 9.6 years) and ranged from 17 to 60 years. In addition, most respondents were enlisted rank (E1–E9; 90%) and had deployed one or more times (55%). Overall, the clinical cohort was similar to the target population (i.e., Ohio National Guard service members) on all demographic and military characteristics.

2.2. Procedures

Study trained clinicians completed face-to-face clinical interviews in private locations (e.g., private library room) with 671 participants from June 2008 to February 2012. Study staff performed monthly inter-rater reliability for the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and Clinician-Administered PTSD Scale (CAPS) to assure that the interviewers were standardized in their diagnostic assessment methods and interviewing techniques; results revealed moderate to excellent inter-rater agreement (> 0.9) and Free-Marginal Multirater Kappas (> 0.85). A comprehensive description of OHARNG Mental Health Initiative sampling strategy and recruitment has been previously published (Prescott et al., 2014). The study was approved by the local institutional review boards and written informed consent was obtained from all participants.

2.3. Measures

The diagnostic interview included both the CAPS (Blake et al., 2000) and the SCID (First et al., 2002, 1996). First, the CAPS was administered twice to assess both lifetime and current PTSD symptoms based on the individuals' self-selected "worst deployment related trauma" and then again for their "worst not related to deployment" (Breslau et al., 1998). Posttraumatic stress disorder diagnosis was based on DSM-IV criteria using the frequency ≥ 1 and intensity ≥ 2 methods (Blake et al., 2000), which is considered the gold standard for identifying PTSD cases for lifetime PTSD diagnosis (Weathers et al., 2001); compared to the SCID, the CAPS has been found to have a test-retest reliability (kappa) of 0.73, 84% sensitivity, and 90% specificity (Weathers et al., 2001). Respondents meeting diagnostic criteria on either the CAPS

Table 1
Baseline characteristics of 671 Ohio Army National Guard study participants, 2008–2012.

Variable	Study Participants (N=671)		Ohio National Guard 2008 Profile (N=10,778)	
	No.	%	No.	%
Age, years				
17–24	278	41.4	6430	39.1
25–34	221	32.9	5477	33.3
35–44	114	17.0	3361	20.5
45+	58	8.6	1166	7.1
Sex				
Male	586	87.3	14,239	86.6
Female	85	12.7	2195	13.4
Race/ethnicity				
White	586	87.3	9512	88.3
African American	48	7.2	1083	10.0
Other	36	5.4	183	1.7
Missing	1	0.2		
Marital status				
Single, never married	345	51.4	5967	55.4
Married	265	39.5	4154	38.5
Divorced/separated/ widowed	61	9.1	657	6.1
Rank				
Enlisted (E1–E9)	603	89.6	9750	90.5
Officer (W1–5/O1–10)	68	10.1	1028	9.5
Prior deployment				
Yes	367	54.7	5863	54.4
No	304	45.3	4915	45.6

Note: E=enlisted; O=officer; W=warrant officer.

related to their worst deployment related traumatic event or the CAPS related to their worst non-deployment related traumatic event were classified as having PTSD.

The SCID was administered to assess Axis I disorders (First et al., 1996), which were then categorized into three overarching groups: anxiety disorder (panic disorder, agoraphobia without panic disorder, specific phobia, social phobia, obsessive-compulsive disorder (OCD)), mood disorders (major depressive disorder (MDD) and bipolar disorder I/II), and substance use disorders (SUD; alcohol and/or drug abuse or dependence). Total unique diagnoses were summed and categorized into a single interval variable representing comorbidity. All diagnoses were based on DSM-IV criteria and subthreshold disorders were not considered for this analysis. Previous reliability studies of the SCID have found that reliability estimates vary across the disorders, ranging from about 0.60 to 1.00 (Lobbestael et al., 2011; Zanarini et al., 2000).

Study clinicians using SCID guidelines determined retrospective age-of-onset. Assessing the reliability of self-reported age-of-onset, Farrer et al. (1989) found perfect agreement for age-of-onset in about 25–33% of persons with MDD and the highest test-retest reliability among persons 18–19 ($r=.91$) and 20–29 ($r=.77$). Likewise, Prusoff et al. (1988) documented similarly high correlation of self-reported age-of-onset among respondents diagnosed with MDD ($r=.71$) and panic disorder ($r=.70$), with moderate correlation among respondents diagnosed with phobic disorders ($r=.58$) and alcohol use disorder ($r=.41$).

Standard demographic and military characteristics were assessed, including: age, sex, race/ethnicity, marital status, rank, and lifetime deployment.

2.4. Statistical analysis

First, cumulative lifetime prevalence was estimated as the proportion of respondents who ever fulfilled DSM-IV diagnostic criteria for a given disorder for at least part of their lives up to their age at baseline interview.

Second, we performed a stratified analysis to assess the presence of a secular trend (i.e., cohort effect). This step was required because we accrued study participants over 4 years and the actuarial method assumes constant conditional risk of disease onset at a given year of life. Upon evidence that there was no secular trend across the cohorts, we assumed constant conditional risk and concatenated all baseline data.

Third, age-of-onset distributions and projected lifetime risk to age 50 years were estimated using the actuarial (life table) method (Halli and Rao, 1992; Rosner, 2006) executed in SAS 9.2 (Cary, NC). The actuarial method differs from the more familiar Kaplan and Meier (1958) method because it takes a time interval (e.g., 1-year) as its primary unit, while the Kaplan-Meier approach calculates the probability of each event at the time it occurs. Therefore, the actuarial method was better suited for our data as we only assessed the age at first diagnosis (i.e., 1-year interval) and not the exact date. The actuarial method calculates the cumulative incidence as the probability of an event in a given interval as the proportion of new events during that period of time, in which the denominator is the initial population corrected for losses. This measure corresponds to the interval-based probability of the event (Rosner, 2006). For this study, cumulative probability of event was estimated for 1-year intervals for 50 years with the probability estimated for every year of age.

3. Results

Lifetime prevalence and projected lifetime risk at age 50 of common mood, anxiety, and substance disorders is presented in Table 2. Overall, 61% of the sample met criteria for at least one lifetime disorder. Substance use disorders were the most prevalent diagnoses (47%), followed by mood (28%) and anxiety disorders (22%). Prevalence of the individual anxiety disorders were evenly distributed within the category with a difference of less than 4% between the least and most common diagnoses, agoraphobia without panic disorder (3%) and PTSD (6%), respectively. Conversely, MDD accounted for the preponderance of diagnosed mood disorders. Finally, comorbidity was substantial; specifically, about 30% of respondents met diagnostic criteria for two or more psychiatric disorders.

Age-of-onset distributions are presented in Table 3. Anxiety disorders (15 years) had an earlier median age-of-onset compared to substance use disorders (19 years) or mood disorders (21 years). There was noticeable variability in median age-of-onset within and between diagnosis categories. For example, within anxiety disorders, age-of-onset clustered within two groups; specific phobia, social phobia, and OCD had a median age-of-onset of 10–13 years, while agoraphobia without panic disorder, PTSD, panic disorder, and other anxiety disorders had a median age-of-onset of 19, 20, 20, and 24 years, respectively. Conversely, substance use disorders had similar median age-of-onsets (16–20 years) and narrow distributions (IQR 4 years). However, while substance abuse had similar means and IQRs, drug use/dependence predominately onset prior to 18 years (67%), compared to the majority of alcohol abuse/dependence that had first onsets between 18 and 24 years (74%). Finally, we observed an inverse association between the number of comorbid psychiatric disorders and age-of-onset, such that respondents who were diagnosed with a greater number of comorbid psychiatric disorders tended to report an

Table 2
Lifetime prevalence and age-of-onset of DSM-IV disorders in Ohio Army National Guard study participants, 2008–2012 (N=671).

Mental disorders	Prevalence		Age-of-onset ^a	
	No.	%	Median	IQR ^b
Anxiety disorders				
Panic disorder	30	4.5	24.0	15.0
Agoraphobia, without panic disorder	20	3.0	19.5	14.0
Specific phobia	39	5.8	10.0	13.0
Social phobia	43	6.4	11.0	7.0
Posttraumatic stress disorder	42	6.3	20.0	11.0
Obsessive compulsive disorder	25	3.7	12.5	13.0
Other anxiety disorder	33	4.9	20.0	13.0
Any anxiety disorder	144	21.5	15.0	14.0
2+ Anxiety disorders	41	6.1	13.0	15.5
Mood disorders				
Major depressive disorder	154	23.0	21.0	13.0
Bipolar I/ II	29	4.3	20.0	12.0
Other mood disorders	41	6.1	24.0	14.0
Any mood disorder	190	28.3	21.0	13.0
2+ Mood disorders	12	1.8	20.0	13.5
Substance use disorders				
Alcohol use disorder ^c	293	43.7	20.0	4.0
Drug use disorder	91	13.6	16.0	4.0
Any	313	46.7	19.0	4.0
Both alcohol and drug abuse	71	10.6	16.5	2.5
Aggregate mental disorders				
0	259	38.6	–	–
1	204	30.4	19.0	4.0
2	115	17.1	17.0	5.0
3+	93	13.9	15.0	8.0

Note: IQR=inter-quartile range.

^a Retrospectively reported age-of-onset.

^b Inter-quartile range (IQR) is the range between then 25th and 75th percentiles on the age-of-onset distribution.

^c Includes abuse and dependence.

earlier age of first disorder onset.

The proportion of disorders with age-of-onset prior to military service aligned well with median age-of-onset, where social phobia (95%), specific phobia (81%), and OCD (73%) had first onsets primarily prior to service (Fig. 1). Additionally, about half of bipolar I/II (52%), agoraphobia without panic (50%), and PTSD (49%) diagnoses had first onsets prior to service.

Fig. 2 presents cumulative onset probability of psychiatric disorders using the actuarial method. This figure supports Table 3 by

showing variability in age-of-onset distributions of psychiatric disorders. For example, while mood disorders are predicted to occur at fairly regular intervals, following a linear trend (albeit with different slopes), substance use disorders are predicted to occur within a fairly small age interval (i.e., less variation around the mean age-of-onset) – aligning with the large IQR of anxiety and mood disorders (13–14 years), compared to substance use disorders (IQR=4 years) documented in Table 3. Further, the lifetime prevalence of alcohol abuse/dependence (59.4%, 95% CI: 53.7, 65.1) and MDD (38.7%, 95%CI: 31.0, 47.5) is relatively higher than all other disorders, which cluster between about 4% and 15%.

4. Discussion

Using data from a representative sample of Ohio Army National Guard soldiers we found that 61% of reservists met diagnostic criteria for one or more psychiatric disorders at some time in their lives. Alcohol abuse/dependence and MDD were the most common individual disorders, whereas anxiety disorders were categorically less prevalent. Importantly, about half of participants reported that disorders onset prior to military service for several assessed psychiatric disorders, including: social phobia, specific phobia, drug abuse/dependence, OCD, PTSD, and bipolar I/II disorders.

We found that the majority of reservists reported disorders starting before military service. We are aware of only two previous studies that attempted to document age-of-onset of DSM-consistent disorders in a military population that may serve as a point of comparison (Gademmann et al., 2012; Kessler et al., 2014). Gademmann et al. (2012) restricted and weighted National Comorbidity Survey Replication (NCS-R) data based on Army socio-demographics to estimate MDD lifetime prevalence and age-of-onset for the U.S. Army. We found higher estimates of lifetime prevalence of MDD (41%) and lower proportion of pre-enlistment onset (47%) compared to Gademmann et al. (2012), who estimated 16% and 70% respectively. That we found higher estimates of lifetime MDD and lower proportion of pre-enlistment onset likely is a product of the Gademmann et al. (2012) study design, which weighted the NCS-R, a national survey of DSM-IV psychiatric disorders in the civilian U.S. household population, to match the sociodemographics of the U.S. Army. Because Gademmann et al. (2012) limited the NCS-R sample to persons meeting very strict military regulations (e.g., high school education/GED, no felony conviction, free from physical or severe psychiatric disorder), military regulations that the military later relaxed during OEF/OIF (Gallaway et al., 2013), their sample is likely to underestimate the

Table 3
Median age-of-onset and distribution of DMS-IV mental disorders in a population-based study of the Ohio Army National Guard, 2008–2012 (N=671).

	Anxiety disorders							Mood disorders			Substance disorders	
	Panic disorder	Agoraphobia, without panic disorder	Specific phobia	Social phobia	Post-traumatic stress disorder	Obsessive compulsive disorder	Other anxiety disorder	Major depressive disorder	Bipolar I/II	Other mood disorder	Alcohol use disorder ^c	Drug use disorder ^c
Median ^a (IQR) ^b	24 (15)	19 (14)	10 (13)	11 (7)	20 (11)	13 (13)	20 (13)	21 (13)	20 (12)	24 (14)	20 (4)	16 (4)
< 18 Years	12.0%	44.4%	70.0%	95.1%	35.9%	68.2%	38.1%	33.6%	39.1%	26.7%	12.1%	66.7%
18–24 Years	44.0%	22.2%	26.7%	2.4%	38.5%	18.2%	28.6%	32.1%	30.4%	40.0%	74.1%	31.2%
25+ Years	44.0%	33.3%	3.3%	2.4%	25.6%	13.6%	33.3%	34.3%	30.4%	33.3%	13.8%	2.2%

^a Retrospectively reported age-of-onset.

^b Inter-quartile range (IQR) is the range between then 25th and 75th percentiles on the age-of-onset distribution.

^c Includes abuse and dependence.

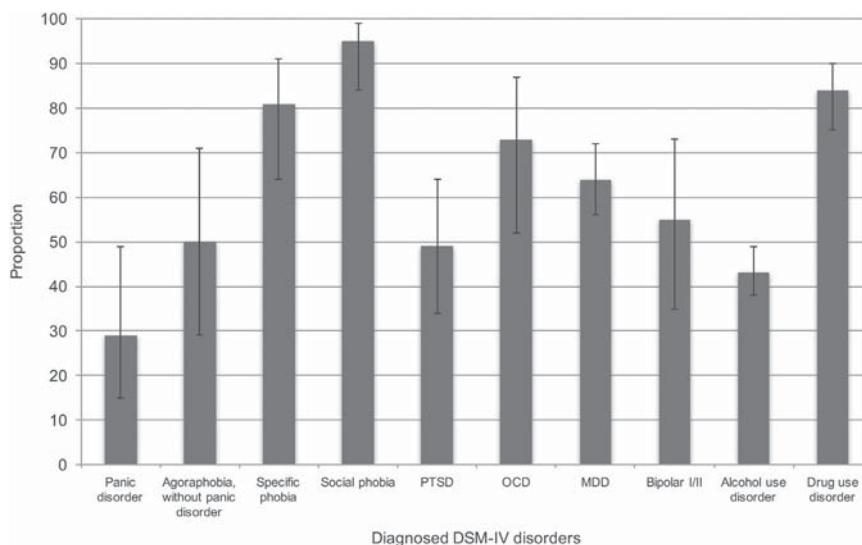


Fig. 1. Proportion of diagnosed psychiatric disorders that had first onsets prior to military service in a representative study of the Ohio Army National Guard, 2008–2012. PTSD, posttraumatic stress disorder; OCD, obsessive-compulsive disorder; MDD, major depressive disorder.

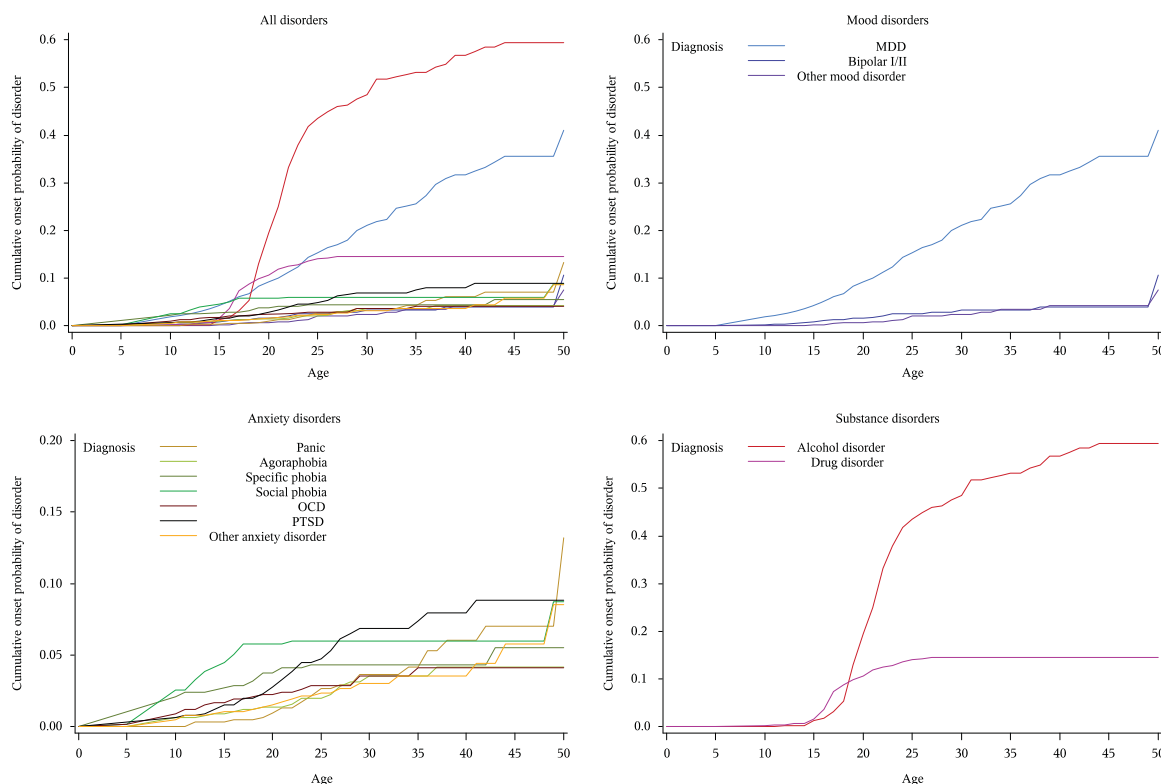


Fig. 2. Cumulative onset probability distributions of common psychiatric disorders within a representative sample of the Ohio Army National Guard service members (N=671). The estimated cumulative onset probabilities were determined using the actuarial (life table) method. Note y-axis for anxiety disorder (lower-left quadrant) is 0.0–0.2; all other y-axis range from 0.0–0.6. Abbreviations: PTSD, posttraumatic stress disorder; OCD, obsessive-compulsive disorder; MDD, major depressive disorder.

true burden of lifetime disorders.

Kessler et al. (2014), using computer-administered questionnaires, estimated 30-day prevalence of DSM disorders and pre-enlistment age-of-onset in a nationally representative sample of active-duty US Army soldiers. We observed a higher prevalence of disorders, but more informative, a higher proportion of pre-enlistment disorders. For example, Kessler et al. (2014) documented 30% of PTSD had pre-military age-of-onset, compared to 49% in this study. That we observed a higher prevalence of both lifetime disorders and disorders with pre-enlistment age-of-onset compared to Kessler et al. (2014) can likely be attributed to differences

in how our studies assessed symptomology. Specifically, Kessler et al. (2014) screened for 30-day prevalence of psychiatric disorders using fully structured, computer-administered, interviews, whereas our study clinicians employed “gold standard” structured clinical interviews to diagnose lifetime psychiatric disorders. Previous studies have documented that both civilians (Hardeveld et al., 2013) and military personnel (Fink et al., 2016) with mental disorders often cycle between stages of remission and recurrence. While our estimates of lifetime diagnosis may include those with remitted symptoms (over-estimating 30 day estimates), our study’s inclusion of lifetime disorders is likely to provide improved

estimates of the population's psychiatric burden compared to previously documented estimates.

Our observation that most soldiers reported that their psychiatric disorders onset prior to military service may explain recent studies that have observed little or no association between deployment and mental and substance use disorders among representative samples of service members (Cerdeira et al., 2014; Larson et al., 2008; LeardMann et al., 2013). For example, Larson et al. (2008) found that U.S. Marines are diagnosed more frequently during the initial months after enlistment rather than after combat deployment. A more recent study of Canadian military forces found that Afghanistan-related deployment contributed to about 9% of past-year psychiatric disorders, whereas child abuse contributed to about 29% of past-year disorders (Boulos and Zamorski, 2016). One explanation for a weaker association between military deployment and psychopathology is the "healthy warrior effect" (Larson et al., 2008; Wilson et al., 2009), which suggests that psychologically unfit personnel are identified early in training and only those service members proven resilient are then eligible for combat tours. In contrast to this literature emphasizing the contribution of pre-military experiences on military mental health, much extant literature has shown that deployment and combat exposures increase psychiatric symptomatology and disorders (Hoge et al., 2004); however, many of these studies exclusively examined deployed service members with no comparison category (Cohen et al., 2015), which may have biased results away from the null. Our findings should not be taken to suggest that deployment and combat exposures are not associated with increased risk for psychiatric disorders, rather that analyses of data from only deployed service members may be oversimplifying a complex association between pre-military experiences and psychiatric symptomatology and recent traumatic event exposure.

The lifetime prevalence and predicted age-of-onset curves in our sample were comparable to previous studies in civilians. Specifically, psychiatric disorders predominately start in youth; with anxiety disorders having the earliest age-of-onset (Kessler et al., 2005) and mood disorders the latest. Anxiety disorders tend to fall into two distinct sets with phobias and OCD occurring earlier, whereas panic, agoraphobia, and PTSD onset later in life (Kessler et al., 2005). And in contrast to the earlier onset anxiety disorders that increase at an exponential rate during childhood, the later onset anxiety (i.e., panic, agoraphobia, PTSD) and mood disorders tend to increase in a roughly linear manner over the entire life course (Kessler et al., 2007, 2005). Moreover, our results are consistent with previous findings that SUDs commonly start during late adolescence and early adulthood in both military and nonmilitary populations (Ames and Cunradi, 2004; Kessler et al., 2007). One hypothesis proposes that the propensity to experiment with psychoactive substances during adolescence increases due to social pressure, but use is curbed during professional integration as a result of social constraints and work environments (Warner et al., 2011). This is particularly true in the military that has a zero tolerance policy towards illegal drugs, while service members perceive a relatively accepting culture towards alcohol use (Ames and Cunradi, 2004). Our results support this discrepancy in perceptions and policy as more than 80% of drug use disorders had first onsets prior to joining the military compared to more than 60% of the alcohol use disorders that onset after joining the military.

5. Limitations

This study is not without limitations. First, self-report data may result in the under-reporting of lifetime psychiatric disorders. While military personnel are likely to provide truthful answers if

they believe a survey will be used for legitimate purposes and individual answers will remain confidential (Warner et al., 2011), the presence or perception of mental illness stigma (Kim et al., 2010) and a bias against reporting embarrassing behaviors (Cannell et al., 1977) remain prevalent in the military. We compensated for this concern by assuring participants that individual answers will remain confidential, both verbally and in writing, prior their volunteering for the study. Additionally, we improved confidentiality by having civilian clinicians conduct all assessments in neutral locations without the presence of military personnel.

Second, lifetime psychiatric disorder symptoms and age-of-onset were self-reported, which may lead to underestimates of the lifetime prevalence of psychiatric disorders (Takayanagi et al., 2014) and recall bias, respectively. In addition, we presented age-of-onset as a binary phenomenon; however, we must acknowledge that the onset of a disorder likely represents a gradual process of symptom development. Although study clinicians asked respondents to report the earliest age at which their symptoms seem to go together, representing a disorder over early subthreshold symptomatology, we cannot rule out the possibility that respondents might have incorrectly recalled the earliest age of disorder onset.

Third, the actuarial method used to estimate lifetime risk assumes that first onset of a disorder is conditionally uniformly distributed within a year of age (Rosner, 2006). While over half of the sample had previously deployed, which is associated with exposure to several traumatic events, the population did not all deploy during the same age interval. Therefore, it is reasonable to assume risk did not change rapidly within a given age interval for all members of the cohort. Additionally, our stratified analysis did not show any age-of-onset differences between birth cohorts. Fourth, the available sample size and number of cases did not allow an examination of stratified tables, such as comparing differences in age-of-onset among deployers and non-deployers. We acknowledge this is an important next step for future studies.

Finally, the sample was predominantly white male US National Guard personnel from the state of Ohio; therefore, the generalizability of our results is limited. Compared to the general US National Guard population, a larger proportion of our sample was younger (age 17–24: 41% *v* 31%) and never married (51% *v* 45%), whereas a similar proportion of our sample was male (87% *v* 85%) and enlisted rank (90% *v* 88%) (Fink et al., 2016). Although our findings were derived from a geographically defined sample and require replication in additional military samples, the similar age-of-onset patterns between our study and Army STARRS (Kessler et al., 2014) provide some confidence in the generalizability of our estimates.

6. Conclusions and implications

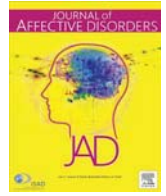
In summary, we documented a high prevalence of psychiatric disorders in this sample with about half of participants reporting pre-military disorder onset. These findings suggest that military leaders aiming to identify soldiers at risk of mental illness should expand current identification methods – assessing contemporary military and civilian stressors – to assess early life mental illness. The observation that a high proportion of participants reported that their psychiatric disorder onset prior to enlistment suggests the need for improved efforts to identify and support incoming soldiers with lifetime mental illness that may affect the potential consequences of traumatic exposure incurred during their military careers.

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Research paper

General distress is more important than PTSD's cognition and mood alterations factor in accounting for PTSD and depression's comorbidity



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ABSTRACT

Background: Posttraumatic stress disorder (PTSD) and major depressive disorder (MDD) are highly comorbid and exhibit strong correlations with each other at both the symptom level and latent factor level. Various theories have attempted to explain this relationship. Results have been inconsistent regarding whether PTSD's negative alterations in cognition and mood factor (NACM) is significantly more related to depression, in contrast to other factors of PTSD.

Methods: Confirmatory factor analysis was used to attempt to address the relationships between PTSD and MDD in a large sample of trauma-exposed combat veterans from the Ohio National Guard as part of a larger longitudinal study.

Results: Confirmatory factor analysis was used to test a bifactor model of PTSD symptoms, testing relations between PTSD's factors and a latent depressive factor. After partitioning out the common variance into the bifactor, we found that in contrast to other PTSD factors, PTSD's NACM factor was not significantly more related to depression. Instead, only the general bifactor predicted depressive symptoms.

Limitations: The limitations of the present study include the following: the specific measures of PTSD and MDD used were based on self-report, and the sample consisted of non-clinical, non-treatment seeking veterans.

Conclusions: The present study suggests that the high rate of comorbidity between posttraumatic stress disorder (PTSD) and major depressive disorder is more related to underlying general distress or negative affectivity than the symptom categories of the PTSD diagnostic criteria.

1. Introduction

Research has shown that posttraumatic stress disorder (PTSD) and major depressive disorder (MDD) are highly comorbid. Epidemiological studies have found that among adults with PTSD, 48–55% have co-occurring MDD (Elhai et al., 2008; Kessler et al., 2005, 1995; Rytwinski et al., 2013). Furthermore, 62% of adolescents with PTSD also met criteria for a major depressive episode (Kilpatrick et al., 2003). The high rates of co-occurrence, and the consistency of

these findings, suggest a need for a better understanding of the relationship between PTSD and MDD.

Previous research has suggested several potential reasons for the high comorbidity rates between PTSD and MDD. First, PTSD and MDD comorbidity could be examined at the symptom-level because they share multiple overlapping symptoms. However, rates of PTSD-MDD comorbidity, using *DSM-IV* criteria, did not change significantly even after the overlapping symptoms are accounted for (Elhai et al., 2008; Franklin and Zimmerman, 2001). In *DSM-5*, the following PTSD

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symptoms are all relevant to or could be confounded by the presence of MDD (American Psychiatric Association, 2013): negative beliefs or expectations related to oneself, others, or the world (D2), persistent negative emotional states, such as anger, guilt, or shame (D4), diminished interest or participation in activities (D5), inability to experience positive emotions (D6), concentration difficulties (E5), and sleep disturbance (E6). Symptoms D2 and D4 are new to the PTSD diagnosis in *DSM-5*. The high rates of co-occurrence between PTSD and MDD could increase in the future due to the addition of these two new symptoms with depressive-based content within PTSD – item content that involves general dysphoria more so than content specific to PTSD.

At the latent-level of analysis, it has been shown that PTSD and MDD have a consistent and robust relationship. Previous research has established that PTSD and MDD have stable factor structures, but these differ by sample and measure. PTSD is commonly analyzed as a four-factor construct (Armour et al., 2016). For example, *DSM-5* is based on the emotional numbing model of King et al. (1998), and is composed of intrusion, avoidance, negative alterations in cognition and mood (NACM), and alterations in arousal and reactivity (AAR) factors. In contrast, the four-factor dysphoria model, consisting of intrusion, avoidance, dysphoria, and hyperarousal factors, has been found to provide good model fit as well (Simms et al., 2002). The *DSM-5* model and the dysphoria model differ in their classification of the symptoms of irritability/anger (E1), difficulty concentrating (E5), and sleep disturbance (E6). In *DSM-5*, these three symptoms are listed under the AAR factor, whereas in the dysphoria model they are considered to be part of the dysphoria factor. Additionally, other researchers have found that the five-factor dysphoric arousal model of PTSD fits the data best by dividing PTSD into intrusion, avoidance, numbing, dysphoric arousal, and anxious arousal factors (Elhai et al., 2011). Recently, other researchers have proposed that six- and seven-factor models of PTSD are significantly better representations of the construct (Armour et al., 2015b; Liu et al., 2014; Tsai et al., 2015). All these various factor models indicate that PTSD is a heterogeneous construct, which makes it more difficult to study empirically and understand clinically.

PTSD has a cluster of symptoms, commonly referred to as emotional numbing (King et al., 1998) or dysphoria (Simms et al., 2002), comprised of symptoms related to other anxiety and mood disorders. In some studies, the relationship between PTSD-MDD has been found to be driven significantly more by the non-specific nature of PTSD's numbing/dysphoria factor than the other three factors of PTSD (Armour et al., 2011; Boelen et al., 2008; Elkit et al., 2010; Grant et al., 2008; Palmieri et al., 2007; Simms et al., 2002). However, other studies have found that PTSD's numbing/dysphoria factor is no more related to depression than other factors of PTSD (Charak et al., 2014; Contractor et al., 2014; Marshall et al., 2010; Miller et al., 2010). Therefore, the non-specific nature of dysphoria or emotional numbing in PTSD is inconsistently found, and leaves a gap in our understanding of the relationship between PTSD and MDD and their comorbidity.

Increasingly, researchers are using statistical techniques to examine comorbidity in a more sophisticated fashion. One of these statistical modeling techniques is bifactor modeling (Holzinger and Swineford, 1937). Bifactor modeling allows for a partitioning out of a construct's specific variance from its shared/generalized variance. In the context of diagnostic comorbidity, the shared variance would be a latent factor of generalized distress that is transdiagnostic, whereas the domain-specific variance represents the variance attributable to the specific diagnosis or diagnostic criteria. The generalized variance is typically referred to as “*p*,” or the general psychopathology factor (Kim and Eaton, 2015; Sharp et al., 2015).

Previous mental health research studies using bifactor modeling have found support for a higher order factor of psychopathology. Adult personality disorder psychopathology has been found to fit a bifactor model (Sharp et al., 2015; Wolf et al., 2011). Including a general bifactor into a model of anxiety and depression significantly improved

the fit in undergraduate students, community adults, and inpatient samples (Simms et al., 2008). In a longitudinal epidemiological study, including a bifactor significantly improved the fit above and beyond a three-factor internalizing-externalizing disorder hierarchy, in which internalizing subsumed fear and distress factors (Lahey et al., 2012). Also in that study, the general psychopathology bifactor predicted pathology over time, above and beyond the variance accounted for by the fear, distress, and externalizing factors. Bifactor models of psychopathology have also been supported in samples of children and adolescents. A general bifactor model of psychopathology significantly better accounted for the relationships between items compared to an internalizing-externalizing model, and negative emotionality was more correlated with the bifactor than either internalizing or externalizing factors (Tackett et al., 2013).

Few studies have examined a bifactor model of psychopathology while including PTSD. Brodbeck et al. (2014) found support for a bifactor model using structured diagnostic interview diagnoses in a large outpatient sample. In this sample, mood disorders, PTSD, and personality disorders were characterized by significantly higher levels of general distress compared to fear-based disorders, somatic disorders, sexual dysfunctions, and eating disorders. However, the authors examined these relationships using diagnoses (coded as present/absent) instead of examining relationships at the symptom level.

The present study addresses the gap in the literature regarding our understanding of how PTSD and MDD are related. PTSD and MDD's high rates of comorbidity have been examined using symptom-level and latent-level analyses, but these have resulted in increasingly mixed findings. This study aims to address the discrepancy regarding the potential factors underlying the relationship between PTSD and MDD in a large sample of trauma-exposed military veterans using a different method of analysis. No previous study that we are aware of has examined PTSD and MDD at the symptom level specifically using bifactor modeling. Further, many of the previous studies examining comorbidity between mental illness diagnoses using bifactor modeling have not included PTSD in their models (Clark and Watson, 2006; Kim and Eaton, 2015; Tackett et al., 2013), which leaves a large gap in the literature because PTSD is highly comorbid with other disorders (Kessler et al., 1995). In addition, with the changed criteria for PTSD in *DSM-5*, relationships between PTSD and MDD could be altered because *DSM-5* introduced new PTSD symptoms that are depression related. Therefore, examining this relationship using a different, unique statistical method in a large veteran sample will improve the current empirical knowledge on PTSD/MDD comorbidity.

Considering the mixed findings regarding the relationship between depression and PTSD's dysphoria factor or numbing factor (now called “negative alterations in mood and cognition” in *DSM-5*), the aim of the present study attempts to determine if this factor of PTSD is more related to depression when compared to a general *p* bifactor derived from the PTSD symptoms. We expected that a confirmatory factor analysis (CFA) of *DSM-5*'s four-factor PTSD model would fit. Because of the inconsistency found in previous empirical research, we could not confidently predict whether in a confirmatory factor analysis (CFA) model, PTSD's negative alterations in mood and cognition would be most related to depression. However, we expected that when adding a general bifactor, the bifactor would be the factor most related to depression.

2. Method

2.1. Participants and procedure

This study was part of a larger prospective study on the mental health of Ohio National Guard (ONG) members. The original sample consisted of 2616 participants, and data were collected using computer-assisted telephone interviewing. The present study only used data from Wave 4, which was collected between 2011 and 2012. Due to

study attrition, 1431 participants were included in Wave 4, and analyses included 683 participants because they were restricted to those participants endorsing deployment-related traumas. The most commonly reported worst traumas, which were referenced when rating PTSD symptoms, were receiving incoming fire ($n=151$, 22.5%), combat/warzone exposure ($n=47$, 7.0%), and unexpected death of a close associate ($n=47$, 5.2%). Further, 11 participants were excluded for missing more than 30% of items on either the PTSD measure or depression measure; therefore, the final sample consisted of 672 participants.

2.2. Instrumentation

2.2.1. PTSD Checklist for DSM-5 (PCL-5)

The PCL-5 (Weathers et al., 2013) is a self-report measure examining PTSD symptom severity, with each of the 20 items anchored to a specific traumatic event. The items are designed to map onto the DSM-5 diagnostic criteria for PTSD. Each item is rated based on symptoms over the previous month on a five-point Likert-type scale (0=“Not at all” to 4=“Extremely”). The PCL-5 has demonstrated excellent internal consistency, in the range of $\alpha=.91-.95$, and test-retest reliability, $r=.82$ over a one-week interval (Wortmann et al., 2016). It has also demonstrated good convergent validity with other measures of PTSD, including the previous PCL for DSM-IV and Posttraumatic Distress Scale (PDS), $r_s=.85-.90$ (Blevins et al., 2015, 2012). Cronbach's alpha=.969 for the current sample.

2.2.2. Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 (Kroenke et al., 2001) is a self-report measure of depressive symptoms from the larger PRIME-MD diagnostic measure. Depressive symptoms are designed to map onto the DSM-5 diagnostic criteria for major depressive disorder. For this study, depressive symptoms were rated in severity over the previous month to be consistent with the PTSD time interval. Each of the nine items is rated on a four-point Likert-type scale (0=“Not at all” to 3=“Nearly every day”). The PHQ-9 has been found to have good internal consistency ($\alpha=.86-.89$), test-retest reliability ($r=.84$), sensitivity (.77-.88), specificity (.88-.94), and construct validity, relative to a thorough diagnostic interview (Kroenke et al., 2010, 2001; Manea et al., 2015). In this wave of data collection, symptoms were rated using a “yes” or “no” format, and a “yes” response was considered a positive endorsement of the symptom. Cronbach's alpha for the PHQ-9 in the present sample was .899.

2.3. Data analyses

Analyses were conducted using Mplus 7 software. For individuals with less than 30% of items missing, missing data were estimated with maximum likelihood (ML) procedures, using a pairwise present approach. Prior to the main analyses, factor correlations between PTSD and depression were examined and reported in Table 1. Five confirmatory factor analyses (CFA) were examined. First, a CFA

Table 1
Bivariate factor correlations between PTSD and MDD without bifactor specified in model.

	IN	AV	NACM	AAR	MDD
IN	–				
AV	.937	–			
NACM	.907	.930	–		
AAR	.927	.890	.943	–	
MDD	.695	.705	.810	.778	–

Note. PTSD=Posttraumatic stress disorder; MDD=Major depressive disorder; IN=Intrusion; AV=Avoidance; NACM=Negative alterations in cognition and mood; AAR=Alterations in arousal and reactivity.

consisting of only the four factors of DSM-5 PTSD was conducted (Model 1). The DSM-5 model of PTSD was used instead of the dysphoria model in order to maximize clinical generalizability.² Model 1 did not include a general bifactor. Second, a depression-only CFA was examined, with the nine depression items loading onto a single factor (Model 2). Next, a CFA specifying the four factors of DSM-5 PTSD each predicting depression was computed (Model 3). Regression values for the four PTSD factors' direct effects on a latent depression factor were determined. Then, a PTSD-only bifactor model was computed, with each item of PTSD loading onto one of the four factors as well as a general bifactor (Model 4). Finally, the same PTSD bifactor model was computed, and then the PTSD individual factors and bifactor were specified to predict a single depression factor (Model 5). This step allowed us to examine if the relationship between PTSD and depression was accounted for by NACM or general distress. Correlations between PTSD factors and the general bifactor were fixed to zero and factor variances were fixed to one. Because the PCL-5 and PHQ-9 have five or fewer responses options, they were treated as ordinal data. Therefore, we used a polychoric covariance matrix, robust weighted least squares estimation with a mean- and variance-adjusted chi-square (WLSMV), and probit regression coefficients. In line with Hu and Bentler (1999) cut off criteria, a well-fitting model would have Comparative Fit Index (CFI) and Tucker Lewis Index (TLI) values > .95 and root mean square error of approximation (RMSEA) value < .06. Standardized model estimates were interpreted.

3. Results

The mean PCL score was 28.60 ($SD=14.19$), and 62 (9.2%) met criteria for probable PTSD, which we adapted for DSM-5 from a DSM-IV algorithm by Cook et al. (2003). Using a DSM-5 diagnostic algorithm (in which the participant responded “yes” to at least five of the nine PHQ-9 items), 96 participants (14.3%) met criteria for a probably major depressive episode (MDE) diagnosis.

For the main analyses, five separate CFAs were conducted to examine the relationship between PTSD factors as they predict a single depression factor, with and without accounting for general distress (specified as a bifactor). The first CFA consisted of the measurement model of the four factors of DSM-5 PTSD (Model 1), and this model demonstrated excellent model fit robust χ^2 (164, $N=672$)=433.622, $p < .0001$, CFI=.994, TLI=.993, RMSEA=.049 (90% CI=.044-.055). Next, the depression-only CFA (Model 2) demonstrated excellent model fit, robust χ^2 (27, $N=672$)=39.274, $p=.060$, CFI=.999, TLI=.999, RMSEA=.026 (90% CI=.000-.043).

Next, Model 3 specified the four-factors of DSM-5 PTSD to predict a single depression factor. This model demonstrated excellent model fit, robust χ^2 (367, $N=672$)=698.69, $p < .0001$, CFI=.993, TLI=.993, RMSEA=.037 (90% CI=.033-.041). Regression values are presented in Table 3. Then, Model 4 used the general bifactor to predict the 20 items of PTSD and also demonstrated excellent fit, χ^2 (144, $N=672$)=255.10, $p < .0001$, CFI=.997, TLI=.997, RMSEA=.034 (90% CI=.027-.041). Finally, the 20 items of PTSD were reanalyzed to specify the four factors as well as a general bifactor, and each of the four factors and the general bifactor were all specified to predict depression (Model 5, see Fig. 1). This CFA also had excellent fit χ^2 (346, $N=672$)=527.085, $p < .0001$, CFI=.996, TLI=.996, RMSEA=.028 (90% CI=.023-.033). Factor loadings and factor correlations are presented in Table 2. When examining which factor(s) best predicted depression, it was found that only the bifactor significantly predicted depression in this model ($B=0.847$, $SE=0.024$, $p < .001$). Regression results are presented in Table 3.

² The dysphoria model of PTSD was also examined in a bifactor model; however, this model would not converge. Non-convergence is not uncommon and is more common when running bifactor solutions. Morgan et al. (2015) also found that non-convergence was not dependent on sample size.

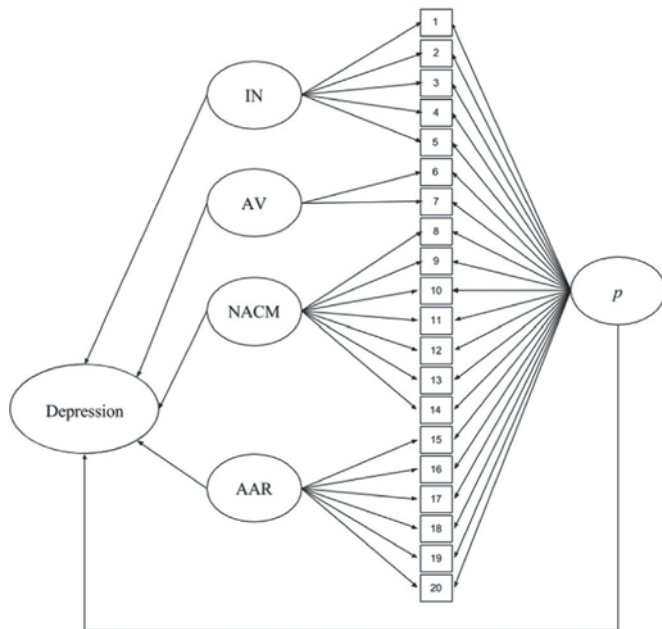


Fig. 1. PTSD bifactor and DSM-5 four factors predicting latent depression factor. Note. IN=Intrusion; AV=Avoidance; NACM=Negative alterations in mood and cognition; AAR=Alterations in arousal and reactivity; *p*=Bifactor; Each numbered item indicates a PTSD symptom item.

Table 2
Standardized factor loadings and factor correlations for PTSD-MDD bifactor model.

Item	IN	AV	NACM	AAR	Bifactor
1. Intrusive thoughts	0.434				0.807
2. Nightmares	0.465				0.800
3. Reliving trauma	0.437				0.806
4. Emotional cue reactivity	0.453				0.824
5. Physiological cue reactivity	0.438				0.808
6. Avoidance of thoughts		0.436			0.814
7. Avoidance of external reminders		0.421			0.837
8. Trauma-related amnesia			0.301		0.640
9. Negative beliefs			0.096		0.906
10. Distorted blame			0.338		0.751
11. Persistent negative emotional state			0.321		0.881
12. Lack of interest			0.124		0.928
13. Feeling detached			0.190		0.930
14. Inability to experience positive emotions			0.127		0.932
15. Irritability/anger				0.215	0.883
16. Recklessness				-0.044	0.813
17. Hypervigilance				0.470	0.832
18. Easily startled				0.488	0.825
19. Difficulty concentrating				0.127	0.938
20. Difficulty sleeping				0.275	0.875
IN	-				
AV	0.716	-			
NACM	0.493	0.628	-		
AAR	0.655	0.387	0.248	-	

Note. PTSD=Posttraumatic stress disorder; MDD=Major depressive disorder; IN=Intrusion; AV=Avoidance; NACM=Negative alterations in mood and cognition; AAR=Alterations in arousal and reactivity; Factor correlations adjusted for presence of bifactor and depression.

4. Discussion

The present study attempted to address the inconsistency in the literature related to the comorbid relationship between PTSD and depression. By using a bifactor model of PTSD, where the 20 items of PTSD were specified to load onto the four factors of PTSD as well as a general *p* factor of distress, we were able to examine if the specific

Table 3
PTSD factors and general bifactor predicting depression.

	<i>B</i>	<i>S.E.</i>	90% <i>CI</i>	β	<i>p</i>
<i>Regression results without a specified bifactor (Model 3)</i>					
IN	-0.215	0.211	-1.37 to -0.67	-1.020	0.308
AV	-0.244	0.243	-1.41 to -0.60	-1.005	0.315
NACM	0.953	0.230	3.77 to 4.53	4.148	<.001
AAR	0.295	0.198	1.16 to 1.81	1.486	0.137
<i>Regression results including bifactor (Model 5)</i>					
IN	-0.025	0.108	-0.20 to 0.15	-0.232	0.816
AV	-0.044	0.111	-0.23 to 0.14	-0.396	0.692
NACM	-0.047	0.097	-0.21 to 0.11	-0.489	0.625
AAR	-0.028	0.074	-0.15 to 0.09	-0.385	0.700
Bifactor	0.847	0.024	0.81 to 0.89	35.863	<.001

Note. IN=Intrusions; AV=Avoidance; NACM=Negative alterations in cognition and mood; AAR=Alterations in arousal and reactivity.

factors of PTSD or general distress were more related to PTSD-MDD comorbidity. Based on our results we found that general distress, not PTSD’s numbing factor (NACM), significantly predicted depression in our sample. Therefore, based on our findings, general distress, rather than a single PTSD factor, may drive the high comorbidity between these two disorders.

Previous research has been inconsistent regarding whether PTSD’s numbing/dysphoria factor is significantly more related to depression than the other factors of PTSD. The present findings support other studies where PTSD’s proposed non-specific factor is no more related to depression than PTSD’s intrusion, avoidance, or arousal factors (Charak et al., 2014; Contractor et al., 2014; Marshall et al., 2010). This suggests that the shared variance between PTSD and MDD is attributable to general distress, which is consistent with hierarchical models of psychopathology where PTSD and MDD load onto the same factor (Brown and Barlow, 2009; Slade and Watson, 2006; Watson, 2005).

In the present study, when the four factors of PTSD (without a bifactor present in the model) are used to predict depression, the NACM factor of PTSD significantly predicts depressive symptoms, whereas the intrusions, avoidance, and arousal do not. However, once the shared variance of general distress was accounted for in the PTSD items, the PTSD factors related to intrusion, avoidance, cognition and mood changes, and arousal no longer significantly predicted the depression factor. This indicates that the NACM factor does not necessarily represent the non-specific variance of PTSD, and instead non-specific distress underlies all PTSD as a whole, not its component parts. Further, this non-specific distress is likely the contributing factor linking PTSD and MDD diagnoses. At the clinical level, this suggests that the high comorbidity between these two diagnoses is associated with general distress. Following a potentially traumatic event, the same distress could manifest as possibly different diagnoses, major depression or PTSD. Therefore, it is important for clinicians to consider various diagnostic possibilities when working with trauma-exposed individuals. Higher levels of generalized distress could result in more severe functional impairment or different trajectories of recovery. Previous studies have found that comorbid PTSD and MDD is associated with greater functional impairment and higher rates of alcohol misuse (Armour et al., 2015a; Thomas et al., 2010). Transdiagnostic treatments targeting generalized distress or negative affect could be a beneficial avenue for symptom reduction based on the present results.

In contrast to previous studies where mental disorders were used to determine the hierarchical structure of their relationships, the present study instead used the individual PTSD items to load onto the general bifactor. By using all the PTSD items instead of dichotomous diagnostic status (present/absent), the analyses maintained higher power to help reduce type II error.

4.1. Limitations

Our study also has some limitations that should be noted. The instruments used to measure PTSD and MDD were based on self-report, which could be influenced by response bias. The estimates of probable PTSD and MDD were established using cut-off scores on the self-report measures, instead of clinical diagnostic interviews. The sample was not composed of clinical patients or treatment-seeking individuals, but instead consisted of trauma-exposed veterans. Thus, the findings may not generalize to other samples with more clinically significant symptomatology. Further, these results are restricted to individuals rating combat traumas. Participants could have experienced multiple traumatic events and distinguishing between symptoms resulting from a single, index trauma versus another trauma could have been difficult for participants. These findings only considered the relationship between PTSD and MDD, and did not include other distress disorders, such as generalized anxiety disorder or persistent depressive disorder (Watson, 2005).

4.2. Strengths and future directions

However, the current sample was relatively large, consisted entirely of combat veterans, and addressed the issue of PTSD-MDD comorbidity in a novel way. Further, the measures and criteria used in this study are representative of DSM-5 diagnoses, and with the continued changes to PTSD's criteria, additional research continuing to explore these diagnostic issues is needed using the new system. Future research is required to replicate the present findings. Only one model of PTSD's conceptualization was currently tested, so investigating the other empirical models of PTSD (i.e., Armour et al., 2015b; Elhai et al., 2011; Liu et al., 2014; Simms et al., 2002; Tsai et al., 2015) should be examined. In addition, it would be beneficial to include other disorders of generalized distress to investigate if a general bifactor best represents the relationship between the other distress disorders beyond just PTSD and MDD. It could also be beneficial to replicate findings using longitudinal data in order to examine if this relationship between variables is consistent across time or changes individuals' quality of life.

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Original article

Coincident alcohol dependence and depression increases risk of suicidal ideation among Army National Guard soldiers



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ABSTRACT

Purpose: Suicide rates among military service members have risen dramatically, while drivers remain poorly understood. We examined the relationship between coincident alcohol dependence and depression in shaping risk of suicidal ideation among National Guard forces.

Methods: We performed a longitudinal analysis using a randomly selected, population-based sample of Ohio Army National Guard soldiers. Telephone-based surveys of 1582 soldiers who participated in both wave 1 (2008–2009) and wave 2 (2009–2010) were analyzed.

Results: Odds ratios (ORs) for suicidal ideation among those with versus without alcohol dependence were similar among nondepressed (OR = 3.85 [95% confidence intervals (CIs) = 1.18–12.52]) and depressed individuals (OR = 3.13 [95% CI = 0.88–11.14]); multiplicative interaction was not observed. In contrast, the risk differences (RDs) among those with versus without alcohol dependence diverged for those without depression (RD = 0.04 [95% CI = 0.02–0.07]) compared with those with depression (RD = 0.11 [95% CI = 0.06–0.18]); strong evidence of additive interaction was observed.

Conclusions: We found that alcohol dependence and depression interact statistically in shaping risk for incident suicidal ideation among Army National Guard service members. A high-risk prevention approach including population-based screening for suicidality among patients with alcohol dependence, depression, and particularly those with both conditions is warranted in military populations.

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Introduction

Suicide and suicide risk among US military forces and veterans have increased substantially in the last decade [1,2]. Suicide in service members has historically been lower than that in the general population [3]; however, this gap has diminished substantially in recent years among service members from Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and

Operation New Dawn (OND) [4–7]. The increase in suicide rates has come despite the investment of tremendous resources aimed at reducing this problem [8].

The suicide rate among Army National Guard soldiers has, in a divergence from earlier trends, recently exceeded that of Active Duty Army and Army Reserves [7,9,10], adjusting for military sub-component demographic composition. In 2010 and 2013, the suicide rate among Army National Guard soldiers exceeded that of Active Duty Army and Army Reserves [7,9,10]. Surveillance data from 2014 suggest that this excess risk among Army National Guard service members may be leveling off [7], but this divergence nonetheless raises concern. Furthermore, rates of suicide in the Army National Guard have consistently remained higher than age-matched civilians, aside from a slight dip in 2013 [11].

Sociodemographic predictors of suicide risk appear to be consistent among both reservists and active duty service members [7,9,10,12]. Despite conflicted findings across individual studies

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[5,6,10,13], a recent meta-analysis suggests that the links between deployment or combat deployment and suicide in OEF/OIF/OND service members are weak to nonexistent, whereas the link to combat exposure is supported by data but weak [14]. Lower rank [5,6,13] has also been associated with increased suicide risk, and while some studies have linked greater suicide risk to men [7,10,13], others have found the opposite [5,15].

Depression is the most common predictor of suicidality both in civilian [16–18] and military populations [5,13,19,20], estimated to be prevalent among 2.7%–14.7% of OEF/OIF/OND National Guard and reserves forces [21]. Given the threefold magnitude of associated risk for suicide [13] and suicidal ideation [5] among service members, depression remains an important target for suicide prevention.

Alcohol misuse is another common condition among military service members, ranking second only to depression in its association with suicide. Whereas a few studies have examined the influence of alcohol misuse [12,13,22], most literature on suicide and suicidality in OEF/OIF/OND service members has focused almost exclusively on depression and PTSD [23,24] as causes, largely considering alcohol misuse only peripherally, as a covariate or comorbidity. Within the general population, alcohol use disorders and acute alcohol intoxication are strongly associated with suicide attempts and suicide [25–27]. Both acute intoxication and chronic use of alcohol (including dependence) are associated with increased risk of suicide and attempted suicide [25,27,28]. Alcohol use disorders are among the most common diagnoses associated with suicide and are implicated in approximately one-quarter of suicides [25].

Of particular concern, the estimated prevalence of alcohol use disorders among Reserve and National Guard forces serving during OEF/OIF/OND was 14%–15% [21]. Among the reserve component, deployment with combat exposures was associated with higher risk of new-onset alcohol misuse, with Army National Guard and Reserve forces having a higher prevalence of new-onset alcohol misuse than Air Force, and Navy/Coast Guard and a lower prevalence than Marines [29]. Among service members with alcohol misuse, the increased risk of suicidal ideation and suicide are approximately threefold [13,19].

Alcohol dependence and depression are clearly risk factors for suicidal ideation in isolation. We hypothesize that in comorbid presentations, they interact in shaping risk of suicidal ideation. Evidence from civilian studies [18,30] suggests that comorbid alcohol dependence and depression act together in shaping suicide risk. These civilian findings, along with the common occurrence and comorbidity of both conditions among military service members [31,32], warrant investigation of their interaction effects in predicting suicidal ideation among service members.

Accordingly, the present investigation aimed to estimate among Army National Guard forces: (1) the effect of alcohol dependence on risk of incident suicidal ideation; (2) the effect of depression on risk of incident suicidal ideation; and (3) the interaction between alcohol dependence and depression on risk of incident suicidal ideation. We use an Ohio Army National Guard (OHARNG) sample and adjust for the influence of sociodemographic characteristics and military service factors. In the interest of temporal proximity, we focus on past year depression and alcohol dependence. To examine the degree to which alcohol dependence and depression act together in predicting suicidal ideation, we examine statistical interaction on both the additive and multiplicative scales.

Materials and methods

Population

We conducted a longitudinal investigation of a sample of the OHARNG. Our sample was drawn from 10,778 soldiers serving in

the OHARNG as of June 2008, and the 1792 who enlisted between then and February 2009. In total, 12,225 OHARNG soldiers were invited to participate through a two-stage process including an opt-out alert letter directly from the OHARNG and a phone call to obtain consent to participate in a phone interview. The number of soldiers opted out was 1013 (8%), and 345 (2.8%) were excluded because of lack of a current address. After 3 weeks, the OHARNG sent us contact information for 11,212 soldiers who did not opt-out. We called 6514 (58.1%) working numbers: 218 (3.3%) were not eligible (i.e., too young, retired, non-English speaker, and hearing problems); 1364 (20.9%) did not wish to participate; and 2316 (35.6%) were not contacted before the cohort closed. Service members deployed at the time of initial contact were called again after return from deployment. The final baseline study sample included 2616 OHARNG soldiers, men and women aged 17 years or older, who were capable of informed consent. Soldiers could have been aged 17 years as opposed to 18 years because emancipated minors are considered adults by the military. The overall cooperation rate (defined as number consented divided by number of successfully contacted numbers) [33] was 68.2%, and the response rate was 43.2% (defined as those who completed the survey plus those who consented but were ineligible, divided by the number of working numbers minus those disqualified) [33]. A second wave of interviews was conducted 1 year later and included 1767 (67.5%) of those interviewed at baseline; we excluded 183 (10.4%) with a lifetime history of suicidal ideation at baseline. Our final analytic sample included 1582 soldiers.

Participants were administered a 60-minute telephone survey, including questions on military history and experiences, health status and medical history, social support, deployment-related and civilian-related trauma and psychopathology, mental health service use, and demographic characteristics. Bachelors-level lay interviewers, trained and managed by professional survey firm Abt-SRBI (>25 years of experience interviewing military personnel), interviewed participants using computer-assisted telephone interviewing techniques. Interviewers received extensive training on working with military service members and conducting psychiatric symptom interviews. Interviewers obtained participant consent from at the start of each interview and offered financial compensation for their time. All human subjects procedures were overseen and approved by the Institutional Review Boards of Columbia University, Case Western Reserve, University of Toledo, University of Michigan, and the Department of Defense.

Traumas

Deployment-related traumatic event experiences were identified with a list of 21 traumatic events specific to military service [34] and asked in reference to most recent deployment. Traumatic event experiences that may have occurred either within or outside of military deployment experiences were additionally identified using a list of 25 traumatic events [35]; if participants endorsed any of these events, they were asked whether the event(s) happened in relation to their most recent deployment. Therefore, we assessed for a total of 46 events related to most recent deployment and 25 events that were not.

Diagnoses

We used the Patient Health Questionnaire-8 version [36] to evaluate depression symptoms. Each of the eight questions asked about symptom frequency within the prior 2 weeks, and possible responses included 0 (not at all), 1 (several days), 2 (more than half the days), and 3 (nearly every day), with total scores ranging from 0 to 24 [37]. We added questions to assess timing, duration, severity

of illness, and disability resulting from symptoms. Major depressive disorder was assessed using Diagnostic and Statistical Manual IV criteria [38] and considered present if five or more of the eight depressive symptoms were present at least “more than half the days” in the past 2 weeks, and one of the symptoms was depressed mood or anhedonia. Other depressive disorder was considered present if two to four depressive symptoms were present at least “more than half the days” in the past 2 weeks, and one of the symptoms was depressed mood or anhedonia. Depression cases included individuals who met criteria for either major depressive disorder or other depressive disorder and reported that his or her symptoms seemed to have occurred together. We included questions to assess the duration and grouping of symptoms. Based on a validation testing of 500 individuals who completed both a telephone and clinical sample interview, we found that excluding the impairment question maximized sensitivity and specificity in our sample [39], and thus did not include it in our case definition. Our telephone-based definition of depression is highly specific (83%) and moderately sensitive (51%), with a positive predictive value (PPV) of 0.46 and a Chronbach’s α (standardized) of 0.66 [39].

Alcohol dependence was assessed using the Mini-International Neuropsychiatric Interview [40] based on Diagnostic and Statistical Manual IV criteria [38]. Alcohol dependence was diagnosed among those who met at least three of seven substance dependence criteria that include tolerance (criteria 1), withdrawal (criteria 2), and compulsive use (criteria 3–7). Participants were asked whether these symptoms had occurred within the past month and year. Our telephone-based alcohol dependence definition is highly specific (81%) and moderately sensitive (60%), with a PPV of 0.46 and a Chronbach’s α (standardized) of 0.76 [39].

Suicidal ideation was assessed using a question from the Patient Health Questionnaire-9 [37], which asks participants about “thoughts that you would be better off dead or of hurting yourself in some way, within the past 30-days?” and “within the past year?” For this investigation, we were interested in predicting incident or new-onset suicidal ideation at wave 2, within the prior year. Accordingly, we omitted this question from our depression measure to avoid overlapping model constructs. Our telephone-based suicidal ideation item was highly specific (0.87), with low sensitivity (0.32), and a PPV of 0.55 [39].

Statistical analyses

All analyses were weighted to (1) calibrate our estimates to reflect the distributions of gender, age, race/ethnicity, education, marital status, rank, deployment history, and years served in the military for the OHARNG universe we sampled from and (2) to adjust for the same factors as predictors of unit nonresponse at 1-year follow-up. Design effects for variables included in this analysis are presented in Table 1. χ^2 tests were used to examine proportions of incident suicidal ideation at 1-year follow-up, within strata of our independent variables. We used logistic regression models to illustrate bivariate relationships between alcohol dependence, depression, and other putative predictors of incident suicidal ideation such as demographics, military rank, lifetime trauma, and past year trauma. We examined interaction between alcohol and depression in predicting suicidal ideation by examining relative measures—odds ratios (ORs) of suicidal ideation for those with alcohol dependence with and without depression and with absolute measures—by plotting conditional risks of suicidal ideation across interaction strata. Finally, we quantitatively examined multiplicative and additive interaction between depression and alcohol dependence using a cross-product term and by calculating the relative excess risk of interaction (RERI), the Attributable Proportion due to Synergy (AP), and the Synergy Index (SI) [41]. We

were particularly interested in investigating departure from additivity, as this is consistent with what is known as public health interaction—a situation in which predicting risk for a given outcome depends on knowing the status of each interaction exposure factor [42,43]. In such a scenario, the removal of one factor alone may have a large impact on the population risk for a given outcome. Statistical analyses were performed with SUDAAN 11 [44] and SAS 9.4 [45].

Results

As shown in Table 1, the final study population was predominantly male (86.3%) and white (88.9%). Approximately, half had some college or technical training (48.2%) and nearly half were married (40%); median age of soldiers was between 18 and 24 years (37.3%). Most soldiers were enlisted personnel (90.2%), had 1–4 deployments (58.9%), 3–6 lifetime traumatic events at baseline (29.4%), and 0 traumatic events between baseline and follow-up (49.7%). At baseline, 6.4% of our sample had current alcohol dependence, and 10.5% had current depression.

Incident suicidal ideation was present among 42% or 2.47% (1.68–3.26) of soldiers at follow-up. Table 2 shows that suicidal ideation at wave 2 was associated with alcohol dependence at baseline (8.97%; $P = .03$) and depression at baseline (8.09%; $P < .001$). In unadjusted logistic regression models, alcohol dependence (OR = 4.76; 95% confidence interval [CI] = 2.05–11.06) and current depression (OR = 4.77; 95% CI = 2.37–9.63) were both associated with incident suicidal ideation at a similar magnitude (Table 2). None of the other predictors evaluated in Table 2 were associated with our outcome at a statistical significance level of $P < .05$.

To evaluate and compare additive versus multiplicative interaction, we first calculated unadjusted ORs and risk differences for those without versus with alcohol dependence, across strata of depression status. ORs for suicidal ideation among those with versus without alcohol dependence were similar among nondepressed (OR = 3.85 [95% CI = 1.18–12.52]) and depressed individuals (OR = 3.13 [95% CI = 0.88–11.14]). Risk differences (RDs) for suicidal ideation among those with versus without alcohol dependence diverged for those without depression (RD = 0.04 [95% CI = 0.02–0.07]) compared with those with depression (RD = 0.11 [95% CI = 0.06–0.18]).

Formal and descriptive analyses of interaction are presented in Figure 1. To descriptively characterize the risk of suicidal ideation within interaction strata, we calculated conditional risks of incident suicidal ideation in those with neither condition (0.02; 95% CI = 0.01–0.02), with alcohol dependence but no depression (0.06; 95% CI = 0.02–0.16), with depression but no alcohol dependence (0.06; 95% CI = 0.03–0.12), and with both conditions (0.17; 95% CI = 0.07–0.38). To assess multiplicative interaction, we fit a multiple logistic regression model including both alcohol dependence (OR = 3.51; 95% CI = 1.45–8.49) and depression (OR = 3.93; 95% CI = 1.90–8.12); we tested a cross-product term for alcohol dependence and depression in a multiple logistic regression model including both conditions, and this term was statistically nonsignificant (beta coefficient = -0.21 , $P = .82$), suggesting absence of multiplicative interaction. To test additive interaction, we computed the RERI, AP, and SI for alcohol dependence and depression, finding strong evidence of interaction on the additive scale (RERI = 5.978 [95% CI = 0.364–11.591], AP = 0.461 [95% CI = 0.199–0.723], and SI = 1.998 [95% CI = 1.163–3.434]).

Discussion

Using a sample of OHARNG soldiers, we found that alcohol dependence and depression interact to place a soldier at greater

Table 1
Characteristics of study sample of Ohio Army National Guard ($n = 1582$)

Characteristics	Unweighted Ns	Weighted % (95% CI)	Design effects (subsample)
Current alcohol dependence ($n = 1582$)			
No	1489	93.61 (92.16–94.81)	1.1854
Yes	93	6.39 (5.19–7.84)	
Current depression ($n = 1582$)			
No	1418	89.50 (87.78–91.01)	1.1353
Yes	164	10.50 (8.99–12.22)	
Gender ($n = 1582$)			
Male	1367	86.29 (84.40–87.99)	1.1190
Female	215	13.71 (12.01–15.60)	
Age ($n = 1582$)			
18–24	490	37.26 (34.64–39.96)	1.2429
25–34	519	34.35 (31.87–36.92)	1.1621
35–44	404	20.76 (18.88–22.77)	0.9433
45+	169	7.63 (6.55–8.87)	0.7773
Race ($n = 1581$)*			
White	1417	88.85 (86.85–90.58)	1.4337
Black	100	9.56 (7.88–11.56)	1.5996
Other	64	1.59 (1.24–2.03)	0.4095
Education ($n = 1582$)			
High school graduate/GED or less	387	30.20 (27.69–32.84)	1.2982
Some college or technical training	763	48.16 (45.53–50.81)	1.1496
College/graduate degree	432	21.64 (19.72–23.69)	0.9537
Household income ($n = 1540$)*			
<\$60,000	868	62.01 (59.45–64.51)	1.0878
≥\$60,000	672	37.99 (35.49–40.55)	
Marital status ($n = 1581$)*			
Married	798	40.01 (37.56–42.51)	1.0510
Divorced/separated/widowed	146	9.40 (7.97–11.06)	1.1467
Never married	637	50.59 (47.95–53.23)	1.1473
Rank ($n = 1582$)			
Officer	236	9.77 (8.59–11.10)	0.7306
Enlisted, cadets, and civilian employees	1346	90.23 (88.90–91.41)	
Number of lifetime deployments ($n = 1582$)			
0	539	39.16 (36.53–41.84)	1.2174
1–4	1005	58.86 (56.17–61.49)	1.2005
5+	38	1.99 (1.44–2.74)	0.8687
Number of lifetime traumatic events at wave 1 ($n = 1582$)			
0–2	297	20.19 (18.10–22.46)	1.2160
3–6	451	29.37 (27.00–31.86)	1.1722
7–11	409	24.97 (22.76–27.31)	1.1357
12+	425	25.47 (23.28–27.28)	1.0978
Number of traumatic events between wave 1 and wave 2 ($n = 1582$)			
0	781	49.69 (47.05–52.34)	1.1525
1	346	21.55 (19.47–23.78)	1.1321
2	182	11.53 (9.96–13.32)	1.1383
3+	273	17.23 (15.31–19.33)	1.1619
Interaction indicator variable ($n = 1582$)			
Neither condition	1352	84.85 (82.84–86.66)	1.1622
Alcohol dependence alone	66	4.65 (3.62–5.95)	1.2315
Depression alone	137	8.76 (7.38–10.38)	1.1476
Alcohol dependence and depression	27	1.74 (1.18–2.55)	1.0658
Suicidal ideation w2 ($n = 1582$)			
Yes	42	2.47 (1.68–3.26)	1.0708
No	1540	97.53 (96.74–98.32)	

* Denotes presence of missing values.

risk of subsequent suicidal ideation. Each condition alone was associated with risk, but the presence of both conditions together had a stronger effect than the sum of their risks in isolation, providing evidence of positive additive interaction. This has implications for screening of soldiers and may help focus our efforts to reduce suicide rates among reservists.

Although no other studies to our knowledge have examined the link between coincident alcohol dependence and depression on incident suicidal ideation in the military prospectively, our key findings are in line with findings in other military samples that have examined the links between each condition individually. Our finding of an association between alcohol dependence and suicidal ideation is consistent with that of a prior National Guard sample that demonstrated this association using cross-sectional data [46].

Our finding of an association between depression and suicidal ideation is consistent with findings in mixed component samples of OEF/OIF veterans [19,22] and with findings in the 2008–2014 Department of Defense Suicide Event Reports [7,9,10]. Griffith [12], who examined suicide in a national sample of the Army National Guard using suicide data spanning from 2007 to 2010, found that an alcohol abuse history was prevalent among 12%–17% of suicide cases, but did not specifically examine alcohol dependence.

Our results are consistent with an extensive civilian population literature demonstrating the link between alcohol dependence and suicidality, both cross-sectionally and prospectively [28,47,48], and the well-established link between depression and suicidality [49]. Indeed, Kessler et al. [17] found that both alcohol dependence and depression were independently associated with suicidal ideation

Table 2
Bivariable associations between study sample characteristics and suicidal ideation in the Ohio Army National Guard ($n = 1582$)

Characteristics	Unweighted frequency of events	Weighted % (95% CI)	χ^2 ; P	Crude weighted OR (95% CI)
Current alcohol dependence ($n = 1582$)			$\chi^2(df = 1) = 4.54; P = .03$	
No	34	2.03 (1.42–2.89)		1
Yes	8	8.97 (4.41–17.38)		4.76 (2.05–11.06)
Current depression ($n = 1582$)			$\chi^2(df = 1) = 7.96; P < .001$	
No	28	1.81 (1.21–2.70)		1
Yes	14	8.09 (4.74–13.48)		4.77 (2.37–9.63)
Gender ($n = 1582$)			$\chi^2(df = 1) = 0.16; P = .69$	
Male	34	2.41 (1.68–3.43)		1
Female	8	2.86 (1.37–5.87)		1.20 (0.52–2.75)
Age ($n = 1582$)			$\chi^2(df = 3) = 0.26; P = .86$	
18–24	15	2.69 (1.58–4.56)		1
25–34	11	2.00 (1.07–3.74)		0.74 (0.32–1.71)
35–44	11	2.73 (1.46–5.02)		1.01 (0.44–2.34)
45+	5	2.79 (1.15–6.60)		1.04 (0.36–2.97)
Race ($n = 1581$)*			$\chi^2(df = 2) = 3.15; P = .21$	
White	38	2.60 (1.86–3.62)		1
Black	1	0.95 (0.13–6.46)		0.36 (0.05–2.67)
Other	3	4.57 (1.47–13.35)		1.80 (0.53–6.07)
Education ($n = 1582$)			$\chi^2(df = 2) = 2.24; P = .11$	
High school graduate/GED or less	6	1.34 (0.59–3.01)		1
Some college or technical training	24	3.04 (1.98–4.63)		2.31 (0.91–5.90)
College/graduate degree	12	2.78 (1.53–5.03)		2.11 (0.75–5.93)
Income ($n = 1540$)*			$\chi^2(df = 3) = 3.55; P = .06$	
<\$60,000	29	3.07 (2.09–4.47)		1.94 (0.93–4.06)
≥\$60,000	12	1.60 (0.86–2.95)		1
Marital status ($n = 1581$)*			$\chi^2(df = 3) = 0.59; P = .74$	
Married	21	2.54 (1.63–3.95)		1
Divorced/separated/widowed	6	3.43 (1.46–7.84)		1.36 (0.51–3.65)
Never married	15	2.24 (1.32–3.76)		0.88 (0.43–1.77)
Rank ($n = 1582$)			$\chi^2(df = 1) = 0.24; P = .62$	
Officer	5	2.02 (0.84–4.81)		1
Enlisted, cadets, and civilian employees	37	2.52 (1.79–3.53)		1.25 (0.48–3.27)
Number of lifetime deployments ($n = 1582$)			$\chi^2(df = 2) = 0.81; P = .44$	
0	11	2.11 (1.14–3.87)		1
1–4	28	2.53 (1.71–3.74)		1.21 (0.57–2.54)
5+	3	7.78 (2.41–22.40)		3.92 (0.99–15.58)
Number of lifetime traumatic events at wave 1 ($n = 1582$)			$\chi^2(df = 3) = 1.02; P = .38$	
0–2	7	2.10 (0.91–4.80)		1
3–6	9	1.63 (0.82–3.22)		0.77 (0.26–2.32)
7–11	12	3.01 (1.67–5.36)		1.44 (0.51–4.11)
12+	14	3.21 (1.85–5.51)		1.54 (0.55–4.30)
Number of traumatic events between wave 1 and wave 2 ($n = 1582$)			$\chi^2(df = 2) = 2.49; P = .06$	
0	11	1.37 (0.72–2.56)		1
1	13	3.99 (1.90–5.98)		2.54 (1.06–6.08)
2	8	3.93 (1.86–8.11)		2.96 (1.09–8.04)
3+	10	3.52 (1.84–6.64)		2.64 (1.05–6.65)
Interaction indicator variable ($n = 1582$)			$\chi^2(df = 3) = 3.43; P = .02$	
Neither condition	24	1.59 (1.03–2.44)		1
Alcohol dependence alone	4	5.85 (2.04–15.66)		3.85 (1.18–12.52)
Depression alone	10	6.26 (3.30–11.56)		4.14 (1.86–9.22)
Alcohol dependence and depression	4	17.31 (6.66–38.06)		12.97 (4.05–41.47)

* Denotes presence of missing values.

and suicide attempts in cross-sectional data from a representative sample of the general US population. Finally, our findings of positive additive interaction between alcohol dependence and depression in suicidal ideation risk are consistent with civilian studies [18,30] demonstrating an increased risk of suicidal ideation and behavior for those with both conditions. The RERI (part of the total effect due to interaction) of 5.978 confirms positive additive interaction as the point estimate and its CIs exceed 0; the AP of 0.461 tells us that almost 50% of the risk of suicidal ideation among those with both conditions is attributable to the synergy between those conditions; the SI (ratio of combined and individual effects) of 1.998 confirms positive additive interaction, as this point estimate and its CIs exceed 1 [42,50]. To examine the possibility that the interaction effect was an artifact of scale [51], we performed a sensitivity analysis that modeled our outcome with a Poisson distribution and

log link. We were heartened to find that our interaction effects were essentially present, even if less strong (see [Supplementary Appendix 1](#) for further detail).

Future studies should confirm the temporal sequence of these exposures and outcomes we observed. More work is needed to illuminate how depression and alcohol dependence work together in shaping risk for suicidal ideation. For example, substance abuse affects risk of suicidality through changes in executive functioning that result in impulsivity [52,53], but the contours of how exactly this interacts with the neuropsychological deficits inherent in depression [54,55] to shape risk for suicidal ideation is less clear. Finally, it is critical to understand how best to treat those with both conditions and do so with reference to the particular set of circumstances and challenges faced by reservists [56,57]. Optimal screening practices for reservists, given their civilian co-status and

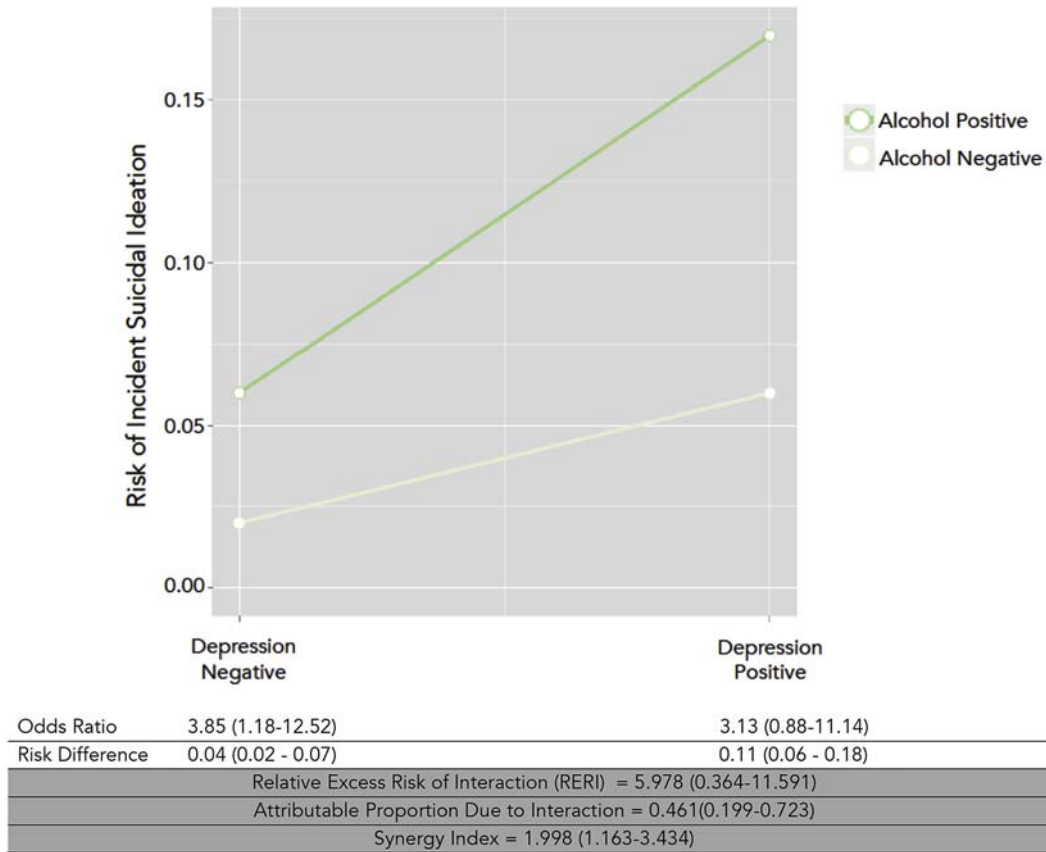


Fig. 1. Assessing interaction between alcohol dependence and depression in predicting incident suicidal ideation. Note: All measures reported in Figure 1 are weighted, but otherwise unadjusted.

one weekend per month of military service, remain a challenge. However, evidence-based treatments for patients with comorbid alcohol dependence and depression are available [58,59], arguing that such treatments along with appropriate screening be further deployed and used for prevention and treatment.

Study limitations include (1) use of telephone interview techniques, a method with less diagnostic validity than clinical interviews, (2) a moderate level of attrition between waves 1 and 2, (3) lack of information on loss to follow-up due to suicide among wave 1 participants, (4) low sensitivity of our outcome measure, (5) a small number of subjects and events across levels of interaction, and (6) quantitative rather than qualitative interaction, raising the possibility of an artifact-based rather than true interaction effect. Despite the inherent limitations with use of telephone interview data, we are reassured about our observations based on a validation study that demonstrated mostly acceptable sensitivity and specificity for the measures used [39]. Although we have a moderate level of attrition between waves 1 and 2, loss to follow-up would have to be unequal both by exposure and disease status to affect our OR estimates [60]. In addition, although loss to follow-up due to suicide is possible among some baseline respondents, this would likely account for only a small percentage of attrition given the low incidence of suicide, and any impact on our effect estimates would likely be negligible or result in an underestimation of our effect measures. Similarly, the low sensitivity of our outcome measure would likely result in an underestimation of our effect estimates. Given knowledge to date on the associations between depression, alcohol misuse and suicide, we would not at all expect a reversal in direction of associations due to any of the previously mentioned limitations. It is possible that the low sensitivity of our outcome

measure threatens inference on the temporal ordering of our exposure outcome relationships, given the possibility that incident cases were truly prevalent cases at baseline. However if this were the case, we do not believe it would change the public health need to identify and treat those with depression, alcohol dependence, or both. While the relatively small number of subjects and events did result in estimates with wide CIs, we are confident in our point estimates and note that the study of suicidal ideation is limited in general given its low frequency. While we are concerned about the difficulty of being confident in quantitative versus qualitative interaction, we are heartened that our result is unlikely due to measurement scale. We hope that future studies can address these limitations.

Conclusions

Notwithstanding the previously mentioned limitations, this study suggests a temporal link between coincident alcohol dependence and depression and risk of suicidal ideation and provides evidence of additive statistical interaction in shaping risk of suicidal ideation. A high-risk suicide prevention strategy that targets military personnel with alcohol dependence, depression, and especially both conditions for screening of suicidal thoughts should receive special attention and further study in suicide prevention efforts.

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Appendix.**Supplementary appendix 1**

To examine the possibility that the interaction effect was an artifact of scale [51], we performed a sensitivity analysis that modeled our outcome with a Poisson distribution and log link. We were heartened to find that our interaction effects were essentially present, even if less strong. In this sensitivity analysis, the Rate Ratios (RRs) were similar to the primary analysis odds ratios for each exposure outcome combination: alcohol

dependence without depression – RR = 3.68 (95% confidence interval [CI] = 2.42–5.61), depression without alcohol dependence – RR = 3.94 (95% CI = 2.86–5.43), and comorbid alcohol dependence and depression – RR = 10.90 (95% CI = 7.28–16.31). The observed relative excess risk of interaction from the Poisson model estimates was 4.27 (95% CI = –0.12 to 8.66), and thus of borderline statistical significance, but convincing on the point estimate. The Attributable Proportion due to Synergy (0.46 [95% CI = 0.12–0.67]) was also convincing at the point estimate and the Synergy Index (SI = 1.76 [95% CI = 1.05–2.94] demonstrated evidence of positive additive interaction.



Practice of Epidemiology

Deployment and Alcohol Use in a Military Cohort: Use of Combined Methods to Account for Exposure-Related Covariates and Heterogeneous Response to Exposure

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Studies have shown that combat-area deployment is associated with increases in alcohol use; however, studying the influence of deployment on alcohol use faces 2 complications. First, the military considers a confluence of factors before determining whether to deploy a service member, creating a nonignorable exposure and unbalanced comparison groups that inevitably complicate inference about the role of deployment itself. Second, regression analysis assumes that a single effect estimate can approximate the population's change in postdeployment alcohol use, which ignores previous studies that have documented that respondents tend to exhibit heterogeneous postdeployment drinking behaviors. Therefore, we used propensity score matching to balance baseline covariates for the 2 comparison groups (deployed and nondeployed), followed by a variable-oriented difference-in-differences approach to account for the confounding and a person-oriented approach using a latent growth mixture model to account for the heterogeneous response to deployment in this prospective cohort study of the US Army National Guard (2009–2014). We observed a nonsignificant increase in estimated monthly drinks in the first year after deployment that regressed to predeployment drinking levels 2 years after deployment. We found a 4-class model that fit these data best, suggesting that common regression analyses likely conceal substantial interindividual heterogeneity in postdeployment alcohol-use behaviors.

alcohol drinking; cohort analysis; military personnel; propensity score

Abbreviations: ATET, average treatment effect for the treated; LGMM, latent growth mixture model.

Alcohol misuse is a widespread problem in the military. In a population-based survey of active duty personnel, about 20% of respondents reported past-month heavy alcohol use (defined as 5 or more drinks per typical occasion at least once per week), and 47% reported binge drinking (5 or more drinks per occasion for men or 4 or more for women, at least once in the past month) (1), compared with approximately 7% and 25%, respectively, among nonmilitary civilians ages 18 or older (2). Among both military personnel and civilians, alcohol use has been linked to aggressive behavior (3–5), injuries (6, 7), marital issues (4, 8–10), and psychiatric comorbidity (11). Preventive strategies against increases in alcohol use and early recognition of risk of abuse are therefore of great interest.

A large body of research has shown that combat-area deployment is associated with increases in alcohol use (1, 12, 13). Several coping models, such as the Tension Reduction Hypothesis (14, 15), affect regulation model (16), and alcohol-stress vulnerability model (17), have been proposed to suggest that some people exposed to stressful events may self-medicate with alcohol to reduce event-related psychopathology. A major shortcoming of these coping models is that the entire group of deployed personnel is assumed to respond similarly to the same stimuli, ignoring the large interindividual differences within the group. Because much literature has documented that stress can have both negative and positive effects on psychopathology and health behaviors (18, 19), the alcohol-stress vulnerability model (17) provides an alternative explanation

for the association between combat-area deployment and alcohol use.

A life-course epidemiology of trauma suggests that the emergence of psychopathology represents a consequence of the complex accumulation and interaction of life experiences that range from social to biological factors that occur over the life span (20). Under the alcohol-stress vulnerability model, this complex accumulation and interaction of life experiences produces each person's vulnerability to alcohol use after stress such that the same stressful stimuli can elicit different patterns of psychopathology as a function of interindividual differences in vulnerability to stress (21, 22). Therefore, estimation of the effect of deployment on alcohol use is challenging for 2 reasons. First, if those factors that increase vulnerability to postdeployment alcohol use are associated with a service member being deployed, a selection bias is introduced. To reduce bias when inferring causal effects from observational data, we must assume that confounding factors (i.e., factors that cause both the exposure and the outcome of interest) are balanced between the 2 groups compared. However, the military considers a confluence of factors before determining whether to deploy a service member, including both operational factors (e.g., need for service members of a particular occupational specialty) and individual factors (e.g., time since last deployment, psychological fitness). As such, deployment is a nonignorable exposure, making it difficult to identify a reasonable group of nondeployed military personnel that has a similar balance of potential confounding factors as do deployed personnel. Unable to identify a defensible reference group of nondeploying service members, studies that have evaluated the association between deployment and alcohol use among service members have often evaluated no control group (23–25).

Second, using regression to identify the average effect of deployment on alcohol use is likely to conceal the different patterns of postdeployment alcohol-use behaviors hypothesized by the alcohol-stress vulnerability model (17). For example, the average causal risk difference is estimated as the average treatment effect for the treated (ATET) (i.e., proportion of respondents increasing their alcohol use after deployment minus the proportion of respondents decreasing their alcohol use after deployment). As such, a positive risk difference suggests that a greater proportion of deployers increased their alcohol use than decreased their alcohol use compared with nondeployers. Given the negative and positive effects of stress on psychopathology and health behaviors (18, 19), heterogeneity in these effects is likely and should be explored using a model that accommodates multiple effects of exposure. For this reason, a major shortcoming of most types of regression analysis is that they assume that respondents come from a single population, which ignores previous studies that have documented heterogeneous postdeployment drinking behaviors among respondents.

To our knowledge, no study has handled selection into deployment in a meaningful way and explored heterogeneity in the course of alcohol use during the postdeployment years. Here, we applied a modeling approach that addresses the nonignorable assignment of deployment and estimates the average effect of deployment on alcohol use for subsets of

persons who share similar characteristics. This modeling approach is applied in 2 steps. First, we propose a propensity score–matched, difference-in-differences analytical strategy to identify the average effect of deployment on alcohol use over 2 years. The strength of this combined approach is that, whereas propensity score matching can account for observed factors that might confound the causal effect of the exposure on the outcome, difference-in-differences models address unobserved factors that are stable over time and might confound the causal effect. However, time-varying factors that are not explicitly adjusted for in the model can still confound the effect estimate under study. Second, we employ a latent growth mixture model (LGMM) to explore the distribution and identifying characteristics for subsets of persons who exhibit similar alcohol-use patterns after deployment (26, 27). And while we aimed to understand those characteristics that determine whether deployment has a negative or positive effect on alcohol use, such an analysis would require prior information about the factors that might modify alcohol-use patterns after deployment. Absent a strong understanding of these factors, we use LGMM to explore both the distribution of and the identifying characteristics for homogeneous subsets of deployers exhibiting heterogeneous patterns of alcohol use after deployment.

Whereas the propensity score–matched difference-in-differences analytical strategy aims to address the nonignorable assignment of deployment to estimate the average effect of deployment among the deployed, the LGMM aims to estimate the average effect for heterogeneous subsets of homogeneous deployers who share similar deployment and nondeployment characteristics. As such, our modeling approach extends previous work by combining methods for propensity score matching (28, 29), to control for confounding variables, with LGMM for visualizing longitudinal data to explore the groups of deployers exhibiting similar patterns of postdeployment patterns of alcohol use in a longitudinal sample of National Guard service members.

METHODS

Study population

Participants were a sample initially recruited as US National Guard service members from the state of Ohio ($n = 2,616$; age, mean = 30.7 (standard deviation, 9.5) years; 85.2% male; 87.8% non-Hispanic white) (30). Data were collected annually for waves 1 to 5 from 2009 to 2014. Retention of wave 1 participants was 80.5%, 68.7%, 60.6%, and 52.2% at waves 2–5, respectively. A second round of baseline interviews for new participants ($n = 578$) was also initiated in 2010 and 2011 to replenish the sample after loss to follow-up.

Regardless of the calendar year that a respondent entered the study, respondents with a baseline interview and 2 additional interviews were eligible for inclusion. Of the total 6,402 person-years observed, 45% of deployers (203 of 314 person-years) and 44% of nondeployers (2,646 of 6,031) met the eligibility criteria.

The study protocol was approved by the Ohio National Guard and the institutional review boards of the University Hospital Case Medical Center, University of Toledo,

University of Michigan, Ann Arbor Veterans Administration Medical Center, Columbia University, Boston University, and the Office of Humans Research Protections of the US Army Medical Research and Materiel Command.

Measures

Deployment. At each wave, respondents were asked whether they had been deployed since their last interview and the location of any deployment. We categorized respondents who reported a deployment to either Iraq or Afghanistan during their most recent deployment as being deployed to a combat area, based on the overlap in dates between this study's data collection (i.e., 2009–2014) and Operation Enduring Freedom (2001 to present) and Operation Iraqi Freedom (2003–2011).

Alcohol use (Quantity-Frequency Index). Past-month alcohol use was measured at each wave with a 2-item measure asking participants "Thinking about just the past 30 days, on how many days did you drink any alcoholic beverage?" and "On the days when you drank alcohol over the past 30 days, on average, how many drinks did you have each day?" The product of these 2 questions provided a measure of the estimated number of drinks consumed over the past month. Because this measure was right skewed, we applied a logarithmic transformation to the alcohol-use measure.

Potentially confounding variables

Twenty-seven potentially confounding sociodemographic, military, psychiatric, and general health variables were included in the model that estimated each respondent's propensity to deploy. See Web Table 1 (available at <https://academic.oup.com/aje>) for full list of variables included in the propensity score model. We gathered information for each of the time-stable potential confounding variables at baseline as well as information for each of the potential time-varying confounding variables at the wave immediately prior to deployment for deployers or immediately prior to the deployment year for their matched deployers among nondeployers.

Statistical analysis

Our analysis occurred in 2 phases, a matching phase and an analysis phase. First, we estimated the propensity score for deployment for each person at each wave and formed a matched data set by connecting each respondent deployed to a combat area with respondents who were not deployed to a combat area and who had the most similar propensity score from the cohort. Propensity scores (predicted probability of deployment) were estimated for each deployed respondent on their index date (i.e., deployment date) and used to match each deployer to a contemporaneous nondeployer. We estimated the predicted probabilities of deployment (propensity scores) for each eligible respondent using logistic regression, with the outcome being deployment between study intervals, and predictors being derived from the respondent characteristics preceding the index date for each respondent. This modeling approach allowed the propensity score to flexibly

account for temporal changes in deployment environment. Within each cohort wave, each eligible deployer was matched to 4 nondeployers using both a nearest-neighbor and an optimal-matching strategy. In accordance with Rosenbaum and Rubin (31), we estimated the standardized mean difference in both the original data and the matched data to determine the best matching strategy. Specifically, a standardized mean difference of less than 0.2 after adjustment indicates balance on the measured covariates between the 2 groups after matching (32). We conducted the propensity score matching in R (R Foundation for Statistical Computing, Vienna, Austria), using the MatchIt package (33).

Second, we conducted both a variable-oriented and a person-oriented analysis to estimate the effect of combat-area deployment on alcohol use. Specifically, we estimated the risk difference using a mixed effects linear regression model that estimated the difference-in-differences of alcohol use among matched deployers and nondeployers (method 1), and we estimated the number and nature of growth curves using LGMM analysis to examine differences in the proportion of deployers and nondeployers assigned to each growth curve (method 2). Method 1 used a difference-in-differences specification with individual-level fixed effects to precisely estimate the effect of deployment on the change in monthly alcohol use:

$$R_{ijk} = \beta_{0jk} + \beta_1(\text{Deployed}_{jk}) + \beta_2(\text{Year}_{ijk}) \\ + \beta_3(\text{Deployed}_{jk} \times \text{Year}_{ijk}) + \mu_{jk} + e_{ijk}$$

R_{ijk} is the annual monthly alcohol-use rate at time i for person j in each propensity score-matched pair k . We used conditional likelihood, stratified propensity score-matched pairs, and estimated individual intercepts for each stratum, represented in this model as β_{0jk} . Deployed_{jk} indicates the deployed-to-a-combat-area exposure versus the nondeployed. Year indicates the follow-up study interview year. The coefficient of interest (β_3) multiplies the interaction term, time \times group, which is equal to 1 for deployers in the postdeployment period. We conducted the difference-in-differences analysis using SAS, version 9.2 (SAS Institute, Inc., Cary, North Carolina).

In method 2, we employed an LGMM to estimate alcohol-use trajectories using the Mplus statistical modeling program, version 7.11 (34). LGMM uses information about interindividual differences and intraindividual changes over time to identify distinct classes of individuals who follow like trajectories of a single outcome variable across multiple time points. Three steps were required to fit the final model. First, we used conventional polynomial growth models to test whether the data exhibited linear or quadratic growth, determining that these data exhibited a quadratic growth. Second, we fit a series of LGMM models to determine best fit, beginning with a 1-class model and progressing to a 6-class model. To allow for differences in baseline drinking levels, we let the intercept vary and held constant the variance of the slope. The best model fit prioritized parsimony, lowest Bayesian information criterion, lowest Akaike information criterion, significant ($P < 0.05$) adjusted Lo-Mendell-Rubin likelihood ratio test, and highest entropy.

RESULTS

Focusing first on the representativeness of the 203 deployed respondents who met the study inclusion criteria (i.e., had a baseline interview and two additional interviews) (Table 1), the included study sample of 203 deployers tended to be more likely to be married (55.7% vs. 38.8%; $d = -0.34$), were less likely to be either never married (36.0% vs. 47.9%; $d = -0.24$) or previously married (8.4% vs. 13.2%; $d = 0.16$), and reported more time in service (10.2 vs. 9.1 years; $d = 0.25$) than excluded deployers. Although no significant differences in percentage with a mental disorder were found (i.e., Cohen's $d \geq 0.2$), a greater proportion of the included study sample met criteria for past-year posttraumatic stress disorder (14.3% vs. 8.3%) and a lesser proportion of the study sample met criteria for current alcohol abuse (29.1% vs. 33.0%).

There were 2,344 respondents (deployers = 203; nondeployers = 2,141) who met the study inclusion/exclusion criteria. The overall incidence of deployment was 8.7% per year. The distribution of propensity score estimates overlapped between the 2 groups: Deployers spanned from 0.02 to 0.48, and nondeployers from 0.00 to 0.52. This overlap indicated a region of common support and suggested that

nondeployed matches could be identified for each deployed respondent (Web Figure 1). Next, we conducted a 1:4 match using both a nearest-neighbor strategy and an optimal-match strategy. After examination of the standardized mean differences after matching, we determined that the optimal match strategy provided the best match. Table 2 shows that the standardized mean differences after matching indicated that the treatment groups were balanced on the measured confounders (i.e., Cohen's $d \geq 0.2$).

Figure 1 shows that deployers, compared with their nondeployed matches, reported a higher mean number of monthly alcohol drinks before deployment and at 1 year after deployment but not at 2 years after deployment. Furthermore, this figure shows that, relative to predeployment, past-month alcohol use was not significantly different at either 1 year or 2 years afterward between matched deployers and nondeployers. Table 3 shows that the difference-in-differences general linear model did not find that the deployers' monthly alcohol use differed between any of the study waves relative to their matched controls. Although we found that the mean number of alcoholic drinks monthly among deployers increased by 2.24 from predeployment to 1 year afterward, decreased by 6.37 from 1 year to 2 years, and decreased by 4.21 from before deployment to 2 years after, compared with their matched

Table 1. Sensitivity Analysis: Descriptive Statistics for Key Variables Among Included and Excluded Deployers, Ohio Army National Guard Mental Health Initiative, 2009–2014

Characteristic	Included Deployers (<i>n</i> = 203)		Excluded Deployers (<i>n</i> = 121)		Cohen's <i>d</i>
	No.	%	No.	%	
Age, years ^a	31.0 (9.1)		30.1 (9.8)		0.13
Male	189	93.1	105	86.8	-0.21
Marital status: Never married	73	36.0	58	47.9	-0.24
Marital status: Married	113	55.7	47	38.8	0.34
Marital status: Previously married	17	8.4	16	13.2	-0.16
Parent or primary caregiver	89	43.8	49	40.5	-0.07
Education: Some college or more	159	78.3	95	78.5	0.07
Annual income > \$40,000	135	66.5	73	62.9	0.15
Currently employed	167	82.3	98	81.0	-0.03
Lifetime deployments: 0	81	39.9	58	48.3	-0.16
Lifetime deployments: 1	53	26.1	30	25.0	0.03
Lifetime deployments: ≥2	69	34.0	33	26.7	0.16
Time since last deployment, days ^a	1,485.7 (1,028.9)		1,450.6 (593.2)		-0.09
Mean time in service, years ^a	10.2 (8.4)		9.1 (9.0)		0.25
Posttraumatic stress disorder ^b	29	14.3	10	8.3	0.19
Depression ^c	3	5.9	0	0.0	0.03
Current alcohol dependence ^d	31	15.1	18	14.9	-0.06
Current alcohol abuse ^e	59	29.1	39	33.0	-0.11

^a Values are presented as mean (standard deviation).

^b *Diagnostic and Statistical Manual of Mental Disorders, Text Revision IV*, criteria (39).

^c Major depression was diagnosed if 5 or more of 9 depressive symptom criteria were present at least "more than half the days" in the prior 2 weeks, and 1 of the symptoms was either depressed mood or anhedonia.

^d Three or more alcohol-dependence symptoms.

^e One or more alcohol-abuse symptoms.

Table 2. Descriptive Statistics for Key Variables in the Propensity Score Model Among the Deployed and Nondeployed Groups, Ohio Army National Guard Mental Health Initiative, 2009–2014

Characteristic	Deployed (n = 203)		Nondeployed (n = 812)		Cohen's d
	No.	%	No.	%	
Age, years ^a	31.0 (9.1)		31.5 (9.5)		-0.04
Male	189	93.1	750	92.4	0.03
Marital status: Never married	73	36.0	305	37.6	-0.03
Marital status: Married	113	55.7	450	55.4	0.00
Marital status: Previously married	17	8.4	57	7.0	0.05
Parent or primary caregiver	89	43.8	371	45.7	-0.04
Education: Some college or more	159	78.3	669	82.4	-0.10
Annual income > \$40,000	135	66.5	555	68.5	-0.01
Currently employed	167	82.3	685	84.4	-0.06
Lifetime deployments: 0	81	39.9	326	40.2	-0.01
Lifetime deployments: 1	53	26.1	217	26.7	-0.01
Lifetime deployments: ≥2	69	34.0	269	33.1	0.02
Time since last deployment, days ^a	1,485.7 (1,028.9)		1,607.8 (1,230.4)		0.01
Mean time in service, years ^a	10.2 (8.4)		11.1 (8.7)		-0.06
Posttraumatic stress disorder ^b	29	14.3	99	12.2	0.06
Depression ^c	3	5.9	12	0.9	0.05
Current alcohol dependence ^d	31	15.1	112	13.8	0.04
Current alcohol abuse ^e	59	29.1	201	24.8	0.08

^a Values are presented as mean (standard deviation).

^b *Diagnostic and Statistical Manual of Mental Disorders, Text Revision IV*, criteria (39).

^c Major depression was diagnosed if 5 or more of 9 depressive symptom criteria were present at least "more than half the days" in the prior 2 weeks, and 1 of the symptoms was either depressed mood or anhedonia.

^d Three or more alcohol-dependence symptoms.

^e One or more alcohol-abuse symptoms.

controls, large standard errors of the estimates resulted in all estimates being insignificant at $\alpha = 0.05$. The large standard errors suggest that the differences in monthly alcohol consumption among the matched sets exhibited substantial heterogeneity. As such, we explored this heterogeneity using LGMM.

Web Table 2 shows the fit indices of past-month alcohol use for the 1-class model through the 6-class model. The 4-class model produced a viable, theoretically defensible solution, with good fit statistics (Akaike information criterion = 9,625.3; Bayesian information criterion = 9,718.8; entropy = 0.83; adjusted Lo-Mendell-Rubin likelihood ratio test: $P < 0.01$). Figure 2 shows that the majority of respondents were assigned to a class with consistently high drinking (47.3%). Other classes were characterized by consistently low drinking (33.2%), high predeployment drinking that became low at 1 year afterward and increased at 2 years (high-decreasing; 6.9%), and low predeployment drinking that increased at 1 year and decreased at 2 years (low-increasing; 12.6%). Table 4 shows that a higher proportion of deployers than nondeployers were in the low-increasing class (14.3% v. 11.2%, respectively), whereas a higher proportion of nondeployers than deployers were in the high-decreasing class (6.4% v. 3.9%, respectively). In a post hoc analysis of deployment-related combat experiences (Web Table 3), deployers in the low-increasing

class were found to have similar deployment experiences as their peers; however, deployers in the low-increasing class tended to be younger, with fewer years of service experience. Because the low-increasing class of deployers tended to be younger than their peers, and alcohol use tends to increase from late adolescents to early adulthood, the increased alcohol use 1 year after deployment among the low-increasing class could represent the influence of age or deployment on alcohol use. Whereas a typical age-related alcohol-use trajectory forms a long arc that changes slowly from one year to the next, the return to near predeployment drinking levels from 1 year to 2 years after deployment suggests a more dramatic change, suggesting that the postdeployment increase in drinking is more likely to represent the association between deployment and alcohol use over and above the influence of age.

DISCUSSION

We have presented a framework for estimating the effect of combat-area deployment on alcohol use over time. The approach we presented used a propensity score–matching method to balance baseline covariates for the 2 comparison

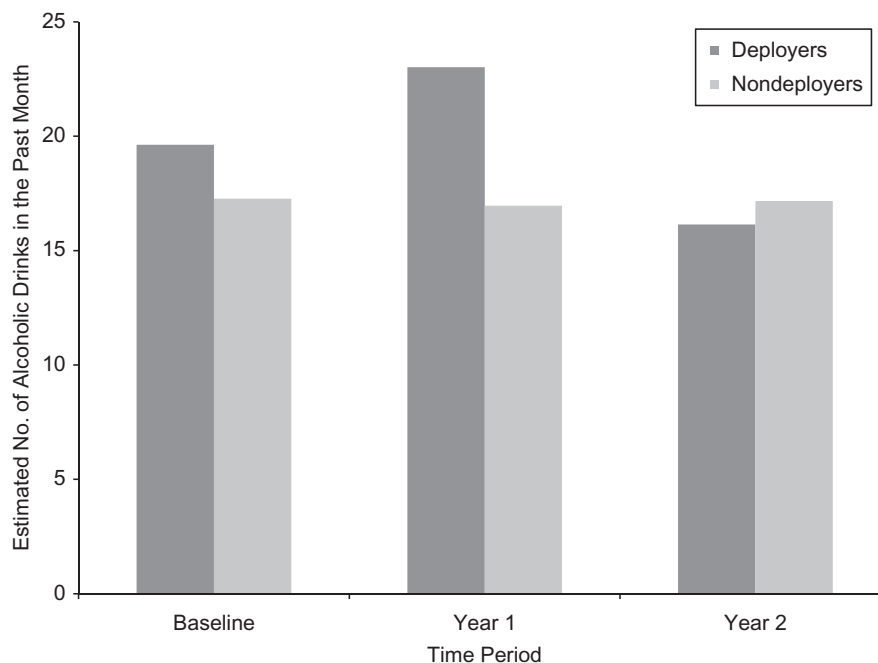


Figure 1. Change in the annual average rate of monthly drinks by deployment status before and after deployment or index date, Ohio Army National Guard Mental Health Initiative, 2009–2014. Estimates result from difference-in-differences regression of the annual rate of monthly drinks between deployed ($n = 203$) and nondeployed ($n = 812$) service members before deployment or index date and at 1 and 2 years afterward.

groups (deployed and nondeployed), followed by a variable-oriented approach based on mixed models to account for the confounding and a person-oriented approach based on LGMM to investigate the heterogeneous response to deployment.

The results of our variable-oriented analysis do not provide evidence of a significant positive association between

combat-area deployment and monthly alcohol use. We obtained positive, although nonsignificant, estimands on the rate of change in alcohol use 1 year after a combat-area deployment relative to nondeployers. This increase in postdeployment alcohol use is consistent with earlier reports in Operation Enduring Freedom/Operation Iraqi Freedom populations (1, 12, 13, 23).

Table 3. Difference-in-Differences Generalized Linear Models Estimating the Number of Monthly Drinks^a by Deployment Status in a Matched Data Set of the Ohio Army National Guard Mental Health Initiative, 2009–2014

Deployment and Year Category	Coefficient	SE	P Value
<i>Before Deployment or Index Date to 1 Year Afterward</i>			
Deployed	3.51	1.65	0.28
Year	1.12	1.66	0.50
Deployed × Year	2.24	3.30	0.62
<i>1 Year to 2 Years After Deployment or Index Date</i>			
Deployed	1.34	1.42	0.52
Year	−3.03	1.43	0.03
Deployed × Year	−6.37	2.83	0.27
<i>Before Deployment or Index Date to 2 Years Afterward</i>			
Deployed	0.29	1.38	0.84
Year	−2.02	1.38	0.14
Deployed × Year	−4.21	2.77	0.13

Abbreviation: SE, standard error.

^a Product of “Thinking about just the past 30 days, on how many days did you drink any alcoholic beverages?” and “On average, how many drinks did you have each day?”

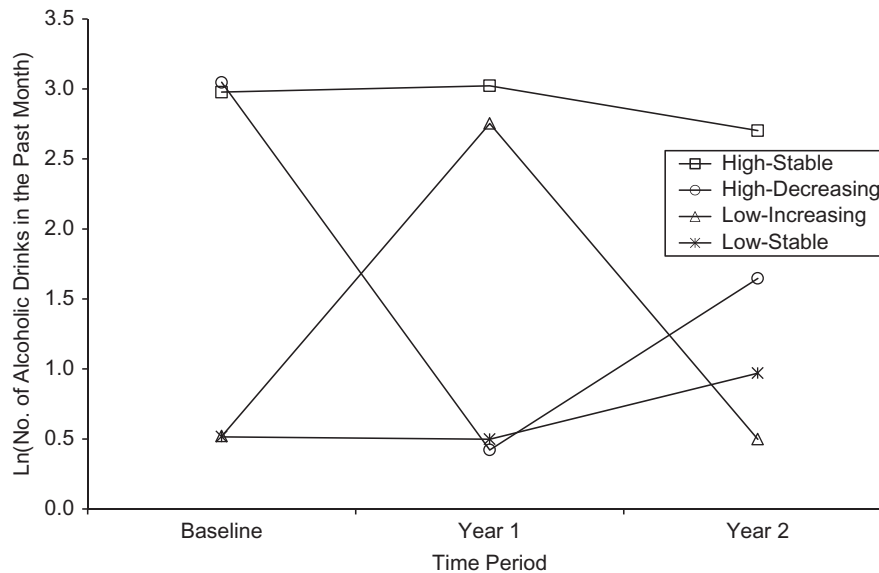


Figure 2. Past-month alcohol-use trajectory over 3 years among study participants in the Ohio Army National Guard Mental Health Initiative, 2009–2014. The 4 groups (and prevalence of group within sample) are depicted with the following symbols: square, high-stable (47.3%); circle, high-decreasing (6.9%); triangle, low-increasing (12.6%); x, low-stable (33.2%).

In our study, however, the increase in alcohol use from predeployment to 1 year after deployment was offset by a subsequent decrease in past-month alcohol use during the subsequent year. Specifically, deployers reported drinking about 7 fewer alcoholic drinks on average between 1 year after deployment (23.0 monthly drinks) and 2 years after deployment (16.1 monthly drinks). To our knowledge, no previous study has looked at the drinking behaviors in Operation Enduring Freedom/Operation Iraqi Freedom veterans across 2 years after deployment; we believe this is the first study to observe that monthly alcohol use regressed to the mean in the period between 1 and 2 years after deployment. While this finding suggests that a critical period for prevention of postdeployment alcohol misuse is isolated to the year immediately after deployment, variable-oriented analyses can conceal the interindividual differences in postdeployment drinking trajectories that we clarified in the LGMM analysis.

Our person-oriented trajectory analysis addressed a key methodological limitation of previous studies using variable-oriented analyses. Although the majority of both the deployers and the nondeployers exhibited a stable trajectory, a substantial proportion of respondents exhibited either an increasing or a decreasing trajectory. That a 4-class solution fit these data best, consistent with other studies (35), exhibits an increasingly recognized finding that a mean alcohol-use trajectory reflects a mixture of multiple trajectories. We observed heterogeneity in alcohol-use trajectories among both the deployers and the nondeployers, which suggests that other factors, beyond the deployment itself, drive the interindividual changes in alcohol use over time. Because studies that have evaluated the influence of deployment on service members have often evaluated no control group (23–25), all the factors that might drive these interindividual changes in alcohol use over time

are uncontrolled. The strength of using a difference-in-differences model, over an approach that does not use a control group, is that unobserved factors that are stable over time and might confound the causal effect are addressed; however, time-varying factors that are not explicitly adjusted for in the model can still confound the effect estimate under study. Therefore, previous studies that have examined alcohol use among deployed personnel, absent a control group, likely have conflated the effects of deployment with other unmeasured factors that are driving whether deployment has a negative or positive effect on alcohol use over time. Whereas variable-oriented analysis (i.e., difference-in-differences) assumes that the factors driving interindividual differences in alcohol-use trajectories are negligible or appropriately controlled for in the model, a person-oriented analysis models this heterogeneity.

To interpret an association as the ATET using a variable-oriented analysis, we most often assume that interindividual differences in response to an exposure are minimal or

Table 4. Trajectory of Estimated Monthly Drinks by Deployment Status Among Participants in the Ohio Army National Guard Mental Health Initiative, 2009–2014

Trajectory	Deployed (n = 203)		Nondeployed (n = 812)	
	No.	%	No.	%
High-stable	117	57.6	380	46.8
High-decreasing	8	3.9	52	6.4
Low-increasing	29	14.3	91	11.2
Low-stable	49	24.1	289	35.6

random; however, previous studies have demonstrated that persons exposed to deployment exhibit heterogeneous changes to psychiatric symptomology (36, 37). When theory does not support a consistent estimator, the ATET is the proportion of persons increasing their alcohol use minus the proportion of persons decreasing their alcohol use between the groups. Thus, we propose that alcohol use increased at a positive rate between baseline and 1 year afterward using a difference-in-differences approach because a greater proportion of persons were in an increasing trajectory than decreasing trajectory among deployers than nondeployers. Future psychiatric epidemiology studies should consider whether the ATET under study might conceal informative and knowable interindividual differences in how the outcome is patterned over time. Under the condition of a consistent estimator, difference-in-differences models address unobserved factors that are stable over time and might confound the causal effect, making this an ideal analytical strategy. However, when a population is likely to be composed of heterogeneous subsets of persons exhibiting homogeneous response patterns over time, LGMM provides the ideal analytical strategy to estimate the average effect for each subset.

Our study findings should be interpreted within the context of 2 limitations. First, we did not consider the influence of time-varying factors on alcohol use. However, previous study findings have suggested that early life experiences (e.g., childhood maltreatment) might have the greatest confounding effect on the relationship between exposure to potentially traumatic events and alcohol use (21, 22). As such, we prioritized addressing any confounding that would arise from a nonignorable treatment assignment and preexposure differences using propensity score matching (31) and fixed-effects modeling (38), respectively. Second, we experienced substantial censoring in our study sample. This censoring was a function of both the overall loss to follow-up among study participants and the exclusion criteria among deployed personnel. At this time, no analytical strategy exists to address the former when applying a propensity score-matched difference-in-differences analysis. As such, the development of a strategy to address censoring that uses, for example, inverse probability weights represents an important avenue for future research. In addition, our study's inclusion criteria required that deployers completed both the data collection immediately prior to their deployment and the 2 data collections immediately after their deployment. Because deployers excluded from this study were more likely than those included to be single, male, and have less time in service—and persons in the increasing alcohol-use trajectory had the lowest mean age and shortest time in service compared with the other alcohol-use trajectories—it is likely that a high proportion of excluded persons would have been classified into the increasing alcohol-use trajectory. Inclusion of these respondents might have resulted in a higher estimate of deployment on alcohol use using the difference-in-differences method.

In conclusion, we observed a nonsignificant increase in estimated monthly drinks in the first year after deployment that regressed to predeployment drinking levels 2 years after deployment. A greater proportion of deployers in the increasing trajectory than in the decreasing trajectory, compared with non-

deployers, likely drove this increase in postdeployment alcohol use at 1 year after deployment. We used combined methods to address challenges to causal identification inherent in studies that examine the psychiatric sequelae of combat-area deployment, specifically nonignorable treatment assignment and heterogeneous response to exposure. Specifically, we used propensity score-matched difference-in-differences and LGMM analyses to address these. Whereas propensity score matching can account for observed factors that might confound the causal effect of the exposure on the outcome, difference-in-differences models address unobserved factors that are stable over time and might confound the causal effect. In addition, whereas difference-in-differences analysis estimates the ATET, an LGMM can investigate the ATET for a subset of persons that share similar characteristics. Future studies should consider using both variable-oriented and person-oriented analyses to better understand the distribution of response patterns that comprise the more often employed variable-oriented approach.

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RESEARCH ARTICLE

Subthreshold PTSD and PTSD in a prospective-longitudinal cohort of military personnel: Potential targets for preventive interventions

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Background: Prevention of PTSD requires identification of subpopulations contributing most to the population burden of PTSD. This study examines the relative contribution of subthreshold PTSD and probable PTSD on future PTSD in a representative military cohort.

Methods: We analyze data on 3,457 U.S. National Guard members from the state of Ohio, assessed by telephone annually from 2008 to 2014. At each wave, participants were classified into one of three groups based on the PTSD Checklist: probable PTSD (DSM-IV-TR criteria), subthreshold PTSD (Criterion A1, at least one symptom in each cluster, symptom lasting longer than 30 days, and functional impairment), and no PTSD. We calculated the exposure rate, risk ratio (RR), and population attributable fraction (PAF) to determine the burden of future probable PTSD attributable to subthreshold PTSD compared to probable PTSD.

Results: The annualized prevalence of subthreshold PTSD and probable PTSD was respectively 11.9 and 5.0%. The RR for probable PTSD was twice as great among respondents with probable PTSD the prior interview than that of those with subthreshold PTSD (7.0 vs. 3.4); however, the PAF was considerably greater in participants with subthreshold PTSD the prior interview (PAF = 35%; 95% confidence interval (CI) = 26.0–42.9%) than in those with probable PTSD (PAF = 28.0%; 95% CI = 21.8–33.8%). Results were robust to changes in subthreshold PTSD definition.

Conclusions: Subthreshold PTSD accounted for a substantial proportion of this population's future PTSD burden. Population-based preventive interventions, compared to an approach focused exclusively on cases of diagnosable PTSD, is likely to affect the greatest reduction in this population's future PTSD burden.

KEYWORDS

anxiety/anxiety disorder, epidemiology, life events/stress, PTSD/posttraumatic stress disorder, trauma

1 | INTRODUCTION

Exposure to potentially traumatic events can elicit a range of psychological symptoms (Fink & Galea, 2015). While symptoms will be mild to moderate for the majority of people, followed by a return to pre-trauma health shortly thereafter, an estimated 1.3 to 8.8% of trauma-exposed persons will experience severe distress and impairment that is consistent with PTSD (Atwoli, Stein, Koenen, & McLaughlin, 2015). Further, another 3.6 to 25.6% of persons experience clinically significant posttraumatic stress symptoms that, despite failure to meet full

diagnostic criteria for PTSD, might cause distress and impairment and warrant treatment (Jakupcak et al., 2011; Mota et al., 2016; Pietrzak, Goldstein, Malley, Johnson, & Southwick, 2009). The dominant lens through which we consider psychiatric disorders is binary, that is, we consider whether individuals have a diagnosis or not. A consequence of this binary model of psychiatric disorders has been a tendency to neglect the people with subsyndromal manifestations of disorder. Thus, persons with symptoms falling below the threshold might not be recognized in clinical care settings or reported in community surveys. Better data on both the course of subthreshold PTSD and the

proportion of future PTSD attributable to subthreshold PTSD within a population would inform decisions about the value of their inclusion or their exclusion in intervention dissemination efforts and clinical care.

PTSD first appeared as a diagnosis in the DSM-III. Although the exact diagnostic criteria for PTSD has varied over time, four features of PTSD have remained stable: (a) experiencing or witnessing a traumatic event; (b) re-experiencing symptoms of the event, including nightmares and/or flashbacks; (c) avoidance of people, situations, or places that are reminders of the event; and (d) hyperarousal symptoms, including irritability and concentration issue (Wilson, 1994). Although a 1-month duration of symptoms is a criterion for PTSD, symptoms can endure anywhere from a few months to several decades (Kessler et al., 2017). During this time, people with PTSD experience a reduced quality of life and increased use of health services (Brunello et al., 2001; Kessler, 2000; Pacella, Hruska, & Delahanty, 2013). Beginning in the 1990s (Stein, Walker, Hazen, & Forde, 1997; Weiss et al., 1992), researchers began to notice that people who do not meet the full diagnostic criteria for PTSD can experience significant impairment, including diminished social and family functioning (Stein et al., 1997), elevated rates of depression, and suicidal ideation (Cukor, Wyka, Jayasinghe, & Difede, 2010; Marshall et al., 2001), and increase health care use (Breslau, Lucia, & Davis, 2004). And, while a complex diagnostic algorithm is necessary to provide reliability, consistency, and communication about a specific disorder, the use of syndrome-based, binary classifications, such as those found in the DSM-III, its successors, and ICD-10, produce artificial boundaries between health and disorder (Kendler & Paranas, 2015; Zachar & Kendler, 2017), which can obfuscate a substantial proportion of trauma-exposed persons who experience subthreshold posttraumatic stress symptoms.

The prevalence of subthreshold PTSD has varied substantially across different studies. A recent meta-analysis by Brancu et al. (2016) found 81 papers reporting the prevalence of subthreshold PTSD published between 1997 and 2014, and among these papers, the prevalence varied from less than 1 to nearly 50%. Brancu et al. (2016) attributed the variability in prevalence estimates to differences in sample composition and population across studies, rather than differences in how studies defined subthreshold PTSD. In particular, Brancu et al. (2016) found that community-based studies (vs. epidemiological) and studies comprised of persons with varying Criterion A events (vs. a single trauma type, such as military combat, natural disaster, or sexual assault) tended to report lower prevalence estimates. Despite the large number of papers that have documented the prevalence of subthreshold PTSD, to the best of our knowledge only a single study has examined the longitudinal course of subthreshold PTSD (Cukor et al., 2010) and no longitudinal studies have been conducted in a military setting.

In this study, we explore the public health burden of subthreshold PTSD using prospective data from a longitudinal study of U.S. Army National Guard soldiers from the state of Ohio. The aim of this study was threefold: (a) to document the prevalence of subthreshold PTSD relative to threshold PTSD; (b) to identify the risk for future PTSD among persons with subthreshold PTSD and PTSD at baseline; and (c) to identify the burden of future PTSD that could be reduced by screening for, and mitigating, subthreshold PTSD.

2 | MATERIALS AND METHODS

2.1 | Study sample

We utilized data from the Ohio Army National Guard Mental Health Initiative (OHARNG MHI; Calabrese et al., 2011). The OHARNG MHI is a longitudinal cohort survey that has annually collected population-based data of Ohio Army National Guard soldiers from November 2008 to present. Addresses were selected from the Guard's complete registry in June 2008 ($N = 12,225$). After an alert letter was sent to all Guard members, 1,013 (8.3%) opted not to participate in the study. After eliminating members without a valid telephone number listed, who did not wish to participate, or who were deemed ineligible due to age, retirement status or language, the official enrollment at baseline was 2,616, representing a cooperation rate and response rate of 68 and 43%, respectively. Retention of Wave 1 participants was 81, 69, 61, and 52% at Waves 2 to 5. In order to replenish the sample after loss to follow-up, a second and third round of baseline interviews for new participants was also initiated in 2010 ($n = 578$) and 2011 ($n = 263$).

Participants were interviewed from 2008 to 2014, approximately 12 months apart for five total waves. Participants in the initial cohort of 2,616 participants contributed a maximum of 4 person-years, whereas participants in 2010 and 2011 supplemental cohorts contributed a maximum of 2 person-years and 1 person-year, respectively. Each person-year began with a completed wave of data collection and ended with the following wave of data collection. Of the 8,053 potential person-years, 5,219 completed the following wave of data collection and 2,834 missed the following wave of data collection. To compensate for non-completed person-years ($n = 2,834$ person-years), response propensity (based on measures available in the prior survey) weighting factors were developed and applied in all analyses of this data. Table 1 shows the distribution of several demographic and psychiatric factors among the 8,053 potential person-years, the 5,219 completed person-years, the 2,834 incomplete person-years (censored), and the censoring-weighted analytic sample.

Study-trained interviewers explained the study and received informed consent before the baseline interview. Ethical approval was granted by the Ohio National Guard and the Institutional Review Boards of University Hospital Case Medical Center, University of Toledo, University of Michigan, Ann Arbor Veterans Administration Medical Center, Columbia University, Boston University, and the Office of Humans Research Protections of the U.S. Army Medical Research and Materiel Command.

2.2 | Definition of subthreshold PTSD

A battery of psychiatric screeners was administered via a 60-min computer-assisted interview at each wave of data collection. Respondent PTSD status was assessed in three phases. First, traumatic events were assessed with the Life Events Checklist—Civilian Version (Gray, Litz, Hsu, & Lombardo, 2004), the Deployment Risk and Resilience Inventory items (King, King, Vogt, Knight, & Samper, 2006), and events used by Breslau et al. (1998). Events could have occurred either during or outside of their most recent deployment. These were all events that met Criterion A1 for the definition of a traumatic event according to

TABLE 1 Comparison of potential person-years, complete person-years, and incomplete person-years, and all person-years censoring-weighted sample

Characteristic	Potential person-years (n = 8,053) %	Complete person-years (n = 5,219) %	Incomplete person-years (n = 2,834) %	Censoring-weight person-years %
Age (years)				
18–24	36.5	32.9	43.3	36.5
25–34	31.7	32.8	29.7	31.7
35–44	22.3	23.3	20.2	22.3
≥45	9.5	11.0	6.8	9.5
Male	85.4	85.8	84.6	85.4
Marital status: Never married	42.1	38.9	48.0	42.0
Marital status: Married	48.2	51.8	41.7	48.3
Marital status: Previously married	9.7	9.4	10.3	9.7
Education: Some college+	77.4	80.8	71.2	77.5
Currently employed	81.4	82.7	78.9	81.5
Baseline probable PTSD	5.8	5.2	7.0	5.1
Baseline probable depression	2.9	2.8	3.1	3.0
Baseline probable alcohol use disorder	5.3	5.3	5.4	5.5

Note. Survey attrition was accounted for using response propensity weights using standardized inverse probability-of-censoring weights to account for baseline covariates associated with censoring: age, sex, marital status, education, income, employment, PTSD, depression, current alcohol use disorder. Baseline PTSD was determined using the PTSD Checklist (PCL), with responses anchored to a Criterion A1 event identified using three screeners of potentially traumatic events, and DSM-IV-TR criterion. Probable major depression was assessed using the patient health questionnaire (PHQ-9) and required respondents to endorse five or more of the nine depressive symptom criteria have been present at least “more than half the days” in the past 2 weeks, and one of the symptoms is either depressed mood or anhedonia. Probable alcohol use disorder required respondents to answer either one or more alcohol abuse symptoms or three or more alcohol dependence symptoms on the Mini International Neuropsychiatric Interview questionnaire (MINI).

the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.; DSM-IV-TR; American Psychiatric Association, 2000). Second, respondents were asked to review the traumatic events they endorsed and identify their “worst event.” Finally, PTSD symptoms were assessed using the PTSD Checklist—Civilian Version (PCL). To better map the screener to the DSM-IV definition of PTSD, respondents were asked to answer each item in relation to their self-selected “worst” Criterion A1 event. In addition to the 17 DSM-IV PTSD symptoms asked during the PCL, respondents were asked three additional questions to assess Criterion E and F. Criterion E was assessed by asking respondents the following question: “What was the longest period of time during which you were having these problems?”—experiencing symptoms for one month or longer was required to meet Criterion E. Criterion F was assessed using the following two questions: “How difficult did these problems make it for you to do your work, take care of things at home, or get along with other people? Would you say—not difficult at all, somewhat difficult, very difficult, or extremely difficult” and “When you had several of these bad moods, feelings, and memories, how distressing was it for you? Was it—not at all distressing, mildly distressing, moderately distressing, or severely distressing?” To meet Criterion F, respondents had to endorse either very or extremely difficult in response to the former question or moderate to severe distress in response to the latter question.

Respondents were categorized as positive for probable DSM-IV PTSD if they reported a Criterion A1 event, being bothered “moderately” or more on at least one intrusion (Criterion B), three

avoidance/numbing (Criterion C), and two hyperarousal (Criterion D) symptoms, with symptoms lasting one month or more (Criterion E) and causing significant distress or impairment (Criterion F). In a clinical reappraisal on a subsample of the telephone survey participants (Prescott et al., 2014), we found past-year telephone diagnosis of PTSD using the PCL had moderate sensitivity (0.54) and high specificity (0.92) and negative predictive value (0.97) compared to the Clinician-Administered PTSD Scale (CAPS).

Because no single definition of subthreshold PTSD exists, we used the three most common subthreshold PTSD definitions according to the recent meta-analysis by Brancu et al. (2016): (a) Criterion B and Criterion C or Criterion D (Definition 1); (b) two of three Criterion (e.g., Criterion B and Criterion D; Definition 2); and (c) at least one symptom in each cluster (Definition 3). In addition to the above criteria, symptoms could not meet DSM-IV PTSD criterion and respondents had to endorse a DSM-IV Criterion A1 event, Criterion E, and Criterion F. Using the Cohen's kappa coefficient, we found agreement among the three definitions of probable subthreshold PTSD was substantial, ranging from 0.78 (95% CI: 0.76–0.80) between Definition 2 and Definition 3 to 0.97 (95% CI: 0.97–0.98) between Definition 2 and Definition 1 (Table 2). To provide the most conservative estimates of exposure rate, risk ratio (RR), and population attributable fraction (PAF), we prioritized the most stringent definition of probable subthreshold PTSD (i.e., Definition 1; Brancu et al., 2016), using Definition 2 and Definition 3 to check robustness of estimates to different definitions of probable subthreshold PTSD.

TABLE 2 Agreement among the three definitions of PTSD in Ohio Army National Guard Mental Health Initiative sample, 2009–2014

Subthreshold PTSD	Kappa (95% CI)		
	Definition 1 ^a	Definition 2 ^b	Definition 3 ^c
Definition 1 ^a	-	0.97 (0.97, 0.98)	0.80 (0.78, 0.82)
Definition 2 ^b	-	-	0.78 (0.76, 0.80)
Definition 3 ^c	-	-	-

^aDefinition 1 requires respondents screen positive for a DSM-IV-TR Criterion A event, Criterion B, Criterion C or Criterion D, plus Criterion E and Criterion F.

^bDefinition 2 requires respondents screen positive for a DSM-IV-TR Criterion A event, two of the three Criterion B, Criterion C, or Criterion D, plus Criterion E and Criterion F.

^cDefinition 3 requires respondents screen positive for a DSM-IV-TR Criterion A event, a response of 3–5 (*Moderately* or above) on at least one Criterion B item, one Criterion C item, and one Criterion D item, plus Criterion E and Criterion F. CI: confidence interval.

2.3 | Statistical analyses

Our analysis was completed in two steps. First, we conducted a series of generalized linear models where lagged variables for probable PTSD and subthreshold PTSD were the predictors of primary interest and next-year probable PTSD was the outcome. To estimate the RR, we specified the model fit with a binomial distribution with a logistic link function (Zou, 2004). All models were adjusted for study year, used robust standard errors to account for repeated observations, and were weighted to account for survey attrition. To account for survey attrition, response propensity weights were estimated in two steps (Rizzo, Kalton, & Brick, 1996; Sommers, Riesz, & Kashihara, 2004; Wun, Ezzati-Rice, Diaz-Tena, & Greenblatt, 2007): (a) fitting a multivariable logit regression of the panel response status at follow-up (i.e., response vs. nonresponse) on a set of baseline variables associated with nonresponse (age, sex, marital status, education, income, employment, PTSD, depression, current alcohol use disorder) and (b) setting the weighting adjustments for the follow-up respondents to the inverse of the response propensity. Results are expressed as adjusted relative risks (RR) with 95% confidence intervals (CIs). Second, we estimated the PAF for probable PTSD and subthreshold PTSD and next-year probable PTSD. The PAF estimates the potential public health impact that would be associated with hypothetically removing the exposure from the population. It was calculated according to the following formula (Rockhill, Newman, & Weinberg, 1998):

Adjusted PAF (regression analysis),

$$PAF = 1 - \sum_{i=0}^k \left(\frac{pd_i}{RR_i} \right),$$

where pd_i is proportion of cases falling into i th exposure level, and RR_i is relative risk comparing i th exposure level with unexposed group ($i = 0$). All statistical analyses were conducted using SAS v9.3 (Cary, NC).

3 | RESULTS

Among the total survey groups, 5.1% screened positive for probable PTSD at baseline and 12.0, 12.5, and 11.9% screened positive for

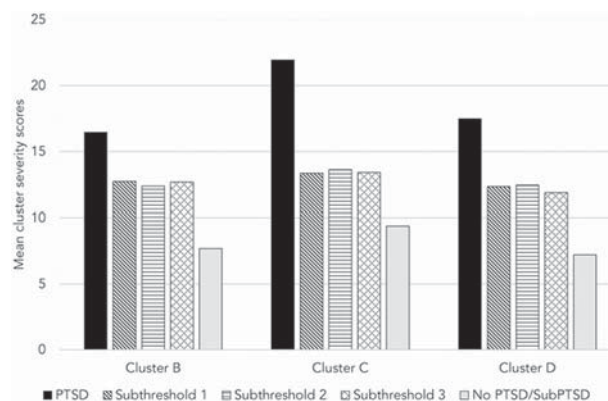


FIGURE 1 Mean symptom cluster severity scores among those meeting criteria for probable DSM-IV PTSD, subthreshold PTSD Definition 1, subthreshold PTSD Definition 2, and subthreshold PTSD Definition 3 compared to persons not meeting criteria for probable PTSD nor any subthreshold definition. Symptom cluster severity score is obtained by summing the scores for the items within the given cluster. Persons with PTSD screened positive for a DSM-IV-TR Criterion A event, Criterion B, Criterion C, Criterion D, Criterion E, and Criterion F. Subthreshold Definition 1 persons screened positive for a DSM-IV-TR Criterion A event, Criterion B, Criterion C or Criterion D, plus Criterion E and Criterion F. Subthreshold Definition 2 Persons screened positive for a DSM-IV-TR Criterion A event, two of the three Criterion B, Criterion C, or Criterion D, plus Criterion E and Criterion F. Subthreshold Definition 3 persons screened positive for a DSM-IV-TR Criterion A event, a response of 3–5 (*Moderately* or above) on at least one Criterion B item, one Criterion C item, and one Criterion D item, plus Criterion E and Criterion F

subthreshold PTSD Definition 1 through Definition 3, respectively. The proportion of respondents with subthreshold PTSD at baseline that progressed to probable PTSD the subsequent year ranged from 15.9% (Definition 1) to 17.3% (Definition 2). Figure 1 shows that the mean symptom cluster score was similar among the three definitions of subthreshold PTSD, and mean symptom cluster scores for subthreshold PTSD fell about halfway between respondents who screened positive for probable PTSD and respondents who did not screen positive for subthreshold PTSD.

The relative risk for diagnosable PTSD at follow-up was twice as high for respondents with probable PTSD at baseline than for respondents with subthreshold PTSD at baseline (Figure 2 and Table 3). The relative risk for respondents with subthreshold PTSD at baseline to screen positive for probable PTSD at follow-up ranged from 3.2 (95% CI = 2.5–4.1) for Definition 1 to 3.7 (95% CI = 2.9–4.7) for Definition 2, whereas respondents with probable PTSD at baseline had 7.0 times (95% CI = 5.9–8.3) the risk of probable PTSD at follow-up compared to respondents without PTSD at baseline. The PAF for probable PTSD at follow-up was uniformly higher for the various baseline measures of subthreshold PTSD than probable PTSD. For example, 28.0% (95% CI = 21.8–33.8%) of all probable PTSD cases at follow-up were attributable to persons with probable PTSD at baseline, compared to about 35% of probable PTSD cases at follow-up, which were attributable to subthreshold PTSD, with the excess fraction ranging from 35.0% (95% CI = 26.0–42.9%) for Definition 3 to 36.4% (95% CI = 27.4–44.3%) for Definition 1.

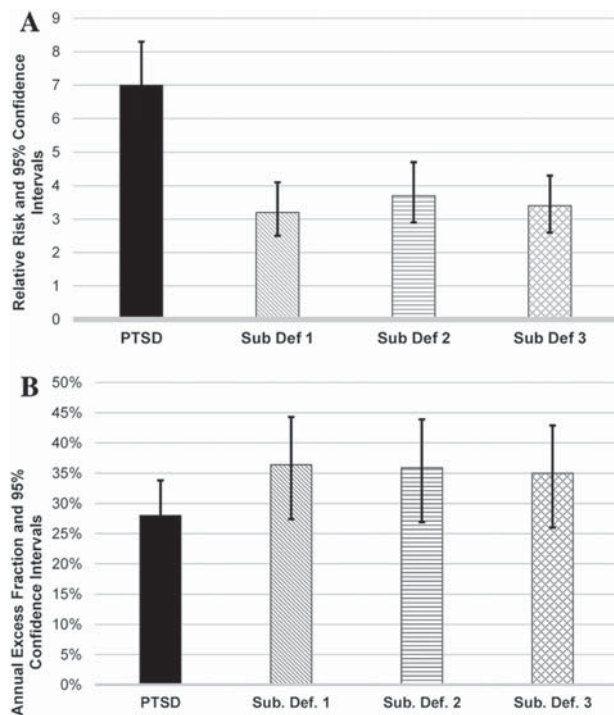


FIGURE 2 Risk ratio associated with PTSD and each subthreshold definition; Graph (a) shows that the risk ratio for future PTSD was twice as great among persons with subthreshold PTSD compared to PTSD. Graph (b) shows the population attributable fraction of PTSD related to persons with subthreshold PTSD the prior year was substantial, suggesting that in the absence of subthreshold PTSD the future population burden of PTSD would fall by about 35 to 36%, relative to 28% for PTSD. Persons with PTSD screened positive for a DSM-IV-TR Criterion A event, Criterion B, Criterion C, Criterion D, Criterion E, and Criterion F. Sub Def 1 persons screened positive for a DSM-IV-TR Criterion A event, Criterion B, Criterion C or Criterion D, plus Criterion E and Criterion F. Sub Def 2 Persons screened positive for a DSM-IV-TR Criterion A event, two of the three Criterion B, Criterion C, or Criterion D, plus Criterion E and Criterion F. Sub Def 3 persons screened positive for a DSM-IV-TR Criterion A event, a response of 3–5 (*Moderately* or above) on at least one Criterion B item, one Criterion C item, and one Criterion D item, plus Criterion E and Criterion F

4 | DISCUSSION

In a cohort of U.S. National Guard soldiers from the state of Ohio, subthreshold PTSD was common, with 12% screening positive for subthreshold PTSD compared to 5% screening positive for probable PTSD. Moreover, even though respondents with probable PTSD had twice the risk of future PTSD than those with subthreshold PTSD, the larger proportion of the population with subthreshold PTSD contributed more to the population's future PTSD burden than those with diagnosable PTSD at prior interviews. Specifically, assuming a causal relationship between subthreshold PTSD and future diagnosable PTSD, the population burden of diagnosable PTSD would have been reduced by about 35 to 36%, if, hypothetically, the symptoms of those with subthreshold PTSD had been reduced to the level of those without subthreshold PTSD, relative to a 28% reduction if those with probable PTSD had

TABLE 3 Baseline PTSD status predicting probable PTSD a year later over five waves (6 years) and annual excess fraction of probable PTSD attributable to baseline PTSD and subthreshold PTSD

PTSD status	PTSD	
	Relative risk (95% CI)	Annual excess fraction (95% CI)
PTSD	7.16 (5.97, 8.59)	28.0% (21.8%, 33.8%)
Subthreshold PTSD Definition 1	3.19 (2.47, 4.13)	36.4% (27.4%, 44.3%)
Subthreshold PTSD Definition 2	3.68 (2.88, 4.71)	35.9% (26.9%, 43.9%)
Subthreshold PTSD Definition 3	3.39 (2.62, 4.39)	35.0% (26.0%, 42.9%)

Note. Persons with PTSD screened positive for a DSM-IV-TR Criterion A event, Criterion B, Criterion C, Criterion D, Criterion E, and Criterion F. Sub Def 1 persons screened positive for a DSM-IV-TR Criterion A event, Criterion B, Criterion C or Criterion D, plus Criterion E and Criterion F. Sub Def 2 persons screened positive for a DSM-IV-TR Criterion A event, two of the three Criterion B, Criterion C, or Criterion D, plus Criterion E and Criterion F. Sub Def 3 persons screened positive for a DSM-IV-TR Criterion A event, a response of 3–5 (*Moderately* or above) on at least one Criterion B item, one Criterion C item, and one Criterion D item, plus Criterion E and Criterion F. CI: confidence interval.

been reduced to the level of those without subthreshold PTSD. Results were robust to changes in definition of subthreshold PTSD.

The prevalence of subthreshold PTSD was similar to those found in previous studies. Indeed, the prevalence of probable subthreshold PTSD in our National Guard sample (12.0%) approached the lower bound of the 95% CI from a random-effects model-based prevalence estimate of subthreshold PTSD from Brancu et al. (2016; 14.7%; 95% CI = 12.3–17.2%); however, our estimate was similar to the estimate from the group of studies that employed the most rigorous methodology (12.6%).

In our study, persons with probable PTSD had a sevenfold increase in their risk of probable PTSD the subsequent year relative to persons without PTSD, compared to about a threefold increase in risk among persons with subthreshold PTSD. The fact that subthreshold PTSD symptoms predicted developing probable PTSD in the future is consistent with studies showing that subthreshold symptoms are at risk factor for developing future psychiatric disorders (Angst & Merikangas, 1997; Fergusson, Horwood, Ridder, & Beautrais, 2005). To the best of our knowledge, however, only a single study has examined the longitudinal course of subthreshold PTSD (Cukor et al., 2010), finding that 14.1% of subthreshold cases progressed to PTSD. Although the previous study was among workers dispatched to the World Trade Center site following the 9/11 terrorist attacks, we observed a similar proportion of persons advancing from subthreshold PTSD to probable PTSD per year (15.9–17.3%).

We found that a greater proportion of future probable PTSD cases could be prevented by reducing PTSD symptoms among the greater proportion of the population with subthreshold PTSD (12.0%) than the smaller, high-risk, group with chronic probable PTSD (5.0%). This finding—that over one in three probable PTSD cases arose from persons with subthreshold PTSD the prior year—is of substantial public

health relevance. A clinical focus on the highest risk minority within the population with PTSD is likely to miss an opportunity to affect the greatest reduction of the future PTSD burden within the population. However, it is difficult to know the best strategy to reduce future PTSD risk among persons with subthreshold PTSD.

One strategy is to apply a broad population prevention strategy focused on the factors that can modify PTSD risk within the population, such as social support (Hobfoll et al., 2007; Ozbay et al., 2007) and alcohol use (Cohen, Fink, Sampson, & Galea, 2015). Through lowering the average risk of PTSD across the entire population, it is likely to follow that persons with subthreshold PTSD will experience a similar shift in PTSD risk. Alternatively, a targeted prevention strategy might focus on identifying, engaging, and linking to care persons exhibiting either subthreshold PTSD or probable PTSD symptoms. While limited guidance is available to clinicians for the best approach to treating persons with subthreshold PTSD symptoms, a growing body of evidence suggests that the same trauma-focused treatments, originally developed for the treatment of PTSD, can be effectively used to treat patients with subthreshold PTSD (Dickstein, Walter, Schumm, & Chard, 2013; Hobfoll, Blais, Stevens, Walt, & Gengler, 2016). Nonetheless, critical questions remain about the urgency with which persons with subthreshold PTSD should be treated and the types of treatment modalities that should be applied to this population.

There are six limitations important for interpretation of this study. First, we used DSM-IV-TR diagnostic criteria to determine probable PTSD, instead of the updated DSM-5 criteria. This decision to use criteria from the DSM-IV instead of the DSM-5 aimed to preserve data from Waves 1 through Waves 3, collected prior to the publication of the DSM-5 and PCL5 in 2013 (American Psychiatric Association, 2013; Weathers et al., 2013). Changes in diagnostic criteria for PTSD from the DSM-IV and DSM-5 included: removal of the subjective component of the index event, clarifying and tightening the definition of a traumatic event, increase the number of symptoms from 17 to 20, and splitting the avoidance and numbing cluster (Criterion C) in DSM-IV into the avoidance cluster (Criterion C) and the cognition and mood group (Criterion D; Pai, Suris, & North, 2017). While these changes to the diagnostic criteria may affect the proportion of respondents screening positive for PTSD, it remains true that future research needs to focus on the spectrum of PTSD symptomology, over an arbitrary cutoff of a binary diagnosis. Second, although we used three well-validated measures to assess respondents' exposure to DSM-IV Criterion A-qualifying traumas, a "gold standard" clinician-interview such as the CAPS was not administered to evaluate whether or not the respondents "worst" event involved actual or threatened death, serious injury, or threat to physical integrity to themselves or others. Further, given that a telephone-administered PCL was used to assess both the presence and the severity of PTSD symptoms, over an independent clinical interview-based diagnosis of PTSD, these results more appropriately reflect the probable presence of PTSD symptoms than DSM-IV algorithm-derived diagnostic classification of PTSD. Although a prior study on the diagnostic utility of the PCL found comparable estimates of symptomatology between the PCL and CAPS in this sample (Fine et al., 2013; Prescott et al., 2014), we used the terms probable PTSD to make clear this limitation—comparison

between the results of this study and other work that uses clinical assessments of PTSD should be made cautiously. Third, respondents with subthreshold PTSD might be comprised of multiple subgroups of people, including: (a) people with symptoms advancing in a linear manner from no PTSD to subthreshold PTSD to diagnosable PTSD; (b) people whose PTSD has remitted to a subthreshold level; and (c) people in a chronic state of subthreshold PTSD. While our data set is insufficiently powered to examine each of these three subgroups independently, future studies should consider heterogeneous symptom trajectories among persons with subthreshold PTSD. Fourth, there was loss to follow-up across the years of our study, requiring additional recruitment. To address this concern, we used an analytic approach to account for the potential influence of missingness, and we show that the distribution of baseline characteristics was similar in our censoring-weighted analytic sample compared to our full baseline sample. Fifth, our findings may not generalize to other populations, including non-military populations and active-duty military populations. Finally, the method of population-attributable fraction assumes causality. It must be noted that elimination of a risk marker may not necessarily improve outcomes. However, our focus on reducing subthreshold PTSD to affect the population burden of PTSD increases the likelihood that reductions of this risk will improve outcomes.

5 | CONCLUSION

In conclusion, our findings that respondents with subthreshold PTSD had an increased risk of future PTSD as compared to persons without PTSD, suggests a need to move beyond a binary PTSD diagnosis. The elevated risk for future PTSD among those with subthreshold PTSD—combined with our finding that persons with subthreshold PTSD contribute more to the future population burden of probable PTSD than persons with chronic PTSD—suggests that it is important to include persons with subthreshold PTSD into intervention dissemination efforts and clinical care. Treatment for persons who go on to develop PTSD can receive current evidence-based PTSD care; however, research is needed to identify when and how to best treat those with subthreshold PTSD.

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CONFLICT OF INTEREST

The authors have no conflicts to report.

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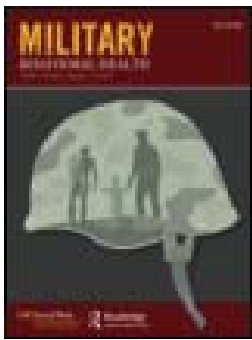
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Examining the Relationship Between PTSD Symptomatology and Cigarette Smoking Among Ohio Army National Guard Soldiers

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ABSTRACT

Evidence suggests that posttraumatic stress disorder (PTSD) increases risk for cigarette smoking in civilian and military populations. There is limited evidence about this relationship among National Guard, a group that may be at higher risk of behavioral health concerns compared to Active Component. The current study used cross-sectional data from a clinical subsample of soldiers ($N=455$) from the Ohio Army National Guard Mental Health Initiative. Soldiers completed self-report and clinician-rated measures, including demographics, smoking status and intensity, and PTSD. Logistic and multinomial regression methods were used to explore the association between PTSD symptomatology and smoking. Higher PTSD symptom severity was modestly associated with an increased likelihood of being a current ($\beta=0.02$, $p=0.049$, OR = 1.02) and heavy smoker ($\beta=0.04$, $p=0.003$, OR = 1.04). Reporting more dysphoria or hyperarousal symptoms was modestly associated with an increased likelihood of being a heavy smoker ($\beta=0.04$, $p=0.001$, OR = 1.05; $\beta=0.03$, $p=0.03$, OR = 1.03). Those with greater PTSD severity are more likely to smoke and have more difficulty quitting; this may have implications for efforts to mitigate the burden of PTSD and smoking among National Guard personnel.

KEYWORDS

Posttraumatic stress disorder; U.S. military; National Guard; soldier; tobacco use; cigarette smoking

Posttraumatic stress disorder (PTSD) and cigarette smoking are consequential and costly (Kessler, Somnoga, Bromet, Hughes, & Nelson, 1995; World Health Organization, 2009). Research indicates that PTSD increases the risk and development of smoking (Feldner, Babson, & Zvolensky, 2007), smoking may worsen PTSD symptoms (e.g., Calhoun et al., 2011), and having PTSD may hinder smoking cessation efforts (Carmody et al., 2012). Individuals with PTSD are two to four times more likely to smoke compared to trauma-exposed only (i.e., no PTSD) and nontrauma-exposed individuals (Feldner, Babson, & Zvolensky, 2007; Fu et al., 2007; Lasser et al., 2000; Lawrence, Mitrou, & Zubrick, 2009); among individuals with PTSD, smoking rates range from 34% to 86% (Feldner, Babson, & Zvolensky, 2007; Fu et al., 2007). Moreover, there is a disproportionate burden of PTSD and smoking among U.S. military personnel as compared to their civilian counterparts. About 5–20% of military personnel deployed to Iraq and/or Afghanistan met criteria for

current PTSD (Kok, Herrell, Thomas, & Hoge, 2012; Ramchand et al., 2010; Seal, Bertenthal, Miner, Sen, & Marmar, 2007; Tanielian & Jaycox, 2008) versus 4.7% of civilians (Goldstein et al., 2016). In regards to smoking, the most recently published Department of Defense survey of active duty military personnel found that 24.0% of service members are current smokers (Barlas, Higgins, Pflieger, & Diecker, 2013) compared to 15.1% of civilians (Jamal et al., 2016).

In a series of studies conducted by Beckham and colleagues, Vietnam veterans with PTSD were more likely to smoke than those without PTSD (Beckham et al., 1997) and more likely to be heavier smokers compared to smokers without PTSD (Beckham et al., 1995; 1997). In addition, Vietnam veterans with PTSD who smoke were more likely to report greater mental health symptoms and physical health problems than nonsmoking veterans with PTSD (Beckham, Gehrman, McClernon, Collie, & Feldman, 2004; Beckham et al., 1995; 1997). Given the evidence

regarding PTSD and cigarette smoking among Vietnam combat veterans, this association was examined to determine whether it is also evident among Operation Enduring Freedom (OEF) and/or Operation Iraqi Freedom/Operation New Dawn (OIF/OND) veterans. Similar to Vietnam combat veterans, OEF/OIF/OND combat veterans who reported greater PTSD severity were also more likely to endorse heavier smoking (Cook, Jakupcak, Rosenheck, Fontana, & McFall, 2009).

Although this prior research has found that PTSD severity predicts smoking intensity, PTSD is usually examined as a homogenous disorder (e.g., total symptom severity), which may not fully capture its complex and heterogeneous nature. Looking at specific PTSD symptom clusters may provide a more nuanced understanding of what symptoms may best be associated with smoking behaviors. For example, among a sample of OEF/OIF/OND male veterans with PTSD, current smokers reported greater emotional numbing symptoms compared to nonsmokers (Kirby et al., 2008). In addition, greater emotional numbing symptoms were most likely to be reported among the heaviest smokers (Cook et al., 2009; Kirby et al., 2008). Veterans not only are smoking to cope with their overall distress but may be specifically smoking as a way to cope with unwanted emotions (Beckham et al., 2008), such as feelings of numbness, depression, and detachment. Although veterans with PTSD smoke to reduce negative affect (Cook et al., 2009), smoking may worsen other PTSD symptoms (Calhoun et al., 2011). Examining smoking behavior at the symptom cluster level is supported by the depression and smoking literature, finding that only some depressive symptoms (e.g., anhedonia, negative affect, somatic symptoms) predict smoking behaviors (Leventhal, Ramsey, Brown, LaChance, & Kahler, 2008). Moreover, specific symptoms, rather than specific diagnoses, may best predict smoking intensity (Morissette, Tull, Gulliver, Kamholz, & Zimering, 2007).

Although the link between PTSD and smoking has been examined among military veterans and Active Component (AC) service members, it has not been specifically addressed among National Guard and Reservists. Understanding the emergent needs of National Guard members is important, as they may face unique post-deployment challenges compared to AC service members, such as being at a higher risk for behavioral health and adjustment problems (e.g., Cohen, Fink, Sampson, & Galea, 2015; Griffith, 2010; Thomas et al., 2010). For example, National Guard soldiers reported higher rates of PTSD symptoms

compared to AC soldiers 12 months post-deployment (30.5% versus 23.7%), even though similar rates of PTSD symptoms were reported between these groups during deployment (Griffith, 2010) and 3 months post-deployment (Thomas et al., 2010). Higher risk of behavioral health and adjustment problems may be due to the strain of National Guard personnel readjusting to their civilian lives, receiving less support from military peers, or barriers to obtaining needed healthcare (Griffith, 2010; Keane, Marshall, & Taft, 2006; King, King, Foy, Keane, & Fairbank, 1999; Thomas et al., 2010). Moreover, due to the wars in Iraq and Afghanistan, National Guard and Reservists experienced more frequent call-ups and longer deployments to combat zones. From 2001 to 2007, approximately 450,000 National Guard and Reservists were deployed, which accounted for almost 30% of all military personnel deployed to Iraq and/or Afghanistan (Waterhouse & O'Bryant, 2008).

Few studies have examined tobacco use solely with National Guard personnel. Widome et al. (2011) conducted focus groups with National Guard soldiers to examine their beliefs and views about tobacco use in combat zones; soldiers described using tobacco as a way to reduce and manage stress, anger, and boredom. Vander Weg et al. (2015) examined the prevalence of smoking among Operation Iraqi Freedom-era and Operation Enduring Freedom-era female veterans and service members from the AC or Reserve/National Guard (RNG). Among female RNG, 17% were current smokers and 21% were former smokers. Among female AC, 19% were current smokers; there was no significant difference in current smoking rates between RNG and AC. Although this accumulating evidence is helping us to better understand this population, to our knowledge, no study has specifically examined the association between PTSD and cigarette smoking within the National Guard population.

Although the relationship between PTSD symptoms and smoking has been found in AC and veteran populations, it needs to be replicated within a National Guard population, as National Guard members may have more behavioral health needs, but have more restricted access to military healthcare services (e.g., Thomas et al., 2010). These findings can then be used to inform healthcare needs, such as developing tailored prevention and intervention programs for National Guard personnel (Tamburrino et al., 2015). In sum, the current study examined the broader relationship between PTSD severity and cigarette smoking by PTSD symptom cluster and intensity of smoking among a sample of Ohio National Guard soldiers.

Table 1. Mean, Standard Deviations, Percentages, and Range for Demographics, Military Characteristics, Smoking, and Trauma Variables ($N = 455$)

Variable	M (SD) or n (%)
Age, range = 17–60	31.38 (9.85)
Gender	
Male	400 (87.9%)
Female	44 (12.1%)
Race/ethnicity	
Caucasian	403 (88.6%)
African American	32 (7.0%)
Other minorities	15 (3.3%)
Hispanic	4 (0.9%)
Marital status	
Unmarried	230 (50.5%)
Married	225 (49.5%)
Education	
High school graduate/GED	89 (19.6%)
Some college/technical training	252 (55.4%)
College graduate/graduate work	114 (25.1%)
Rank	
Enlisted/cadet	402 (88.3%)
Warrant officer/officer	51 (11.2%)
Deployment	
Never	140 (30.8%)
1 or more times	315 (69.2%)
Smoking status	
Current smoker	160 (35.2%)
Current nonsmoker (former/never)	295 (64.8%)
Smoking intensity (current smokers only)	
Light (1–9 cigarettes smoked daily)	79 (49.4%)
Moderate (10–19 cigarettes smoked daily)	36 (22.5%)
Heavy (20+ cigarettes smoked daily)	45 (28.1%)
PTSD severity (CAPS, range = 0–76) ^a	10.91 (13.30)
PTSD diagnosis (CAPS)	
Current PTSD	9 (2.0%)
Past PTSD	23 (5.1%)
Lifetime PTSD	31 (6.8%)

Note: Some percentages will not add up to 100% due to missing data. One person met for both current and lifetime posttraumatic stress disorder (PTSD) for two separate traumas. Lifetime includes current and prior PTSD diagnosis. CAPS = Clinician-Administered PTSD Scale.

^aAnalyses based on CAPS for most severe trauma, civilian- and/or deployment-related.

Method

Participants

Participants were 455 Ohio National Guard soldiers who were randomly selected from the Ohio Army National Guard Mental Health Initiative (OHARNG MHI) parent study ($N = 2,616$). The OHARNG MHI is an ongoing longitudinal investigation that is primarily aimed at assessing the behavioral health risk and resilience factors among OHARNG soldiers. In the current study, the sample was majority White (88.6%), male (87.9%), and cadet/enlisted (88.3%). See Table 1 for more demographic information about the current study sample.

The study was approved by the National Guard Bureau and the institutional review boards of the Office of Human Research Protections of the U.S. Army Medical Research and Materiel Command, University Hospitals Case Medical Center, University of Toledo, University of Michigan, Ann Arbor

Veterans Administration Medical Center, and Columbia University. Verbal informed consent was obtained from all participants. Further details of the methods used by the OHARNG MHI have been published elsewhere (Calabrese et al., 2011; Tamburrino et al., 2015).

Measures

Demographics

Demographical information, including age, gender, race/ethnicity, marital status, education, rank, and deployment, were collected during the baseline telephone survey and/or in-person clinical interview.

Clinician-administered PTSD scale (CAPS; Blake et al., 1995)

Current and past civilian- and/or deployment-related DSM-IV-TR (American Psychiatric Association [APA], 2000) PTSD diagnosis and severity was assessed via the CAPS, a clinician-rated measure that was conducted as part of the in-person clinical interview. PTSD symptoms were assessed based on an individual's self-selected worst traumatic civilian- and/or deployment-related event; if a participant endorsed experiencing both civilian- and deployment-related traumatic events, we used the CAPS with the highest severity score. Frequency ratings were made on a 5-point continuum, ranging from 0 (*never*) to 4 (*daily or almost every day*), and intensity ratings were made on a 5-point continuum, ranging from 0 (*no effort*) to 4 (*extreme, drastic attempts at avoidance*). PTSD symptoms were considered present if an item was scored a frequency of 1 or higher and an intensity 2 or higher (Weathers, Ruscio, & Keane, 1999). This rule is considered the most sensitive of scoring methods for the CAPS (Blake et al., 1995; Weathers et al., 1999). The frequency and intensity score were summed to produce a severity score for each item; total severity scores were calculated by the sum total of all the individual severity scores. The CAPS has good psychometrics (test-retest reliability = 0.77–0.98, $\alpha = 0.85$ –0.94, $\kappa = 0.78$) and is considered the “gold standard” for PTSD assessment (Blake et al., 1995; Weathers, Keane, & Davidson, 2001). In the current study, the CAPS had good internal consistency ($\alpha = 0.88$ –0.96).

We investigated overall PTSD severity and PTSD symptom clusters in relation to smoking status and intensity. When examining by PTSD symptom clusters, we used the Simms, Watson, and Doebbellings (2002) four-factor model as meta-analytic findings indicate it provides a better fit to the PTSD symptom

structure in analyses that used the CAPS as compared to the King, Leskin, King, and Weathers (1998) model (Yufik & Simms, 2010). The four PTSD symptom clusters are intrusions (five items; intrusive recollections or memories, distressing dreams, flashbacks, psychological reactivity to trauma cues, physiological reactivity to trauma cues), avoidance of traumatic stimuli (two items; avoidance of trauma-related thoughts or feelings, avoidance of trauma reminders, such as people, places, activities), dysphoria or general distress (eight items; inability to recall important aspects of the trauma, loss of interest in activities, detachment, restricted affect, sense of foreshortened future, sleep disturbance, irritability, difficulty concentrating), and hyperarousal (two items; hypervigilance and exaggerated startle response).

Cigarette smoking status and intensity

Questions about smoking status and intensity used in the current study originated from the National Survey on Drug Use and Health (Hunter, Feder, Granger, Piper, & Chromy, 2006) and were asked as part of the baseline telephone survey. Smoking status was determined by inquiring about cigarette use in the past 30 days. Soldiers were classified as current smoker (smoked in past 30 days) or current nonsmoker (not smoked in past 30 days or no history of tobacco use). Current smokers were also asked how many cigarettes they smoked daily (one pack = 20 cigarettes). Based on the number of cigarettes smoked daily, we classified soldiers as being a light smoker (1-9 cigarettes), moderate smoker (10-19 cigarettes), and heavy smoker (20+ cigarettes) (Cook et al., 2009). For the current study, we focused on the comparison between current versus current nonsmoker (former or never).

Procedure

The current study used a cross-sectional design to analyze data from the clinical subsample of soldiers, who were randomly selected from the OHARNG MHI parent study. OHARNG members serving between June 2008 to February 2009 with valid address ($N=12,225$) were sent an initial mailing, inviting them to participate in the OHARNG MHI. From the 12,225 soldiers invited to participate, soldiers were initially excluded for the following reasons: opting out of the study ($n=1,013$), having an inactive or incorrect phone numbers ($n=3,568$), or not having a phone number listed with the Guard ($n=1,130$). This resulted in 6,514 possible participants remaining. From the 6,514, soldiers were additionally excluded

based age restriction (e.g., younger than 17 or retired; $n=187$), declined to participate when contacted by phone ($n=1,364$), had English comprehension or hearing difficulties ($n=31$), and not contacted before recruitment closed ($n=2,316$). This resulted in the OHARNG MHI parent study of 2,616 participants, who completed the Wave 1 (baseline) telephone survey conducted between November 2008 and December 2009.

From the 2,616 soldiers who completed the telephone survey, 1,052 were randomly selected to participate in the in-person clinical interview. Of the 1,052 invited, soldiers were excluded for the following reasons: not interested ($n=100$), declined after initial interest ($n=25$), did not attend scheduled interview ($n=21$), and not included before cohort closed ($n=406$). This resulted in the OHARNG MHI clinical subsample of 500 soldiers, who completed both the baseline telephone survey and an in-person clinical interview lasting approximately 2 hours and were compensated for their time (Tamburrino et al., 2015).

Data analysis

As we were most interested in the association between PTSD symptomatology and smoking, we excluded soldiers from the original clinical subsample ($N=500$) who did not endorse any trauma exposure on the CAPS ($n=44$) and had missing smoking data on current cigarette use ($n=1$). Analyses were conducted with the remaining 455 soldiers. We examined if there were any significant differences between our trauma-exposed sample ($N=455$) and those who were excluded ($n=45$). Soldiers who reported trauma exposure were significantly older ($p < 0.001$, $d = 0.57$) and more likely to have had a prior deployment ($p = 0.02$, $phi = 0.01$) compared to the soldiers who reported no trauma exposure. There were no statistically significant differences by gender, race, education, rank, and marital status ($ps = 0.20-0.99$) between soldiers who reported trauma exposure versus no trauma exposure.

Chi-square tests of independence were conducted between categorical variables (e.g., smoking status, PTSD diagnosis); if the results were significant, we followed up with 2×2 chi-squares. Independent sample t -tests and one-way analyses of variance (ANOVAs), with Tukey post hoc tests, were conducted for continuous (e.g., PTSD severity) and categorical (e.g., smoking status, smoking intensity) variables. If the ANOVA results were significant, we followed up post hoc analyses, examining differences between light, moderate, and

heavy smokers. We reported respective effect sizes: Cohen's d for t -tests, Cramer's V or phi for chi-square tests, and eta-squared (η^2) for ANOVAs.

Binary logistic regression was conducted to determine if current PTSD symptoms from the most severe trauma were associated with smoking status (0 = current nonsmoker versus 1 = current smoker). Multinomial logistic regression was conducted to determine if PTSD symptomatology (overall and symptom clusters) was associated smoking intensity (i.e., light, moderate, or heavy); reference category was current nonsmoker. For ease of interpretation, the predictor variables (CAPS total score and four symptom cluster scores) were standardized (T -scores: $M = 50$, $SD = 10$) and the reciprocal of the odds ratio (OR) were reported. We used Agras and colleagues (Agras et al., 2000) criteria to determine the size of the effect, 0.2 (OR = 1.2) small, 0.5 (OR = 1.6) medium, and 0.8 (OR = 2.2) large. To determine covariates to include in the regression analyses, we examined which military and demographic characteristics were significantly related to smoking outcomes of interest (smoking status and smoking intensity). IBM SPSS Statistics Version 24 was used to perform all statistical analyses for the current study.

Results

Preliminary analyses

For most severe trauma, 66.2% of soldiers reported civilian-related trauma, 19.1% reported deployment-related trauma, and 14.7% reported equal PTSD severity for civilian- and deployment-related traumas. Regarding PTSD diagnosis, 0.9% ($n = 4$) met for current civilian-related PTSD, 3.1% ($n = 14$) met for past civilian-related PTSD, 1.3% ($n = 6$) met for current deployment-related PTSD, and 2.0% ($n = 9$) met for past deployment-related PTSD.¹ Because of the small number of soldiers who met for civilian- and/or deployment-related PTSD, we collapsed across trauma type: 2.0% met for current PTSD and 5.1% met for past PTSD. In total, 6.8% met for lifetime (current and/or past) PTSD.² See Table 1. Soldiers with lifetime PTSD (61.3%) were more likely than soldiers with trauma exposure only (33.3%) to be current

smokers, $\chi^2 (1, N = 455) = 8.77$, $p = 0.003$, $phi = 0.15$. Soldiers with lifetime PTSD (90.3%) were more likely than soldiers with trauma exposure (67.7%) to have had a prior deployment, $\chi^2 (1, N = 455) = 5.93$, $p = 0.02$, $phi = 0.12$. Soldiers with lifetime PTSD reported significantly greater PTSD symptoms than soldiers with trauma exposure, $t (32.27) = 8.38$, $p < 0.001$, $d = 1.77$. All of the soldiers with lifetime PTSD were cadet/enlisted. There was no statistically significant differences by age, gender, race/ethnicity, education, and marital status ($ps = 0.14$ – 0.99). See Table 2.

In regard to smoking status, 35.2% of soldiers identified as current smokers. On average, current smokers reported smoking on most days in past month ($M = 22.19$, $SD = 10.63$, range = 1–30) and about $\frac{1}{2}$ pack per day ($M = 11.16$, $SD = 8.88$, range = 1–40). Among current smokers, 49.4% were light smokers, 22.5% were moderate smokers, and 28.1% were heavy smokers; see Table 1. Current smokers were significantly younger than current nonsmokers, $t(349.38) = 3.77$, $p < 0.001$, $d = 0.37$. Tukey post-hoc tests revealed that light smokers ($M = 25.62$, $SD = 6.81$) were significantly younger than moderate ($M = 33.03$, $SD = 10.19$) and heavy smokers ($M = 32.09$, $SD = 9.90$), $F (3) = 11.76$, $p < 0.001$, $\eta^2 = 0.07$. Current smokers (28.9%) were less likely to be married than current nonsmokers (71.1%), $\chi^2 (1, N = 455) = 7.16$, $p = 0.01$, $phi = -0.13$. There was an association between smoking intensity and marital status, $\chi^2 (3, N = 455) = 17.88$, $p < 0.001$, Cramer's $V = 0.20$. Specifically, light smokers (33.8%) were less likely to be married than moderate or heavy smokers (66.2%), $\chi^2 (1, N = 160) = 9.54$, $p = 0.002$, $phi = -0.26$. There was an association between smoking status and education, $\chi^2 (2, N = 455) = 29.25$, $p < 0.001$, $phi = 0.25$. Specifically, current smokers (11.3%) were less likely to have a college degree than current nonsmokers (32.5%), $\chi^2 (1, N = 455) = 23.93$, $p < 0.001$, $phi = -0.24$. There was no statistically significant difference by smoking intensity and education ($p = 0.61$). Current smokers (30.8%) were less likely than current nonsmokers (69.2%) to have had a prior deployment, $\chi^2 (1, N = 455) = 7.97$, $p = 0.01$, $phi = -0.14$. There was an association between smoking intensity and deployment, $\chi^2 (3, N = 455) = 16.55$, $p = 0.001$, Cramer's $V = 0.19$. Specifically, light smokers (41.2%) were less likely to have had a prior deployment than moderate or heavy smokers (58.8%), $\chi^2 (1, N = 160) = 5.43$, $p = 0.02$, $phi = -0.20$. Almost all current smokers (99.4%) were cadet/enlisted. Current smokers reported significantly more PTSD symptoms compared to current

¹One participant met diagnostic criteria for current PTSD for both civilian-related and deployment-related traumas. They were counted separately in both current PTSD categories, but only counted once in the current PTSD category.

²One participant met diagnostic criteria for both current and past PTSD for two separate civilian and deployment-related traumas. They are counted separately both current and past PTSD categories, but only counted once in the lifetime PTSD category.

Table 2. Mean, Standard Deviations, Percentages, and Range for Demographics, Military Characteristics, Smoking, and Trauma Variables for Trauma-Exposure Only And Lifetime PTSD.

Variable	Trauma-exposure only (<i>n</i> = 424) <i>M</i> (<i>SD</i>) or <i>n</i> (%)	Lifetime PTSD (<i>n</i> = 31) <i>M</i> (<i>SD</i>) or <i>n</i> (%)
Age, range = 17–60	31.37 (10.04)	31.55 (6.71)
Gender		
Male	374 (88.2%)	26 (83.9%)
Female	50 (11.8%)	5 (16.1%)
Race/ethnicity		
Caucasian	378 (89.2%)	25 (80.6%)
African American	29 (6.8%)	3 (9.7%)
Other minorities	13 (3.1%)	2 (6.5%)
Hispanic	3 (0.7%)	1 (3.2%)
Marital status		
Unmarried	214 (50.5%)	16 (51.6%)
Married	210 (49.5%)	15 (48.4%)
Education		
High school graduate/GED	83 (19.6%)	6 (19.4%)
Some college/technical training	232 (54.7%)	20 (64.5%)
College graduate/graduate work	109 (25.7%)	5 (16.1%)
Rank		
Enlisted/cadet	370 (87.3%)	31 (100%)
Warrant officer/officer	51 (12.0%)	0 (0%)
Deployment		
Never	137 (32.3%)	3 (9.7%)
1 time or more	287 (67.7%)	28 (90.3%)
Smoking status		
Current smoker	141 (33.3%)	19 (61.3%)
Current nonsmoker	283 (66.7%)	12 (38.7%)
PTSD severity (CAPS, range = 0–76) ^a	9.23 (11.42)	33.81 (16.03)

Note: Some percentages will not add up to 100% due to missing data. One person met for both current and lifetime post-traumatic stress disorder (PTSD) for two separate traumas. Lifetime includes current and prior PTSD diagnosis. CAPS = Clinician-Administered PTSD Scale.

^aAnalyses based on CAPS for most severe trauma, civilian- and/or deployment-related.

nonsmokers, $t(453) = 2.54$, $p = 0.01$, $d = 0.25$. There was no statistically significant differences by gender and race/ethnicity for smoking status and intensity ($ps = 0.20$ – 0.44). See Table 3.

Association between PTSD symptomatology and smoking

Binary logistic regression examined the association between overall PTSD symptomatology and smoking status. Age, marital status, deployment, and education were retained as covariates as they were significantly associated with smoking status. Rank was not retained as 99.4% of current smokers were cadet/enlisted soldiers. The full model containing all predictors was statistically significant, $\chi^2(6, N = 455) = 44.25$, $p < 0.001$. Reporting more PTSD symptoms was associated with an increased likelihood of endorsing being a current smoker ($\beta = 0.02$, $p = 0.049$, OR = 1.02, 95% confidence interval: 1.00–1.04).

Multinomial logistic regression examined the association between overall PTSD symptomatology and smoking intensity; reference category was current nonsmoker. Age, marital status, and deployment were retained as covariates that they were significantly associated with smoking intensity. Rank was not retained

as 99.4% of current smokers were cadet/enlisted. Higher PTSD symptom severity was associated with an increased likelihood of heavy smoking ($\beta = 0.04$, $p = 0.003$, OR = 1.04). Next, multinomial logistic regressions examined the association between the four PTSD symptom clusters (intrusions, avoidance, dysphoria, and hyperarousal) and smoking intensity; reference category was current nonsmoker and age, marital status, and deployment were retained as covariates. Reporting more avoidance symptoms was associated with an increased likelihood of being a light smoker ($\beta = 0.02$, $p = 0.049$, OR = 1.02). Endorsing more dysphoria symptoms was associated with an increased likelihood of heavy smoking ($\beta = 0.04$, $p = .001$, OR = 1.05). Reporting more hyperarousal symptoms was associated with an increased likelihood of heavy smoking ($\beta = 0.03$, $p = 0.03$, OR = 1.03). See Table 4.

Discussion

We found modest evidence that Ohio National Guard soldiers who reported more PTSD symptoms may have an increased likelihood of identifying as a current smoker. Rates of cigarette smoking found in the current study map onto the broader cigarette smoking

Table 3. Mean, Standard Deviations, Percentages, and Range for Demographics, Military Characteristics, and Trauma Variables for Current Smokers and Current Nonsmokers.

Variable	Current smokers (<i>n</i> = 160), <i>M</i> (<i>SD</i>) or <i>n</i> (%)	Current nonsmokers (<i>n</i> = 295), <i>M</i> (<i>SD</i>) or <i>n</i> (%)
Age, range = 17–60	29.11 (9.21)	32.62 (9.97)
Gender		
Male	137 (85.6%)	263 (89.2%)
Female	23 (14.4%)	32 (10.8%)
Race/ethnicity		
Caucasian	146 (91.3%)	257 (87.1%)
African American	9 (5.6%)	23 (7.8%)
Other minorities	3 (1.9%)	12 (4.1%)
Hispanic	1 (0.6%)	3 (0.1%)
Marital status		
Unmarried	95 (59.4%)	135 (45.8%)
Married	65 (40.6%)	160 (54.2%)
Education		
High school graduate/GED	45 (28.1%)	44 (14.9%)
Some college/technical training	97 (60.6%)	155 (52.5%)
College graduate/graduate work	18 (11.3%)	96 (32.5%)
Rank		
Enlisted/cadet	158 (99.4%)	244 (83.0%)
Warrant officer/officer	1 (0.6%)	50 (17.0%)
Deployment		
Never	63 (39.4%)	77 (26.1%)
1 or more times	97 (60.6%)	218 (73.9%)
PTSD severity (CAPS, range = 0–76) ^a	13.05 (14.03)	9.75 (12.76)
PTSD diagnosis (CAPS)		
Current PTSD	4 (2.5%)	5 (1.7%)
Past PTSD	16 (10.0%)	7 (2.4%)
Lifetime PTSD	19 (11.9%)	12 (4.1%)

Note: Some percentages will not add up to 100% due to missing data. One person met for both current and past posttraumatic stress disorder (PTSD) for two separate traumas. Lifetime includes current and past PTSD diagnosis. CAPS = Clinician-Administered PTSD Scale.

^aAnalyses based on CAPS for most severe trauma, civilian- and/or deployment-related.

Table 4. Results From Multinomial Regressions Examining the Association Between PTSD Symptomatology (Overall and Symptom Clusters) and Smoking Intensity.

Models	<i>B</i>	<i>p</i> -value	Odds ratio	95% CI	Chi-square (χ^2)	Pseudo R-squares
Total PTSD symptoms					55.28	0.06–0.13
Light smoker	0.02	0.07	1.02	1.00–1.05		
Moderate smoker	0.01	0.69	1.01	0.97–1.04		
Heavy smoker	0.04	0.003	1.04	1.01–1.07		
Intrusion symptoms					49.35	0.05–0.12
Light smoker	0.02	0.18	1.02	0.99–1.04		
Moderate smoker	0.02	0.23	1.02	0.99–1.05		
Heavy smoker	0.01	0.50	1.01	0.98–1.04		
Avoidance symptoms					52.35	0.06–0.13
Light smoker	0.02	0.049	1.02	1.00–1.05		
Moderate smoker	0.01	0.69	1.01	0.97–1.05		
Heavy smoker	0.02	0.10	1.02	1.00–1.05		
Dysphoria symptoms					58.96	0.07–0.14
Light smoker	0.03	0.06	1.03	1.00–1.05		
Moderate smoker	0.00	0.83	1.00	0.96–1.04		
Heavy Smoker	0.04	0.001	1.05	1.02–1.07		
Hyperarousal symptoms					50.92	0.06–0.12
Light smoker	0.01	0.43	1.01	0.98–1.04		
Moderate smoker	0.01	0.71	1.01	0.97–1.04		
Heavy Smoker	0.03	0.03	1.03	1.00–1.06		

Note: Models included age, marital status, and deployment as covariates. Reference category used was current nonsmoker. PTSD = posttraumatic stress disorder; CI = confidence interval.

literature showing that military personnel are more likely to be cigarette smokers than civilians (Barlas et al., 2013). Our study found an even higher rate of current cigarette smoking; 35.2% endorsed being current cigarette smokers compared to 24.0% of active duty personnel (Barlas et al., 2013). In addition, this

rate is even higher among individuals with a PTSD diagnosis; more than half of soldiers with a lifetime PTSD diagnosis reported being current smokers. In comparison, Kirby et al. (2008) found that 32% of male OEF/OIF/OND veterans with PTSD reported being current smokers. Our current findings suggest

that soldiers who reported more PTSD symptoms may be more likely to not only be a current smoker, but a heavy smoker. Previous work has suggested that veterans with greater PTSD severity are more likely to smoke to cope with their distress (Beckham et al., 2008). Similarly, we found modest evidence to suggest that soldiers who reported more dysphoria and hyperarousal symptoms were more likely to be heavy smokers. Our findings are similar to prior research that has examined the link between smoking intensity and specific PTSD cluster symptoms endorsed. For example, OEF/OIF/OND veterans who reported more emotional numbing symptoms (dysphoria symptom cluster, as used in the present study, includes both emotional numbing and general distress symptoms) were also most likely to be the heaviest smokers (Cook et al., 2009; Joseph et al., 2012; Kirby et al., 2008) and that smoking may exacerbate hyperarousal symptoms (e.g., Calhoun et al., 2011).

Understanding the relationship between PTSD and smoking has potential implications for prevention and treatment. Despite calls for broad tobacco prevention and cessation efforts across military branches (e.g., Institute of Medicine, 2009; Smith et al., 2014), large scale prevention of tobacco use efforts have been small and unsuccessful (e.g., Klesges et al., 2006). Moreover, there is still a conflicting message about tobacco use for military personnel, as while it is banned during basic training and associated with negatively impacting “military readiness,” tobacco use is still positively related to some aspects of military culture (e.g., Haddock et al., 2009; Nelson & Pederson, 2008). For behavioral health practice with National Guard soldiers, it is important to do routine screenings of both PTSD symptoms and tobacco use, which can help identify soldiers who may be in need of PTSD treatment and smoking cessation programming. However, National Guard soldiers only have access to free military healthcare for a limited period of time, depending on their activation status (e.g., Thomas et al., 2010), which may impact their ability to have uninterrupted care if they have to obtain additional healthcare coverage. Yet, even with increased access, getting military personnel and veterans to engage in tobacco cessation programming can be challenging. For example, in an analysis of national Veterans Health Administration (VHA) data (FY2012), only 5.5% of veterans with comorbid PTSD and tobacco use disorder used VHA tobacco cessation services (Kelly, Wang, & Rosenheck, 2017). Cessation rates among veteran smokers with PTSD remain low compared to veterans without PTSD (Carmody et al., 2012). Limited cessation efforts

may be due to worse withdrawal symptoms and greater urges to smoke to reduce negative affect among individuals with PTSD (Dedert et al., 2012).

Even with these barriers, getting individuals into mental health treatment may help to increase cessation rates. For example, individuals who received mental health treatment within a 12-month period were more likely to quit smoking (37.2%) compared to individuals who did not receive mental health treatment (33.1%; Lê Cook et al., 2014). In addition, evidence suggests that smoking cessation treatment should be integrated into standard PTSD treatment care. For example, providing integrated PTSD and smoking cessation treatment to veterans with PTSD was not only safe and effective (Dedert et al., 2016; McFall et al., 2005) but led to higher rates of prolonged abstinence compared to veterans who were referred to smoking cessation clinics (McFall et al., 2010). This indicates that incorporating smoking cessation efforts into behavioral health treatment may help address both physical and behavioral health concerns, as well as potentially being a cost-effective approach to care (Barnett et al., 2016).

The study has several strengths, among which was the use of a clinical subsample drawn from the OHARNG MHI parent study. Diagnosis of PTSD was based on *DSM* criteria (APA, 2000) and assessed using psychometrically sound instruments that have been standardized with our study population. However, when interpreting our results, some limitations should be taken into consideration. First, as diagnosis of PTSD was based on *DSM-IV-TR* criteria (APA, 2000) in the current study, it is important that these results be replicated with the *DSM-5* PTSD diagnostic criteria (APA, 2013), given the addition of the new symptom cluster negative cognitions and mood. Second, our findings regarding the association between PTSD symptomatology and smoking status and intensity were modest at best. That said, our findings are consistent with other studies that also found modest results (e.g., reciprocal odds ratios reported were below 2) when examining the relationship between PTSD severity (overall and symptom cluster) and smoking (e.g., Cook et al., 2009; Joseph et al., 2012; Kirby et al., 2008). One possible explanation for our modest findings is that our current sample is a relatively healthy cohort of soldiers, as they reported low PTSD severity, only a small percentage met for current or past PTSD, and were a nontreatment seeking sample. Third, we used data from a cross-sectional design. Fourth, there may be self-reporting recall bias as the soldiers were asked to recall information

happening across their lifetime. However, the self-report measures were supplemented by clinician-rated measures, such as the CAPS. Finally, the findings from the OHARNG MHI clinical subsample may not be generalizable to other military samples.

The present study reinforces findings from prior literature regarding the relationship between PTSD and cigarette smoking, while also providing novel insights regarding this association in a National Guard sample. Further longitudinal research is needed to better understand this temporal relationship and its underlying mechanisms. In addition, future research should investigate whether these findings hold true for other types of tobacco products used, such as smokeless tobacco. For example, Hermes et al. (2012) found that smoking and PTSD symptoms increased odds of smokeless tobacco initiation among deployed military personnel. In sum, this study not only provides more evidence regarding the relationship between PTSD symptomatology and cigarette smoking within a National Guard sample, but also highlights the importance of examining this unique population specifically, separately, and in comparison to the AC of the Armed Forces.

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Prevalence and covariates of problematic gambling among a US military cohort

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ABSTRACT

The availability of and participation in gambling has increased substantially the past several decades, however studies of military members' gambling behaviors are limited. The present study aimed to investigate potential problematic gambling and its association with demographics and behavioral characteristics in a US military cohort. We analyzed cohort data from a telephone survey during 2015–2016 of 1,553 Ohio Army National Guard members. We assessed potential problematic gambling by using the 3-item National Opinion Research Center Diagnostic Screen—Loss of Control, Lying, and Preoccupation Screen (NODS-CLiP). Potential correlates examined were demographics, depression, suicidal ideation, smoking status, alcohol use, legal and financial problems, perceived general health status, pain, and impulsivity. Results indicated past-year frequent gambling (at least once per week) and lifetime potential problematic gambling was reported by 13% and 8% of respondents, respectively. Problematic gambling and past-year gambling behaviors were associated in a dose-response relationship from 18% among soldiers gambling once per week to 44% among those gambling 4 or more times per week. Correlates of screening positive for potential problematic gambling included the following: being male, currently unmarried, having left the Guard or retired, minor depression, alcohol dependence, legal problems, and increased pain. Given the higher prevalence of frequent gambling in this military cohort (8%), nearly twice the US prevalence (5%), and the association with negative psychological and behavioral outcomes, routine screening of gambling frequency and problem gambling may be needed to ensure military and veteran populations live the healthiest lives possible.

Keywords: gambling, alcohol, military, depression, impulsivity, mental health

1. Introduction

Gambling opportunities have increased rapidly over the past several decades in the United States (US) and worldwide. Expansion of online gaming coupled with the recent rise in popularity of urban casinos have reduced barriers to gaming and normalized gambling behaviors. Although the majority of people who participate will never experience adverse outcomes, approximately 5% of adults in the general population will experience some form of gambling problem during their life (1, 2), with rates likely to be higher in populations exhibiting the same sociodemographic characteristics correlated with problem gambling, including being male, younger, single or divorced, unemployed, and having lower income or less education (3). Given that the majority of US military personnel are male (84%), younger than 30 years (72%), with less than a college degree (92%) (4), the burden of problem gambling may be particularly high in military populations. Despite this, little is known about the burden of problem gambling in military personnel.

Compared to the general population, military and veteran populations have a higher risk of substance abuse (5), mental health issues (6), and suicide (7), all conditions that are highly associated with problem gambling (8-12). Likewise, service members share demographic characteristics associated with problem gambling (e.g., male, young, less educated, unmarried) (6). In addition, problem gambling may be associated with increased risk-taking (13) and impulsivity (14), both of which have been observed to increase post-deployment (15, 16). However, with the exception of a few studies (17-19), gambling behaviors among military and veteran populations have not been well studied. In a study of gambling-related problems among new Air Force recruits, 6% reported gambling problems (i.e., feeling bad about gambling or its related negative consequences in the past 12 months) (17). In another study of patients seeking care at a naval psychiatric clinic, approximately 2% of incoming patients were diagnosed with lifetime prevalence of pathological gambling (19). Finally, a recent assessment found that during 2011–2015, less than 1% of active-duty and reserve component service members examined were diagnosed with a gambling disorder or seen for problem gambling each year in the military health system (18). Most of these studies provide prevalence estimates from convenience samples (i.e., new recruits or patients seeking care) or were completed more than 10 years ago.

Aiming to fill this gap, we investigated the prevalence of potential problematic gambling by specific sociodemographic and military factors and the association between potential problematic gambling and behavioral characteristics among a cohort of US National Guard members from the state of Ohio.

2. Materials and methods

2.1 Design

We used data from the Ohio Army National Guard Mental Health Initiative (OHARNG MHI). The OHARNG MHI is a multiwave cohort survey that has annually collected data from US Army National Guard soldiers from November 2008 to present. The methods used in the survey have been described in detail by Calabrese and colleagues.(20) The cooperation rate and response rate for this study is 67.5% and 43.2%, respectively. For this study, we used data from participants interviewed from 2015 to 2016.

2.2 Participants

A battery of psychiatric screeners were administered via a 60-min computer-assisted telephone interview at each wave of data collection. All participants were informed about the study procedures before giving their written consent. Ethical approval was granted by the Ohio National Guard and the Institutional Review Boards of University Hospital Case Medical Center (UHCMC), University of Toledo (UT), University of Michigan, Ann Arbor Veterans Administration Medical Center, Columbia University, Boston University, and the Office of Human Research Protections of the US Army Medical Research and Materiel Command.

2.3 Measures

2.3.1 Gambling behaviors

Past-year and lifetime gambling history was assessed by using two questions. First, respondents were asked, "In the past 12 months, how often have you bet money or gambled in any way?" with responses ranging from "not at all" to "4 or more times a week." Those who responded "not at all" were asked a follow-up question, "Thinking about your entire lifetime, have you ever bet money or gambled in any way?" Respondents who had gambled one or more times during their lifetime were assessed by using the 3-item National Opinion Research Center Diagnostic Screen—Loss of Control, Lying, and Preoccupation Screen (NODS-CLiP) (21, 22). Derived from the NODS (23), a 17-item measure based on DSM-IV criteria for pathological gambling, the NODS-CLiP comprises 3 NODS items that best identified problem gambling across 8 separate community surveys. Respondents who endorsed one or more items on the screen were considered to screen positive for problematic gambling. By using this cut-off, the NODS-CLiP has been found to have good sensitivity (0.80–0.99) and specificity (0.82–0.94) (21, 22).

2.3.2 Demographic and behavioral questionnaires

Sociodemographic variables included sex, education, marital status, age, annual household income, employment status, homelessness status, military status, and lifetime military deployment to a combat zone. Behavioral variables included depression symptoms (Patient Health Questionnaire-9 [PHQ-9]) (24, 25), smoking status, alcohol use (Mini International Neuropsychiatric Interview [MINI]) (26, 27),

legal and financial problems (28), perceived general health, pain, and impulsivity (Barratt Impulsiveness Scale-Brief [BIS-Brief]) (29).

2.4 Analytic strategy

The extent to which problem gambling differed across demographic, behavioral, and mental health characteristics was assessed. Chi-square t-distribution test statistics were calculated to test for significant differences across relevant categorical strata and continuous variables, respectively. *P*-values less than 0.05 were considered statistically significant. Unadjusted odds ratios (OR), adjusted odds ratios (aORs), and 95% confidence intervals (CI) were computed for the association between potential problematic gambling and behavioral characteristics. All models were adjusted for age, sex, education, and marital status. SAS (SAS Institute, Cary, NC) Enterprise Guide version 7.11 was used to complete all analyses.

3. Results

3.1 Descriptive analyses

This sample of 1,553 current ($n = 911$ [59%]) and former ($n = 642$ [41%]) Ohio Army National Guard members was predominantly male (85%), had at least some college education (87%), were employed full-time (79%), and had deployed one or more times to a conflict area (79%) (not shown).

3.2 Problem gambling

About half (50%) reported gambling at least once during the past year, with 36% gambling less than 10 times and 13% gambling one or more times per week. Lifetime potential problematic gambling was reported by 8% of participants (Table 1). Positive screening for potential problematic gambling increased with past-year gambling behaviors, from 18% among soldiers gambling at least once per week to 44% among those gambling four or more times per week (not shown).

3.3 Correlates of problem gambling

Demographic correlates of screening positive for lifetime potential problematic gambling included being male ($P = 0.02$), currently unmarried ($P = 0.003$), or having left the Guard or retired ($P = 0.007$) (Table 2).

After adjusting for demographics (i.e., age, gender, education, marital status), respondents screening positive for potential problematic gambling were 2.6 times (95% CI = 1.5, 4.8) more likely to screen positive for minor depression than those with minimal symptoms, 3.6 times (95% CI = 2.1, 6.4) more likely to be dependent on alcohol than those who did not use it, and 1.4 times (95% CI = 1.1, 1.7) more likely to report increased pain than those who did not (Table 3). Finally, respondents screening positive

for potential problematic gambling were 1.9 times (95% CI = 1.0, 3.5) more likely to report legal problems than those who did not.

4. Discussion

This study is the first to examine the burden of problem gambling among a cohort of military personnel in which 13% reported past-year frequent gambling (at least once per week) and 8% screened positive for lifetime potential problem gambling. Lifetime potential problem gambling was significantly associated with two demographic factors (i.e., male gender, being unmarried) and four behavioral characteristics (i.e., depression, alcohol dependence, legal problems, increased pain). Although these correlates are consistent with those observed in studies of gambling nonmilitary populations (3, 30-33), the prevalence of problem gambling was nearly twice as great for military personnel in this cohort (8%) than among the general US population (5%) (2).

Problem gambling among men in both military (17, 19) and nonmilitary (3, 34-36) populations has been shown, but this is the first study to show that it is higher among service members who have never been married or were previously married (37). It is possible that the additional time, availability of more discretionary income, loneliness, or disconnectedness may contribute to more problem gambling among this military population (because similar reasons have been found among the general population) (3, 34, 37).

There is a body of literature to support that problem gambling is associated with alcohol abuse or dependence (3, 17, 19) legal issues and financial problems (31, 32), and poor general health (31, 33), which are common among other addictive behaviors (38-40). Persons with less money may see gambling as a means to improve their financial position; however, we found that respondents with potential gambling problems had higher odds of legal issues, and it is unlikely that gambling will improve a person's economic well-being over time. Moreover, these findings highlight the need for prevention efforts that target multiple problem behaviors, not just problem gambling (40, 41). Our findings showed a similar pattern among a military population with alcohol dependence and legal issues, suggesting that service members entering treatment for an addictive behavior, such as alcohol dependence, may also benefit from screening for problem gambling.

Gambling disorder has only recently been included in substance abuse policies and guidance documents (18). Routine screening for problem gambling may be a means to reduce barriers to mental health treatment among people reluctant to seek these services because of stigma or other issues (42). Moreover, incorporating a gambling disorder screener into the intake and periodic assessments of persons seeking military mental health treatment may identify persons with comorbid problem gambling

before they experience adverse outcomes (18). It may be important to routinely screen and monitor military personnel for frequency of gambling behaviors as part of routine (e.g., sick call), periodic (e.g., PHA) and post-deployment (e.g., PDHA/PDHRA) health assessments because some service members may be missed as they do not actively seek mental health treatment.

Our study findings have four limitations common among epidemiologic surveys. First, gambling behaviors and problem gambling were self-reported and could be subject to recall bias or underreporting because of social desirability. However, recall of gambling frequencies that were of greatest interest in this study (e.g., past-month, past-week) may be less subject to this bias because of their temporal proximity. Moreover, although a bias against reporting embarrassing behavior (61) and the perception of psychiatric illness stigma is prevalent in the military (62), we compensated for this concern by assuring participants' confidentiality, both verbally and in writing, before volunteering for this study and by conducting all assessments by telephone using civilian interviewers and no military personnel. Second, we used a short, three-item screener for lifetime problem gambling. Although a previous investigation of problem gambling screeners found the three-item NODS-CLiP to adequately detect both problem gambling and moderate-risk gambling, its ability to detect low-risk gambling was less than satisfactory (22). Any such misclassification of low-risk gambling as no-risk gambling would lead to an underestimate of the true population prevalence of problem gambling. Third, as our study is cross-sectional, we are unable to make any temporal claims about the associations between any demographic or psychosocial characteristics and problem gambling. Longitudinal research is needed to examine both the course of problem gambling and the direction of association. An analysis over time of this cohort and the planned capture of additional gambling measures may enable a more robust assessment of the relationship between problem gambling and behavioral characteristics. Finally, our findings may not be generalizable to other reservists (e.g., Navy Reserve) from other states or active-duty military personnel. Although the OHARNG population is similar in several key demographic and social factors to the U.S. population (e.g., proportion of high school graduates, per-capita income) (43) and National Guard population (e.g., age, sex, rank) (44),¹⁵ our study sample had a higher proportion of respondents who were divorced, separated, or widowed, a group shown to be at increased risk for mood or anxiety disorder. The higher number of divorced, separated, and widowed respondents may have resulted in increased incidence rates.

5. Conclusions

In summary, we found that lifetime potential problematic gambling was associated with negative psychological and behavioral outcomes among a large cohort of current and former Army National Guard members. Specifically, lifetime potential problematic gambling was significantly more likely among those reporting minor depression, alcohol dependence, legal problems, or increased physical

pain. Problematic gambling was also significantly more common among males, unmarried persons, and soldiers who had separated or retired from the Guard. Although personal gambling is a relatively low-prevalence disorder among the general population, it is becoming a substantial concern for population health, the preoccupation it brings, its financial hardship, and its association with other psychiatric disorders and substance use. (18). Given the higher prevalence of frequent gambling among military and veteran populations, routine screening of gambling frequency and problem gambling may be needed so that they can live the healthiest lives possible.

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Table 1. Prevalence of reported gambling behaviors among Ohio Army National Guard members, 2015–2016 (N = 1,553)

	n	%
Total	1,553	100.0
Gambling History:		
Past 12 Months ^a		
Not at all	776	50.0
Less than 10 times	565	36.4
1–4 times month/1 time per week	146	9.4
2–3 times per week	35	2.3
4+ times per week	17	1.1
Lifetime ^b		
No	289	18.6
Yes	1,246	80.2
Problematic Gambling Behaviors (Lifetime):		
Potential problematic gambler ^c		
No	1,424	91.7
Yes	119	7.7
Spent a lot of time thinking about gambling		
No	1,487	95.8
Yes	59	3.8
Tried to control gambling		
No	1,474	94.9
Yes	70	4.5
Lied to family or friends about gambling		
No	1,501	96.7
Yes	46	3.0

^aIn the past 12 months, how often have you bet money or gambled in any way?

^bThinking about your entire lifetime, have you ever bet money or gambled in any way?

^cNODS-CLiP Short Problem Gambling Screen - Classified as "Potential Problematic Gambler" (i.e., further assessment is advised) if answered "Yes" to at least 1 of the 3 questions.

Table 2. Demographic and military characteristics stratified by potential problem gambling (N = 1,543)

	Potential Problematic Gambler ^a				Chi-Square
	Yes		No		
	n	%	n	%	P
Total	119	7.7	1,424	91.7	
Sex					0.02
Men	111	93.3	1,223	85.9	
Women	8	6.7	201	14.1	
Education ^b					0.38
High School	11	9.2	190	13.3	
Some college	51	42.9	550	38.6	
College degree	57	47.9	684	48	
Marital status ^c					0.003
Married or living with partner	62	52.1	950	66.7	
Previously married	22	18.5	154	10.8	
Never married	35	29.4	319	22.4	
Age (years)					0.16
18–24	9	7.6	148	10.4	
25–34	46	38.7	631	44.3	
35–44	35	29.4	300	21.1	
45+	29	24.4	344	24.2	
mean(standard deviation)	37.1 (10.1)		36.1 (10.5)		
Annual household income					0.2
<\$40,000	35	29.4	318	22.3	
\$40,000–\$80,000	46	38.7	572	40.2	
>\$80,000	38	31.9	525	36.9	
Employment status					0.3
Full-time	88	74.0	1,128	79.2	
Part-time	19	16.0	158	11.1	
Unemployed	9	7.6	87	6.1	
Other	3	2.5	51	3.6	
Homeless					0.4
Yes	3	2.5	21	1.5	
Guardsman					0.007
Current	56	47.1	852	59.8	
Former	63	52.9	572	40.2	
Previously deployed					0.62
Yes	93	78.2	1,084	76.1	

^aNODS-CLiP Short Problem Gambling Screen - Yes to at least 1 of 3 questions below (further assessment is advised).

^bEducation – High School (some high school, GED equivalency, high school graduate, technical training); some college (including Associates Degree); college degree (college graduate, graduate work or degree).

°Marital status - Married or living with partner; previously married (divorced, separated, widowed); never married.

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Table 3. Adjusted^a odds ratios (aOR) for the association between individual behavioral characteristics and potential problematic gambling^b (N = 1,543)

	Potential Problematic Gambler		aOR ^a	95% CI
	Yes	No		
	n	n		
Total	117	1,424		
Depression ^c				
Minimal symptoms	88	1,243	1.00	
Minor depression	20	91	2.64	(1.46, 4.78)
Major depression, moderate/severe	8	57	2.07	(0.93, 4.57)
Major depression, severe	3	33	1.45	(0.43, 4.93)
Current smoker ^d				
No	94	1,179	1.00	
Yes	19	192	1.29	(0.75, 2.21)
Alcohol use ^e				
None/normal	87	1,238	1.00	
Abuse	10	111	1.23	(0.60, 2.55)
Dependence	22	75	3.64	(2.08, 6.38)
Legal problems (in past year) ^f				
No	104	1,325	1.00	
Yes	15	98	1.90	(1.04, 3.46)
Financial problems (in past year) ^g				
No	98	1,259	1.00	
Yes	21	165	1.66	(0.98, 2.82)
	<u>mean</u>	<u>mean</u>		
General health ^h	2.3	2.5	1.23	(1.00, 1.52)
Bodily pain ⁱ	2.0	2.2	1.39	(1.11, 1.72)
Impact of pain ^j	1.7	2.2	1.31	(1.09, 1.57)
Impulsivity ^k	19.5	19.6	0.97	(0.90, 1.05)

^aThe association between each individual characteristic and problematic gambling was adjusted for age, sex, education, and marital status.

^bNODS-CLiP Short Problem Gambling Screen - Yes to at least 1 of 3 questions (further assessment is advised).

^cDepression (PHQ-9 cut-point thresholds: minimal symptoms [5–9]; minor depression, dysthymia, major depression-mild [10–14]; major depression-moderately severe [15–10]; major depression-severe [>20]).

^dCurrent smoker (smoked cigarettes every day in the past 12 months or used e-cigarettes every day in the past 30 days).

^eAlcohol use (DSM-IV criteria for alcohol abuse or alcohol dependence [self-reported]).

^fExperienced stressful legal problems (e.g., being sued or suing someone else).

^gHad serious financial problems (e.g., filed for bankruptcy).

^hGeneral health self-reported on Likert scale from excellent (1) to poor (5).

ⁱBodily pain self-reported in the past 4 weeks from none (1) to very severe (5).

^jExtent to which pain interfered with work in the past 4 weeks from not at all (1) to extremely (5).

^kBIS-Brief (summary score).

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Highlights

- Burden of problem gambling and its correlates were investigated in a US military cohort.
- Military members reported frequent gambling at nearly twice the US prevalence.
- Problem gambling was correlated with depression, alcohol use and legal problems.
- Routine screening for problem gambling may be needed for military populations.

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Contributions

All of the authors have made substantive intellectual contributions to the study. MSG and DSF designed the study and executed the analysis. MSG, DSF, LS, and MT were involved in drafting the first version of the manuscript. LS, GC, MT, IL, JC, and SG were involved in obtaining funding, developing the data collection protocol, and management of data collection. All authors contributed to, read, and approved the final manuscript.

Conflict of Interest

None

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None

A machine learning approach to predicting new-onset depression in a military population.

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Abstract:

Objectives: Depression is one of the most common mental disorders in the United States in both civilian and military populations, but few prospective studies assess a wide range of predictors across multiple domains for new-onset (incident) depression in adulthood. Supervised machine learning methods can identify predictors of incident depression out of many different candidate variables, without some of the assumptions and constraints that underlie traditional regression analyses. The objectives of this study were to identify predictors of incident depression across five years of follow-up using machine learning, and to assess prediction accuracy of the algorithms. **Method:** Data were from a cohort of Army National Guard members free of history of depression at baseline (n = 1951 men and 298 women), interviewed once per year for probable depression. Classification trees and random forests were constructed and cross-validated, using 84 candidate predictors from the baseline interviews. **Results:** Stressors and traumas such as emotional mistreatment and adverse childhood experiences, demographics such as being a parent or student, and military characteristics including paygrade and deployment location were predictive of probable depression. Cross-validated random forest algorithms were moderately accurate (68% for women and 73% for men). **Conclusions:** Events and characteristics throughout the life course, both in and outside of deployment, predict incident depression in adulthood among military personnel. Although replication studies are needed, these results may help inform potential intervention targets to reduce depression incidence among military personnel. Future research should further refine and explore interactions between identified variables.

Key words: Depressive disorders, military psychiatry, machine learning, prediction, traumatic events

INTRODUCTION

Depressive disorders are among the most common mental disorders in both civilian and military populations in the United States (U.S.) (1,2). Major Depressive Disorder (MDD) was the second leading cause of disability in the U.S. in 2010 out of all medical conditions (3). Given this high burden, there is a need to identify characteristics of persons at high risk for developing depression, particularly in a military environment where soldiers may frequently deploy to high-stress situations and may be more feasible to monitor and intervene on compared to most civilian populations.

The broad goal of supervised machine learning is optimized prediction, and it comprises algorithmic, data-driven approaches that can handle large numbers of predictor variables (4,5). In particular, classification tree and random forest classifiers construct nonparametric algorithms that promote visual inspection of the data and an understanding of complicated interactions and nonlinear associations that are more difficult to identify and interpret using other methods (4,6,7) or that would not otherwise be detected (8–10), allowing for identification of complex risk profiles without *a priori* hypotheses (7).

Among military populations, most studies investigating predictors of mental health problems have focused on military—and particularly deployment—experiences rather than a full range of characteristics and stressors occurring both in and outside of military service. A broader picture of risk is needed, particularly for part-time soldiers including the National Guard, who frequently transition between military and civilian life. Supervised machine learning methods can identify a wide array of factors associated with incident depression in this group.

Supervised learning has been used to predict psychiatric outcomes including suicide (11–13), posttraumatic stress disorder (PTSD) (14,15), depression in very specific groups (e.g.,

elderly populations; 16), comorbid depression among patients with chronic physical conditions (17), and depression treatment response in clinical samples (18–20). To our knowledge, classification trees and random forest have not yet been applied to predicting new-onset (incident) depression in a military population.

Our objectives for this study were to (a) use a range of potentially predictive characteristics and experiences from across the life course to discern which variables and their interactions predict incident depression, using classification tree and random forest algorithms, and (b) assess predictive accuracies of these algorithms using cross-validation, in a cohort of U.S. Army National Guard members.

METHOD

Data source

We used data from the Ohio Army National Guard Mental Health Initiative (OHARNG-MHI), an ongoing cohort study that began in 2008-2009. Details of recruitment are described elsewhere (21). This cohort—and the Ohio Army National Guard in general—is representative of the U.S. Army National Guard population as a whole in terms of many demographic and social factors such as military rank, gender, and age (21,22).

The first and primary cohort of the study (n=2,616 participants at baseline) completed telephone interviews approximately once per year for six years. The baseline interview assessed demographics, mental health disorders, military experiences, and potentially traumatic life events (“traumas,” e.g., major accidents, abuse) that occurred throughout the life course, whereas the follow-up interviews primarily assessed past-year events. In order to mitigate loss of sample size over time and related changes in demographics due to attrition, smaller samples of newer recruits

to the Guard replenished the original group of respondents each year, beginning in the third year of the study, creating a dynamic cohort study design (23). The analytic sample (1,951 men and 298 women) included respondents from OHARNG-MHI who were present for at least one follow-up interview and had no history of depression at baseline (their first interview, regardless of the calendar year of entry into the study).

The Ohio National Guard and the institutional review boards of University Hospitals Case Medical Center, University of Toledo, University of Michigan, Ann Arbor Veterans Administration Medical Center, Columbia University, Boston University Medical Campus, and the Office of Human Research Protections of the US Army Medical Research and Materiel Command approved this study protocol. Respondents provided verbal informed consent after receiving a complete description of the study.

Outcome

Probable depression (henceforth referred to as “depression”) was measured with the Patient Health Questionnaire (PHQ-9) (24) and classified according to the Diagnostic and Statistical Manual for Mental Disorders version IV (DSM-IV) criteria. The construct was validated as part of the parent study, using a Structured Clinical Interview for DSM-IV-TR (SCID) Axis I Disorders (non-patient version) in-person interview among a random subsample of 500 members of the original cohort (25). Any Depressive Disorder, which includes the DSM-IV categories of MDD and Other Depressive Disorder, was used to define depression in this study due to higher sensitivity compared to MDD only (51% vs. 35%), without sacrificing specificity (83%), when validated against the in-person psychiatric interviews.

This definition corresponds to reporting a period of at least two weeks in the past year

with two or more co-occurring symptoms, where one of the symptoms is depressed mood or anhedonia (inability to feel pleasure), with a frequency of “more than half the days” or “nearly every day.” Having thoughts of self-harm or suicide is an exception to the frequency criteria, counting as a symptom when reported at any frequency.

Incident depression was established by collapsing up to five years of follow-up data into one binary measure for each participant, to represent whether the individual had new-onset depression at any point during their follow-up.

Predictors

In order to preserve temporality, all potential predictors were collected from the baseline interviews, with the exception of four adverse childhood experiences (ACEs) which were added to the study in the second year for the original cohort (but which were assessed at baseline for the following three cohorts).

Our set of *a priori* predictors included all questions or constructs (i.e., variables created from groups of questions or symptoms) from the baseline surveys, as long as the variables had at least five respondents per cell (category). There were 84 total potential predictors for men and 72 for women; women had fewer potential predictors due to their smaller sample (variables with less than five individuals per cell were either removed, or where possible, categories were combined).

These potential predictors included 12 demographic variables, 7 military characteristic variables (e.g., rank), 8 health-related variables (e.g., other mental health disorders, substance use), 2 social support variables, 8 general life stressors (e.g., financial problems), and 47 traumas, including ACEs and also more recent traumas (e.g., witnessing death), both in and

outside of deployment. All potential predictors and their prevalence in the sample are listed in eTable 1 (appendix), and details of the predictors are provided in the text of the appendix.

Statistical analysis

All analyses were gender-stratified due to known differences in correlates of depression among men and women (26,27). We first ran single classification trees for each gender-specific sample using the *partykit* package in R, specifying no random variable selection at each node, minimums of 20 observations per split and 10 observations for the terminal nodes, and stop criterion based on univariate p -values with a cutoff of $p < 0.01$. We plotted these trees in order to visually evaluate the data structure and identify key predictive variables and their interactions.

Next, we constructed 10-fold cross-validated random forests, which a) consolidate across multiple classification trees to add random variation and avoid overfitting to any particular subsample, and b) test and train the algorithms on different combinations of subsets of the sample. We used the *caret* and *RandomForest* packages with 1,000 trees (28), 5 predictor variables randomly sampled at each node, and minimums of 20 observations per split and 1 observation for the terminal nodes. As described in the appendix, we tuned the algorithms to sample only from a subset of data for each tree (90% of true cases and an equal number of non-cases), in order to adjust for the class imbalance in our sample (29,30). Tuning this parameter provided better sensitivity compared to algorithms calculated from default methods.

Using the cross-validated predicted values, the average area under the receiver operating characteristic curve (AUC) was calculated for each gender-specific algorithm, in addition to the average sensitivity, specificity, and accuracy (the overall proportion of correctly classified individuals). We assessed and plotted variable importance using average decrease in accuracy for

each variable, which represents the reduction in accuracy that would result if a variable were randomly permuted (29). All analyses are explained in detail in the appendix. For the tree classification, missing data was handled using surrogate splits (see appendix). For the cross-validated random forests, a complete-case analysis was performed, as surrogate splits cannot be used across folds.

RESULTS

Men

Incidence of depression over follow-up was 14.9% among men (other descriptive information is provided in the appendix including eTables). Figure 1 shows the single classification tree among men. Past-year PTSD was the most predictive of depression overall. Among men with past-year PTSD, having had casualties in the unit with which they were most recently deployed was the next most predictive variable. Among those without past-year PTSD, parental verbal abuse in childhood (one of the ACEs) was next-most important in predicting depression, and so on, down each branch. The combination of characteristics with the highest probability of incident depression was having both past-year PTSD and reporting a unit casualty during the most recent deployment (n=15, incidence=73.3%). The subgroup with the next highest incidence of depression (53.8%) included men who were parents or guardians of children under the age of 18 and who reported fair or poor general health compared to good or great health, but who reported no traumatic injuries/accidents (other than transportation accidents), no financial problems, no childhood verbal abuse, and no past-year PTSD (n=13).

Figure 2 shows a variable importance plot (of mean decreases in accuracy when each variable is removed) for the top 40 predictive variables among men from the cross-validated random forest (the values for all variables are listed in eTable 2). Reporting general life stressors (having been emotionally mistreated, financial problems, divorce); some demographic characteristics (being a current student, being a parent or guardian, being aged 35 or older); being deployed to a non-conflict area; and various traumas (including two ACEs) had the highest mean decreases in accuracy, meaning they were the top predictors. The cross-validated AUC and accuracy were 0.67 and 73.0%, respectively, with 46.8% sensitivity and 77.0% specificity when using the default threshold of predicted risk of 0.50.

Women

Incidence of depression over follow-up was 24.8% among women. Figure 3 shows the single classification tree. Given the small sample size, only one split of the data was made, for alcohol abuse: women with a history of alcohol abuse at baseline had a 42.5% incidence of depression, whereas those who never had alcohol abuse had a 22.1% incidence of depression.

Figure 4 depicts the variable importance plot for all predictive variables from the cross-validated random forest (these values are also listed in eTable 3). Life stressors (having a family member addicted to drugs or alcohol, having been mistreated); demographics (being Enlisted with a relatively low paygrade, a student, and aged 25 or older); having a close friend or family member seriously injured in an accident other than a car accident; low psychosocial support; and childhood verbal abuse were among the top predictors. The cross-validated AUC was 0.67 and the average accuracy was 68.1%, with 75.3% specificity and 45.9% sensitivity when using the default threshold of predicted risk of 0.50.

DISCUSSION

To our knowledge, this study is the first to use classification trees and random forests to assess predictors of probable incident depression in a military sample. We found that, among both men and women, traumas and ACEs (particularly verbal abuse by a parent or guardian), stressors such as being emotionally mistreated, and demographics such as being a current student were predictive of incident depression during follow-up. Military characteristics (e.g., paygrade), low psychosocial support, and hearing about traumas happening to friends or family (e.g., a friend was in a serious accident) appeared more predictive of depression for women than for men, whereas PTSD, deployment location, personally experienced traumas (including combat-related experiences), and financial problems appeared more predictive among men compared to women.

Among men, recent deployment to a non-conflict area was predictive of depression, compared to being deployed to either a conflict area (Iraq or Afghanistan) or never having been deployed. This may be due to stressful and unexpected domestic deployments to areas affected by natural disasters—which have been increasing in recent years—or to areas of civil unrest after riots or massive protests, which can involve National Guard deployment. These types of domestic deployment may be more distressing for soldiers than combat deployments overseas, because they can involve confronting fellow citizens (at protests that become violent, for example) or witnessing citizens suffer (in natural disaster contexts). This finding should be replicated, but it could indicate that additional resiliency training may be warranted for these unique deployment experiences. We were unable to compare incidence of depression by exact location or type of recent deployments, given small cells and lack of detailed questions on the surveys.

Past-year PTSD was the most predictive variable for incident depression among men in the single tree (and moderately predictive in the random forest, suggesting there may have been some overfitting in the single tree). This finding is broadly consistent with both with the only other study to use random forests to predict incident depression in a population-based sample (31) and with many non-machine learning studies that have consistently found comorbidity between PTSD and depression (32–35). The combination of having both past-year PTSD and reporting a unit casualty during the most recent deployment was particularly predictive of depression among men in the classification tree, for which the incidence of depression was 73.3%, or five times larger than the overall incidence of depression among men in this sample.

Among women in our study, PTSD was not predictive of incident depression, but lifetime PTSD status was included in the algorithm instead of past-year status, given the small number of women with PTSD in the past year in an already-small sample of women. This may be the reason why PTSD was not selected among women as being highly predictive, since history of PTSD may have occurred many years before onset of depression, and thus not as clinically or statistically relevant.

Our findings that ACEs and more recent traumas and stressors were predictive of incident depression (for both men and women) is also consistent with a prior machine learning study (31) as well as many non-machine-learning studies that have modeled incident or prevalent depression with similar types of events as exposures or predictors (36–38). Traumas and stressors such as being mistreated have long been known to associate with depression outcomes (39–42), particularly when they occur during childhood, while brain is still developing (42,43).

Finally, our findings on financial problems, being a student, being of lower paygrade, and having children may all be related to financial stress, debt, and concern about being able to

provide for one's family, which have been found in non-machine learning contexts to be associated with depression (44–47).

Based on ten-fold cross-validation, our random forest algorithms were moderately accurate overall (73% accuracy for men and 68% for women). These values are in line with other studies predicting depression outcomes; Kautzky and colleagues (18), who used random forests to predict treatment-resistant depression, found accuracies of 68-75%. Similarly, Jin and colleagues (17), who used four different prediction methods including random forests to model depression (also measured using the PHQ-9) among patients with diabetes, found comparable levels of accuracy (approximately 73%).

Limitations of our study include the use of baseline information alone to predict incident depression over follow-up. It follows that we lack (a) time-varying information assessed on the follow-up surveys that could be temporally closer to onset of depression compared to baseline variables, and (b) information on exact timing of prior events and experiences, as the baseline surveys primarily assessed events that occurred at some point in the past, without asking detailed information on timing (with the exception of other mental disorders). However, using only baseline predictors in this study established temporality between our predictors and outcome—a crucial aspect of valid prediction.

Another limitation is our use of the PHQ-9 for measuring depression. Although the PHQ-9 has been validated against a gold standard depression measure within this cohort as well as in many other populations (24,25), it is primarily a screening tool and was not designed as a diagnostic test. Thus, it is possible that there are individuals in this study with incorrectly classified depression status, which could have affected which variables were chosen as being

predictive. Future studies should aim to replicate these results using diagnostic measures of depression.

Finally, we used a complete case analysis for the cross-validated random forests. Missing data in this study stems primarily from the fact that ACEs were not asked on the baseline survey for the first (and largest) cohort of participants. For those individuals, the ACEs were assessed in the second wave of the study, at which not all respondents were present. A smaller portion of missing data came from responses of “don’t know” or declining to answer questions such as income. As this is a prediction study and thus we are not aiming to isolate and measure the effect of any particular variable on depression, missing data is not as problematic of an issue as in an explanatory study. Generally, missing data among predictors in prediction modeling is thought to only create bias if missingness is related to the outcome variable (9,48). We have no reason to believe that this is the case in our study, as all predictors are from the baseline interview, at which time the outcome had not yet occurred (with the exception of the four ACEs assessed at wave 2 for the primary cohort, which were missing by design, not by refusal to answer).

Despite these limitations, these results may help inform potential screening interventions for depression in this population. Algorithms represent concrete ways officials might identify characteristics associated with high risk of developing outcomes, regardless of underlying causal relationships; this might be especially useful in a military setting given that military personnel are feasible to monitor. For example, the REACH VET algorithm, built by researchers using machine learning, helped the U.S. Department of Veterans’ Affairs to identify veterans at high risk for suicide (49,50), as part of a crucial undertaking at a time when suicides among military personnel have been increasing.

Future analytic work that aims to predict depression—preferably using larger samples and more specifically timed predictors than we were able to utilize in this study—should aim to replicate our findings and further refine interactions between variables identified here. Machine learning might also be used to predict particular subtypes of depression, given that the overall disorder is heterogeneous and takes on different forms in different individuals; this may improve prediction accuracy. Predictive accuracies of the algorithms could also be compared with individual-level prediction using more traditional types of regressions, or using other types of machine learning algorithms, including ensemble methods such as Super Learner which average across different types of algorithms. Finally, broader environmental and context-level variables—like unit-level characteristics in a military study or residential neighborhood-level characteristics in a general population survey—may be important for prediction of individual incident depression (51,52), and should be included as predictors in future studies, where sampling designs allow.

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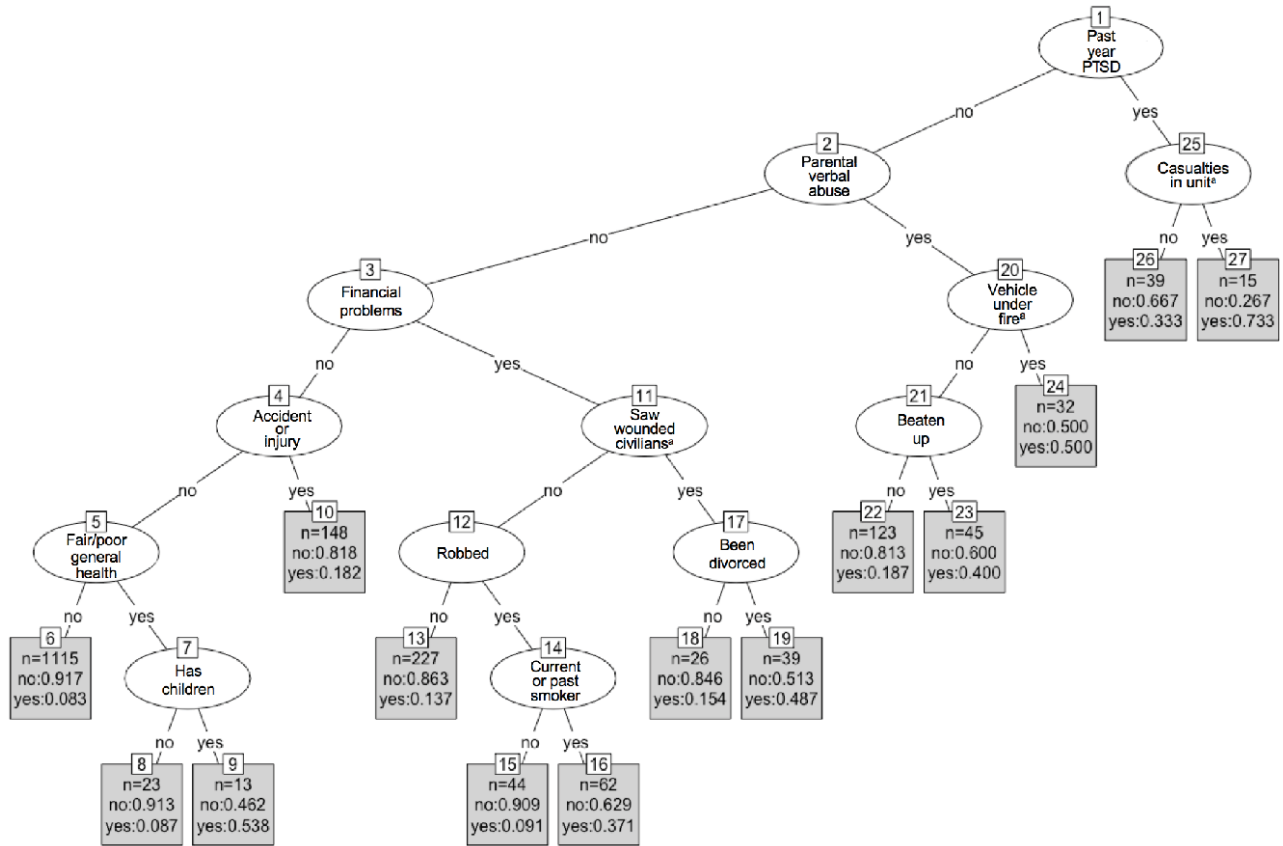
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Figure 1. Classification tree for incident depression during follow-up among men (n = 1,951).

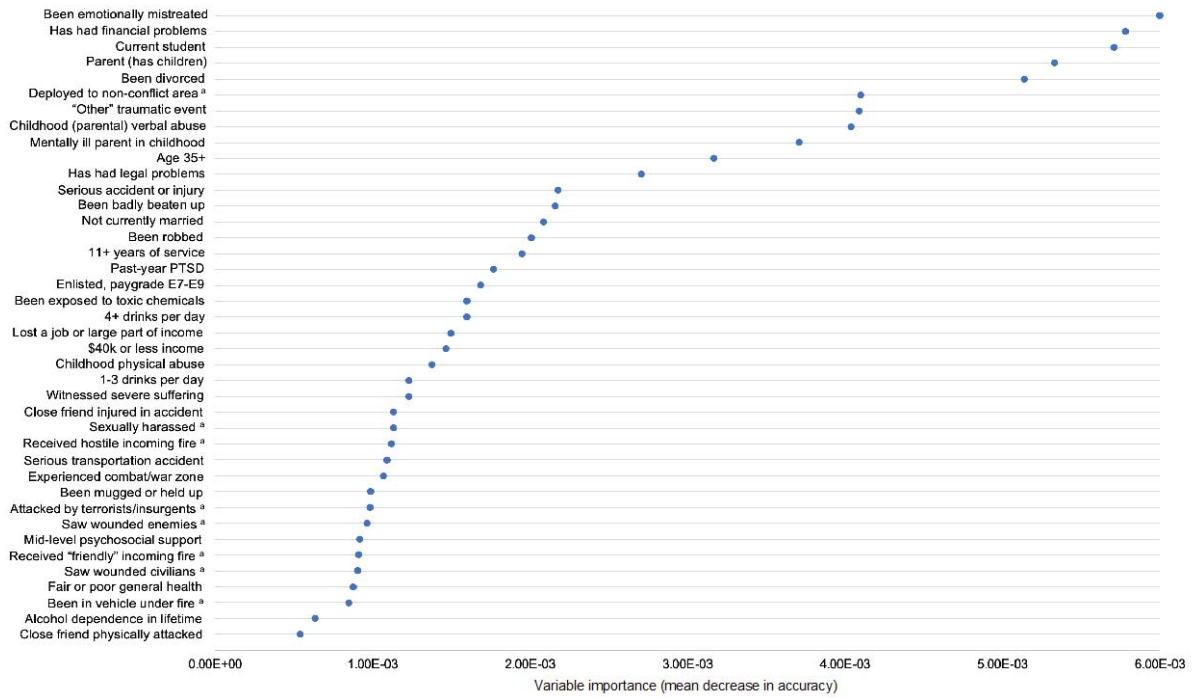


^a During most recent deployment.

PTSD = posttraumatic stress disorder.

In grey boxes: n = number of individuals with selected combination of predictors; “no” = proportion without incident depression in this group; “yes” = proportion with incident depression in this group.

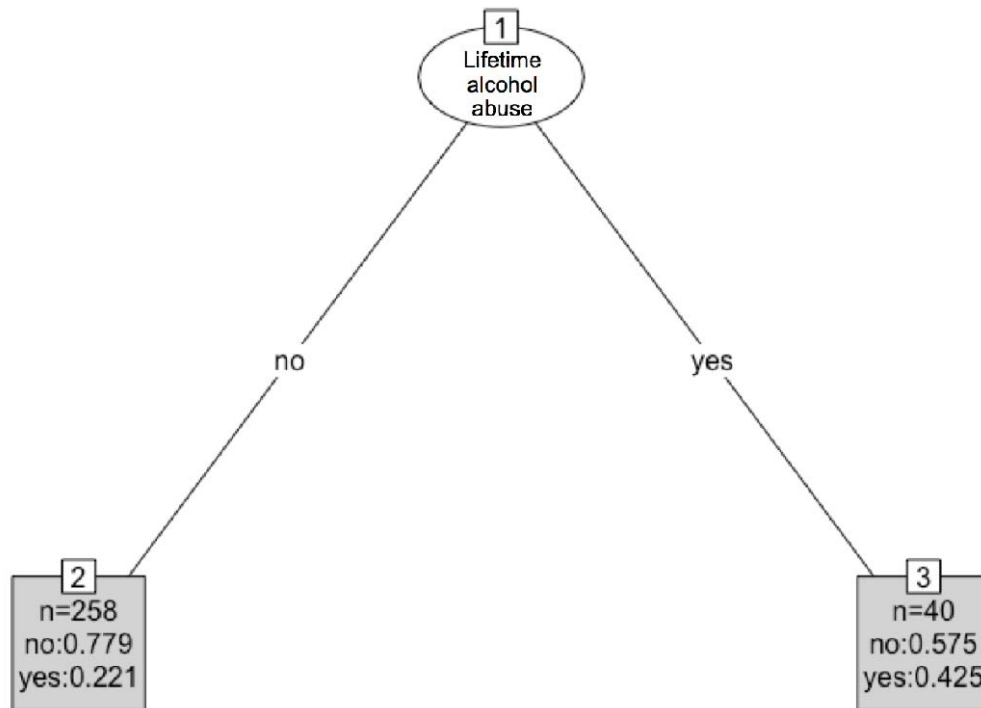
Figure 2. Variable importance plot from 10-fold cross-validated random forest for incident depression during follow-up, among men with no missing data (n = 1,409).



^a During most recent deployment.

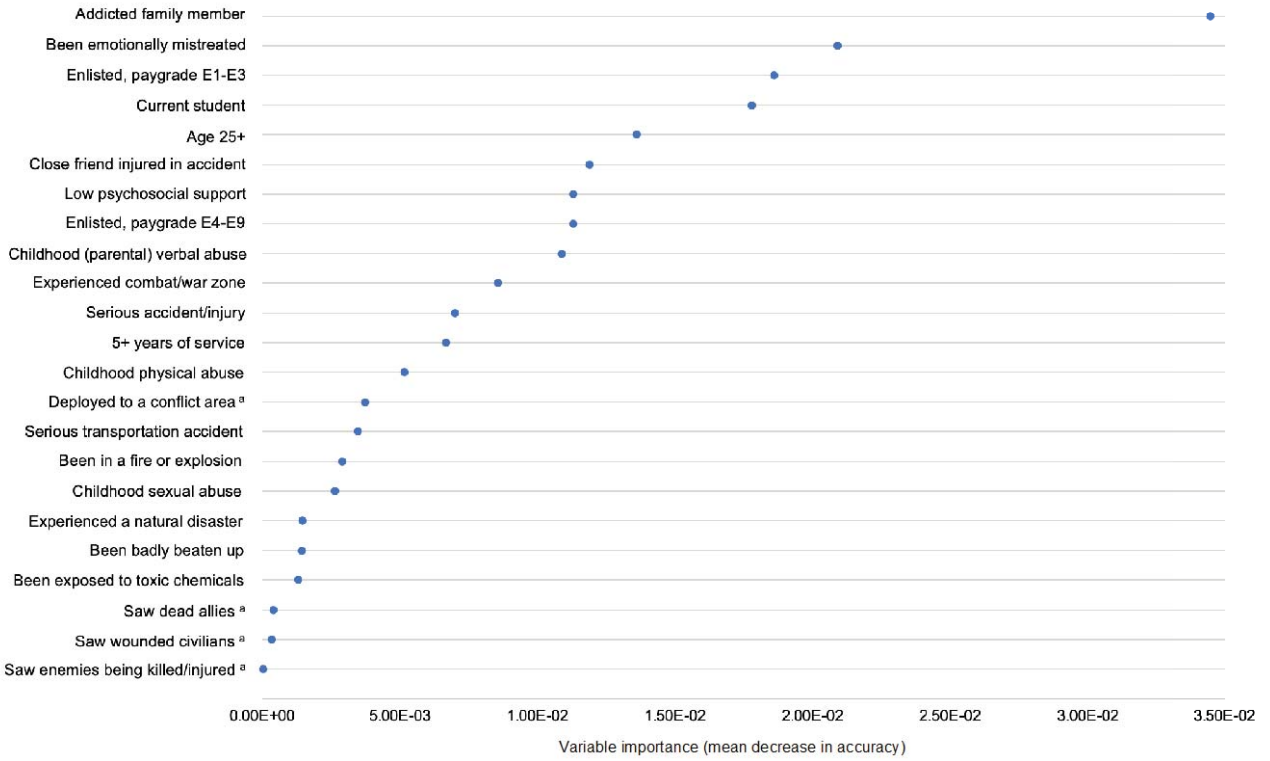
PTSD = posttraumatic stress disorder.

Figure 3. Classification tree for incident depression during follow-up among women (n = 298).



In grey boxes: n = number of individuals with selected combination of predictors; “no” = proportion without incident depression in this group; “yes” = proportion with incident depression in this group.

Figure 4. Variable importance plot from 10-fold cross-validated random forest for incident depression during follow-up, among women with no missing data (n = 251).



^a During most recent deployment.

Appendices:

Description of potential predictors in algorithms:

The potential predictors included the following general categories (detailed in eTable 1): demographics, military characteristics, health-related variables, potentially traumatic events from the respondent's most recent deployment as assessed by the Deployment Risk and Resilience Inventory (DRRI) (1), additional potentially traumatic events from the Life Events Checklist-Civilian Version (2) and the Detroit Area Survey of Trauma (3) (regardless of whether or not they occurred during deployment), individual traumatic events specific to childhood (four out of seven questions from the Adverse Childhood Experiences (ACEs) study (4)), individual stressful experiences that could occur at any point during the lifecourse (e.g., divorce, having serious financial trouble), responses to a psychosocial support and resources scale (six items adapted from the DRRI (1) which were summed and tertiled given the importance of relative differences in perceived social support among individuals in relation to mental health outcomes found in prior work using this cohort) (5), and the following Diagnostic and Statistical Manual for Mental Disorders, version IV (DSM-IV) mental disorders (DSM-5 criteria was not yet available at the time of the baseline interviews for the majority of cohorts): Generalized Anxiety Disorder (GAD, measured using the GAD-7 (6) with a cutoff score of 10 or a reported doctor's diagnosis, and with a timescale of any point in lifetime for women and any point in the past year for men given their larger sample), posttraumatic stress disorder (PTSD; measured using the PTSD Check List-Civilian version (7) or a reported doctor's diagnosis; lifetime for women and past-year for men), and both lifetime and past-year (tested separately, to avoid multicollinearity) alcohol abuse and alcohol dependence, included as separate alcohol use disorders according to the DSM-IV, assessed using the Mini-International Neuropsychiatric Interview (8).

All variables were operationalized as categorical variables. Most predictors were inherently categorical, (e.g., trauma experience, location of most recent deployment), but variables that were originally continuous, such as age or years of military service, were coded into categories based on their distribution (e.g., split into tertiles or quartiles), as listed in eTable 1. All variables were entered into the algorithms as binary dummy variables. (For a variable with n different categories, n-1 dummy variables were entered, with one category left out as a reference group.) The reason for this categorization and use of dummy variables is that if some predictor variables have more categories than others (including continuous variables which would be treated by classification trees and random forests as having as many categories as they do values), they would automatically be retained by the algorithms more often than those with fewer categories, due to greater variation in the outcome variable by category of the predictor, which obscures the true predictive ability of each variable (9).

Since these variables were from the baseline interviews, they primarily describe events throughout the lifecourse without reference to specific timing (designed in order to keep the baseline interview relatively short), but some critical constructs were asked with reference to specific timing, such as mental disorder symptoms. As recency is likely relevant for prediction, we included past-year baseline constructs where available and where sample size allowed (e.g., we included past-year PTSD for men, but only included more general lifetime PTSD for women (still measured at baseline), due to the small number of women with past-year disorder).

Description of tree classification, random forests, and cross-validation:

Classification trees

Classification trees (also known as “decision trees”) choose key predictive variables from the larger group of potential predictors using the probabilities of the known outcome, in order of magnitude of bivariate associations (10). Trees are constructed by making repetitive partitions of the data—called splits—by

such predictive variables, in order to form a hierarchical structure of nodes (variables or combinations of variables), which also serve as decision rules for the algorithm to predict the outcome (10–12). When creating these splits, the tree classification method uses “surrogate” splits for respondents who are missing data on predictors, based on variables other than the one used for the primary split (11). The ultimate goal of the classification tree is to end up with groups of observations that are relatively homogenous with respect to the outcome, at the terminal nodes (the end of the branches) (13).

Random forests and cross-validation

A Random forest can be conceptualized as an ensemble prediction method, consolidating across multiple decision trees, to avoid overfitting to any particular subsample. By combining different trees, the random forest capitalizes on the fact that individual trees can be unstable by themselves, but tend to produce the right prediction, on average (14). In random forests, the classification tree analysis (as described above) is generated on many different “training sets” or bootstrapped samples of the data (drawn with replacement), and tested on the observations not included in the training sample (also referred to as the “out of bag” sample) (13). Each tree within the random forest uses a different bootstrap sample and testing sample, and then the results are combined in order to produce an aggregated final result with less overall variance and better prediction than a single classification tree (9,15,16). As Bi and colleagues explain, when the trees are combined, they can “borrow strength” from one another, in order to achieve higher overall average predictive accuracy (12).

Cross-validation is performed to evaluate whether the random forest may be generalizable to an independent dataset (17). This is particularly important given that in general, a model trained and tested on the same sample tends to be overoptimistic (17,18). In cross-validation, the data are randomly split into ten subsets, or folds. A random forest is then generated—as described above—using nine of the folds and tested on the one remaining fold (which is considered an independent sample). This process is

repeated over all combinations of folds, while computing the prediction accuracy each time. Finally, these estimates are averaged together across all iterations (13).

We ran the 10-fold cross-validations on non-missing data only, given that the surrogate split method for missing data cannot be applied to cross-validation as it can in single classification trees. We first ran the cross-validation with all possible predictor variables included, and then removed a few variables that contributed negatively to prediction (i.e., had a negative variable importance, meaning the model was more accurate without them) one at a time, in a stepwise fashion, until there were either no remaining negative values or the performance metrics were maximized.

To address the class imbalance in our sample (more non-cases than cases), we instructed the algorithm to sample from 90% of true cases (the maximum number of cases that could be chosen for the training phase, given that 10% of the sample is always saved for the testing phase), and an equal number of non-cases, in order to have the same number of true cases and true non-cases when building each tree. If this parameter is not tuned, the algorithm tends to do a better job of predicting the dominant class (14,19), which in this sample is being a non-case. For the sample of men ($n = 1,409$ total non-missing observations), 171 cases and 171 non-cases were sampled at each node. For the women ($n = 251$ total non-missing observations), 54 cases and 54 non-cases were sampled at each node.

Important predictors from random forests are compared using the average improvement in classification accuracy that each variable achieved across all different trees in the forest (13). In order to determine importance, the prediction accuracy of each tree is computed with each variable of interest and then again with a version of that variable that is randomly permuted (i.e., removing any true predictive power of that variable), and the difference in accuracy between these two versions is averaged across every tree (15,20). This is repeated for each variable, and the average differences in accuracy for all variables across all trees and folds are then plotted in order of magnitude, or variable “importance” (see Figures 2 and 4). The values of variable importance are relative to each other; large breaks between variables in the plot represent large relative differences in prediction; the numbers are not meaningful in

isolation or when comparing across studies. In the variable importance plots in Figures 2 and 4, the predictors shown had a positive average decrease in classification accuracy (when removed from the trees) after the cross-validation.

Descriptive information about sample

As can be seen in eTable 1, about 41% of men were between the ages of 18 and 24; 29% were between the ages of 25 and 34; and 30% were older than 35. The women were younger overall, with 57.4% between the ages of 18 and 24. There was a very small proportion of individuals who identified as Hispanic overall, and only 6.8% of men were black while 4.4% identified as being of a race other than white or black. Slightly more than 37% of men had an annual income of \$40,000 or less, while almost half of women reported that same income category. eTable 1 lists the prevalence for all demographics and other characteristics of the sample by gender.

eTable 1. Prevalence of all predictors entered into algorithms, by category and stratified by gender.

	Men (n = 1,951)		Women (n = 298)	
	n	%	n	%
Demographics				
Age 25-34	566	29.01	127	42.62
Age 35+ (ref = age 18-25)	587	30.09		
Hispanic ethnicity	53	2.72	N <5	-
Black race	133	6.83	61	20.47
“Other” race (ref = white)	85	4.37		
\$40,000 or less annual income	711	37.32	138	48.76
\$41,000-\$80,000 annual income (ref = more than \$80,000)	742	38.95	90	31.80
Not currently married	1068	54.77	243	81.54
High school or less education	546	27.99	80	26.85
Some college education (ref = more than college education)	924	47.36	147	49.33
Parent or dependent of someone younger than 18	769	39.42	64	21.48
Current student	561	28.83	135	45.30
Military characteristics				
2-4 total years of service in U.S. military (for women)	-	-	107	35.91
5+ total years of service in U.S. military (for women; ref = 0-1 years)	-	-	105	35.23

3-10 total years of service in U.S. military (for men)	659	33.81	-	-
11+ total years of service in U.S. military (for men; ref = 2 or fewer years)	648	33.25	-	-
Enlisted, paygrade E1-E3	508	26.12	109	36.70
Enlisted, paygrade E4-E6	924	47.51	150	50.51
Enlisted, paygrade E7-E9 (ref = Officer or Warrant Officer)	204	10.49		
Deployed to an area of conflict during most recent deployment	515	26.51	36	12.08
Deployed to an area of NON-conflict during most recent deployment (reference = never deployed)	556	28.62	64	21.48
Health-related variables				
Fair or poor self-rated general health (ref = good or great) ^a	97	4.98	70	23.57
Current or former smoker (ref = never smoked)	1065	54.64	154	51.68
1-2 drinks per day on average days of drinking in past month (for women)	-	-	98	32.89
3+ drinks per day on average days of drinking in past month (for women; ref = no drinking in past month)	-	-	82	27.52
1-3 drinks per day on average days of drinking in past month (for men)	811	41.98	-	-
4+ drinks per day on average days of drinking in past month (for men; ref = no drinking in past month)	593	30.69	-	-
DSM-IV alcohol dependence in lifetime	372	19.07	24	8.05

DSM-IV alcohol abuse in lifetime	479	24.55	40	13.42
DSM-IV PTSD (in past-year for men; in lifetime for women)	54	2.77	23	7.72
DSM-IV GAD (in past-year for men; in lifetime for women)	24	1.27	25	8.71
Low tertile of psychosocial support score	655	33.83	103	34.68
Middle tertile of psychosocial support score (ref= top tertile)	736	38.02	81	27.27
Adverse childhood experiences (ACEs)				
Verbal abuse by a parent or other adult in home	158	9.34	30	11.81
Physical abuse by a parent or other adult in home	147	8.69	27	10.63
Sexual abuse by a parent or other adult in home	10	0.59	12	4.72
Parent or other adult in home was mentally ill	166	9.81	38	15.02
Stressful events in lifetime				
Lost a job or a large part of income	613	31.42	69	23.15
Been divorced	779	39.93	149	50.00
Been emotionally mistreated	404	20.73	94	31.54
Had legal problems (e.g., have been sued)	329	16.88	48	16.11
Been unemployed for 3 months or more	670	34.38	92	30.87
Had financial problems	519	26.62	64	21.55
Been robbed or had your house broken into	495	25.37	60	20.13
Had a family member with a serious drug or alcohol problem	166	9.81	165	55.37

Traumatic events in lifetime (in or outside of deployment)				
Experienced combat or a war zone	740	37.99	48	16.11
Sexually assaulted or raped	76	3.90	85	28.52
Been in a fire or explosion	536	27.52	27	9.06
Been shot or stabbed	138	7.08	N <5	-
Been kidnapped or tortured	5	0.26	N <5	-
Been mugged or held up	556	28.53	29	9.73
Been badly beaten up	272	13.95	15	5.03
Been in a serious transportation accident	486	24.91	67	22.48
Been in another type of serious accident or injury	305	15.67	29	9.73
Experienced a natural disaster in which you were hurt or property was damaged	284	14.56	37	12.42
Been diagnosed with a serious illness	123	6.31	19	6.40
Your child was diagnosed with a serious illness	43	2.21	N <5	-
Witnessed serious injury or death	769	39.52	39	13.09
Unexpectedly discovered a dead body	344	17.65	21	7.05
A close friend or family member was sexually assaulted	615	31.55	134	45.12
A close friend or family member was physically attacked	535	27.42	80	26.85
A close friend or family member was hurt in a serious transportation accident	996	51.10	143	47.99

A close friend or family member was hurt in another kind of accident	571	29.30	85	28.62
Experienced the sudden, unexpected death of a loved one	1228	63.04	191	64.09
Injured or killed someone else	180	9.34	N <5	-
Witnessed severe human suffering	566	29.13	44	14.77
Had a serious operation	245	12.57	34	11.45
Been exposed to toxic substances or chemicals	407	21.41	29	9.80
Had another type of traumatic event	372	19.09	56	18.79
Traumatic events that happened specifically during most recent deployment^b				
Encountered land/water mines or booby traps	362	18.69	17	5.70
Received hostile incoming fire from small arms, artillery, rockets, mortars, bombs, or IEDs	570	29.37	39	13.09
Received “friendly” incoming fire from small arms, artillery, rockets, mortars, bombs, or IEDs	123	6.38	10	3.39
Been in a vehicle under fire	331	17.05	13	4.36
Attacked by terrorists, insurgents, or civilians	465	24.16	27	9.12
Engaged in a battle with casualties in unit	195	10.05	19	6.38
Witnessed allies being seriously wounded or killed	235	12.09	8	2.68
Witnessed enemies being seriously wounded or killed	222	11.42	10	3.36
Fired weapon at enemy	231	11.89	N <5	-
Killed or think you killed someone in combat	129	6.83	N <5	-

Saw enemy soldiers after they had been severely wounded or disfigured	243	12.51	11	3.69
Saw bodies of dead enemies	230	11.86	7	2.36
Saw civilians after they had been severely wounded or disfigured	262	13.51	18	6.04
Saw bodies of dead civilians	200	10.31	16	5.37
Saw allies after they had been severely wounded or disfigured	294	15.13	13	4.36
Saw bodies of dead allies	189	9.72	7	2.35
Injured or wounded in combat	38	1.95	N <5	-
Sexually harassed (during most recent deployment)	173	8.88	50	16.84
Head injury (during most recent deployment)	43	2.22	N <5	-

^a Good, fair or poor health for women (vs. very good or excellent).

^b Respondents who had never been deployed at baseline have a 0 for these variables.

Ref = reference group when entered into algorithms.

PTSD = posttraumatic stress disorder.

GAD = generalized anxiety disorder.

IED = improvised explosive device.

Percentages calculated among non-missing values.

eTable 2. Mean decrease in accuracy of predictors from 10-fold cross-validated random forest among men with no missing data (n = 1,409).

Predictor	Mean decrease in accuracy
Been emotionally mistreated	6.00E-03
Has had financial problems	5.78E-03
Current student	5.71E-03
Parent (has children)	5.33E-03
Been divorced	5.14E-03
Deployed to an area of non-conflict ^a	4.10E-03
"Other" traumatic event	4.09E-03
Childhood (parental) verbal abuse	4.04E-03
Parent mentally ill in childhood	3.71E-03
Age 35+	3.17E-03
Has had legal problems	2.71E-03
Serious accident/injury (other)	2.18E-03
Been badly beaten up	2.16E-03
Not currently married	2.09E-03
Been robbed	2.01E-03
11+ years of service	1.95E-03
Past-year PTSD	1.77E-03
Enlisted, paygrade E7-E9	1.69E-03
Been exposed to toxic substances	1.60E-03
4+ drinks per day	1.60E-03

Lost a job or a large part of income	1.50E-03
\$40k or less income per year	1.47E-03
Childhood physical abuse	1.38E-03
1-3 drinks per day	1.23E-03
Witnessed severe human suffering (ever)	1.23E-03
Close friend injured in [other] accident	1.13E-03
Sexually harassed ^a	1.13E-03
Received hostile incoming fire ^a	1.12E-03
Serious transportation accident	1.09E-03
Experienced combat/war zone	1.07E-03
Been mugged or held up	9.89E-04
Attacked by terrorists, insurgents, or civilians ^a	9.84E-04
Saw wounded enemies ^a	9.65E-04
Mid-level psychosocial support	9.17E-04
Received "friendly" incoming fire ^a	9.11E-04
Saw wounded civilians ^a	9.04E-04
Fair or poor self-rated general health	8.78E-04
Been in a vehicle under fire ^a	8.48E-04
Alcohol dependence in lifetime	6.34E-04
Close friend physically attacked	5.40E-04
Experienced natural disaster	5.27E-04
Injured or killed someone else	5.14E-04
Saw dead civilians ^a	5.13E-04
Unexpectedly discovered dead body (ever)	5.07E-04
Head injury ^a	4.73E-04

Encountered land mines ^a	4.69E-04
Sexually assaulted or raped (ever)	4.06E-04
Enlisted, paygrade E1-E3	3.80E-04
Been shot or stabbed	3.75E-04
Low psychosocial support	3.72E-04
Age 25-34	3.72E-04
Enlisted, paygrade E4-E6	3.21E-04
Had a serious operation	3.14E-04
Some college education	2.86E-04
\$41k-80k income per year	2.66E-04
Saw dead enemies ^a	2.32E-04
“Other” race (not white, not black)	1.71E-04
Past-year GAD	1.30E-04
Child diagnosed with serious illness	1.13E-04
Hispanic	8.11E-05
Injured or wounded in combat ^a	7.76E-05
Saw enemies being killed/injured ^a	6.95E-05
Black race	5.59E-05
Diagnosed with serious illness	5.42E-05
Childhood sexual abuse	3.89E-05
Deployed to an area of conflict ^a	7.24E-06
Been kidnapped	-1.75E-06
Killed or think you killed someone in combat ^a	-3.06E-05
Close friend sexually assaulted	-5.78E-05
Current or former smoker	-1.17E-04

Been in a fire or explosion

-8.56E-04

^a During most recent deployment.

PTSD = posttraumatic stress disorder.

GAD = generalized anxiety disorder.

eTable 3. Mean decrease in accuracy of predictors from 10-fold cross-validated random forest among women with no missing data (n = 251).

Predictor	Mean decrease in accuracy
Addicted family member	3.45E-02
Been emotionally mistreated	2.09E-02
Enlisted, paygrade E1-E3	1.86E-02
Current student	1.78E-02
Age 25+	1.36E-02
Close friend injured in [other] accident	1.19E-02
Low psychosocial support	1.13E-02
Enlisted, paygrade E4-E9	1.13E-02
Childhood (parental) verbal abuse	1.09E-02
Experienced combat or a war zone	8.57E-03
Experienced a serious accident/injury (other than car accident)	7.01E-03
5+ years of service	6.66E-03
Childhood physical abuse	5.15E-03
Deployed to an area of conflict ^a	3.74E-03
Serious transportation accident	3.47E-03
Been in a fire or explosion	2.90E-03
Childhood sexual abuse	2.63E-03
Experienced a natural disaster	1.46E-03
Been badly beaten up	1.43E-03

Been exposed to toxic substances	1.30E-03
Saw dead allies ^a	3.94E-04
Saw wounded civilians ^a	3.31E-04
Saw enemies being killed/injured ^a	2.01E-05

^a During most recent deployment.

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Summary of Publications

1. Biehn, TL, Contractor, AA, Elhai, JD, Tamburrino, M, Fine, TH, Cohen, G, Shirley, E, Chan, PK, Liberzon, I, Calabrese, JR, Galea, S. Latent dimensions of posttraumatic stress disorder and their relations with alcohol use disorder. *Social Psychiatry and Psychiatric Epidemiology. Soc Psychiatry Psychiatr Epidemiol.* 2016 Mar;51(3):421-9. Epub 2015 Oct 31. PMID: 26520448

The objective of this study was to evaluate the relationship between factors of posttraumatic stress disorder (PTSD) and alcohol use disorder (AUD) using confirmatory factor analysis (CFA) in order to further our understanding of the substantial comorbidity between these two disorders. CFA was used to examine which factors of PTSD's dysphoria model were most related to AUD in a military sample. Ohio National Guard soldiers with a history of overseas deployment participated in the survey (n = 1215). Participants completed the PTSD Checklist and a 12-item survey from the National Survey on Drug Use used to diagnosis AUD. The results of the CFA indicated that a combined model of PTSD's four factors and a single AUD factor fit the data very well. Correlations between PTSD's factors and a latent AUD factor ranged from correlation coefficients of 0.258-0.285, with PTSD's dysphoria factor demonstrating the strongest correlation. However, Wald tests of parameter constraints revealed that AUD was not more correlated with PTSD's dysphoria than other PTSD factors. All four factors of PTSD's dysphoria model demonstrate comparable correlations with AUD. The role of dysphoria to the construct of PTSD is discussed.

2. Sampson L, Cohen GH, Calabrese JR, Fink DS, Tamburrino M, Liberzon I, Chan P, Galea S. Mental health over time in a military population: the impact of alcohol use disorder on trajectories of psychopathology after deployment *J Trauma Stress.* 2015 Dec;28(6):547-55. PMID: 26625353

To identify trajectories of posttraumatic stress (PTS) and depression symptoms after deployment and determine the effect of alcohol use disorder on these trajectories, PTS symptoms were modeled using the PTSD Checklist in 472 Ohio National Guard members, and depression symptoms were modeled using the 9-item Patient Health Questionnaire in 727 Ohio National Guard members. Forty-two percent of participants were resistant to PTS symptoms across all four years and 55.9% were resistant to depression symptoms. Nineteen percent and 42.2% of participants showed resilience (experiencing slightly elevated symptoms followed by a decline) to depression and PTS symptoms, respectively. Mild and chronic dysfunction constituted the smallest trajectory groups across disorders. Marital status, deployment to an area of conflict, and number of lifetime stressors were associated with membership into different latent groups for depression (beta estimates range: 0.69-1.37). Deployment to an area of conflict, number of lifetime potentially traumatic events and education predicted membership into different latent groups for PTS (beta estimate range: 0.83-3.17). Alcohol use disorder was associated with an increase in both symptom outcomes (beta estimate range: 0.20-9.45). These results suggest that alcohol use disorder may have contributed substantially to the burden of psychopathology in this population.

3. Fink DS, Gallaway MS, Tamburrino MB, Liberzon I, Chan P, Cohen GH, Sampson L, Shirley E, Goto T, D'Arcangelo N, Fine T, Reed PL, Calabrese JR, Galea S. Onset of alcohol

use disorders and comorbid psychiatric disorders in a military cohort: Are there critical periods for prevention of alcohol use disorders? *Prev Sci.* 2016 Apr;17(3):347-56. PMID: 26687202

Alcohol use disorders (AUD) are commonly comorbid with anxiety and mood disorders; however, a strategy for AUD prevention remains unclear in the presence of three competing etiological models that each recommends different high-risk groups. Therefore, the investigation of the three hypotheses in a characteristically unique cohort is critical to identifying pervasive characteristics of AUD that can inform a universal prevention strategy. The current study evaluated the temporality and onset of comorbid AUD and psychiatric disorders in a representative sample of 528 Ohio Army National Guard soldiers using structured clinical interviews from 2009 to 2012. We examined temporality both statistically and graphically to identify patterns that could inform prevention. General estimating equations with dichotomous predictor variables were used to estimate odds ratios between comorbid psychiatric disorders and AUDs. An annualized rate of 13.5 % persons per year was diagnosed with any AUD between 2010 and 2012. About an equal proportion of participants with comorbid psychiatric disorders and AUD initiated the psychiatric disorder prior to the AUD and half initiated the psychiatric disorder after the AUD. Regardless of onset, however, the majority (80 %) AUD initiated during a short interval between the ages of 16 and 23. Focused primary prevention during this narrow age range (16-23 years) may have the greatest potential to reduce population mental health burden of AUD, irrespective of the sequencing of comorbid psychiatric disorder.

4. Ganocy SJ, Goto T, Chan PK, Cohen GH, Sampson L, Galea S, Liberzon I, Fine T, Shirley E, Sizemore J, Calabrese JR, Tamburrino MB. Association of Spirituality with Mental Health Conditions in Ohio National Guard Soldiers. *J Nerv Ment Dis.* 2016 Jul;204(7):524-9. PMID: 27065107

Research exploring mental health in military populations is a relatively new field with limited published reports. This study used the Spiritual Well-Being Scale (SWBS) to examine the association of spiritual well-being with suicidal ideation/behavior, posttraumatic stress disorder (PTSD), and depression and alcohol use disorders in a randomized sample of Ohio Army National Guard soldiers. The participants were 418 soldiers, mostly white and male, with nearly three-quarters indicating they had been deployed at least once during their careers. Higher spirituality, especially in the existential well-being subscale, was associated with significantly less lifetime PTSD, depression, and alcohol use disorders and with less suicidal ideation over the past year. Future research in this area may benefit from a longitudinal design that can assess spirituality and mental health behaviors in addition to diagnoses at different time points, to begin to explore spirituality in a larger context.

5. Fink DS, Chen Q, Liu Y, Tamburrino MB, Liberzon I, Shirley E, Fine T, Cohen GH, Galea S, Calabrese JR. Incidence and Risk for Mood and Anxiety Disorders in a Representative Sample of Ohio Army National Guard Members. *Public Health Reports.* 2016 Jul-Aug; 131:614-22. PMID: PMC4937124

This study investigated the incidence of first-onset psychiatric disorders among Ohio Army National Guard members and the sociodemographic and military factors associated with

these incident disorders. We analyzed data on a representative sample of 528 Ohio Army National Guard members who were assessed in person annually for first-onset psychiatric disorders from 2008 through 2012 using structured clinical interviews. We used a multivariable discrete-time Cox proportional hazard model to determine risk factors of first-onset anxiety or mood disorders. The annualized incidence rate of any first-onset psychiatric disorder was 9.8 per 100 person-years at risk. Alcohol use disorder and major depressive disorder had the highest incidence rates among the unique disorders under study (5.0 and 4.2 per 100 person-years at risk, respectively). We found an association between respondents endorsing past-year deployment and a 29% increase in the risk of incident anxiety or mood disorder, whereas the past-year experience of any non-deployment traumatic event was associated with a 32% increase in risk of incident anxiety or mood disorder. Soldiers experience a substantial burden of first-onset alcohol use disorder and major depressive disorder annually; the experience of non-deployment-related traumatic events contributes substantially to increasing risk, suggesting that any effort aimed at mitigating mood and anxiety disorders in this population must consider the soldier's life experience and military experience.

6. Fink et al. Retrospective age-of-onset and projected lifetime prevalence of psychiatric disorders among U.S. Army National Guard soldiers. *J Affect Disord.* 2016 Sep 15; 202:171-177. PMID: 27262639

The study of military-related mental health has been disproportionately focused on current symptomology rather than potentially more informative life course mental health. Indeed, no study has assessed age-of-onset and projected lifetime prevalence of disorders among reservists. Age-of-onset and projected lifetime DSM-IV anxiety, mood, and substance use disorders were assessed in 671 Ohio Army National Guard soldiers aged 17–60 years. Between 2008 and 2012, face-to-face clinical assessments and surveys were conducted using the Structured Clinical Interview for DSM-IV and Clinician-Administered PTSD Scale. Lifetime prevalence of psychiatric disorders was 61%. Alcohol abuse/dependence (44%) and major depressive disorder (23%) were the most common disorders. The majority (64%) of participants reported disorders antedating enlistment. Median age-of-onset varied with anxiety disorders – particularly phobias and OCD – having the earliest (median=15 years) and mood disorders the latest median age-of-onset (median=21 years). Each psychiatric disorder exhibited a distinct age-of-onset pattern, such that phobias and OCD onset earliest, substance use disorders onset during a short interval from late-adolescence to early adulthood, and mood disorders onset the latest. Our finding that the majority of participants reported disorders antedating enlistment suggests that an assessment of lifetime psychopathology is essential to understanding the mental health burden of both current and former military personnel.

7. Byllesby BM, Elhai JD, Tamburrino M, Fine TH, Cohen G, Sampson L, Shirley E, Chan PK, Liberzon I, Galea S, Calabrese JR. General distress is more important than PTSD's cognition and mood alterations factor in accounting for PTSD and depression's comorbidity. *J Affect Disord.* 2017 Mar 15;211:118-123. PMID: 28110158

Confirmatory factor analysis was used to test a bifactor model of PTSD symptoms, testing relations between PTSD's factors and a latent depressive factor. After partitioning out the

common variance into the bifactor, we found that in contrast to other PTSD factors, PTSD's NACM factor was not significantly more related to depression. Instead, only the general bifactor predicted depressive symptoms. The present study suggests that the high rate of comorbidity between posttraumatic stress disorder (PTSD) and major depressive disorder is more related to underlying general distress or negative affectivity than the symptom categories of the PTSD diagnostic criteria.

8. Cohen GH, Fink DS, Sampson L, Tamburrino M, Liberzon I, Calabrese JR, Galea S. Coincident alcohol dependence and depression increases risk of suicidal ideation among Army National Guard soldiers. *Ann Epidemiol.* 2017 Mar;27(3):157-163. PMID: 28139369

Suicide rates among military service members have risen dramatically, while drivers remain poorly understood. We aimed to examine the relationship between coincident alcohol dependence and depression in shaping subsequent risk of suicidal ideation among National Guard forces. We performed a longitudinal analysis using a randomly selected, population-based sample of Ohio Army National Guard soldiers. Telephone-based surveys of 1582 soldiers who participated in both wave 1 (data collected 2008–2009) and wave 2 (data collected 2009–2010) were analyzed. Incident suicidal ideation was present among 2.47% of soldiers at follow-up. Odds ratios (ORs) for suicidal ideation among those with vs. without alcohol dependence were similar among non-depressed [OR=3.85 (95% Confidence Intervals (CI) = 1.18–12.52)] and depressed individuals [OR = 3.13 (95% CI = 0.88–11.14)]; a logistic model cross-product term confirmed an absence of multiplicative interaction (beta coefficient=-0.21, p=0.82). In contrast, the risk differences (RD) for suicidal ideation among those with vs. without alcohol dependence diverged for those without depression [RD = 0.04 (95% CI = 0.02–0.07)] compared to those with depression [RD 0.11(95% CI=0.06–0.18)]; strong evidence of additive interaction was observed - [Relative Excess Risk of Interaction (RERI) = 5.978(95% CI=0.364–11.591)]. We found that alcohol dependence and depression worked together to shape risk for incident suicidal ideation among Army National Guard service members. Because coincident alcohol dependence and depression is relatively rare, a high-risk prevention approach is recommended. Population-based screening for suicidality among patients with alcohol dependence, depression, and particularly those with both conditions is warranted in military populations.

9. Fink DS, Keyes KM, Calabrese JR, Liberzon I, Tamburrino MB, Cohen GH, Sampson L, Galea S. Deployment and Alcohol Use in a Military Cohort: Use of Combined Methods to Account for Exposure-Related Covariates and Heterogeneous Response to Exposure. *Am J Epidemiol.* 2017 Aug 15;186(4):411-419. PMID: PMC5860008

Studies have shown that combat-area deployment is associated with increases in alcohol use; however, studying the influence of deployment on alcohol use faces 2 complications. First, the military considers a confluence of factors before determining whether to deploy a service member, creating a nonignorable exposure and unbalanced comparison groups that inevitably complicate inference about the role of deployment itself. Second, regression analysis assumes that a single effect estimate can approximate the population's change in postdeployment alcohol use, which ignores previous studies that have documented that respondents tend to exhibit heterogeneous postdeployment drinking behaviors. Therefore, we

used propensity score matching to balance baseline covariates for the 2 comparison groups (deployed and nondeployed), followed by a variable-oriented difference-in-differences approach to account for the confounding and a person-oriented approach using a latent growth mixture model to account for the heterogeneous response to deployment in this prospective cohort study of the US Army National Guard (2009-2014). We observed a nonsignificant increase in estimated monthly drinks in the first year after deployment that regressed to predeployment drinking levels 2 years after deployment. We found a 4-class model that fit these data best, suggesting that common regression analyses likely conceal substantial interindividual heterogeneity in postdeployment alcohol-use behaviors.

10. Fink DS, Gradus JL, Keyes KM, Calabrese JR, Liberzon I, Tamburrino MB, Cohen GH, Sampson L, Galea S. Subthreshold PTSD and PTSD in a prospective-longitudinal cohort of military personnel: Potential targets for preventive interventions. *Depress Anxiety*. 2018 Nov; 35(11):1048-1055. PMID: 30099820

Prevention of PTSD requires identification of subpopulations contributing most to the population burden of PTSD. This study examines the relative contribution of subthreshold PTSD and probable PTSD on future PTSD in a representative military cohort. We analyze data on 3,457 U.S. National Guard members from the state of Ohio, assessed by telephone annually from 2008 to 2014. At each wave, participants were classified into one of three groups based on the PTSD Checklist: probable PTSD (DSM-IV-TR criteria), subthreshold PTSD (Criterion A1, at least one symptom in each cluster, symptom lasting longer than 30 days, and functional impairment), and no PTSD. We calculated the exposure rate, risk ratio (RR), and population attributable fraction (PAF) to determine the burden of future probable PTSD attributable to subthreshold PTSD compared to probable PTSD. The annualized prevalence of subthreshold PTSD and probable PTSD was respectively 11.9 and 5.0%. The RR for probable PTSD was twice as great among respondents with probable PTSD the prior interview than that of those with subthreshold PTSD (7.0 vs. 3.4); however, the PAF was considerably greater in participants with subthreshold PTSD the prior interview (PAF = 35%; 95% confidence interval (CI) = 26.0-42.9%) than in those with probable PTSD (PAF = 28.0%; 95% CI = 21.8-33.8%). Results were robust to changes in subthreshold PTSD definition. In conclusion, subthreshold PTSD accounted for a substantial proportion of this population's future PTSD burden. Population-based preventive interventions, compared to an approach focused exclusively on cases of diagnosable PTSD, is likely to affect the greatest reduction in this population's future PTSD burden.

11. Bergman HE, Chan P, Cooper AA, Shirley E, Goto T, Fine T, Cohen GH, Sampson L, Ganocy S, Tamburrino M, Liberzon I, Calabrese J, Galea S, Feeny NC. Examining the impact of PTSD symptomatology on cigarette smoking among Ohio Army National Guard soldiers. *Military Behavioral Health*. 2019;7(1): 46-56.

Evidence suggests that posttraumatic stress disorder (PTSD) increases risk for cigarette smoking in civilian and military populations. There is limited evidence about this relationship among National Guard, a group that may be at higher risk of behavioral health concerns compared to Active Component. The current study used cross-sectional data from a clinical subsample of soldiers (N = 455) from the Ohio Army National Guard Mental Health

Initiative. Soldiers completed self-report and clinician-rated measures, including demographics, smoking status and intensity, and PTSD. Logistic and multinomial regression methods were used to explore the association between PTSD symptomatology and smoking. Higher PTSD symptom severity was modestly associated with an increased likelihood of being a current ($\beta = 0.02$, $p = 0.049$, $OR = 1.02$) and heavy smoker ($\beta = 0.04$, $p = 0.003$, $OR = 1.04$). Reporting more dysphoria or hyperarousal symptoms was modestly associated with an increased likelihood of being a heavy smoker ($\beta = 0.04$, $p = 0.001$, $OR = 1.05$; $\beta = 0.03$, $p = 0.03$, $OR = 1.03$). Those with greater PTSD severity are more likely to smoke and have more difficulty quitting; this may have implications for efforts to mitigate the burden of PTSD and smoking among National Guard personnel.

12. Gallaway MS, Fink DS, Sampson L, Cohen GH, Tamburrino M, Liberzon I, Calabrese J, Galea S. Prevalence and covariates of problematic gambling among a US military cohort. *Addict Behav.* 2019 Aug; 95:166-171. PMID: PMC6574081

The availability of and participation in gambling has increased substantially the past several decades, however studies of military members' gambling behaviors are limited. The present study aimed to investigate potential problematic gambling and its association with demographics and behavioral characteristics in a US military cohort. We analyzed cohort data from a telephone survey during 2015-2016 of 1553 Ohio Army National Guard members. We assessed potential problematic gambling by using the 3-item National Opinion Research Center Diagnostic Screen-Loss of Control, Lying, and Preoccupation Screen (NODS-CLiP). Potential correlates examined were demographics, depression, suicidal ideation, smoking status, alcohol use, legal and financial problems, perceived general health status, pain, and impulsivity. Results indicated past-year frequent gambling (at least once per week) and lifetime potential problematic gambling was reported by 13% and 8% of respondents, respectively. Problematic gambling and past-year gambling behaviors were associated in a dose-response relationship from 18% among soldiers gambling once per week to 44% among those gambling 4 or more times per week. Correlates of screening positive for potential problematic gambling included the following: being male, currently unmarried, having left the Guard or retired, minor depression, alcohol dependence, legal problems, and increased pain. Given the higher prevalence of frequent gambling in this military cohort (8%), nearly twice the US prevalence (5%), and the association with negative psychological and behavioral outcomes, routine screening of gambling frequency and problem gambling may be needed to ensure military and veteran populations live the healthiest lives possible.

13. Sampson L, Jiang T, Gradus JL, Cabral HJ, Rosellini AJ, Calabrese JR, Cohen GH, Fink DS, King AP, Liberzon I, Galea S. A machine learning approach to predicting new-onset depression in a military population. *Psychiatric Research and Clinical Practice*. In press.

This study found that stressful and traumatic events—including those that occurred in childhood—were predictive of first-time depression in adulthood among United States military personnel. Additionally, demographics like being a parent or student—and military characteristics including paygrade and deployment location—were predictive of first-time depression. We conclude that it may be important to consider characteristics and events both

in and outside of deployment—not just those that occur during deployment—when studying mental health among military personnel.

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INTRODUCTION

Altered glucocorticoid receptor function has been reported in PTSD. FK506 binding protein-5 (FKBP5) regulates glucocorticoid receptor sensitivity, and FKBP5 gene single nucleotide polymorphism (SNP) at rs1360780 is linked to severity of PTSD. The same FKBP5 SNP (T-carriers) has been linked to smaller anterior cingulate cortex (ACC) volumes. Smaller ACC volume has also been reported in some PTSD patients and might be a contributing factor for PTSD symptom development in T-carriers. To test the possible link between the T allele, ACC volumes and PTSD, we compared the ACC volume among both T-carriers and non-T-carriers with and without PTSD.

METHOD

Participants and Procedures

Male veterans and healthy civilians were participants in two PTSD MRI studies at the University of Toledo and the University of Michigan.

PTSD Assessment

Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995) was used to diagnose current and lifetime full or partial PTSD. Full PTSD met criteria of at least 1 reexperiencing symptom, 3 avoidance/numbing symptoms, and 2 hyperarousal symptoms. Partial PTSD met criteria of at least 1 reexperiencing symptom, and either 3 avoidance/numbing symptoms or 2 hyperarousal symptoms, but not both.

Genetic Analysis

Genotyping was performed using a custom microarray (Infinium; Illumina).

Brain Structural Imaging Processing

Structural MRI images were processed using FreeSurfer, measuring the rostral and caudal ACC (rACC and cACC) volumes bilaterally.

Data Analyses

All variables were normally distributed according to benchmarks of skewness < 2 and kurtosis < 7. A One-way Analysis of Covariance (ANCOVA) using IBM SPSS v.21 was utilized to examine statistically significant differences between veterans with or without a PTSD diagnosis, and veterans that were T-carriers and non-T-carriers of the FKBP5 gene. The groups served as the independent variable (PTSD and genotype), and the rACC served as the dependent variable. Additionally, in these analyses we controlled for intracranial volume (ICV). All assumptions for ANCOVA were tested and appeared to have been met for these analyses.

RESULTS

Demographics and PTSD symptoms

Table 1 Demographics

	PTSD	non-PTSD
N of subjects	24	42
veteran	24	27
civilian	0	15
T-carrier	13	22
non-T-carrier	11	20
age	34±12	30±8
CAPS score	69±19.92	8.78±8.2

Our sample consisted of 66 male subjects that ranged in age from 20 to 63 years (M = 31.17, SD = 9.73). CAPS total scores ranged from 0 to 111, with an average score of 37.12 (SD = 33.75). Approximately 36.4% (n = 24) of the sample met criteria for PTSD, and 53% (n = 35) were T-carriers of the FKBP5 gene.

PTSD and non-PTSD groups are not different in age (p>0.05).

Effects of genetics and PTSD diagnosis on the right rACC volume

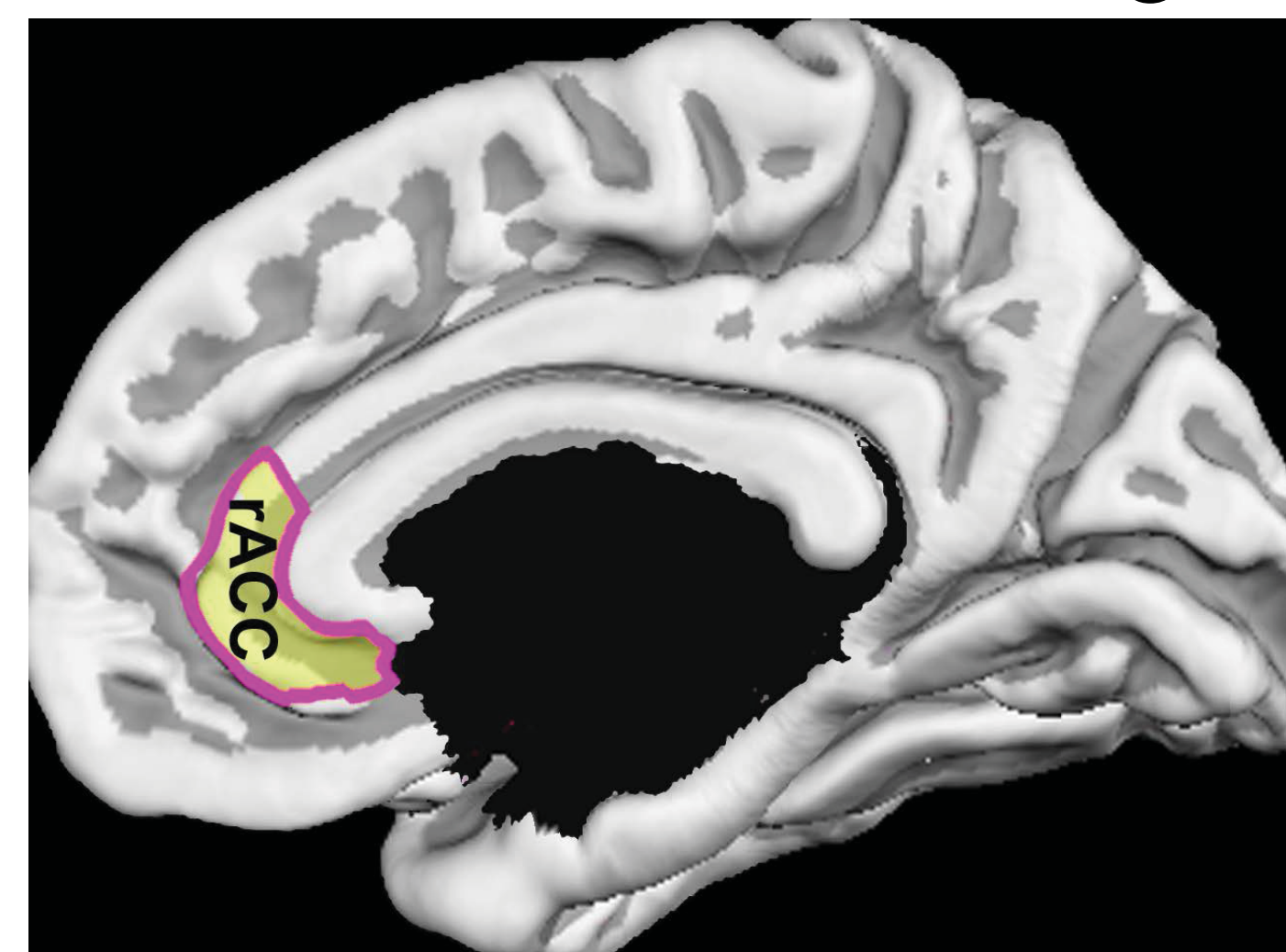


Table 2 right rACC volume influenced by PTSD and genotype

	F	df	p	η_p^2
PTSD	0.151	1, 61	0.7	0.002
genotype	0.865	1, 61	0.356	0.014
PTSD by genotype interaction	6.494	1, 61	0.013	0.096

There were no significant main effects after controlling for ICV for PTSD diagnosis (Yes/No) or genotype (Yes/No). There was a significant interaction after controlling for ICV for the PTSD diagnosis by genotype on the right rACC volume.

PTSD group differences in T-Carriers and non-T-carriers

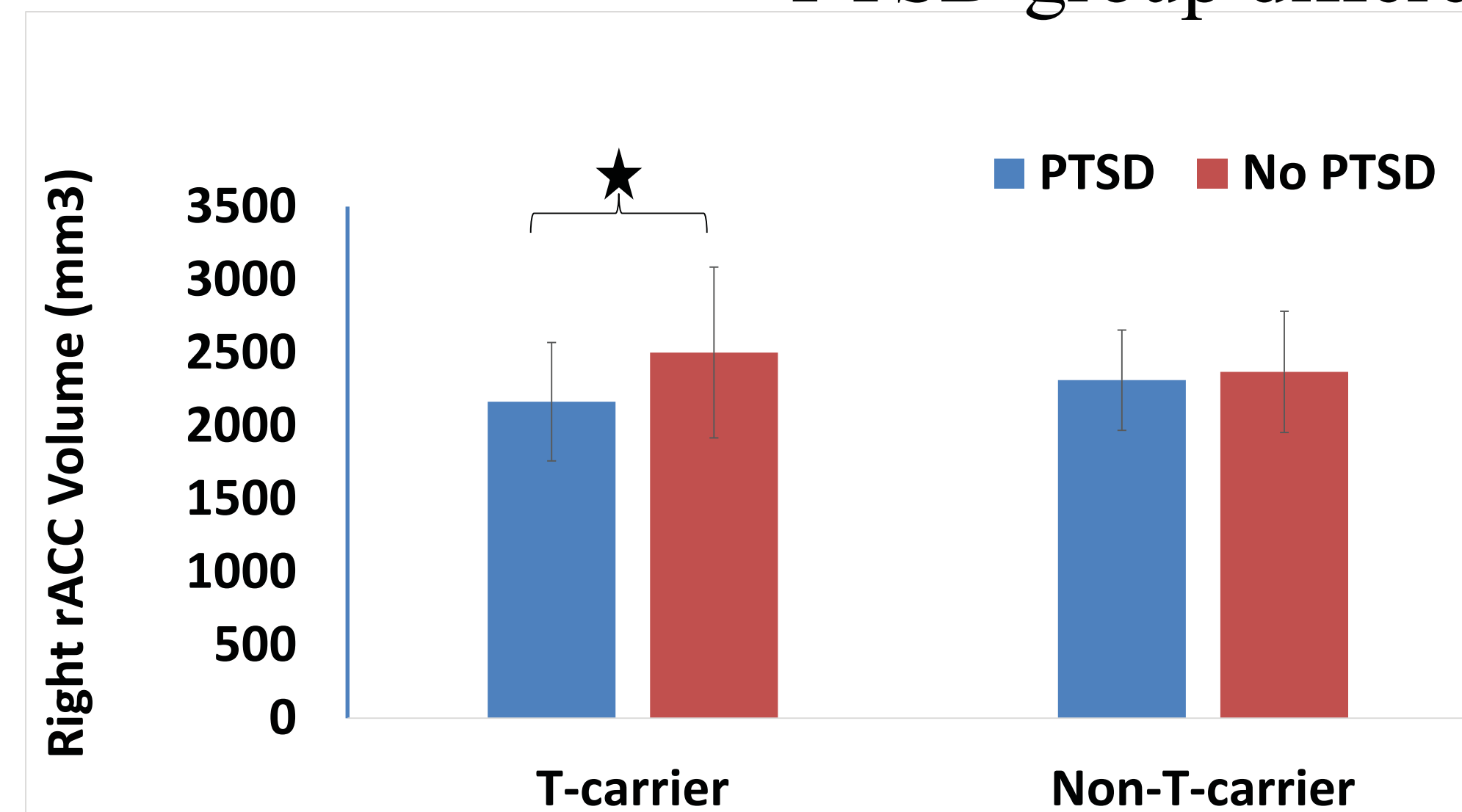


Table 3. group differences in right rACC volumes (mm³)

	PTSD	non-PTSD	p
T-carrier	2166.31±405.05	2502.23±583.90	0.033
Non-T-carrier	2313.36 + 342.89	2369.85±414.12	0.158

Simple-effects post-hoc analyses revealed that T-carrier veterans with PTSD have smaller rACC than T-carriers without PTSD, but non-T-carrier veterans with PTSD were not significantly different from non-T-carriers without PTSD.

★ indicates p<0.05

CONCLUSION

1. PTSD diagnosis alone, and the FKBP5 rs1360780 status alone did not affect right rACC volumes in trauma survivors.
2. Significant interaction between PTSD diagnosis and FKBP5 rs1360780 genotype was found, such that right rACC volume reduction was associated with PTSD development in FKBP5 rs1360780 T-carriers, but not in non-T-carriers.

ACKNOWLEDGEMENT

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Introduction

Our ability to reduce alcohol misuse among service members is predicated on identifying its causes. Although a large body of literature has shown that combat area deployment is associated with increases in alcohol use, do we believe the evidence?

Studying the causal effects of deployment on post-deployment health behaviors brings in two complications:

1. Deployment is a non-ignorable exposure: The military considers a confluence of factors before determining whether to deploy a service member, creating a *nonignorable exposure* and *unbalanced comparison group* that will inevitably complicate inferences about the role of deployment itself

2. Heterogeneous response to deployment: Previous studies have shown that military personnel exposed to deployment exhibit *heterogeneous post-deployment drinking behaviors*. Thus, describing an entire population (i.e., deployed personnel) using a single effect estimate is likely to conceal a heterogeneous population comprised of homogenous subgroups.

To address these complications:

1. Deployment is a non-ignorable exposure:

- We estimated the average treatment effect on the treated (ATET) using a combined approach comprised of propensity score matching to balance baseline covariates for the two groups (deployed and non-deployed), followed by a variable-oriented difference-in-differences analysis to account for unknown factors

2. Heterogeneous response to deployment:

- We employed a person-oriented approach to account for heterogeneous response to deployment

Methods

Study population

We analyzed longitudinal data from a representative sample of Ohio Army National Guard soldiers (N=3194). Data were collected annually from 2009 and 2014.

Inclusion criteria: baseline interview *and* 2 additional interviews

- 65% of deployers (203 of 314 persons)
- 44% of non-deployers (2646 of 6031 persons)

Measures

Exposure: Past-year deployment

- Respondents reporting a deployment to either Iraq or Afghanistan since their last interview

Outcome: Past-month alcohol use (Quantity-Frequency Index)

- Past month alcohol use was the product of 2 questions that asked respondents to report “how many days did you drink” and “on the(se) days...how many drinks did you have each day”.

Statistical analysis

1. Deployment is a non-ignorable exposure

- Propensity score estimation and matching to address the deployment variable as an exposure with non-ignorable assignment
- Difference-in-differences approach to estimate the ATET

2. Heterogeneous response to deployment

- LGMM approach to investigate interindividual differences in alcohol use behaviors over time

Results

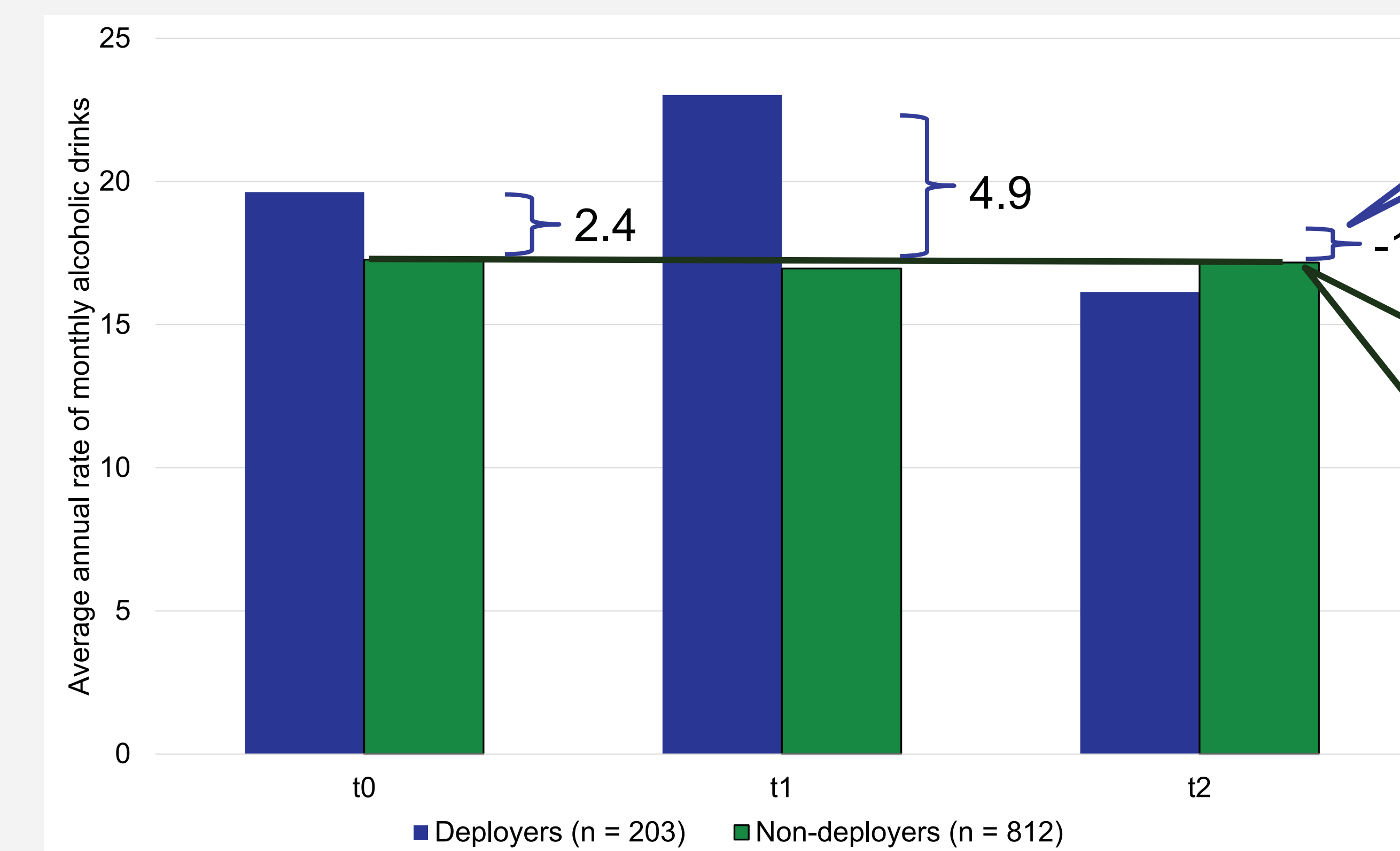
1. Propensity score estimation and matching to address the deployment variable as an exposure with non-ignorable assignment

Table 1. Descriptive statistics for key variables in propensity score model: Deployed and non-deployed groups

Characteristic	Deployers (n=203)		Non-deployers (n=812)		Effect sizes Std. Mean Diff.
	Mean (SD)	No. %	Mean (SD)	No. %	
Age, years	31.0 (9.1)		31.5 (9.5)		-0.04
Male		189 93.1		750 92.4	0.03
Marital status: Never married		73 36.0		305 37.6	-0.03
Marital status: Married		113 55.7		450 55.4	0.00
Marital status: Previously married		17 8.4		57 7.0	0.05
Parent or primary caregiver		89 43.8		371 45.7	-0.04
Education: Some college+		159 78.3		669 82.4	-0.10
Income: \$ 40 000+		135 66.5		555 68.5	-0.01
Currently employed		167 82.3		685 84.4	-0.06
Lifetime deployments: 0		81 39.9		326 40.2	-0.01
Lifetime deployments: 1		53 26.1		217 26.7	-0.01
Lifetime deployments: 2+		69 34.0		269 33.1	0.02
Time since last deployment, days	1485.7 (1028.9)		1607.8 (1230.4)		0.01
Time in service, years	10.2 (8.4)		11.1 (8.7)		-0.06
PTSD ^a		29 14.3		99 12.2	0.06
Depression ^a		3 5.9		12 0.9	0.05
Current alcohol dependence ^b		31 15.1		112 13.8	0.04
Current alcohol abuse ^c		59 29.1		201 24.8	0.08

A standardized mean difference after matching >0.2 indicates exposure groups were balanced on the measure confounders after matching

Figure 1. Change in the annual average rate of monthly drinks by deployment status. Estimates result from difference-in-differences regression of the annual rate of monthly drinks among deployed and non-deployed service members.



Annual average monthly drinks remained consistent among non-deployers

Compared to their matched non-deployers, deployers reported a higher mean number of monthly drinks at pre-deployment (t0) and first post-deployment wave (t1), but not the second post-deployment wave (t2)

2. Heterogeneous response to deployment

Table 2. Fit indices of past-month alcohol use trajectories

Profile	AIC ^b	E
1 Profile	9979.208	1
2 Profiles	9857.145	9
3 Profiles	9805.043	9
4 Profiles	9625.317	9
5 Profiles	9595.665	9
6 Profiles	9540.437	9

Abbreviations: AIC, akaike information criterion; aLRT, adjusted Lo Mendelkron test.
^a Slope and quadratic 0 variance; ^b Lower is better

Figure 2. Past-month alcohol use trajectories

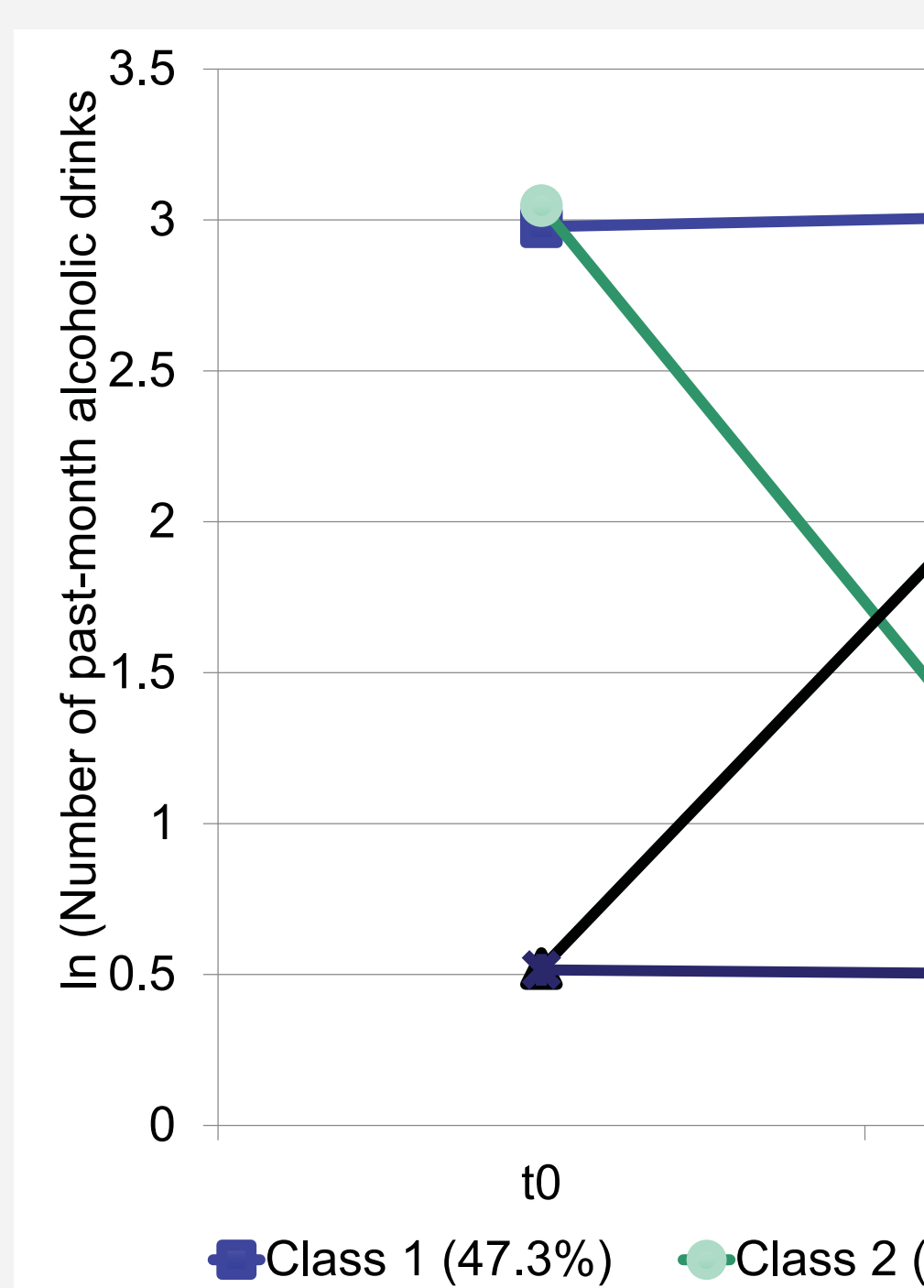


Table 3. Trajectory of estimate

Trajectory	N
1. High-stable	1
2. High-decreasing	1
3. Low-increasing	1
4. Low-stable	1

Conclusions

1. Deployment is a non-ignorable exposure:

- Using a combined analytical approach that both balanced baseline covariates (propensity score matching) and adjusted for unknown confounders (difference-in-differences analysis), we found insufficient evidence of a significant effect of combat area deployment on monthly alcohol use; however, a significant, effect on the rate of change in alcohol use one year after deployment relative to non-deployers. This is the first study to regress to the mean in the period between 1-year and 2-years post-deployment.

2. Heterogeneous response to deployment

- We found a 4 class solution fit these data best. This finding exhibits that estimating the average change in alcohol use following deployment reflects a mixture of multiple trajectories. Because we observed heterogeneity in alcohol use trajectories among both groups, it is important to consider individual differences in alcohol use behaviors over time.

Acknowledgments

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INTRODUCTION

Emerging literature suggests that religiosity/spirituality may be associated with positive mental health outcomes in military personnel. Religiosity generally refers to one's practice of an institutionalized religion, such as attending church or temple services, whereas spirituality is much more broadly defined to include existential qualities such as self-awareness and a sense of meaning or purpose in life (Hufford et al, 2010). Spiritual fitness has recently been added to the Total Force Fitness initiative of the Department of Defense to promote the health and resiliency of U.S. troops (DOD Task Force Final Report, 2010).

Research in spirituality/religiosity and mental health in military populations is a relatively new field with limited investigations. However, a number of studies have reported associations between spirituality and mental conditions of depression, posttraumatic stress disorder (PTSD), suicide risk, and alcohol use disorders. Berg (2011) studied Vietnam combat veterans and found that both depression and PTSD were associated with spiritual distress. Chang's group (2003) reported that attending religious services was protective in mitigating against depression in a group of male veterans with a history of sexual assault. In another study, spiritual well-being similarly showed a protective effect for both genders among homeless veterans with a history of childhood abuse and combat experience (Benda 2004).

The aim of the current study was to explore whether spiritual well-being in a National Guard sample would be associated with better mental health outcomes; the reserve population has been relatively understudied regarding spirituality/religiosity.

METHODS

A population-based sample of 418 Ohio Army National Guard (OHARNG) soldiers participated in a clinician-based in-person interview as a subset of a larger sample of soldiers interviewed through a telephone survey. Among the assessments administered to the subjects were a 20 item Spirituality Well-Being Survey (SWBS), a 15-item Columbia Suicide Severity Rating Scale (C-SSRS), the Structured Clinical Interview for DSM-IV-TR (SCID) Axis I Disorders (non-patient version), and the Clinician-Administered PTSD Scale (CAPS) for DSM-IV. On the SWBS the Religious Well-Being (RWB) score is based on the sum of responses to the odd-numbered questions, the Existential Well-Being (EWB) score based on the sum of responses to the even-numbered questions. The overall Spiritual Well-Being (SWB) score is defined as the sum of the Religious and Existential scores.

Both suicidal ideation and suicidal behavior are determined as dichotomous responses on the C-SSRS. Assessment for lifetime depression and PTSD employed the SCID and CAPS. To examine the association of spiritual well-being with suicidal ideation/ behavior, PTSD, and depression while adjusting for other covariates, logistic regression models were employed. The common covariates were age, gender, race, deployment status. Age and SWBS scores were treated as continuous while gender, race and lifetime diagnoses were categorical. Separate logistic regression models were run incorporating overall spiritual, existential or religious well-being scores individually along with the common covariates as predictors of either suicidal ideation or behavior, lifetime diagnoses of PTSD and Depression. Statistical significance was taken to be 0.05. The full regression models are presented in Tables 2 – 3.

RESULTS

- Overall spiritual well-being and existential well-being were significantly associated with past year suicidal ideation (Table 2).
- None of the spirituality scores were related to lifetime suicidal behavior. White soldiers were associated with decreased risk (59%) in both the overall SWB and RWB models.
- Higher overall spiritual well-being and existential well-being were associated with less lifetime PTSD (Table 3).
- No statistically significant relationship between religious well-being and PTSD.
- Overall spiritual well-being and religious well-being were not significantly associated with less lifetime depression (Table 3). There was a relationship between age and less lifetime depression in the overall spiritual well-being model. Decreased risk of lifetime depression was statistically significant in the EWB. Male soldiers had significantly decreased risk of lifetime depression in all three models; SWB, RWB and EWB.

Table 1. Demographics

	N = 418	n	%
Gender	Male	368	88.0
	Female	50	12.0
Race	White	373	89.2
	Black	28	6.7
	Other	17	4.1
Age	17 – 24	125	29.9
	25 – 34	154	36.8
	35 – 44	90	21.5
	45+	49	11.7
Marital Status	Married	222	53.1
	Divorced/Separated/Widowed	47	11.2
	Single	146	34.9

Spirituality Well-Being Survey (SWBS)	
1.	I don't find much satisfaction in private prayer with a Higher Power.
2.	I don't know who I am, where I came from, or where I'm going.
3.	I believe that a Higher Power loves me and cares about me.
4.	I feel that life is a positive experience.
5.	I believe that a Higher Power is impersonal and not interested in my daily situations.
6.	I feel unsettled about my future.
7.	I have a personally meaningful relationship with a Higher Power.
8.	I feel very fulfilled and satisfied with life.
9.	I don't get much personal strength and support from a Higher Power.
10.	I feel a sense of well-being about the direction my life is headed in.
11.	I believe that a Higher Power is concerned about my problems.
12.	I don't enjoy much about life.
13.	I don't have a personally satisfying relationship with a Higher Power.
14.	I feel good about my future.
15.	My relationship with a Higher Power helps me not to feel lonely.
16.	I feel that life is full of conflict and unhappiness.
17.	I feel most fulfilled when I'm in close communion with a Higher Power.
18.	Life doesn't have much meaning.
19.	My relation with a Higher Power contributes to my sense of well-being.
20.	I believe there is some real purpose for my life.

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Table 2. Relationship between spirituality and both current suicidal ideation and lifetime suicidal behavior among OHARNG soldiers.

Effect	Unadjusted Model			Adjusted Model ^a		
	OR	95% Confidence Interval		OR	95% Confidence Interval	
<u>Current suicidal ideation</u>						
Overall spiritual well-being	0.97	0.95	0.99	0.97	0.95	0.99
Religious well-being	0.98	0.95	1.01	0.98	0.95	1.00
Existential well-being	0.92	0.88	0.96	0.92	0.88	0.96
<u>Lifetime suicidal behavior</u>						
Overall spiritual well-being	0.99	0.98	1.01	0.99	0.98	1.01
Religious well-being	1.01	0.98	1.03	1.01	0.98	1.04
Existential well-being	0.96	0.92	1.00	0.96	0.92	1.00

Table 3 Relationship between spirituality and both the occurrence of lifetime PTSD and depression among OHARNG soldiers.

Effect	Unadjusted Model			Adjusted Model ^a		
	OR	95% Confidence Interval		OR	95% Confidence Interval	
<u>Lifetime PTSD</u>						
Overall spiritual well-being	0.97	0.94	0.99	0.96	0.94	0.99
Religious well-being	0.98	0.95	1.01	0.98	0.95	1.01
Existential well-being	0.91	0.87	0.96	0.92	0.87	0.96
<u>Lifetime Depression (MDD)</u>						
Overall spiritual well-being	1.00	0.98	1.01	0.99	0.98	1.01
Religious well-being	1.01	0.99	1.03	1.01	0.99	1.03
Existential well-being	0.96	0.93	0.98	0.95	0.93	0.98

CONCLUSIONS

- In this sample of OHARNG members, we found that higher spirituality measured by SWBS was associated with lower levels of mental health problems of lifetime PTSD and depression. Similarly, higher spirituality was associated with less suicidal ideation over the past year.
- Our results indicated that religious well-being was not a determining factor when compared to existential well-being, and no evidence of any indirect effect of Religious well-being through Existential well-being on any of mental health outcomes was found in this cohort. The effect of Existential well-being was independent of Religious well-being in our sample.
- Having a positive outlook as is described in Existential well-being is more relevant to positive mental health outcomes, and future interventions could be developed regardless of one's religious beliefs.

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On the Assessment of Subthreshold PTSD: Content and Construct Validity According to Various Definitions

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Introduction

Some people exposed to traumatic events develop posttraumatic symptomatology falling below diagnostic threshold for PTSD; often, these people are categorized as subthreshold PTSD cases. However, no consensual definition of subthreshold PTSD exists. Variations in definitions can affect both treatment of subthreshold cases and bias population estimates of psychopathology and future health care needs.

The three most common definitions of subthreshold PTSD (Brancu et al., 2016):

Def 1: Screen positive for cluster B and cluster C or cluster D

Def 2: Screen positive for 2 of 3 clusters

Def 3: At least 1 symptom in each cluster B, C, and D

To recommend a standardized subthreshold PTSD definition, we examined the content, criterion, and construct validity of these three most often used subthreshold PTSD definitions in a population-based military sample.

Methods

Study population

We analyzed longitudinal data from a representative sample of Ohio Army National Guard soldiers (N=3194). Data were collected annually from 2009 and 2014.

Measures

Posttraumatic stress disorder (PCL):

- **Positive screen for PTSD:** A response of 3 to 5 ("Moderately" or above) on 1 or more "B" items (Q1-5) (Criterion B), 3 or more "C" items (Q6-12) (Criterion C), and 2 or more "D" items (Q13-17) (Criterion D)
- **Positive screen for subthreshold PTSD**
 - **Def 1:** Screen positive for Criterion B and Criterion C or Criterion D
 - **Def 2:** Screen positive for 2 of 3 Criteria
 - **Def 3:** A response of 3 to 5 ("Moderately" or above) on at least 1 Criterion B item, 1 Criterion C item, and 1 Criterion D item

Depression (Patient Health Questionnaire); Positive screen for depression: five out of nine symptoms endorsed minimally as "more than half the days," and one of the symptoms being depressed mood or anhedonia.

Alcohol use disorder (M.I.N.I.): Positive screen for alcohol use disorder: one or more alcohol abuse questions or three or more alcohol dependence questions endorsed

Generalized anxiety disorder (GAD-7): Positive screen for generalized anxiety disorder (GAD): a score of ten or greater on the GAD-7

Results

1. Content validity

A good subthreshold PTSD definition should identify persons exhibiting symptomatology within each cluster that falls somewhere between persons with PTSD and persons without PTSD.

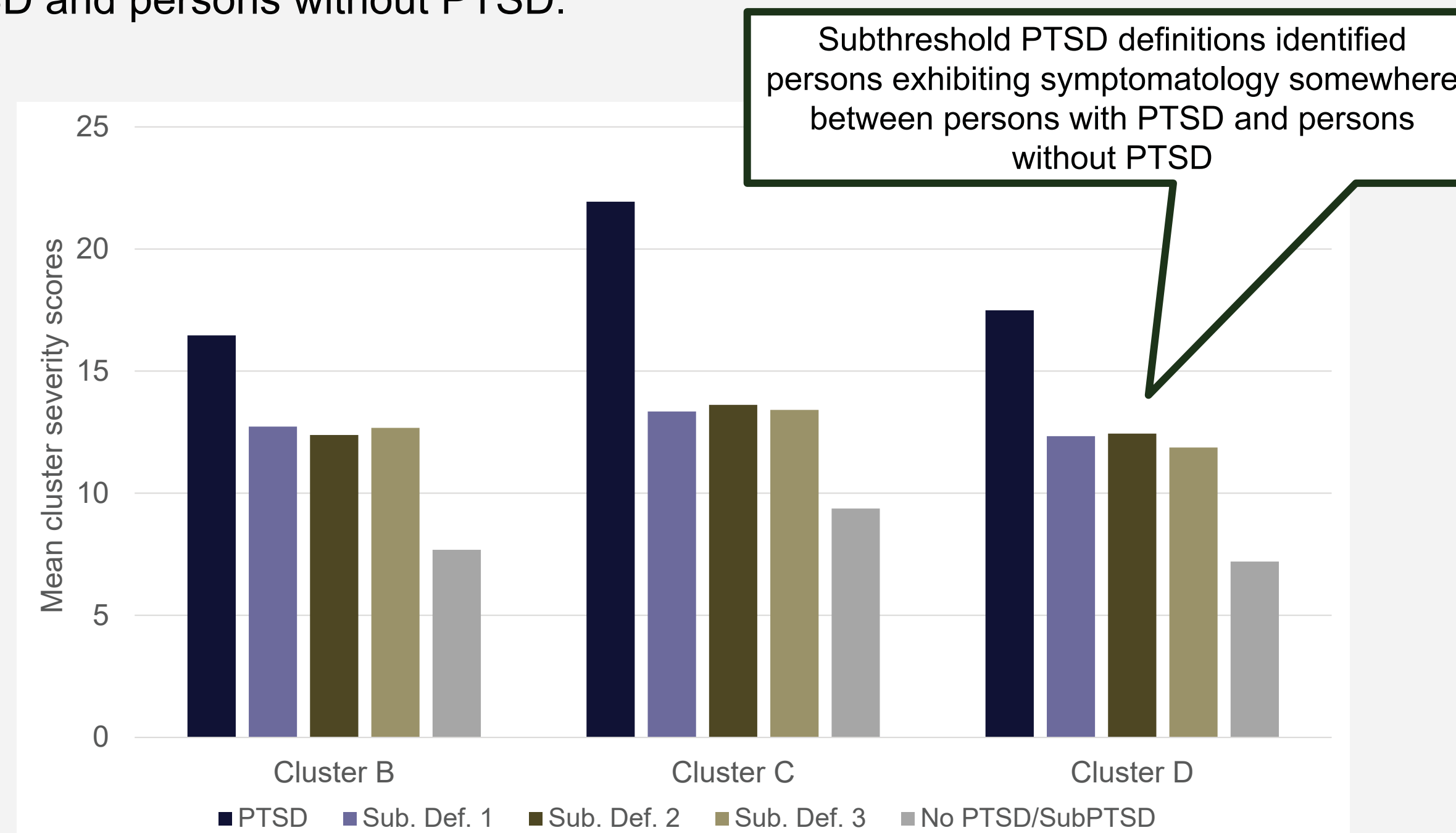


Figure 1. Mean symptom cluster severity scores among those meeting criteria for DSM-IV PTSD criteria, each subthreshold PTSD definition, neither PTSD criteria nor any subthreshold definition. The item scores within each cluster were summed to give the symptom cluster severity score.

Why did all three definitions perform equally well?

Subthreshold PTSD	Kappa (95% CI)		
	Sub. Def. 1	Sub. Def. 2	Sub. Def. 3
Sub. Def. 1	-	.963 (.953, .973)	.712 (.684, .740)
Sub. Def. 2	-	-	.683 (.655, .712)
Sub. Def. 3	-	-	-

The 3 subthreshold PTSD definitions largely identify the same people

2. Criterion validity

A good subthreshold PTSD definition should predict future PTSD.

PTSD status	PTSD at subsequent data collection (+1 year)		Rel. Risk (95% CI) Adjustment for study wave + robust SE
	Yes	No	
PTSD	180 (40.6%)	263 (59.4%)	7.00 (5.88, 8.32)
Sub. Def. 1	66 (15.8%)	353 (84.2%)	3.17 (2.45, 4.10)
Sub. Def. 2	77 (17.2%)	370 (82.8%)	3.68 (2.88, 4.70)
Sub. Def. 3	68 (16.2%)	351 (83.8%)	3.36 (2.61, 4.34)

3. Construct validity

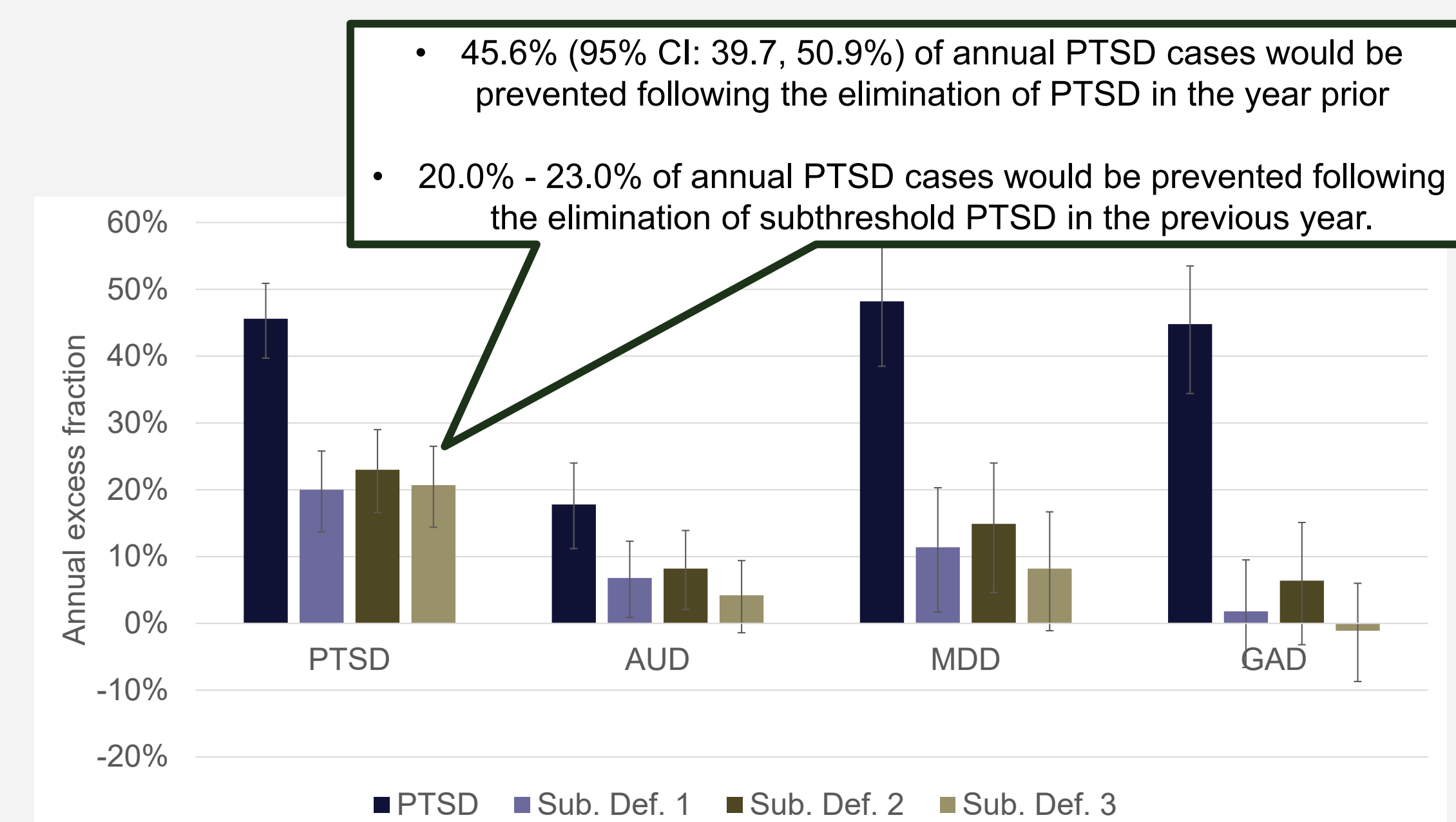
A good subthreshold PTSD definition should be positively associated with increased risk of psychiatric disorders commonly comorbid with PTSD

	Relative risk for disorder at subsequent data collection (Rel. Risk, 95% CI)		
	Alcohol use disorder	Major depressive disorder	Generalized anxiety disorder
PTSD	2.9 (2.2, 3.9)	8.9 (6.7, 11.8)	8.63 (6.3, 11.9)
Sub. Def. 1	1.8 (1.2, 2.6)	2.3 (1.4, 3.9)	1.2 (0.6, 2.4)
Sub. Def. 2	1.9 (1.3, 2.7)	2.8 (1.7, 4.5)	1.7 (0.9, 3.2)
Sub. Def. 3	1.4 (0.9, 2.1)	1.8 (1.0, 3.2)	0.8 (0.4, 1.9)

Results (cont.)

4. Public health effect

The population attributable fraction (excess fraction) is the proportion of disease cases over a year that would be prevented following elimination of the exposures, assuming the exposures are causal.



Conclusions

1. Summary of findings:

- The 3 subthreshold PTSD definitions identified persons:
 - a. exhibiting substantial posttraumatic stress symptomatology falling below those screening positive for DSM-IV PTSD.
 - b. exhibiting an increased risk for screening positive for PTSD the subsequent year.
 - c. exhibiting an increased risk of screening positive for alcohol use disorder, major depressive disorder, and generalized anxiety disorder.
- The 3 subthreshold PTSD definitions are largely equivalent in their ability to identify persons with substantial psychopathology, albeit Def. 2 appears to represent a slightly more severe condition than Defs. 1 and 3.
- Subthreshold PTSD was found to be more of an attenuated form of PTSD than a standalone disorder that is discernable from PTSD
- Increased risk for psychopathology among persons with subthreshold PTSD suggests that the identification and treatment of persons exhibiting subthreshold PTSD symptomatology is likely to improve population health

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Is the relationship between stressful events and depression mediated by unit social support during deployment among National Guard members?

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Background and study aims

- Stressful events (stressors) such as job loss or divorce are associated with depression in both the general population and in the military (Carter-Visscher et al., 2010; Thoits 1995)
- Stressors can also strain social support networks, leading to perceived or real lower social support (Lin & Ensel 1989; Thoits 1995)
- Low social support is associated with higher risk of depression (Paykel 1994)
- Using a cohort of Ohio National Guard soldiers, we investigated a path from lifetime civilian stressors to current depression through low social support during deployment (low unit support)
- We hypothesized that lifetime stressors may put soldiers in a more vulnerable position when deployed - this may manifest in trouble connecting with peers and concern with stressful matters at home, and potentially make these soldiers more likely to have symptoms of depression post-deployment

Proposed mediation relationship

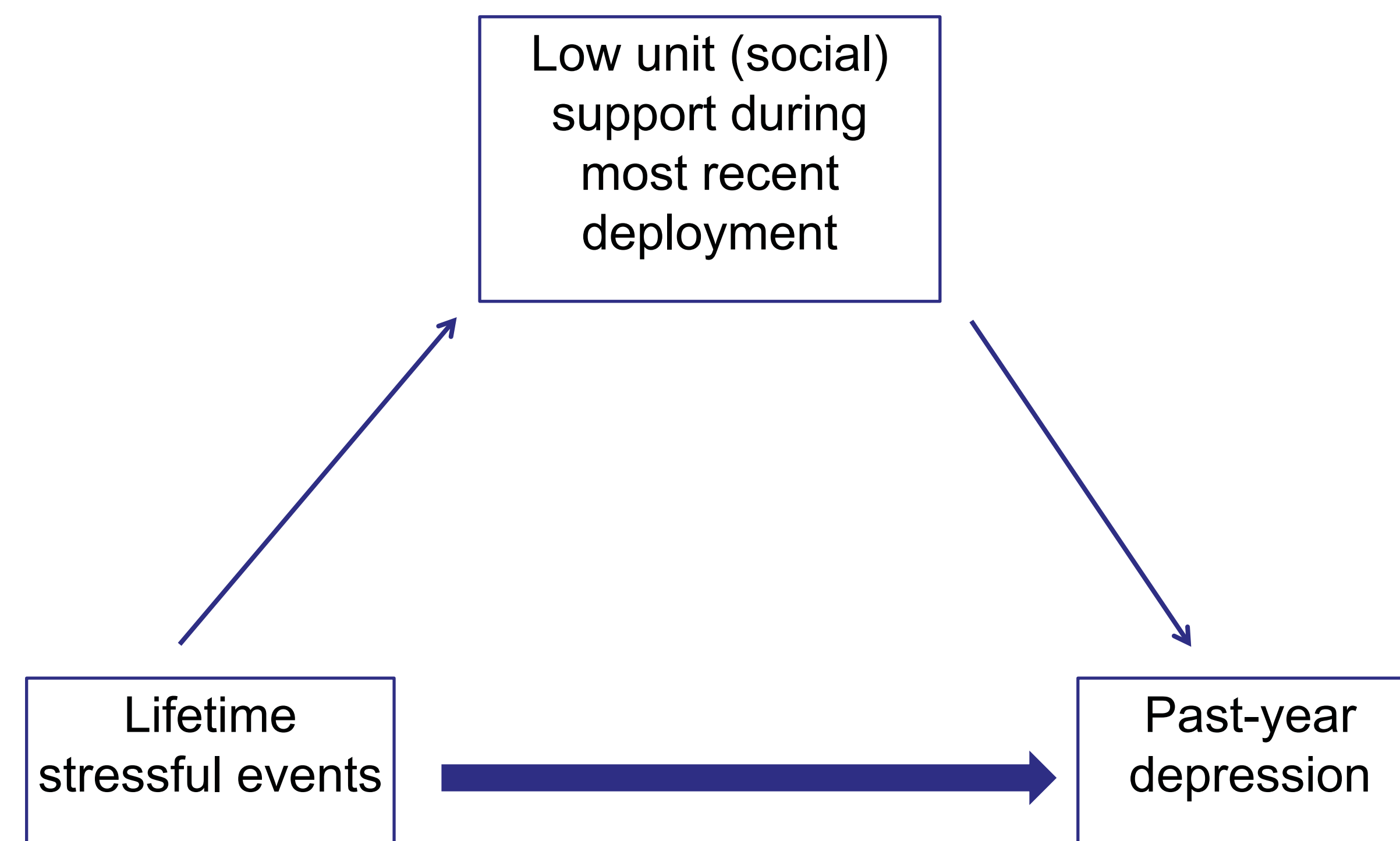


Table 1

	n	%
Female	44	10.6%
High school education or less	85	20.5%
Low unit support	184	44.3%
4+ lifetime stressors	197	47.5%
Past-year depression	51	12.3%

Methods

- Participants were drawn from a representative sample of Ohio Army National Guard members in 2008-2009
- Telephone interviews were completed once a year for four years
- Analyses were restricted to soldiers who had been deployed within four years but not in the past year, and present in at least two waves, in order to ensure temporality (n = 415)
- Lifetime stressors were measured at baseline using the positive count of 12 possible stressors, dichotomized at the median split (4 or more)
- Social support was asked in the form of 7 questions in relation to the unit the soldier most recently deployed with, and dichotomized at the median split
- Past-year DSM-IV depression was measured using the 9-item Patient Health Questionnaire
- Sex and education (dichotomized at median split) were controlled for in all analyses based on prior literature
- Baron and Kenny steps for mediation analysis were used with logistic regression in SAS version 9.4

Mediation results

Model	Odds ratio	95% lower limit	95% upper limit
Stressors → depression	2.91	1.53	5.52
Stressors → low unit support	1.46	0.99	2.16
Low unit support → depression with stressors in model	0.95	0.52	1.73
Stressors → depression with low unit support in model	2.92	1.54	5.56

Conclusions

- Experiencing 4+ lifetime stressors was associated with a 46% increased odds of low unit support and 291% increased odds of past-year depression
- There was no significant mediation found using the Baron and Kenny method
- The observed effect from stressors to depression appears to be a strong direct effect, which supports previous research that civilian exposures throughout the lifecourse are predictive of post-deployment mental health (Stevanovic et al., 2016)
- In this sample, low unit social support was not associated with depression, contrary to previous findings (Paykel 1994)

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narratives that have substantially different policy implications.

A harm reduction model has prioritized the potential for e-cigarettes to reduce the harms from combustible cigarettes (“c-cigarettes”) until a smoker is able to quit, whereas a transition model considers the potential for e-cigarettes to increase the risk of c-cigarette initiation among nonsmokers.

We investigate the harm reduction model in a high-risk cohort, evaluating the longitudinal use of c-cigarettes and e-cigarettes in a representative military cohort from 2014 to 2016.

Methods

Study population

We analyzed longitudinal data from a representative sample of Ohio Army National Guard soldiers. Respondents who answered the tobacco use measure in both the 2014 and the 2016 data collection waves were included in this analysis (n=1385).

Measures

Electronic cigarette (e-cigarette) use:

- **Lifetime e-cigarette use:** “Have you ever used an e-cigarette or other electronic “vaping” product, even just one time, in your entire life?”
- **Ever daily e-cigarette use:** “At any point in your life, did you use electronic cigarettes, e-cigarettes, or other electronic “vaping” products every day?”
- **Past-month e-cigarette use:** “Out of the past 30 days, how many days did you use electronic cigarettes, e-cigarettes, or other electronic “vaping” products?”

Combustible cigarette (c-cigarette) use:

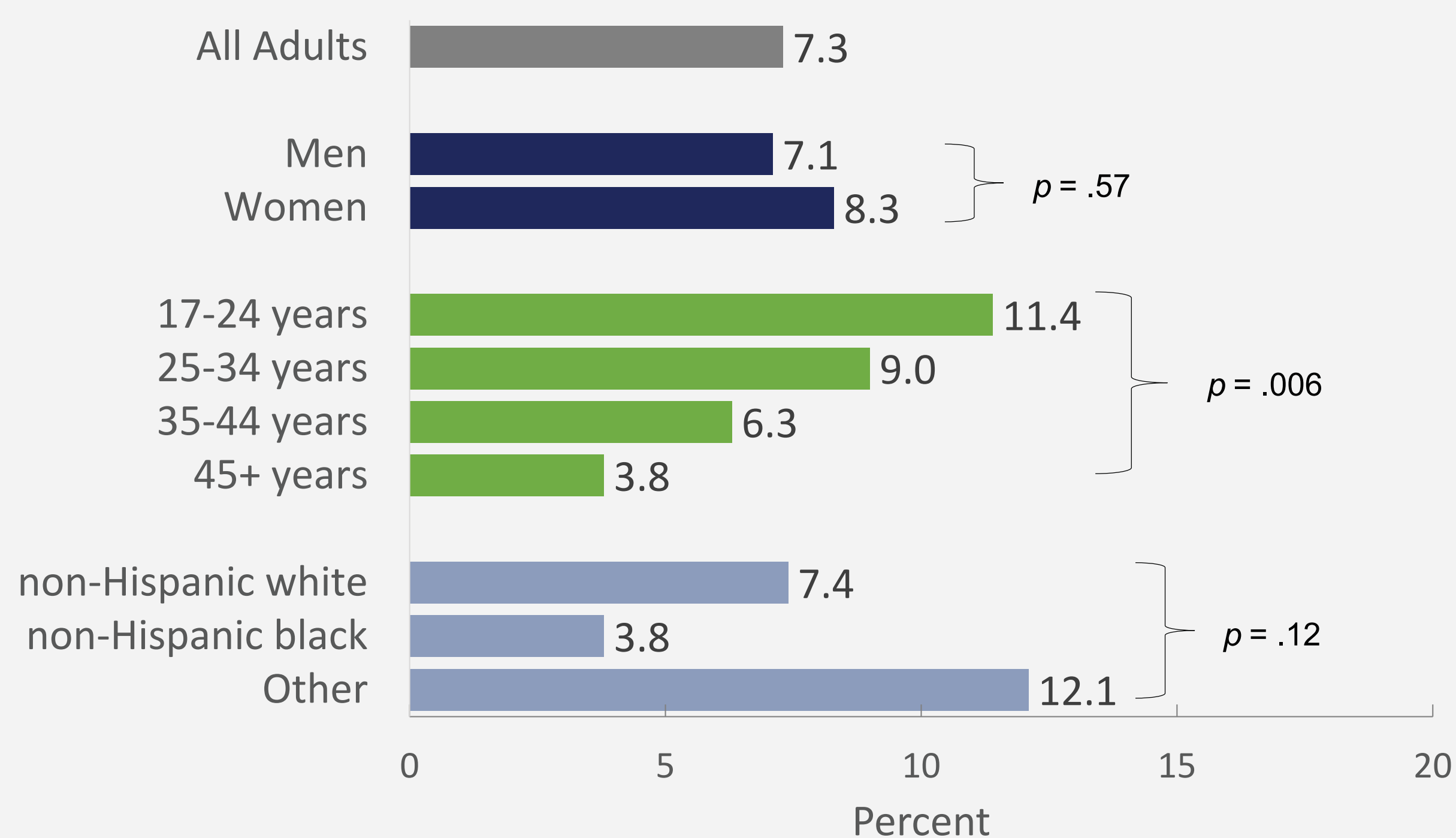
- **Past-month c-cigarette use:** Endorsed smoking at least one cigarette on at least one day out of the past 30 days
- **Cigarette consumption:** the product of number of days smoked c-cigarettes per month (frequency) and c-cigarettes per day on days smoked (quantity).

Statistical analysis

- We created a four-level nominal variable from respondents’ c-cigarette smoking patterns from 2014 to 2016: Nonsmokers, reported no past-month c-cigarette use in either 2014 or 2016 (n=973, 70%); Quitters, reported past-month c-cigarette use in 2014, but not in 2016 (n=138, 10%); Initiators, reported no past-month use in 2014 and past-month use in 2016 (n=62, 5%); and Chronic smokers, reported past-month use in both 2014 and 2016 (n=212, 15%).
- We used a difference-in-differences approach to estimate change in monthly individual rate of c-cigarette use adjusting for age. Inclusion of individual fixed effects adjusts for time-stable differences that might exist between persons who use e-cigarettes and persons who do not use e-cigarettes.

Results

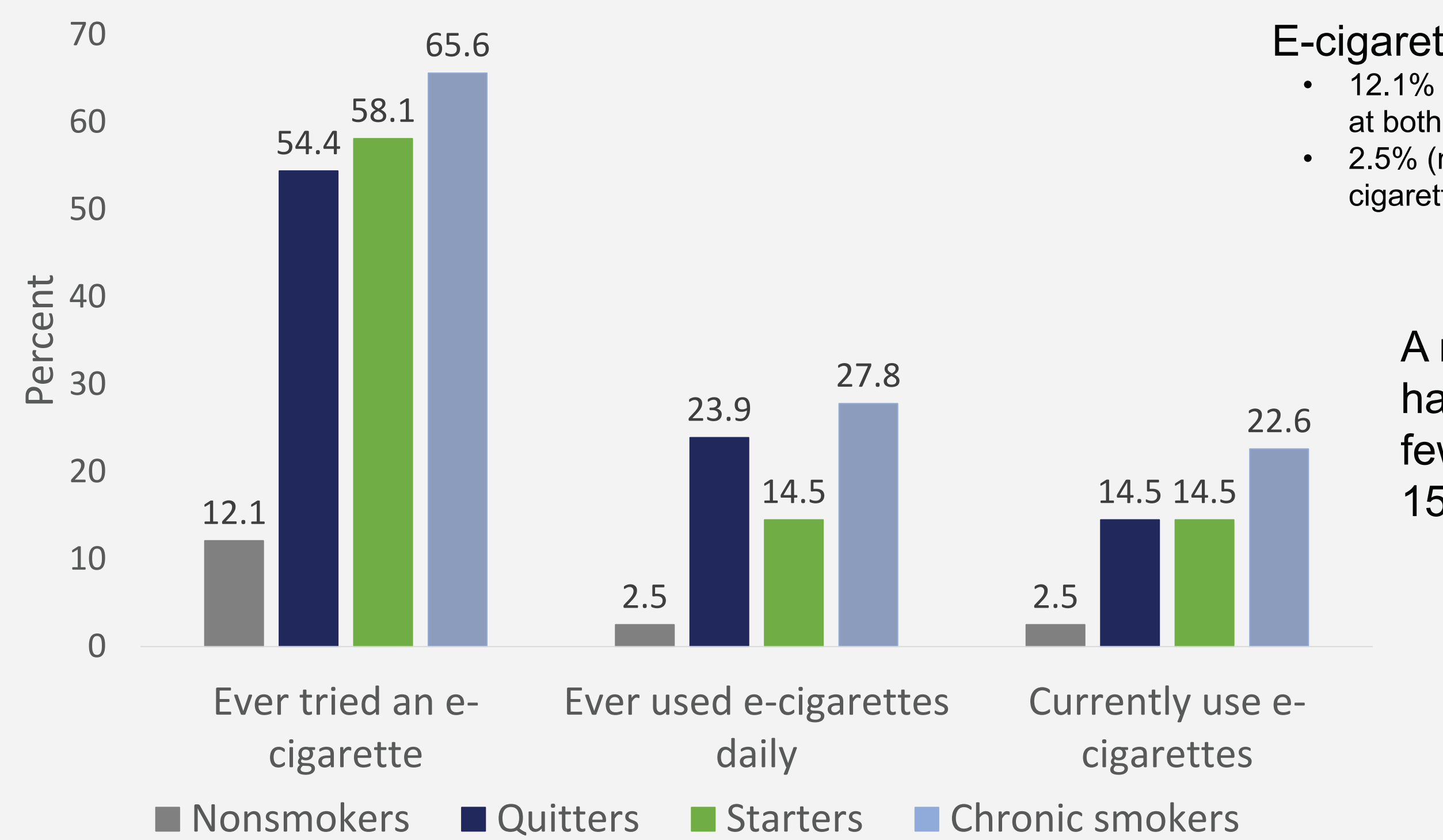
Figure 1. Percentage of soldiers who currently use e-cigarettes, by sex, age, and race/ethnicity: National Guard Soldiers, 2016



Acknowledgments

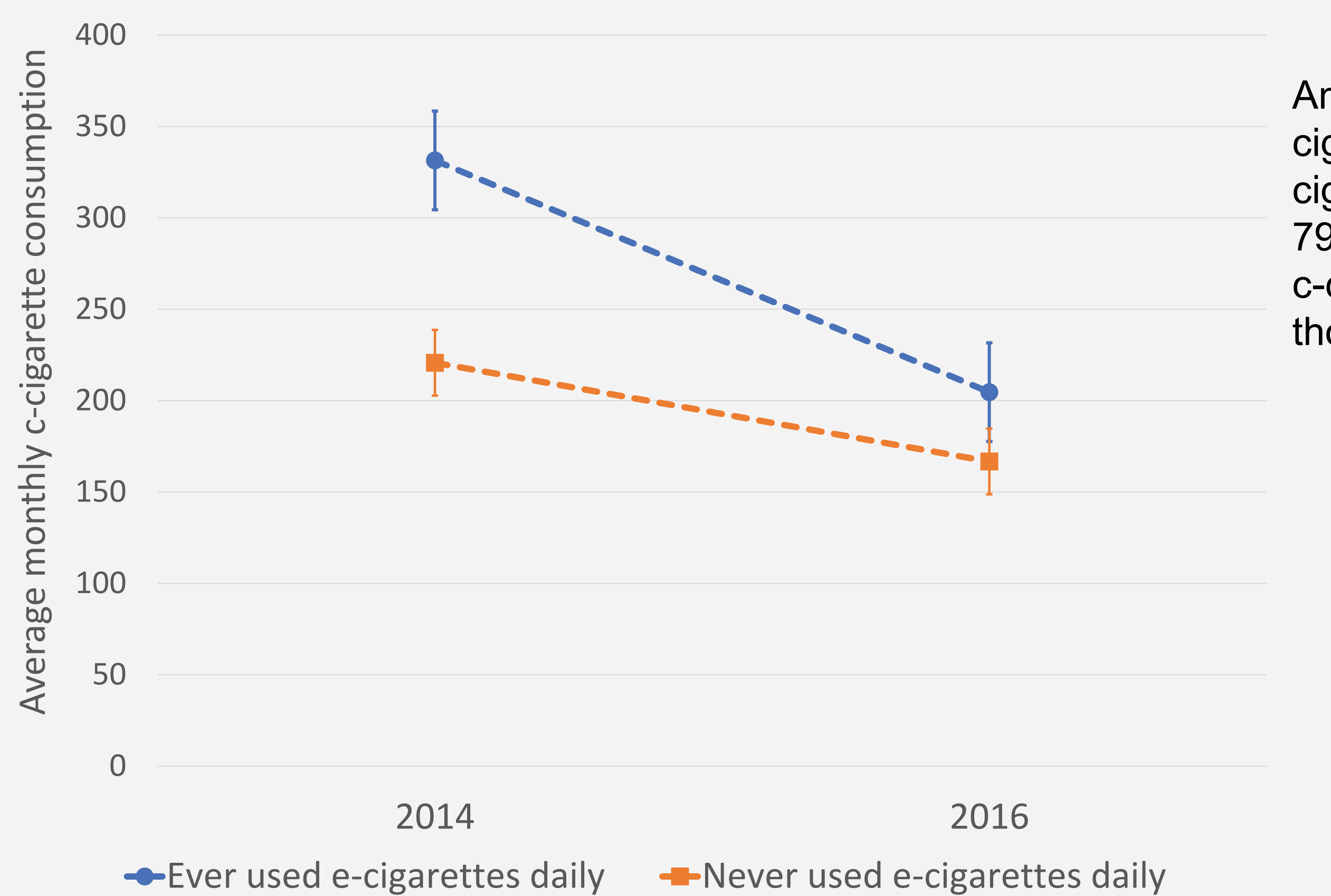
This work was supported by the Office of the Assistant Secretary of Defense for Health Affairs through the Joint Warfighter Medical Research Program (Grants W81XWH-15-1-0080, W81XWH-07-1-0409, and W81XWH-07-1-0409) and the National Institute on Drug Abuse at the National Institutes of Health (Grant T32DA031099 to D.S.F.). The U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD 21702-5014 is the sponsor of this work. All interpretations, conclusions, and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.

currently use e-cigarettes, by c-cigarette smoking status in 2016



NOTES: Current e-cigarette users have ever tried an e-cigarette and currently used them every day or some days during the past month in 2016. Nonsmokers reported no past-month c-cigarette use in either 2014 or 2016. Quitters reported using c-cigarettes every day or some days during the past month in 2014, and no past-month c-cigarette use in 2016. Starters reported no past-month c-cigarette use in 2014, and reported using c-cigarettes every day or some days during the past-month in 2016. Chronic smokers reported using c-cigarettes every day or some days during the past-month in both 2014 and 2016.

Figure 3. Change in the average rate of past-month c-cigarette smoking by



NOTES: Estimates result from difference-in-differences regression of the monthly individual rate of c-cigarette use adjusting for age. Individual fixed effects included. Difference-in-differences F-value = 7.75, p-value = .006

Conclusions

To our knowledge, this is the first test of the longitudinal change in combustible

Our study had three findings:

1. E-cigarette use is uncommon among non-smokers
2. A small proportion of new-onset smokers have ever used e-cigarettes daily (15%)
3. Among persons who smoked cigarettes at baseline, ever use of e-cigarettes resulted in significant reductions in cigarette use, two years later, at the follow up

Under an assumption that e-cigarette use is less harmful than combustible cigarettes, the harm reduction model for e-cigarette use

New onset of mental disorders across five years of follow-up among U.S. National Guard members

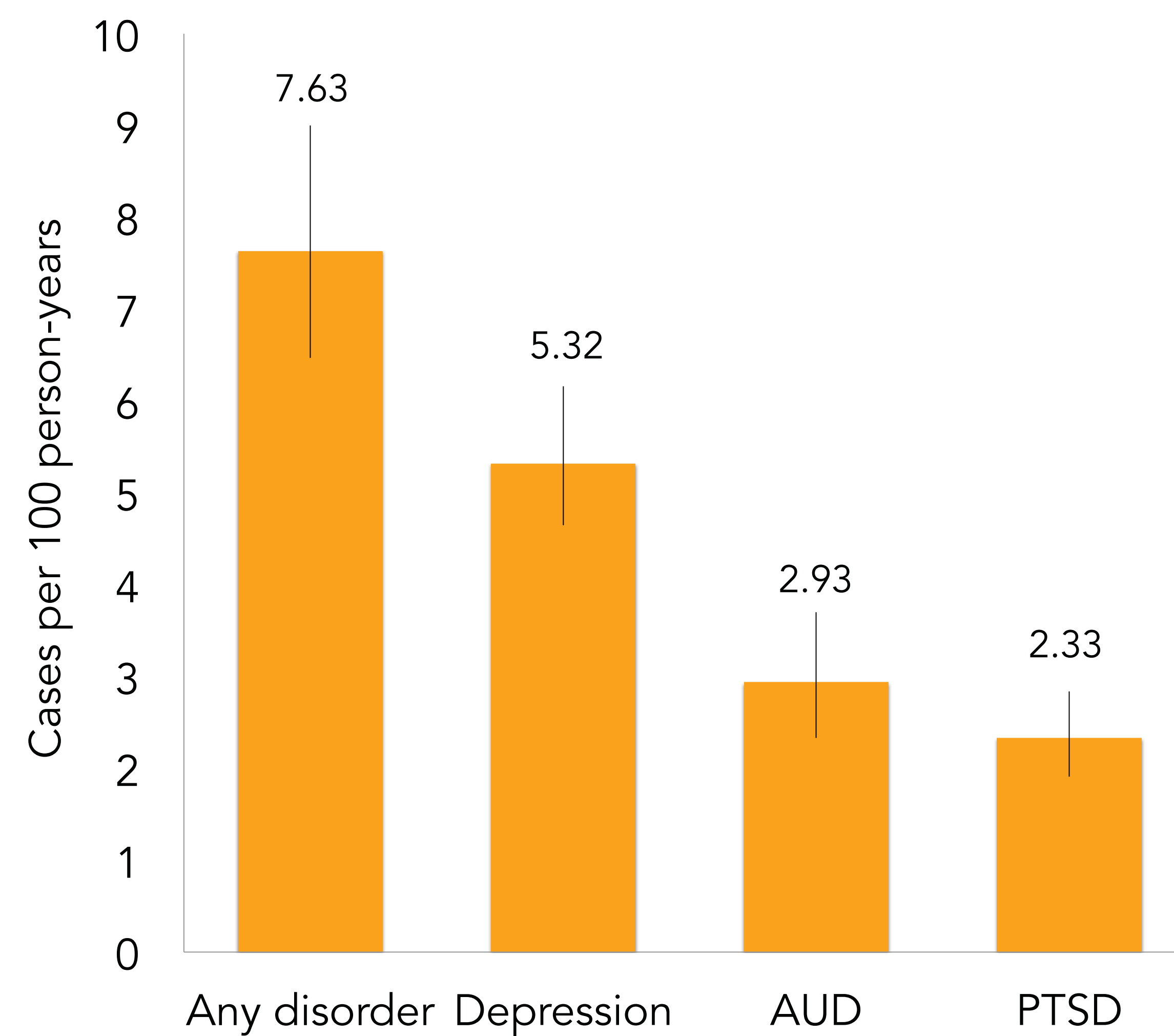
Laura Sampson¹, David S. Fink², Gregory H. Cohen^{1,2}, Israel Liberzon³, Marijo Tamburrino⁴, Joseph R. Calabrese⁵

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Background and study aims

- There are very few long-term studies that estimate incident cases of mental disorders over time in U.S. military populations
- This is particularly true among Reservists, who have seen more exposure to combat in recent years compared to past U.S. conflicts, in addition to being mobilized for humanitarian relief following natural disasters
- Reservists face a different set of burdens compared to the Active Duty Military, including differential access to health care and other resources, unpredictable deployment schedules, and the frequent balance of civilian jobs on top of military engagement
- The aim for this study was to estimate the rate of and predictors for new-onset depression, alcohol use disorder (AUD), and posttraumatic stress disorder (PTSD) across five follow-up years in a representative sample of National Guard members

Rates of disorder



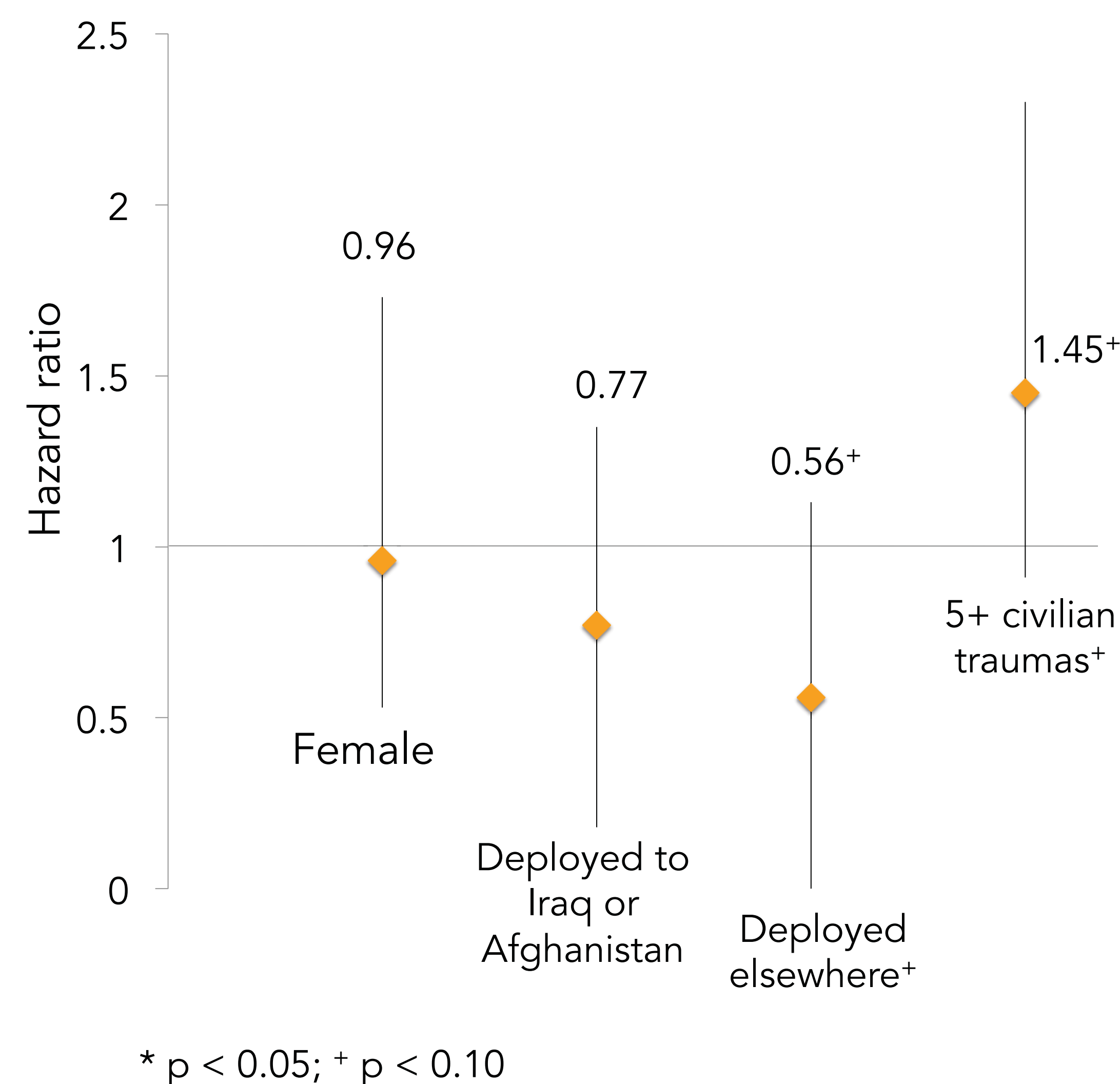
Risk factors for depression onset



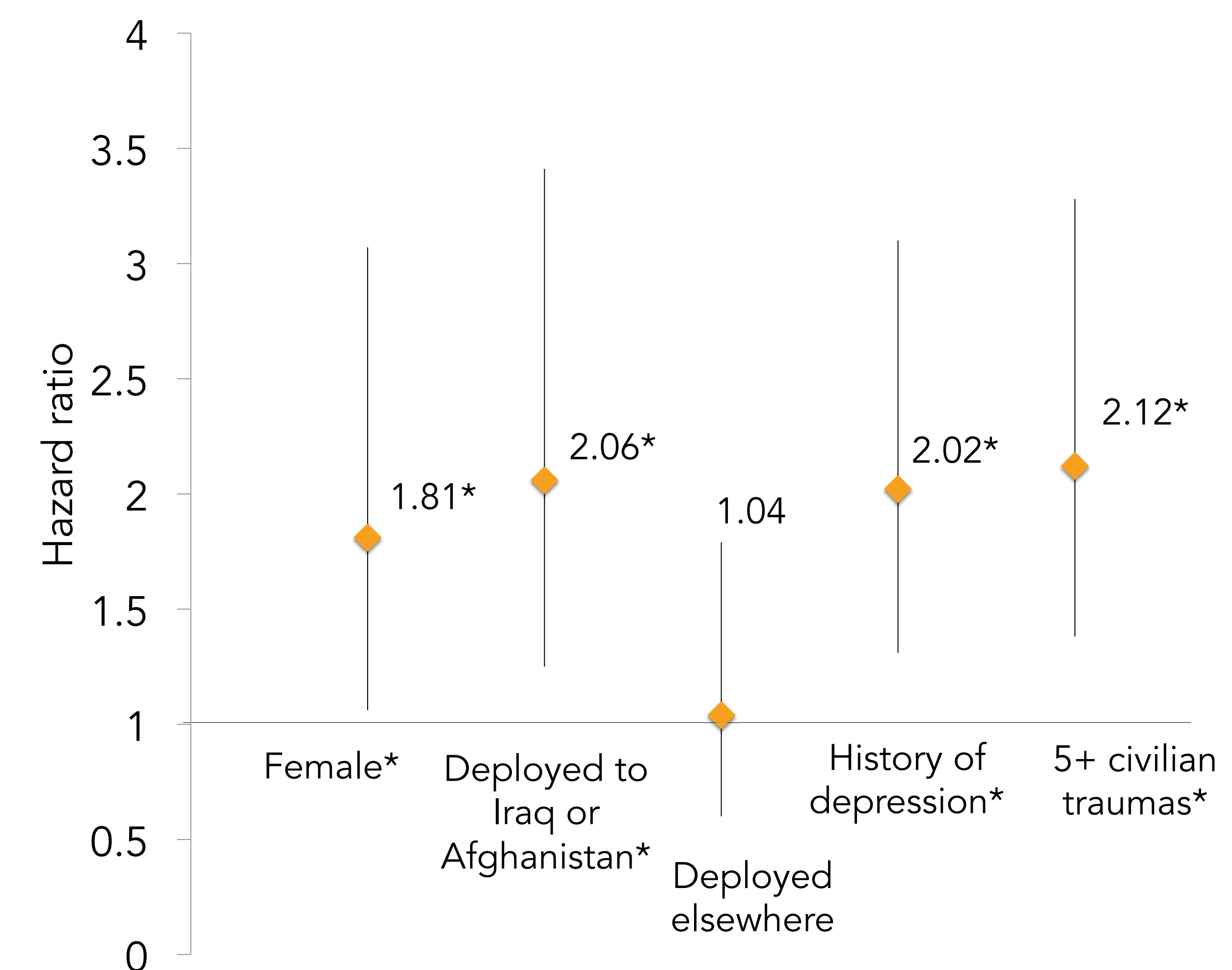
Methods

- Participants were from a random sample of Ohio Army National Guard members drawn in 2008-2009
- Telephone interviews were completed approximately once per year for five years of follow-up after baseline
- In order to assess DSM IV disorders, we administered the Patient Health Questionnaire for depression, the PTSD Checklist - Civilian Version for PTSD, and the Mini-International Neuropsychiatric Interview for AUD
- Participants who contributed at least one year of follow-up and had no history of disorder at baseline were included in analyses (n=737 for any disorder; n=1393 for depression; n=917 for AUD; n=1520 for PTSD)
- Cox proportional hazards models were used to estimate hazard ratios

Risk factors for AUD onset



Risk factors for PTSD onset



Conclusions

These results suggest that particular attention to National Guard soldiers who are women, who have been deployed to Iraq or Afghanistan, who experienced adverse childhood events or more than the median number of traumatic events outside of military engagement, and who have comorbid conditions, is warranted to mitigate the consequences of new onset mental disorders



On the Assessment of Subthreshold PTSD: Content and Construct Validity According to Various Definitions

David S. Fink¹, Jaimie L. Gradus², Katherine M. Keyes¹, Marijo B. Tamburrino³, Israel Liberzon⁴ Joseph R. Calabrese⁵, Gregory H. Cohen⁶, Laura Sampson⁶, Sandro Galea⁷

¹Columbia University, Department of Epidemiology, New York, NY; ²National Center for PTSD, Boston VA Medical Center and Boston University School of Medicine, Boston, MA; ³University of Toledo, Department of Psychiatry, Toledo, OH; ⁴University of Michigan, Department of Psychiatry, Ann Arbor, MI; ⁵Case Western Reserve University, Department of Psychiatry, Cleveland, OH; ⁶ Boston University, Department of Epidemiology, Boston, MA; ⁷ Boston University, School of Public Health, Boston, MA

Introduction

Some people exposed to traumatic events develop posttraumatic symptomatology falling below diagnostic threshold for PTSD; often, these people are categorized as subthreshold PTSD cases. However, no consensual definition of subthreshold PTSD exists. Variations in definitions can affect both treatment of subthreshold cases and bias population estimates of psychopathology and future health care needs.

The three most common definitions of subthreshold PTSD (Brancu et al., 2016):

Def 1: Screen positive for cluster B and cluster C or cluster D

Def 2: Screen positive for 2 of 3 clusters

Def 3: At least 1 symptom in each cluster B, C, and D

To recommend a standardized subthreshold PTSD definition, we examined the content, criterion, and construct validity of these three most often used subthreshold PTSD definitions in a population-based military sample.

Methods

Study population

We analyzed longitudinal data from a representative sample of Ohio Army National Guard soldiers (N=3194). Data were collected annually from 2009 and 2014.

Measures

Posttraumatic stress disorder (PCL):

- **Positive screen for PTSD:** A response of 3 to 5 ("Moderately" or above) on 1 or more "B" items (Q1-5) (Criterion B), 3 or more "C" items (Q6-12) (Criterion C), and 2 or more "D" items (Q13-17) (Criterion D)
- **Positive screen for subthreshold PTSD**
 - **Def 1:** Screen positive for Criterion B and Criterion C or Criterion D
 - **Def 2:** Screen positive for 2 of 3 Criteria
 - **Def 3:** A response of 3 to 5 ("Moderately" or above) on at least 1 Criterion B item, 1 Criterion C item, and 1 Criterion D item

Depression (Patient Health Questionnaire); Positive screen for depression: five out of nine symptoms endorsed minimally as "more than half the days," and one of the symptoms being depressed mood or anhedonia.

Alcohol use disorder (M.I.N.I.): Positive screen for alcohol use disorder: one or more alcohol abuse questions or three or more alcohol dependence questions endorsed

Generalized anxiety disorder (GAD-7): Positive screen for generalized anxiety disorder (GAD): a score of ten or greater on the GAD-7

Results

1. Content validity

A good subthreshold PTSD definition should identify persons exhibiting symptomatology within each cluster that falls somewhere between persons with PTSD and persons without PTSD.

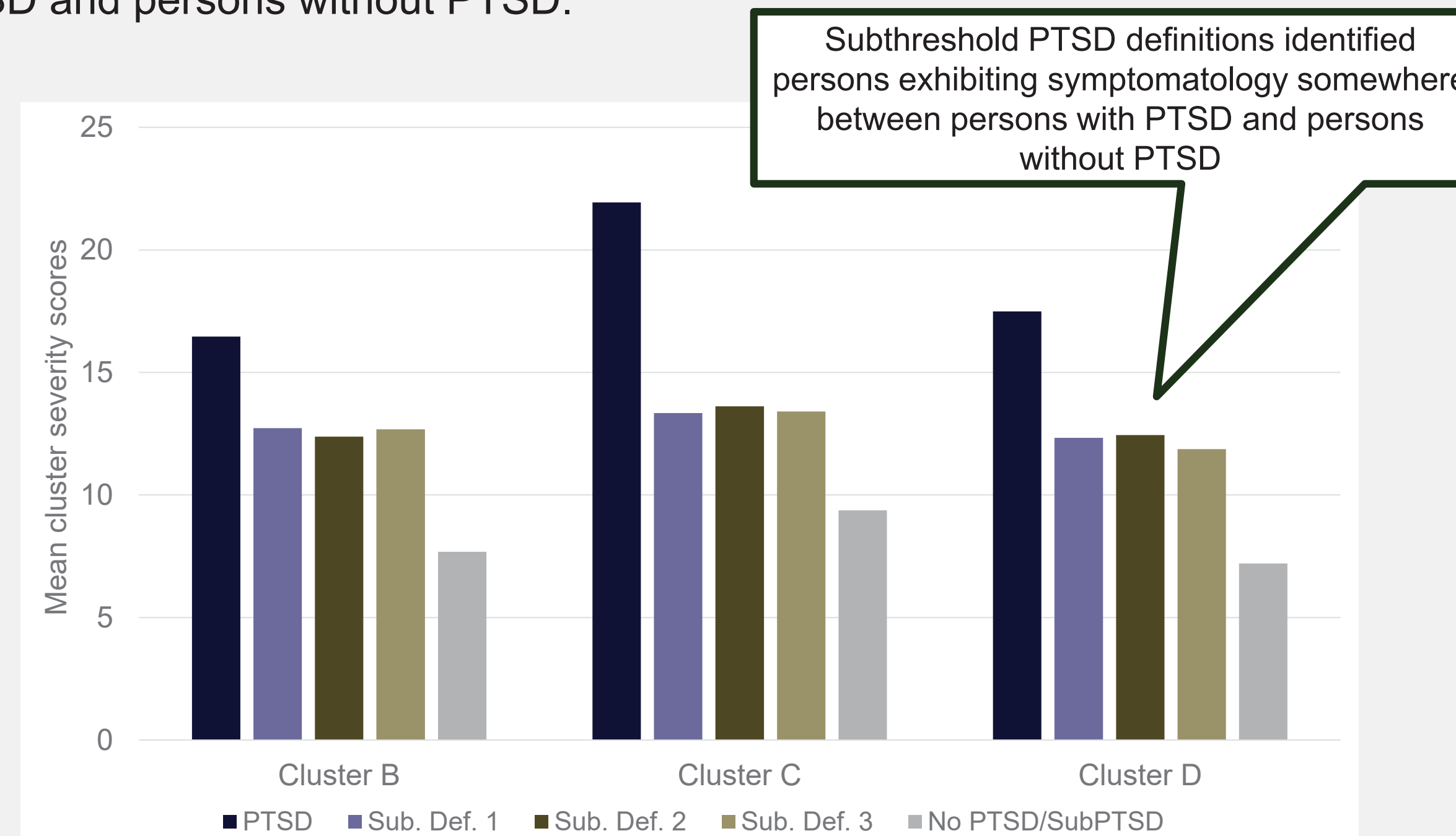


Figure 1. Mean symptom cluster severity scores among those meeting criteria for DSM-IV PTSD criteria, each subthreshold PTSD definition, neither PTSD criteria nor any subthreshold definition. The item scores within each cluster were summed to give the symptom cluster severity score.

Why did all three definitions perform equally well?

Subthreshold PTSD	Kappa (95% CI)		
	Sub. Def. 1	Sub. Def. 2	Sub. Def. 3
Sub. Def. 1	-	.963 (.953, .973)	.712 (.684, .740)
Sub. Def. 2	-	-	.683 (.655, .712)
Sub. Def. 3	-	-	-

The 3 subthreshold PTSD definitions largely identify the same people

2. Criterion validity

A good subthreshold PTSD definition should predict future PTSD.

PTSD status	PTSD at subsequent data collection (+1 year)		Rel. Risk (95% CI) Adjustment for study wave + robust SE
	Yes	No	
PTSD	180 (40.6%)	263 (59.4%)	7.00 (5.88, 8.32)
Sub. Def. 1	66 (15.8%)	353 (84.2%)	3.17 (2.45, 4.10)
Sub. Def. 2	77 (17.2%)	370 (82.8%)	3.68 (2.88, 4.70)
Sub. Def. 3	68 (16.2%)	351 (83.8%)	3.36 (2.61, 4.34)

3. Construct validity

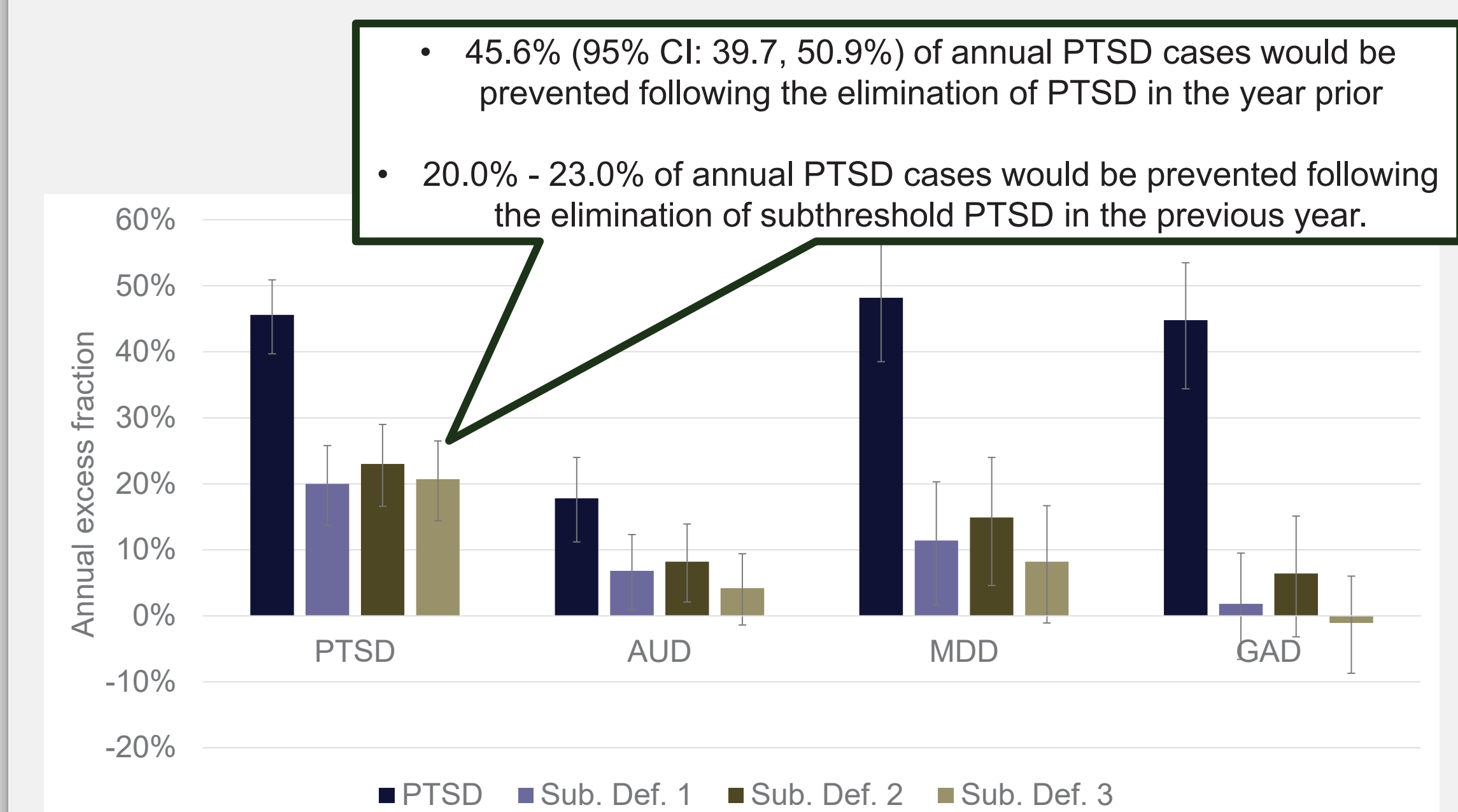
A good subthreshold PTSD definition should be positively associated with increased risk of psychiatric disorders commonly comorbid with PTSD

	Relative risk for disorder at subsequent data collection (Rel. Risk, 95% CI)		
	Alcohol use disorder	Major depressive disorder	Generalized anxiety disorder
PTSD	2.9 (2.2, 3.9)	8.9 (6.7, 11.8)	8.63 (6.3, 11.9)
Sub. Def. 1	1.8 (1.2, 2.6)	2.3 (1.4, 3.9)	1.2 (0.6, 2.4)
Sub. Def. 2	1.9 (1.3, 2.7)	2.8 (1.7, 4.5)	1.7 (0.9, 3.2)
Sub. Def. 3	1.4 (0.9, 2.1)	1.8 (1.0, 3.2)	0.8 (0.4, 1.9)

Results (cont.)

4. Public health effect

The population attributable fraction (excess fraction) is the proportion of disease cases over a year that would be prevented following elimination of the exposures, assuming the exposures are causal.



Conclusions

1. Summary of findings:

- The 3 subthreshold PTSD definitions identified persons:
 - a. exhibiting substantial posttraumatic stress symptomatology falling below those screening positive for DSM-IV PTSD.
 - b. exhibiting an increased risk for screening positive for PTSD the subsequent year.
 - c. exhibiting an increased risk of screening positive for alcohol use disorder, major depressive disorder, and generalized anxiety disorder.

- The 3 subthreshold PTSD definitions are largely equivalent in their ability to identify persons with substantial psychopathology, albeit Def. 2 appears to represent a slightly more severe condition than Defs. 1 and 3.

- Subthreshold PTSD was found to be more of an attenuated form of PTSD than a standalone disorder that is discernable from PTSD

- Increased risk for psychopathology among persons with subthreshold PTSD suggests that the identification and treatment of persons exhibiting subthreshold PTSD symptomatology is likely to improve population health

Reference

Brancu, M., Mann-Wrobel, M., Beckham, J.C., Wagner, H.R., Elliott, A., Robbins, A.T., Wong, M., Berchuck, A.E., Runnals, J.J. (2016). Subthreshold Posttraumatic Stress Disorder: A Meta-Analytic Review of DSM-IV Prevalence and a Proposed DSM-5 Approach to Measurement. *Psychological Trauma: Theory, Research, Practice, and Policy*, 8, 2, 222-232.

Acknowledgments

This work was supported by the Office of the Assistant Secretary of Defense for Health Affairs through the Joint Warfighter Medical Research Program (Grants W81XWH-15-1-0080, W81XWH-07-1-0409, and W81XWH-10-1-0579 to J.R.C., I.L., M.T.B., S.G.) and National Institute on Drug Abuse at the National Institutes of Health (Grant T32DA031099 to D.S.F.). The U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD 21702-5014 is the awarding and administering acquisition office. Opinions, interpretations, conclusions, and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.

Childhood adversity and trajectories of depression symptoms in adulthood across six years in a U.S. Army National Guard cohort

Laura Sampson¹, Gregory H. Cohen^{1,2}, David S. Fink², John Wryobeck³, Israel Liberzon⁴, Joseph R. Calabrese⁵

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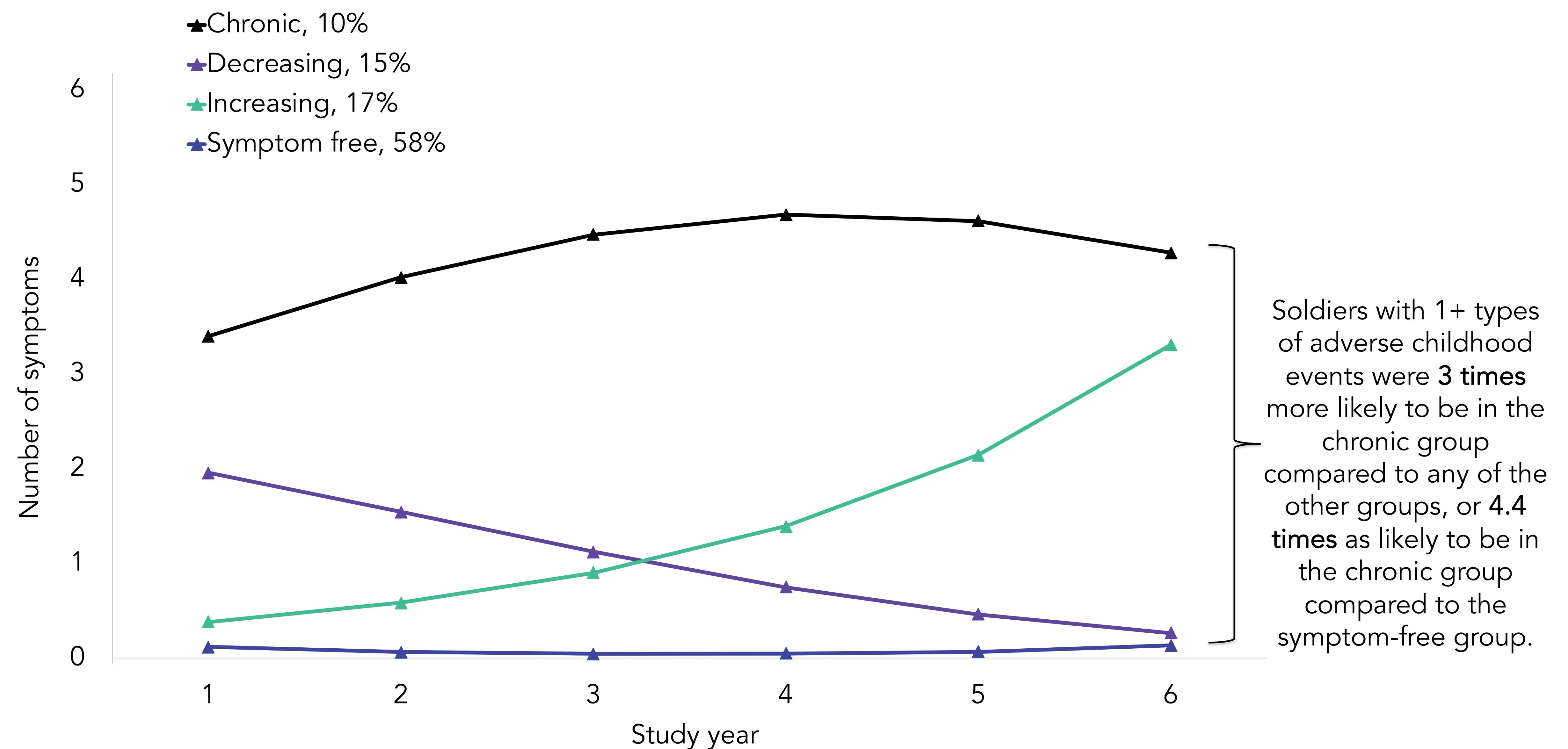
Background

- Depression is the most common mental disorder among U.S. military populations. Despite its high burden and relationship to suicide, physical health problems, and retention in the military, little is known about the course of depression symptoms over time among military personnel.
- The Army National Guard (ARNG), a force of the U.S. military that has been increasingly deployed during recent conflicts, differs from the Active Duty component in terms of demographic characteristics and deployment experiences, and is studied much less frequently.
- Traumatic events throughout the civilian lifecourse have been shown to associate with depression in adulthood among other groups, but not yet within an ARNG population.
- Identifying the course of symptoms over time in a longitudinal study is crucial, especially for cases of sub-threshold depression, which may not be discernible when modeling binary outcomes of depression.
- We set out to identify (1) latent trajectories of depression symptoms in an ARNG cohort and (2) whether childhood events predict these trajectory groups.

Methods

- The primary cohort of participants was from a random sample of Ohio Army National Guard members drawn in 2008-2009.
- Telephone interviews were completed approximately once per year for five years of follow-up after baseline.
- In order to mitigate loss to follow-up over time, a dynamic cohort design was employed, with three smaller random samples drawn and added to the cohort in study years 3, 4, and 5.
- Childhood adverse events included physical, sexual, and emotional abuse, as well mental illness of a parent.
- Past 30 day depression symptoms were assessed with the 9-item Patient Health Questionnaire at each study year.
- We used latent class growth analysis with a zero-inflated Poisson distribution on 2,407 participants who were present in two or more study waves, and selected the ideal number of groups based on fit statistics and entropy.
- An adjusted multinomial model was run to predict group membership using childhood adversity.

Trajectories of depression symptoms in the past 30 days



Multinomial model predicting trajectory group membership

	Decreasing vs. symptom free group			Increasing vs. symptom free group			Chronic vs. symptom free group		
	Odds ratio	95% CI lower limit	95% CI upper limit	Odds ratio	95% CI lower limit	95% CI upper limit	Odds ratio	95% CI lower limit	95% CI upper limit
Age 17-24	1.04	0.77	1.40	0.98	0.74	1.29	0.37	0.26	0.51
Age 25-34	1.47	1.07	2.00	1.14	0.84	1.54	0.64	0.46	0.90
White	0.92	0.64	1.31	0.88	0.63	1.23	0.77	0.51	1.15
Female	1.35	0.97	1.88	1.55	1.13	2.11	1.63	1.11	2.38
1+ childhood events	3.02	2.32	3.92	2.09	1.60	2.73	4.40	3.27	5.90

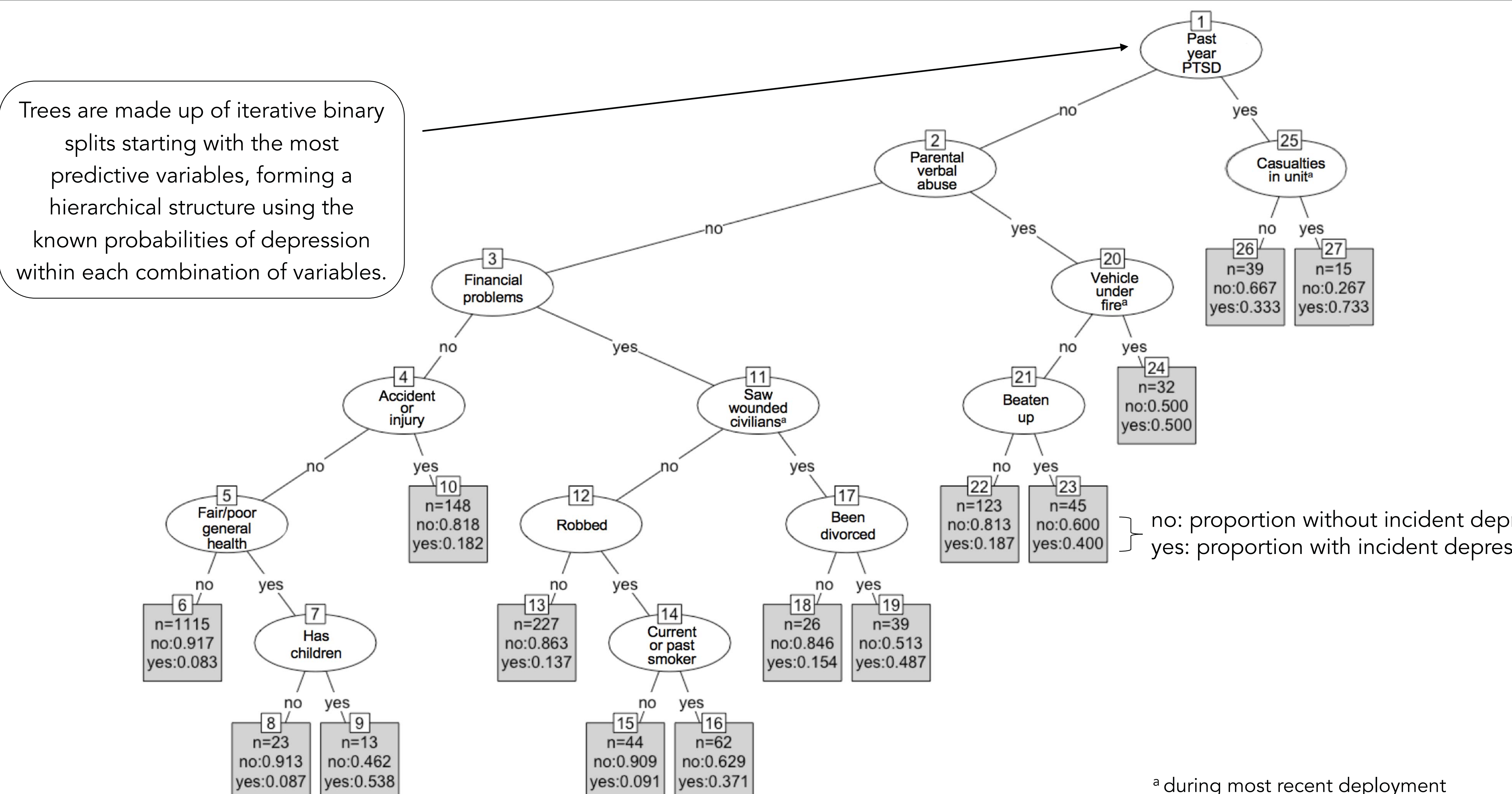
Conclusions

- We identified four distinct latent trajectory groups of depression symptoms across six years in a representative ARNG cohort.
- ARNG Soldiers who reported adverse events during childhood were more likely to have chronically high, decreasing, or increasing numbers of depression symptoms over time, compared to no symptoms.
- This study highlights the importance of considering events throughout the entire lifecourse, not only those that occur during deployment or military engagement, when studying or treating mental health in the U.S. National Guard.

Background and study aim

- Depression is one of the most common mental disorders in the United States (US).
- The US Army National Guard may be particularly at risk for depression, given unique deployment experiences and demographics.
- Traditional statistical methods may fall short on individual-level prediction.
- Machine learning can improve on traditional methods for individual-level prediction.
- Our aim was to determine which variables and combinations of variables are identified as predictors of incident depression across five years in an Army National Guard cohort, using tree classification and random forests, followed by cross-validation.

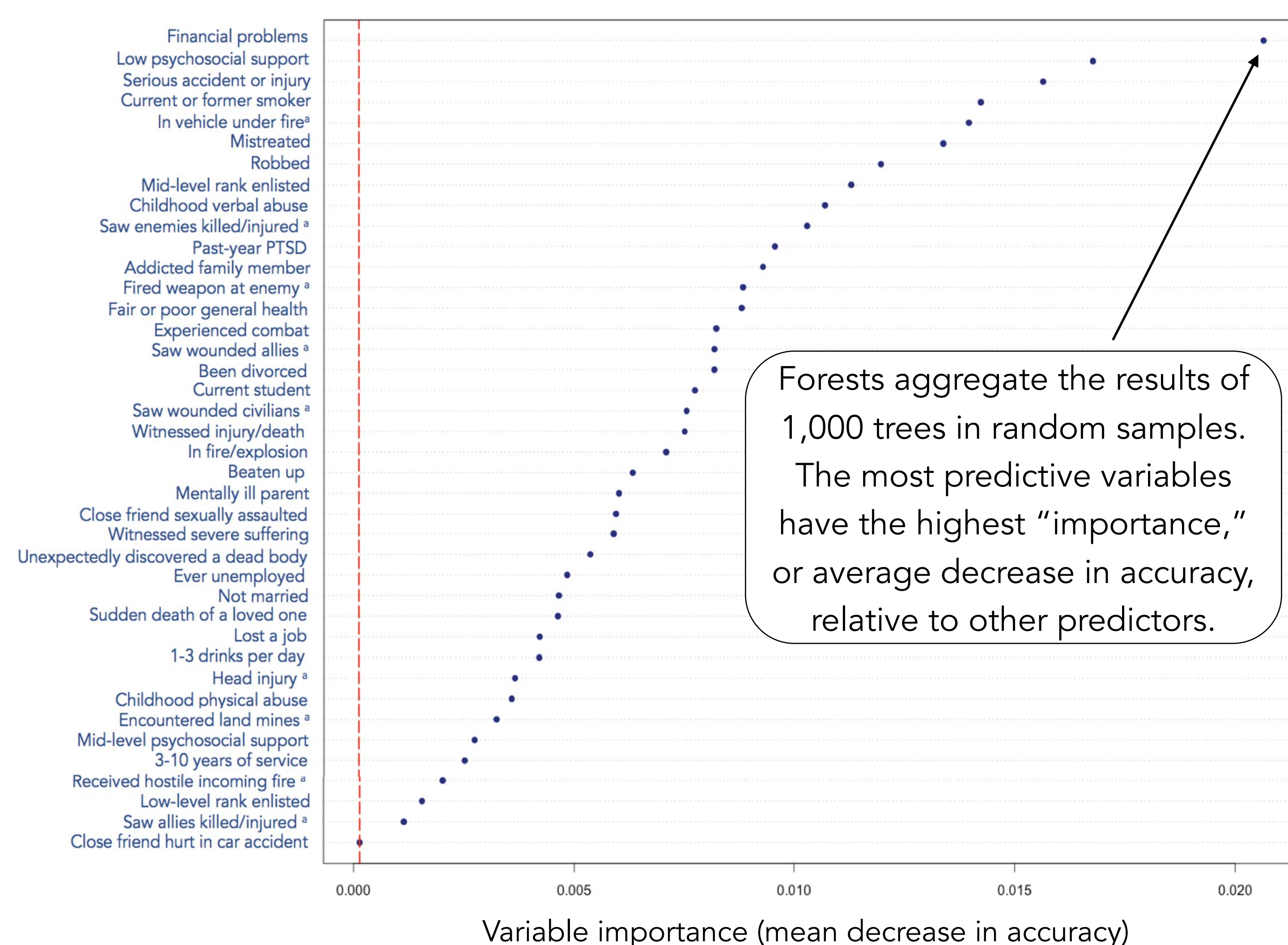
Tree classification for men



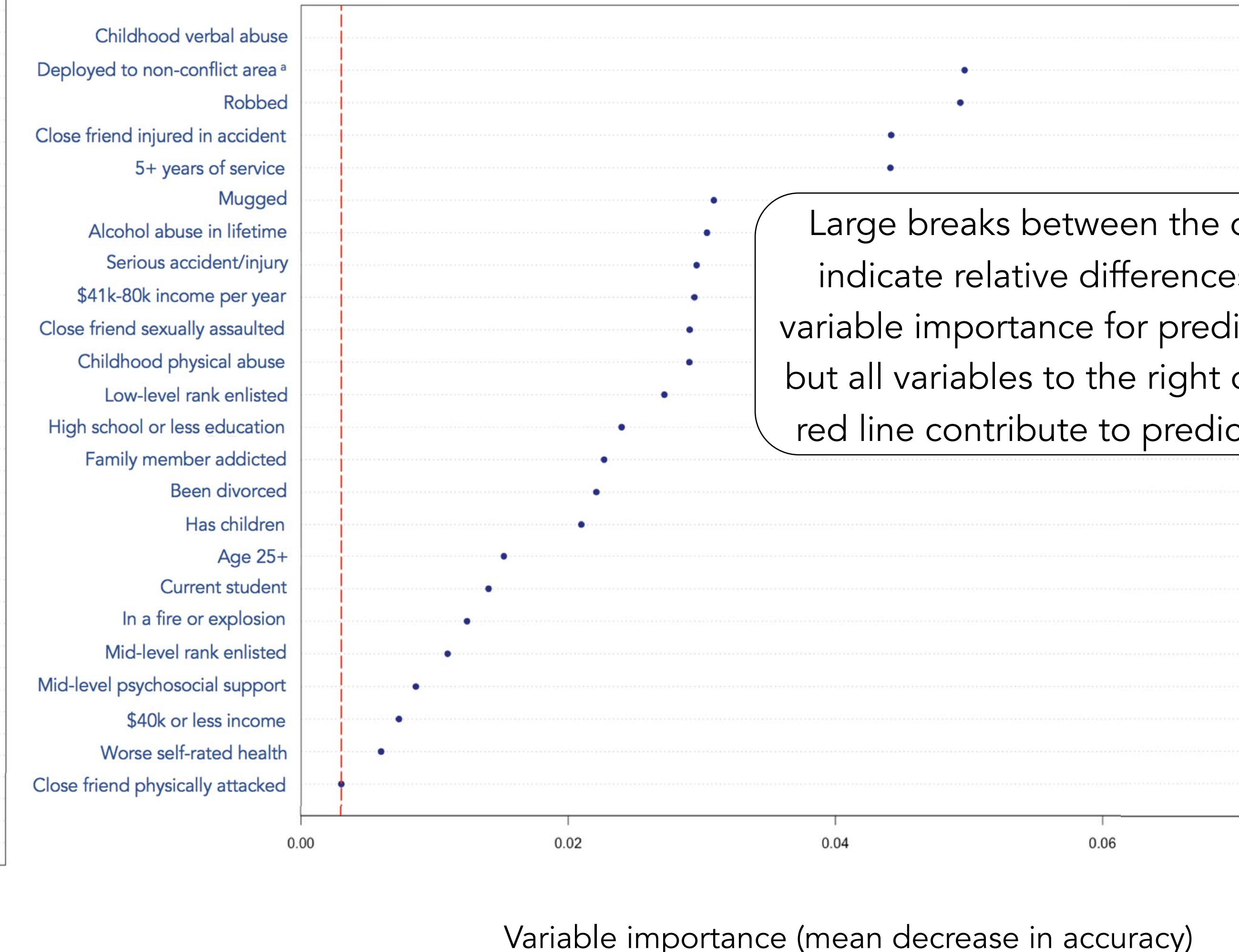
Methods

- Sample: Ohio Army National Guard Mental Health Initiative cohort (n=1,951 men and 298 women).
- Outcome: Binary incident depression during any of the 5 years of follow-up, defined using DSM-IV criteria with the 9-item Patient Health Questionnaire.
- Tree classification was run followed by random forests with 1,000 trees, a minimum of 20 observations per split, and 86 predictor variables with 5 sampled at each node.
- Forests were validated with 10-fold cross-validation.

Variable importance plot for men



Variable importance plot for women



Results

- Across five years of follow-up, incidence of depression was 14.9% among men and 24.8% among women.
- After cross-validation, the random forest AUC was 0.68 for both men and women.

Conclusions

- Stressful and traumatic events, including childhood-specific traumas, were among the most predictive variables.
- Demographic and military characteristics were more predictive of depression for women than for men, for whom deployment experiences tended to be more predictive compared to demographic characteristics.
- This is an important first step at identifying novel interactions between predictors using machine learning methods and helps to bridge the gap between population-level and individual-level prediction of depression.

Ohio Army National Guard Mental Health Initiative

Scientific Advisory Meeting
May 14, 2020



Scientific Investigators

- Joseph Calabrese, MD
 - Coordinating administrative investigator
- Sandro Galea, MD, DrPH
 - Scientific Principal Investigator
- Israel Liberzon, MD
 - Director, Translational Research
- **Nirmala Rajaram, PhD**
 - **Took over for Dr. Liberzon as PI of VERAM when Dr. Liberzon left**

Scientific Investigators

- Cheryl McCullumsmith, M.D., Ph.D.
 - Took over for Dr. Wyrobeck when he went on medical leave
 - Lead on dissemination
- Survey Research Firm: Abt. Associates

Ohio Army National Guard Mental Health Initiative

- Mission and Vision -

- The original vision funded through congressional allocations 2005-2007
 - Longitudinal data, molecular genetics, and primary project as platform for other translational research
- Congressional support for Waves 1-4 (~2009-2012) and Joint Warfighter support for Waves 5-9 (2014-2019)
 - Enrollment suspended during 2013

Achievements

Data Dissemination

- 35 publications
- 60 poster presentations
- 36 oral presentations
- Study website

Recruitment

- 3,841 OHARNG members enrolled
- 11,383 telephone interviews completed
- 1,283 OHARNG members enrolled in to the genetics repository

Agenda

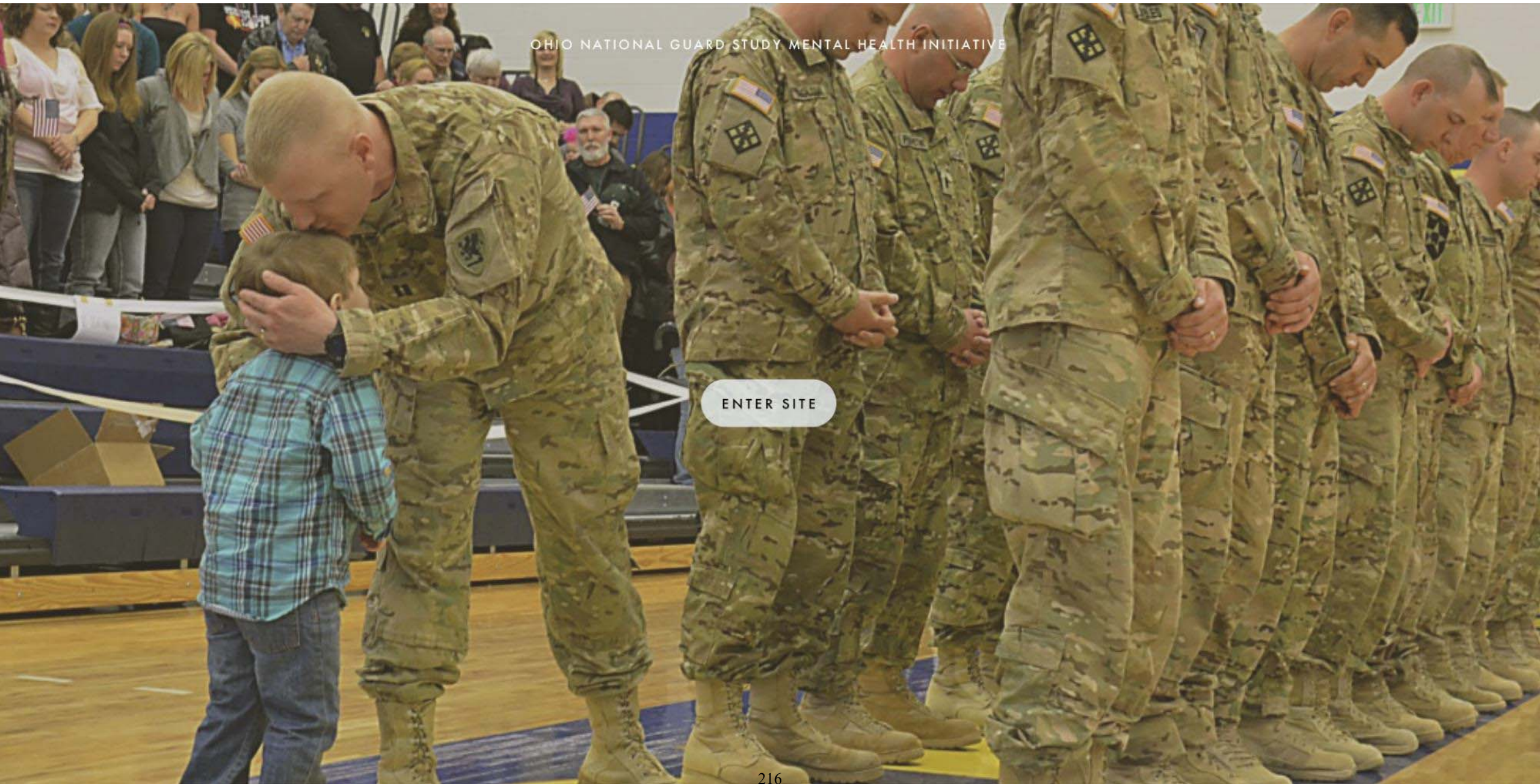
11:00am – 11:15am	Welcome – Dr. Calabrese
11:15am – 11:25am	Dissemination Initiative - Dr. Jon Elhai
11:25am – 11:30am	Q&A
11:30am – 11:50am	Genetics Repository – Dr. Anthony King,
11:50am – 12:00pm	Q&A
12:00pm – 12:30pm	Project GUARD (Alcohol Misuse Study) - Dr. Fred Blow
12:30pm – 12:45pm	Q&A
12:45pm – 1:15pm	Break
1:15pm – 3:15pm	Results Presentation & Discussion – Dr. Sando Galea, Laura Sampson, Greg Cohen and David Fink
3:15pm – 3:45pm	Q&A
3:45pm – 4:00pm	Wrap up

Dissemination Initiative:

www.militarybehavioralhealth.org

Jon Elhai
University of Toledo
Department of Psychology

The Website: Rebuilt On Squarespace



ENTER SITE



Ohio National Guard Study

Mental Health Initiative

This ongoing, 9 year longitudinal study of Ohio Army National Guard members assesses, through annual surveys, military and civilian factors related to mental health risk and resilience. Reserve members, primarily National Guard, have served in significant numbers in recent wars, accounting for over one quarter of all deployments.

This study assesses, over time:

- The development of behavioral health problems; including PTSD, hazardous use of alcohol and other risk-taking behavior, depression, suicidality, and military sexual trauma.
- Resilience, military culture and social support, and personal coping factors.
- Health issues, including traumatic brain injury
- Biological factors for risk and resilience, using genetics and brain imaging in associated studies.

Website Analytics

Traffic

Tue, Jan 1 – Tue, Dec 31, 2019

Last Year

Unique Visitors

110

Visits

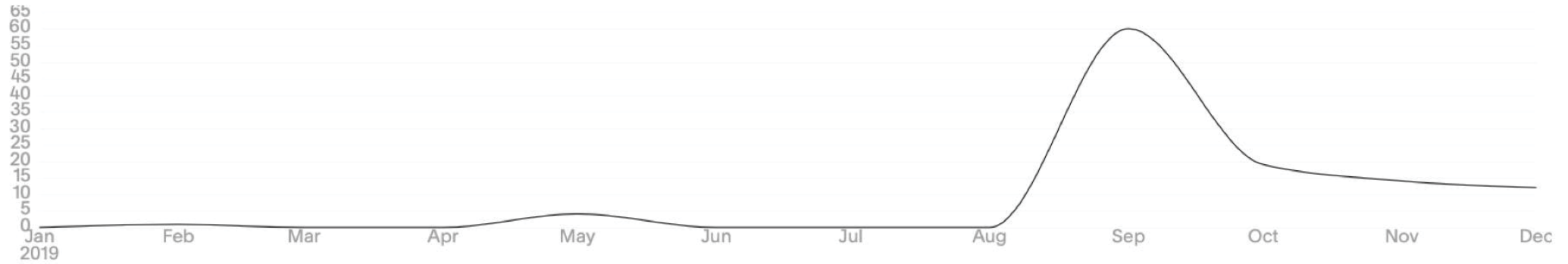
110

Pageviews

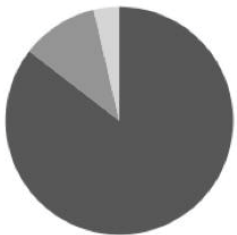
265

Visits

Monthly



Visits by Device Type



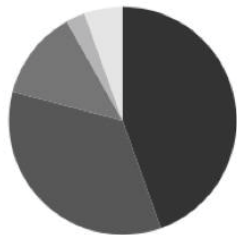
- Desktop
94 (85%)
- Mobile
12 (11%)
- Tablet
4 (4%)

Visits by Source



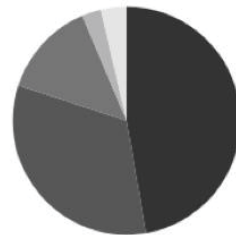
- Direct
65 (60%)
- military...
30 (28%)
- Facebo...
6 (6%)
- Google
2 (2%)
- Others
6 (6%)

Visits by Browser



- Safari
49 (45%)
- Chrome
38 (35%)
- Mobile ...
14 (13%)
- IE
3 (3%)
- Others
6 (5%)

Visits by Operating System



- macOS
52 (47%)
- Windows
36 (33%)

Traffic

Wed, Jan 1 – Thu, May 7, 2020

Year To Date ▾

Unique Visitors

88

+1,157.1% yr/yr

Visits

85

+1,600.0% yr/yr

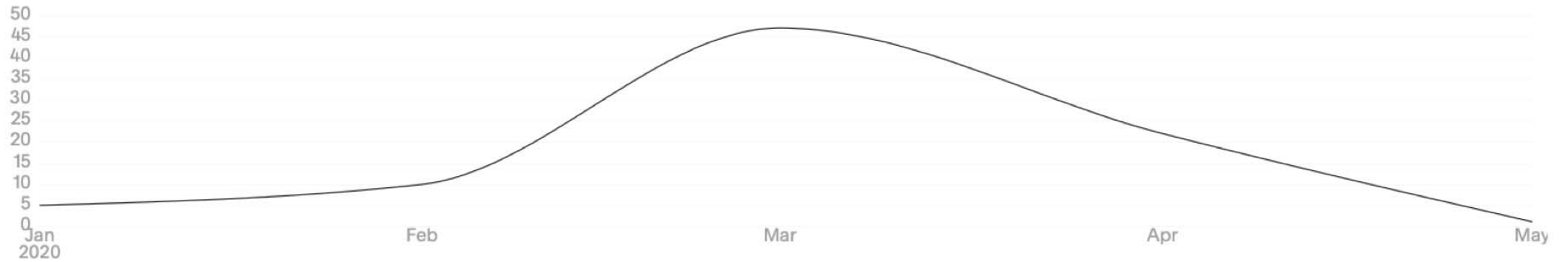
Pageviews

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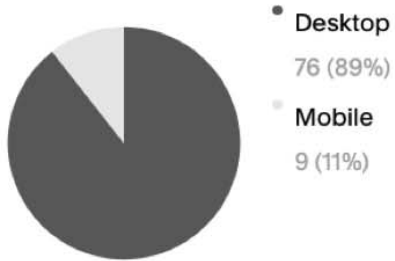
+463.4% yr/yr

Visits

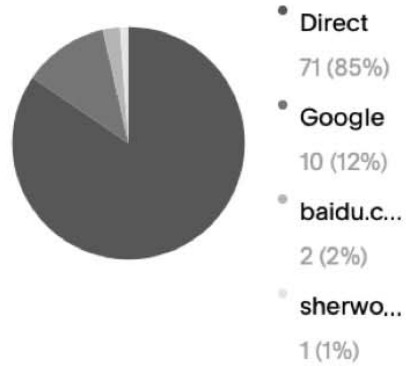
Monthly ▾



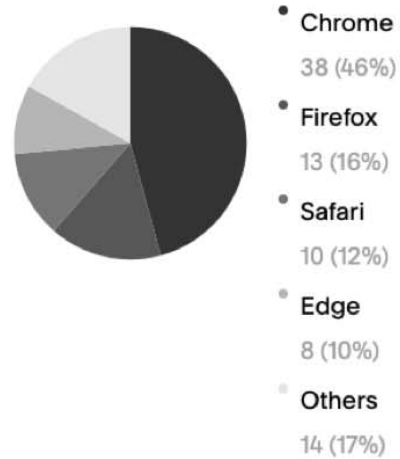
Visits by Device Type



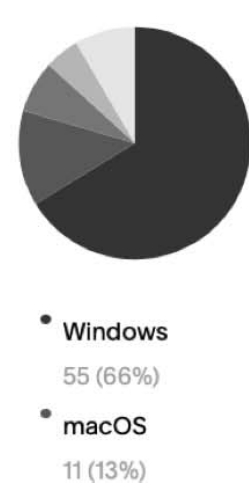
Visits by Source



Visits by Browser



Visits by Operating System



Thanks!

Ohio National Guard Risk and Resilience Project Scientific Advisory Meeting Final Report, May 14, 2020

**OHARNG Translation Studies & PTSD
Genetics Repository**

Site PI: Israel Liberzon, MD, Texas A&M University

Co-I: Anthony King, PhD, Univ. Michigan

Lab Manager: Niramala Rajaram, PhD, Univ. Michigan

PTSD Risk and resilience: gene x environment interactions

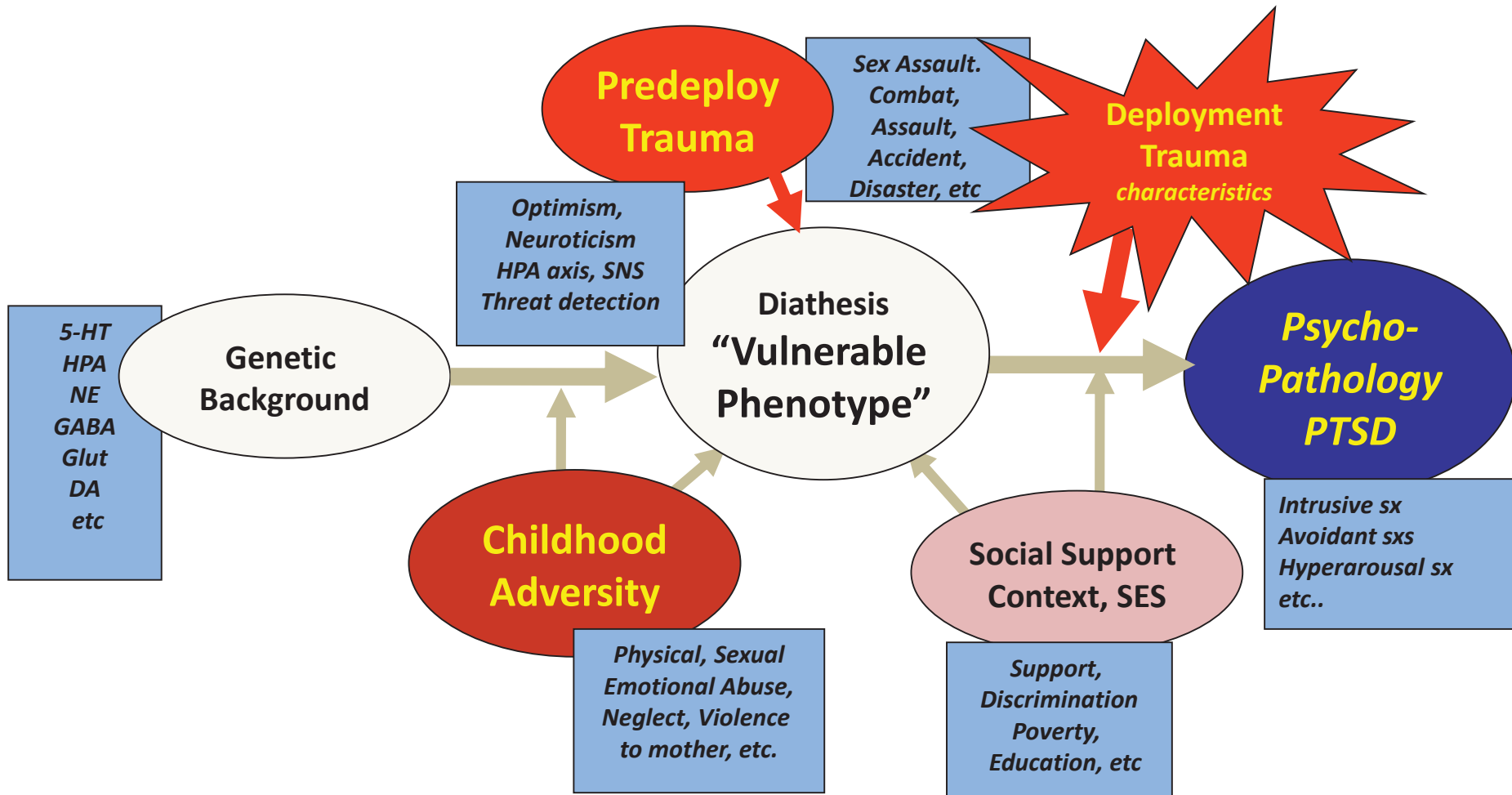


Table 1 Genome-wide association studies (GWAS) in PTSD

Study	Sample size	Significant SNP(s)	Nearest gene	<i>p</i> value	Notes
Logue et al. [39]	Discovery: <i>N</i> = 491 European American Replication: <i>N</i> = 600 African American	rs8042149	RAR related orphan receptor A (RORA)	2.50E-08	
Xie et al. [40]	Discovery: <i>N</i> = 1838 European American <i>N</i> = 3380 African American Replication: <i>N</i> = 1578 European American <i>N</i> = 744 African American	rs6812849	Tolloid like 1 (TLL1)	3.10E-09	
Guffanti et al. [41•]	Discovery: <i>N</i> = 413 African American Replication: <i>N</i> = 2541 European American	rs10170218	LINC01090 (long non-coding RNA)	5.09E-08	
Wolf et al. [42]	Discovery: 484 Non-Hispanic White	rs263232	ADCY8 adenylate cyclase 8 (ADCY8)	6.12E-07	Outcome: Dissociation
Nievergelt et al. [43•]	Discovery: <i>N</i> = 3494 European American, African American, East Asian, Latin American Replication: <i>N</i> = 491 European American	rs6482463	Phosphoribosyl transferase domain containing 1 (PRTFDC1)	2.04E-09	
Almli et al. [44]	Discovery: <i>N</i> = 147 European American, African American, East Asian, Latin American Replication: <i>N</i> = 2006 African American	rs717947	BC036345 (long non-coding RNA)	1.28E-08	
Ashley-Koch et al. [45]	Discovery: 949 Non-Hispanic Black 759 Non-Hispanic White	rs7866350 Non-Hispanic White	TBC1 domain family member 2 (TBC1D2)	1.10E-06	
Stein et al. [46•]	Discovery: 5049 European American 1312 African American 1413 Latin American Replication: 4007 European American 667 African American 1242 Latin American	rs159572 rs11085374	Ankyrin repeat domain 55 (ANKRD55) Zinc finger protein 626 (ZNF626)	2.34E-08 4.59E-08	
Kilaru et al. [47]	Discovery: 3678 African American Replication: <i>N</i> = 205 South African	N/A N/A	Neurologin 1 (NLGN1) ZNRD1-AS1 (long non-coding RNA)	minSNP: 1.00E-06 VEGAS: 1.00E-06	Method: Gene-based
Melroy-Greif et al. [48]	Discovery: 254 Mexican Americans 258 American Indians	rs6681483 rs6667389 rs10888255 rs10888257	Olfactory receptor family 11 subfamily L Member 1 (OR11L1)	1.83E-06	
Duncan et al. [12••]	Discovery: 9954 European American 9691 African American 698 Latin American 387 South African	rs139558732 African American	Kelch-like protein 1 (KLHL1)	3.33E-08 LDSC = 0.36 s.e. = 0.12, <i>p</i> = 3.00E-03 GCTA = 0.21, s.e. = 0.09, <i>p</i> = 1.90E-03	Method: SNP-based heritability Method: SNP-based heritability

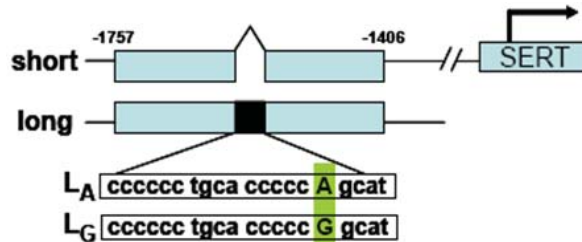
Recent Genetics and Epigenetics Approaches to PTSD

Models for gene Association and Gene x Environment interactions

- Main Effects of SNPs on PTSD symptoms
 - $Y = b_0 + b_1 \text{ SNP} + b_2 \text{ gender}$
- ME Gene, ME Adverse Childhood Event, Gene x CAE interaction
 - $Y = b_0 + b_1 \text{ SNP} + b_2 \text{ CAE} + b_3 \text{ SNP} \times \text{ACE} + b_4 \text{ gender}$
- ME Gene, ME Adverse Childhood Event, Gene x CAE interaction, Lifetime Trauma load, Gene x LT trauma load interaction
 - $Y = b_0 + b_1 \text{ SNP} + b_2 \text{ CAE} + b_3 \text{ SNP} \times \text{ACE} + b_4 \text{ LT trauma} + b_5 \text{ SNP} \times \text{LT trauma} + b_6 \text{ gender}$

Gene x Environment interactions in psychiatric genetics: the role of childhood adversity

Serotonin Transporter Promoter



FKBP5 Interaction with ACE in adult PTSD
Binder, 2007, Klengel 2014

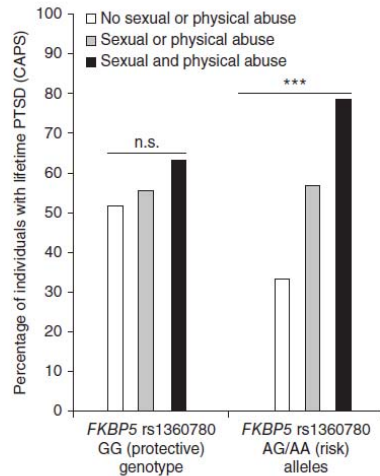
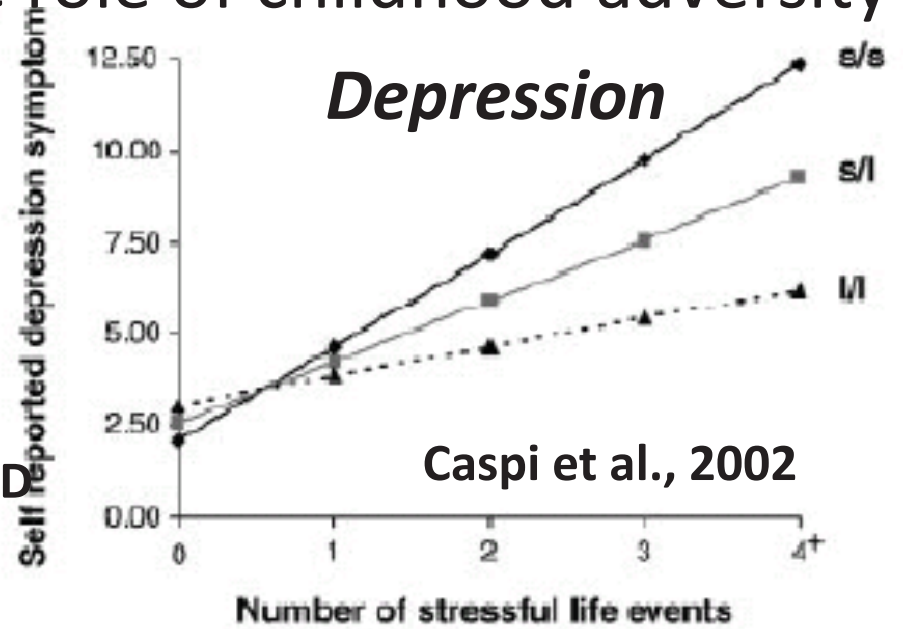
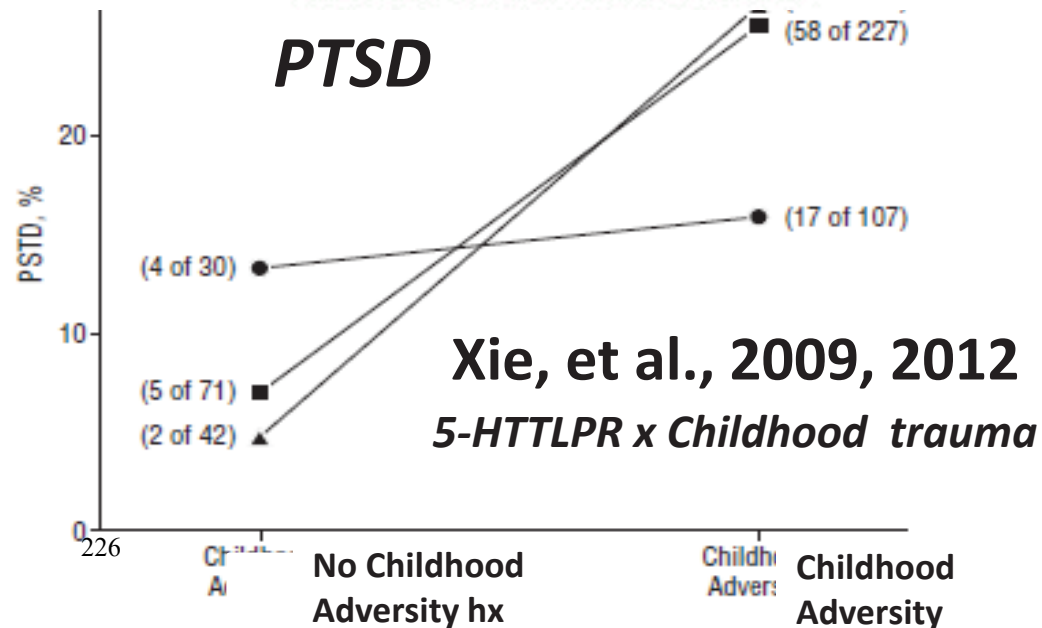


Figure 1 *FKBP5* × childhood abuse interaction on PTSD lifetime diagnosis. Shown is the interaction of child abuse and *FKBP5* rs1360780 protective genotype (left) or risk allele carrier status (right) on percentage lifetime PTSD (CAPS). *FKBP5* protective genotype: no abuse, $N = 133$; one type, $N = 27$; two types, $N = 16$; *FKBP5* risk allele carriers: no abuse, $N = 252$, one type, $N = 69$; two types, $N = 22$ (n.s. $P > 0.05$, *** $P < 0.001$).

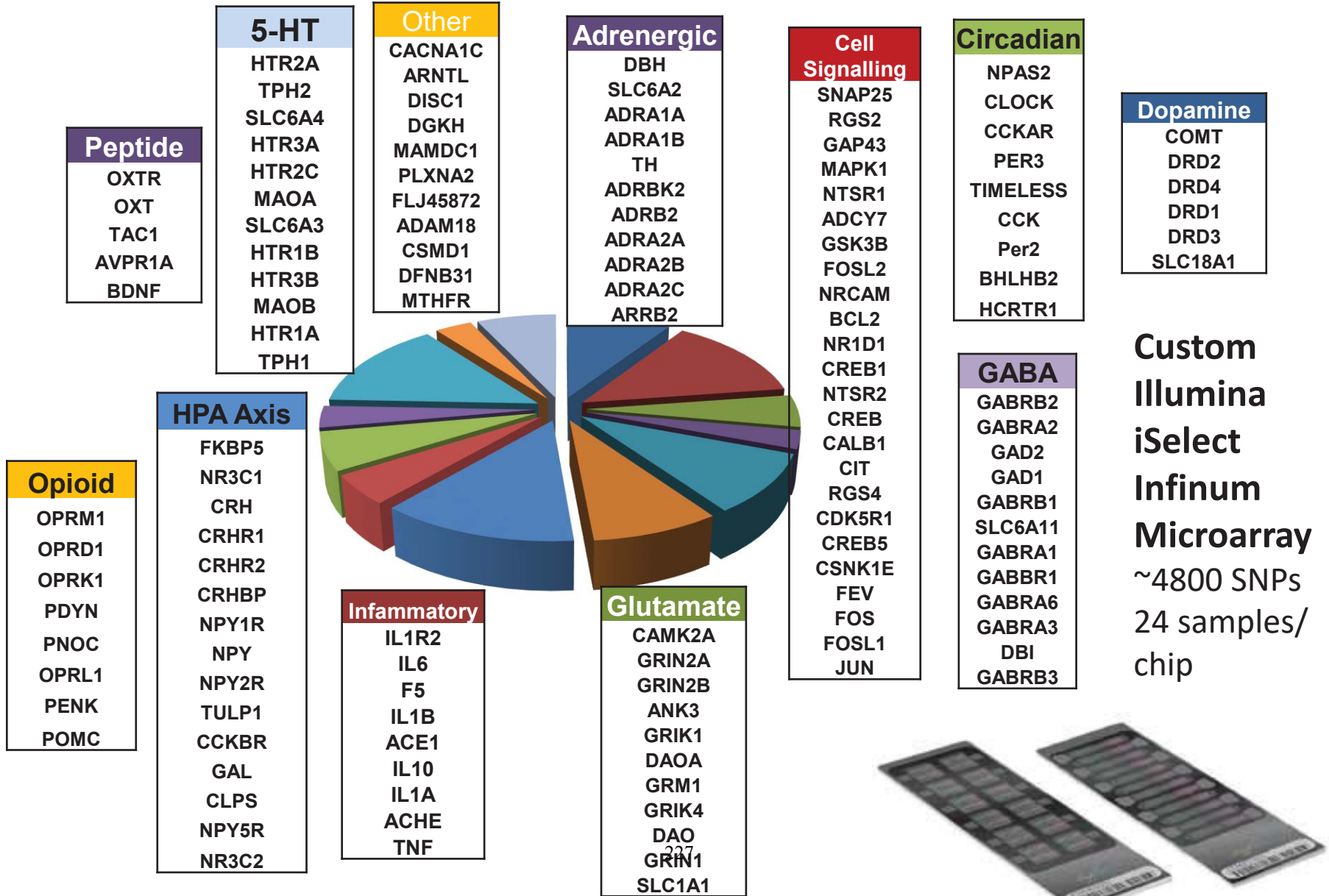


C



Xie, et al., 2009, 2012
5-HTTLPR × Childhood trauma

Initial OHANRG genetic analysis – candidate gene (4800 SNP) Illumina array

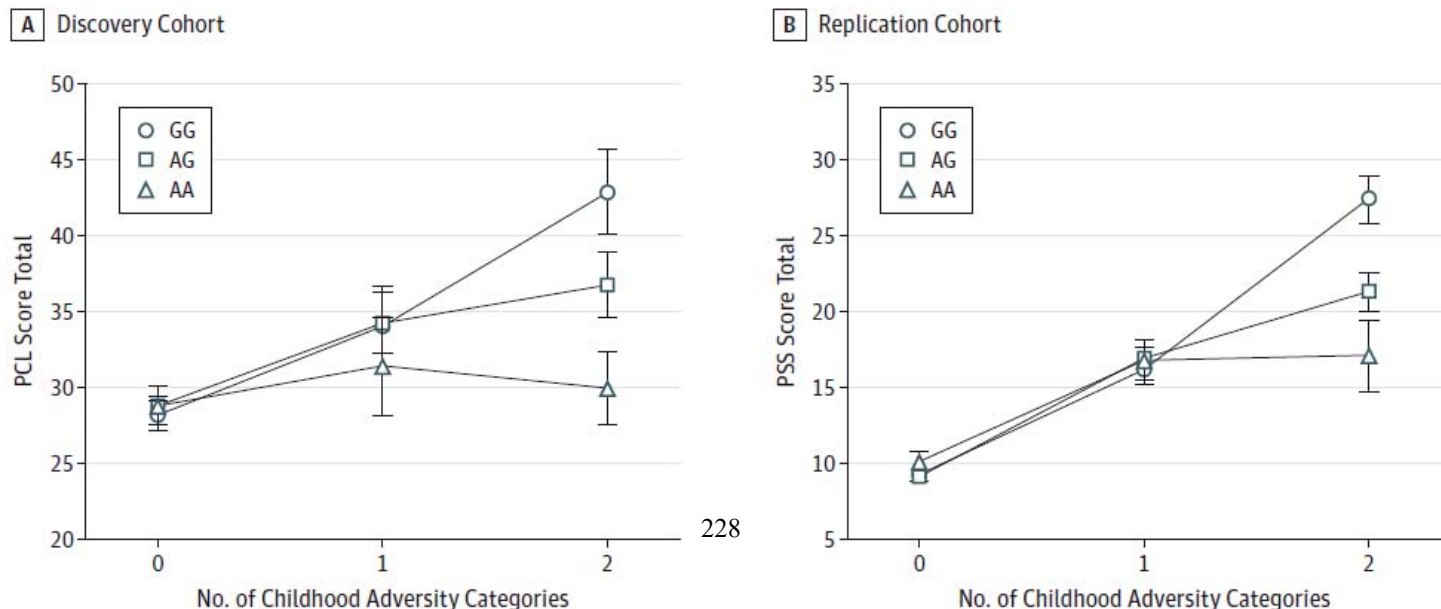


Interaction of the *ADRB2* Gene Polymorphism With Childhood Trauma in Predicting Adult Symptoms of Posttraumatic Stress Disorder

Israel Liberzon, MD; Anthony P. King, PhD; Kerry J. Ressler, MD, PhD; Lynn M. Almlí, PhD; Peng Zhang, PhD; Sean T. Ma, PhD; Gregory H. Cohen, MPH; Marijo B. Tamburrino, MD; Joseph R. Calabrese, MD; Sandro Galea, MD, MPH

- No main effect of SNP in this small array
- SNP x Childhood maltreatment interaction in Discovery (N=715), replication in Grady (N=2100, Ressler et al)
- Subsequent replication in second independent cohort (Hauser, 2017, N=949 African American combat veterans)

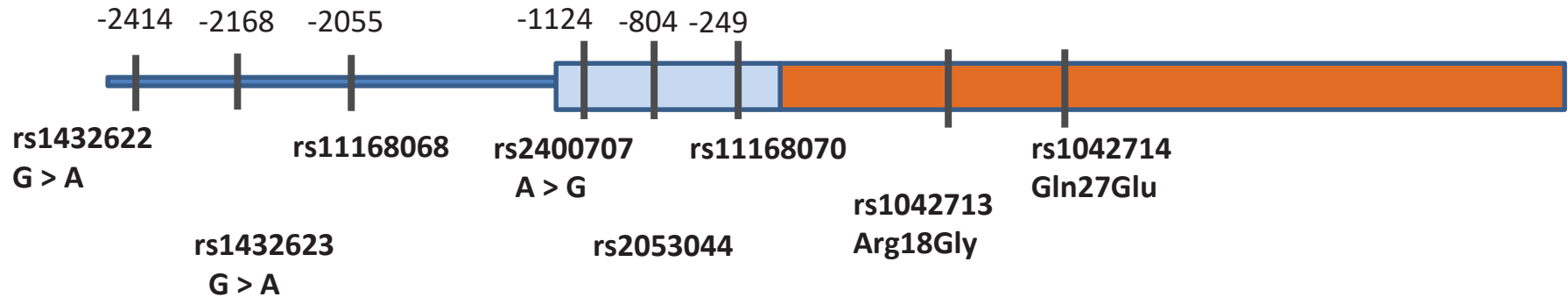
Figure 1. Interaction of *ADRB2* Single-Nucleotide Polymorphism rs2400707 With Childhood Adversity in Adult Posttraumatic Stress Disorder



Beta 2 Adrenergic Receptor SNPs showing G x E interaction

mRNA transcript

ADRB2



SNP	P value
rs1432622	5.41×10^{-6}
rs1432623	5.41×10^{-6}
rs11168068	5.41×10^{-6}
rs2400707	3.82×10^{-6}
rs2053044	5.2×10^{-6}
rs12654778	0.000247
rs11168070	6.74×10^{-6}
rs1042713	0.000193
rs1042714	6.6×10^{-6}

- **Beta 2 Adrenergic Receptor central player in sympathetic nervous system**
- May be important in Brain-Immune system cross-signalling (Elenkov, 2008)
- Haplotypes of these SNPs predict depressed mood, pain sensitivity, and chronic pain (Diatchenko, 2006, 2008)



Further evidence for a role of the ADRB2 gene in risk for posttraumatic stress disorder



Michael A. Hauser^{a, b, *}, Melanie E. Garrett^{a, c}, Yutao Liu^a, Michelle F. Dennis^{d, e, f},
Nathan A. Kimbrel^{d, e, f},
Veterans Affairs Mid-Atlantic Mental Illness Research, Education, and Clinical Center
Workgroup^e, Jean C. Beckham^{d, e, f}, Allison E. Ashley-Koch^{a, c}

Partial Replication of ADRB2 rs2400707 x Childhood Trauma Interaction and adult PTSD

- Veteran cohort of non-Hispanic blacks (NHB; n = 949)
- Veteran cohort of non-Hispanic whites (NHW; n = 759).
- *No main effects were observed for rs2400707 on PTSD diagnosis.*
- **NHB: Gene x Childhood trauma interaction in ADRB2 rs2400707**
- rs2400707 each additional A allele, the odds of having PTSD increased by 1.31,
- but only among those who had experienced childhood trauma (p = 0.038).

[Interaction of the ADRB2 gene polymorphism with childhood trauma in predicting adult symptoms of posttraumatic stress disorder.](#)

Liberzon I, King AP, Ressler KJ, Almli LM, Zhang P, Ma ST, Cohen GH, Tamburrino MB, Calabrese JR, Galea S. JAMA Psychiatry. 2014 71(10):1174-82. doi: 10.1001/jamapsychiatry.2014.999.

[Largest GWAS of PTSD \(N=20 070\) yields genetic overlap with schizophrenia and sex differences in heritability.](#)

Duncan LE, Ratanatharathorn A, Aiello AE, Almli LM, Amstadter AB, Ashley-Koch AE, Baker DG, Beckham JC, Bierut LJ, Bisson J, Bradley B, Chen CY, Dalvie S, Farrer LA, Galea S, Garrett ME, Gelernter JE, Guffanti G, Hauser MA, Johnson EO, Kessler RC, Kimbrel NA, King A, Koen N, Kranzler HR, Logue MW, Maihofer AX, Martin AR, Miller MW, Morey RA, Nugent NR, Rice JP, Ripke S, Roberts AL, Saccone NL, Smoller JW, Stein DJ, Stein MB, Sumner JA, Uddin M, Ursano RJ, Wildman DE, Yehuda R, Zhao H, Daly MJ, **Liberzon I, Ressler KJ, Nievergelt CM, Koenen KC.**

Mol Psychiatry. 2018 23(3):666-673. doi: 10.1038/mp.2017.77

[International meta-analysis of PTSD genome-wide association studies identifies sex- and ancestry-specific genetic risk loci.](#)

Nievergelt CM, Maihofer AX, Klengel T, Atkinson EG, Chen CY, Choi KW, Coleman JRI, Dalvie S, Duncan LE, Gelernter J, Levey DF, Logue MW, Polimanti R, Provost AC, Ratanatharathorn A, Stein MB, Torres K, Aiello AE, Almli LM, Amstadter AB, Andersen SB, Andreassen OA, Arbisi PA, Ashley-Koch AE, Austin SB, Johnson EO, Jones I, Jovanovic T, Qin XJ, Junglen AG, Karstoft KI, Kaufman ML, Kessler RC, Khan A, Kimbrel NA, King AP, Koen N, Kranzler HR, Luykx JJ, Lyons MJ, Maples-Keller J, Marmar C, Martin AR, Martin NG, Maurer D, Mavissakalian MR, McFarlane A, McGlinchey RE, McLaughlin KA, McLean SA, McLeay S, Mehta D, Milberg WP, Miller MW, Morey RA, Morris CP, Mors O, Mortensen PB, Neale BM, Nelson EC, Nordentoft M, WK, Trapido E, Uddin M, Ursano RJ, van den Heuvel LL, Van Hooff M, Vermetten E, Vinkers CH, Voisey J, Wang Y, Wang Z, Werge T, Williams MA, Williamson DE, Winternitz S, Wolf C, Wolf EJ, Wolff JD, Yehuda R, Young RM, Zhao H, Zoellner LA, **Liberzon I, Ressler KJ, Haas M, Koenen KC.**

Nature Commun. 2019 Oct 8;10(1):4558. doi: 10.1038/s41467-019-12576-w.

OHARNG Contributions to Psychiatric Genomics Consortium PTSD Committee

	Initial cohort	remainder	Total
PTSD Cases	125	82	207
Combat Controls (Matched)	125	759	884
			1091



Illumina Psych Array BeadChip. Developed w/ Psychiatric Genomics Consortium for large-scale genetic studies of psychiatric disorders.

Content for the Infinium PsychArray-24

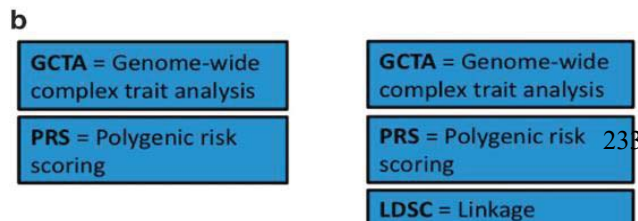
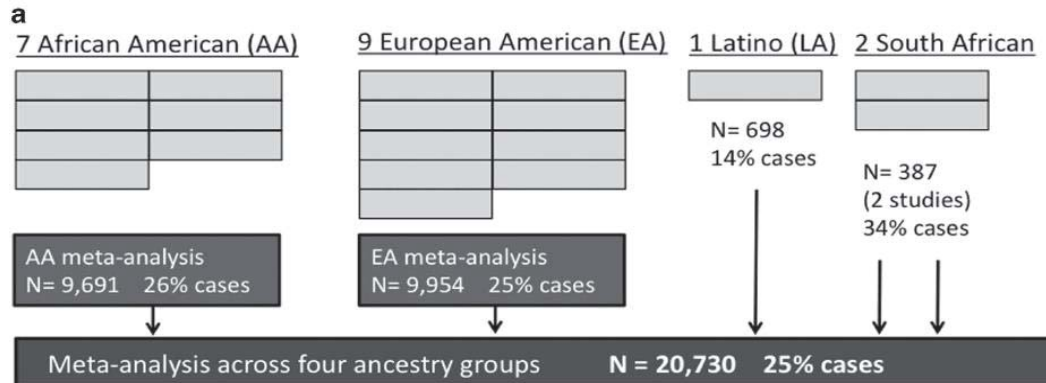
- 265,000 proven tag SNPs found on the Infinium Core-24
- 245,000 markers from the Infinium Exome-24 BeadChip,
- 50,000 additional markers associated with common psychiatric disorders
- (Schizophrenia, bipolar disorder, ASD, ADHD, OCD, anorexia, Tourette's syndrome)

- Obtained permissions from Dept VA ORD to share OHARNG genetic (GWAS) and limited phenotype data (e.g. demographics, trauma exposures, PTSD, MDD, AUD) with Psychiatric Genomics Consortium
- This allowed us obtain funding from CVB for Genome-wide genotyping for our OHARNG sample

ORIGINAL ARTICLE

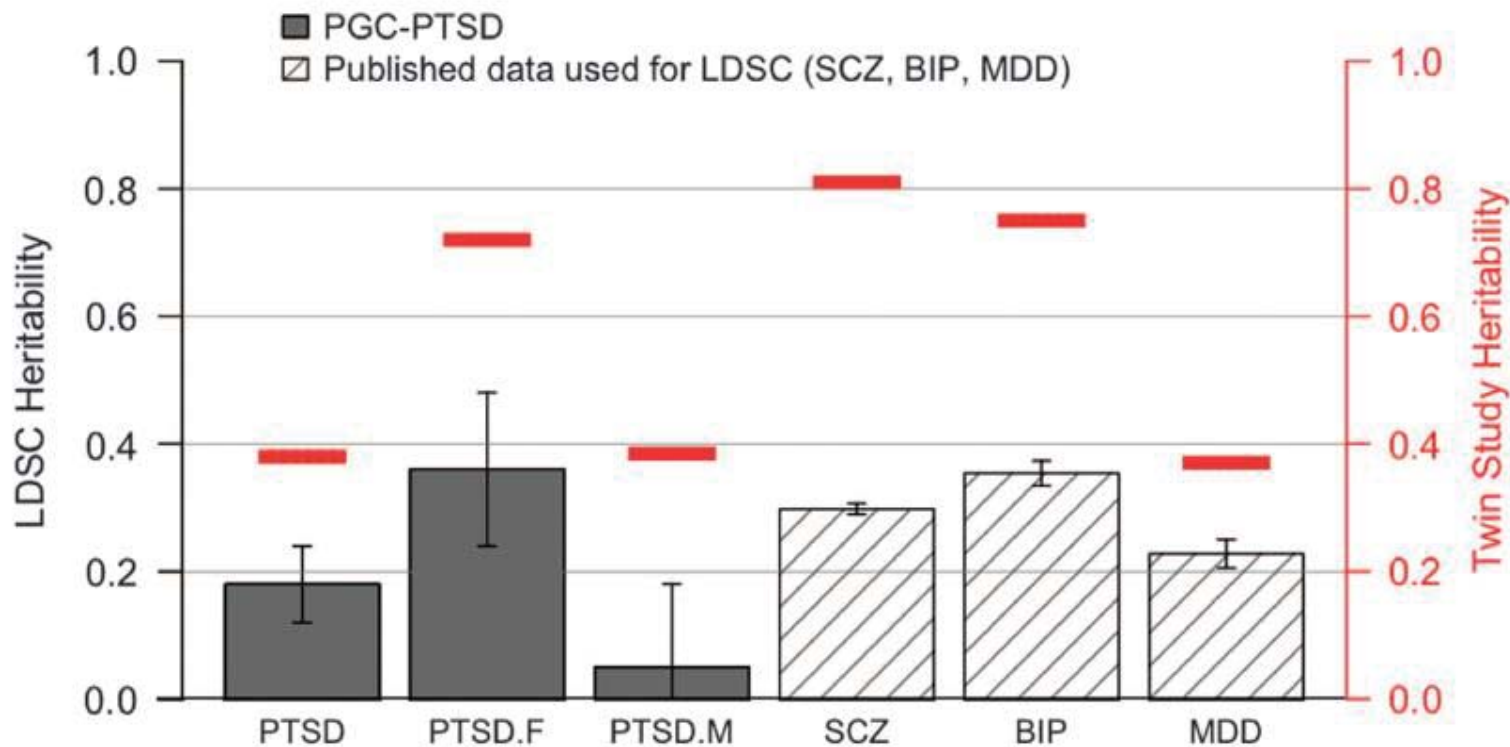
Largest GWAS of PTSD ($N = 20070$) yields genetic overlap with schizophrenia and sex differences in heritability

LE Duncan^{1,2,3}, A Ratanatharathorn⁴, AE Aiello⁵, LM Almli⁶, AB Amstadter⁷, AE Ashley-Koch⁸, DG Baker^{9,10}, JC Beckham^{11,12}, LJ Bierut¹³, J Bisson¹⁴, B Bradley^{15,16}, C-Y Chen^{3,17,18}, S Dalvie¹⁹, LA Farrer²⁰, S Galea²¹, ME Garrett⁸, JE Gelernter²², G Guffanti^{18,23}, MA Hauser⁸, EO Johnson²⁴, RC Kessler²⁵, NA Kimbrel^{11,12}, A King²⁶, N Koen^{27,28}, HR Kranzler²⁹, MW Logue^{30,31}, AX Maihofer³², AR Martin^{2,3}, MW Miller^{30,33}, RA Morey^{12,34}, NR Nugent^{35,36}, JP Rice³⁷, S Ripke^{2,3,38}, AL Roberts³⁹, NL Saccone⁴⁰, JW Smoller^{2,17}, DJ Stein^{27,28}, MB Stein^{32,41,42}, JA Sumner⁴³, M Uddin⁴⁴, RJ Ursano⁴⁵, DE Wildman⁴⁶, R Yehuda^{47,48}, H Zhao⁴⁹, MJ Daly^{2,3}, I Liberzon^{26,50}, KJ Ressler^{18,23}, CM Nievergelt^{9,10} et al.



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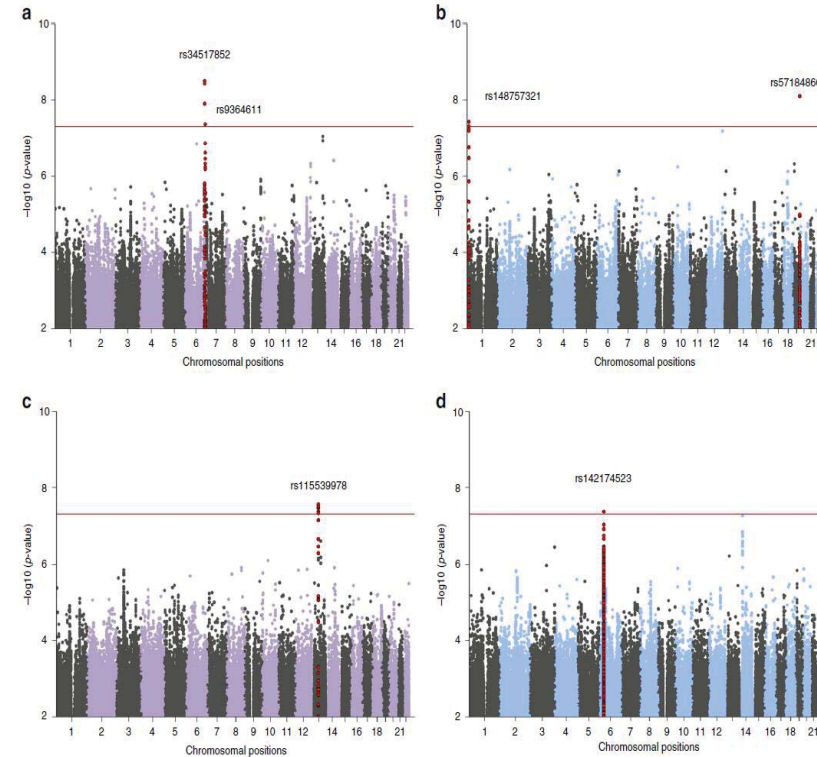
PGC=psychiatric genomics consortium, PTSD=posttraumatic stress disorder, LDSC=Linkage Disequilibrium Score Regression, SCZ=schizophrenia, BIP=bipolar disorder, MDD=major depressive disorder

International meta-analysis of PTSD genome-wide association studies identifies sex- and ancestry-specific genetic risk loci

Caroline M. Nievergelt et al.[#]

Largest to date – Meta-analysis

- 30,000 PTSD cases
- 170,000 controls
- 5-20% SNP-based heritability of PTSD
- 6 Genome-wide SNPs overall
- 2 in European, 1 in African ancestry
- 3 in men only
- PARK2 – a Parkinson's disease associated gene regulates dopamine
- Polygenic Risk scores (PRS) predict PTSD re-experiencing, in MVP **but specific loci are not replicated in MVP**



OHARNG Genetics – Adult and childhood trauma data available for future G x E studies?

- **ONG contributed >1,000 genetic samples to GWAS**
- GWAS 1: Duncan et al., 2018: 20,000 subjects – a single genome-wide SNP (main effect of SNP on PTSD diagnosis) in African ancestry only and lack of replications of previous SNPs
- GWAS 2: Nievergelt et al., 2019: 200,000 subjects identification of 6 genome-wide SNPs, including one in PARK2 – dopamine regulation genes – did not replicate previous and were not replicated in MVP
- *Considerable variability in world-wide PGC trauma exposure data – different samples, assessments, measures, etc.*

Gene x Environment (Childhood and Adult Trauma) Interaction analyses?

- **OHARNG has detailed assessment of both Deployment-related Traumas as well as Life-time adult “non-deployment” traumas, and PCL-S scores indexed to these traumas**
- OHARNG “yes/no” items assessing childhood physical, sexual, emotional abuse/ maltreatment and SMI adult in childhood home
- OHARNG relatively homogeneous sample with shared exposures

Longitudinal psychiatric measures?

Early Intervention to Reduce Alcohol Misuse and Abuse in the Ohio Army Reserve National Guard

Scientific Advisory Board Meeting

May 14, 2020



Principal Investigators

Coordinating PI: Joseph R. Calabrese, MD
Case Western Reserve University

Scientific PI: Frederic Blow, PhD
Department of Veterans Affairs and
University of Michigan

Site PI: Cheryl McCullumsmith, M.D., Ph.D.
University of Toledo

Collaborators & Acknowledgements

University of Michigan

Amy Bohnert, PhD

Kristen Barry Haenchen, PhD

Mark Ilgen, PhD

Maureen Walton, PhD

Case Western Reserve University

Richard McCormick, PhD

Ohio Army National Guard

CPT David Kirker

Colin Fowler, LPCC-S

Background and Rationale

Problem Addressed

- Hazardous use of alcohol is a significant problem in the National Guard members that contributes to and complicates other problems including PTSD, depression, suicidality, lowered resilience and work performance.
- Studies consistently find that substantial number of Guard members misuse alcohol.
- Addressing misuse is particularly challenging in reserve component soldiers who are geographically dispersed and must divide their time between military and civilian responsibilities.

Theoretical Rationale

- Screening, Brief Intervention and Referral to Treatment model has been shown to effectively impact misuse on population basis.
- An eHealth intervention, tailored to National Guard, could provide a cost effective tool to enhance alcohol programming. New surveys verify that over half of Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) veterans willing to use E-mental health (highest rates for youngest)

Research Questions and Hypotheses

The specific aims are to compare SP-BI and EUC in:

1. Reducing the frequency and intensity of at-risk drinking at 4 -, 8- and 12-months;
2. Decreasing binge drinking at 4-, 8- and 12 months.

Hypotheses for specific aims:

1. Participants randomized to the SP-BI condition will report significantly fewer days/week drinking and fewer drinks/day than participants in the EUC condition at follow-ups.
2. Participants randomized to the SP-BI condition will report significantly fewer binge drinking episodes compared to the EUC participants at follow-ups.

Design and Methodology

Phase I: Development of Phone App Intervention

- Informed by literature and initial experience in NIAAA-funded Michigan National Guard Web-based study
- Investigators and app developers, in collaboration with a team of Ohio Guard members, brainstormed best options for phone app
- Focused on shortening initial interaction (compared to web approaches) and maximizing engagement in an ongoing therapeutic/educational interaction
- Emphasized relevance to complex life patterns of Guard members (e.g. military commitment, civilian employment, other civilian roles, deployment disruptions and stress)

Design and Methodology

Phase II: Randomized Trial of App Intervention

- Participants were pre-screened for eligibility, then consented
- Eligibility:
 - Past 4-month AUDIT-C score of 5 for men and 4 for women
 - Current or former member of the OHARNG
 - Not in substance use treatment
 - Own a smartphone
- Complete baseline assessment (~40 minutes)
- Randomization stratified by gender and severity of use
- Two groups:
 - Smart Phone App Brief Intervention (SP-BI) (12 weeks)
 - Enhanced Usual Care (EUC) (Brochure with Resources)
- 4, 8, 12 month follow-up assessments
- Payment: \$35 for Baseline, 4-month and 8-month surveys; \$40 for 12-month survey; additional \$15 for those in SP-BI who complete a post-app survey

Study Progress

Regulatory:

- All sites have Instructional Review Board (IRB) and U.S. Army Medical Research and Materiel Command Human Research Protections Office (USAMRMC) approval
- Certificate of Confidentiality obtained from NIH

Phase I: Development of Intervention App

- App modified and IRB changes made for removal of contingency management functions as requested by USAMRMC
- App has been fully developed, beta tested for both iOS and Android platforms, and is available in app stores
- Early enrollees carefully monitored for glitches in app that might reduce compliance

Study Progress

Phase II: Recruitment

- Enrollment began March, 2017 and was completed February, 2020.
- Enrollment was conducted with three parallel approaches:
 - 1) Ohio Army National Guard Mental Health Initiative (OHARNG-MHI) longitudinal platform study, ongoing cohort: These subjects (N=3,651) have participated for the past six years in an annual assessment, and have participated in other studies. For this study we will include only those who are still presently in the Guard (~45%) and meet drinking criteria.
 - 2) OHARNG-MH longitudinal platform, replenishment cohorts: Each year new subjects are added to the platform to replenish the sample, we will have access to the 2017 and 2018 samples (N=1,000). All will be currently in the ONG.
 - 3) Active Ohio Army National Guard members recruited at their Periodic Health Assessments (PHA): ONG brings all units to a central location early in the calendar year for a full day to complete the PHA. We have obtained the required approvals and now have a physical presence at the PHA's to recruit in person.

Study Progress

Changes implemented to improve recruitment

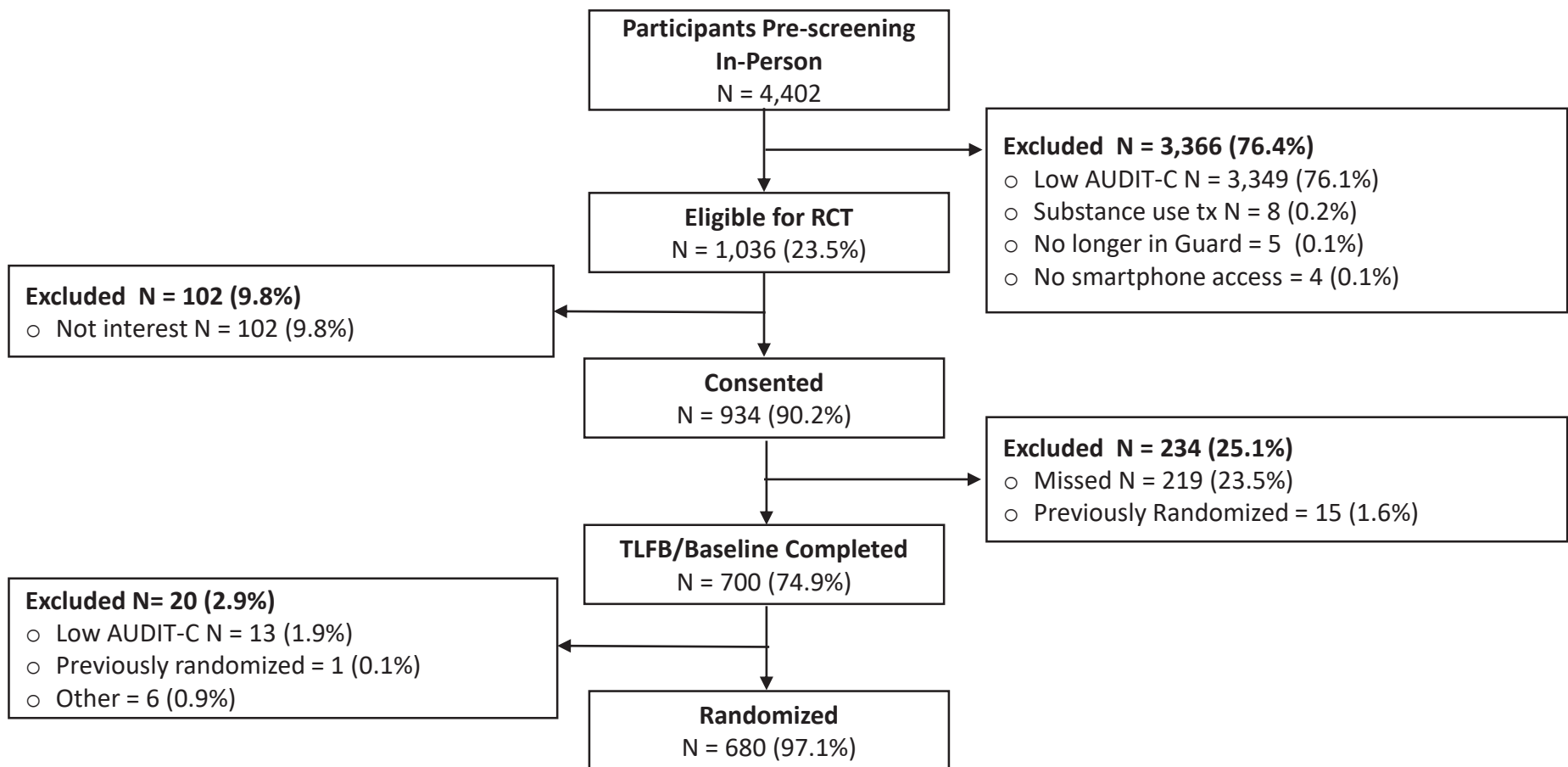
- Changed inclusion criteria to allow for OHARNG members who were no longer active in the Guard
- Provided those who pre-screened with a \$10 Amazon e-gift card and small gifts as a thank you (mini-notebooks and small wallets)

Changes implemented to improve retention

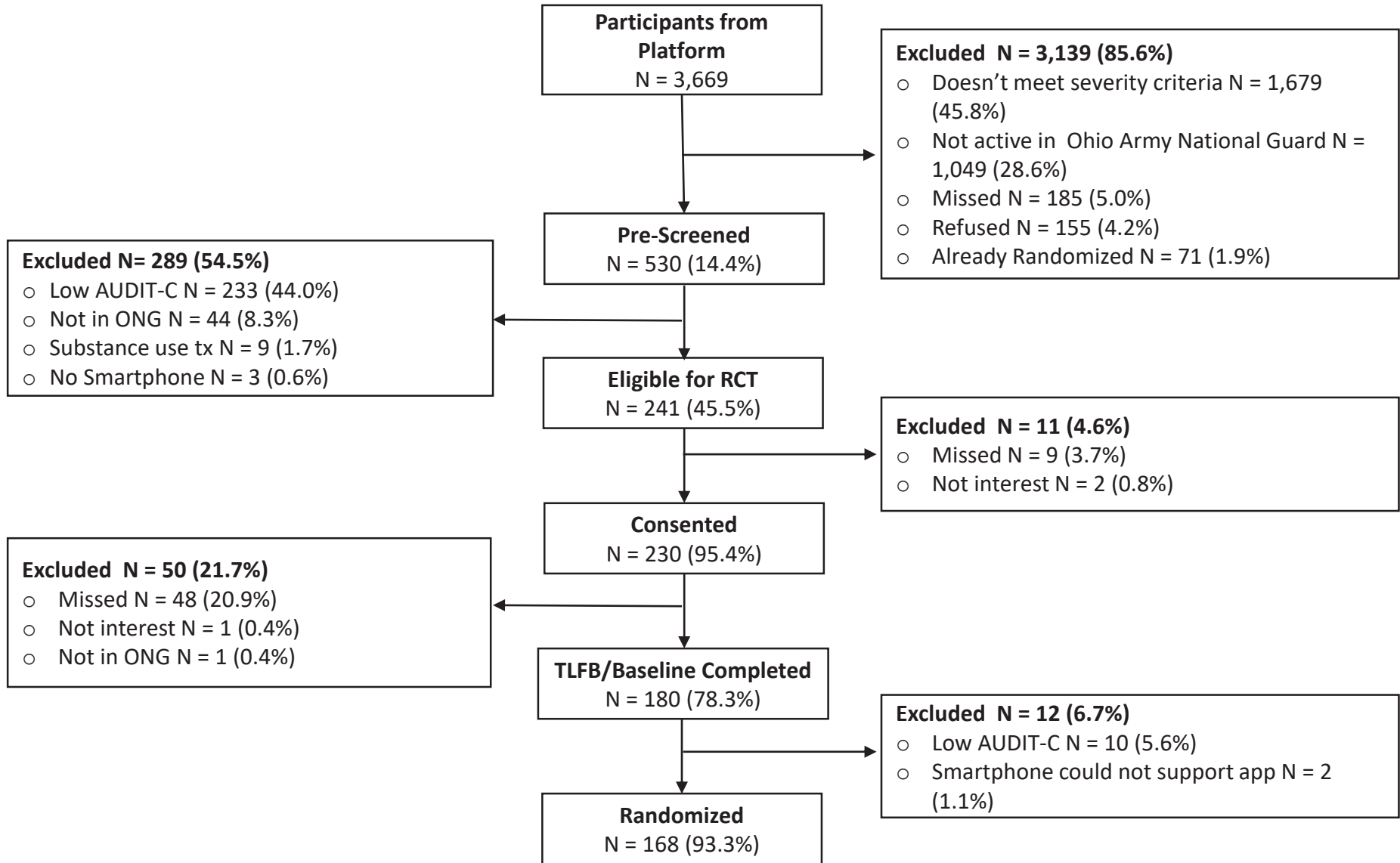
- Provided small gifts in between survey time points (calendar magnets, letter openers, ear buds, cellphone pockets)
- Working to increase 12-month stipend from \$40 to \$50

In order to account for lower than anticipated follow-up rates, we increased the total number of subjects randomized from 750 to 850

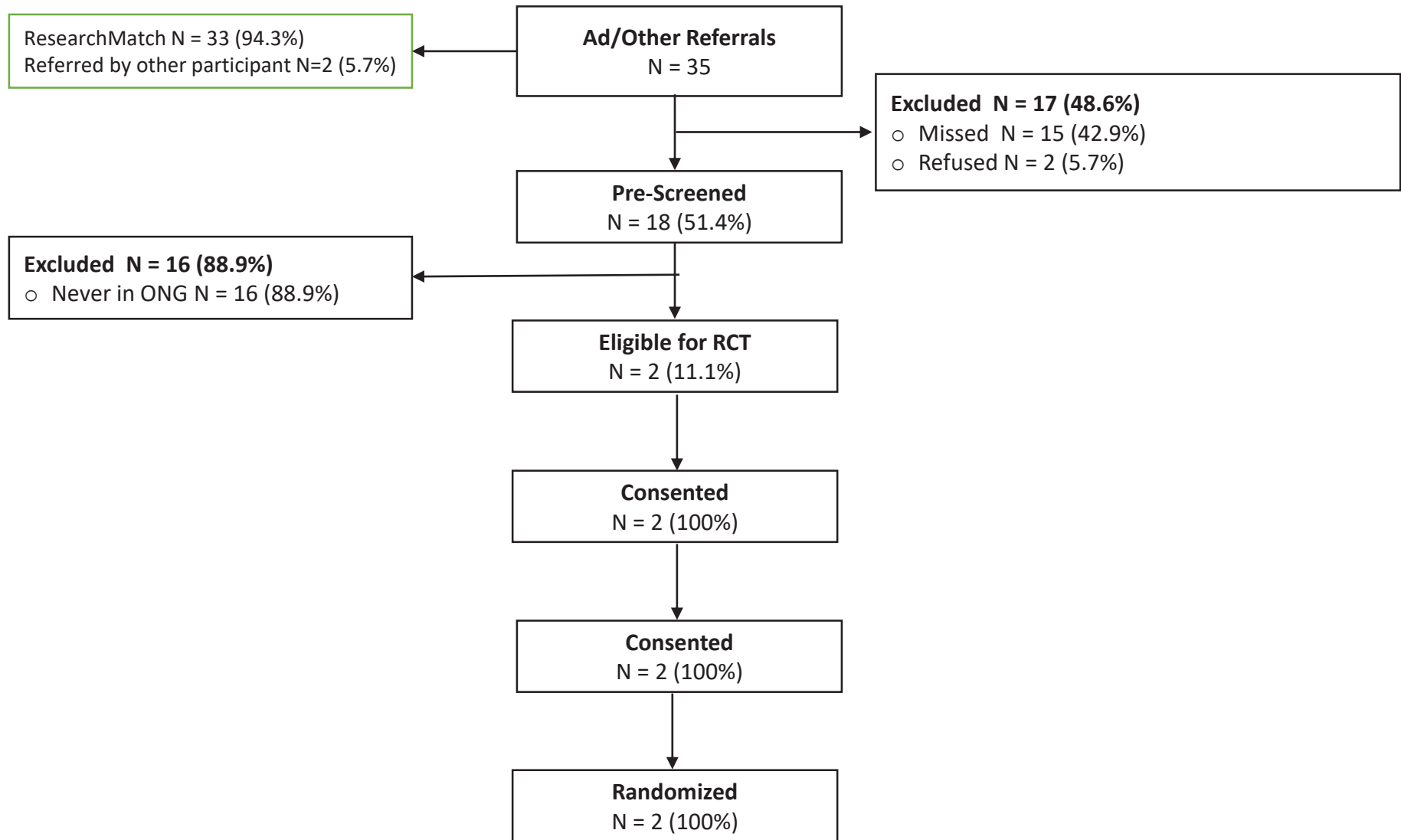
Enrollment – In-Person



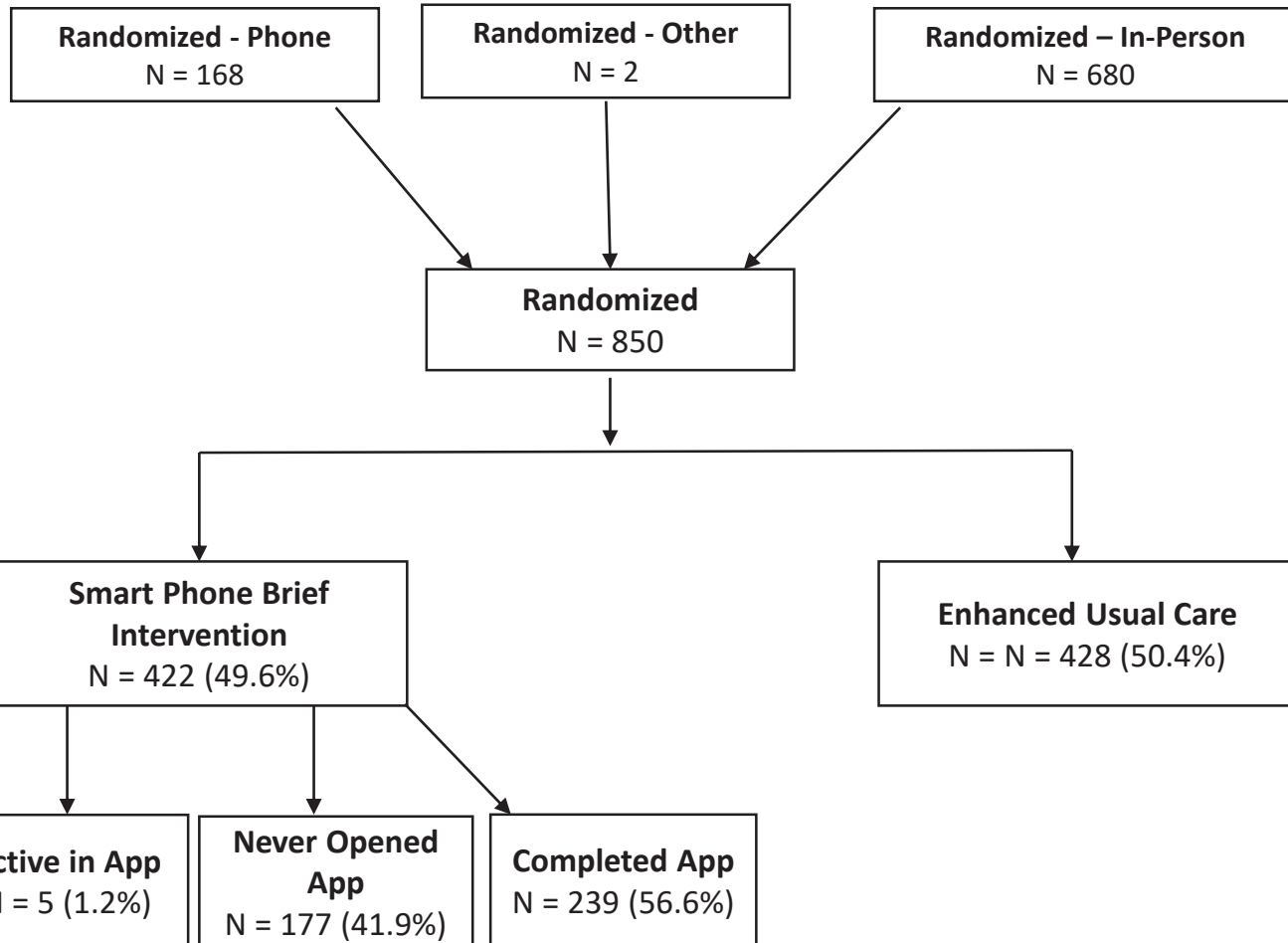
Enrollment - Phone



Enrollment – Ad/Other Referrals



Randomization



4 Month Follow Up

	Smart Phone		Control		Total	
	372		378		750	
	N	%	N	%	N	%
In Progress (≤ 14 days)	7	1.9%	5	1.3%	12	1.6%
Outstanding (>15 days)	43	11.6%	24	6.3%	67	8.9%
Completed	190	51.1%	256	67.7%	446	59.5%
Not Completed	132	35.5%	93	24.6%	225	30.0%

8 Month Follow Up

	Smart Phone		Control		Total	
	256		265		521	
	N	%	N	%	N	%
In Progress (≤ 14 days)	6	2.3%	7	2.6%	13	2.5%
Outstanding (>15 days)	14	5.5%	18	6.8%	32	6.1%
Completed	127	49.6%	141	53.2%	268	51.4%
Not Completed	109	42.6%	99	37.4%	208	39.9%

12 Month Follow Up

	Smart Phone		Control		Total	
	198		206		404	
	N	%	N	%	N	%
In Progress (≤ 14 days)	6	3.0%	5	2.4%	11	2.7%
Outstanding (>15 days)	32	16.2%	29	14.1%	61	15.1%
Completed	111	56.1%	123	59.7%	234	57.9%
Not Completed	49	24.7%	49	23.8%	98	24.3%

Enrollment



Follow On Work

- eHealth app interventions have many advantages, including the ability to present detailed interactive interventions and allow the Guard member to establish personalized plans for change and receive frequent reminders, updated information and virtual support services.
- Based on results of these two studies (this phone app intervention and the NIAAA Web-based intervention) additional innovations will be proposed and tested in National Guard and other Reserve components.
- Results from this study will inform future studies that attempt to further refine and increase the impact of population eHealth interventions on key substance use and other mental health problems in reserve component members.

Ohio Army National Guard Mental Health Initiative

Final Presentation to the Scientific and
Administrative Advisory Boards

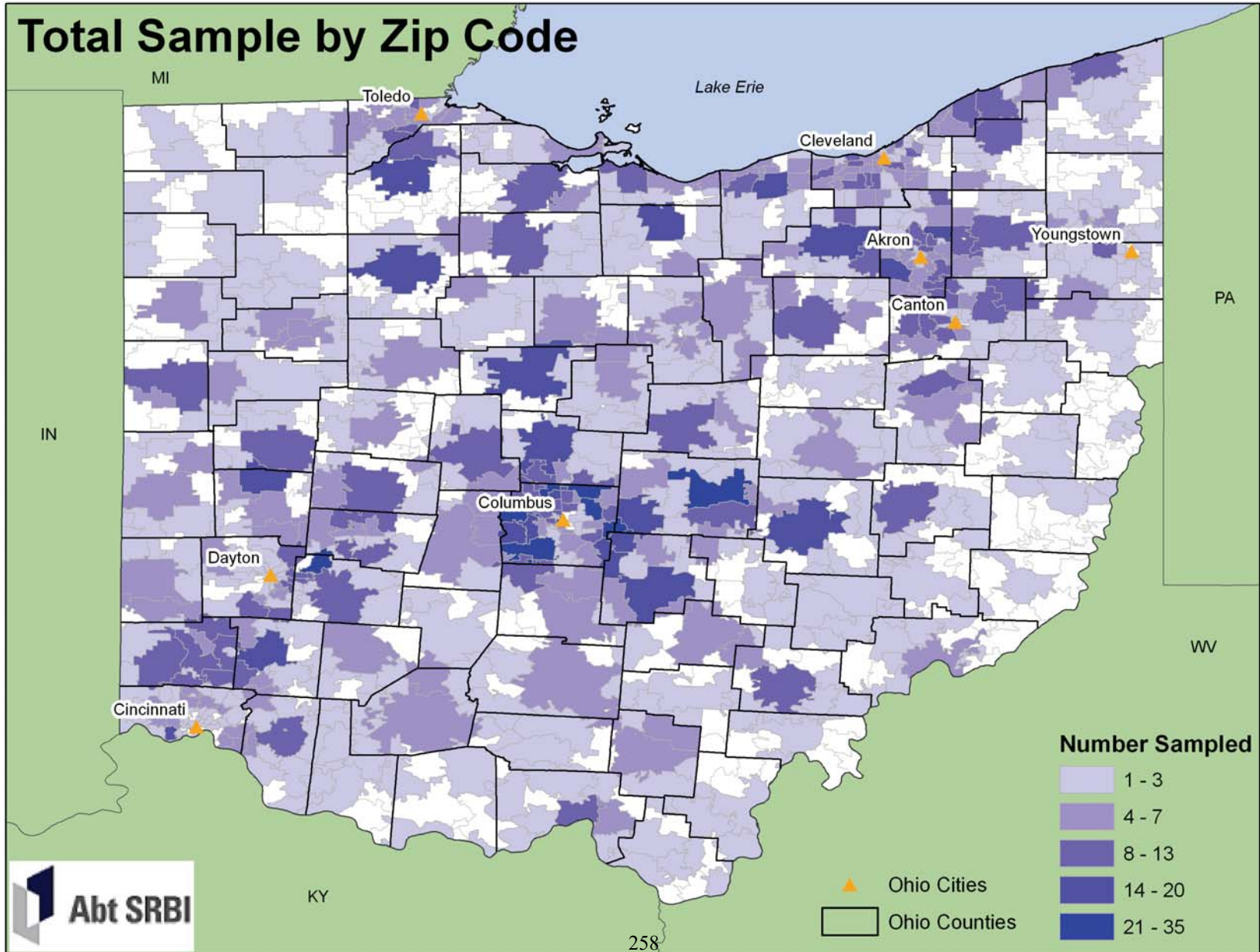
May 14, 2020



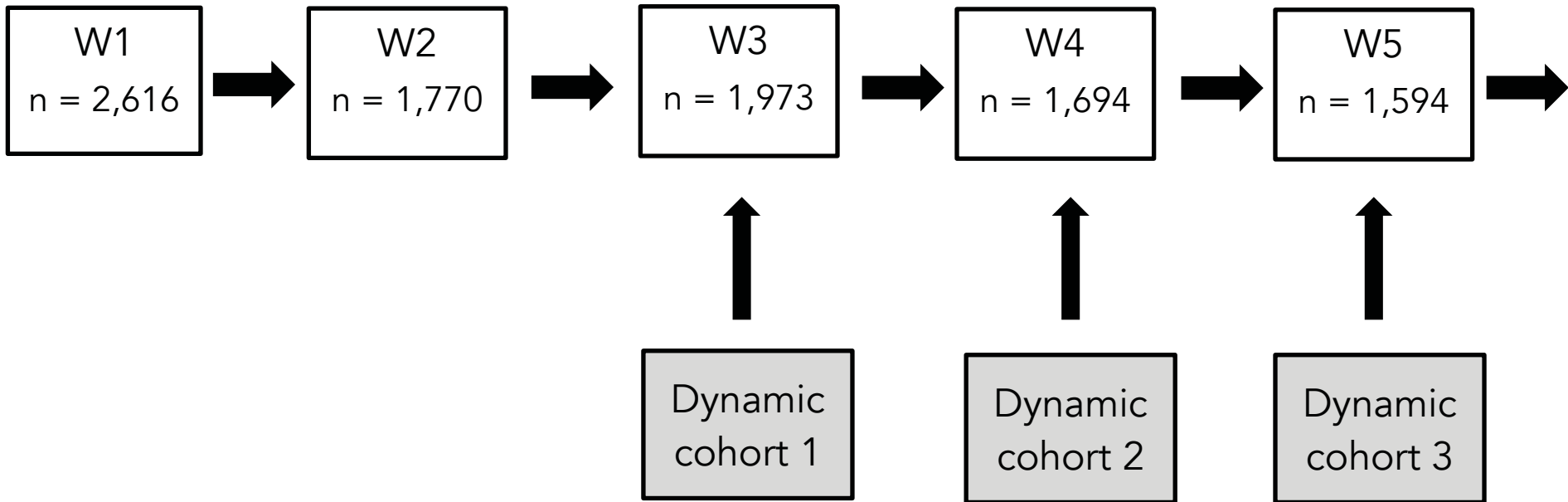
OHIO NATIONAL GUARD STUDY

Study overview

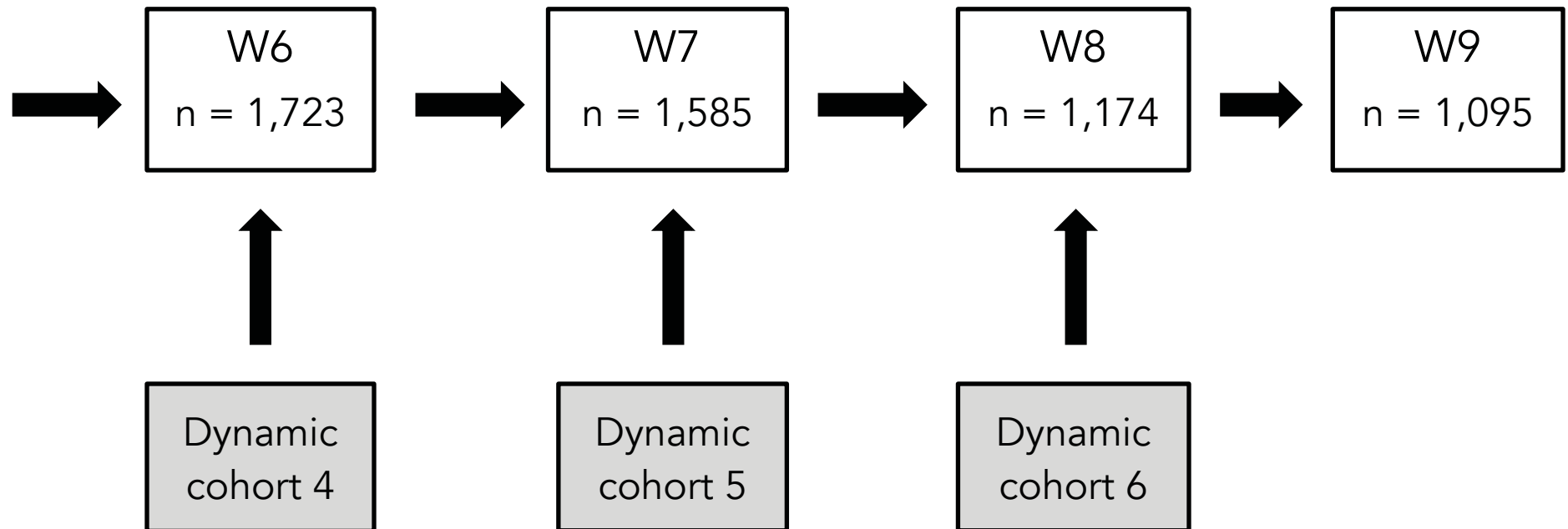
Total Sample by Zip Code



Telephone survey participation flow chart (1)

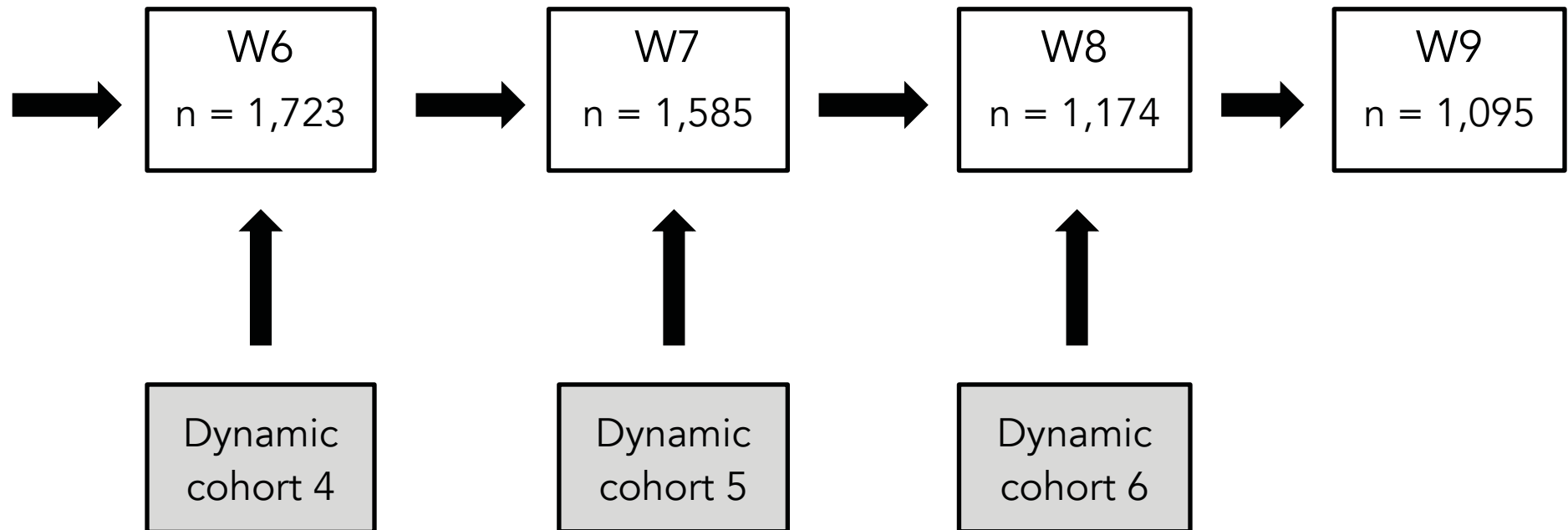


Telephone survey participation flow chart (2)

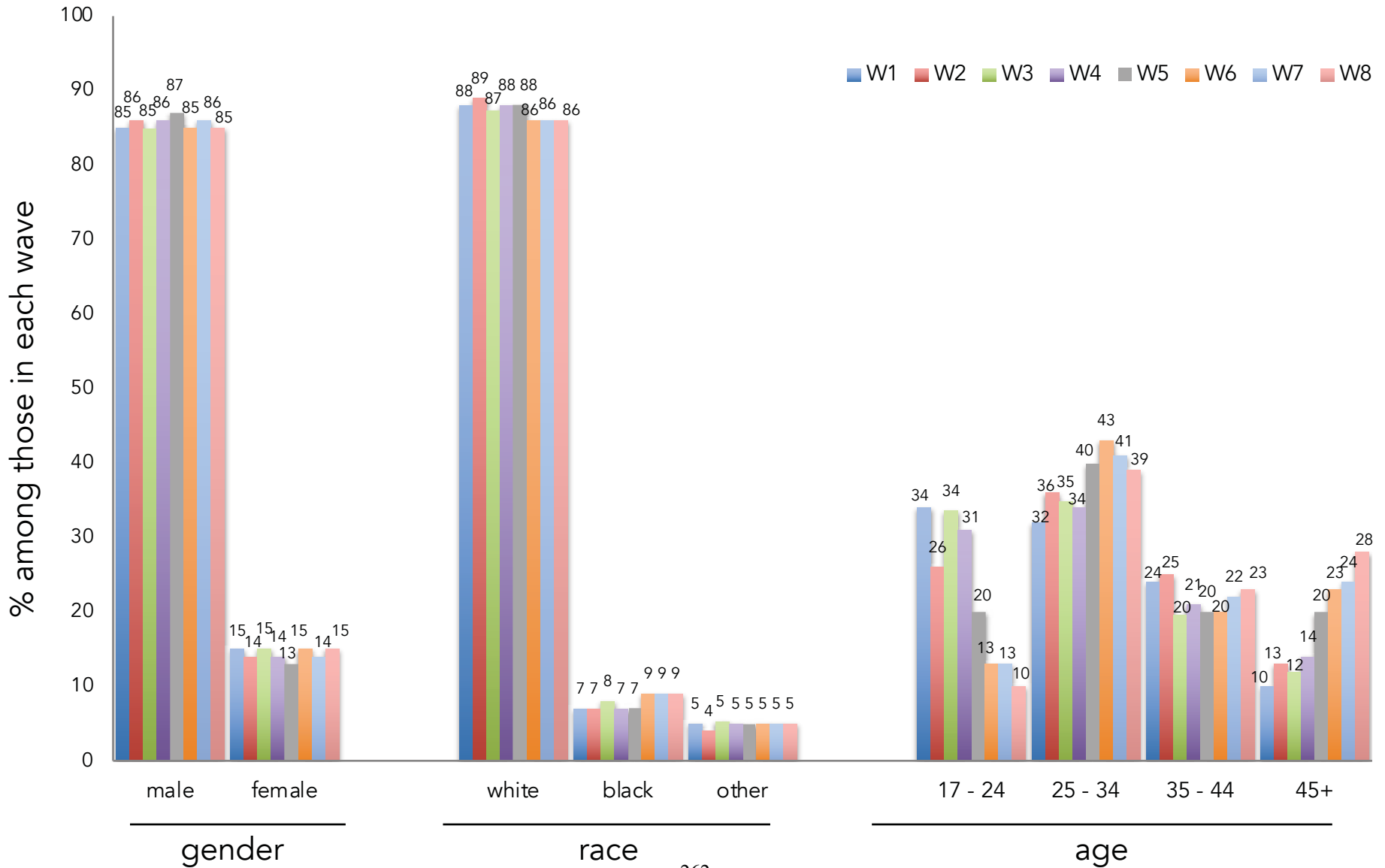


Telephone survey participation flow chart (2)

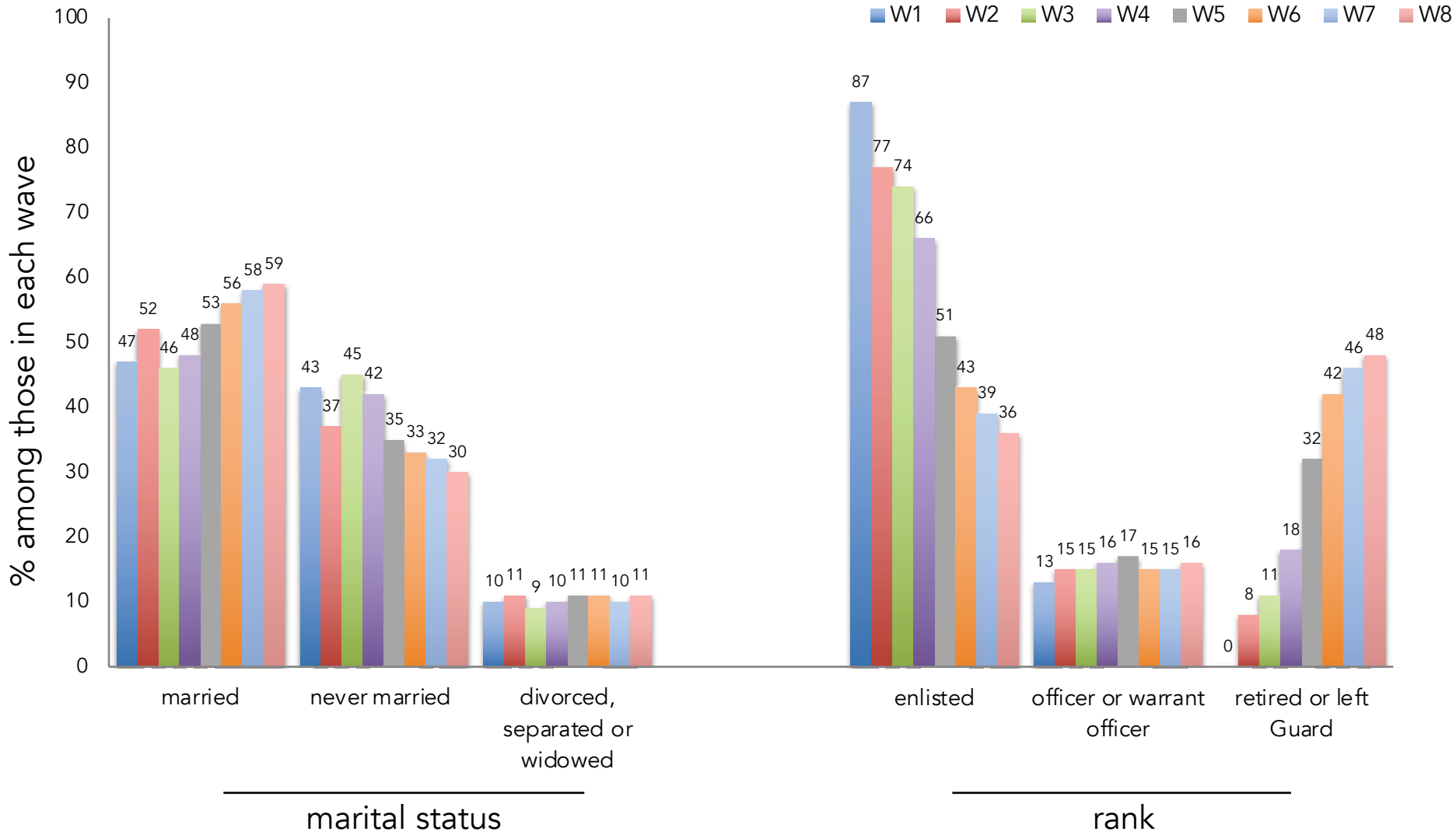
Total number of unique participants across all waves:
3,841



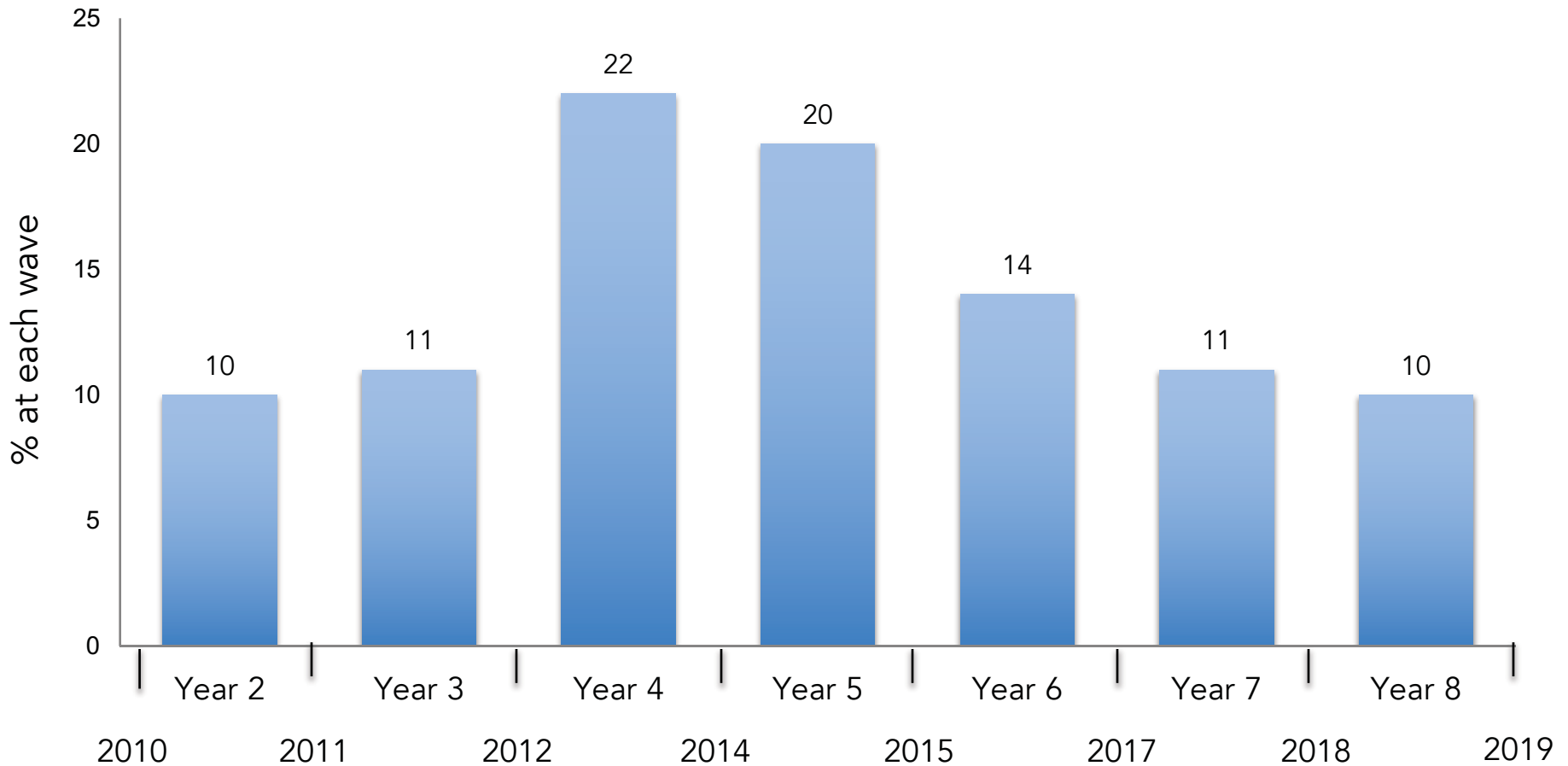
Telephone sample demographics (1)



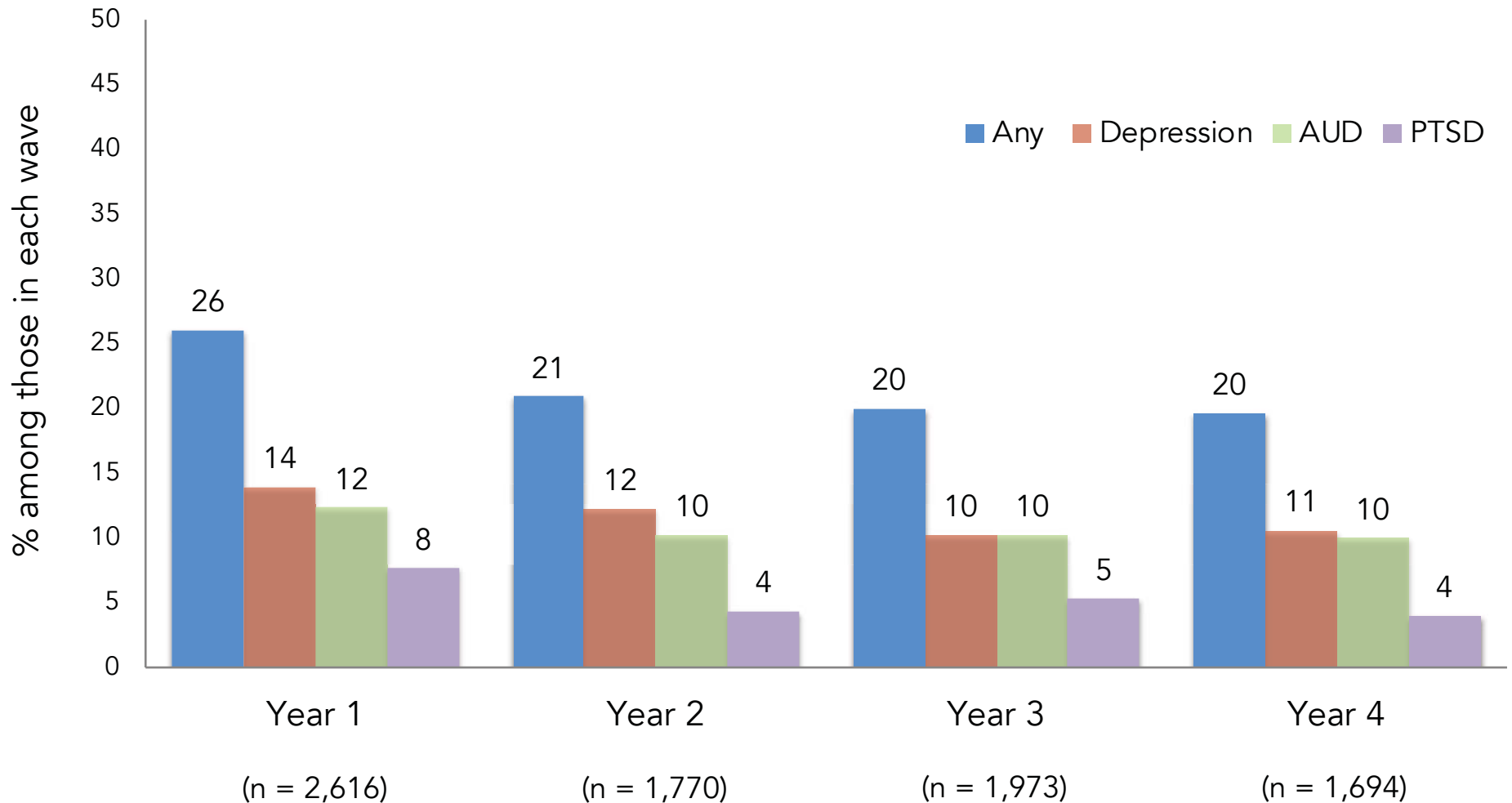
Telephone sample demographics (2)



Proportion deployed between interviews throughout the study

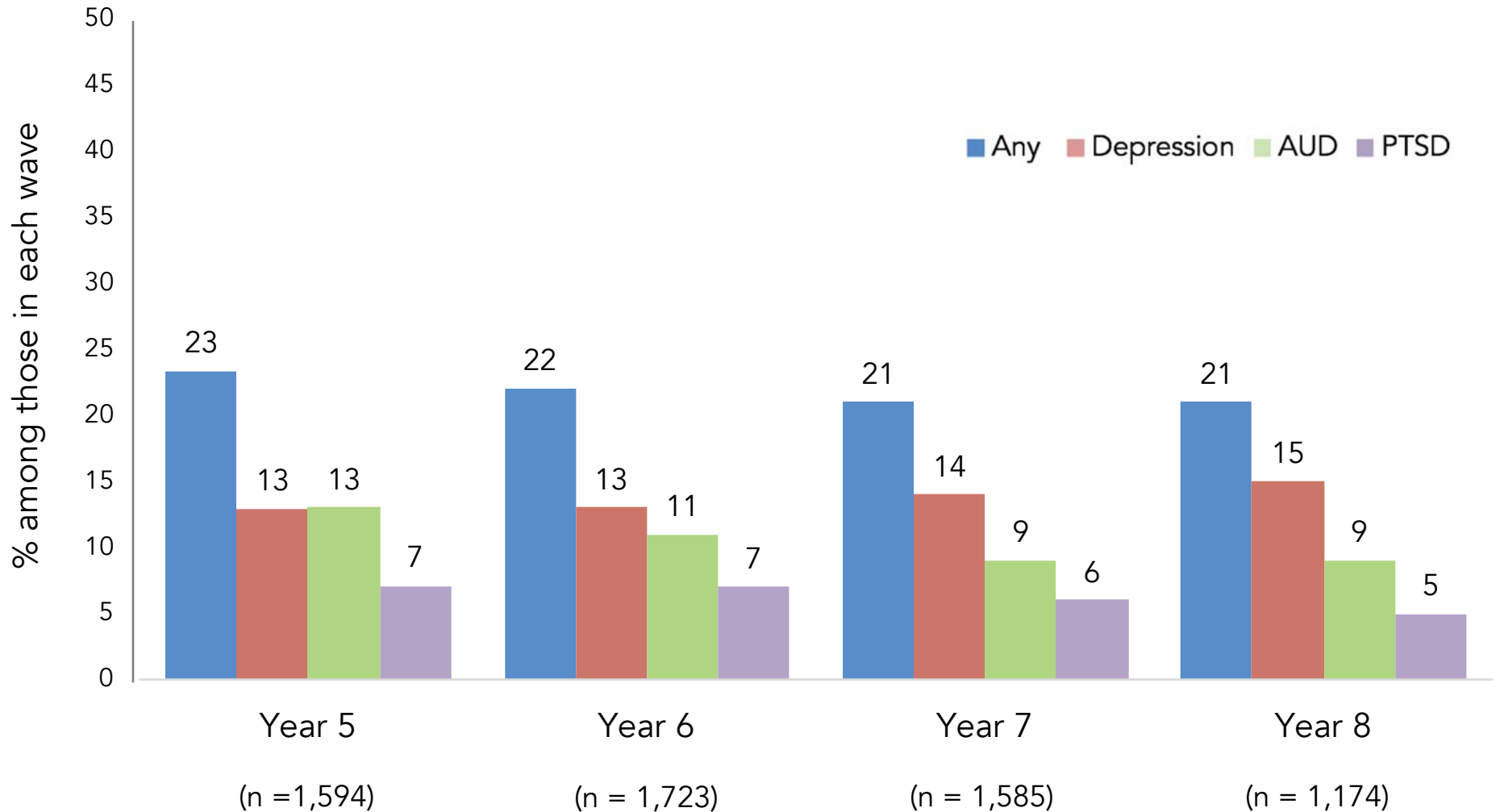


Past-year DSM-IV Mental Health Overview (1)



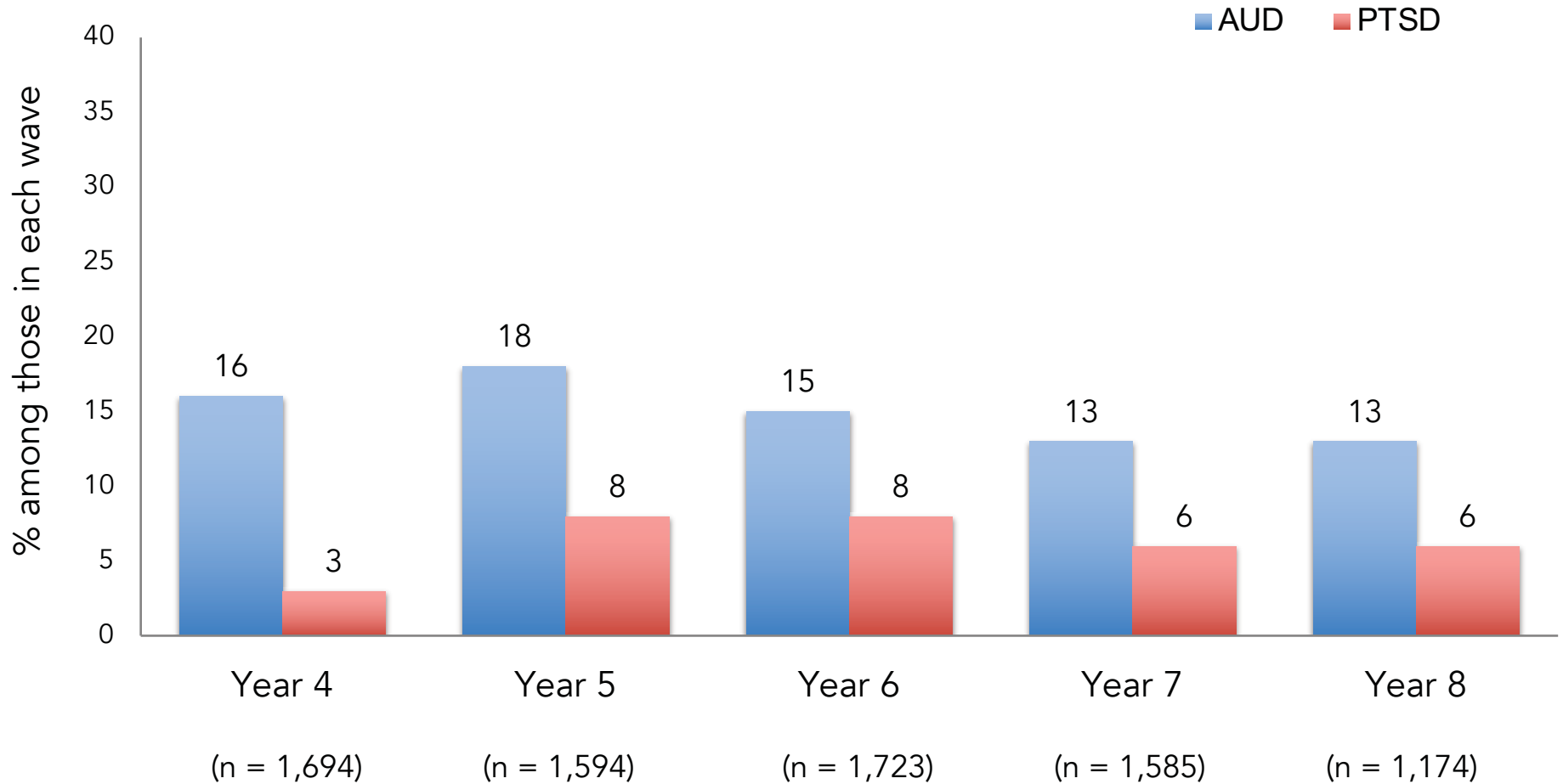
AUD = Alcohol use disorder (dependence or abuse). PTSD = posttraumatic stress disorder.
Waves 3-8 include the dynamic cohorts' baseline interviews. Respondents with no potentially traumatic events are not included in PTSD denominator.

Past-year DSM-IV Mental Health Overview (2)



AUD = Alcohol use disorder (dependence or abuse). PTSD = posttraumatic stress disorder.
Waves 3-8 include the dynamic cohorts' baseline interviews. Respondents with no potentially traumatic events are not included in PTSD denominator.

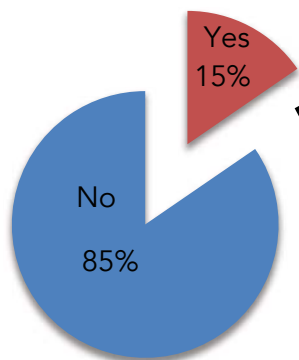
Past-year DSM-5 Mental Health Overview



Mental health service use updates

Mental health service use may be increasing over time

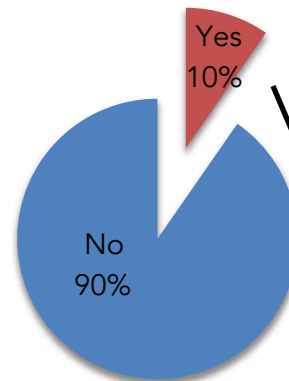
Wave 2 follow-up
(2010-2011)



n = 1,770

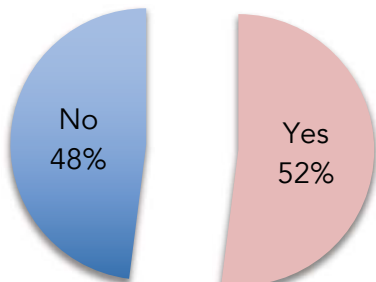
Did you feel a need for services since last interview?

Wave 4 follow-up
(2012-2014)



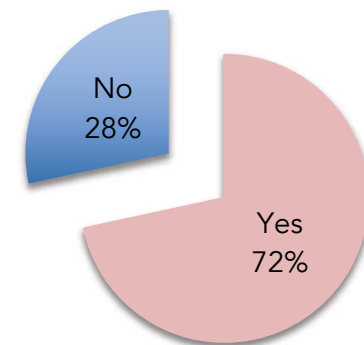
n = 1,431

If so, did you use services since last interview?



n = 273

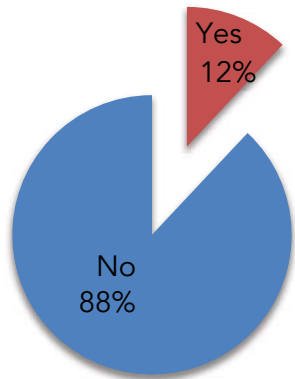
269



n = 148

Mental health service use may be increasing over time

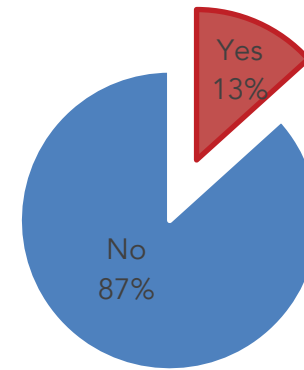
Wave 7 follow-up
(2017-2018)



n = 1,429

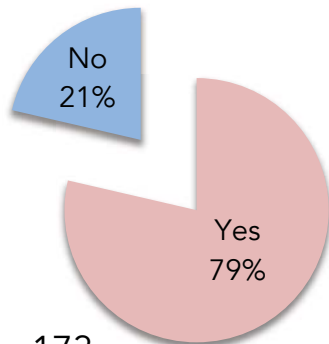
Did you feel a need for services since last interview?

Wave 8 follow-up
(2018-2019)



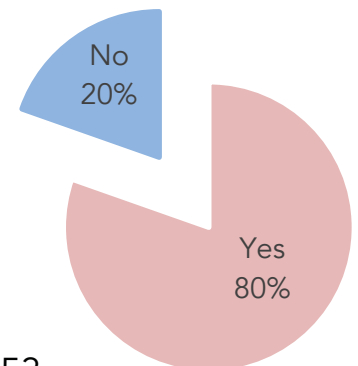
n = 1,140

If so, did you use services since last interview?



n = 173

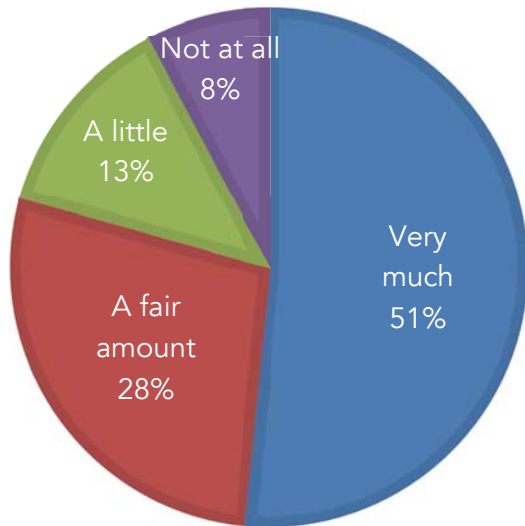
270



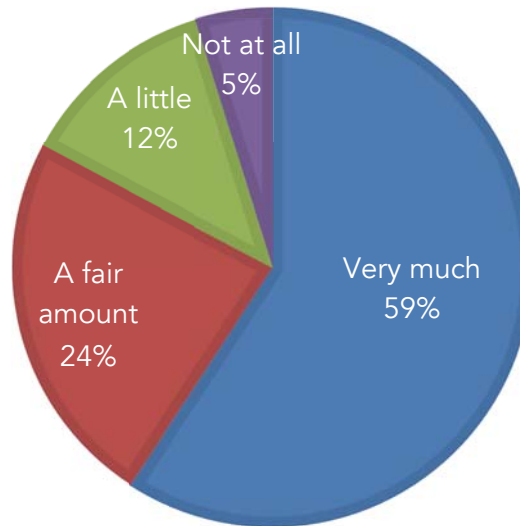
n = 153

Reasons for seeking care (wave 8)

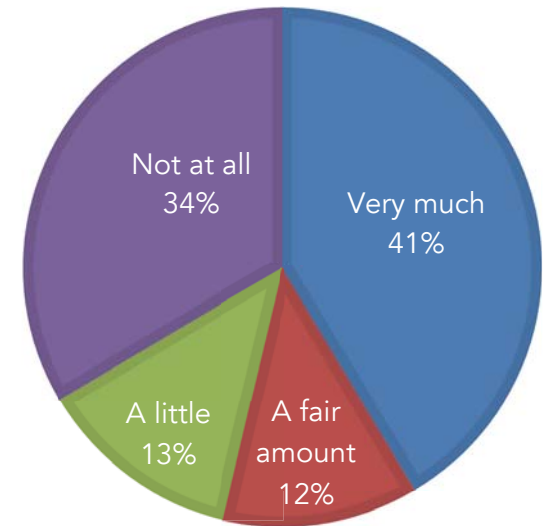
You didn't like the way you were feeling or behaving:



You knew something was wrong:

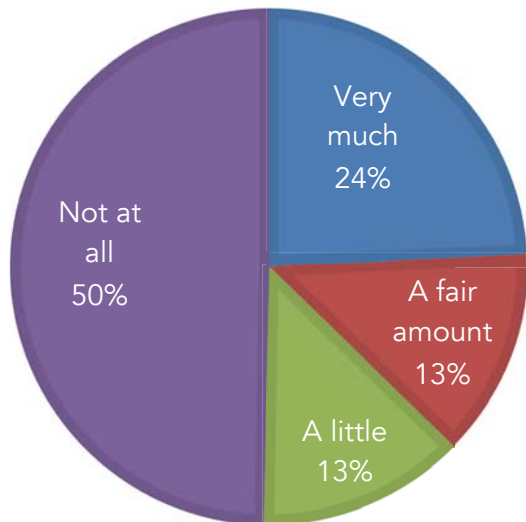


You had a positive mental health experience in the past:

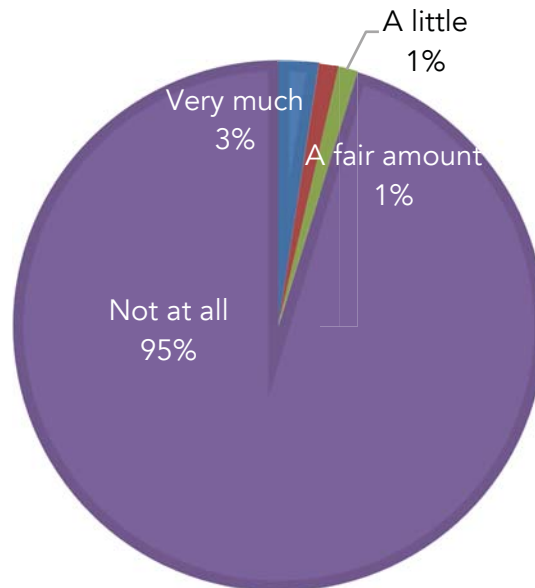


Reasons for seeking care (wave 8)

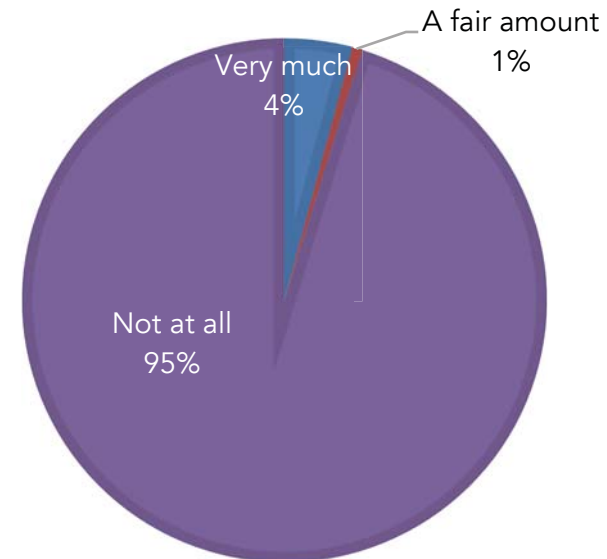
A family member asked you to talk to a mental health professional:



Your commanding officer suggested you talk to a mental health professional:



Mental health treatment was mandated by court order:



New analytic findings

Associations between stressful life events and the rate of incident depression

Study rationale and aims

- Very few general population studies assess incident depression
- Stressful life events throughout the civilian lifecourse—especially in childhood—have been shown to cause adult depression in other groups
 - Not typically studied within the military
 - May be especially salient for a National Guard population

The aims for this study were to estimate:

- the associations between reporting (a) traumatic childhood events and (b) stressful events during adult, civilian life with the rate of incident depression, using survival analysis across 4 years of follow-up
- effect measure modification of these relationships

Methods

- Sample: respondents free of lifetime history of depression at baseline and present in at least one follow-up wave
- Outcome: time to incident DSM-IV depression (in intervals of one year), measured with the PHQ-9
- Multiple imputation ($m = 5$)
- Stratified by sex
- Cox-proportional hazards regression
- Confounders and modifiers chosen from prior literature; effect measure modification assessed by stratification
- Quantitative bias analysis

Exposure A: Childhood traumatic events: one or more of the following:

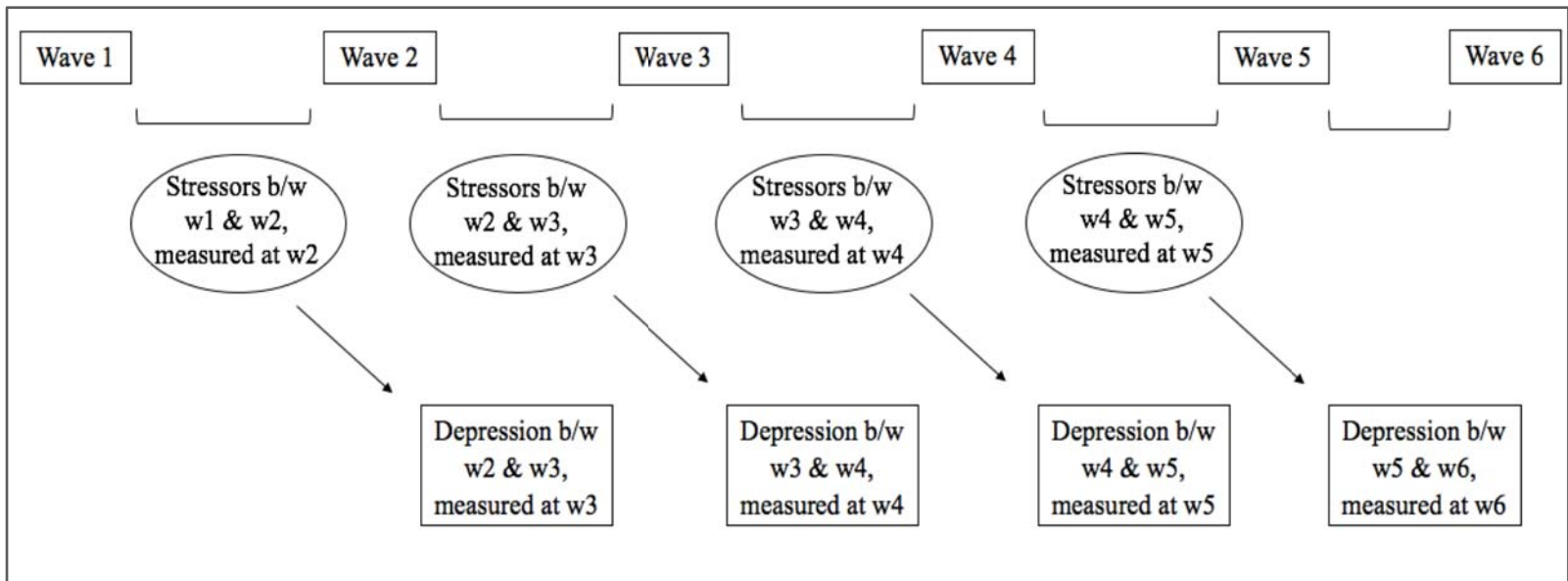
Did a parent or other adult in the household you grew up in...

- (1) often or very often insult you, put you down, or act in a way that made you afraid you would be physically hurt?
- (2) often or very often grab, shove, or slap you, or hit you so hard you had marks or were injured?
- (3) touch you or have you touch them in a sexual way, or attempt to or actually have oral, anal, or vaginal intercourse with you?
- (4) Was a parent or other adult in the household you grew up in depressed or mentally ill, or ever attempt suicide?

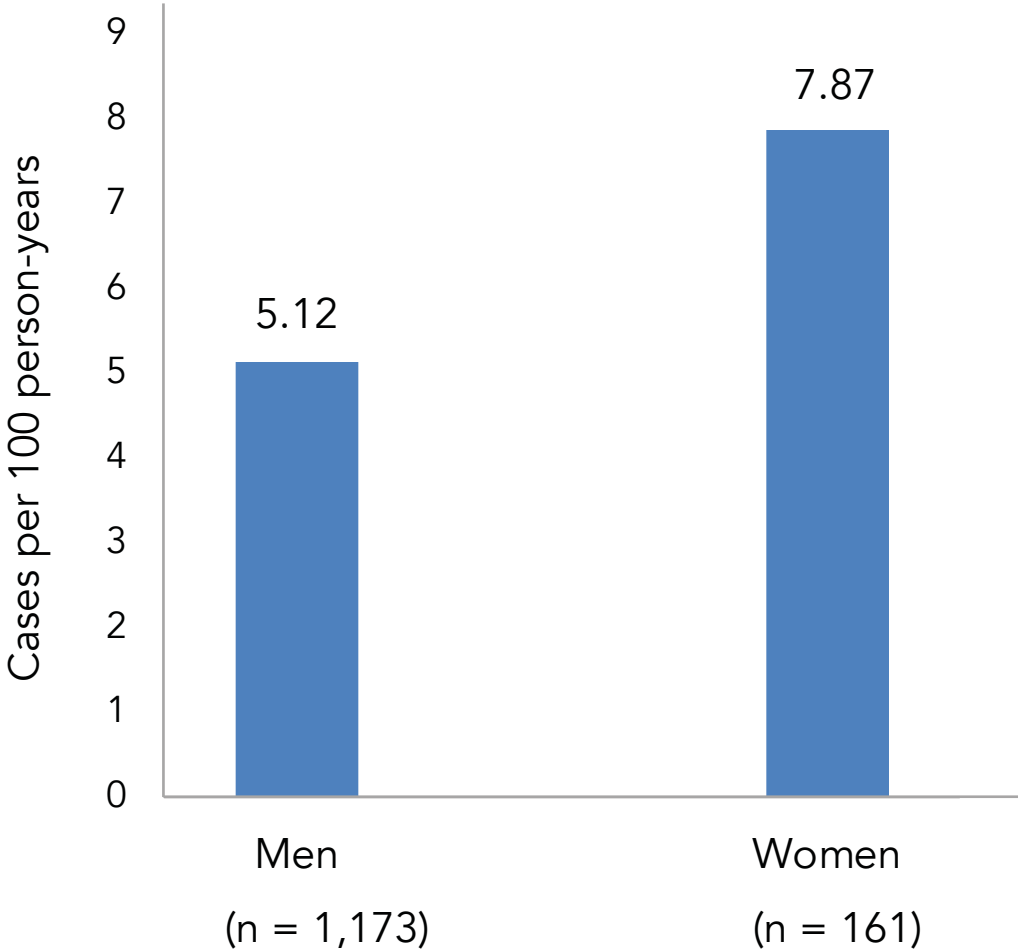
Exposure B: Adult stressful events: one or more of the following:

- Lost a job, been laid off, or lost a large part of income
- Lost your house or were homeless
- Been through a divorce or “break up” with a partner or significant other
- Had a family member with a serious drug or alcohol problem
- Experienced stressful legal problems (e.g., being sued or suing someone else)
- Been unemployed and seeking employment for at least 3 months
- Had serious financial problems
- Been emotionally mistreated (e.g., shamed, embarrassed, ignored, or repeatedly told you were no good)
- Been robbed or had your home broken into

Lagged time-varying stressors



Incidence rate of depression across four years of follow-up



Results among men (n = 1,173)

Relationship between 1+ childhood traumatic events and time to incident depression

	Hazard ratio	95% CI
1+ traumatic childhood events, crude	1.73	(1.26, 2.38)
1+ traumatic childhood events, adjusted ^a	1.77	(1.33, 2.49)
1+ traumatic childhood events, adjusted, including PTSD ^b	1.71	(1.24, 2.35)

CI = confidence interval

PTSD = posttraumatic stress disorder

^a Adjusted for race and age group

^b Adjusted for race, age group, and PTSD

Relationship between 1+ childhood traumatic events and time to incident depression, by income level

	\$40,000 or less annual income (n = 410)		More than \$40,000 annual income (n = 763)	
	Hazard ratio	95% CI	Hazard ratio	95% CI
1+ traumatic childhood events, adjusted ^a	2.06	(1.22, 3.49)	1.63	(1.09, 2.45)

CI = confidence interval

^a Adjusted for race and age group

Relationship between 1+ past-year stressful events and time to incident depression

	Hazard ratio	95% CI
1+ past-year stressful events, crude	2.17	(1.63, 2.89)
1+ past-year stressful events, adjusted ^a	2.04	(1.52, 2.72)

CI = confidence interval

^a Adjusted for race and age group, and time-varying, lagged past-year PTSD Stressors are lagged by one year

Conclusions

- Among men, both traumatic childhood events and adult stressful events were associated with higher rates of incident depression
 - The relationship between childhood trauma and incident depression was stronger among men with lower income in adulthood
- Unmeasured confounding and misclassification are potential limitations but are unlikely to fully account for the observed effects, according to quantitative bias analyses

A machine learning approach to predicting incident depression

Study rationale and aim

- Traditional population-level statistical methods fall short on individual-level prediction
- Machine learning can help
 - Can identify complex risk profiles and combinations of predictors that we might not otherwise detect with traditional regression modeling which typically require hypotheses/prior knowledge
 - More flexible, fewer assumptions
- The aim of this study was to determine which variables and their interactions are identified as predictors of incident depression across 5 years using tree classification and random forest algorithms

Outcome

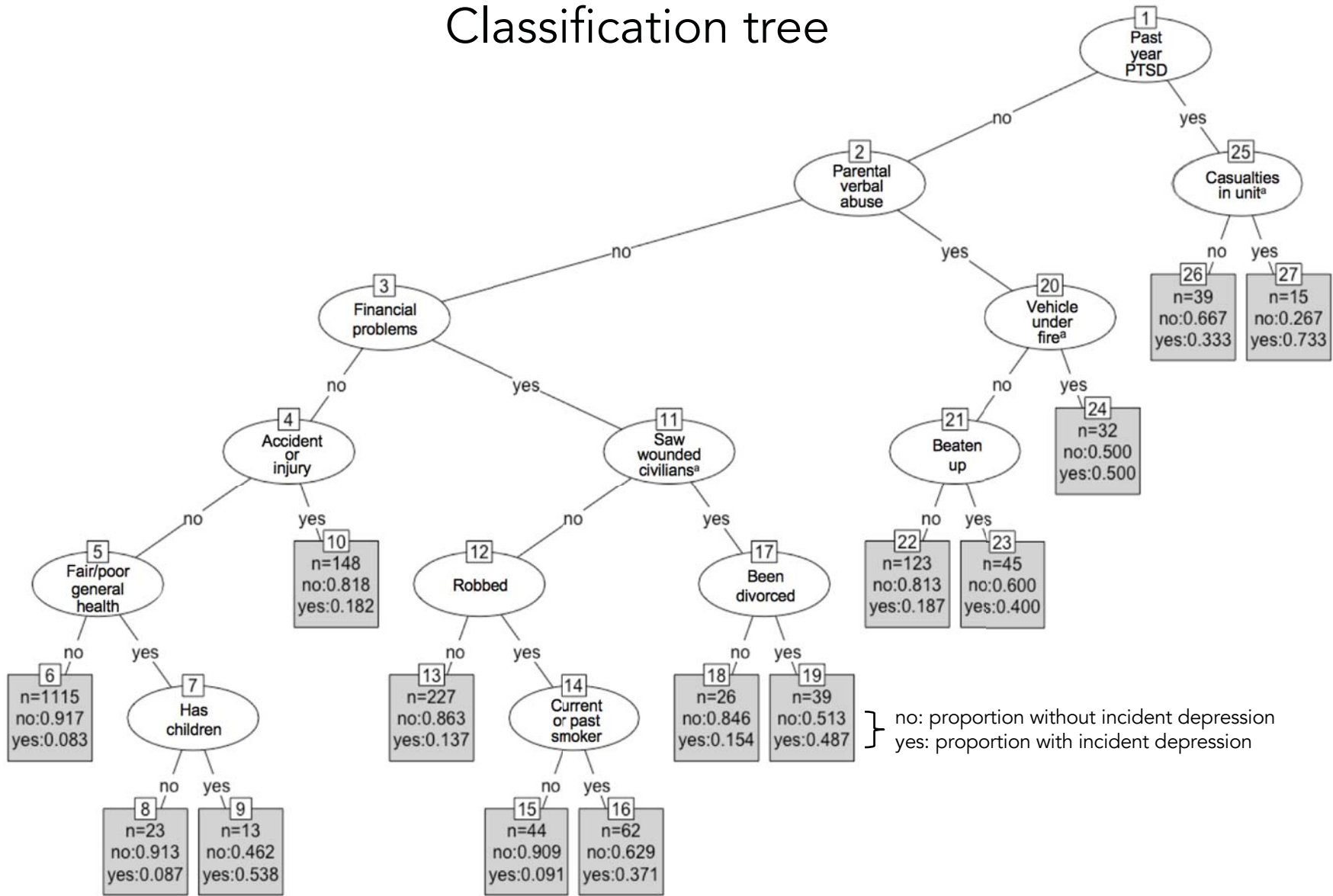
- Cumulative incidence of depression during follow-up
- Defined using DSM-IV criteria, measured with the PHQ-9
 - 14.9% among men
 - 24.8% among women

Predictors entered into algorithms

- 4 childhood traumatic events
- 8 lifetime stressful events
- 43 lifetime traumatic events
- Race
- Hispanic ethnicity
- Age
- Income
- Marital status
- Education level
- Student status
- Parent status
- Years of military service
- Paygrade/rank
- Deployment status and most recent location
- Sexual harassment during deployment
- Head injury during deployment
- Sexual assault at any time
- Self-reported physical health
- Psychosocial support
- Alcohol dependence
- Alcohol abuse
- Average number of drinks per day
- Smoking status
- Past year and lifetime posttraumatic stress disorder
- Past year and lifetime generalized anxiety disorder

Results among men (n = 1,951)

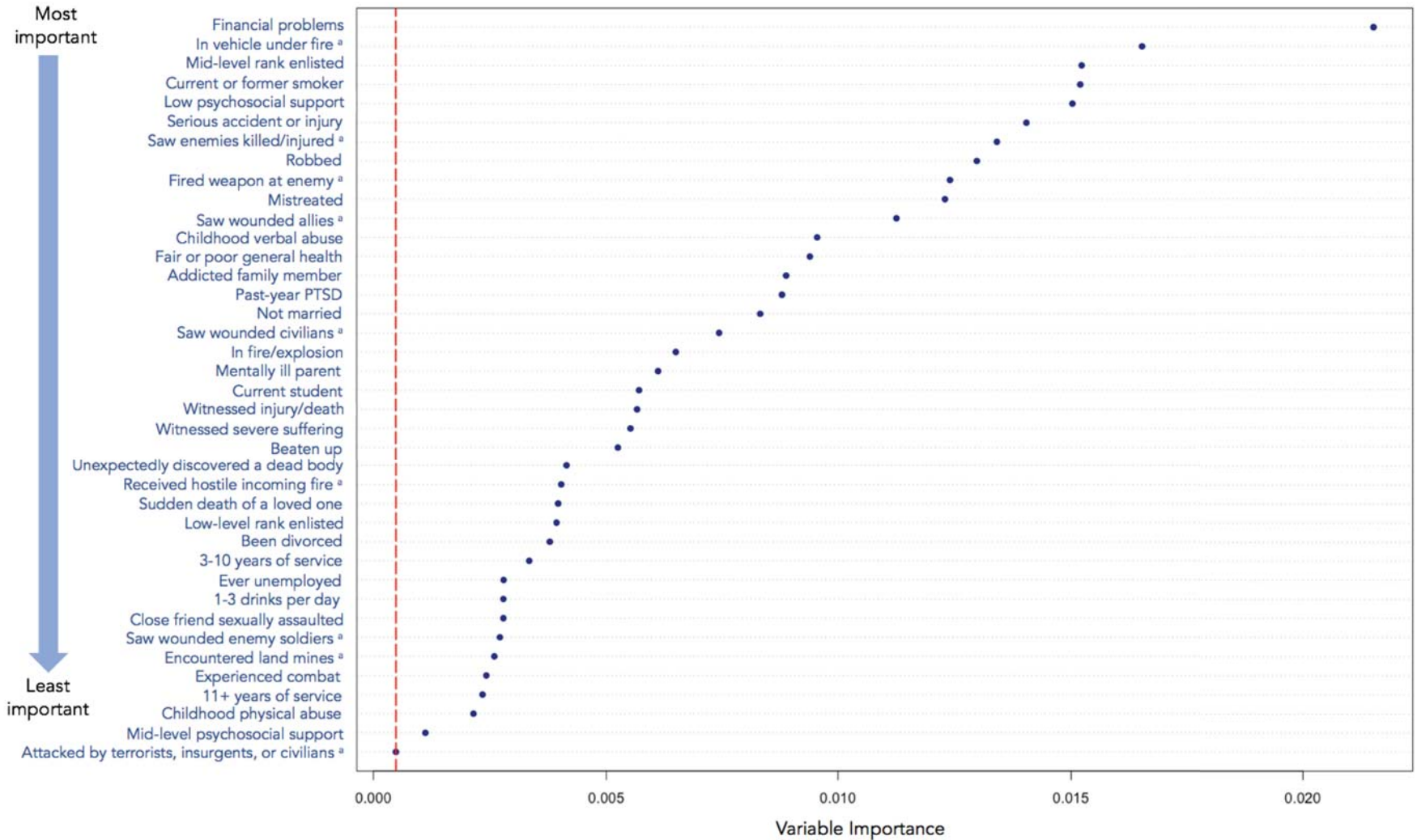
Classification tree



no: proportion without incident depression
 yes: proportion with incident depression

^a during most recent deployment

Variable importance plot



^a during most recent deployment

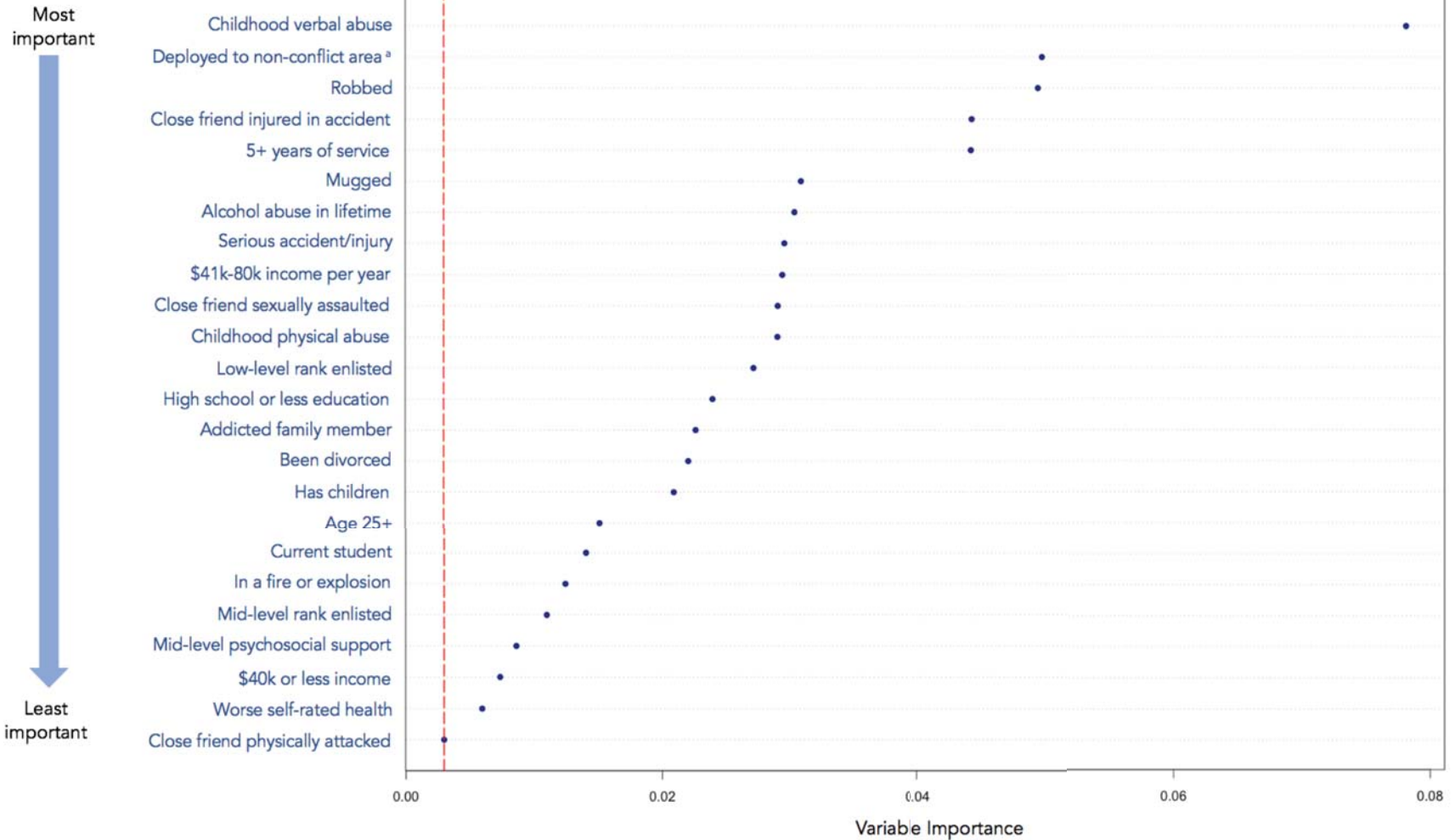
Results among women (n = 298)

Classification tree



no: proportion without incident depression
yes: proportion with incident depression

Variable importance plot



^a during most recent deployment

Conclusions

- Lifetime stressors and traumas, childhood-specific traumas, and military characteristics were consistently among the most predictive variables for both men and women
 - Results are consistent with traditional epidemiologic methods
- Hearing about traumatic events happening to others was more predictive of depression for women compared to men, whose life experiences tended to be the most predictive variables
- Overall, there was moderate accuracy in prediction after cross-validation (68-85%); in line with other depression studies
 - If depression as a whole is difficult to predict, future research might focus on specific symptom clusters

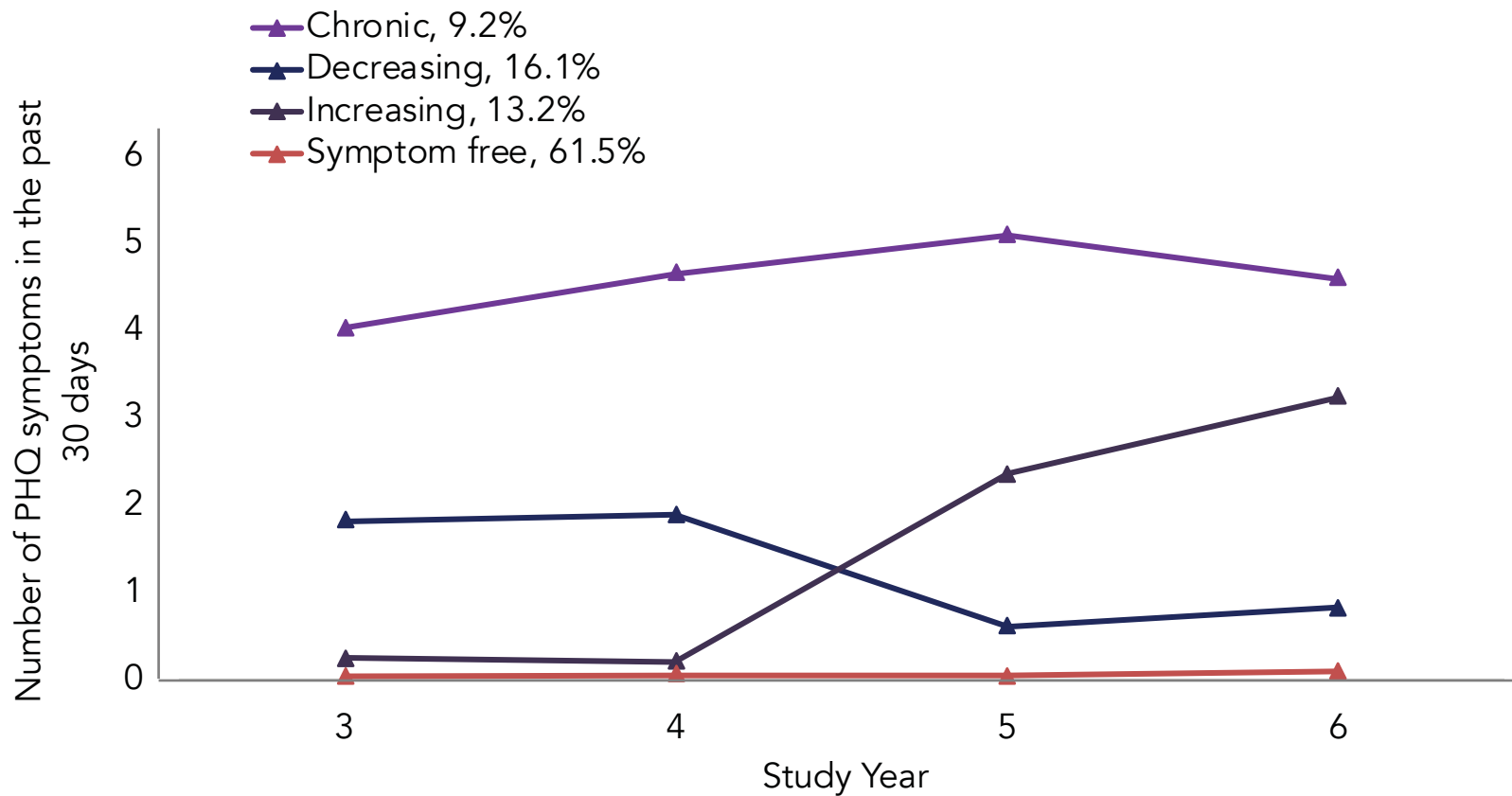
Stressful life events in relation to trajectories of depression symptoms over time

Study rationale and aims

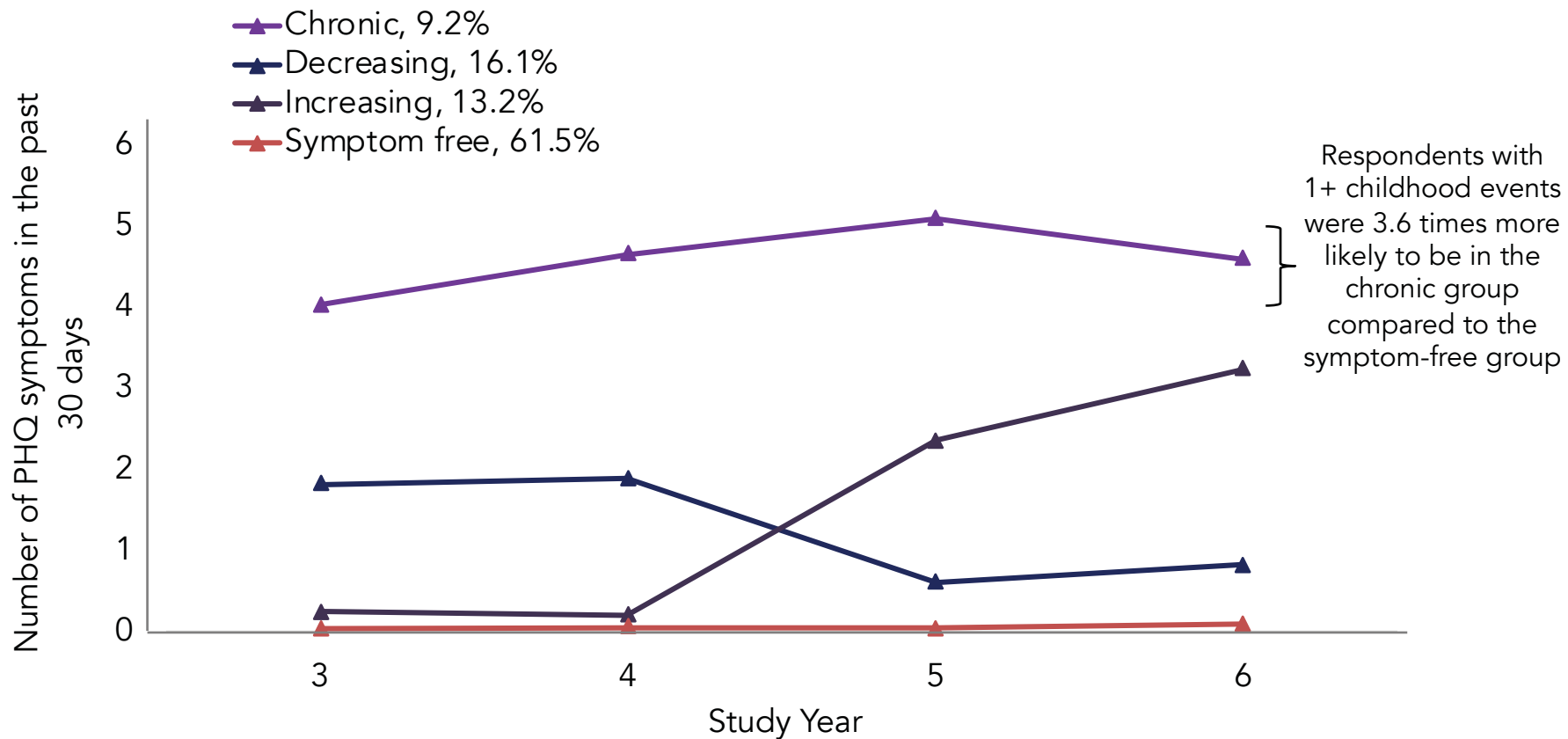
- Incidence does not tell us about previously depressed or chronically depressed individuals
- It may be overly reductionist to lump different sub-types of depression together into one single, binary outcome
 - Heterogeneity of symptom profiles
 - Sub-threshold depression are not be discernible when modeling binary outcomes
- Identifying the course – or trajectories – of respondents' symptoms in a longitudinal study is crucial (recovery, relapse, etc.)
- Group-based trajectory methods cluster respondents together based on the “growth” or shape of their symptom patterns over time
- How do childhood traumatic events and stressful adult events relate to trajectories of symptoms?

Results among men and women together (n = 1,844)

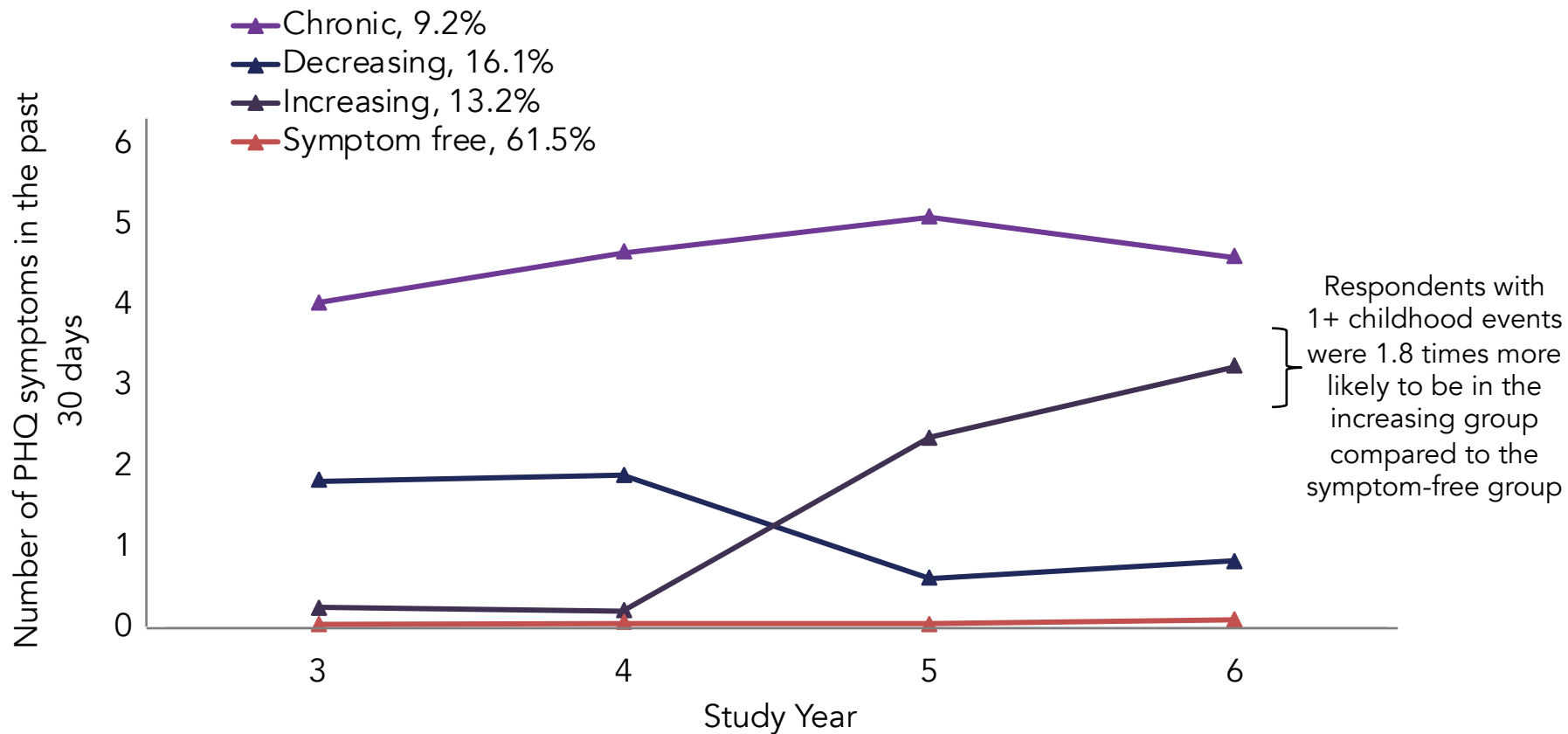
Trajectories of depression symptoms over four years



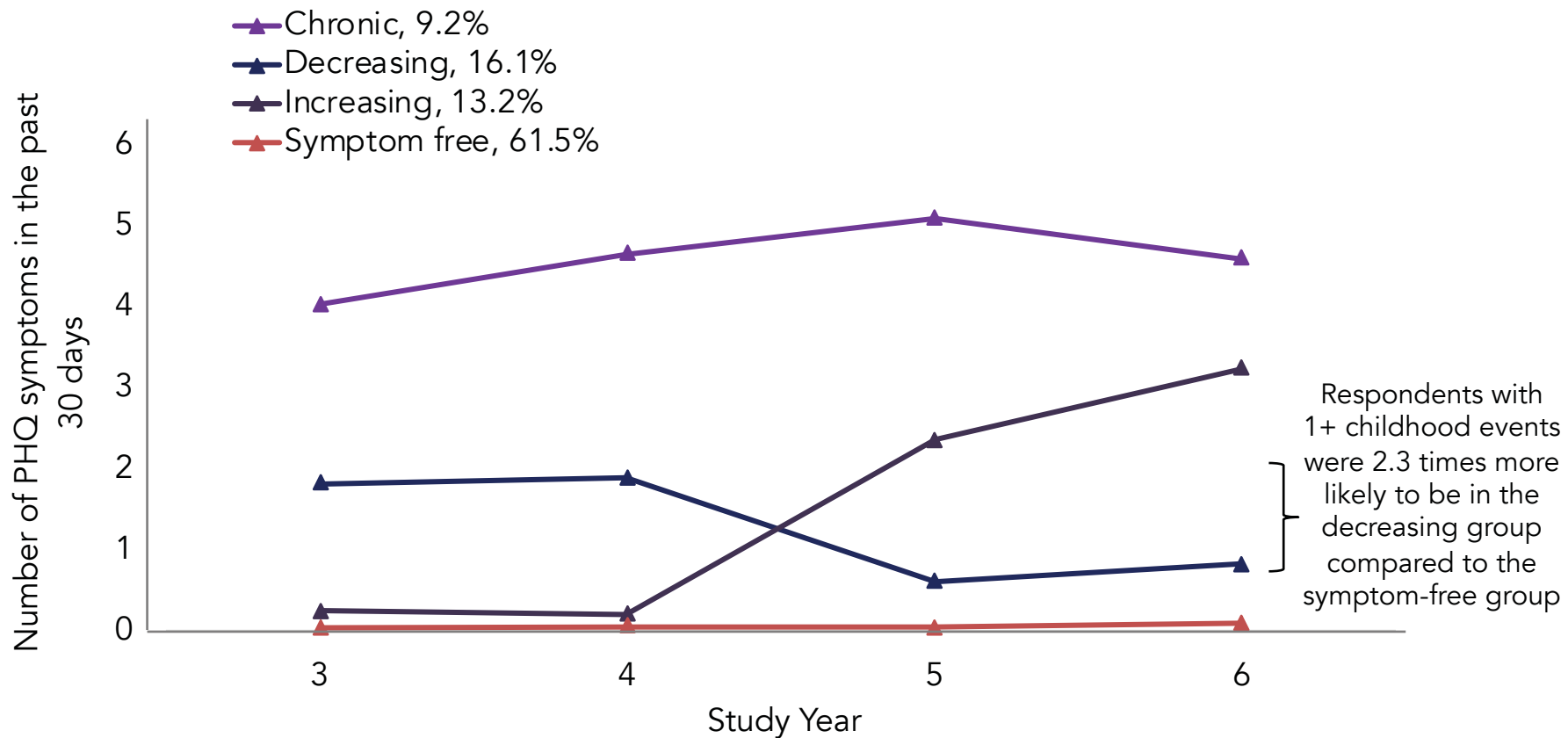
Trajectories of depression symptoms over four years



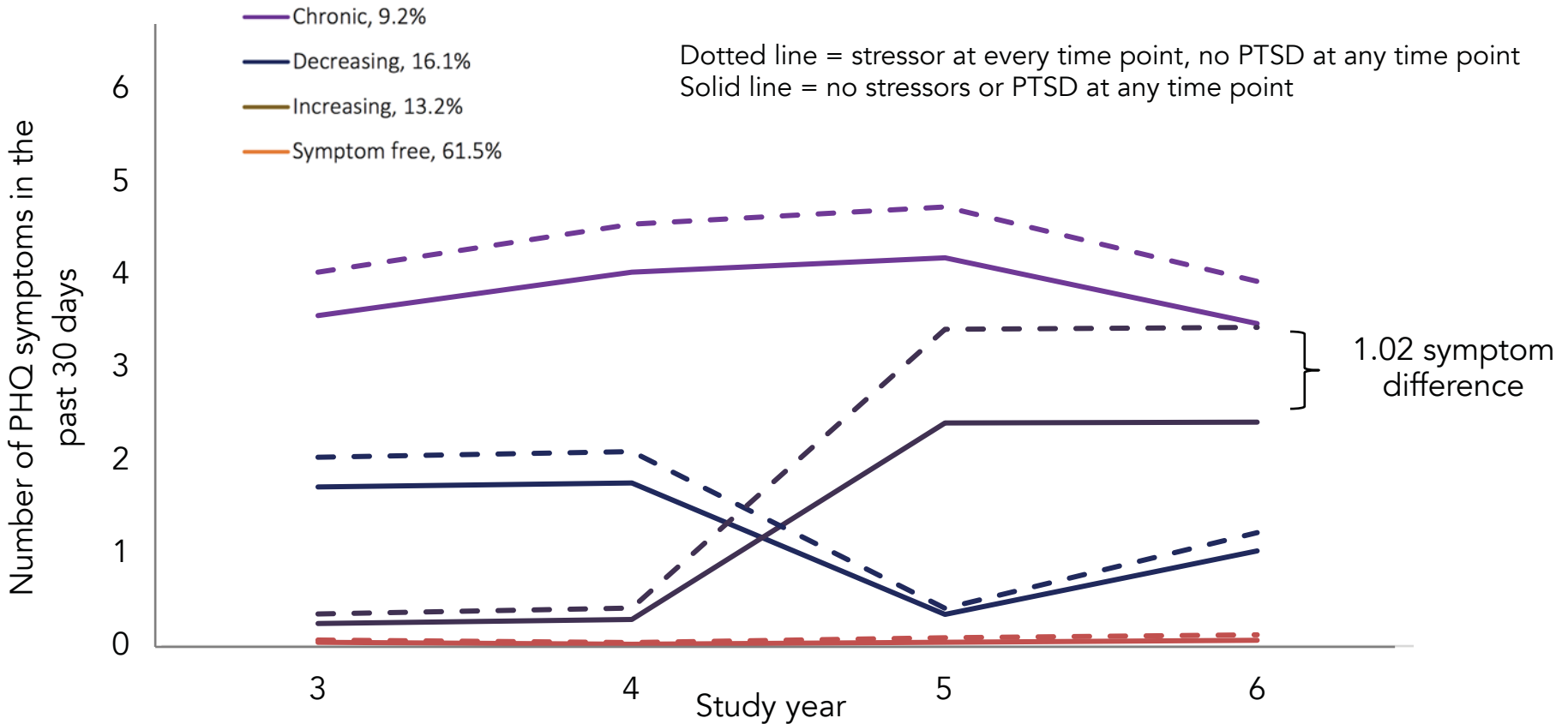
Trajectories of depression symptoms over four years



Trajectories of depression symptoms over four years



Relationship between lagged, past-year stressors and depression symptoms



Conclusions

- Identified 4 distinct latent trajectory groups of depression symptoms across 4 years
 - The majority of respondents had consistently no symptoms
- Reporting 1+ traumatic childhood events was associated with chronically high, decreasing, and increasing numbers of depression symptoms over time, compared to no symptoms
 - Recall bias may be a limitation but is unlikely to fully explain the observed associations, according to quantitative bias analyses
- Reporting 1+ stressors at each time point was associated with a positive difference in depression symptoms among all trajectory groups
 - Biggest difference for the increasing group; reverse causation?
- All results were consistent among both men and women

Conclusions from three studies on depression

- It is important to consider the entire lifecourse when studying the mental health of military personnel
 - Not only recent or deployment-related factors
- Across 3 different analytic methods and 3 different ways of conceptualizing depression, consistency of relationships between childhood traumatic events, adult stressful events, and depression
- Random forests are a feasible method for predicting incident depression in this population, and can help to bridge the gap between individual- and population-level health

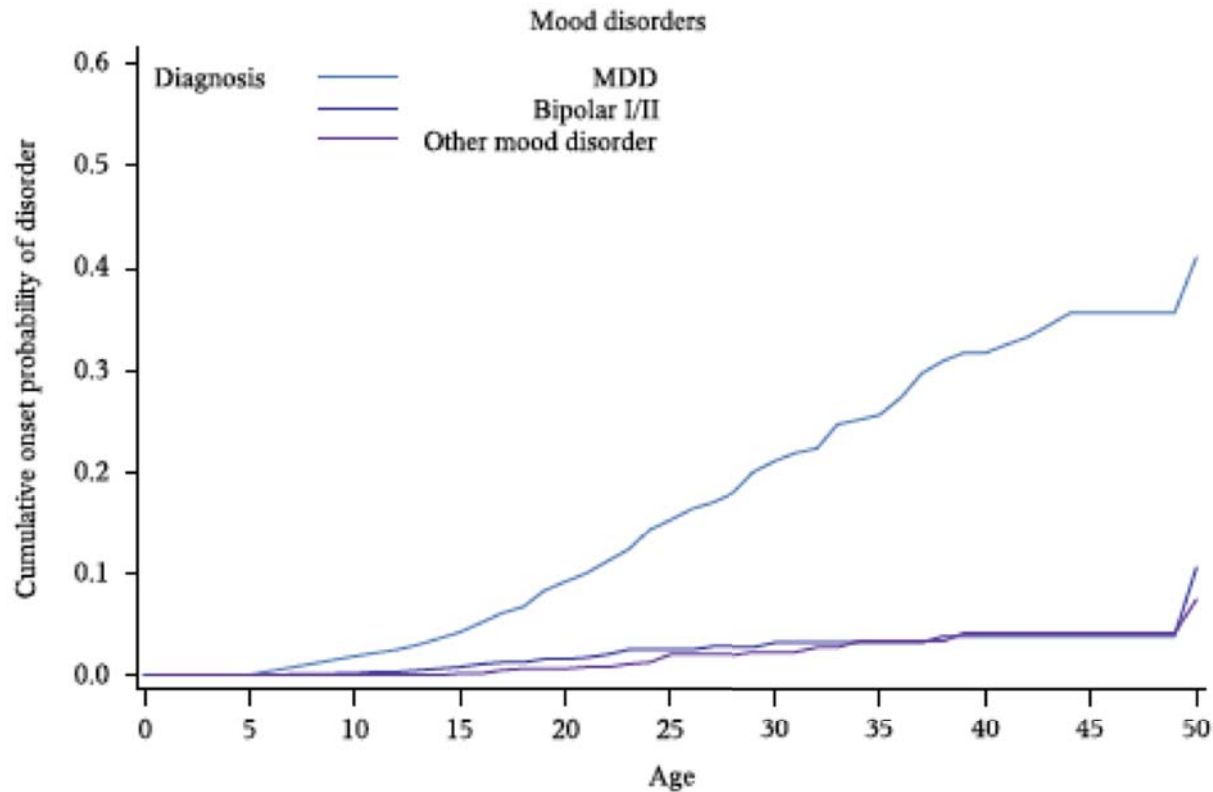
Selected analytic findings from prior years

Age of onset and projected lifetime prevalence of psychiatric disorders

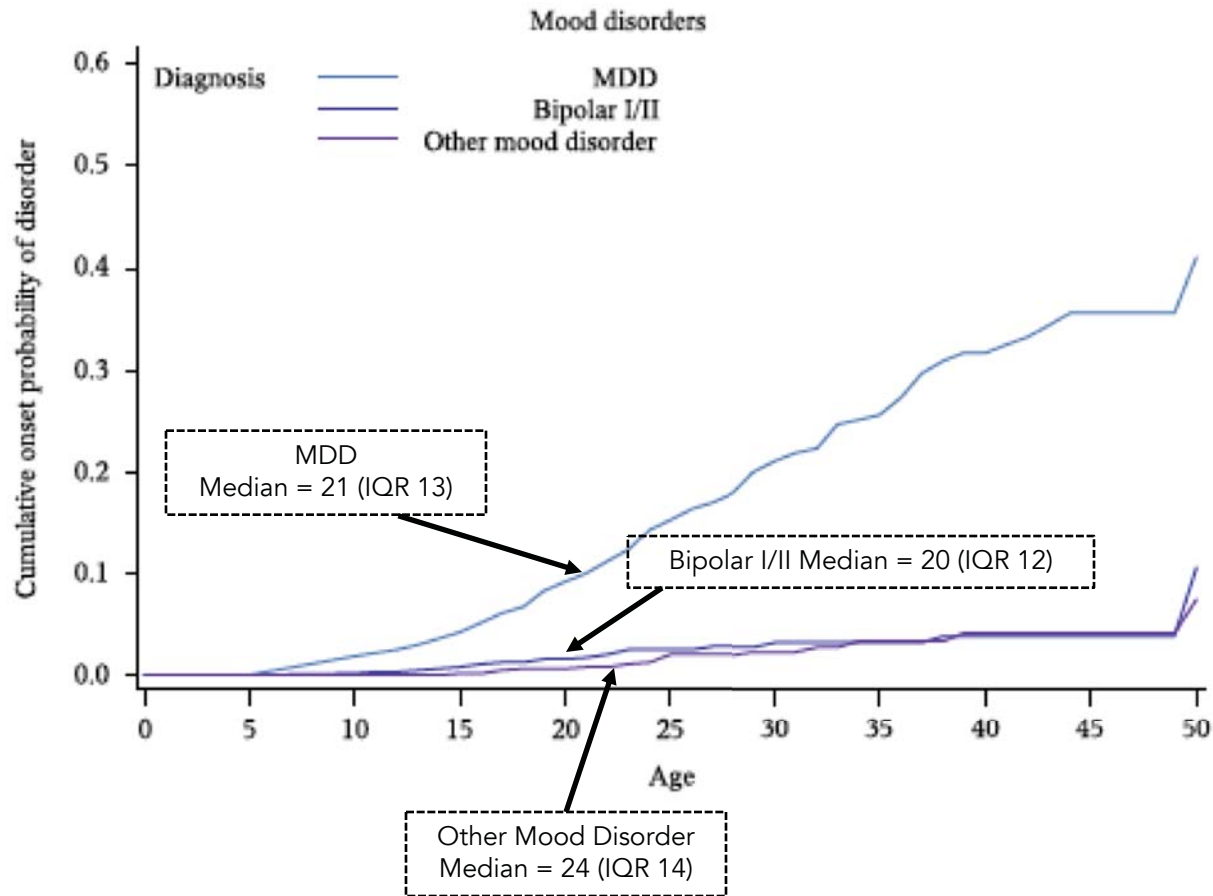
Study aims

- Document the age of onset and projected lifetime prevalence of psychiatric disorders
- Determine the prevalence of disorders that onset prior to military service

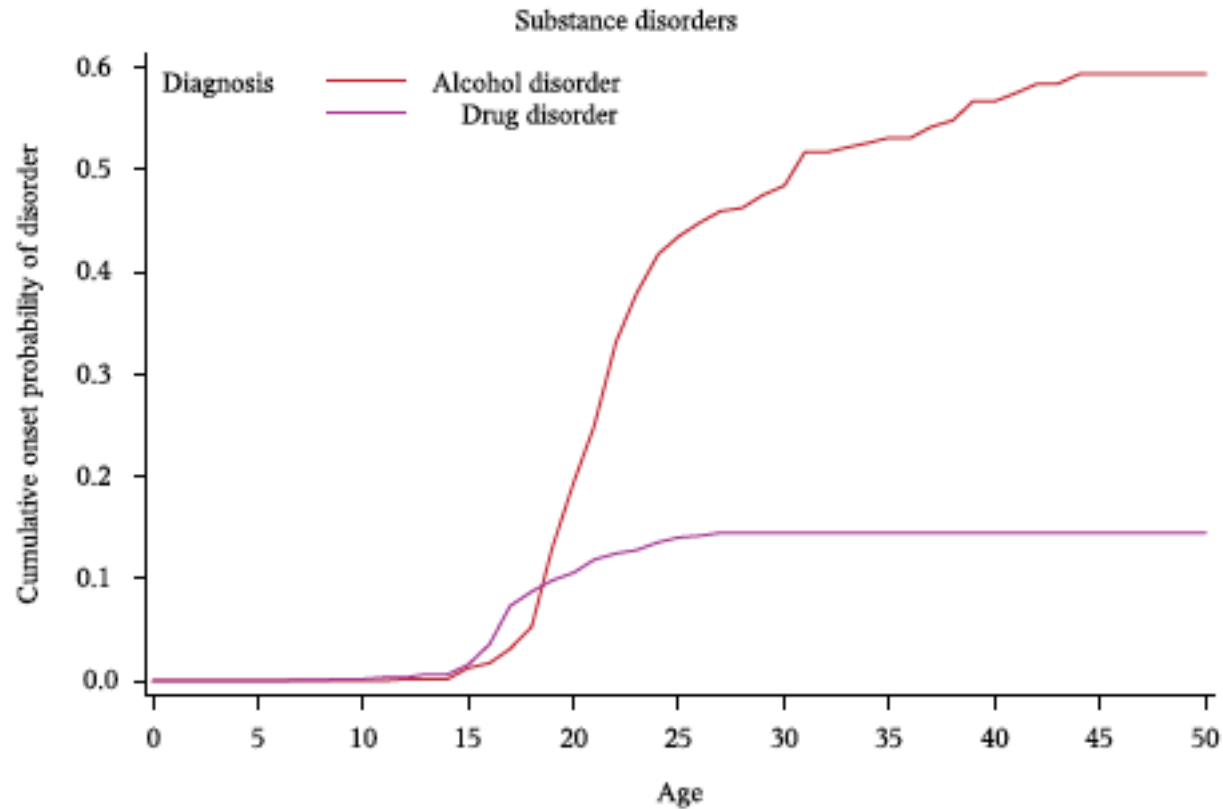
Age of onset: Mood disorders



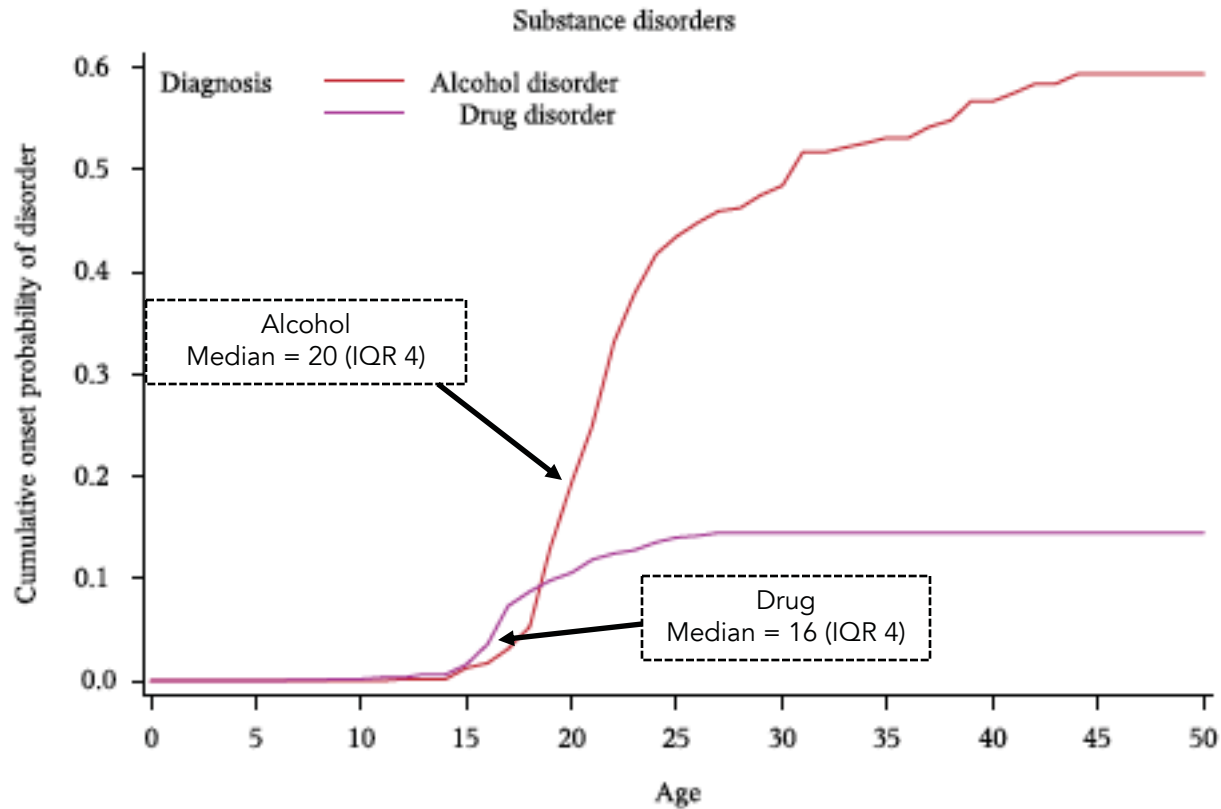
Age of onset: Mood disorders



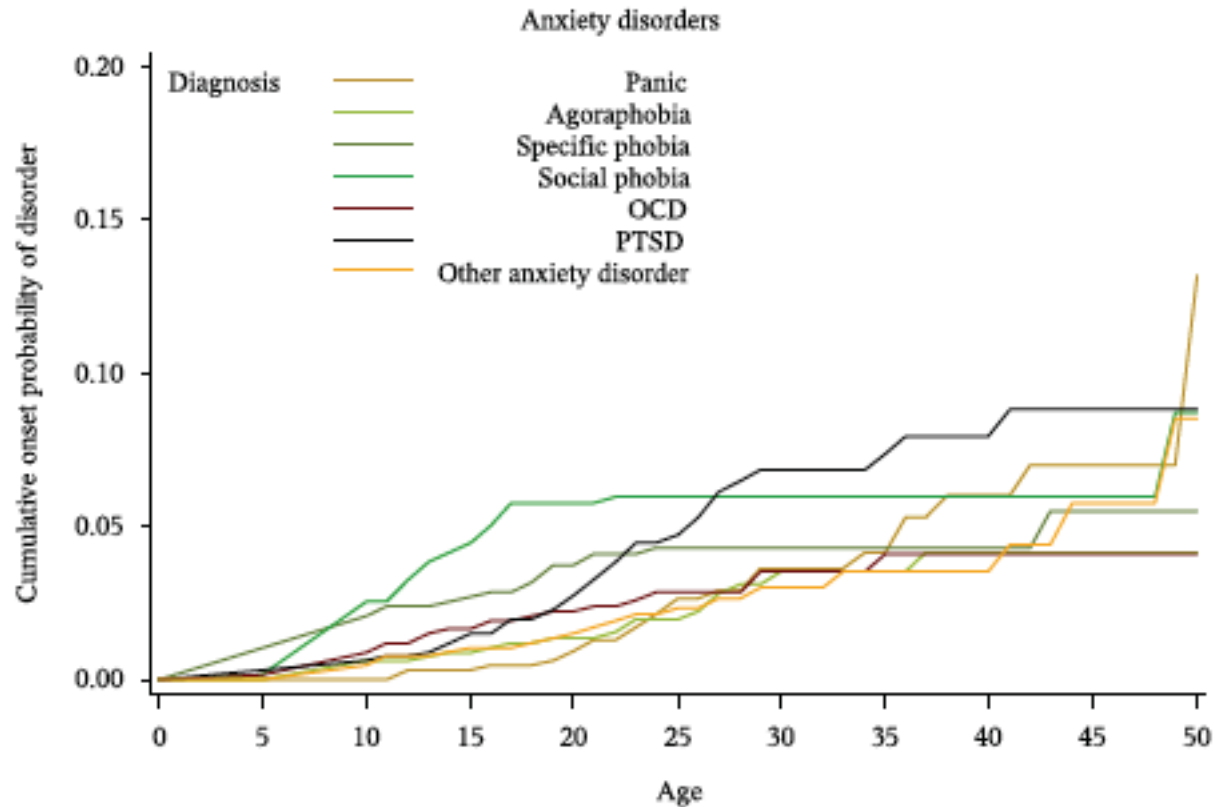
Age of onset: Substance disorders



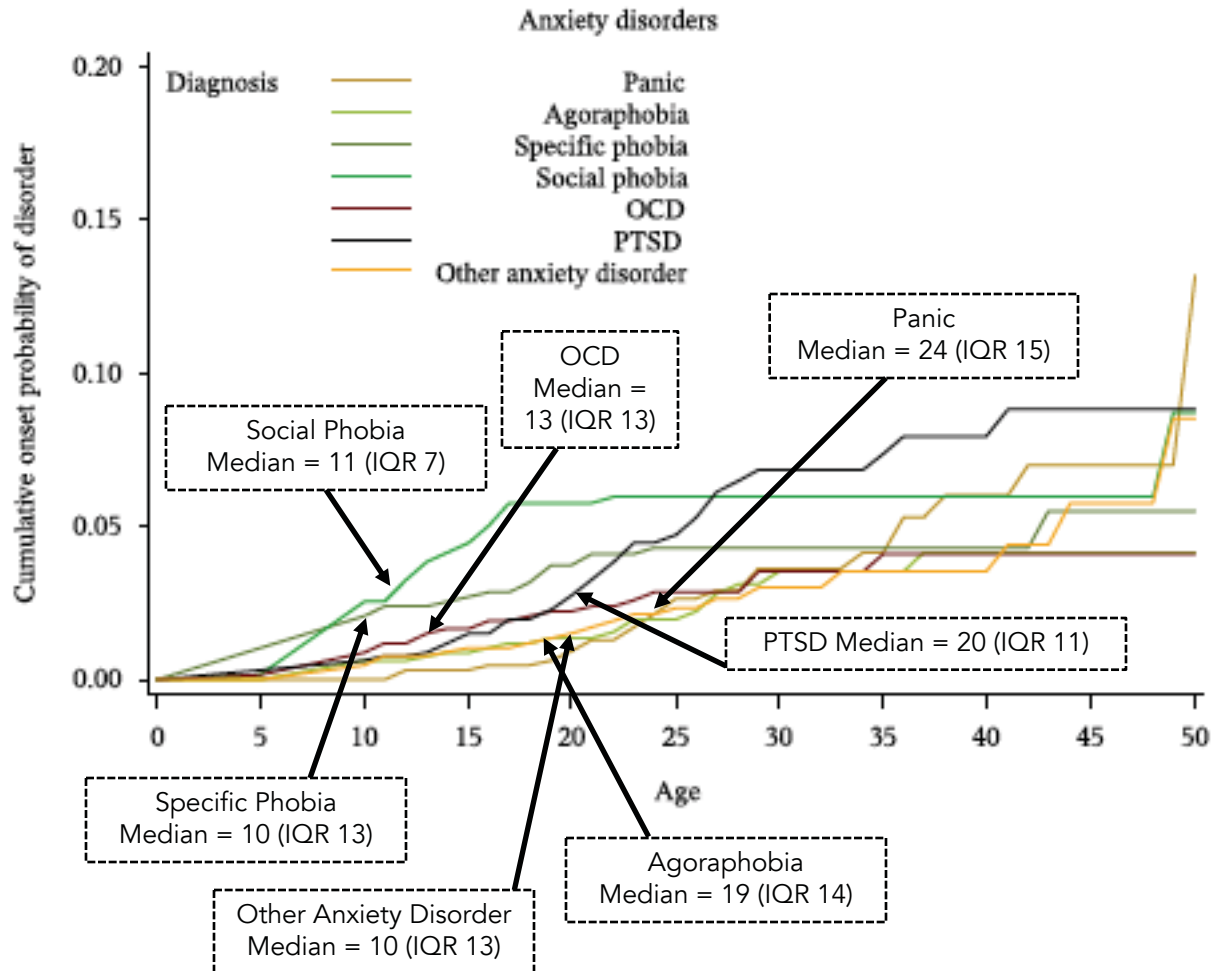
Age of onset: Substance disorders



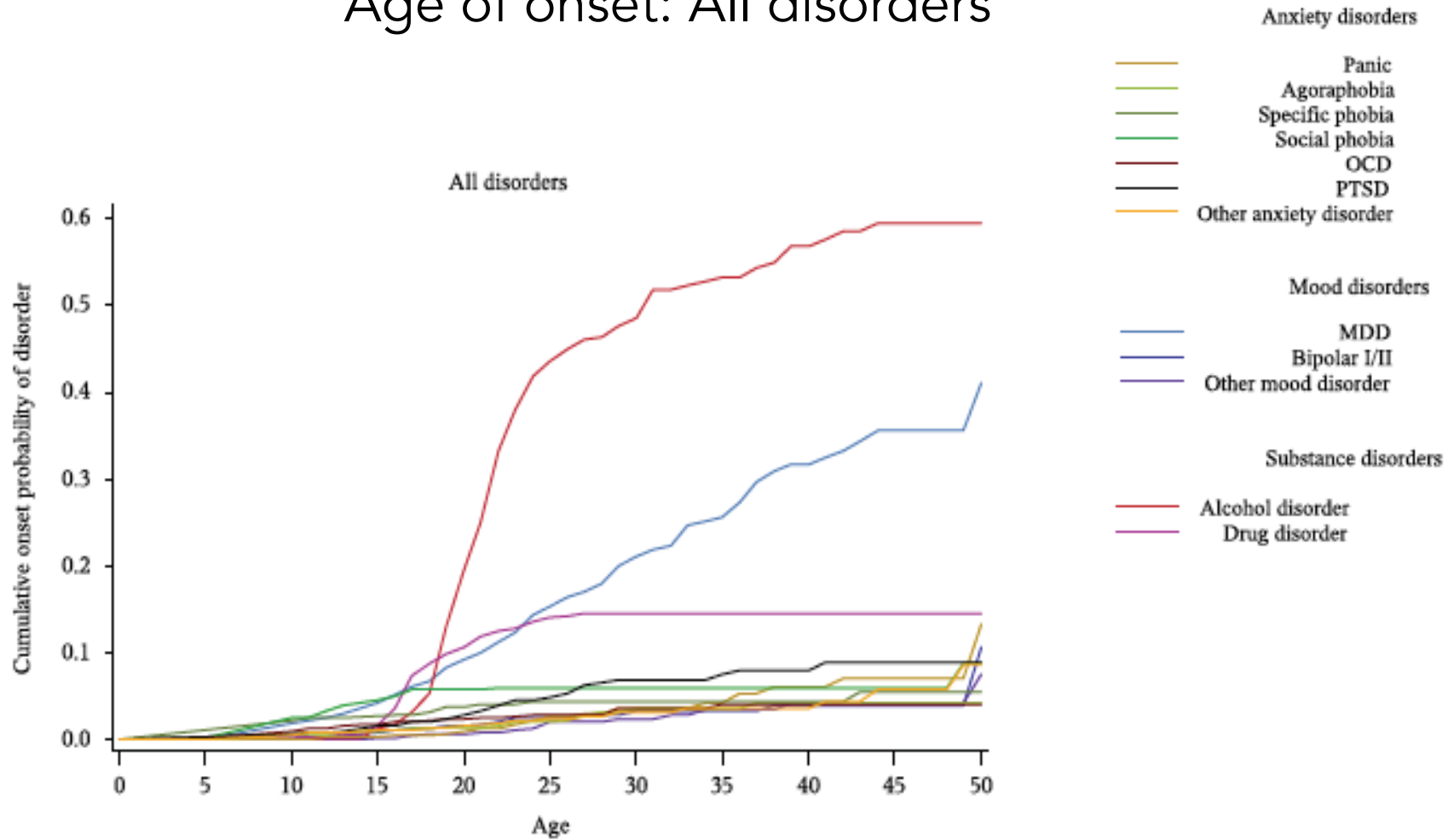
Age of onset: Anxiety disorders



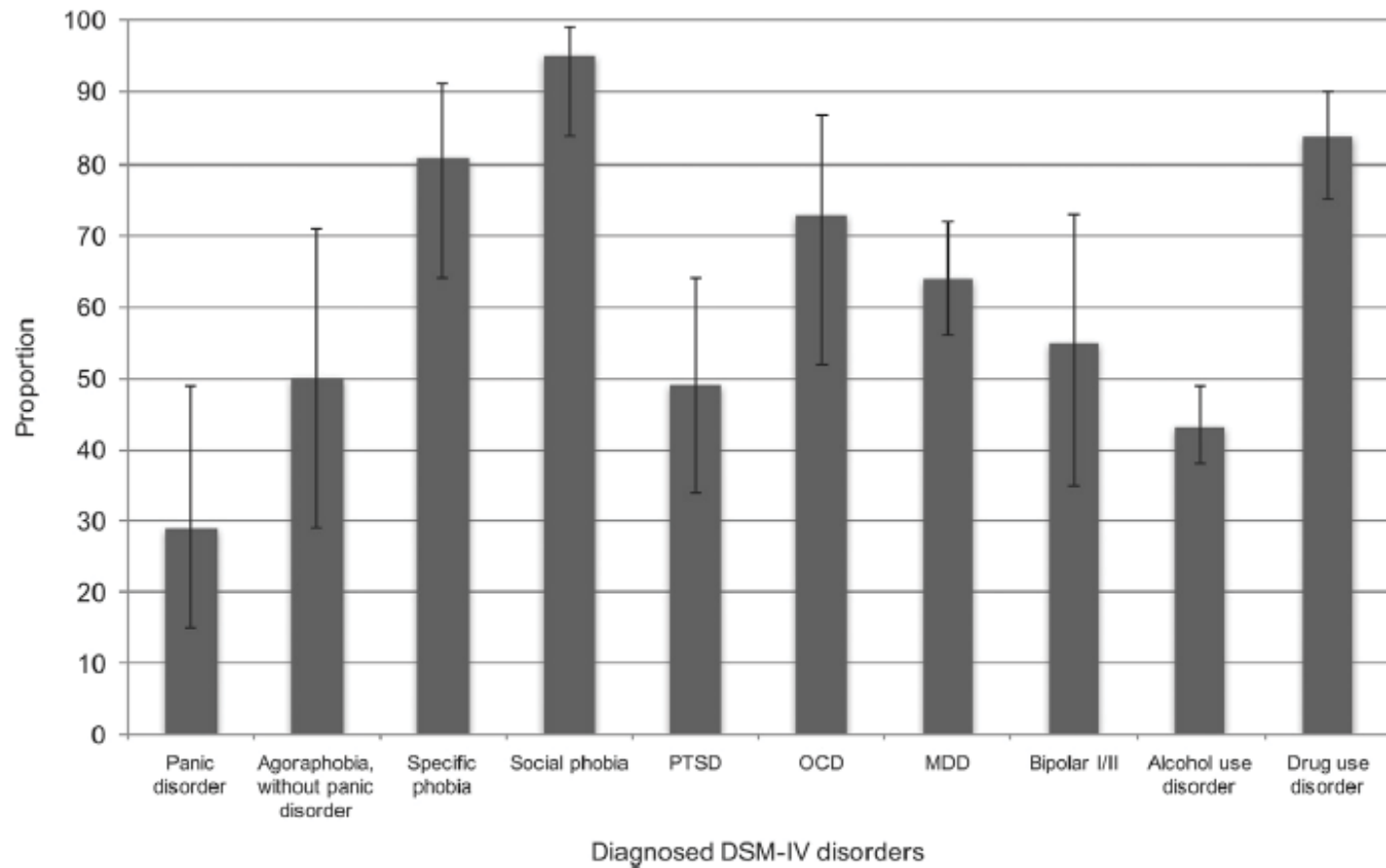
Age of onset: Anxiety disorders



Age of onset: All disorders



The majority of participants reported pre-enlistment onset of their mental health disorder



Conclusions

- About 61% of soldiers met criteria for 1 or more lifetime psychiatric disorders
- Alcohol abuse/dependence and Major Depressive Disorder were the most common individual disorders
- The majority of those disorders onset before military enlistment
- The military may want to expand current identification and support programs to include lifetime mental illness, which may affect soldiers' function and vulnerability to the effects of future potentially traumatic event exposure

Are there critical periods for prevention of alcohol use disorders?

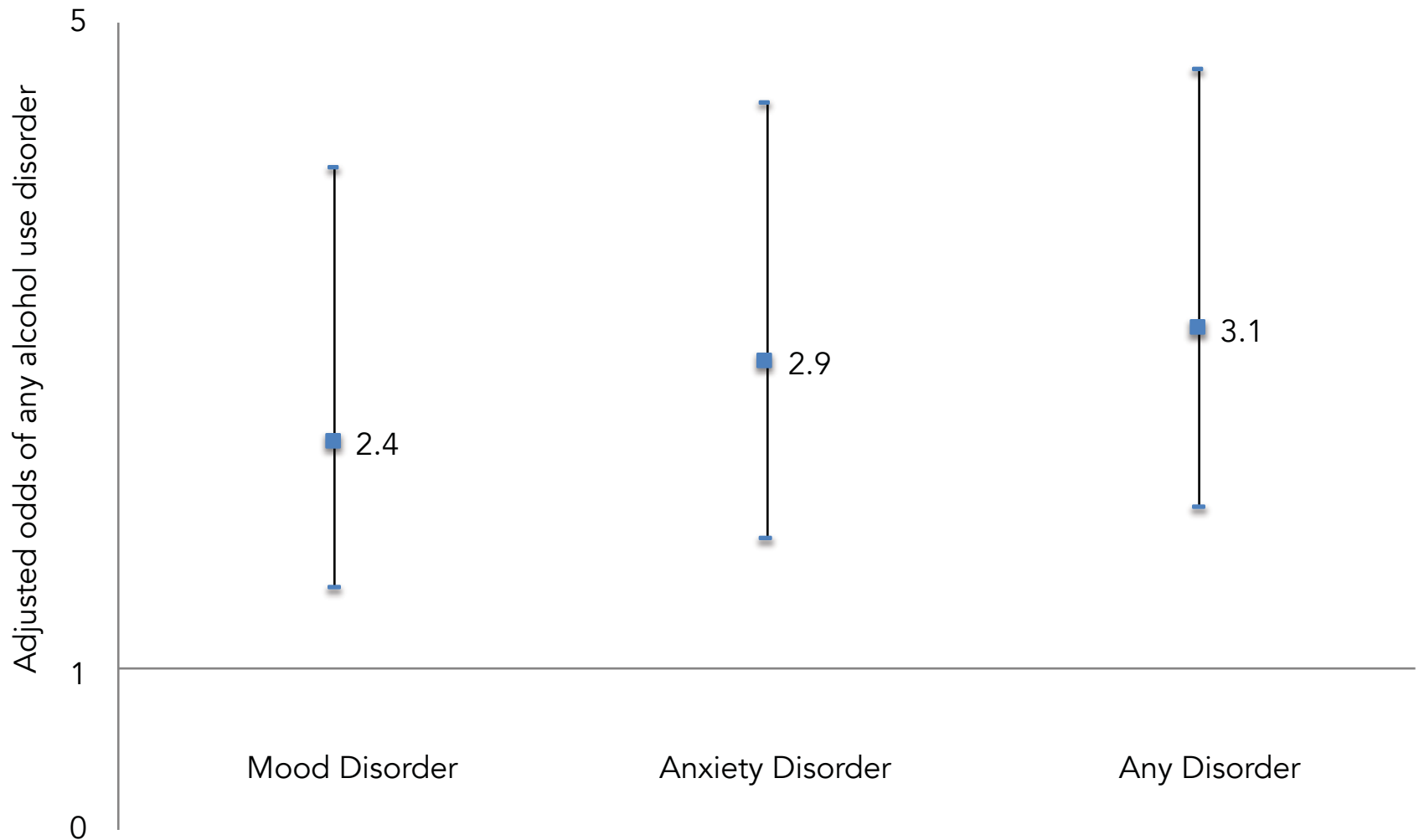
Study aims

- To investigate the temporal relationship between alcohol use disorders and anxiety or mood disorders
- To investigate whether alcohol use disorders were more likely to be diagnosed in the presence of a current mood or anxiety disorder

Competing hypotheses for comorbidity of alcohol use disorders and mood and anxiety disorders

- Self-medication
- Downward Spiral
- Shared Exogenous Factor

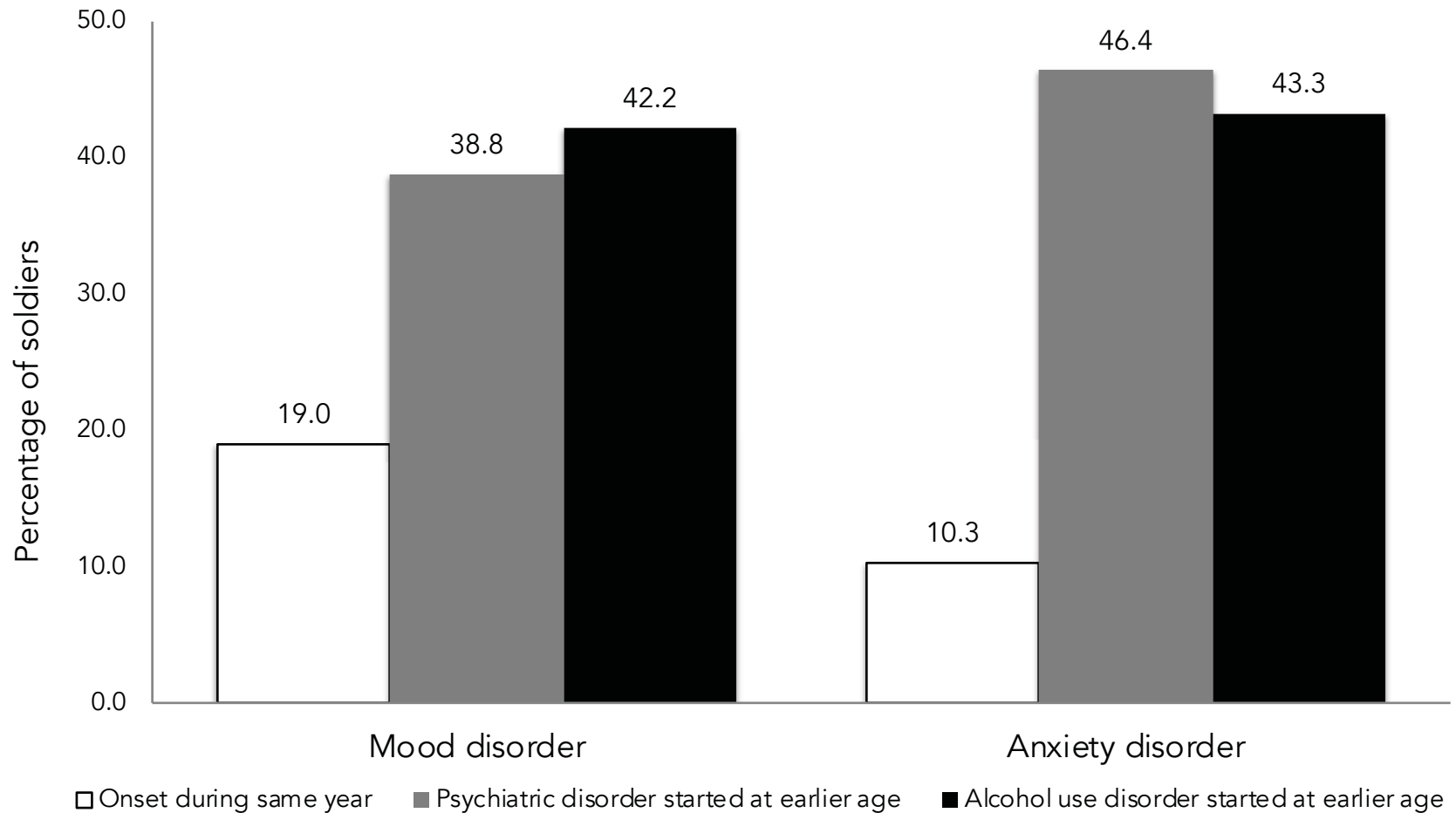
Mood, anxiety and any disorder were each associated with any alcohol use disorder in adjusted analyses



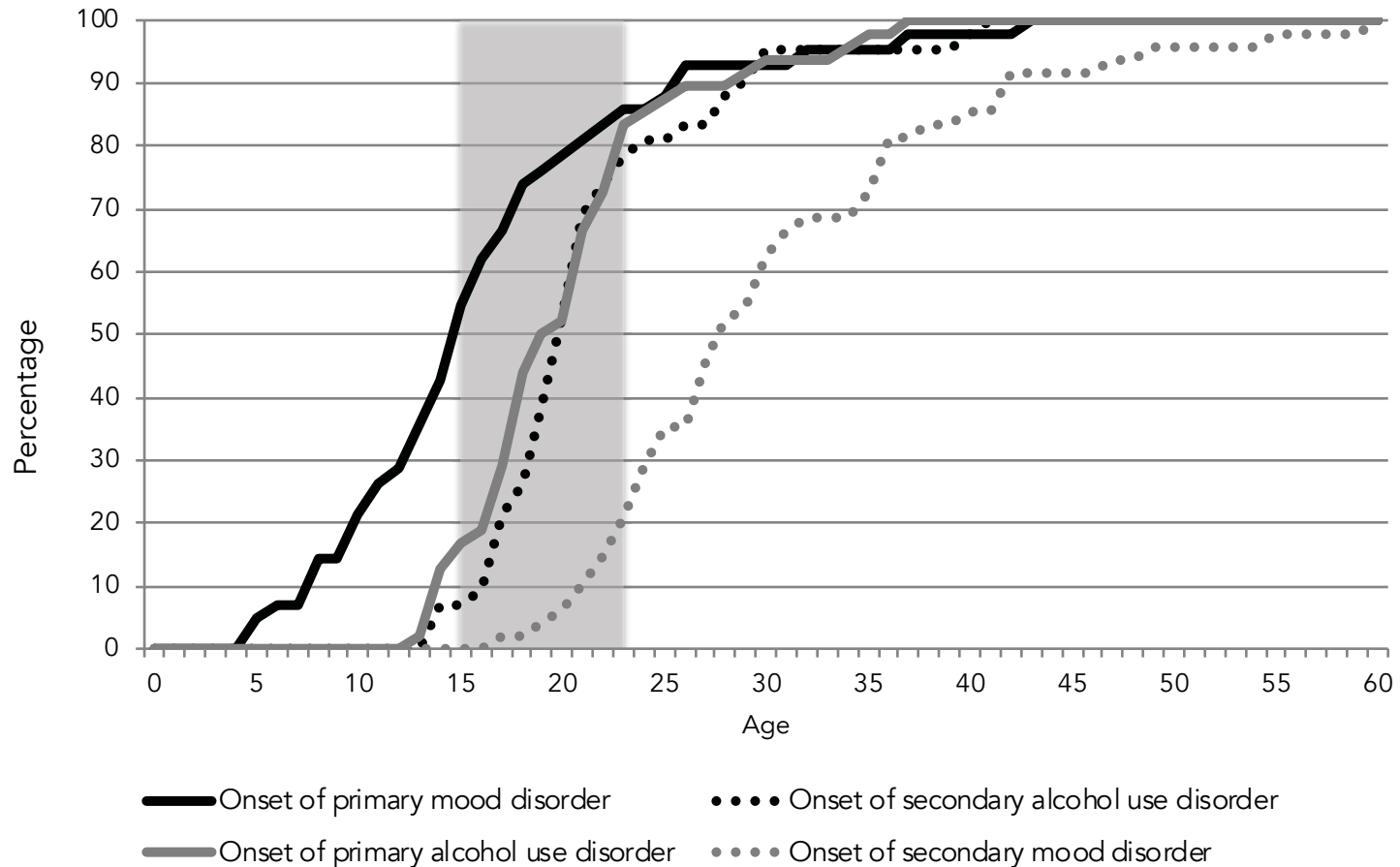
n=163; results adjusted for gender, age, race/ethnicity, rank and lifetime deployment status

Fink DS, Gallaway MS, Tamburrino MB, Liberzon I, Chan P, Cohen GH, Sarpal L, Shirley E, Goto T, D'Arcangelo N, Fine T., Reed PL, Calabrese JR, Galea S. Onset of alcohol use disorders and comorbid psychiatric disorders in a military cohort: are there critical periods for prevention of alcohol use disorders? *Prevention Science* 2016; 17(3): 347-56.

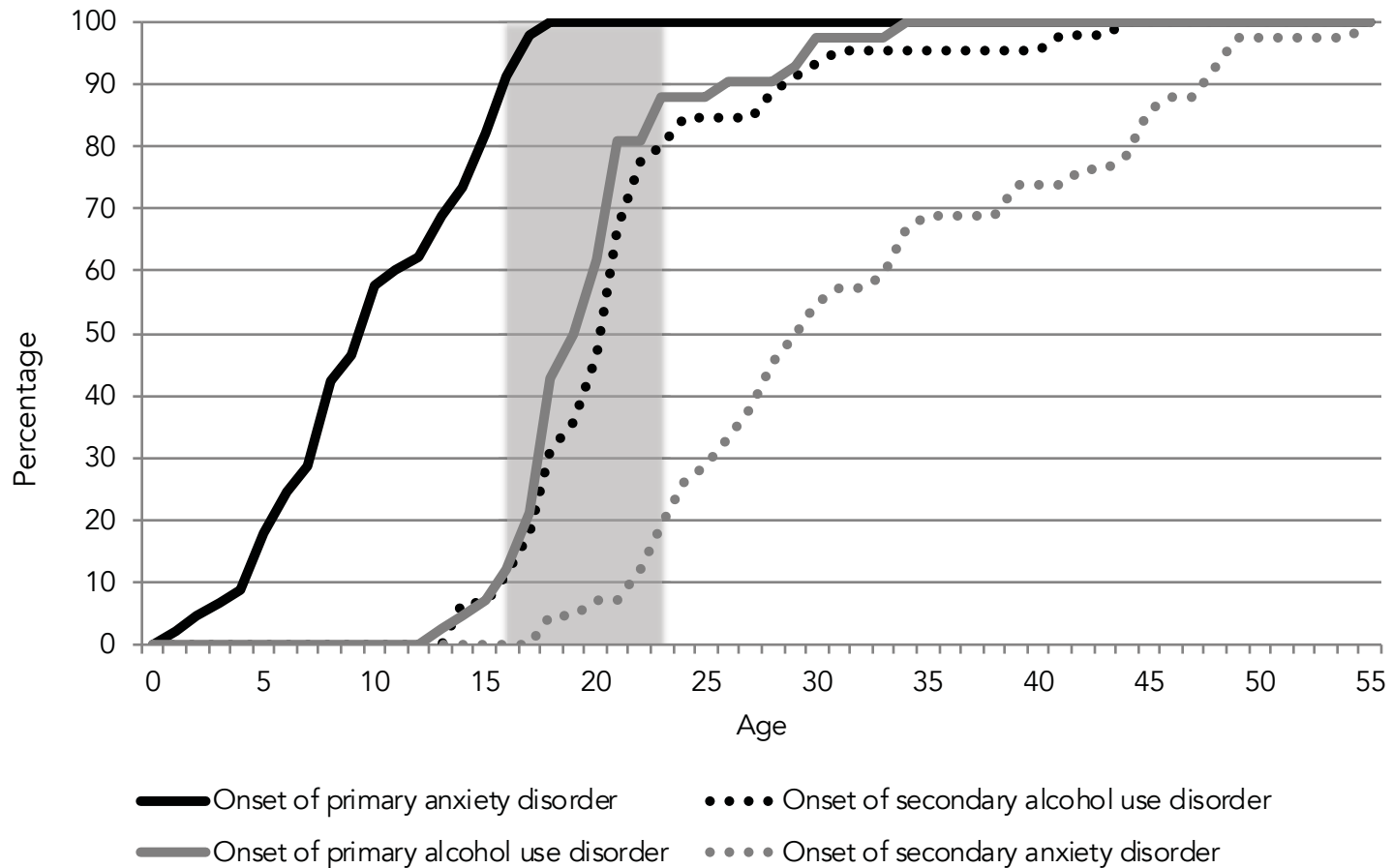
Distributions of comorbidity in our sample were similar across mood and anxiety disorders



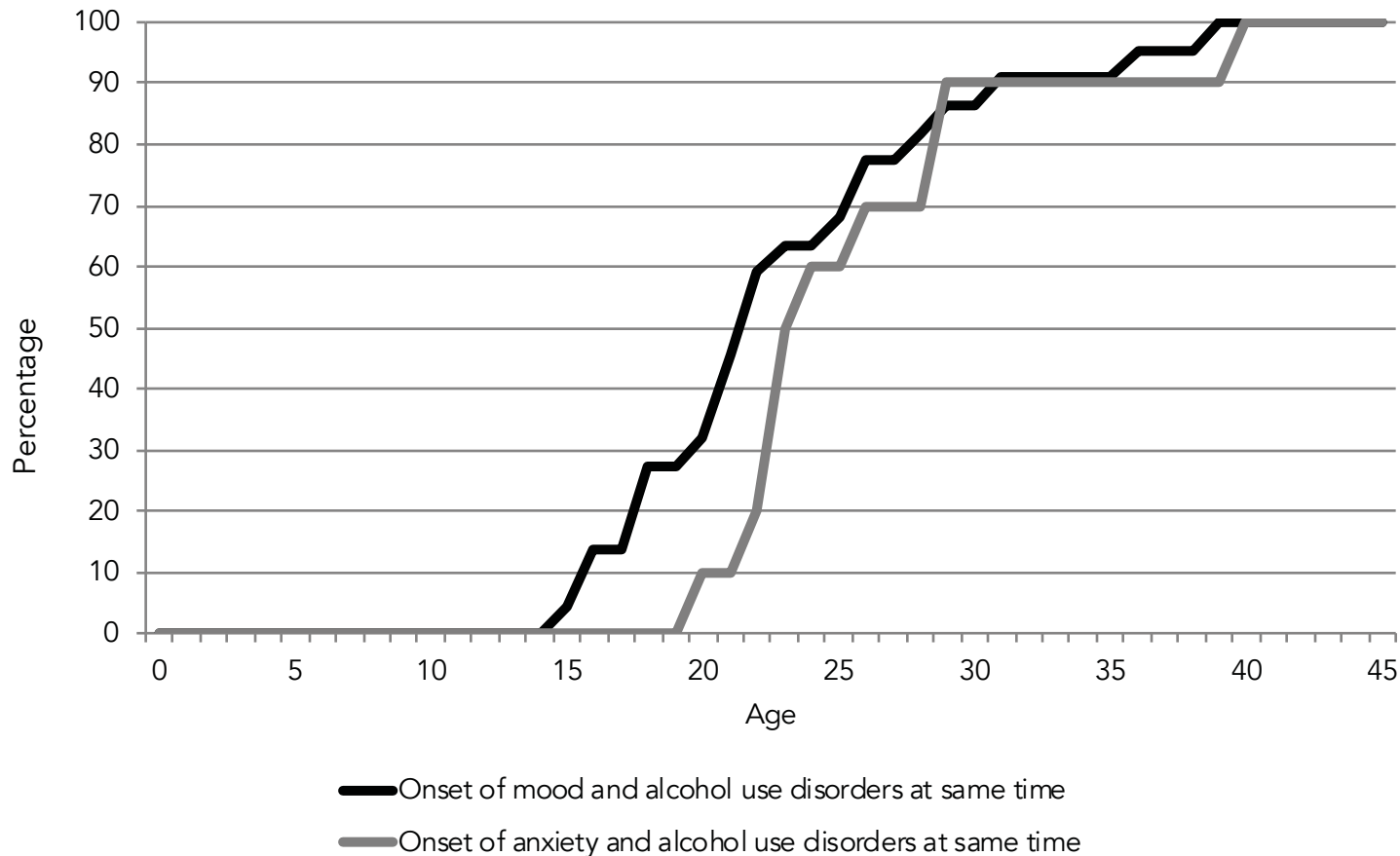
Cumulative age of onset distributions for mood and alcohol use disorders



Cumulative age of onset distributions for anxiety and alcohol use disorders



Age of onset distributions for alcohol use disorders coincident with mood or anxiety disorders

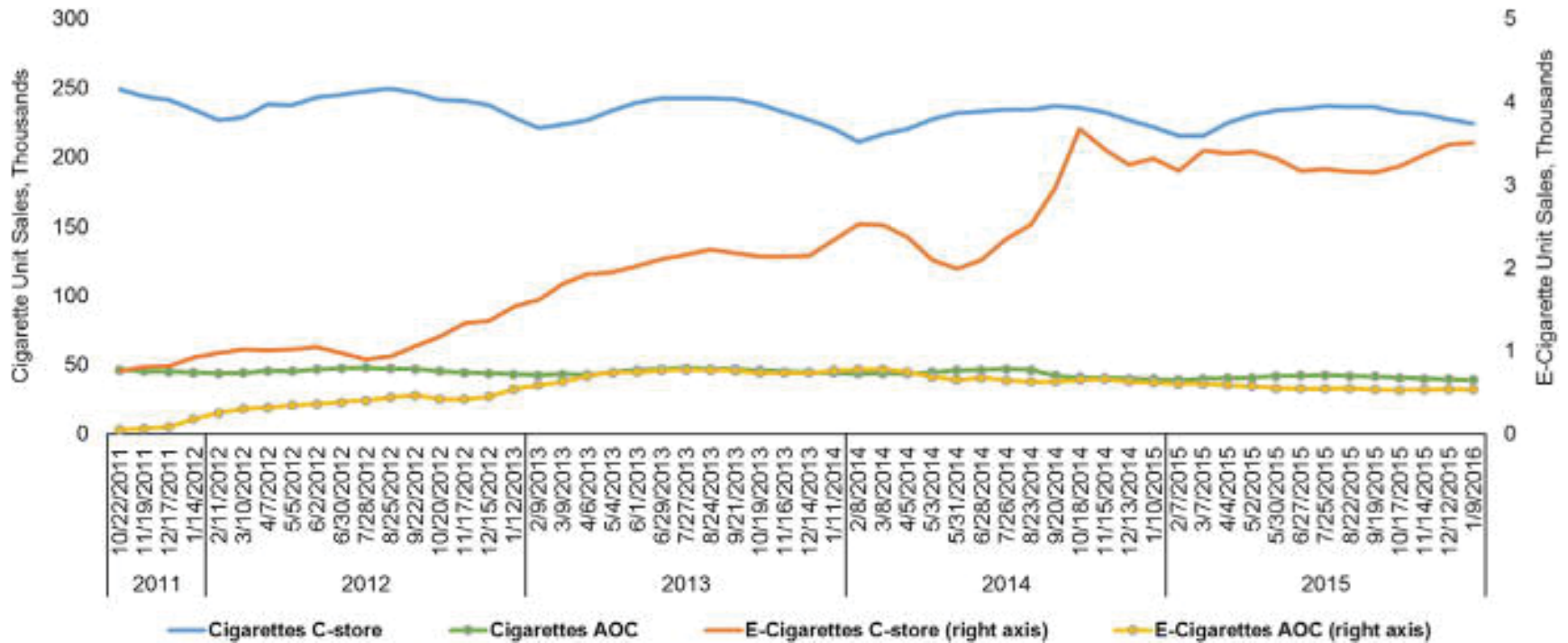


Conclusions

- In lifetime comorbid alcohol use and mood or anxiety disorder, the vast majority of alcohol use disorders start during a narrow age interval between 16 and 23 years old
- Universal interventions for individuals in this age range may provide the greatest population impact

E-cigarette and combustible cigarette use

Cigarette and e-cigarette unit sales, U.S. 2011–2015

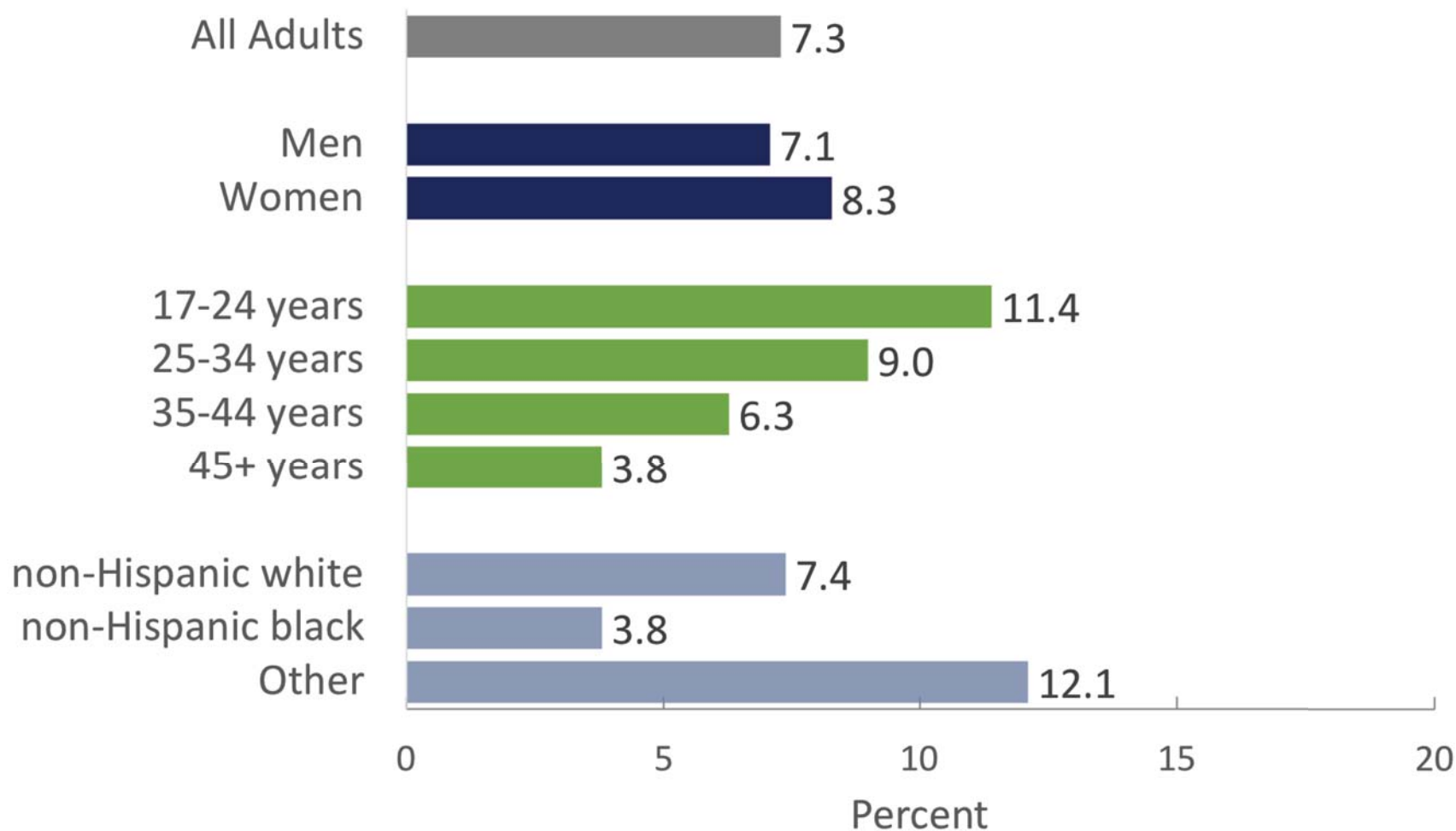


Note: Unit sales per 100,000 people.
 AOC, all other outlets combined; C-store, convenience stores.

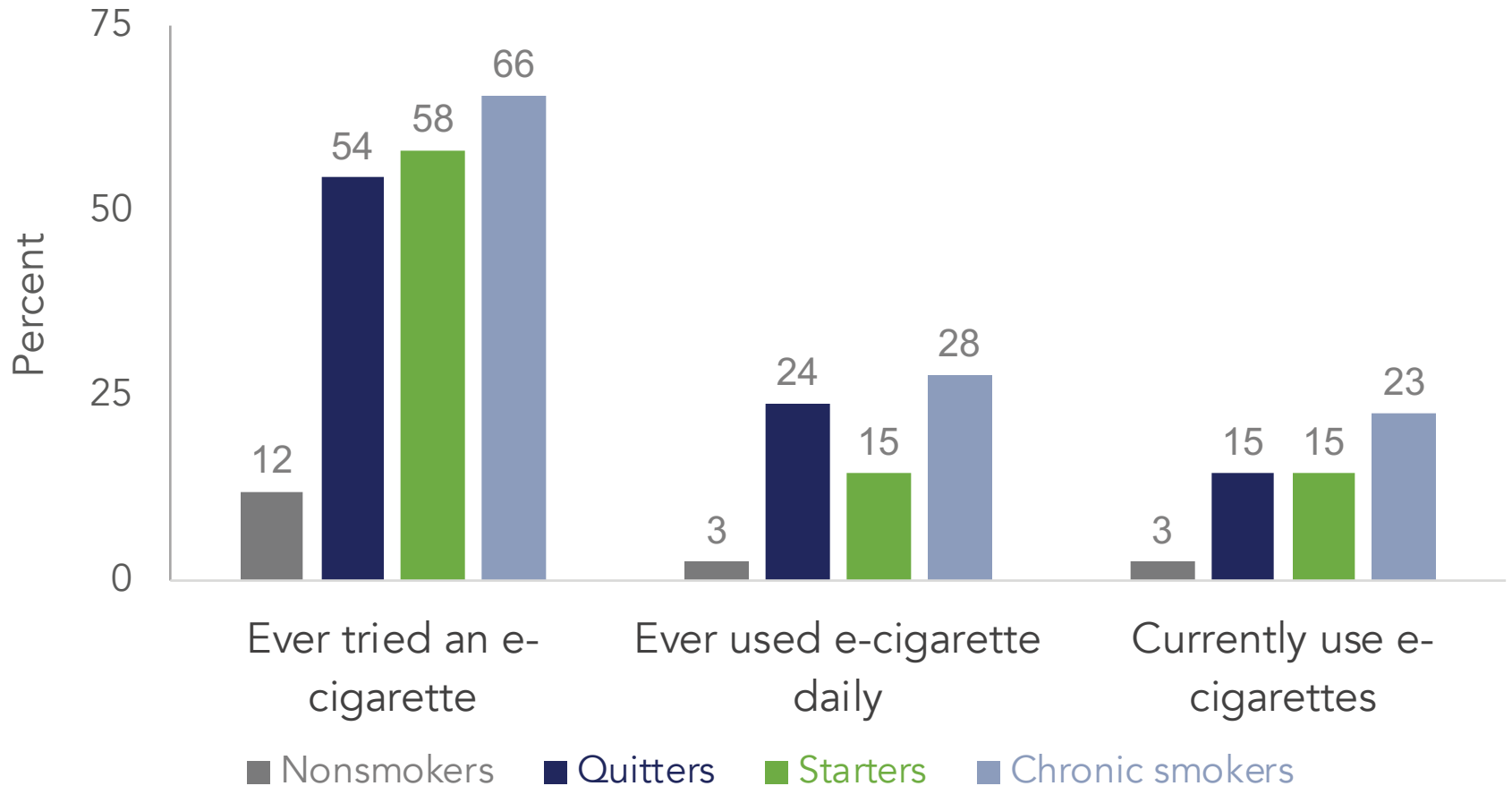
Study rationale and aim

- Two models of e-cigarette and cigarette use
 - A harm reduction model prioritizes the potential for e-cigarettes to reduce the harms from combustible cigarettes until a smoker is able to quit
 - A transition model considers the potential for e-cigarettes to increase the risk of combustible cigarette initiation among nonsmokers
- We investigated the harm reduction model using waves 4 and 6 of the OHARNG-MHI

Percentage of soldiers who currently use e-cigarettes, by sex, age, and race/ethnicity, 2016

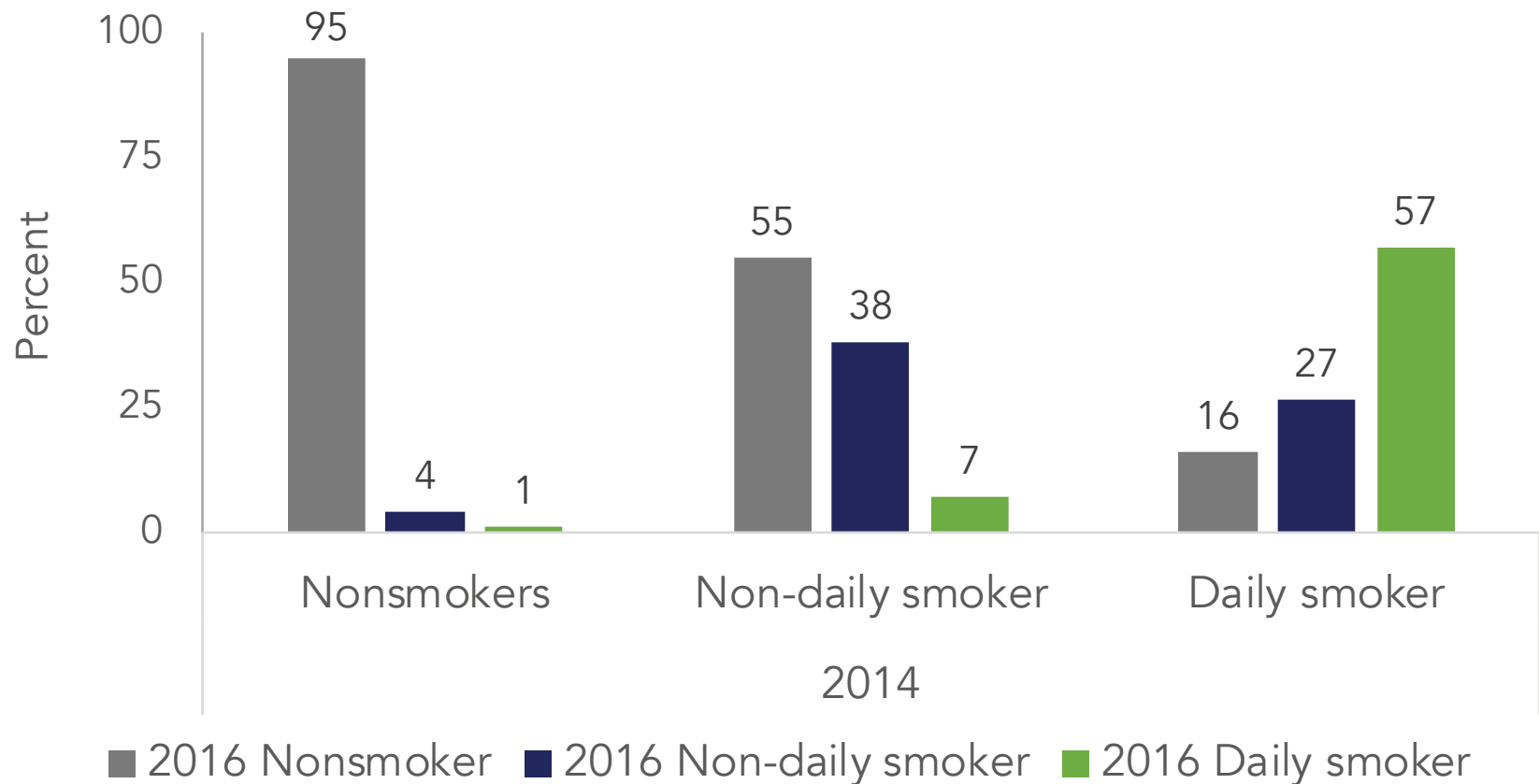


Percentage of soldiers who had ever tried an e-cigarette, ever used e-cigarettes daily, and currently use e-cigarettes, by cigarette smoking status, 2014 and 2016



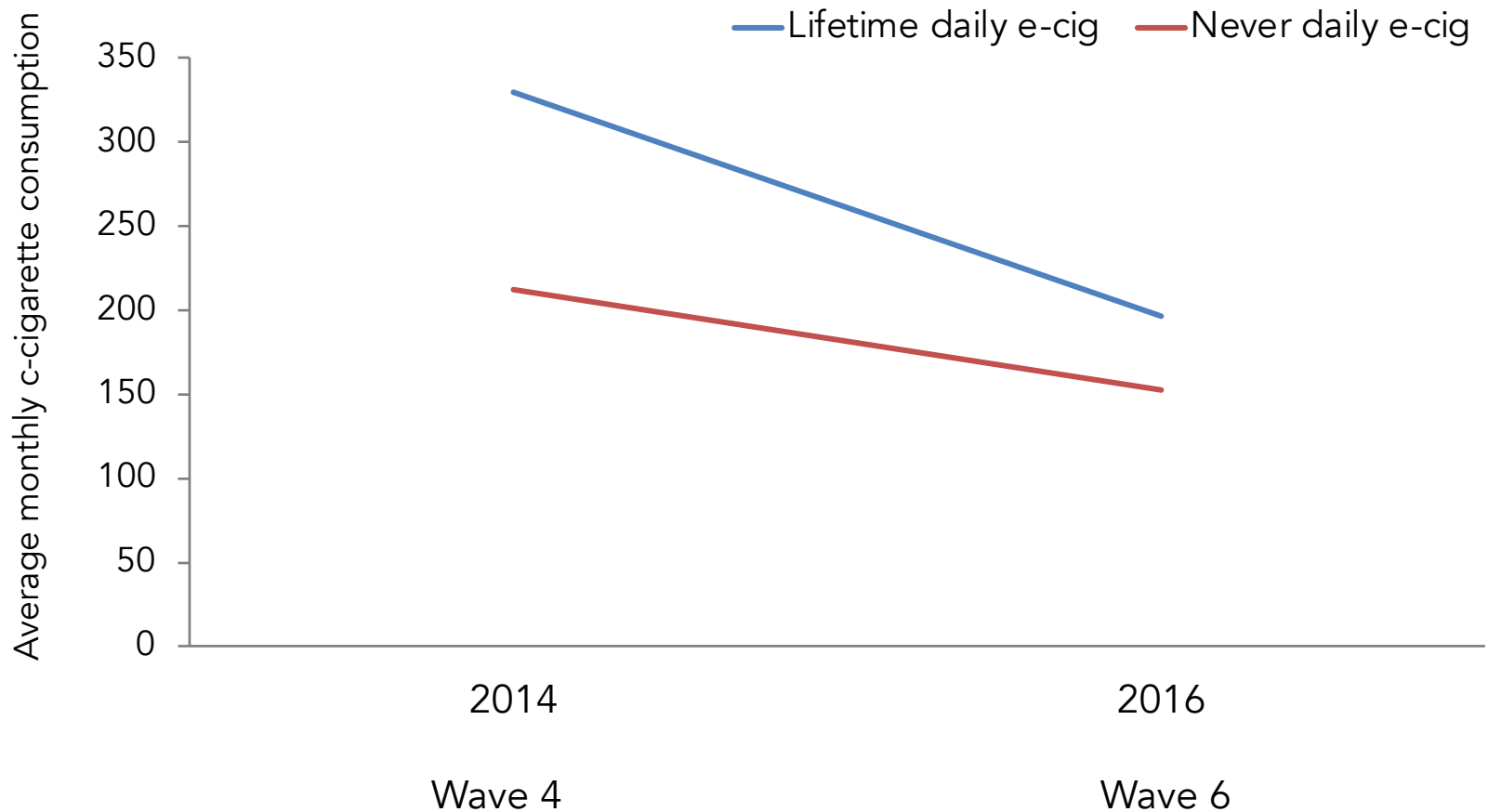
Current e-cigarette users have ever tried an e-cigarette and currently used them every day or some days during the past month. Nonsmokers reported no past-month cigarette use at either wave 4 or wave 6. Quitters reported using cigarettes every day or some days during the past month at wave 4, and no past-month cigarette use at wave 6. Starters reported no past-month cigarette use at wave 4, and reported using cigarettes every day or some days during the past-month at wave 6. Chronic smokers reported using cigarettes every day or some days during the past-month at both wave 4 and wave 6.

The vast majority of nonsmokers in 2014 remained nonsmokers in 2016. Many nondaily and daily smokers in 2014 reduced their smoking in 2016



Nonsmokers reported no past-month cigarette use. Non-daily smoker reported past-month use, but no everyday use. Daily smokers reported smoking cigarettes everyday during the past month.

Change in the average rate of past-month cigarette smoking by ever daily e-cigarette use



Conclusions

- Nonsmokers largely remained nonsmokers
- Nearly half of smokers reduced their smoking
- Few new-onset smokers reported ever using (15%) or currently using e-cigarettes daily (15%)
- Smokers in 2014 who reported ever using e-cigarettes daily smoked, on average, 4 packs less per-month in 2016

Prevalence and covariates of problematic gambling

Recent legalization and expansion of gambling in Ohio



2012:

Jack Cleveland (Cleveland)
Hollywood Casino (Toledo)
Scioto Downs Racino (Columbus)
Hollywood Casino (Columbus)

2013:

Jack Cincinnati (Cin.)
Jack Thistledown Racino (N. Randall)
Maimi Valley (Turtlecreek)
Hard Rock Casino (Northfield)

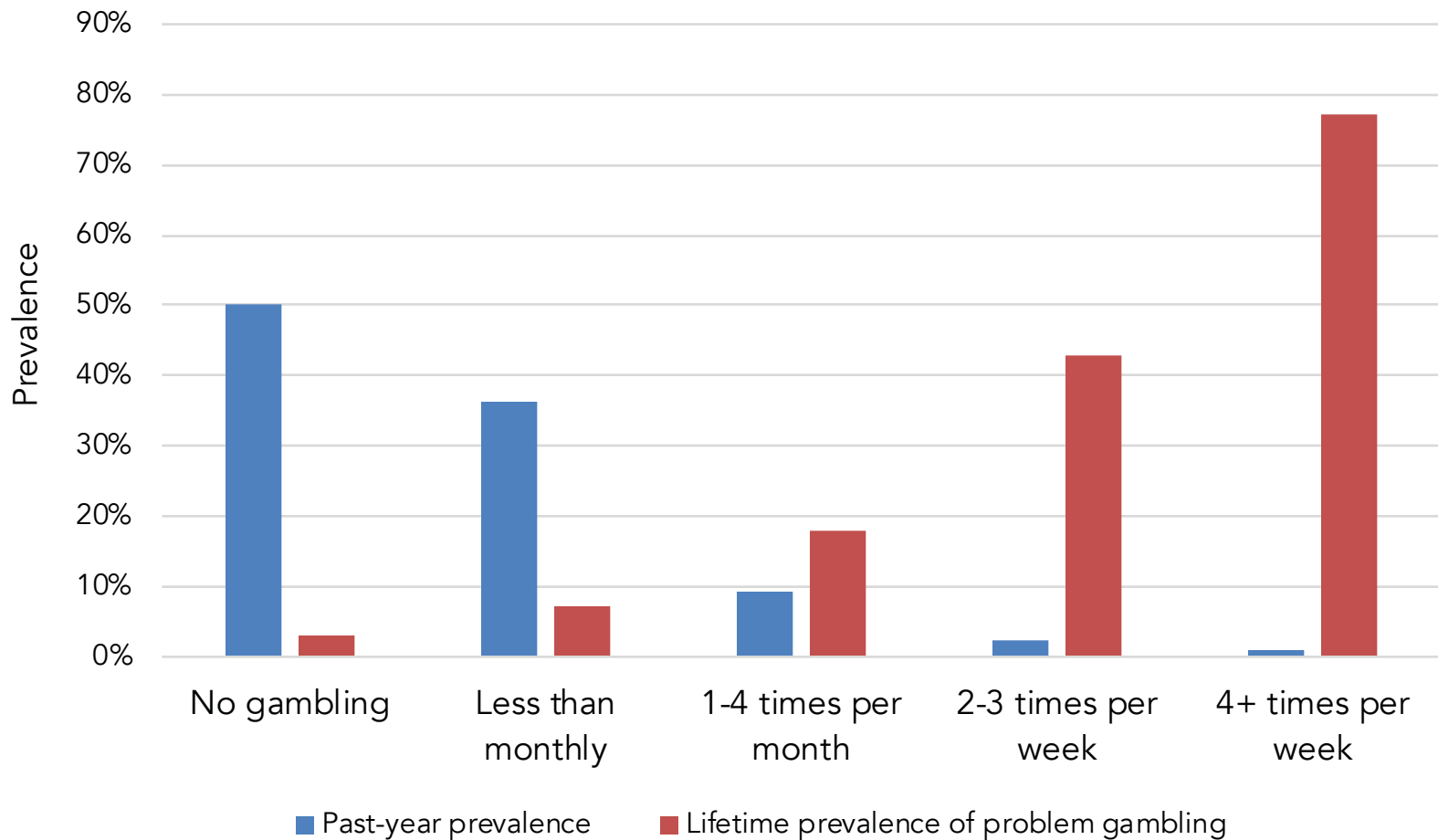
2014:

Belterra Park (Anderson)
Hollywood Gaming (Dayton)
Hollywood Gaming (Austintown)

Rationale and study aim

- About 5% of adults have experienced some form of gambling problem during their lifetime
- Gambling problems are highly correlated with mental health and substance use issues
- Gambling opportunities in Ohio have increased rapidly and are become more accessible through various platforms (e.g., online gaming, sports betting, lottery)
- This study investigates the prevalence of potential problematic gambling behaviors and their relationship with sociodemographic and military factors

Frequency of past-year gambling and lifetime problem gambling, 2016



Correlates of screening positive for lifetime problematic gambling

Demographic correlates

Male

Unmarried

Left the Guard or retired

Psychosocial correlates

Alcohol use disorder

Minor depression

Poor general health

Increasing pain

Legal problems

Financial problems

Impulsivity scores and suicidal ideation were similar between those who screened positive for problematic gambling and those who did not.

Conclusions

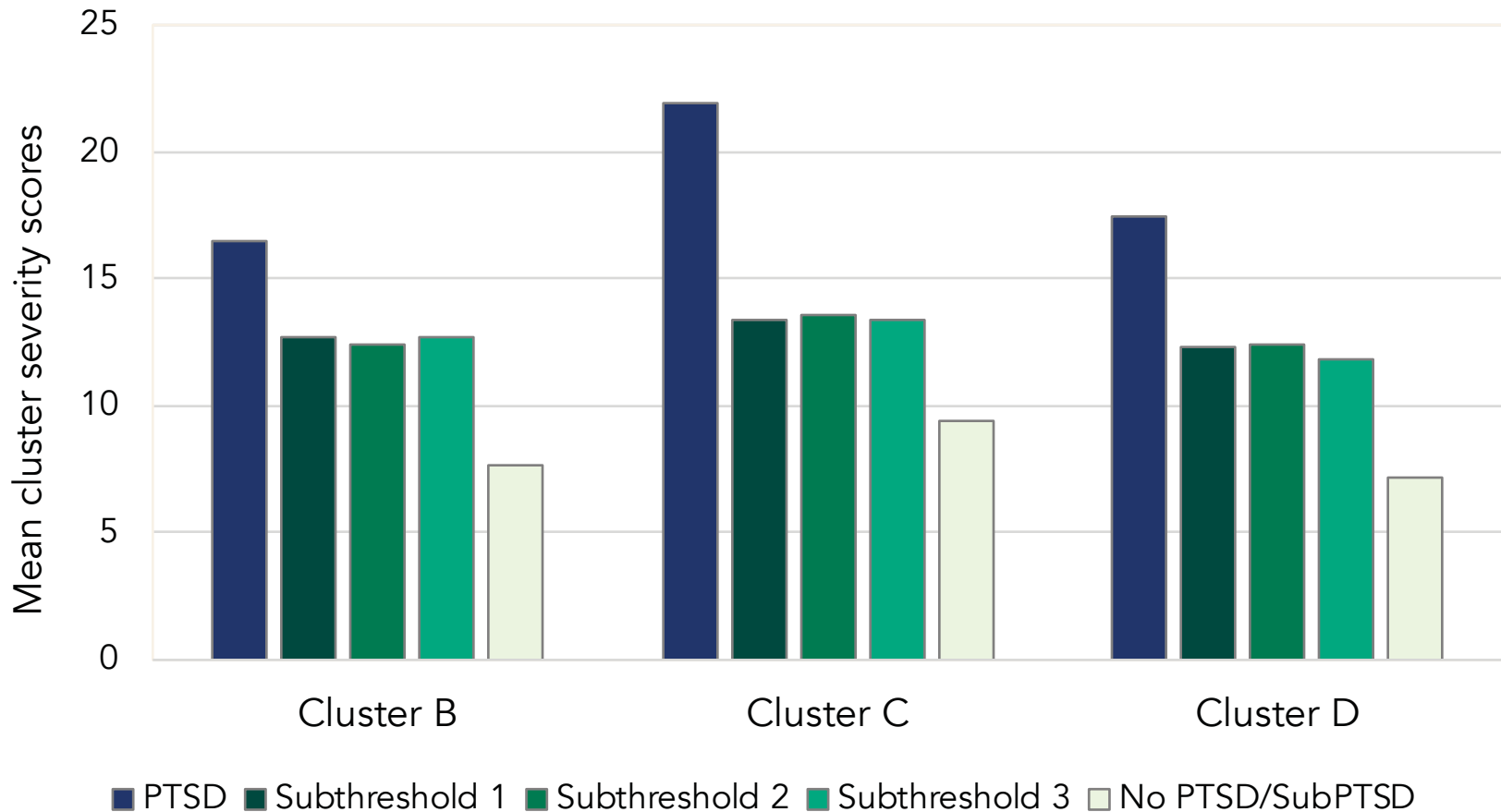
- High frequency gambling (1+ times per week) is common
- Lifetime problem gambling is twice as prevalent in this sample than the general US population
- Given the prevalence of frequent gambling and psychosocial correlates of problem gambling, it may be important to routinely screen and monitor military personnel for frequency of gambling behaviors.

Subthreshold PTSD and PTSD: Potential targets for preventive interventions

Rationale, study aim, and methods

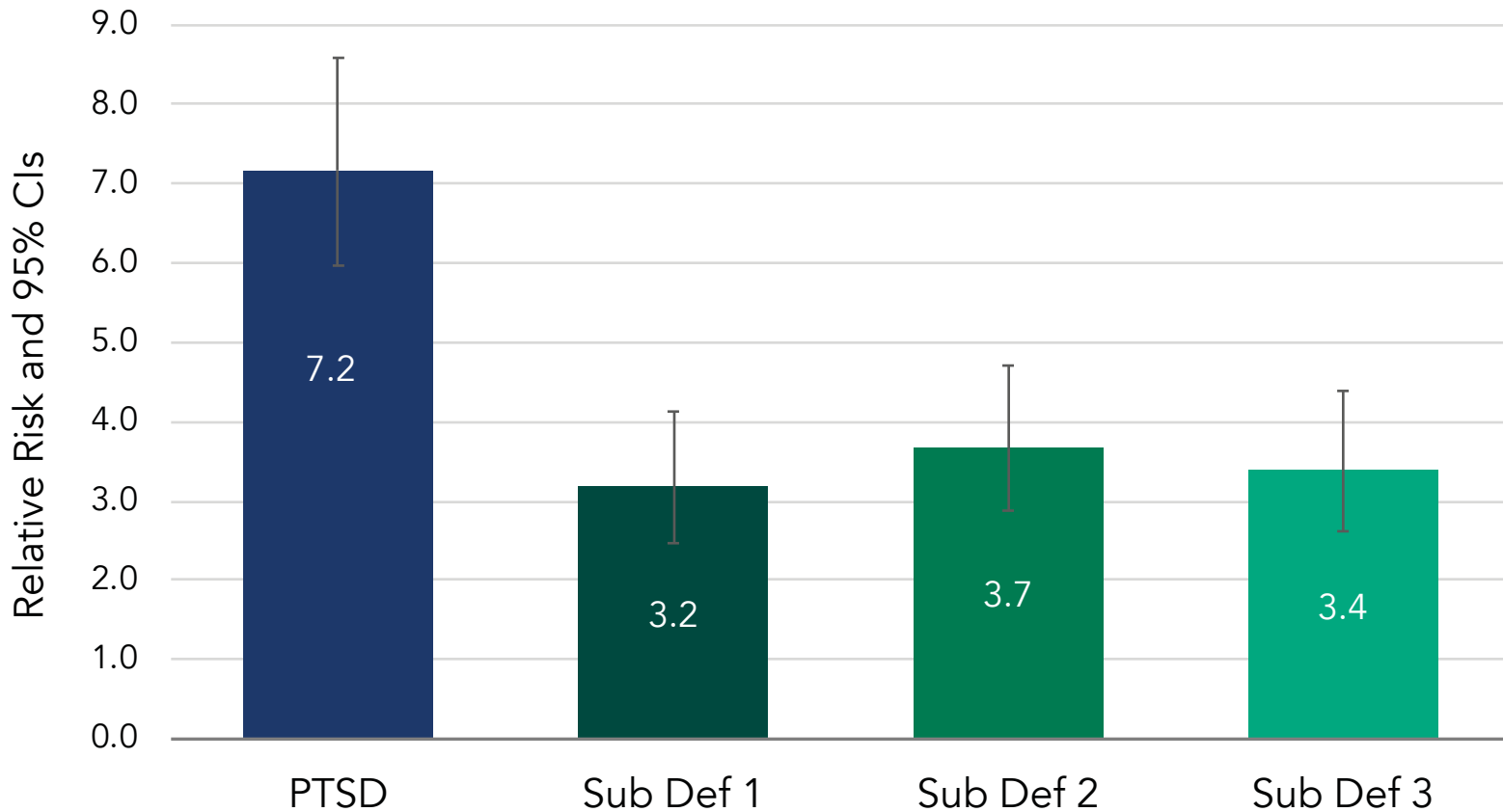
- Prevention of PTSD requires identification of subpopulations contributing most to the population burden of PTSD
- This study examined the relative contribution of subthreshold PTSD and diagnosable PTSD on later PTSD in the ONG
- We classified ONG respondents into 3 groups at each wave based PTSD symptoms:
 - Current PTSD (Criteria A, DSM-IV criteria, functional impairment)
 - Subthreshold PTSD (Criteria A, at least one symptom in each cluster)
 - No PTSD
- We calculated the exposure rate, risk ratio, and population attributable fraction (PAF)

Mean symptom cluster scores among respondents screening positive for probable PTSD, subthreshold PTSD, and no PTSD

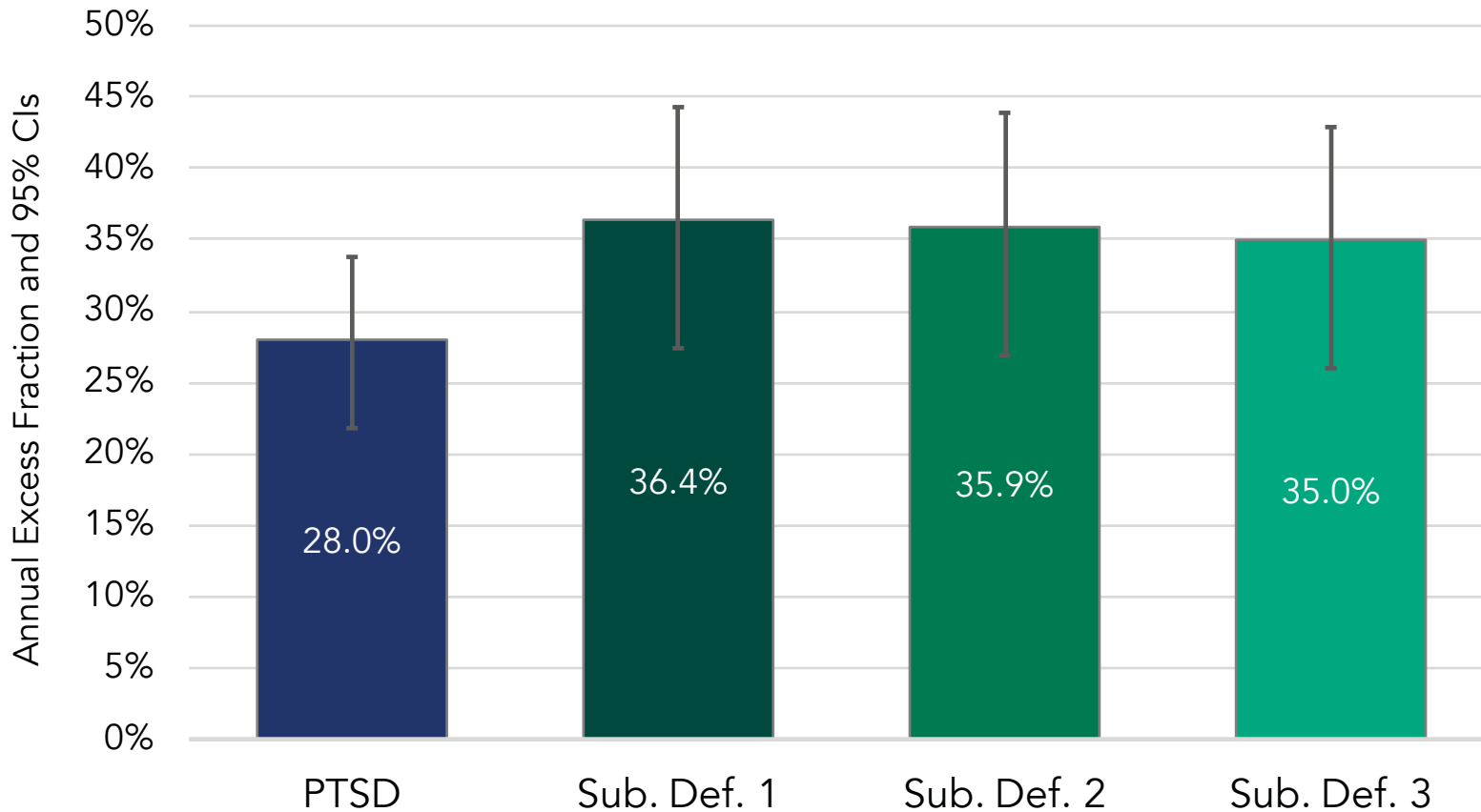


Note. Symptom cluster severity score is obtained by summing the scores for the items within the given cluster.

Relative risk for probable PTSD was twice as great among respondents with probable PTSD the prior interview than that of those with subthreshold PTSD



Population attributable fraction of PTSD related to persons with subthreshold PTSD the prior year was substantial



Conclusions

- The annualized prevalence of subthreshold PTSD and PTSD was 11.9% and 5.0%, respectively
- Subthreshold PTSD accounted for a substantial proportion of this population's future PTSD burden, the future population burden of PTSD would fall by about 35% to 36%, relative to 28% for PTSD
- Population-based preventive interventions, compared to an approach focused on cases of diagnosable PTSD, is likely to affect the greatest reduction in this population's future PTSD burden

Deployment and Alcohol Use

Study aims

- To estimate the effect of deployment on alcohol use behaviors over time
 - No study to date has examined multiple years of post-deployment alcohol use
- Two problems:
 - Soldiers deployed to combat zones can differ substantially from non-deployed Soldiers
 - Deployment to a combat zone is not a homogenous experience and can vary substantially from one Soldier to the next

Soldiers deployed to combat zones can differ substantially from non-deployed Soldiers

Characteristic	Included Deployers (n = 203)		Excluded Deployers (n = 121)		Cohen's d
	No.	%	No.	%	
Age, years ^a	31.0 (9.1)		30.1 (9.8)		0.13
Male	189	93.1	105	86.8	-0.21
Marital status: Never married	73	36.0	58	47.9	-0.24
Marital status: Married	113	55.7	47	38.8	0.34
Marital status: Previously married	17	8.4	16	13.2	-0.16
Parent or primary caregiver	89	43.8	49	40.5	-0.07
Education: Some college or more	159	78.3	95	78.5	0.07
Annual income > \$40,000	135	66.5	73	62.9	0.15
Currently employed	167	82.3	98	81.0	-0.03
Lifetime deployments: 0	81	39.9	58	48.3	-0.16
Lifetime deployments: 1	53	26.1	30	25.0	0.03
Lifetime deployments: ≥2	69	34.0	33	26.7	0.16
Time since last deployment, days ^a	1,485.7 (1,028.9)		1,450.6 (593.2)		-0.09
Mean time in service, years ^a	10.2 (8.4)		9.1 (9.0)		0.25
Posttraumatic stress disorder ^b	29	14.3	10	8.3	0.19
Depression ^c	3	5.9	0	0.0	0.03
Current alcohol dependence ^d	31	15.1	18	14.9	-0.06
Current alcohol abuse ^e	59	29.1	39	33.0	-0.11

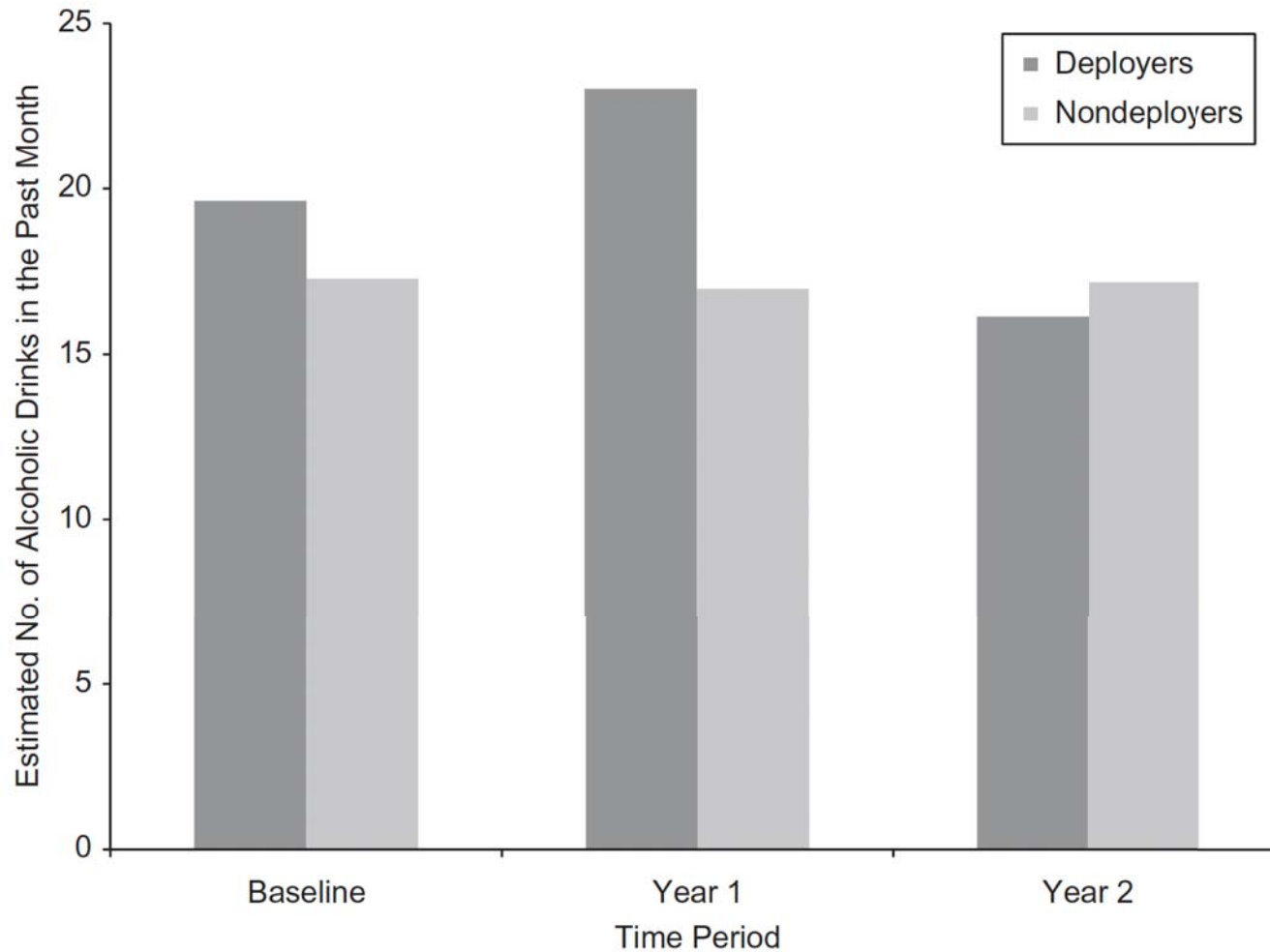
Soldiers deployed to combat zones can differ substantially from non-deployed Soldiers

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Marital status: Never married	73	36.0	58	47.9	-0.24
Marital status: Married	113	55.7	47	38.8	0.34
Marital status: Previously married	17	8.4	16	13.2	-0.16
Parent or primary caregiver	89	43.8	49	40.5	-0.07
Education: Some college or more	159	78.3	95	78.5	0.07
Annual income > \$40,000	135	66.5	73	62.9	0.15
Currently employed	167	82.3	98	81.0	-0.03
Lifetime deployments: 0	81	39.9	58	48.3	-0.16
Lifetime deployments: 1	53	26.1	30	25.0	0.03
Lifetime deployments: ≥2	69	34.0	33	26.7	0.16
Time since last deployment, days ^a	1,485.7 (1,028.9)		1,450.6 (593.2)		-0.09
Mean time in service, years ^a	10.2 (8.4)		9.1 (9.0)		0.25
Posttraumatic stress disorder ^b	29	14.3	10	8.3	0.19
Depression ^c	3	5.9	0	0.0	0.03
Current alcohol dependence ^d	31	15.1	18	14.9	-0.06
Current alcohol abuse ^e	59	29.1	39	33.0	-0.11

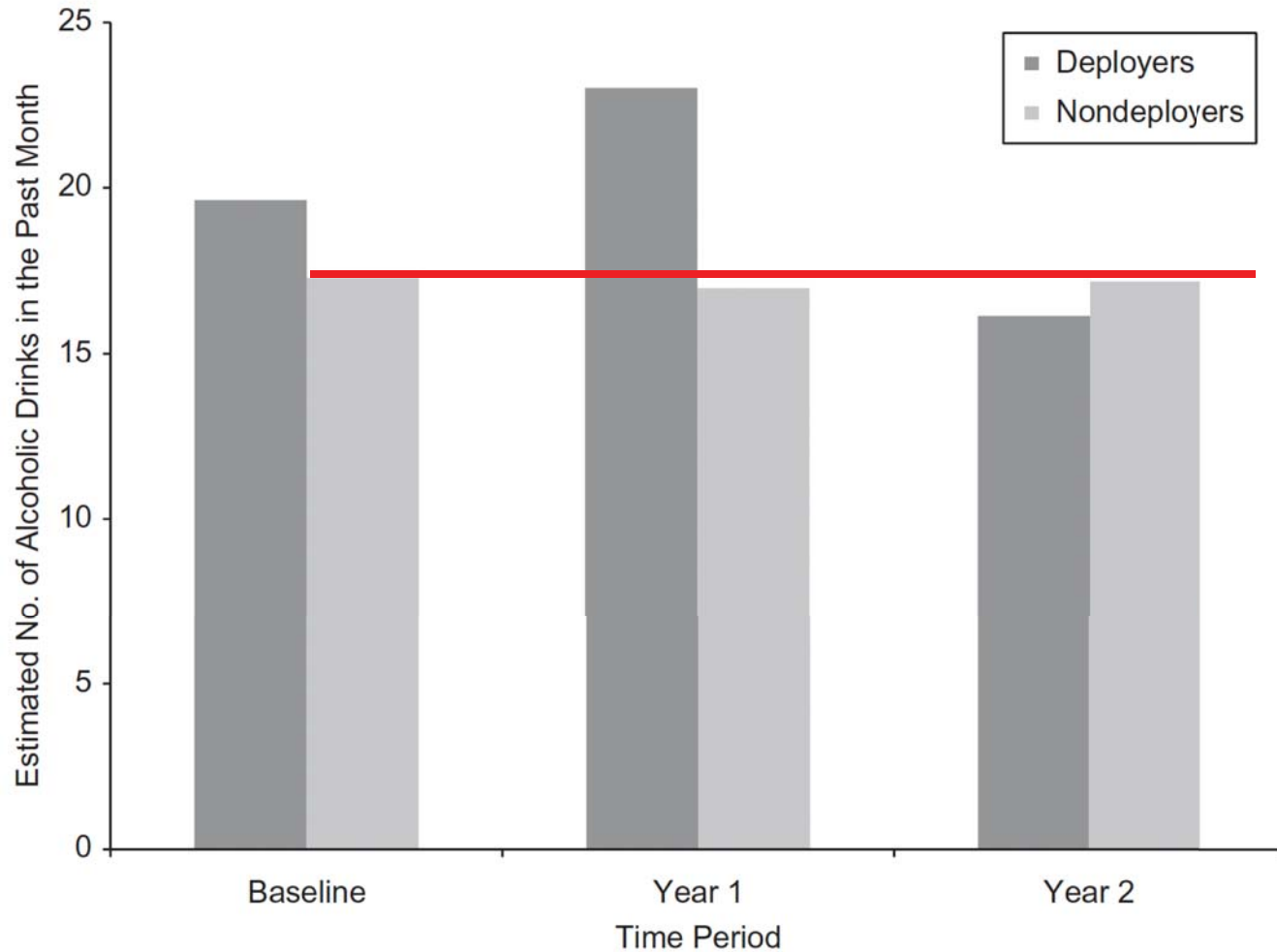
Soldiers deployed to combat zones can differ substantially from non-deployed Soldiers

Characteristic	Included Deployers (n = 203)		Excluded Deployers (n = 121)		Cohen's d
	No.	%	No.	%	
Age, years ^a	31.0 (9.1)		30.1 (9.8)		0.13
Male	189	93.1	105	86.8	-0.21
Marital status: Never married	73	36.0	58	47.9	-0.24
Marital status: Married	113	55.7	47	38.8	0.34
Marital status: Previously married	17	8.4	16	13.2	-0.16
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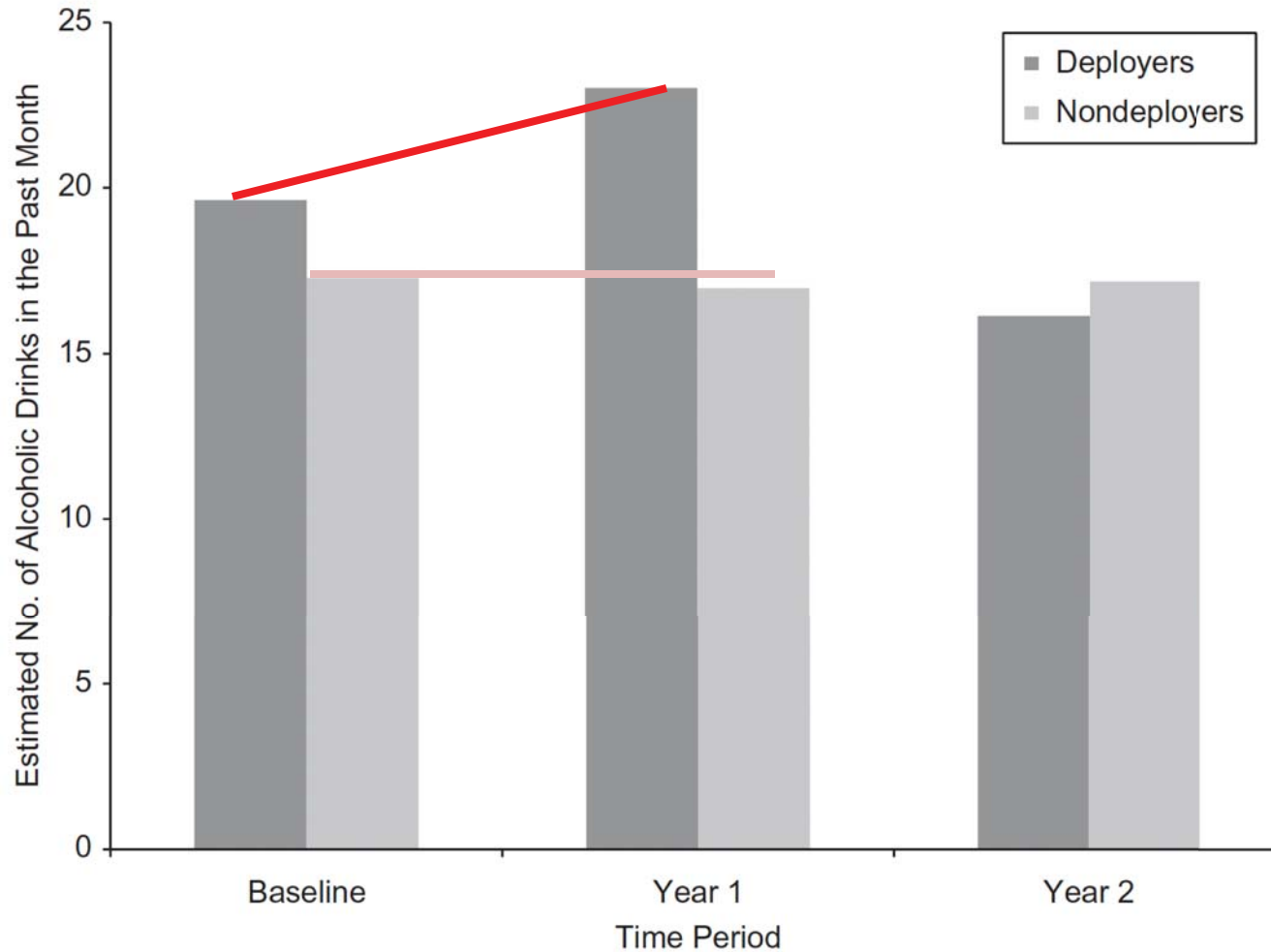
Alcohol use increases 1-year post-deployment, but returns to pre-deployment levels at 2-years post-deployment



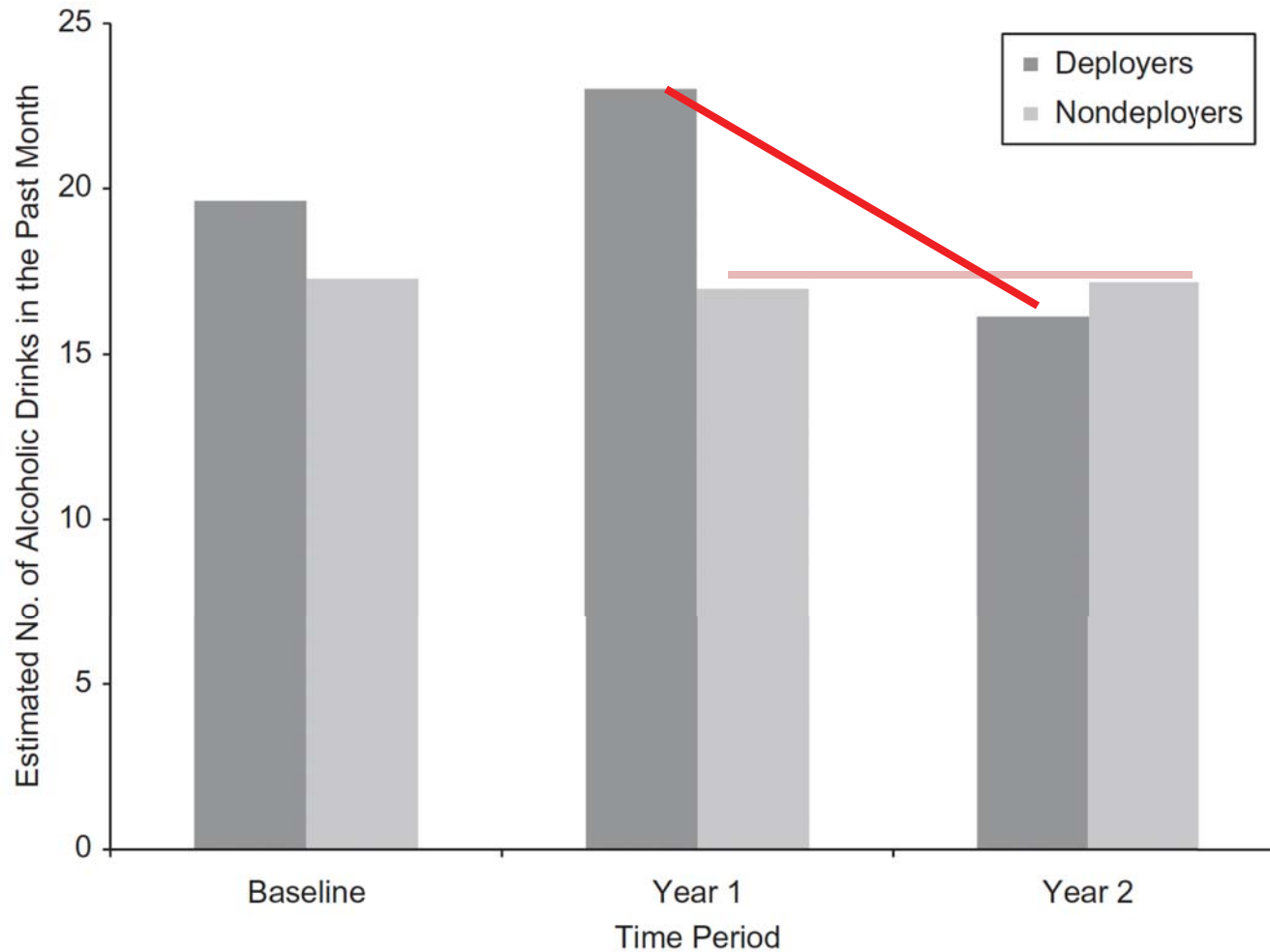
Alcohol use increases 1-year post-deployment, but returns to pre-deployment levels at 2-years post-deployment



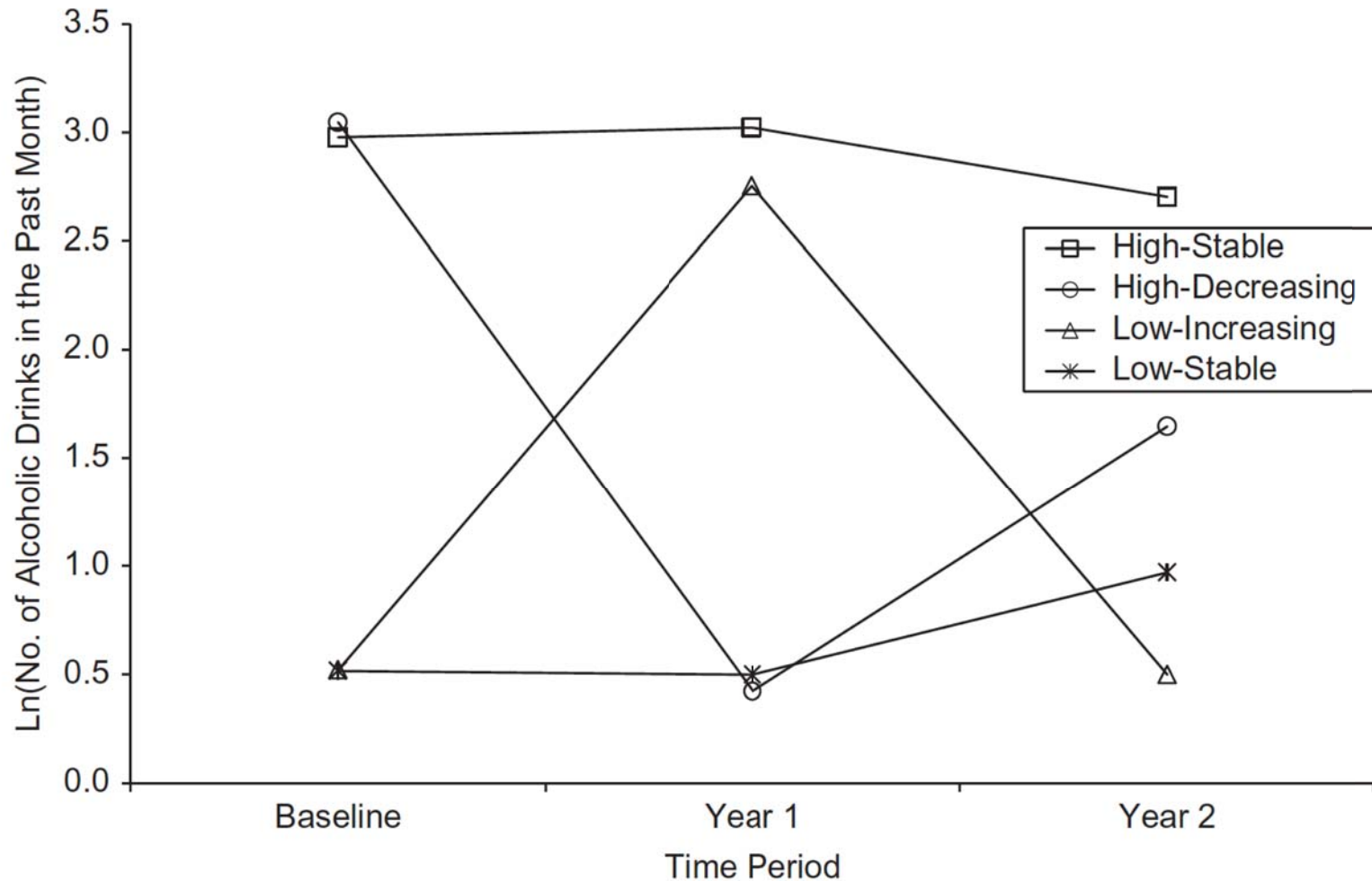
Alcohol use increases 1-year post-deployment, but returns to pre-deployment levels at 2-years post-deployment



Alcohol use increases 1-year post-deployment, but returns to pre-deployment levels at 2-years post-deployment



Deployment to a combat zone is not a homogenous experience and can vary substantially among soldiers



Conclusions

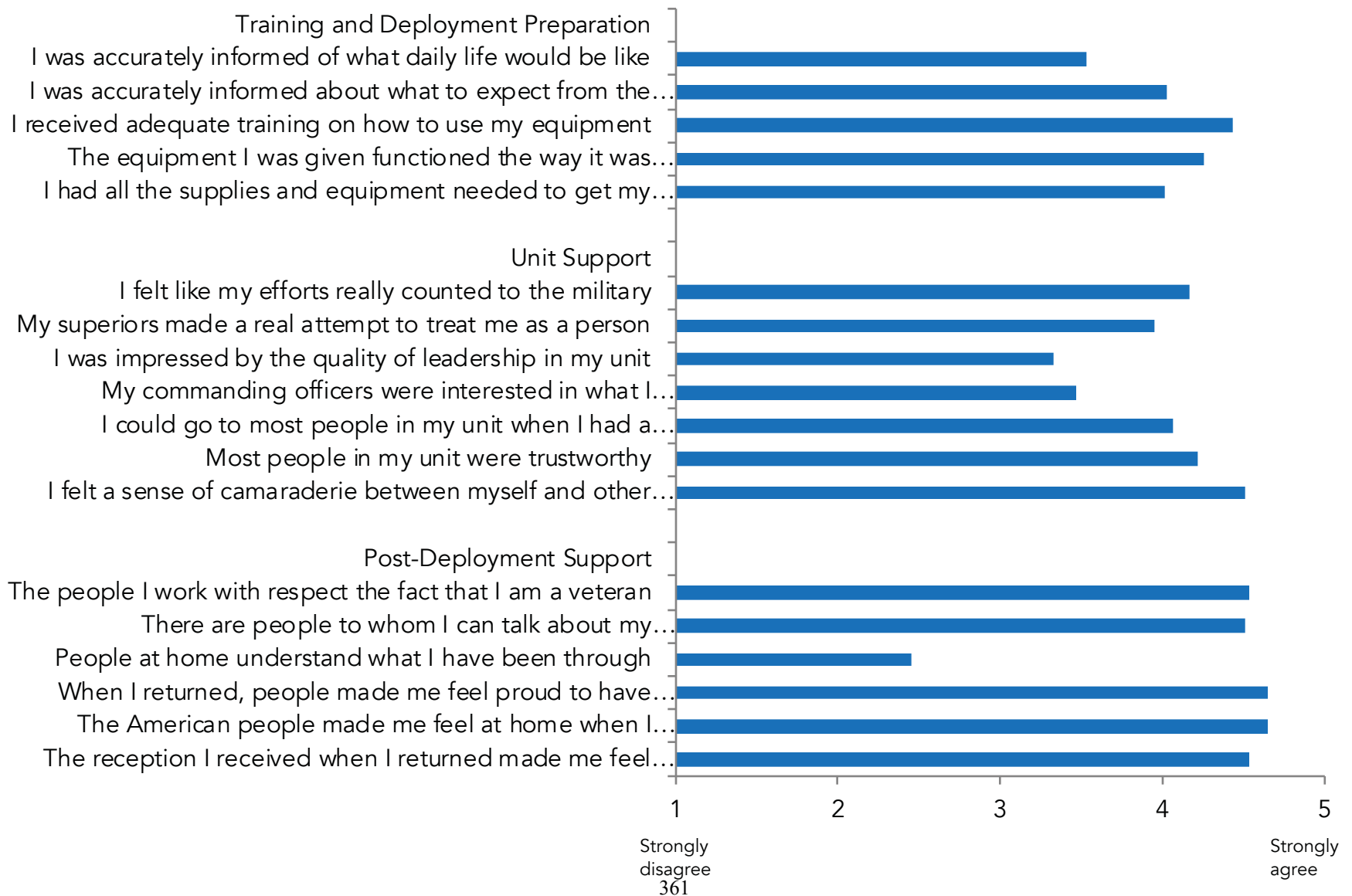
- Although deployers increased their rate of alcohol use 1 year after combat-area deployment relative to non-deployers, this increase was offset by a subsequent decrease in alcohol use during the subsequent year
- This suggests that a critical period for prevention of postdeployment alcohol misuse is isolated to the year immediately after deployment
- Although most Soldiers exhibited a stable drinking trajectory, heterogeneity in alcohol-use trajectories existed among both deployers and non-deployers
- This suggests that the average change in post-deployment alcohol use conceals substantial heterogeneity among Soldiers

Potentially modifiable pre-, peri-, and post-deployment characteristics associated with deployment-related posttraumatic stress disorder

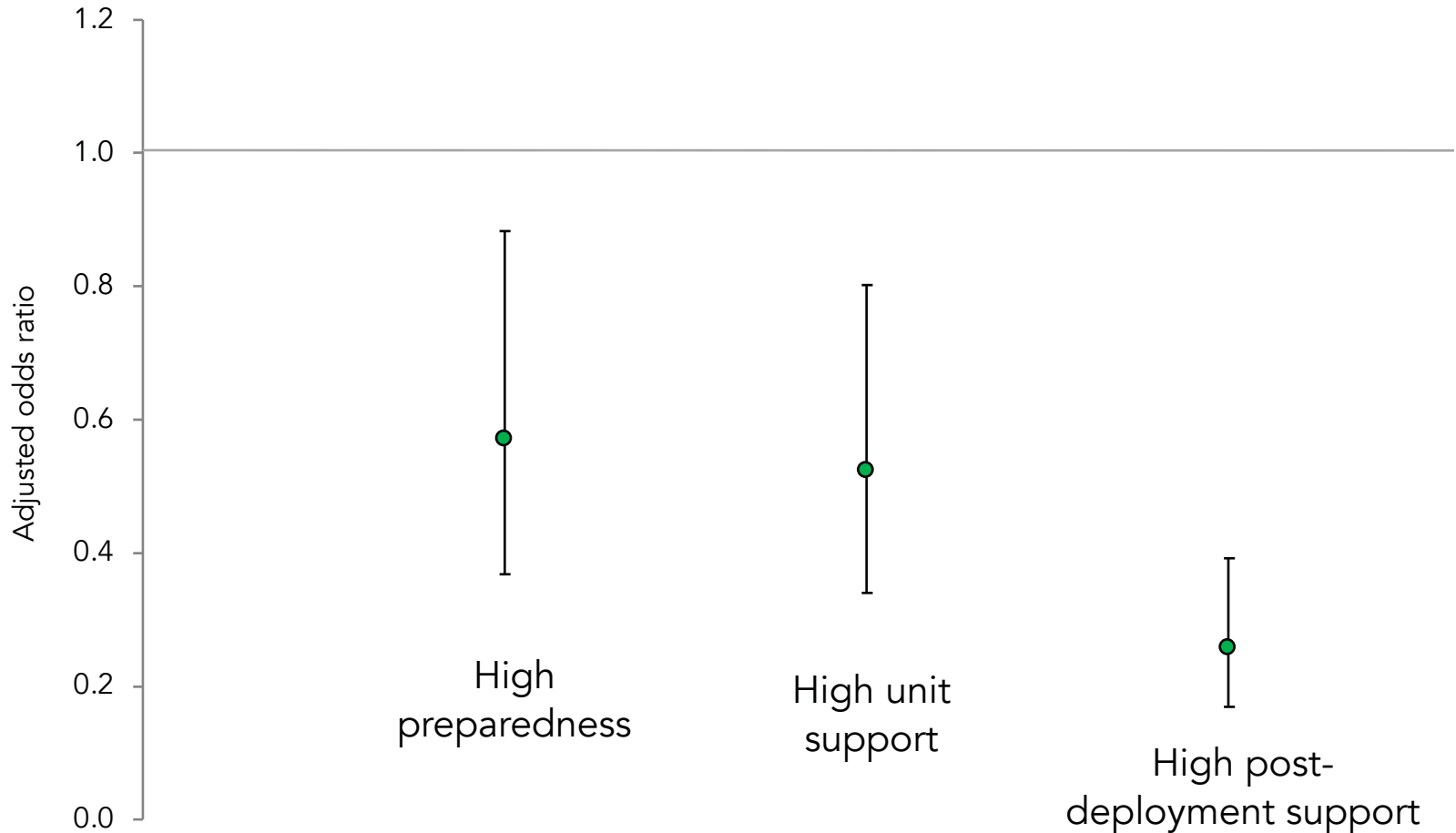
Study aim

- Considering potentially modifiable risk factors, pre-, peri- and post-deployment that may influence development of PTSD, we aimed to:
 - Identify potential areas of intervention that can be modified throughout the course of deployment to mitigate the consequences of deployment
 - Identify one modifiable deployment characteristic whose improvement will have the greatest benefit to soldiers' post-deployment psychological wellbeing

Pre-, peri-, and post-deployment factors



Each deployment condition is independently associated with deployment-PTSD

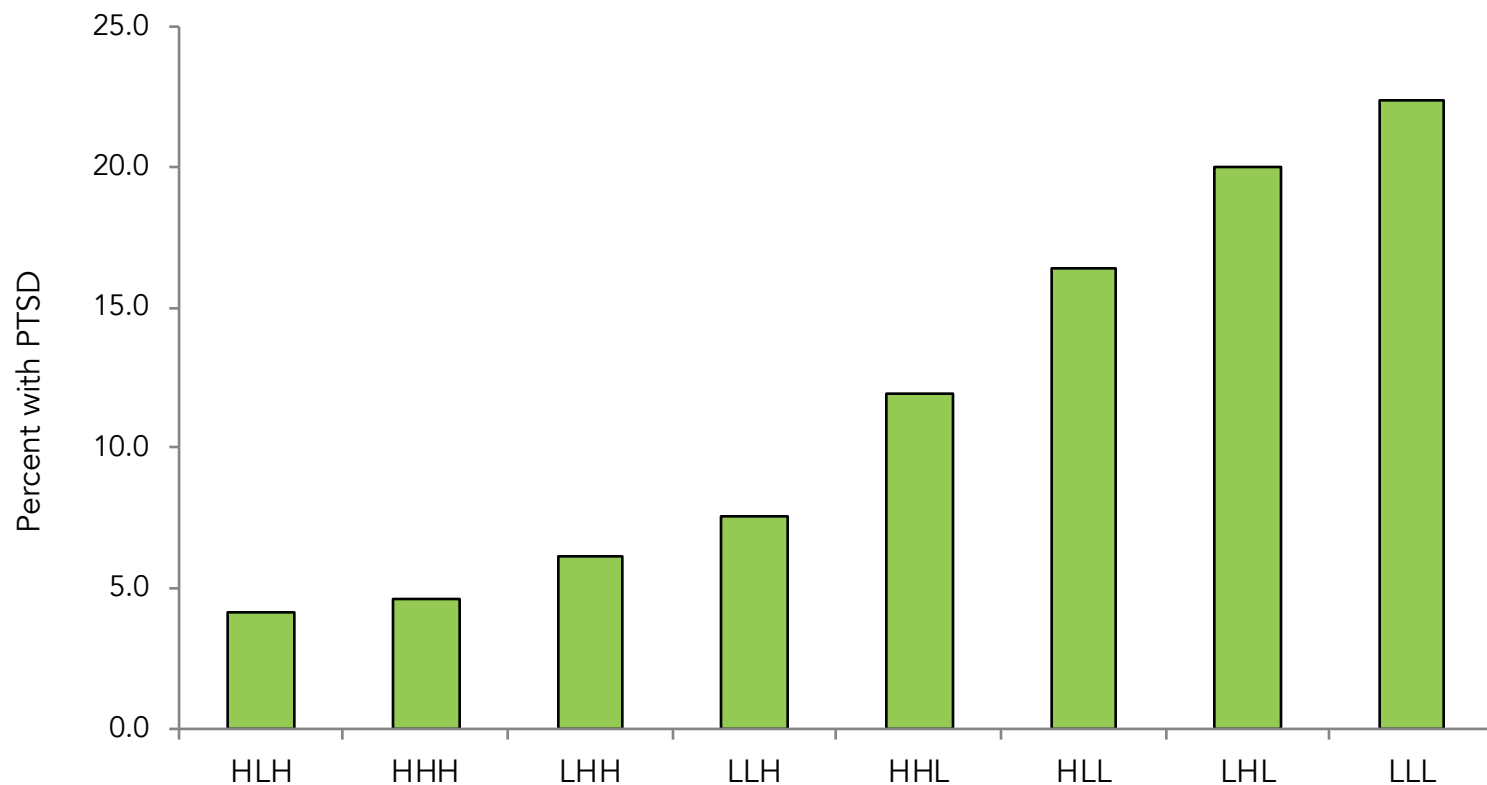


Low levels of each factor are reference groups.

Models are adjusted for gender, age, race, income, educational attainment, marital status, rank (officer vs. enlisted, cadets, and civilian employees), most recent deployment location (to non-conflict area vs. conflict area), and total number of deployment-related traumatic events experienced

Those with low levels of preparedness, unit support and post-deployment support have the highest prevalence of PTSD

Among those who have been deployed and experienced a traumatic event during their most recent deployment (n=1294)



e.g. HLH = high preparedness, low unit support, high post-deployment support

*Scores above 21, 29, and 24 indicated high preparedness, high unit support, and high post-deployment support, respectively.

Conclusions

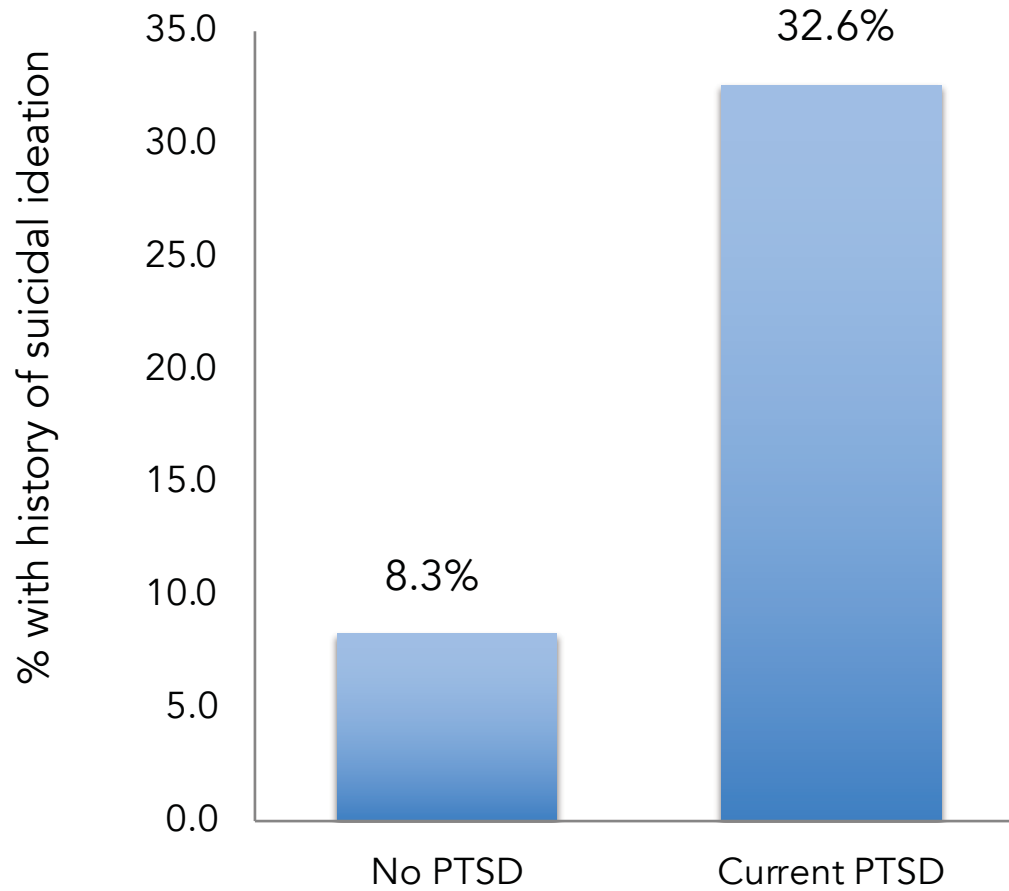
- Reporting high levels (compared to low-levels) of preparedness, unit support, and post-deployment support were independently associated with lower odds of deployment-related PTSD
- Soldiers who report high training and deployment preparedness may be more psychologically prepared for deployment-related potentially traumatic events
- Low post-deployment support appears to be particularly influential for higher odds of PTSD

PTSD comorbidity and suicidal ideation

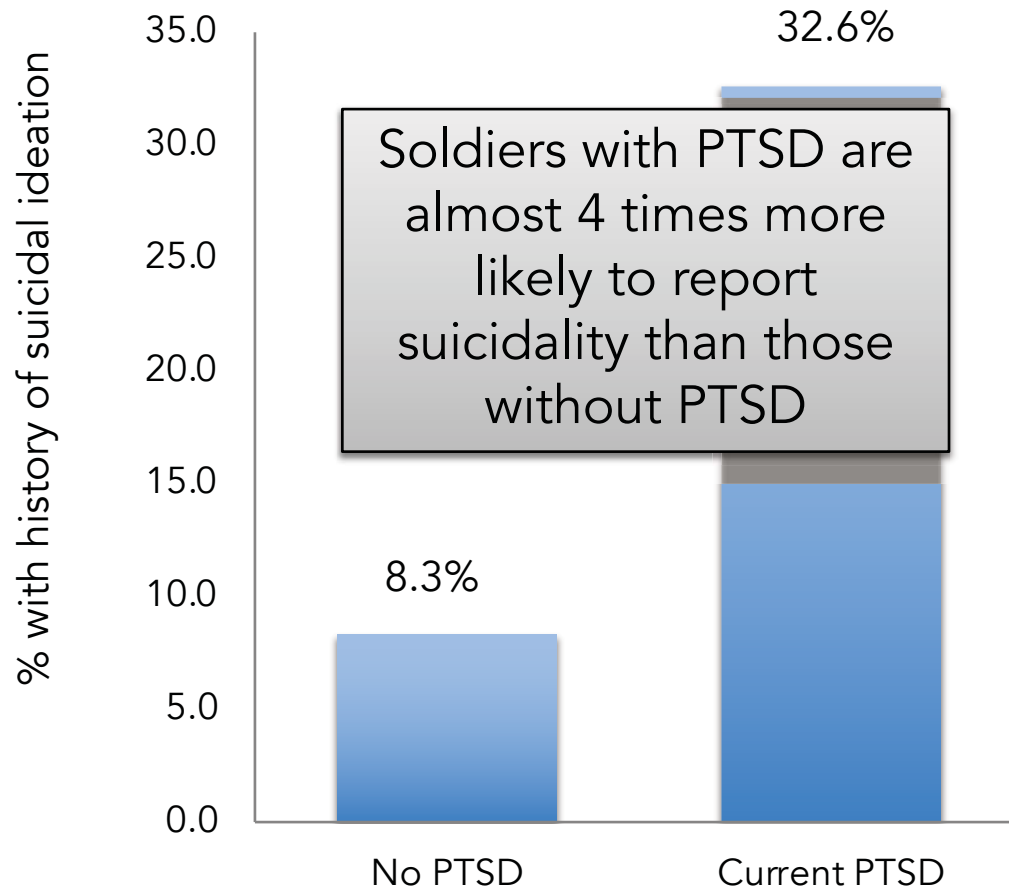
Study aims

- To study the relationship between PTSD, psychiatric comorbidity, and suicidal ideation, examining:
 - The prevalence of other psychiatric conditions among those with PTSD compared to those without PTSD
 - The association between PTSD comorbidity and suicidal ideation

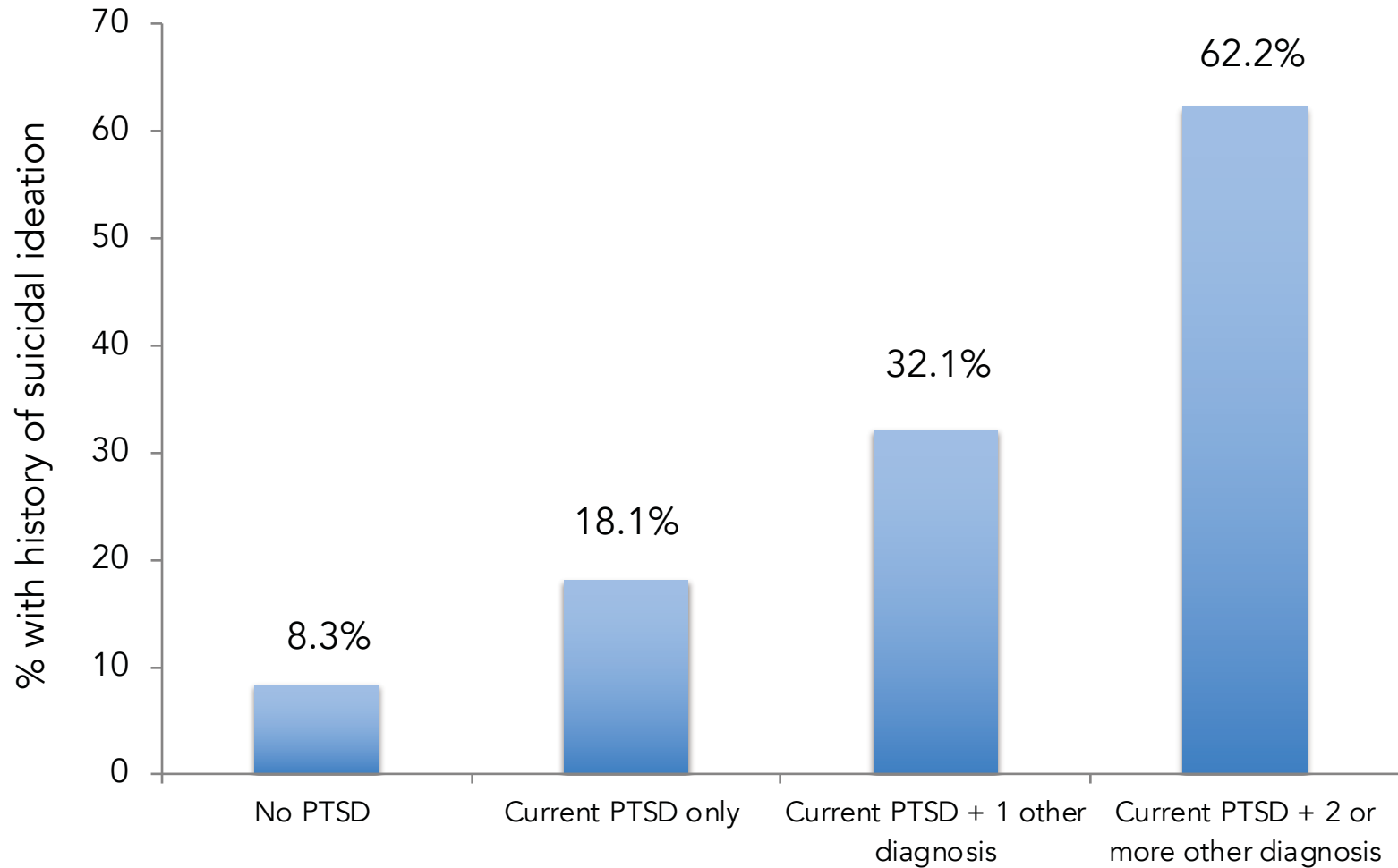
PTSD and suicidality



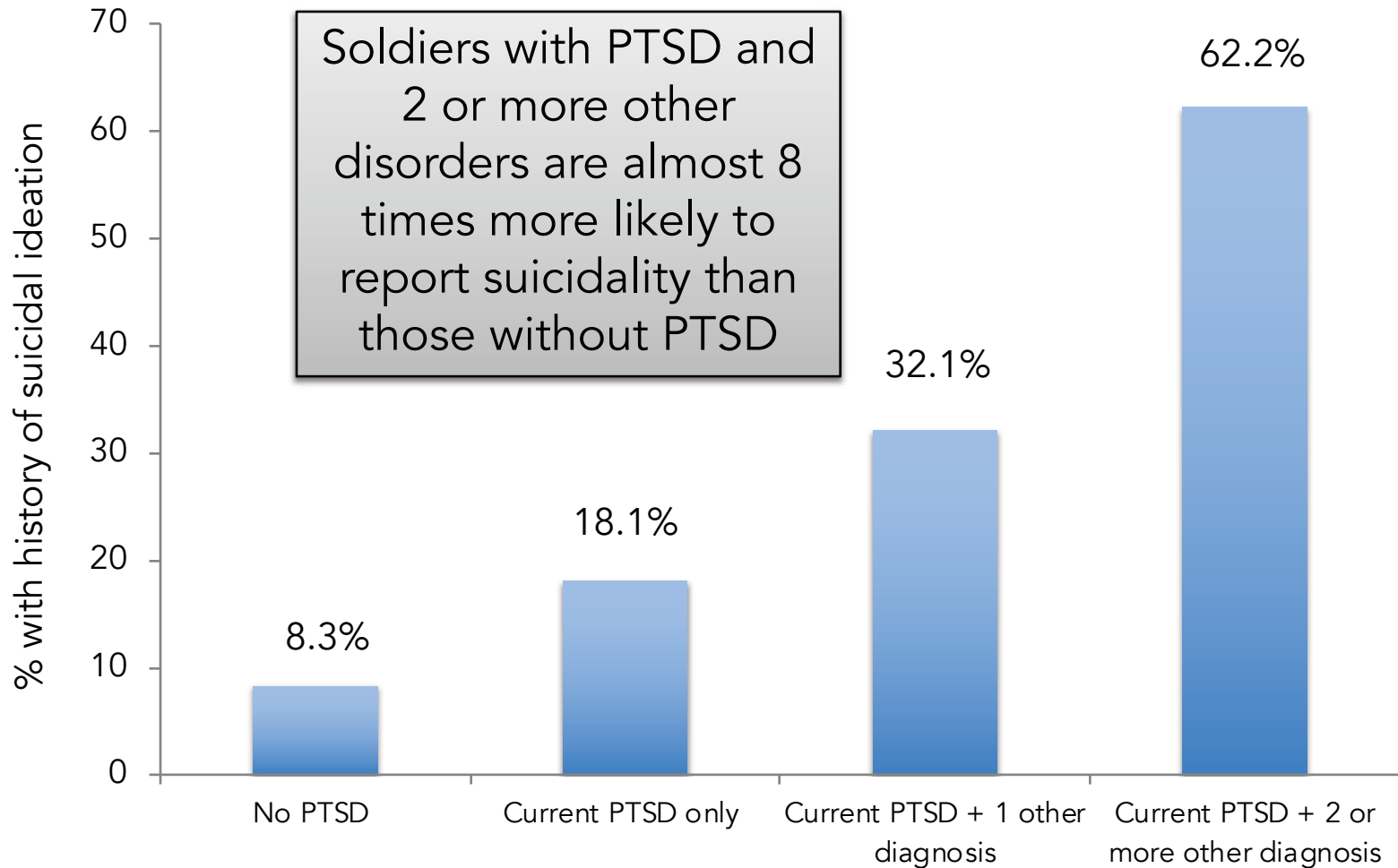
PTSD and suicidality



Comorbid PTSD and suicidality



Comorbid PTSD and suicidality



Conclusions

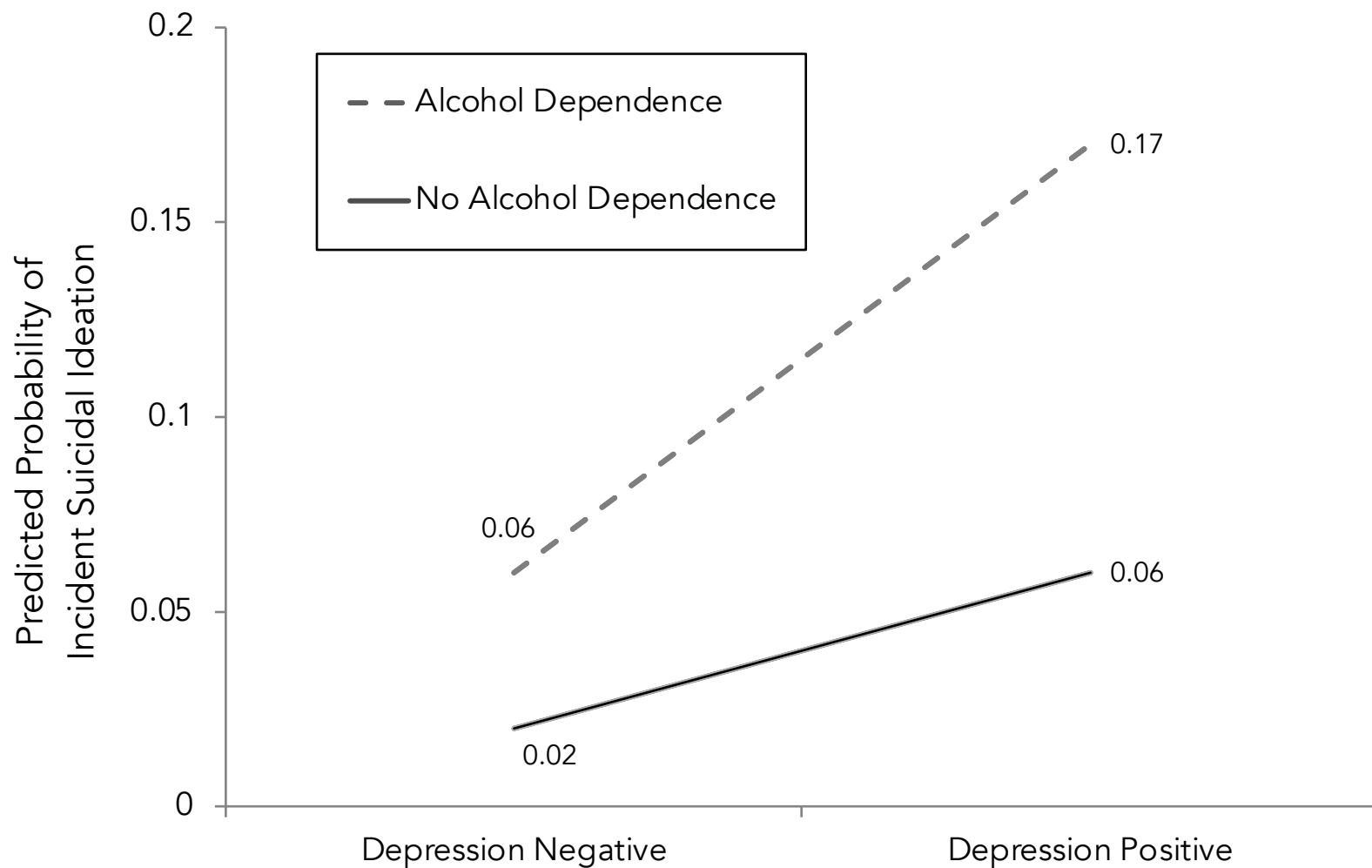
- Soldiers with PTSD were at increased risk for suicidal ideation
- Among those with PTSD, those who have at least 2 additional psychiatric conditions were at highest risk of suicidal ideation
- Future research should address mechanisms that contribute to multimorbidity in this group
- Future research should also address appropriate treatment methods in this group

Coincident alcohol misuse and depression, and increased risk for new-onset suicidal ideation

Study aims

- To identify the independent influence of alcohol dependence and depression on incident suicidal ideation, accounting for lifetime and past year trauma and sociodemographic factors
- To examine and quantify the interaction between depression and alcohol dependence in predicting incident suicidal ideation

The effects of depression and alcohol dependence on suicidal ideation are greater than the sum of their individual effects



Results

- Strong additive interaction was confirmed with multiple measures of synergy:
 - Relative Excess Risk of Interaction = 6.0 (0.4 - 11.6)
 - Attributable Proportion Due to Interaction = 0.5 (0.2 - 0.7)
 - Synergy Index = 2.0 (1.2 - 3.4)
- In contrast, multiplicative interaction was not present

Conclusions

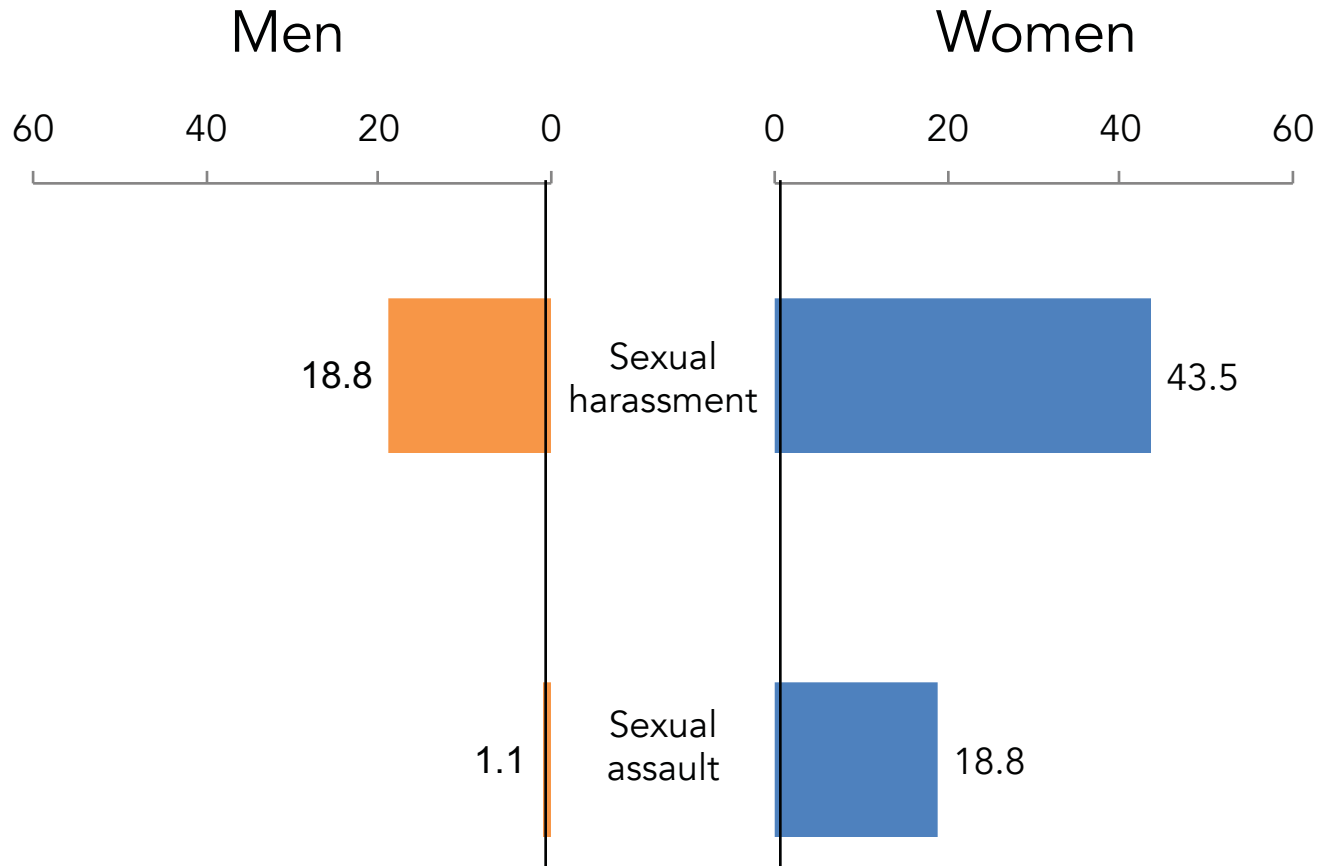
- Alcohol dependence and depression work together to shape risk for new-onset suicidal ideation among ONG soldiers
- A high-risk prevention approach including population based screening for suicidality among those with alcohol dependence, depression, and particularly both conditions may be warranted in military populations

Unit support protects against
sexual harassment and assault

Study rationale and aim

- Little research has examined military factors that could prevent sexual harassment and assault during deployment
- Most of the research to date on sexual harassment has focused on individual risk characteristics, including minority race, female gender, enlisted rank, and longer length of deployment
- This study examined whether unit support, a potentially malleable construct, which reflects the quality of service members' relationships within their unit, protects against sexual harassment and assault during deployment

Nearly 1/2 of women and 1/5 of men reported sexual harassment, while 1/5 of women and 1% of men reported sexual assault



N=1674 (Men: n=1504; Women: n=170); Timing of reported events was during most recent deployment

Higher unit support predicted lower adjusted odds of sexual harassment and assault for both men and women



N=1674 (Men: n=1504; Women: n=170); Timing of reported events was during most recent deployment

Conclusions

- A substantial proportion of men and women reported sexual harassment/assault
- Greater unit support was associated with diminished odds of sexual harassment/assault during deployment
- Programming designed to improve unit cohesion has the potential to reduce sexual harassment and assault
- Updated longitudinal analyses in progress

Spirituality and Mental Health

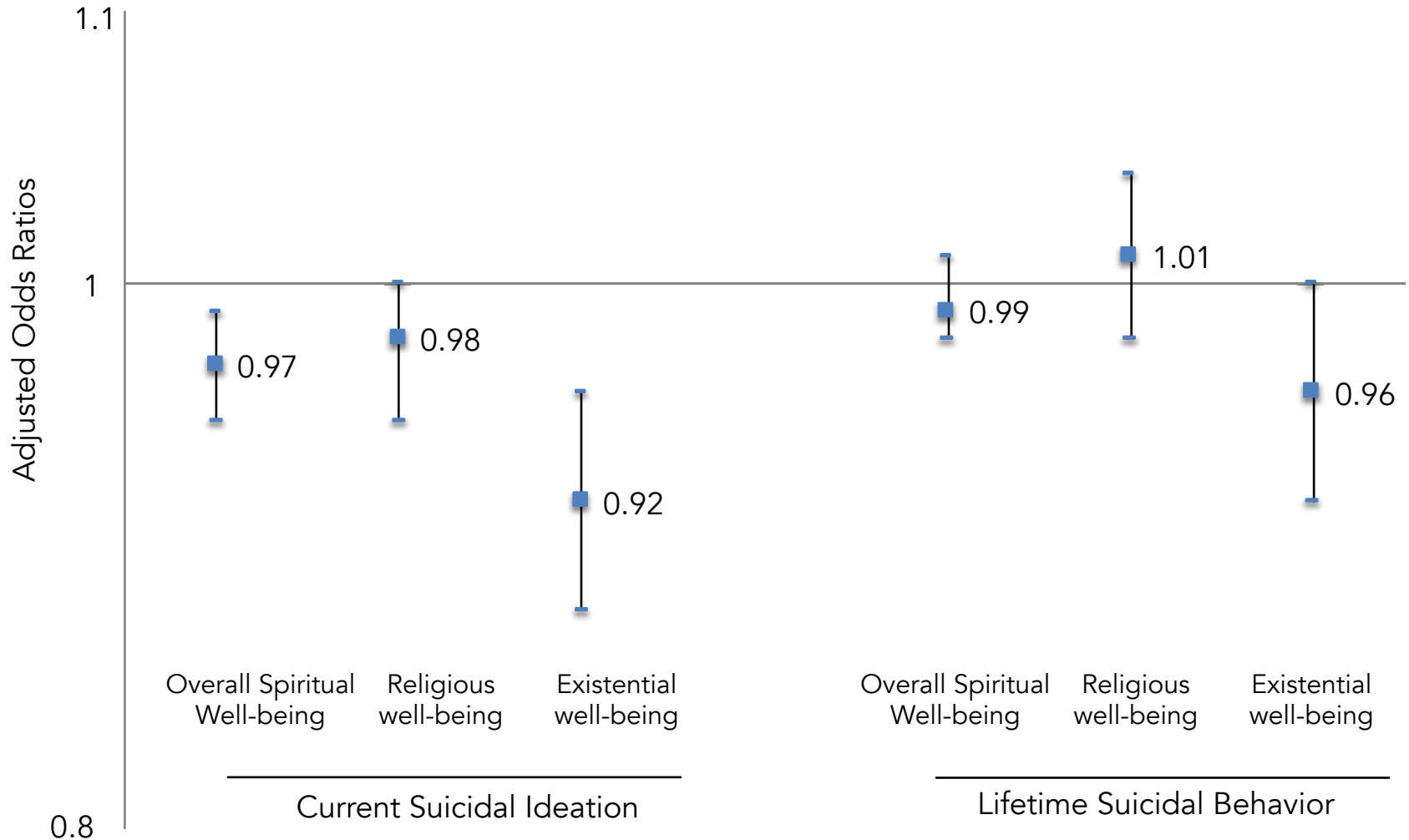
Study aim

- To explore whether spiritual wellbeing is associated with mental health outcomes
 - Suicidal thoughts
 - Depression
 - PTSD

Dimensions of spiritual wellbeing

- Overall Spiritual Well-being
 - Full scale construct
- Religious Well-being
 - Sub-scale construct pertaining to one's relationship with a higher power
- Existential Well-being
 - Sub-scale construct pertaining to life satisfaction, purpose and meaning

Spiritual well-being is protective against suicidal ideation, not behavior

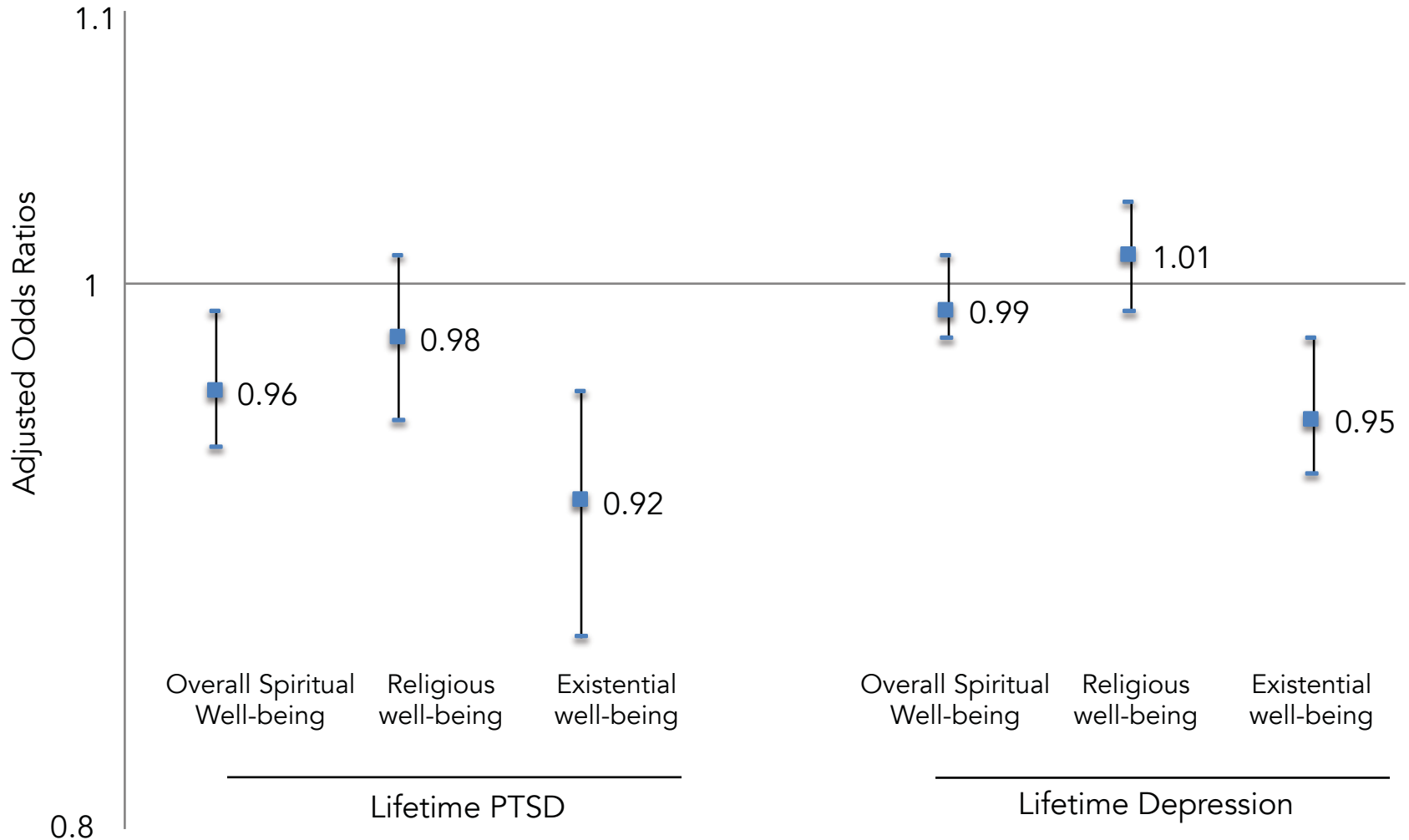


n=418; results adjusted for gender, age, race, and deployment status.

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Ganocy SJ, Goto T, Chan PK, Cohen GH, Sampson L, Galea S, Liberzon I, Fine T, Shirley E, Sizemore J, Calabrese JR, Tamburrino MB. Association of spirituality with mental health conditions in Ohio National Guard soldiers. *The Journal of nervous and mental disease*. 2016.

Spiritual well-being is protective against lifetime depression and PTSD



n=418; results adjusted for gender, age, race, and deployment status.

386

Ganocy SJ, Goto T, Chan PK, Cohen GH, Sampson L, Galea S, Liberzon I, Fine T, Shirley E, Sizemore J, Calabrese JR, Tamburrino MB. Association of spirituality with mental health conditions in Ohio National Guard soldiers. *The Journal of nervous and mental disease*. 2016.

Results

- Spiritual well-being was associated with:
 - Lower adjusted odds of current suicidal ideation
 - Lower adjusted odds of lifetime PTSD
 - Lower adjusted odds of lifetime depression
- The associations observed in these analyses were driven mostly by the existential wellbeing subscale

Conclusions

- Higher levels of spirituality were associated with lower prevalence of lifetime mental health disorders and less suicidal ideation over the prior year
- Future studies should examine this question with a longitudinal structure to examine the effect of changes in spirituality on mental health and vice-versa

Questions?