

**THE ARMY STUDY TO ASSESS RISK AND RESILIENCE IN SERVICEMEMBERS  
(Army STARRS)  
and  
THE STUDY TO ASSESS RISK AND RESILIENCE IN SERVICEMEMBERS – LONGITUDINAL STUDY  
(STARRS-LS)  
2009 – 2025**

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*This document is an ongoing continuous summary of Army STARRS and STARRS-LS publications*

## **INTRODUCTION:**

Army STARRS (2009-2015) was the largest and most comprehensive research project of mental health ever conducted in the U.S. Army. The project was designed to examine a broad range of risk and resilience (protective) factors across a complex set of outcomes. Army STARRS scientists created a series of extensive databases with the potential to achieve groundbreaking results. These databases allow scientists to investigate a diverse combination of factors from demographic, psychological, biological, neurological, behavioral, and social domains to help identify risk and resilience factors for Soldier suicidal behaviors and associated mental health issues. The project was designed using an adaptive approach which means it evolved as new information became available over the course of the project. With the goal of generating actionable findings, the research team shared preliminary findings with the Army as they become available so that the Army could apply them to its ongoing health promotion, risk reduction, and suicide prevention efforts.

Army STARRS included the following component studies:

- 1) the Historical Administrative Data Study (HADS) of Army and Department of Defense (DoD) administrative data systems (including records of suicidal behaviors) for all Soldiers on active duty from 2004 to 2009 aimed at finding administrative record predictors of suicides;
- 2) two retrospective case-control studies of fatal and nonfatal suicidal behaviors;
- 3) a study of new Soldiers assessed just before beginning basic combat training (BCT) with self-administered questionnaires (SAQ), neurocognitive tests, and blood samples;
- 4) a cross-sectional study of Soldiers representative of all other active duty Soldiers (exclusive of BCT);
- 5) a pre-post deployment study (with blood samples) of Soldiers in Brigade Combat Teams about to deploy to Afghanistan, with sub-samples assessed again one, three, and nine months after returning from deployment.

Army STARRS Component Studies and Soldier Sample Size:

Historical Administrative Data Study (HADS)	>1.6 million
Soldier Health Outcomes Study A (SHOS-A)	186 cases and 375 controls
Soldier Health Outcomes Study B (SHOS-B)	150 cases and 270 controls
New Soldier Study (NSS)	55,814
All Army Study (AAS)	41,210
Pre-Post Deployment Study (PPDS)	10,116

Army/DoD administrative data were linked prospectively to the large-scale survey samples to examine predictors of subsequent suicidality and related mental health outcomes.

STARRS-LS (2015-2020 and 2020-2025) is continuing, extending and expanding the Army STARRS research to discover additional findings for the Army and the DoD. STARRS-LS also includes a multi-wave survey longitudinal follow-up study to collect additional data from a subset of Soldiers who participated in Army STARRS.

## **SUMMARY OF FINDINGS:**

The following is a brief summary of published findings to-date from Army STARRS and STARRS-LS. Findings followed by an asterisk (\*) were included in USU press releases.

### **1. The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Ursano, et al 2014)**

- Component study cooperation rates are comparatively high.
- Sample biases are relatively small.
- Inefficiencies introduced into parameter estimates by using nonresponse adjustment weights and time-space clustering are small.
- Initial findings show that the suicide death rate, which rose over 2004–2009, increased for those deployed, those never deployed, and those previously deployed.
- Analyses of administrative records show that those deployed or previously deployed were at greater suicide risk.
- Receiving a waiver to enter the Army was not associated with increased risk.
- Being demoted in the past two years was associated with increased risk.
- Time in current deployment, length of time since return from most recent deployment, total number of deployments, and time interval between most recent deployments (known as dwell time) were not associated with suicide risk.
- Initial analyses of survey data show that 13.9% of currently active non-deployed regular Army Soldiers considered suicide at some point in their lifetime, while 5.3% had made a suicide plan, and 2.4% had attempted suicide.\*
- 47–60% of these outcomes first occurred prior to enlistment.\*
- Prior mental disorders (in particular major depression and intermittent explosive disorder) were the strongest predictors of these self-reported suicidal behaviors.
- Most onsets of plans-attempts among ideators (58.3–63.3%) occurred within the year of onset of ideation.

- About 25.1% of non-deployed U.S. Army personnel met 30-day criteria for a DSM-IV anxiety, mood, disruptive behavior, or substance disorder (15.0% an internalizing disorder; 18.4% an externalizing disorder) and 11.1% for multiple disorders.\*
- Three-fourths of these disorders had pre-enlistment onsets.\*
- Integration across component studies creates strengths going well beyond those in conventional applications of the same individual study designs.
- These design features create a strong methodological foundation from which Army STARRS can pursue its substantive research goals.
- The early findings reported here illustrate the importance of the study and its approach as a model of studying rare events particularly of national security concern.
- Continuing analyses of the data will inform suicide prevention for the U.S. Army.

## **2. Sociodemographic and Career History Predictors of Suicide Mortality in the United States Army 2004–2009 (Gilman, et al 2014)**

- Several novel results were found that could have intervention implications.
- Significantly elevated suicide rates among enlisted Soldiers deployed either during their first year of service or with less than expected (based on time in service) junior enlisted rank (69.6–80.0 suicides per 100,000 person-years compared with 18.5 suicides per 100,000 person-years in the total Army)
- Substantially greater rise in suicide among women than men during deployment
- Protective effect of marriage against suicide only during deployment.
- Career history approach produces several actionable insights missed in less textured analyses of administrative data predictors.
- Expansion of analyses to a richer set of predictors might help refine understanding of intervention implications.

## **3. Predictors of Suicide and Accident Death in the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Schoenbaum, et al, 2014)**

- The suicide rate rose between 2004 and 2009 among never deployed and currently and previously deployed Regular Army Soldiers.

- The accident death rate fell sharply among currently deployed Soldiers, remained constant among the previously deployed, and trended upward among the never deployed.
- Increased suicide risk was associated with being a man (or a woman during deployment), white race/ethnicity, junior enlisted rank, recent demotion, and current or previous deployment.
- Sociodemographic and Army experience predictors were generally similar for suicides and accident deaths.
- Time trends in these predictors and in the Army's increased use of accession waivers (which relaxed some qualifications for new Soldiers) do not explain the rise in Army suicides.
- Predictors of Army suicides were largely similar to those reported elsewhere for civilians, although some predictors distinct to Army service emerged that deserve more in-depth analysis.
- The existence of a time trend in suicide risk among never-deployed Soldiers argues indirectly against the view that exposure to combat-related trauma is the exclusive cause of the increase in Army suicides.

#### **4. Thirty-Day Prevalence of DSM-IV Mental Disorders among Nondeployed Soldiers in the U.S. Army: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Kessler, et al 2014)**

- A total of 25.1% of respondents met criteria for any 30-day disorder (15.0% internalizing; 18.4% externalizing) and 11.1% for multiple disorders.
- A total of 76.6% of cases reported pre-enlistment age at onset of at least one 30-day disorder (49.6% internalizing; 81.7% externalizing).\*
- 12.8% of respondents reported severe role impairment.
- Controlling for sociodemographic and Army career correlates (which were broadly consistent with other studies) 30-day disorders with pre-enlistment and post-enlistment ages at onset both significantly predicted severe role impairment
- Pre-enlistment disorders were more consistent powerful predictors than post-enlistment disorders.

- Population-attributable risk proportions of severe role impairment were 21.7% for pre-enlistment disorders, 24.3% for post-enlistment disorders, and 43.4% for all disorders.
- Interventions to limit accession or increase resilience of new Soldiers with pre-enlistment mental disorders might reduce prevalence and impairments of mental disorders in the U.S. Army.

#### **5. Prevalence and Correlates of Suicidal Behavior among Soldiers: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Nock, et al 2014)**

- The lifetime prevalence estimates of suicidal ideation, suicide plans, and suicide attempts are 13.9%, 5.3%, and 2.4%.\*
- Most reported cases (47.0%-58.2%) had pre-enlistment onsets.\*
- Pre-enlistment onset rates were lower than in a prior national civilian survey (with imputed/simulated age at enlistment).
- Post-enlistment onsets of ideation and plans were higher, and post-enlistment first attempts were equivalent to civilian rates.
- Most reported onsets of plans and attempts among ideators (58.3%-63.3%) occur within the year of onset of ideation.
- Post-enlistment attempts are positively related to being a woman, lower rank, and previously deployed, and are negatively related to being unmarried and assigned to Special Operations Command.
- Five mental disorders predict post-enlistment first suicide attempts in multivariate analysis:
  - pre-enlistment panic disorder
  - pre-enlistment posttraumatic stress disorder
  - post-enlistment depression
  - pre-enlistment intermittent explosive disorder
  - post-enlistment intermittent explosive disorder
- 4 of these 5 (posttraumatic stress disorder is the exception) predict ideation.
- Only post-enlistment intermittent explosive disorder predicts attempts among ideators.

- Population-attributable risk proportions of lifetime mental disorders predicting post-enlistment suicide attempts are:
  - 31.3% for pre-enlistment onset disorders
  - 41.2% for post-enlistment onset disorders
  - 59.9% for all disorders
- The fact that approximately one-third of post-enlistment suicide attempts are associated with pre-enlistment mental disorders suggests that pre-enlistment mental disorders might be targets for early screening and intervention.
- The possibility of higher fatality rates among Army suicide attempts than among civilian suicide attempts highlights the potential importance of means control (i.e., restricting access to lethal means [such as firearms]) as a suicide prevention strategy.

**6. Risk Factors for Accident Death in the U.S. Army, 2004-2009 (Lewandowski-Romps, et al 2014)**

- Delayed rank progression or demotion and being male, unmarried, in a combat arms specialty, and of low rank/service length increased odds of accident death for enlisted Soldiers.
- Unique to officers was high risk associated with aviation specialties.
- Accident death risk decreased over time for currently deployed, enlisted Soldiers and increased for those never deployed.
- Mental health diagnosis was associated with risk only for previous and never-deployed, enlisted Soldiers.
- Models did not discriminate not-line-of-duty from line-of-duty accident deaths.
- Adding more refined person-level and situational risk indicators to current models could enhance understanding of accident death risk specific to Soldier rank and deployment status.
- Stable predictors could help identify high risk of accident deaths in future cohorts of Regular Army Soldiers.

## **7. Predicting Suicides after Psychiatric Hospitalization in U.S. Army Soldiers: The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Kessler, et al 2015)**

- Sixty-eight Soldiers died by suicide within 12 months of hospital discharge (12.0% of all U.S. Army suicides), equivalent to 263.9 suicides per 100,000 person-years compared with 18.5 suicides per 100,000 person-years in the total U.S. Army.
- The strongest predictors included sociodemographics:
  - male sex
  - late age of enlistment
  - criminal offenses (verbal violence and weapons possession)
  - prior suicidality
  - aspects of prior psychiatric inpatient and outpatient treatment (e.g., number of antidepressant prescriptions filled in the past 12 months), and disorders diagnosed during the focal hospitalizations (e.g., non-affective psychosis)
- A total of 52.9% of post-hospitalization suicides occurred after the 5% of hospitalizations with highest predicted suicide risk (3,824.1 suicides per 100,000 person-years).\*
- These highest-risk hospitalizations also accounted for significantly elevated proportions of several other adverse post-hospitalization outcomes (unintentional injury deaths, suicide attempts, and subsequent hospitalizations).\*
- The high concentration of risk of suicide and other adverse outcomes might justify targeting expanded post-hospitalization interventions to Soldiers classified as having highest post-hospitalization suicide risk, although final determination requires careful consideration of intervention costs, comparative effectiveness, and possible adverse effects.

## **8. Lifetime Prevalence of DSM-IV Mental Disorders among New Soldiers in the U.S. Army: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Rosellini, et al 2015)**

- Lifetime prevalence of having at least one internalizing, externalizing, or either type of disorder did not differ significantly between new Soldiers and civilians
- Three specific disorders (generalized anxiety, posttraumatic stress, and conduct disorders) and multi-morbidity were significantly more common among new Soldiers than civilians.



- Several socio-demographic characteristics were significantly associated with disorder prevalence and persistence (these associations were uniformly weak).
- New Soldiers differ somewhat, but not consistently, from civilians.

**9. Prevalence and Correlates of Suicidal Behavior among New Soldiers in the U.S. Army: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Ursano, et al 2015)**

- Lifetime prevalence estimates of pre-enlistment suicide ideation, plans, and attempts were 14.1, 2.3, and 1.9%, respectively.
- Most reported onsets of suicide plans and attempts (73.3–81.5%) occurred within the first year after onset of ideation.
- Odds of these lifetime suicidal behaviors among new Soldiers were positively, but weakly associated with being female, unmarried, religion other than Protestant or Catholic, and a race/ethnicity other than non-Hispanic White, non-Hispanic Black, or Hispanic.
- Lifetime prevalence estimates of suicidal behaviors among new Soldiers are consistent with retrospective reports of pre-enlistment prevalence obtained from Soldiers later in their Army careers.
- Given that prior suicidal behaviors are among the strongest predictors of later suicides, consideration should be given to developing methods of obtaining valid reports of pre-enlistment suicidality from new Soldiers to facilitate targeting of preventive interventions.

**10. Mental Disorders, Comorbidity, and Pre-enlistment Suicidal Behavior Among New Soldiers in the U.S. Army: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Nock, et al 2015)**

- Most new Soldiers with a pre-enlistment history of suicide attempt reported a prior mental disorder (59.0%).
- Each disorder examined was associated with increased odds of suicidal behavior.
- Only PTSD and disorders characterized by irritability and impulsive/aggressive behavior (i.e., bipolar disorder, conduct disorder, oppositional defiant disorder, and attention-deficit/hyperactivity disorder) predicted unplanned attempts among ideators.

- Mental disorders are important predictors of pre-enlistment suicidal behavior among new Soldiers and should figure prominently in suicide screening and prevention efforts.

### **11. Understanding the Elevated Suicide Risk of Female Soldiers during Deployments (Street, et al 2015)**

- The suicide rate of currently deployed women (14.0/100,000 person-years) was 3.1 to 3.5 times the rates of other (i.e., never-deployed/previously deployed) women.
- The suicide rate of currently deployed men (22.6/100,000 person years) was 0.9 to 1.2 times the rates of other men.
- The adjusted (for time trends, sociodemographics, and Army career variables) female to male odds ratio comparing the suicide rates of currently deployed vs. other women vs. men was 2.8 (95% confidence interval 1.1–6.8), became 2.4 after excluding Soldiers with Direct Combat Arms occupations, and remained elevated (in the range 1.9–2.8) after adjusting for the hypothesized explanatory variables.
- None of the explanatory variables considered could fully account for the disproportionately elevated female suicide rate during deployment among Regular Army enlisted Soldiers over the years 2004–2009.
- These results are valuable in excluding otherwise plausible hypotheses for the elevated suicide rate of deployed women and point to the importance of expanding future research on the psychological challenges of deployment for women.

### **12. Nonfatal Suicidal Behaviors in U.S. Army Administrative Records, 2004-2009: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Ursano, et al 2015)**

- U.S. Army suicide rate is known to have risen sharply over the past decade, but information about medically documented, non-fatal suicidal behaviors (suicide attempts, suspicious injuries, and suicide ideation) is far more limited.
- There were 21,740 unique Regular Army Soldiers with a non-fatal suicidal event at some point during 2004-2009.
- There were substantial increases in the annual incidence rates of suicide attempts (179–400/100,000 person-years) and suicide ideation (557–830/100,000 person-years), but not suspicious injuries.



- Using hierarchical classification rules to identify the first instance of each Soldier's most severe behavior, there was an increased risk of all outcomes among those who were female, Non-Hispanic White, never married, lower-ranking enlisted, less educated, and of younger age when entering Army service.
- Socio-demographic associations significantly differed across outcomes, despite some patterns that appear similar.

### **13. Suicide Attempts in the U.S. Army during the Wars in Afghanistan and Iraq, 2004-2009 (Ursano, et al 2015)**

- The study included 9,791 medically documented suicide attempts among Regular Army Soldiers during the period 2004 to 2009. Predictor variables were constructed from Army personnel and medical records.
- Enlisted Soldiers accounted for 98.6% of all suicide attempts, with an overall rate of 377/100,000 person-years, versus 27.9/100,000 person-years for officers.\*
- Significant predictors among enlisted Soldiers included socio-demographic characteristics (female gender, older age at Army entry, younger current age, lower education, non-Hispanic white), short length of service, never or previously deployed, and the presence and recency of mental health diagnoses. Risk was highest early in the Army career.\*
- Among officers, only socio-demographic characteristics (female gender, older age at Army entry, younger current age, and low education) and the presence and recency of mental health diagnoses were significant.\*
- The results represent the most comprehensive accounting of U.S. Army suicide attempts to date and reveal unique risk profiles for enlisted Soldiers and officers, and highlight the importance of focusing research and prevention efforts on enlisted Soldiers in their first tour of duty.\*

### **14. Occupational Differences in U.S. Army Suicide Rates (Kessler, et al 2015)**

- Military research has found elevated suicide rates in combat arms occupations, but has not evaluated variation in this pattern by deployment history which is the indicator of occupational stress widely considered responsible for the recent rise in military suicide rates.
- This study analyzed associations of Army occupation and deployment history in predicting suicide among 729,337 male enlisted Regular Army Soldiers in 2004-2009.

- There were 496 suicides (22.4/100,000 person-years) during the study period and only two occupational categories (both in combat arms) had significantly elevated suicide rates: infantrymen (37.2/100,000 person-years) and combat engineers (38.2/100,000 person-years).
- Suicide rates in these two occupational categories were significantly lower when currently deployed (30.6/100,000 person-years) than never deployed or previously deployed (41.2-39.1/100,000 person years).
- The suicide rate of other Soldiers was significantly higher when currently deployed and previously deployed (20.2-22.4/100,000 person-years) than never deployed (14.5/100,000 person-years).
- Adjusted suicide rate for infantrymen and combat engineers was most elevated when never deployed (OR=2.9, 95% CI=2.1-4.1), less so when previously deployed (OR=1.6, 95% CI=1.1-2.1) and not at all when currently deployed (OR=1.2, 95% CI=0.8-1.8).
- Adjustment for a differential “healthy warrior effect” cannot explain this variation in the relative suicide rates of never deployed infantrymen and combat engineers by deployment status.

**15. Prospective Longitudinal Evaluation of the Effect of Deployment-Acquired Traumatic Brain Injury on Posttraumatic Stress and Related Disorders: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Stein, et al 2015)**

- Approximately one in five Soldiers reported exposure to TBI during the index deployment (mild TBI 18.0% and more-than-mild TBI 1.2%).
- Even after adjusting for other risk factors (e.g., pre-deployment mental health status, severity of deployment stress, prior TBI history), deployment-acquired TBI was associated with elevated adjusted odds of PTSD, generalized anxiety disorder, and major depressive episode.

**16. Predicting Non-Familial Major Physical Violent Crime Perpetration in the U.S. Army from Administrative Data (Rosellini, et al 2015)**

- A machine learning model was developed aimed at predicting which Soldiers would subsequently commit a severe, physical violent crime.
- Model was based on an analysis of administrative data for all 975,057 Regular Army Soldiers on active duty from 2004 to 2009. Hundreds of potential predictors were examined from the extensive administrative records available.

- 5,771 of these Soldiers committed a first founded major physical violent crime (murder-manslaughter, kidnapping, aggravated arson, aggravated assault, robbery) over that time period.
- The 5% of Soldiers classified by the model as having highest predicted risk accounted for 36.2% of all major physical violent crimes committed by men, and 33.1% by women, over the six years of study.
- When the model was applied to a more recent cohort in 2011-2013 (a validation sample), the 5% of Soldiers with highest predicted risk accounted for 50.5% of all major physical violent crimes.
- Key predictors were indicators of disadvantaged social/socio-economic status, early career stage, prior crime, and mental disorder treatment. Area under the receiver operating characteristic curve was .80-.82 in 2004-2009 and .77 in 2011-2013.
- Although these results suggest that the model could be used to target Soldiers at high risk of violent crime perpetration for preventive interventions, final implementation decisions would require further validation and weighing of predicted effectiveness against intervention costs and competing risks.

#### **17. Mental Health Treatment among Soldiers with Current Mental Disorders in the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Colpe, et al 2015)**

- This analysis included a representative sample of 5,428 non-deployed Regular Army Soldiers who completed a self-administered questionnaire (SAQ) and consented to linking SAQ data with administrative records.
- The SAQ included information about prevalence and treatment of mental disorders among respondents with current Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) internalizing (anxiety, mood) and externalizing (disruptive behavior, substance) disorders.
- 21.3% of Soldiers with any current disorder reported current treatment.
- Seven significant predictors of being in treatment were identified.
  - Four were indicators of psychopathology (bipolar disorder, panic disorder, post-traumatic stress disorder, 8 or more months duration of disorder).
  - Two were sociodemographics (history of marriage, not being non-Hispanic Black).

- The final predictor was history of deployment.
- Treatment rates varied between 4.7 and 71.5% depending on how many positive predictors the Soldier had. The vast majority of Soldiers had a low number of these predictors.
- These results document that most non-deployed Soldiers with mental disorders are not in treatment and that untreated Soldiers are not concentrated in a particular segment of the population that might be targeted for special outreach efforts. Analysis of modifiable barriers to treatment is needed to help strengthen outreach efforts.

**18. Prognostic Indicators of Persistent Post-Concussive Symptoms after Deployment-Related Mild Traumatic Brain Injury: A Prospective Longitudinal study in U.S. Army Soldiers (Stein, et al 2016)**

- Persistent and severe post-concussive symptoms (PCS) were found among Soldiers who experienced a mild TBI while deployed to Afghanistan.
- The study sample consisted of 4,518 Soldiers from three Brigade Combat Teams who deployed an average of 10 months to Afghanistan in 2012. Of these Soldiers, 822 experienced a mild TBI during the deployment.
- Based on surveys administered 1, 3, and 9 months following redeployment, the Soldiers with mild TBI were three times more likely to report PCS than other Soldiers in the BCTs.
- More severe symptoms were reported by Soldiers with a history of TBI(s) or mental health problems (depression, anxiety, irritability, etc.) prior to this deployment, or more severe deployment-related stress.
- Persistent and more severe symptoms were also more likely when there was loss of consciousness or memory problems associated with the TBI (versus being “dazed” only).
- Female Soldiers were more likely than male Soldiers to experience poor recovery following mild TBI.

## **19. Genome-Wide Association Studies of Posttraumatic Stress Disorder in 2 Cohorts of U.S. Army Soldiers (Stein, et al 2016)**

- The analysis was designed to discover genetic loci associated with lifetime PTSD risk in the U.S. Army. Two coordinated genome-wide association studies (GWAS) of mental health were conducted for nearly 13,700 consenting Soldiers in two cohorts from Army STARRS.\*
- These were the largest genome-wide association studies (GWAS) of PTSD to date.\*
- GWAS were performed on 3,167 Soldiers with PTSD (cases) and 4,607 trauma-exposed control Soldiers from the New Soldier Study (NSS), and 947 Soldiers with PTSD (cases) and 4,969 trauma-exposed control Soldiers from the Pre/Post Deployment Study (PPDS). The primary analysis compared lifetime DSM-IV PTSD cases to trauma-exposed controls without lifetime PTSD.\*
- Two statistically significant genetic variants were found associated with PTSD among Soldiers who were part of the NSS. One variant, in samples from African American Soldiers with PTSD, was in a gene (ANKRD55) on chromosome 5. In prior research, this gene has been found to be associated with various autoimmune and inflammatory disorders, including multiple sclerosis, type 2 diabetes, celiac disease, and rheumatoid arthritis. The other variant was found on chromosome 19 in European American samples.\*
- There were no significant genetic correlations observed between PTSD and six mental disorders and nine immune-related disorders. However there was significant evidence of pleiotropy (i.e., genetic factors having effects on multiple traits) for PTSD and rheumatoid arthritis, and to a lesser extent, psoriasis.\*
- Further efforts are needed to replicate the genome-wide significant association researchers found with the gene ANKRD55, and to clarify the nature of the genetic overlap observed between PTSD and rheumatoid arthritis and psoriasis.\*

## **20. Risk Factors, Methods, and Timing of Suicide Attempts among U.S. Army Soldiers (Ursano, et al 2016)**

- This analysis used Army STARRS historical administrative data for more than 1.6 million Soldiers on active duty from 2004 to 2009. The study identified 9,650 incident suicide attempts among regular Army Soldiers (excluding National Guard and Reserve) during 2004-2009.\*

- The 40% of enlisted Soldiers who had never deployed accounted for 61% of enlisted suicide attempters. Regardless of deployment status, suicide attempts were more likely among Soldiers who were female, in their first 2 years of service, or had recently received a mental health diagnosis.\*
- Risk among never deployed Soldiers was highest the 2nd month of service. Risk among currently deployed Soldiers on their 1st deployment was highest at the 6th month of deployment. Previously deployed Soldiers were at highest risk at 5 months after return.\*
- Drug overdose was the most common method of suicide attempt and accounted for more than 50% of all attempts. Although not overall very frequent, the use of firearms was most likely to occur among currently deployed (21/100,000 person-years) or previously deployed Soldiers (14/100,000 person-years), compared to 5/100,000 person-years among Soldiers who had never deployed.\*
- As in other studies, a history of any mental health diagnosis was associated with suicide attempts in all deployment groups. The highest odds occurred in the month following the most recent diagnosis and then decreased over time.\*
- Soldiers with depression in the previous month had the highest odds of suicide attempt across the deployment groupings.\*
- PTSD and substance use disorder were associated with suicide attempts, but varied by deployment status with the greatest risk among the never deployed Soldiers.
- The odds of a suicide attempt increased with the number of mental health diagnoses a Soldier received. The effect of multiple diagnoses was most pronounced among currently deployed Soldiers.
- Suicide attempt has rarely been studied with data as comprehensive as the data used in this research. The findings highlight the complexity of risk and protective factors in different settings and contexts, and the importance of life and career history in understanding suicide attempts in the U.S. Army.
- A better understanding of suicide attempts may provide opportunities for the prevention of suicidal behavior in the Army as well as in other populations.



## **21. Predicting Suicides after Outpatient Mental Health Visits in the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Kessler, et al 2016)**

- Given that clinician-based assessments are not known to be strong predictors of suicide, this study investigated whether a precision medicine model using administrative data after outpatient mental health specialty visits could be developed to predict suicides among outpatients.
- This analysis used Army STARRS historical administrative data for more than 1.6 million Soldiers on active duty from 2004 to 2009 and focused on male non-deployed Regular U.S. Army Soldiers because they account for the vast majority of such suicides.
- The study calculated the observed proportions of suicide deaths within 5 weeks of each ventile (5% grouping) of specialty mental health outpatient visits ranked by predicted suicide risk based on the optimal prediction model out of the population of all such visits made by male non-deployed Regular U.S. Army Soldiers in 2004-2009.
- 41.5% of Army suicides in 2004-2009 occurred among the 12.0% of Soldiers seen as outpatient by mental health specialists, with risk especially high within 26 weeks of visits.
- An elastic net classifier with 10-14 predictors optimized sensitivity (45.6% of suicide deaths occurring after the 15% of visits with highest predicted risk).
- The 5% of visits with highest risk included only 0.1% of Soldiers (1047.1 suicides/100,000 person-years in the 5 weeks after the visit).
- This is a high enough concentration of risk to have implications for targeting preventive interventions. An even better model might be developed in the future by including the enriched information on clinician-evaluated suicide risk mandated by the VA/DoD CPG to be recorded.

## **22. Cross-Phenotype Polygenic Risk Score Analysis of Persistent Post-Concussive Symptoms in U.S. Army Soldiers with Deployment-Acquired Traumatic Brain Injury (Polimanti, et al 2016)**

- This study used a prospective longitudinal survey of three Brigade Combat Teams to assess deployment-acquired TBI and persistent physical, cognitive, and emotional post-concussive symptoms (PCS).
- A cross-phenotype high-resolution polygenic risk score (PRS) analysis of persistent post-concussive symptoms (PCS) was conducted in 845 U.S. Army Soldiers who sustained TBI during deployment.

- PRS was derived from summary statistics of large genome-wide association studies of Alzheimer’s disease, Parkinson’s disease, schizophrenia, bipolar disorder, and major depressive disorder; and for years of schooling, college completion, childhood intelligence, infant head circumference (IHC), and adult intracranial volume.
- Although the study had more than 95% of statistical power to detect moderate-to-large effect sizes, no association was observed with neurodegenerative and psychiatric disorders, suggesting that persistent PCS does not share genetic components with these traits to a moderate-to-large degree.
- Subjects with high IHC PRS recovered better from cognitive/emotional persistent PCS than the other individuals.
- Enrichment analysis identified two significant Gene Ontology (GO) terms related to this result: GO:0050839~Cell adhesion molecule binding and GO:0050905~Neuromuscular process.
- The study indicated that the genetic predisposition to persistent PCS after TBI does not have substantial overlap with neurodegenerative and psychiatric diseases, but mechanisms related to early brain growth may be involved.

### **23. An Examination of Potential Misclassification of Army Suicides: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Cox, et al 2016)**

- Systematic review of CID investigative files for 510 suicides, and 488 accident, homicide and undetermined deaths from 2005-2009.
- Using research criteria, 35 of 488 (8.2%) of non-suicides were reclassified to “definite, probable, or possible” suicide.
- Only 1 of 488 (0.2%) was reclassified to definite suicide.
- CID investigative practices reflect the “true” population of Army suicides. Flagrant misclassification was uncommon.

### **24. Barriers to Initiating and Continuing Mental Health Treatment Among Soldiers in the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Naifeh, et al 2016)**

- Army Soldiers with mental disorders report a variety of barriers to initiating and continuing treatment.

- This study involved a representative sample of 5,428 non-deployed Regular Army Soldiers who completed a self-administered questionnaire and consented to linking their questionnaire data with administrative records.
- The study examined reported treatment barriers (perceived need, structural reasons, attitudinal reasons) among respondents with current Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, mental disorders who either did not seek treatment in the past year (n = 744) or discontinued treatment (n = 145).
- 82.4% of Soldiers who did not initiate treatment, and 69.5% of Soldiers who discontinued treatment, endorsed at least two barriers.
- 69.8% of never-treated Soldiers reported no perceived need.
- Attitudinal reasons were cited more frequently than structural reasons among never-treated Soldiers with perceived need (80.7% vs. 62.7%) and Soldiers who discontinued treatment (71.0% vs. 37.8%).
- Multivariate associations with socio-demographic, Army career, and mental health predictors varied across barrier categories.
- These findings suggest most Soldiers with mental disorders do not believe they need treatment and those who do typically face multiple attitudinal and, to a lesser extent, structural barriers.
- Improved understanding of these treatment barriers can help direct mental health services to Soldiers in need.

## **25. Developing a Risk Model to Target High-Risk Preventive Interventions for Sexual Assault Victimization Among Female U.S. Army Soldiers (Street, et al 2016)**

- Sexual violence victimization is a significant problem among female U.S. military personnel. Preventive interventions for high-risk individuals might reduce prevalence but would require accurate targeting.
- This study attempted to develop a targeting model for female Regular U.S. Army Soldiers based on theoretically guided predictors abstracted from administrative data records.

- Because administrative reports of sexual assault victimization are known to be incomplete, parallel machine learning models were developed to predict administratively recorded (in the population) and self-reported (in a representative survey) victimization. Capture–recapture methods were used to combine predictions across models.
- Key predictors included low status, crime involvement, and treated mental disorders.
- Area under the receiver operating characteristic curve was .83–.88.
- Between 33.7% and 63.2% of victimizations occurred among Soldiers in the highest risk ventile (5%).
- This high concentration of risk suggests that the models could be useful in targeting preventive interventions, although final determination would require careful weighing of intervention costs, effectiveness, and competing risks.

## **26. Using Administrative Data to Identify U.S. Army Soldiers at High-Risk of Perpetrating Minor Violent Crimes (Rosellini, et al 2016)**

- Interventions exist to reduce violent crimes in high-risk populations, but optimal implementation requires evidence-based targeting.
- The goal of this study was to use machine learning methods to develop models to predict minor violent crime perpetration among U.S. Army Soldiers.
- Predictors were abstracted from administrative data available for all 975,057 Soldiers in the U.S. Army from 2004 to 2009. There were 25,966 men and 2,728 women who committed a first founded minor violent crime (simple assault, blackmail-extortion-intimidation, rioting, or harassment).
- Temporally prior administrative records measuring socio-demographic, Army career, criminal justice, medical/pharmacy, and contextual variables were used to build separate male and female prediction models that were then tested in an independent sample of U.S. Army Soldiers from 2011 to 2013.
- Final model predictors included young age, low education, early career stage, prior crime involvement, and outpatient treatment for diverse emotional and substance use problems.

- 30.5–28.9% (men-women) of all administratively-recorded crimes in 2004–2009 were committed by the 5% of Soldiers having highest predicted risk, with similar proportions (28.5–29.0%) when the 2004–2009 coefficients were applied to the 2011–2013 test sample.
- These results suggest that it may be possible to target Soldiers at high-risk of violence perpetration for preventive interventions.
- Final decisions about such interventions would require weighing predicted effectiveness against intervention costs and competing risks.

## **27. Neurocognitive Function and Suicide in U.S. Army Soldiers (Naifeh, et al 2016)**

- This study used administrative data from 2004 to 2009 to examine associations between neurocognitive functioning and subsequent suicidal events among Regular Army enlisted Soldiers.
- Cases were all Soldiers who completed the Army’s Automated Neuropsychological Assessment Metrics (ANAM) computerized testing battery prior to documented suicide attempt (n = 607), ideation (n = 955), or death (n = 57). Controls were an equal-probability sample of 9,893 person-months from other Soldiers.
- Exploratory factor analysis of five ANAM tests identified a general neurocognitive factor that excluded the mathematic processing test (MTH). When examined separately in logistic regression analyses that controlled for sociodemographics and prior mental health diagnosis, both the general neurocognitive factor and MTH were associated with all outcomes.
- When both predictors were examined simultaneously, the general neurocognitive factor continued to be associated with all outcomes and MTH continued to be associated with suicide attempt and ideation.
- These small but robust associations suggest that future research must continue to examine the extent to which objective neurocognitive tests may enhance understanding and prediction of suicide risk.

## **28. Alcohol Misuse and Co-Occurring Mental Disorders Among New Soldiers in the U.S. Army (Stein, et al 2016)**

- This study used cross-sectional survey data from Soldiers reporting for basic combat training to retrospectively assess lifetime alcohol consumption and substance abuse/dependence, enabling estimation of the prevalence of lifetime binge drinking and heavy drinking in a sample of 30,583 Soldiers and of probable alcohol use disorder (AUD) among 26,754 Soldiers with no or minimal lifetime use of other drugs.
- Co-occurrence of mental disorders and other adverse outcomes with binge drinking, heavy drinking, and AUD was examined. Discrete-time survival analysis, with person-year the unit of analysis and a logistic link function, was used to estimate associations of AUD with subsequent onset of mental disorders and vice versa.
- Prevalence of lifetime binge drinking was 27.2% among males and 18.9% among females; respective estimates for heavy drinking were 13.9% and 9.4%.
- Among Soldiers with no or minimal drug use, 9.5% of males and 7.2% of females had lifetime AUD.
- Relative to no alcohol misuse, binge drinking, heavy drinking, and AUD were associated with increased odds of all mental disorders and other adverse outcomes under consideration.
- Prior mental disorders and suicidal ideation were associated with onset of AUD, and prior AUD was associated with onset of mental disorders and suicidal ideation.
- Strong bidirectional associations between alcohol misuse and mental disorders were observed. Recognition of alcohol misuse and mental disorders upon enlistment may provide opportunities for risk mitigation early in a Soldier's career.

## **29. Medically Documented Suicide Ideation Among U.S. Army Soldiers (Ursano, et al 2016)**

- This study used administrative data to examine predictors of medically documented suicide ideation (SI) among Regular Army Soldiers from 2006 through 2009. The study included 10,466 ideators and 124,959 control person-months.
- Enlisted ideators (97.8% of all cases) were more likely than controls to be female, younger, older when entering service, less educated, never or previously deployed, and have a recent mental health diagnosis.
- Officer ideators were more likely than controls to be female, younger, younger when entering service, never married, and have a recent mental health diagnosis.

- Risk among enlisted Soldiers peaked in the second month of service then declined steadily, whereas risk among officers remained relatively stable over time.
- Risk of SI is highest among enlisted Soldiers early in Army service, females, and those with a recent mental health diagnosis.
- Most cases of medically documented SI in the U.S. Army occurred among enlisted Soldiers in their first tour of duty.
- Risk was particularly elevated among enlisted Soldiers during the initial months of training, and among Soldiers with a mental health diagnosis recorded during a recent health care encounter.
- Given apparent similarities between our findings on SI and recently published evidence on suicide attempts, it is important for future studies to examine how risk may differ across suicide-related outcomes of increasing severity.

### **30. Genetic Risk Variants for Social Anxiety (Stein, et al 2017)**

- This study used genome-wide association analysis (GWAS) to determine SNP-based heritability of social anxiety, discern genetic risk loci for social anxiety, and determine shared genetic risk with neuroticism and extraversion.
- GWAS were conducted within ancestral groups, European Americans (EUR), African Americans (AFR) and Latin Americans (LAT), using linear regression models for each of the three component studies in Army STARRS, and then meta-analyzed across studies.
- SNP-based heritability for social anxiety was significant in EUR. One meta-analytically genome-wide significant locus was seen in each of the EUR and AFR samples.
- Social anxiety was significantly genetically correlated (negatively) with extraversion but not with neuroticism or with an anxiety disorder factor score from external GWAS meta-analyses.
- This first GWAS of social anxiety confirms a genetic basis for social anxiety, shared with extraversion but possibly less so with neuroticism.

### **31. Frequency of Improvised Explosive Devices and Suicide Attempts in the U.S. Army (Ursano, et al 2017)**

- This study examined the association of monthly IED rates with risk of Soldier suicide attempt among those deployed and non-deployed among all active duty Regular Army suicide attempters 2004-2009 (n = 9,791) and an equal-probability sample of control Soldiers.
- Logistic regression analyses examined Soldiers' risk of attempting suicide as a function of monthly IED frequency, controlling for socio-demographics, service-related characteristics, rate of deployment/redeployment, combat deaths and injuries. The association of IED frequency with suicide attempt was examined overall and by time in service and deployment status.
- Soldiers' risk of suicide attempt increased with increasing numbers of IEDs. Suicide attempt was 26% more likely for each 1,000 IED increase in monthly frequency.
- The association of IED frequency with suicide attempt was greater for Soldiers in their first 2 years of service than for those with 3 or more years of service.
- Among Soldiers in their first 2 years of service, the association was constant, regardless of deployment status. Among soldiers with 3 or more years of service, the association was higher for those never deployed and currently deployed than for those previously deployed.
- To our knowledge, this is the first study to examine and demonstrate an association between the aggregate frequency of IEDs and risk of suicide attempts among U.S. Army Soldiers. The findings suggest that the threat of new weapons may increase stress burden among Soldiers. Targeting risk perception and perceived preparedness, particularly early in a Soldier's career, may improve psychological resilience and reduce suicide risk.

### **32. A Genome-Wide Gene-by-Trauma Interaction Study of Alcohol Misuse in Two Independent Cohorts Identifies PRKG1 as a Risk Locus (Polimanti, et al 2017)**

- Traumatic life experiences are associated with alcohol use problems, an association that is likely to be moderated by genetic predisposition.
- To better understand these interactions, a gene-by-environment genome-wide interaction study (GEWIS) of alcohol use problems was conducted in two independent cohorts: Army STARRS (N=16,361) and Yale-Penn (N=8,084).



- In African-American subjects, an interaction of PRKG1 with trauma exposure in the STARRS cohort was identified and replicated in the Yale-Penn cohort.
- PRKG1 encodes cyclic GMP-dependent protein kinase 1, which is involved in learning, memory and circadian rhythm regulation.
- Considering the loci identified in stage-1 that showed same effect directions in stage-2, the gene ontology (GO) enrichment analysis showed several significant results, including calcium-activated potassium channels, cognition, locomotion and Stat3 protein regulation.
- This was the largest GEWIS performed in psychiatric genetics, and the first GEWIS examining risk for alcohol misuse. The results add to a growing body of literature highlighting the dynamic impact of experience on individual genetic risk.

### **33. Sexual Assault Victimization and Mental Health Treatment, Suicide Attempts, and Career Outcomes among Women in the U.S. Army (Rosellini, et al 2017)**

- This study examined associations of administratively recorded sexual assault victimization during military service with subsequent mental health and negative career outcomes among U.S. Army women controlling for non-random victimization exposure.
- Used propensity score methods to match all 4,238 female Regular Army Soldiers with administratively recorded sexual assault victimization during 2004 to 2009 to five controls per case with similar composite victimization risk.
- Examined associations of this victimization measure with administratively recorded mental health treatment, suicide attempt, and Army career outcomes over the subsequent 12 months by using survival analysis for dichotomous outcomes and conditional generalized linear models for continuous outcomes.
- Women with administratively recorded sexual assault had significantly elevated odds ratios of subsequent mental health treatment, posttraumatic stress disorder treatment, suicide attempt, demotion, and attrition.
- Conclusion was sexual assault victimization is associated with considerable suffering and likely decreased force readiness.

### **34. Health Care Contact and Suicide Risk Documentation Prior to Suicide Death: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Ribeiro, et al 2017)**

- Prior research has shown that a substantial portion of suicide decedents access health care in the weeks and months before their death. This study examined whether this is true among Soldiers.
- The sample included the 569 Regular Army Soldiers in the U.S. Army who died by suicide on active duty between 2004 and 2009 compared to 5,690 matched controls.
- Analyses examined the prevalence and frequency of health care contacts and documentation of suicide risk (i.e., the presence of prior suicidal thoughts and behaviors) over the year preceding suicide death. Predictors of health care contact and suicide risk documentation were also examined.
- Approximately 50% of suicide decedents accessed health care in the month prior to their death, and more than 25% of suicide decedents accessed health care in the week prior to their death.
- Mental health encounters were significantly more prevalent among suicide decedents. Despite this, risk documentation was rare among suicide decedents (4 weeks: 13.8%; 52 weeks: 24.5%).
- Suicide decedents who were male, never married, and non-Hispanic Black were less likely to access care prior to death. Number of mental health encounters was the only predictor of suicide risk documentation among decedents at 4 weeks and 52 weeks prior to their death.
- Conclusion was many Soldiers who die by suicide access health care shortly before death, presenting an opportunity for suicide prevention. However, in most cases, there was no documentation of prior suicidal thoughts or behaviors, highlighting the need for improvements in risk detection and prediction. Increasing the frequency, scope, and accuracy of risk assessments, especially in mental health care settings, may be particularly useful.

### **35. Associations of Childhood Bullying Victimization with Lifetime Suicidal Behaviors among New U.S. Army Soldiers (Campbell-Sills, et al 2017)**

- Prior studies have documented associations of childhood bullying victimization with suicidal behaviors. Many failed to adjust for concomitant risk factors and none investigated this relationship in military personnel. The aim of this study was to estimate independent associations of childhood bullying victimization with suicidal behaviors among U.S. Army soldiers.
- Soldiers reporting for basic training completed a cross-sectional survey assessing mental disorders, suicidal behaviors, and childhood adversities including two types of bullying victimization: (1) Physical Assault/Theft and (2) Bullying Comments/Behaviors.
- Associations of childhood bullying experiences with suicidal behaviors were estimated using discrete-time survival analysis of person–year data from 30,436 Soldiers. Models adjusted for sociodemographic factors, childhood maltreatment by adults, and mental disorders.
- After comprehensive adjustment for other risk factors, more frequent Physical Assault/Theft by peers during childhood was associated with increased odds of lifetime suicidal ideation and attempt.
- More frequent Bullying Comments/Behaviors were associated with increased risk of ideation, plan, attempt, and onset of plan among ideators.
- Relative to no bullying victimization, exposure to the most persistent bullying was associated with two- to fourfold increase in risk for suicidal behaviors.
- The conclusion was childhood bullying victimization is associated with lifetime suicidal behaviors in new Soldiers. Exposure to Bullying Comments/Behaviors during childhood is associated with progression from suicidal ideation to plan. Improved recognition of these relationships may inform risk mitigation interventions for Soldiers.

### **36. Using Self-Report Surveys at the Beginning of Service to Develop Multi-Outcome Risk Models for New Soldiers in the U.S. Army (Rosellini, et al 2017)**

- The Army uses universal preventive interventions for several negative outcomes (e.g., suicide, violence, sexual assault) with especially high risks in the early years of service. More intensive interventions exist, but would be cost-effective only if targeted at high-risk Soldiers. This study developed models for such targeting from self-report surveys administered at the beginning of Army service.

- The study included 21,832 new Soldiers who completed a self-administered questionnaire (SAQ) in 2011–2012 and consented to link administrative data to SAQ responses. Penalized regression models were developed for 12 administratively recorded outcomes occurring by December 2013: suicide attempt, mental hospitalization, positive drug test, traumatic brain injury (TBI), other severe injury, several types of violence perpetration and victimization, demotion, and attrition.
- The best-performing models were for TBI, major physical violence perpetration, sexual assault perpetration, and suicide attempt. Although predicted risk scores were significantly correlated across outcomes, prediction was not improved by including risk scores for other outcomes in models.
- 40.5% of suicide attempts occurred among the 10% of new Soldiers with highest predicted risk, 57.2% of male sexual assault perpetrations among the 15% with highest predicted risk, and 35.5% of female sexual assault victimizations among the 10% with highest predicted risk.
- The conclusion was data collected at the beginning of service in self-report surveys could be used to develop risk models that define small proportions of new Soldiers accounting for high proportions of negative outcomes over the first few years of service.

**37. Childhood Adversity, Adult Stress, and the Risk of Major Depression or Generalized Anxiety Disorder in U.S. Soldiers: a Test of the Stress Sensitization Hypothesis (Bandoli, et al 2017)**

- The stress sensitization theory hypothesizes that individuals exposed to childhood adversity will be more vulnerable to mental disorders from proximal stressors. This study aimed to test this theory with respect to risk of 30-day major depressive episode (MDE) and generalized anxiety disorder (GAD) among new U.S. Army Soldiers.
- The sample consisted of 30,436 new Soldier recruits in the Army Study to Assess Risk and Resilience (Army STARRS). Generalized linear models were constructed, and additive interactions between childhood maltreatment profiles and level of 12-month stressful experiences on the risk of 30-day MDE and GAD were analyzed.
- Stress sensitization was observed in models of past 30-day MDE and GAD. This sensitization only occurred at high (3+) levels of reported 12-month stressful experiences.

- In pairwise comparisons for the risk of 30-day MDE, the risk difference between 3+ stressful experiences and no stressful experiences was significantly greater for all maltreatment profiles relative to no maltreatment.
- Similar results were found with the risk for 30-day GAD with the exception of the risk difference for episodic emotional and sexual abuse, which did not differ statistically from no maltreatment.
- This study found that new Soldiers are at an increased risk of 30-day MDE or GAD following recent stressful experiences if they were exposed to childhood maltreatment.
- Particularly in the military with an abundance of unique stressors, attempts to identify this population and improve stress management may be useful in the effort to reduce the risk of mental disorders.

**38. Psychological Autopsy Study Comparing Suicide Decedents, Suicide Ideators, and Propensity Score Matched Controls: Results from the Study to Assess Risk and Resilience in Service Members (Army STARRS) (Nock, et al 2017)**

- The suicide rate has increased significantly among U.S. Army Soldiers over the past decade. This study reports the first results from a large psychological autopsy study using two control groups designed to reveal risk factors for suicide death among Soldiers beyond known socio-demographic factors and the presence of suicide ideation.
- Informants were next-of-kin and Army supervisors for 135 suicide cases, 137 control Soldiers propensity-score-matched on known socio-demographic risk factors for suicide and Army history variables, and 118 control Soldiers who reported suicide ideation in the past year.
- Results revealed that most (79.3%) Soldiers who died by suicide have a prior mental disorder; mental disorders in the prior 30-days were especially strong risk factors for suicide death.
- Approximately half of suicide decedents tell someone that they are considering suicide.
- Virtually all of the risk factors identified in this study differed between suicide cases and propensity-score-matched controls, but did not significantly differ between suicide cases and suicide ideators.

- The most striking difference between suicides and ideators was the presence in the former of an internalizing disorder (especially depression) and multi-morbidity (i.e., 3+ disorders) in the past 30 days.
- This study found that most Soldiers who die by suicide have identifiable mental disorders shortly before their death and tell others about their suicidal thinking, suggesting that there are opportunities for prevention and intervention. However, few risk factors distinguish between suicide ideators and decedents, pointing to an important direction for future research.

### **39. Childhood Maltreatment and Lifetime Suicidal Behaviors among New Soldiers in the U.S. Army: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Stein, et al 2017)**

- Understanding suicide risk is a priority for the U.S. military. This study aimed to estimate associations of childhood maltreatment with pre-enlistment suicidal behaviors in new Army Soldiers using cross-sectional survey data from 38,237 Soldiers reporting for basic training from April 2011 through November 2012.
- Scales assessing retrospectively reported childhood abuse and neglect were derived and subjected to latent class analysis, which yielded 5 profiles: No Maltreatment, Episodic Emotional Maltreatment, Frequent Emotional/Physical Maltreatment, Episodic Emotional/Sexual Abuse, and Frequent Emotional/Physical/Sexual Maltreatment.
- Discrete-time survival analysis was used to estimate associations of maltreatment profiles with suicidal behaviors (assessed with a modified Columbia-Suicide Severity Rating Scale), adjusting for socio-demographics and mental disorders.
- Nearly 1 in 5 new Soldiers was classified as experiencing childhood maltreatment.
- Relative to No Maltreatment, all multivariate maltreatment profiles were associated with elevated odds of lifetime suicidal ideation, attempt, and onset of plan among those with ideation.
- Several profiles also predicted attempts among those with plans, and Frequent Emotional/Physical/Sexual Maltreatment predicted unplanned attempts among ideators.
- Adjustment for mental disorders attenuated but did not eliminate these associations.
- Childhood maltreatment is strongly associated with suicidal behavior among new Soldiers, even after adjusting for intervening mental disorders.

- Among soldiers with lifetime ideation, certain maltreatment profiles are associated with elevated odds of subsequently planning and/or attempting suicide.
- Focus on childhood maltreatment might reveal avenues for risk reduction among new Soldiers.

#### **40. Suicide Attempts in U.S. Army Combat Arms, Special Forces and Combat Medics (Ursano, et al 2017)**

- The U.S. Army suicide attempt rate increased sharply during the wars in Iraq and Afghanistan. Risk may vary according to occupation, which significantly influences the stressors that Soldiers experience.
- Using administrative data from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS), this study identified person-month records for all active duty Regular Army enlisted Soldiers who had a medically documented suicide attempt from 2004 through 2009 (n = 9,650) and an equal-probability sample of control person-months (n = 153,528).
- Logistic regression analyses examined the association of combat occupation (combat arms, special forces, combat medics) with suicide attempt, adjusting for socio-demographics, service-related characteristics, and prior mental health diagnosis.
- In adjusted models, the odds of attempting suicide were higher in combat arms and combat medics, but lower in special forces, compared to all other occupations.
- Combat arms and combat medics had higher odds of suicide attempt than other occupations if never deployed or previously deployed, but not when currently deployed.
- Occupation was associated with suicide attempt in the first ten years of service, but not beyond.
- In the first year of service, primarily a time of training, combat medics had higher odds of suicide attempt than both combat arms and other occupations.
- Discrete-time hazard functions revealed that these occupations had distinct patterns of monthly risk during the first year of service.
- This study found that military occupation can inform the understanding suicide attempt risk among Soldiers.

#### **41. Lifetime Suicidal Behaviors and Career Characteristics Among U.S. Army Soldiers (Millner, et al 2017)**

- This study presented data on lifetime prevalence of suicide ideation and non-fatal attempts as reported by the large representative sample of U.S. Army Soldiers who participated in the Consolidated All Army Study (n = 29,982). The study also examined associations of key Army career characteristics with these outcomes.
- Prevalence estimates for lifetime suicide ideation were 12.7% among men and 20.1% among women, and for lifetime suicide attempts were 2.5% and 5.1%, respectively.
- Retrospective age-of-onset reports suggested that 53.4% to 70% of these outcomes had pre-enlistment onsets.
- Results revealed that, for both men and women, being in the Regular Army, compared with being in the National Guard or Army Reserve, and being in an enlisted rank, compared with being an officer, is associated with increased risk of suicidal behaviors and that this elevated risk is present both before and after joining the Army.

#### **42. Risk of Suicide Attempt Among Soldiers in Army Units With a History of Suicide Attempts (Ursano, et al 2017)**

- This study examined whether a Soldier's risk of suicide attempt is influenced by previous suicide attempts in that Soldier's unit.
- Using administrative data from the Army Study to Assess Risk and Resilience in Servicemembers (STARSS), this study identified person-month records for all active-duty, regular U.S. Army, enlisted Soldiers who attempted suicide from January 1, 2004 through December 31, 2009 (n = 9,650), and an equal-probability sample of control person-months (n = 153,528).
- Logistic regression analyses examined the number of past-year suicide attempts in a Soldier's unit as a predictor of subsequent suicide attempt, controlling for socio-demographic features, service-related characteristics, prior mental health diagnosis, and other unit variables, including suicide-, combat-, and unintentional injury-related unit deaths.
- The study also examined whether the influence of previous unit suicide attempts varied by military occupational specialty (MOS) and unit size.



- Of the final analytic sample of 9,512 enlisted Soldiers who attempted suicide and 151,526 control person-months, most were male (86.4%), 29 years or younger (68.4%), younger than 21 years when entering the Army (62.2%), white (59.8%), high school educated (76.6%), and currently married (54.8%).
- In adjusted models, Soldiers were more likely to attempt suicide if 1 or more suicide attempts occurred in their unit during the past year (odds ratios [ORs], 1.4-2.3;  $P < .001$ ), with odds increasing as the number of unit attempts increased.\*
- The odds of suicide attempt among Soldiers in a unit with 5 or more past-year attempts was more than twice that of Soldiers in a unit with no previous attempts (OR, 2.3; 95%CI, 2.1-2.6).
- The association of previous unit suicide attempts with subsequent risk was significant whether Soldiers had a combat arms MOS or other MOS (ORs, 1.4-2.3;  $P < .001$ ) and regardless of unit size, with the highest risk among those in smaller units (1-40 Soldiers) (ORs, 2.1-5.9;  $P < .001$ ).\*
- The population-attributable risk proportion for 1 or more unit suicide attempts in the past year indicated that, if this risk could be reduced to no unit attempts, 18.2% of attempts would not occur.
- Units with a history of suicide attempts may be important targets for preventive interventions.

#### **43. Predicting Sexual Assault Perpetration in the U.S. Army Using Administrative Data (Rosellini, et al 2017)**

- This study developed actuarial models to identify male U.S. Army Soldiers at high risk of administratively recorded sexual assault perpetration.
- This study investigated administratively recorded sexual assault perpetration among the 821,807 male Army Soldiers serving 2004–2009.
- Penalized discrete-time (person-month) survival analysis was used to select the smallest possible number of stable predictors to maximize number of sexual assaults among the 5% of Soldiers with highest predicted risk of perpetration (top-ventile concentration of risk). Separate models were developed for assaults against non-family and intra-family adults and minors.
- There were 4,640 male Soldiers found to be perpetrators against non-family adults, 1,384 against non-family minors, 380 against intra-family adults, and 335 against intra-family minors.

- Top-ventile concentration of risk was 16.2%–20.2% predicting perpetration against non-family adults and minors, and 34.2%–65.1% against intra-family adults and minors. Final predictors consisted largely of measures of prior crime involvement and the presence and treatment of mental disorders.
- Administrative data can be used to develop actuarial models that identify a high proportion of sexual assault perpetrators. If a system is developed to consolidate administrative predictors routinely, then predictions could be generated periodically to identify those in need of preventive intervention. Whether this would be cost effective, though, would depend on intervention costs, effectiveness, and competing risks.

#### **44. Genome-wide Association Studies of Suicide Attempts in U.S. Soldiers (Stein, et al 2017)**

- This study utilized population-based non-clinical cohorts of U.S. military personnel (discovery: n = 473 cases and n = 9778 control subjects; replication: n = 135 cases and n = 6879 control subjects) and a clinical case-control sample of recent suicide attempters (n = 51 cases and n = 112 control subjects) to conduct GWAS of suicide attempts (SA).
- Genome-wide association was evaluated within each ancestral group (European-, African-, Latino-American) and study using logistic regression models.
- Meta-analysis of the European ancestry discovery samples revealed a genome-wide significant locus in association with SA near MRAP2 (melanocortin 2 receptor accessory protein 2) and CEP162 (centrosomal protein 162); 12 genome-wide significant SNPs in the region; peak SNP rs12524136-T, OR = 2.88, p = 5.24E-10.
- These findings were not replicated in the European ancestry subsamples of the replication or suicide attempters samples. However, the association of the peak SNP remained significant in a meta-analysis of all studies and ancestral subgroups (OR = 2.18, 95%CI 1.70, 2.80).
- Polygenic risk score (PRS) analyses showed some association of SA with bipolar disorder.
- The association with SNPs encompassing MRAP2, a gene expressed in brain and adrenal cortex and involved in neural control of energy homeostasis, points to this locus as a plausible susceptibility gene for suicidality that should be further studied. Larger sample sizes will be needed to confirm and extend these findings.

#### **45. Prior Mental Disorders and Lifetime Suicidal Behaviors among U.S. Army Soldiers in the Army Study to Assess Risk and Resilience in Servicemembers (Millner, et al 2017)**

- This study examined associations of prior mental disorders and Army career characteristics with subsequent first onset of suicidal behaviors in a large, representative sample of U.S. Army Soldiers from the consolidated All Army Study (n=29,982).
- Among men and women, all self-reported lifetime disorders measured (some assessed with screening scales) are associated with subsequent onset of suicide ideation.
- Among men, three disorders characterized by agitation and impulsiveness (intermittent explosive disorder, panic disorder, and substance disorders) predict the transition from suicide ideation to attempt.
- For both men and women, being in the Regular Army (vs. National Guard or Army Reserve) predicts suicide attempts in the total sample.
- For men, a history of deployment and junior rank are predictors of suicide attempts after adjusting for pre-enlistment disorders but not accounting for pre- and post-enlistment disorders, suggesting that post-enlistment disorders account for some of the increased suicide risk among these career characteristics.
- The results highlight associations between mental disorders and suicidal behaviors, but underscore limitations predicting which people with ideation attempt suicide.

#### **46. Documented Family Violence and Risk of Suicide Attempt among U.S. Army Soldiers (Ursano, et al 2017)**

- Person-month records of active duty, Regular Army, enlisted Soldiers with medically documented suicide attempts (SA) (n=9,650), and a sample of control person-months (n=153,528), were selected from administrative data in 2004 to 2009 to examine associations of family violence (FV) history with SA risk among Soldiers. Logistic regression analyses were used to examine associations of FV with SA, adjusting for socio-demographics, service-related characteristics, and prior mental health diagnosis.
- Odds of SA were higher in Soldiers with a FV history and increased as the number of FV events increased.
- Soldiers experiencing past-month FV were almost five times as likely to attempt suicide as those with no FV history.

- Odds of SA were elevated for both perpetrators and those who were exclusively victims. Male perpetrators had higher odds of SA than male victims, whereas female perpetrators and female victims did not differ in SA risk.
- A discrete-time hazard function indicated that SA risk was highest in the initial months following the first FV event.
- Findings indicate that FV is an important consideration in understanding risk of SA among Soldiers.

#### **47. Prospective Risk Factors for Post-Deployment Heavy Drinking and Alcohol or Substance Use Disorder among U.S. Army Soldiers (Campbell-Sills, et al 2017)**

- This study estimated prevalence of alcohol misuse among 4,645 U.S. Army Soldiers who participated in a longitudinal survey.
- Assessment occurred 1–2 months before Soldiers deployed to Afghanistan in 2012 (T0), upon their return to the U.S. (T1), 3 months later (T2), and 9 months later (T3).
- Weights-adjusted logistic regression was used to evaluate associations of hypothesized risk factors with post-deployment incidence and persistence of heavy drinking (HD) (consuming 5 + alcoholic drinks at least 1–2×/week) and alcohol or substance use disorder (AUD/SUD).
- Prevalence of past-month HD at T0, T2, and T3 was 23.3% (S.E. = 0.7%), 26.1% (S.E. = 0.8%), and 22.3% (S.E. = 0.7%); corresponding estimates for any binge drinking (BD) were 52.5% (S.E. = 1.0%), 52.5% (S.E. = 1.0%), and 41.3% (S.E. = 0.9%).
- Greater personal life stress during deployment (e.g., relationship, family, or financial problems) – but not combat stress – was associated with new onset of HD at T2 [per standard score increase: adjusted odds ratio (AOR) = 1.20, 95% CI 1.06–1.35,  $p = 0.003$ ]; incidence of AUD/SUD at T2 (AOR = 1.54, 95% CI 1.25–1.89,  $p < 0.0005$ ); and persistence of AUD/SUD at T2 and T3 (AOR = 1.30, 95% CI 1.08–1.56,  $p = 0.005$ ).
- Any BD pre-deployment was associated with post-deployment onset of HD (AOR = 3.21, 95% CI 2.57–4.02,  $p < 0.0005$ ) and AUD/SUD (AOR = 1.85, 95% CI 1.27–2.70,  $p = 0.001$ ).
- Alcohol misuse is common during the months preceding and following deployment. Timely intervention aimed at alleviating/managing personal stressors or curbing risky drinking might reduce risk of alcohol-related problems post-deployment.

#### **48. Predictive Validity and Correlates of Self-Assessed Resilience among U.S. Army Soldiers (Campbell-Sills, et al 2017)**

- This study evaluated the validity of self-assessed resilience among U.S. Army Soldiers, including whether pre-deployment perceived resilience predicted post-deployment emotional disorder.
- Resilience was assessed via self-administered questionnaire among 35,807 new Soldiers reporting for basic training and 8,558 experienced Soldiers preparing to deploy to Afghanistan. Concurrent validity of self-assessed resilience was evaluated among recruits by estimating its association with past-month emotional disorder.
- Predictive validity was examined among 3,526 experienced Soldiers with no lifetime emotional disorder pre-deployment. Predictive models estimated associations of pre-deployment resilience with incidence of emotional disorder through 9 months post-deployment and with marked improvement in coping at 3 months post-deployment.
- Soldiers characterized themselves as very resilient on average [ $M = 14.34$ ,  $SD = 4.20$  (recruits);  $M = 14.75$ ,  $SD = 4.31$  (experienced Soldiers); theoretical range = 0-20].
- Demographic characteristics exhibited only modest associations with resilience, while severity of childhood maltreatment was negatively associated with resilience in both samples.
- Among recruits, resilience was inversely associated with past-month emotional disorder [adjusted odds ratio (AOR) = 0.65, 95% CI = 0.62-0.68,  $P < .0005$  (per standard score increase)].
- Among deployed Soldiers, greater pre-deployment resilience was associated with decreased incidence of emotional disorder (AOR = 0.91; 95% CI = 0.84-0.98;  $P = .016$ ) and increased odds of improved coping (AOR = 1.36; 95% CI = 1.24-1.49;  $P < .0005$ ) post-deployment.
- Findings supported validity of self-assessed resilience among Soldiers, although its predictive effect on incidence of emotional disorder was modest. In conjunction with assessment of known risk factors, measurement of resilience could help predict adaptation to foreseen stressors like deployment.

#### **49. Medical-encounter Mental Health Diagnoses, Non-fatal Injury and Polypharmacy Indicators of Risk for Accident Death in the U.S. Army Enlisted Soldiers, 2004-2009 (Lewandowski-Romps, et al 2017)**

- Accidents are a leading cause of deaths in active duty personnel and understanding accident deaths during wartime could facilitate future operational planning and inform risk prevention efforts.
- This study used 2004-2009 military records for enlisted, active duty, Regular Army Soldiers to identify mental health, injury, and polypharmacy (multiple narcotic and/or psychotropic medications) predictors of accident deaths for current, previously, and never deployed groups during the Afghanistan and Iraq wars.
- Deployed Soldiers with anxiety diagnoses showed higher risk for accident deaths. More than half had anxiety diagnoses prior to being deployed, suggesting anticipatory anxiety or symptom recurrence may contribute to high risk.
- Traumatic brain injury (TBI) indicated higher risk for accident deaths among previously deployed Soldiers. Two-thirds of these Soldiers had first TBI medical-encounter while non-deployed, but mild, combat-related TBIs may have been undetected during deployments.
- Post-Traumatic Stress Disorder (PTSD) predicted higher risk of accident death for never deployed Soldiers, as did polypharmacy which may relate to reasons for deployment ineligibility.
- The higher risk of accident death predicted by PTSD among those never deployed suggests the importance of identification, treatment, and prevention of non-combat traumatic events.
- Accident death risk predictors overlapped with those identified for suicides which suggests effective intervention might reduce both types of deaths.

#### **50. Trauma Exposure Interacts with the Genetic Risk of Bipolar Disorder in Alcohol Misuse of U.S. Soldiers (Polimanti, et al 2017)**

- This study investigated whether trauma exposure modified the association of genetic risks for mental disorders with alcohol misuse and nicotine dependence (ND) symptoms by calculating high-resolution polygenic risk scores (PRSs) for 10,732 U.S. Army Soldiers (8,346 trauma-exposed and 2,386 trauma-unexposed) based on genome-wide association studies of bipolar disorder (BD), major depressive disorder, and schizophrenia.

- The study found a significant BD PRS-by-trauma interaction with respect to alcohol misuse; a positive correlation between BD PRS and alcohol misuse in trauma-exposed Soldiers; and a negative correlation in trauma-unexposed Soldiers.
- The variants included in the BD PRS-by-trauma interaction showed significant enrichments for gene ontologies related to high voltage-gated calcium channel activity and for Beta1/Beta2 adrenergic receptor signaling pathways.
- The results indicated that the genetic overlap between alcohol misuse and BD is significantly moderated by trauma exposure. This study provides molecular insight into the complex mechanisms that link substance abuse, psychiatric disorders, and trauma exposure.

### **51. Genome-Wide Analysis of Insomnia Disorder (Stein, et al 2018)**

- Insomnia is a worldwide problem with substantial deleterious health effects. Twin studies have shown a heritable basis for various sleep-related traits, including insomnia, but robust genetic risk variants have just recently begun to be identified.
- This study involved genome-wide association studies (GWAS) of Soldiers in Army STARRS. GWAS were carried out separately for each ancestral group (EUR, AFR, LAT) using logistic regression for each of the STARRS component studies (including 3,237 cases and 14,414 controls), and then meta-analysis was conducted across studies and ancestral groups.
- Heritability (SNP-based) for lifetime insomnia disorder was significant in EUR. A meta-analysis including three ancestral groups and three study cohorts revealed a genome-wide significant locus on Chr 7 and a genome-wide significant gene-based association in EUR for RFX3 on Chr 9. Polygenic risk for sleeplessness/insomnia severity in UK Biobank was significantly positively associated with likelihood of insomnia disorder in STARRS.
- Genetic contributions to insomnia disorder in STARRS were significantly positively correlated with major depressive disorder and type 2 diabetes, and negatively with morningness chronotype and subjective well-being in external datasets.
- Insomnia associated loci may contribute to the genetic risk underlying a range of health conditions including psychiatric disorders and metabolic disease.

## **52. Risk Factors for the Transition from Suicide Ideation to Suicide Attempt: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Nock, et al 2018)**

- Prior research has shown that most known risk factors for suicide attempts in the general population actually predict suicide ideation rather than attempts among ideators. Yet clinical interest in predicting suicide attempts often involves the evaluation of risk among patients with ideation.
- This study examined a number of characteristics of suicidal thoughts hypothesized to predict incident attempts in a retrospective analysis of lifetime ideators (N = 3,916) drawn from a large (N = 29,982), representative sample of U.S. Army Soldiers.
- The most powerful predictors of first nonfatal lifetime suicide attempt in a multivariate model controlling for previously known predictors (e.g., demographics, mental disorders) were: recent onset of ideation, presence and recent onset of a suicide plan, low controllability of suicidal thoughts, extreme risk-taking or “tempting fate,” and failure to answer questions about the characteristics of one’s suicidal thoughts.
- A predictive model using these risk factors had strong accuracy (area under the curve [AUC] = .93), with 66.2% of all incident suicide attempts occurring among the 5% of Soldiers with highest composite predicted risk.
- This high concentration of risk in this retrospective study suggests that a useful clinical decision support model could be constructed from prospective data to identify those with highest risk of subsequent suicide attempt.

## **53. Improving risk prediction accuracy for new soldiers in the U.S. Army by adding self-report survey data to administrative data (Bernecker, et al 2018)**

- The Army STARRS New Soldier Survey was administered to 21,790 Regular Army Soldiers who agreed to have their survey data linked to their administrative data. Machine-learning models using administrative data as predictors found that small proportions of high-risk Soldiers accounted for high proportions of negative outcomes including mental disorders, suicidality, and interpersonal violence.
- This study examined the extent to which this survey information increased prediction accuracy, over models based solely on administrative data, for these outcomes.



- The study used discrete time survival analysis to estimate a series of models predicting first occurrence, assessing how model fit improved and concentration of risk increased when adding the predicted risk score based on survey data to the predicted risk score based on administrative data.
- The addition of survey data improved prediction significantly for all outcomes. In the most extreme case, the percentage of reported sexual violence victimization among the 5% of female soldiers with highest predicted risk increased from 17.5% using only administrative predictors to 29.4% adding survey predictors, a 67.9% proportional increase in prediction accuracy. Other proportional increases in concentration of risk ranged from 4.8% to 49.5% (median = 26.0%).
- The researchers concluded that the Army may benefit from routinely administering surveys that assess additional risk factors, such as the New Soldier Survey, because the data from the surveys could substantially improve accuracy of risk models compared to models based exclusively on administrative predictors.

#### **54. Associations of Time-Related Deployment Variables with Risk of Suicide Attempt Among Soldiers (Ursano, et al 2018)**

- This study was designed to determine whether risk of suicide attempt (SA) among Soldiers is associated with time-related deployment characteristics such as time in service prior to first deployment, length of deployment, and length of time between deployments (dwell time).\*
- It was a longitudinal, retrospective cohort study that used administrative data from 2004 through 2009 to identify person-month records of active-duty Regular Army enlisted Soldiers who had served continuously in the Army for at least 2 years. Study included 593 medically-documented suicide attempters and 19,034 control person-months for Soldiers who deployed exactly twice.\*
- Findings indicate the risk of SA during or after second deployment was higher for those who initially deployed within the first 12 months of service, and for those with a dwell time of 6 months or less.\*
- Length of first deployment was not associated with subsequent SA.
- Time in service prior to first deployment and dwell time are modifiable risk factors for SA risk among Soldiers.\*
- The Army's continued focus on dwell time may help mitigate a range of negative outcomes and reduce risk of suicidal behavior.

### **55. Nonfatal Suicidal Behaviors in the Administrative Records of Activated U.S. Army National Guard and Army Reserve Soldiers, 2004–2009 (Ursano, et al 2018)**

- The Army suicide rate increased sharply during the wars in Iraq and Afghanistan. There is limited information about medically-documented, nonfatal suicidal behaviors among Soldiers in the Army's Reserve Component (RC), which is composed of the Army National Guard and Army Reserve.
- This study used administrative records for all Soldiers on active duty for the years 2004 through 2009 (n = 1.66 million) to examine trends and socio-demographic correlates of suicide attempts, suspicious injuries, and suicide ideation among activated RC Soldiers. The study identified 2,937 unique RC Soldiers with a documented nonfatal suicidal event.
- The study found increases in the annual incidence rates of suicide attempts (71 to 204/100,000 person-years) and suicide ideation (326 to 425/100,000 person years). Incidence rates for suspicious injuries also generally increased but were more variable.
- Using hierarchical classification rules, the study identified the first instance of each Soldier's most severe behavior (suicide attempt versus suspicious injury versus suicide ideation). For each of those suicide- or injury-related outcomes, the study found increased risk among those who were female, younger, non-Hispanic White, less educated, never married, and lower-ranking enlisted.
- The socio-demographic associations differed significantly across outcomes, although the patterns were similar.
- The results provide a broad overview of nonfatal suicidal trends in the RC during the period 2004 through 2009, and demonstrate that integration of multiple administrative data systems enriches analysis of the predictors of such events.

### **56. Pre-deployment Predictors of Psychiatric Disorder-Symptoms and Interpersonal Violence during Combat Deployment (Rosellini, et al 2018)**

- Preventing suicides, mental disorders, and noncombat-related interpersonal violence during deployment are priorities of the U.S. Army.

- This study used pre-deployment survey and Army administrative data to develop actuarial models to identify Soldiers at high risk of these outcomes during combat deployment. The models were developed for Soldiers in the Pre-Post Deployment Study, a panel study of Soldiers deployed to Afghanistan in 2012–2013 who completed self-administered questionnaires before deployment and one month (T1), three months (T2), and nine months (T3) after deployment, and consented to linking their survey data to their Army administrative data.
- Seven “during-deployment” outcomes were assessed using post-deployment surveys either at T1 (n = 7,048) or at T2–T3 (n = 7,081). Machine learning was used to develop a model for each outcome from 273 pre-deployment predictors which were compared to simple logistic regression models.
- The relative improvement in area under the receiver operating characteristic curve (AUC) obtained by machine learning compared to the logistic models ranged from 1.11 (major depression) to 1.83 (suicidality). The best-performing machine learning models were for major depression (AUC=0.88), suicidality (0.86), and generalized anxiety disorder (0.85).
- Roughly 40% of these outcomes occurred among the 5% of Soldiers with highest predicted risk.
- Actuarial models could be used to identify high risk Soldiers either for exclusion from deployment or preventive interventions. The ultimate value of this approach depends on the associated costs, competing risks (e.g., stigma), and effectiveness of to-be-determined interventions.

#### **57. Risk Factors Associated with Attempted Suicide among U.S. Army Soldiers without a History of Mental Health Diagnosis (Ursano, et al 2018)**

- This study was designed to examine predictors of suicide attempt among Soldiers without a previous mental health diagnosis.
- Using Army and DoD administrative data from 2004-2009, the study identified person-month records for all active duty Regular Army enlisted Soldiers who had a medically documented suicide attempt (n=9,650), and an equal-probability sample of control person-months (n=153,528), then examined whether predictors of suicide attempt varied by history of mental health diagnosis.

- Suicide attempts were identified using DoD Suicide Event Report records and ICD-9 E95x diagnostic codes. Mental health diagnoses and related codes (as well as socio-demographic, service-related, physical healthcare, crime, and family violence variables) were constructed from Army personnel, medical, legal, and family services records.
- The study found 36.3% (n=3,507) of Soldiers who attempted suicide did not have a previous mental health diagnosis.\*
- Among Soldiers with no previous diagnosis, the highest adjusted odds of suicide attempt were for females, less than high school education, in first year of service, previously deployed, promotion delayed 2 months or less, past-year demotion, 8 or more outpatient physical health care visits in the past 2 months, past-month injury-related outpatient and inpatient health care visit, previous combat injury, minor violent crime victimization, major violent crime perpetration, and family violence.\*
- Most of these variables were also associated with suicide attempts among Soldiers with a previous mental health diagnosis, although the strength of associations differed.\*
- The study concluded that suicide attempt risk among Soldiers with unrecognized mental health problems is a significant and important challenge, and administrative records from personnel, medical, legal, and family services systems can assist in identifying Soldiers at risk.\*

#### **58. Patterns and Predictors of Persistence of Suicide Ideation: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (Nock, et al 2018)**

- Persistent suicide ideation (SI) is known to be a risk factor for subsequent suicidal behaviors. Reducing SI persistence among people with a history of SI may be a useful target for preventive intervention, but basic information is lacking about patterns and predictors of SI persistence.
- Based on retrospective data on annual SI persistence in a representative sample of 3,501 U.S. Army Soldiers with lifetime SI, age-of-onset and number of years with SI were used to estimate two definitions of persistence: persistence beyond year-of-onset and proportional annual persistence.
- For 47.8% of respondents with lifetime SI, their SI did not persist beyond the year-of-onset. For the 52.2% whose SI did persist beyond the year-of-onset, the median (inter-quartile range) proportional annual persistence was 33% (17-67%).

- Significant predictors of increased persistence were different for respondents with pre-enlistment SI onset (prior histories of attention-deficit/hyperactivity disorder [ADHD], bipolar disorder, and panic disorder) and post-enlistment SI onset (male, combat support military occupation specialty, prior histories of ADHD, panic disorder, and posttraumatic stress disorder).
- These predictors of persistence are different from the predictors of SI onset, suggesting that secondary preventive interventions to reduce SI persistence may need to focus on different factors than primary preventive interventions to reduce SI onset.

### **59. Attention Deficit Hyperactivity Disorder and Risk of Posttraumatic Stress and Related Disorders: A Prospective Longitudinal Evaluation in U.S. Army Soldiers (Howlett, et al 2018)**

- Aim of this study was to examine whether pre-deployment ADHD is associated with increased risk of post-deployment PTSD among U.S. Army Soldiers.
- Soldiers (n=4,612) who completed all assessments in the prospective Pre/Post Deployment Study of Soldiers deployed to Afghanistan comprised the sample to estimate association of pre-deployment ADHD with post-deployment PTSD.
- Also examined relationships of pre-deployment ADHD with post-deployment major depressive episode (MDE), generalized anxiety disorder (GAD), and suicidal ideation.
- Weighted prevalence of ADHD pre-deployment was 6.1% (SE=0.4%). Adjusting for other risk factors and pre-deployment PTSD, pre-deployment ADHD was associated with elevated odds of post-deployment PTSD (AOR= 2.13, 95% CI=1.51–3.00, p<.001).
- Pre-deployment ADHD was similarly associated with incidence of PTSD among Soldiers with no lifetime history (AOR= 2.50, 95% CI=1.69–3.69, p<.001).
- ADHD also displayed associations with post-deployment MDE (AOR=2.80, 95% CI=2.01-3.91, p<0.0005) and GAD (AOR=3.04, 95% CI=2.10-4.42, p<.001), but not suicidal ideation.
- Recognition of associations between pre-deployment ADHD and post-deployment PTSD, MDE, and GAD may inform targeted prevention efforts. Future research should examine whether treatment of ADHD is protective against PTSD and related disorders in trauma-exposed individuals.

## **60. Pre-deployment Insomnia is Associated with Post-deployment PTSD and Suicidal Ideation in US Army Soldiers (Wang, et al 2018)**

- Insomnia is prevalent among military personnel and may increase risk of mental disorders and suicidal ideation. This study examined associations of pre-deployment insomnia with post-deployment post-traumatic stress disorder (PTSD) and suicidal ideation among U.S. Army Soldiers.
- Study included Soldiers from 3 Brigade Combat Teams who completed surveys 1–2 months before deploying to Afghanistan in 2012 (T0), on return from deployment (T1), 3 months later (T2), and 9 months later (T3). Logistic regression was used to estimate associations of pre-deployment (T0) insomnia with post-deployment (T2 or T3) PTSD and suicidal ideation among those who completed surveys at all waves (n = 4,645).
- Pre-deployment insomnia was associated with increased risk of post-deployment PTSD (adjusted odds ratio [AOR] = 3.14, 95% confidence interval [CI] = 2.58% to 3.82%, p < .0005) and suicidal ideation (AOR = 2.78, 95% CI = 2.07% to 3.74%, p < .0005) in models adjusting for socio-demographic characteristics and prior deployment history.
- Adjustment for other pre-deployment risk factors and deployment experiences attenuated these associations, but insomnia remained significantly associated with post-deployment PTSD (AOR = 1.50, 95% CI = 1.19% to 1.89%, p = .001) and suicidal ideation (AOR = 1.43, 95% CI = 1.04% to 1.95%, p = .027).
- Subgroup models showed that pre-deployment insomnia was associated with incident PTSD (AOR = 1.55, 95% CI = 1.17% to 2.07%, p = .003) and suicidal ideation (AOR = 1.67, 95% CI = 1.16% to 2.40%, p = .006) among Soldiers with no pre-deployment history of these problems.
- Study found that pre-deployment insomnia contributed to prediction of post-deployment PTSD and suicidal ideation in Army Soldiers, suggesting that detection of insomnia could facilitate targeting of risk mitigation programs.

## **61. Predicting Suicide Attempts among Soldiers who deny Suicidal Ideation (Bernecker, et al 2018)**

- Most non-fatal suicide attempts and suicide deaths occur among patients who deny suicidal ideation (SI) during suicide risk screenings. But little is known about risk factors for suicidal behaviors among such patients. The study investigated this using a representative sample of U.S. Army Soldiers who denied lifetime SI in a survey and were then followed through administrative records for up to 45 months to learn of administratively-recorded suicide attempts (SA).

- Study used a novel two-stage risk assessment approach that combined first-stage prediction from administrative records to find the subsample of SI deniers with highest subsequent SA risk, then used survey reports to estimate a second-stage model identifying the subset of individuals in the high-risk subsample at highest SA risk.
- 70% of survey respondents denied lifetime SI. Administrative data identified 30% of this 70% who accounted for 81.2% of subsequent administratively-recorded SAs. A relatively small number of self-report survey variables were then used to create a prediction model that identified 10% of the first-stage high-risk sample (i.e., 3% of all Soldiers) at highest SA risk (accounting for 45% of SAs in the total sample).
- Study discussed potential applications of this approach for identifying future SI deniers at highest SA risk.

## **62. Transition to Suicide Attempt from Recent Suicide Ideation in U.S. Army Soldiers (Naifeh, et al 2018)**

- Most people with suicide ideation (SI) do not attempt suicide (SA). Understanding the transition from current/recent SI to SA is important for mental health care. The objective of this study was to identify characteristics that differentiate SA from 30-day SI among representative U.S. Army Soldiers.
- The study used a unique case–control design including Soldiers recently hospitalized for SA (n = 132) and representative Soldiers from the same four communities (n = 10,193) who were administered the same questionnaire.
- The study systematically identified variables that differentiated suicide attempters from the total population, then examined whether those same variables differentiated all 30-day ideators (n = 257) from the total population, and attempters from non-attempting 30-day ideators.
- In univariable analyses, 20 of 23 predictors were associated with SA in the total population (0.05 level). The best multivariable model included 8 significant predictors: interpersonal violence, relationship problems, major depressive disorder, post-traumatic stress disorder (PTSD), and substance use disorder (all having positive associations), as well as past 12-month combat trauma, intermittent explosive disorder (IED), and any college education (all having negative associations).

- Six of these predictors differentiated 30-day ideators from the population. Three of these predictors differentiated attempters from ideators: past 30-day PTSD (OR = 6.7 [95% CI = 1.1–39.4]), past 30-day IED (OR = 0.2 [95% CI = 0.1–0.5]), and any college education (OR = 0.1 [95% CI = 0.0–0.6]). The 5% of ideators with highest predicted risk in this final model included 20.9% of attempters, a four-fold concentration of risk.
- Study concluded that combat exposure did not differentiate attempters from ideators, many SA risk factors in the Army population are actually risk factors for SI, and prospective Army research examining transition from SI to SA should consider PTSD, IED, and education.

### **63. Suicide Attempts among Activated Soldiers in the U.S. Army Reserve Components (Naifeh, et al 2019)**

- Although the majority of active duty Soldiers are full-time personnel in the Active Component (AC), a substantial minority are in the Reserve Components (RCs). These “citizen-Soldiers” (Army National Guard and Army Reserve) experience many of the same stressors as AC Soldiers as well as stressors that are unique to their intermittent service. Despite the important role of RC Soldiers, the vast majority of military mental health research focuses on AC Soldiers. One important goal of Army STARRS was to address this gap.
- This was a longitudinal, retrospective cohort study that examined predictors of suicide attempts among activated RC Soldiers using individual-level person-month records from Army and Department of Defense administrative data systems to examine socio-demographic, service-related, and mental health predictors of medically documented suicide attempts from 2004 to 2009.
- Analysis used a discrete-time survival framework and included data from all 1,103 activated RC suicide attempters and an equal-probability sample of 69,867 control person-months.
- Study found that enlisted Soldiers comprised 84.3% of activated RC Soldiers and accounted for 95.7% of all activated RC suicide attempts (overall rate = 108/100,000 person-years, more than four times the rate among officers).



- Multivariable predictors of enlisted RC suicide attempts included being female, entering Army service at age  $\geq 25$ , current age  $< 30$ , non-Hispanic white,  $<$ high school education, currently married, having 1–2 years of service, being previously deployed (vs. currently deployed), and history of mental health diagnosis (particularly when documented in the previous month). Predictors among RC officers (overall rate = 26/100,000 person-years) included being female and receiving a mental health diagnosis in the previous month.
- Discrete-time hazard models showed suicide attempt risk among enlisted Soldiers was inversely associated with time in service.
- Study concluded that risk factors for suicide attempt in the RCs were similar to those previously observed in the AC, highlighting the importance of research and prevention focused on RC enlisted Soldiers in the early phases of Army service and those with a recent mental health diagnosis.

#### **64. Prospective Associations of Perceived Unit Cohesion with Post-deployment Mental Health Outcomes (Anderson, et al 2019)**

- Prior investigations have found negative associations between military unit cohesion and posttraumatic stress disorder (PTSD); however, most relied on cross-sectional data and few examined relationships of unit cohesion to other mental disorders. This study evaluated prospective associations of perceived unit cohesion with a range of mental health outcomes following combat deployment.
- Soldiers were surveyed approximately 1–2 months before deployment to Afghanistan (T0); and 1 month (T1), 3 months (T2), and 9 months (T3) after return from deployment. Logistic regression was performed to estimate associations of perceived unit cohesion at T0 with risk of PTSD, major depressive episode (MDE), generalized anxiety disorder (GAD), alcohol or substance use disorder (AUD/SUD), and suicidal ideation at T2 or T3 among 4,645 Soldiers who completed all study assessments. Models were adjusted for socio-demographic and Army service characteristics, pre-deployment history of the index outcome, and deployment stress exposure.
- Higher perceived unit cohesion at T0 was associated with lower risk of PTSD, MDE, GAD, AUD/SUD, and suicidal ideation at T2 or T3 (AORs = 0.72 to 0.85 per standard score increase in unit cohesion; P-values  $< 0.05$ ). Models of incidence of mental disorders and suicidal ideation among Soldiers without these problems pre-deployment yielded similar results, except that perceived unit cohesion was not associated with incident AUD/SUD.

- Soldiers who reported strong unit cohesion before deployment had lower risk of post-deployment mental disorders and suicidal ideation.
- Awareness of associations of perceived unit cohesion with post-deployment mental health may facilitate targeting of prevention programs.

#### **65. Nicotine Dependence and Pre-Enlistment Suicidal Behavior Among U.S. Army Soldiers (Campbell-Sills, et al 2019)**

- This study investigated associations of nicotine dependence with suicidal behaviors among incoming Soldiers. Lifetime DSM-IV nicotine dependence, mental disorders, suicidal behaviors, and their ages of onset were retrospectively assessed in Soldiers entering the Army in 2011–2012.
- Discrete-time survival analysis of person-year data from 30,436 Soldiers was performed to evaluate associations of nicotine dependence with subsequent suicidal ideation, plans, and attempts. Among respondents with lifetime ideation (n=4,060), models tested associations of nicotine dependence with progression from ideation to first onset of plan, from plan to first attempt, and, among ideators without plans, from ideation to first unplanned attempt. A hierarchy of models incorporated increasing controls for other risk factors.
- In models controlling for socio-demographic characteristics, nicotine dependence was associated with onset of all suicidal behaviors (AORs, 2.07–4.08, p <0.001) and with each type of progression of suicidal behavior (AORs, 1.48–2.44, p <0.005). After adjusting for childhood adversities and mental disorders, nicotine dependence remained associated with onset of ideation (AOR=1.27, 95%CI=1.10, 1.46, p=0.001) and attempt (AOR=1.83, 95% CI=1.41, 2.37, p <0.001); and with progression from ideation to unplanned attempt (AOR=2.03, 95% CI=1.17, 1.74, p <0.001).
- Nicotine dependence exhibited associations with onset of suicidal ideation and suicide attempt (and with progression from ideation to unplanned attempt) that were independent of other measured risk factors.
- Awareness of associations of nicotine dependence with suicidal behaviors may inform risk assessment, facilitate targeting of prevention efforts, and provide further impetus for reducing nicotine dependence.

## 66. Assessment of a Risk Index for Suicide Attempts among U.S. Army Soldiers with Suicide Ideation (Zuromski, et al 2019)

- The Department of Veterans Affairs recently began requiring annual suicide ideation (SI) screening of all patients and additional structured questions for patients reporting SI. Related changes are under consideration at the Department of Defense. These changes will presumably lead to higher SI detection, which will require hiring additional clinical staff and/or developing a clinical decision support system to focus in-depth suicide risk assessments on patients considered high risk.
- This study was designed as a proof-of-concept for whether a brief structured question battery from a survey of Soldiers can help target in-depth suicide risk assessments by identifying Soldiers with self-reported lifetime SI who are at highest risk of subsequent administratively recorded nonfatal suicide attempts (SAs).
- This was a cohort study with prospective observational design involving data collection from May 2011 to February 2013, and participant follow-up through December 2014.
- Analyses included a logistic regression model to assess risk for subsequent administratively recorded nonfatal SAs among a total of 3,649 Soldiers who reported lifetime SI in surveys and were followed-up for 18-45 months from baseline to assess administratively reported nonfatal SAs between survey response and December 2014.
- The 3,649 survey respondents were 80.5% male and had a median (interquartile range) age of 29 (25-36) years (range, 18-55 years); 69.4% were white non-Hispanic, 14.6% were black, 9.0% were Hispanic, 7.0% were another racial/ethnic group.
- Sixty-five respondents had administratively recorded nonfatal SAs between survey response and December 2014. One additional respondent died by suicide without making a nonfatal SA but was excluded from analysis based on previous evidence that predictors are different for suicide death and nonfatal SAs.
- Significant risk factors were SI recency (odds ratio [OR], 7.2; 95% CI, 2.9-18.0) and persistence (OR, 2.6; 95% CI, 1.0-6.8), positive screens for mental disorders (OR, 26.2; 95% CI, 6.1-112.0), and Army career characteristics (OR for junior enlisted rank, 30.0; 95% CI, 3.3-272.5 and OR for senior enlisted rank, 6.7; 95% CI, 0.8-54.9). Cross-validated area under the curve was 0.78. The 10% of respondents with highest estimated risk accounted for 39.2% of subsequent SAs.

- Results suggest the feasibility of developing a clinically useful risk index for SA among Soldiers with SI using a small number of self-report questions. If implemented, a continuous quality improvement approach should be taken to refine the structured question series.

#### **67. Prospective Study of Polygenic Risk, Protective Factors, and Incident Depression following Combat Deployment in US Army Soldiers (Choi, et al 2019)**

- This study examined whether trait resilience and/or unit cohesion could protect against the onset of MDD following combat deployment, even in Soldiers at high polygenic risk.
- Study analyzed data from 3,079 Soldiers of European ancestry assessed before and after their deployment to Afghanistan. Incident MDD was defined as no MDD episode at pre-deployment, followed by a MDD episode following deployment.
- Polygenic risk scores were constructed from a large-scale genome-wide association study of major depression. Study first examined the main effects of the MDD PRS and each protective factor on incident MDD. Then study tested the effects of each protective factor on incident MDD across strata of polygenic risk.
- Study found that polygenic risk showed a dose–response relationship to depression, such that Soldiers at high polygenic risk had greatest odds for incident MDD.
- Both unit cohesion and trait resilience were prospectively associated with reduced risk for incident MDD. The protective effect of unit cohesion persisted even in Soldiers at highest polygenic risk.
- Study concluded that polygenic risk was associated with new-onset MDD in deployed Soldiers. Unit cohesion (an index of perceived support and morale) was protective against incident MDD even among those at highest genetic risk, and may represent a potent target for promoting resilience in vulnerable Soldiers.
- Findings illustrate the value of combining genomic and environmental data in a prospective design to identify robust protective factors for mental health.

**68. Utilization of and Barriers to Treatment among Suicide Decedents: Results from the Army Study to Assess Risk and Resilience among Servicemembers (Army STARRS) (Zuromski, et al 2019)**

- This was a psychological autopsy study that examined suicide decedents' use of mental health treatment and perceived barriers to initiating and maintaining treatment. This study compared suicide decedents (n=135) to Soldiers in two control conditions: those propensity-score-matched on known socio-demographic and Army history variables (n=137) and those with a history of suicidal thoughts in the past 12 months (n=118). Informants were next-of-kin and Army supervisors.
- Study results revealed that suicide decedents were significantly more likely to be referred to services and to use more intensive treatments (e.g., medication, overnight stay in hospital) than propensity-matched controls. Decedents were also more likely to perceive significant barriers to treatment-seeking.
- All differences observed in this study were between propensity-matched controls and decedents, with no observed differences between suicide ideators and decedents.
- The study concluded that many suicide decedents used some form of mental health care at some point in their lives, but they also were more likely than propensity-matched controls to perceive barriers that may have prevented service use.
- The lack of differences between suicide ideators and decedents suggests that more information is needed, beyond knowledge of treatment utilization or perceived barriers, to identify and intervene with those at highest risk for suicide.
- These findings underscore the importance of reducing attitudinal barriers that may deter suicidal Soldiers from seeking treatment, and also improving risk detection among those who are attending treatment.

**69. Genome-wide Analyses of Psychological Resilience in U.S. Army Soldiers (Stein, et al 2019)**

- There is a growing body of preclinical and translational research illuminating a biological basis for resilience to stress, but little is known about the genetic basis of psychological resilience in humans.
- For this study, genome-wide association studies (GWASs) were conducted of self-assessed (by questionnaire) and outcome-based (incident mental disorders from pre-deployment to post-deployment) resilience among European (EUR) ancestry Soldiers.

- Self-assessed resilience (n=11,492) was found to have significant common-variant heritability and to be significantly negatively genetically correlated with neuroticism.
- GWAS results from the EUR Soldiers revealed a genome-wide significant locus on an intergenic region on Chr 4 upstream from *doublecortin-like kinase 2* (DCLK2) (four single nucleotide polymorphisms (SNPs) in LD; topSNP: rs4260523 is an eQTL in frontal cortex), a member of the doublecortin family of kinases that promote survival and regeneration of injured neurons. A second gene, *kelch-like family member 36* (KLHL36) was detected at gene-wise genome-wide significance. A polygenic risk score derived from the self-assessed resilience GWAS was not significantly associated with outcome-based resilience.
- In very preliminary results, genome-wide significant association with outcome-based resilience was found for one locus (top SNP: rs12580015) on Chr 12 downstream from solute carrier family 15 member 5 (SLC15A5) in subjects (n=581) exposed to the highest level of deployment stress.
- Further study of genetic determinants of resilience has the potential to illuminate the molecular bases of stress-related psychopathology and point to new avenues for therapeutic intervention.

#### **70. Association of Firearm Ownership, Use, Accessibility, and Storage Practices with Suicide Risk among U.S. Army Soldiers (Dempsey, et al 2019)**

- Since 2004, the suicide rate among Army Soldiers has exceeded the rate of death from combat injury. It is critical to establish factors that increase risk of acting on suicidal thoughts to guide early intervention and suicide prevention.
- This study included 135 cases of Army Soldiers who died by suicide while on active duty from Aug 1, 2011 to Nov 1, 2013. Cases were compared with propensity-matched controls and control Soldiers with past year suicidal ideation. Next-of-kin (NOK) and Army supervisors of case and control Soldiers were interviewed. Firearm ownership, storage, and accessibility were assessed using items from the World Health Organization Composite International Diagnostic Interview screening scales along with items created for Army STARRS.
- For the 135 cases, the NOK reported greater accessibility to firearms compared with propensity-matched controls. Specifically, when compared with propensity-matched controls, suicide decedents were:
  - 2 times as likely to own 1 or more handguns
  - 4 times as likely to store a loaded gun at home

- 3 times as likely to publicly carry a gun when not required for military duty
  - The combination of these 3 items was associated with 3-fold increase in the odds of suicide death
  - Storing a loaded gun with ammunition at home or publicly carrying a gun when not on duty was associated with 4-fold increase in odds of suicide death
  - In addition to gun ownership, ease and immediacy of firearm access were associated with an increased suicide risk
- The study concluded that discussion with family members and supervisors about limiting firearm accessibility should be evaluated for potential intervention.

### **71. Associations of Lifetime Traumatic Brain Injury Characteristics With Prospective Suicide Attempt Among Deployed U.S. Army Soldiers (Campbell-Sills, et al 2019)**

- This study estimated associations of lifetime traumatic brain injury (TBI) characteristics with prospective suicide attempt among U.S. Army Soldiers. The data were from the Army STARRS Pre/Post Deployment Study that surveyed 3 Brigade Combat Teams that were deployed to Afghanistan in 2012.
- Lifetime TBI and past-month post-concussive/post-TBI symptoms were evaluated at pre-deployment baseline. Recency and number of TBIs were quantified, and TBI severity was classified on the basis of reports of alteration/loss of consciousness and memory lapse. Suicide attempt data came from administrative records and surveys administered after return from deployment.
- Logistic regression models estimated associations of TBI characteristics with prospective suicide attempt among baseline respondents who were deployed (n=7,677), adjusting for other risk factors including lifetime mental disorder. One hundred three Soldiers made a suicide attempt over a median follow-up period of 30 months.
- In the final model estimating joint associations of TBI severity/recency and past-month post-concussive/post-TBI symptoms, only post-concussive/post-TBI symptoms were associated with a higher risk of suicide attempt.
- The study concluded that among the lifetime TBI characteristics evaluated at pre-deployment baseline, only past-month post-concussive/post-TBI symptoms were prospectively associated with an increased risk of suicide attempt following deployment. Detection of post-concussive/post-TBI symptoms could facilitate targeting of Army suicide prevention programs.

## **72. The Association of Lifetime and Deployment-Acquired Traumatic Brain Injury With Postdeployment Binge and Heavy Drinking (Adams, et al 2019)**

- This was a prospective, longitudinal study to investigate associations of lifetime traumatic brain injury (LT-TBI) prior to an index deployment, and/or deployment-acquired TBI (DA-TBI), with post-deployment binge and heavy drinking.
- The study included 4,645 Soldiers from 3 Brigade Combat Teams deployed to Afghanistan in 2012 who participated in the Pre/Post Deployment Study and completed all 4 study assessments: T0 (1-2 months pre-deployment), T1 (upon return to the U.S.), T2 (3 months post-deployment), and T3 (9 months post-deployment).
- The measures included self-reported past month binge drinking (5+ alcoholic beverages on the same day) and past month heavy drinking (binge drinking at least weekly) at T2 and T3. The study controlled for baseline binge drinking.
- In total, 34.3% screened positive for LT-TBI, and 19.2% screened positive for DA-TBI. At T2 only, LT-TBI, but not DA-TBI, was associated with increased odds of binge drinking (adjusted odds ratio [AOR] = 1.39, 95% confidence interval [CI]: 1.20-1.60,  $P < .001$ ) and heavy drinking (AOR = 1.28, 95% CI: 1.09-1.49,  $P = .007$ ). Among the subgroup with LT-TBI, also having DA-TBI was associated with increased risk of heavy drinking at T3 (AOR = 1.42, 95% CI: 1.03-1.95,  $P = .047$ ).
- The study concluded that routine screening for LT-TBI may help target efforts to prevent alcohol misuse among military members.

## **73. Developing an Optimal Short-Form of the PTSD Checklist for DSM-5 (PCL-5) (Zuromski, et al 2019)**

- Although several short-forms of the posttraumatic stress disorder (PTSD) checklist (PCL) exist, all were developed using heuristic methods. This study worked with Army STARRS datasets to create an optimal short-form PCL for DSM-5 (PCL-5) using both machine learning and conventional scale development methods.
- A training dataset ( $n=8,917$ ) was used to fit short-form scales with 1 to 8 items using different statistical methods (exploratory factor analysis, stepwise logistic regression, and a new machine learning method to find an optimal integer-scored short-form scale) to predict dichotomous PTSD diagnoses that were determined using the full PCL-5.



- A smaller subset of best short-form scales was then evaluated in an independent validation sample (n=11,728) to select one optimal short-form scale based on multiple operating characteristics (area under curve [AUC], calibration, sensitivity, specificity, net benefit).
- Inspection of AUCs in the training sample and replication in the validation sample led to a focus on 4-item integer-scored short-form scales selected with stepwise regression. Brier scores in the validation sample showed that a number of these scales had comparable calibration (0.015–0.032) and AUC (0.984–0.994), but that one had consistently highest net benefit across a plausible range of decision thresholds.
- The study concluded that the recommended 4-item integer-scored short-form PCL-5 generated diagnoses that closely parallel those of the full PCL-5, making it well-suited for screening.

#### **74. Postconcussive, Posttraumatic Stress and Depressive Symptoms in Recently Deployed U.S. Army Soldiers with Traumatic Brain Injury (Aggarwal, et al 2019).**

- Prior studies raise questions about whether persistent post-concussive symptoms (PCS) are differentiable from mental health sequelae of traumatic brain injury (TBI). Using data from the Army STARRS Pre/Post Deployment Study that surveyed 3 Brigade Combat Teams that were deployed to Afghanistan in 2012, this study evaluated the structure of post-concussive, posttraumatic stress, and depressive symptoms following TBI, to investigate whether PCS represented a distinct symptom domain.
- Data from 1,229 participants who sustained probable TBI during deployment completed ratings of past-30-day post-concussive, posttraumatic stress, and depressive symptoms three months after return from deployment. Exploratory factor analysis (EFA; n=300) and confirmatory factor analysis (CFA; n=929) of symptom ratings were performed in independent subsamples.
- EFA suggested a model with three correlated factors resembling PCS, posttraumatic stress, and depression. CFA confirmed adequate fit of the 3-factor model (CFI=.964, RMSEA=.073 [.070-.075]), contingent upon allowing theoretically defensible cross-loadings.
- Bifactor CFA indicated that variance in all symptoms was explained by a general factor but also provided evidence of domain factors defined by: (1) re-experiencing/hyperarousal, (2) cognitive/somatic symptoms, and (3) depressed mood/anhedonia.

- Soldiers with more severe TBI had higher cognitive/somatic scores, while Soldiers with more deployment stress had higher general and re-experiencing/hyperarousal scores. The variance in PCS was attributable to both a specific cognitive/somatic symptom factor and a general factor that also explained variance in posttraumatic stress and depression.
- Measurement of specific domains representing cognitive/somatic symptoms, re-experiencing/hyperarousal, and depressed mood/anhedonia may help clarify the relative severity of PCS, posttraumatic stress, and depression among individuals with recent TBI.

#### **75. Early First Deployment and Risk of Suicide Attempt Among First-term Enlisted Soldiers in the U.S. Army (Naifeh, et al 2019)**

- The study examined early first deployment and subsequent suicide attempt among U.S. Army Soldiers using 2004–2009 administrative data and person-month records of first term, Regular Army, enlisted Soldiers with one deployment (89.2% male). The study identified 1,704 Soldiers with a documented suicide attempt during or after first deployment and an equal-probability control sample (n = 25,861 person-months).
- Logistic regression analyses indicated Soldiers deployed within the first 12 months of service were more likely than later deployers to attempt suicide (OR = 1.7 [95% CI = 1.5–1.8]). Adjusting for sociodemographic characteristics, service-related characteristics, and previous mental health diagnosis slightly attenuated this association (OR = 1.6 [95% CI = 1.5–1.8]). Results were not modified by gender, deployment status, military occupation, or mental health diagnosis.
- The population-attributable risk proportion for deploying within the first 12 months of service was 17.8%. Linear spline models indicated similar risk patterns over time for early and later deployers, peaking at month 9 during deployment and month 5 post-deployment; however, monthly suicide attempt rates were consistently higher for early deployers.
- The study concluded that enlisted Soldiers deployed within the first 12 months of service had elevated risk of suicide attempt during and after first deployment. Improved understanding of why early deployment increases risk can inform the development of policies and intervention programs.

## **76. Risk Factors and Timing of Suicide Attempts among US Army Reserve Component Soldiers during Deployment to the Afghanistan and Iraq Wars (Stokes, et al 2019)**

- During the wars in Afghanistan and Iraq, suicidal behaviors increased among U.S. Army Soldiers. Although Reserve Component (RC) Soldiers (National Guard and Army Reserve) comprise approximately one third of those deployed in support of the wars, few studies have examined suicidal behaviors among these “citizen-soldiers.” The objective of the study was to examine suicide attempt risk factors and timing among RC enlisted Soldiers.
- This longitudinal, retrospective cohort study used individual-level person-month records from Army and Department of Defense administrative data systems to examine socio-demographic, service-related, and mental health predictors of medically documented suicide attempts among enlisted RC Soldiers during deployment from 2004–2009. Data were analyzed using discrete-time survival models. A total of 230 enlisted RC Soldiers attempted suicide.
- Overall, the in-theater suicide attempt rate among RC Soldiers was 81/100,000 person-years. Risk was highest in the fifth month of deployment (13.8 per 100,000 person-months). Suicide attempts were more likely among Soldiers who were women (adjusted odds ratio, aOR = 2.5 [95% CI: 1.8–3.5]), less than high school educated (aOR = 1.8 [95% CI: 1.3–2.5]), in their first 2 years of service (aOR = 2.0 [95% CI: 1.2–3.4]), were currently married (aOR = 2.0 [95% CI: 1.5–2.7]), and had received a mental health diagnosis in the previous month (aOR = 24.7 [95% CI: 17.4–35.0]).
- The study concluded that being female, early in service and currently married are associated with increased odds of suicide attempt in RC soldiers. Risk of suicide attempt was greatest at mid deployment. These predictors and the timing of suicide attempt for RC Soldiers in-theater are largely consistent with those of deployed Active Component (Regular) Soldiers. Results also reinforce and replicate the findings among Active Component Soldiers related to the importance of a recent mental health diagnosis and the mid-deployment as a period of enhanced risk.

## **77. Economic Evaluation of Brief Cognitive Behavioral Therapy vs Treatment as Usual for Suicidal US Army Soldiers (Bernecker, et al 2019)**

- Brief cognitive behavioral therapy (BCBT) is a clinically effective intervention for reducing risk of suicide attempts among suicidal Army Soldiers. Because specialized treatments can be resource intensive, more information is needed on costs and benefits of BCBT compared with existing treatments. This study was designed to evaluate the cost-effectiveness of BCBT compared with treatment as usual for suicidal Army Soldiers.

- This study used a decision analytic model to compare effects and costs of BCBT vs treatment as usual. Input data were drawn from epidemiologic data sets and a clinical trial of suicidal Soldiers. The study compared treatment as usual alone versus treatment as usual plus 12 individual BCBT sessions. Treatment as usual could include a range of pharmacologic and psychological treatment options.
- BCBT was expected to avert about 23-25 more suicide attempts and 1-3 more suicide deaths per 100 patients treated than treatment as usual. Sensitivity analyses showed BCBT to be cost saving in most scenarios. Using the federal discount rate, the DoD was estimated to save \$15,000-\$16,630 per patient with BCBT vs treatment as usual. In a worst-case scenario (i.e., assuming the weakest plausible BCBT effect sizes), BCBT cost an additional \$1,910 to \$2,250 per patient compared with treatment as usual.
- Results suggest BCBT may be a cost-saving intervention for suicidal active-duty Soldiers. The costs of ensuring treatment fidelity would also need to be considered when assessing the implications of disseminating BCBT across the entire DoD.

#### **78. Pre-deployment predictors of suicide attempt during and after combat deployment (Zurmoski, et al 2019)**

- Deployment-related experiences might be risk factors for Soldier suicides in which case identification of vulnerable Soldiers before deployment could inform preventive efforts. This study investigated this possibility by using pre-deployment survey and administrative data in a sample of US Army Soldiers to develop a risk model for suicide attempt (SA) during and shortly after deployment.
- Soldiers in the Pre-Post Deployment Survey (PPDS) completed a baseline survey shortly before deploying to Afghanistan in 2011–2012. Survey measures were used to predict SAs, defined using administrative and subsequent survey data, through 30 months after deployment. Models were built using penalized regression and ensemble machine learning methods.
- Significant pre-deployment risk factors were history of traumatic brain injury, 9+ mental health treatment visits in the 12 months before deployment, young age, female, previously married, and low relationship quality. Cross-validated AUC of the best penalized and ensemble models were .75–.77.
- 21.3–40.4% of SAs occurred among the 5–10% of Soldiers with highest predicted risk and positive predictive value (PPV) among these high-risk Soldiers was 4.4–5.7%.
- Study concluded that SA can be predicted significantly from pre-deployment data, but intervention planning needs to take PPV into consideration.

### **79. Genome-wide association study of shared liability to anxiety disorders (Hettema, et al 2019)**

- Anxiety disorders (ANX), namely generalized anxiety, panic disorder, and phobias, are common, etiologically complex syndromes that show increasing prevalence and comorbidity throughout adolescence and beyond. Few genome-wide association studies (GWAS) examining ANX risk have been published and almost exclusively in individuals of European ancestry.
- In this study, participants were phenotyped to approximate DSM-based ANX diagnoses and each subject was factor-analyzed to create a single dimensional anxiety score. GWAS were conducted using that score within each of three ancestral groups (EUR, AFR, LAT) and then meta-analyzed across ancestries (N Total = 16,510).
- The study sought to (a) replicate prior ANX GWAS findings in ANGST; (b) determine whether results extended to other ancestry groups; and (c) meta-analyze with ANGST for increased power to identify novel susceptibility loci.
- No reliable genome-wide significant SNP associations were detected. However, SNPs within the CAMKMT gene located in region 2p21 associated with shared ANX risk in ANGST were replicated in EUR Soldiers but not in other ancestry groups.
- Combining EUR STARRS and ANGST (N = 28,950) yielded a more robust 2p21 association signal ( $p = 9.08 \times 10^{-11}$ ). Gene-based analyses supported three genes within 2p21 and LBX1 on chromosome 10. More powerful ANX genetic studies will be required to identify further loci.

### **80. Factors associated with suicide ideation in US Army soldiers during deployment in Afghanistan (Ursano, et al 2020)**

- This study was designed to better understand suicide ideation (SI) during combat deployment to help inform prevention and treatment during and after deployment. The study examined associations of sociodemographic characteristics, lifetime and past-year stressors, and mental disorders with 30-day SI among a representative sample of US Army Soldiers deployed in Afghanistan.

- Soldiers who were deployed to Afghanistan completed self-administered questionnaires and the sample was weighted to represent all 87,032 Soldiers serving in Afghanistan. Prevalence of lifetime, past-year, and 30-day SI and mental disorders was determined and logistic regression analyses was used to examine risk factors associated with SI. The study assessed SI, lifetime and 12-month stressors, and mental disorders using questionnaires. Administrative records identified sociodemographic characteristics and suicide attempts.
- A total of 3,957 Soldiers (3,473 [weighted 87.5%] male; 2,135 [weighted 52.6%] aged 29 years) completed self-administered questionnaires during their deployment in Afghanistan. Lifetime, past-year, and 30-day SI prevalence estimates were 11.7%, 3.0%, and 1.9%, respectively. Among Soldiers with SI, 44.2% had major depressive disorder (MDD) and 19.3% had PTSD in the past 30-day period.
- A series of analyses of the 23 grouped variables potentially associated with SI resulted in a final model of sex; race/ethnicity; lifetime noncombat trauma; past 12-month relationship problems, legal problems, and death or illness of a friend or family member; and MDD. In this final multivariable model, white race/ethnicity, lifetime noncombat trauma, and MDD were associated with SI. Among the 85 Soldiers with past 30-day SI, from survey administration through 12 months after returning from deployment, 6% (5 participants) had a documented suicide attempt vs 0.14% (6 participants) of the 3,872 Soldiers without SI.
- This study suggests that major depressive disorder and noncombat trauma are important factors in identifying SI risk during combat deployment.

#### **81. Self-injurious thoughts and behaviors that differentiate soldiers who attempt suicide from those with recent suicide ideation (Naifeh, et al 2020)**

- Because risk for suicide attempt (SA) versus suicide ideation (SI) is clinically important and difficult to differentiate, this study examined whether a history of self-injurious thoughts and behaviors (SITBs) differentiates Soldiers with a recent SA from non-attempting Soldiers with current or recent SI.
- This study used a unique case-control design and administered the same questionnaire (assessing the history of SITBs and psychosocial variables) to representative Soldiers recently hospitalized for SA (n = 132) and Soldiers from the same Army installations who reported 30-day SI but did not make an attempt (n = 125). Logistic regression analyses examined whether SITBs differentiated attempters and ideators after controlling for previously identified covariates.

- In separate models that weighted for systematic non-response and controlled for gender, education, post-traumatic stress disorder, and intermittent explosive disorder, SA was positively and significantly associated with the history of suicide plan and/or intention to act, difficulty controlling suicidal thoughts during the worst week of ideation, and non-suicidal self-injury (NSSI). Area under the curve was 0.87 in a full model that combined these SITBs and covariates. The top ventile based on predicted risk had a sensitivity of 24.7%, specificity of 99.8%, and positive predictive value of 97.5%.
- The study concluded that history of suicide plan/intention, difficult to control ideation, and NSSI differentiate Soldiers with recent SA from those with current/recent SI independent of sociodemographic characteristics and mental disorders. Longitudinal research is needed to determine whether these factors are prospectively associated with the short-term transition from SI to SA.

**82. Unit cohesion during deployment and post-deployment mental health: is cohesion an individual- or unit-level buffer for combat-exposed soldiers? (Campbell-Sills, et al 2020)**

- Unit cohesion may protect Soldier mental health by mitigating effects of combat exposure, but questions remain about the origins of potential stress-buffering effects.
- This study examined buffering effects associated with two forms of unit cohesion (peer-oriented horizontal cohesion and subordinate-leader vertical cohesion) defined as either individual-level or aggregated unit-level variables.
- Using mixed-effects regression, the study analyzed longitudinal survey data from Soldiers who deployed to Afghanistan in 2012. Models evaluated individual- and unit-level interaction effects of combat exposure and cohesion during deployment on symptoms of post-traumatic stress disorder (PTSD), depression, and suicidal ideation reported at 3 months post-deployment (model n's = 6684 to 6826). Given the small effective sample size (k = 89), the significance of unit-level interactions was evaluated at a 90% confidence level.
- The study found, at the individual-level, buffering effects of horizontal cohesion for PTSD symptoms and depressive symptoms, while a buffering effect of vertical cohesion was observed for PTSD symptoms only.
- At the unit-level, buffering effects of horizontal (but not vertical) cohesion were observed for PTSD symptoms, depressive symptoms, and suicidal ideation.

- The study concluded that policies and interventions that enhance horizontal cohesion may protect combat-exposed units against post-deployment mental health problems. Efforts to support individual Soldiers who report low levels of horizontal or vertical cohesion may also yield mental health benefits.

### **83. A test of the interpersonal theory of suicide in a large, representative, retrospective and prospective study (Chu, et al 2020)**

- The interpersonal theory of suicide hypothesizes that perceived burdensomeness, thwarted belongingness, and hopelessness lead to active suicidal thoughts and individuals with active suicidal thoughts and elevated capability for suicide are most likely to attempt suicide.
- This study retrospectively and prospectively tested this theory in a large sample of 7,677 Soldiers who were followed post-deployment for up to nine months.
- The study found that interaction of perceived burdensomeness and hopelessness (OR = 2.59) was significantly associated with lifetime suicidal thoughts, and the interactions of thwarted belongingness and perceived burdensomeness and of thwarted belongingness and hopelessness were not.
- The study also found that, consistent with the theory, capability for suicide prospectively predicted suicide attempts during and following deployment (OR = 1.22). However, among Soldiers reporting lifetime suicidal thoughts, capability did not predict attempts, only perceived burdensomeness did (OR = 1.36).
- Study results supported some, but not all, theory hypotheses, suggesting that additional constructs may be needed to better identify the psychological factors that lead Soldiers to attempt suicide.

### **84. Association between neurocognitive functioning and suicide attempts in US Army Soldiers (Hoffman, et al 2020)**

- This study sought to discover objective predictors of suicide and non-fatal suicidal behaviors by examining the association between neurocognitive functioning and pre-military history of suicide attempts (SA) and post-enlistment onset of SA.
- The study included 38,507 new Soldiers reporting for Basic Combat Training who completed a comprehensive computerized neurocognitive assessment battery and self-report questionnaires. A subset of Soldiers (n=6,216) completed a follow-up survey, including assessment of lifetime SA, 3–7 years later.



- Six hundred eighty-nine Soldiers indicated lifetime SA at baseline and 210 Soldiers indicated new-onset SA at follow-up. Regression analyses, adjusted for demographic variables, revealed significant bivariate associations between neurocognitive performance on measures of sustained attention, impulsivity, working memory, and emotion recognition and lifetime SA at baseline.
- In a multivariable model including each of these measures as predictors, poorer impulse control and quicker response times on an emotion recognition measure were significantly and independently associated with increased odds of lifetime SA. A second model predicted new-onset SA at follow-up for Soldiers who did not indicate a history of SA at baseline. Poorer impulse control on a measure of sustained attention was predictive of new-onset SA. Effect sizes were small and of unlikely clinical predictive utility.
- The study simultaneously examined multiple neurocognitive domains as predictors of SA in a large, representative sample of new Army Soldiers. The study found that impulsivity most strongly predicted past and future SA over and beyond other implicated cognitive-emotional domains.

#### **85. Sex differences in US Army suicide attempts during the wars in Iraq and Afghanistan (Naifeh, et al 2021)**

- This study examined sex differences in risk for administratively documented suicide attempt (SA) among US Army Soldiers during the Iraq/Afghanistan wars using administrative person-month records of Regular Army enlisted Soldiers from 2004 to 2009. The study identified 9,650 person-months with a first documented SA and an equal-probability control sample (n=153,528 person-months). Person-months were weighted to the population and pooled over time.
- After examining the association of sex with SA in a logistic regression analysis, predictors were examined separately among women and men. The study found that women (an estimated 13.7% of the population) accounted for 25.2% of SAs and were more likely than men to attempt suicide after adjusting for sociodemographic, service-related, and mental health diagnosis (MHDx) variables. Women with increased odds of SA in a given person-month were younger, non-Hispanic White, less educated, in their first term of enlistment, never or previously deployed (vs. currently deployed), and previously received a MHDx.
- Interactions indicated significant but generally small differences between women and men on 6 of the 8 predictors, the most pronounced being time in service, deployment status, and MHDx. Discrete-time survival models were used to examine risk by time in

service and demonstrated that patterns for women and men were similar, and that women's initially higher risk diminished as time in service increased.

- The study concluded that predictors of documented SAs are similar for US Army women and men. Differences associated with time in service, deployment status, and MHDx require additional research. Future research should consider stressors that disproportionately affect women.

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## **PUBLICATIONS FROM COLLABORATION WITH THE PSYCHIATRIC GENOMICS CONSORTIUM:**

The following publications represent an example of the broader impact of STARRS resulting from our collaboration and data sharing. STARRS investigators shared STARRS GWAS and other data with the NIMH Psychiatric Genomics Consortium (PGC) to yield the largest sample ever examined of the GWAS of PTSD. STARRS was the largest contributor of GWAS data to this effort. These publications are based on analyses of pooled data from a consortium of investigators conducting genetic studies on PTSD and other psychiatric disorders.

1. Dunn, E. C., Sofer, T., Gallo, L. C., Gogarten, S. M., Kerr, K. F., Chen, C. Y., Stein, M. B., Ursano, R. J., Guo, X., Jia, Y., Qi, Q., Rotter, J. I., Argos, M., Cai, J., Penedo, F. J., Perreira, K., Wassertheil-Smoller, S., & Smoller, J. W. Genome-wide association study of generalized anxiety symptoms in the Hispanic Community Health Study/Study of Latinos. (2017). *Am J Med Genet B Neuropsychiatr Genet.* Mar; 174(2): 132-143.
  - This study aimed to discover potential loci by conducting a genome-wide analysis of GAD symptoms in a large, population-based sample of Hispanic/Latino adults using data from 12,282 participants, aged 18-74, of the Hispanic Community Health Study/Study of Latinos.
  - Using a shortened Spielberger Trait Anxiety measure, the study analyzed: (1) a GAD symptoms score restricted to the 3 items tapping diagnostic features of GAD as defined by DSM-V; and (2) a total trait anxiety score based on summing responses to all 10 items. Study first calculated heritability due to common variants (h<sup>2</sup>SNP) and then conducted a genome-wide association study (GWAS) of GAD symptoms. Replication was attempted in 3 independent Hispanic cohorts (Multi-Ethnic Study of Atherosclerosis, Women's Health Initiative, Army STARRS).
  - The GAD symptoms score showed evidence of modest heritability while the total trait anxiety score did not. One genotyped SNP (rs78602344) intronic to thrombospondin 2 (THBS2) was nominally associated in the primary analysis adjusting for psychiatric medication use and significantly associated with the GAD symptoms score in the analysis excluding medication users. Meta-analysis of the replication samples did not support this association.
  - The study identified a genome-wide significant locus in this sample, but was unable to replicate this finding. Evidence for heritability was also only detected for GAD symptoms, and not the trait anxiety measure, suggesting differential genetic influences within the domain of trait anxiety.



2. Wolf, E. J., Maniates, H., Nugent, N., Maihofer, A. X., Armstrong, D., Ratanatharathorn, A., Ashley-Koch, A. E., Garrett, M., Kimbrel, N. A., Lori, A., VA Mid-Atlantic Mirecc Workgroup, Aiello, A. E., Baker, D. G., Beckham, J. C., Boks, M. P., Galea, S., Geuze, E., Hauser, M. A., Kessler, R. C., Koenen, K. C., Miller, M. W., Ressler, K. J., Risbrough, V., Rutten, B. P. F., Stein, M. B., Ursano, R. J., Vermetten, E., Vinkers, C. H., Uddin, M., Smith, A. K., Nievergelt, C. M., & Logue, M. W. (2017). Traumatic stress and accelerated DNA methylation age: A meta-analysis. *Psychoneuroendocrinology*, *92*, 123-134. doi: 10.1016/j.psyneuen.2017.12.007.
  - This study involved a meta-analysis of trauma exposure, PTSD diagnosis, and symptom severity in association with accelerated DNA methylation age using data from 9 cohorts contributing to the PGC-PTSD Epigenetics Workgroup (combined N = 2186). The study also examined associations between demographic and cellular variables and accelerated DNA methylation age.
  - The results revealed that childhood trauma exposure, measured with the Childhood Trauma Questionnaire, and lifetime PTSD severity show significant meta-analytic associations with accelerated DNA methylation age. The study also found that sex, CD4T cell proportions, and natural killer cell proportions were significantly associated with accelerated DNA methylation age.
  - Findings suggest that traumatic stress is associated with advanced epigenetic age and raises the possibility that cells integral to immune system maintenance and responsivity play a role in this. The study highlights the need for additional research into the biological mechanisms linking traumatic stress to accelerated DNA methylation age and the importance of furthering our understanding of the neurobiological and health consequences of PTSD.
3. Dunn, E. C., Sofer, T., Wang, M., Soare, T. S., Gallo, L. C., Gogarten, S. M., Kerr, K. F., Chen, C., Stein, M. B., Ursano, R. J., Guo, X., Jia, Y., Yao, J., Rotter, J. I., Argos, M., Cai, J., Ferreira, K., Wassertheil-Smoller, S., & Smoller, J. W. Genome-wide association study (GWAS) of depressive symptoms in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). (2018). *Journal of Psychiatric Research*, *99*, 167-176. doi: 10.1016/j.jpsychires.2017.12.010.
  - This study involved a genome-wide analysis of depression in a large, population-based sample of Hispanics/Latinos. This is the largest GWAS of depression related phenotypes in Hispanic/Latino adults ever conducted.
  - Three phenotypes were examined: a total depression score, a total score modified to account for psychiatric medication use, and a score excluding antidepressant medication users. The study included a GWAS of the three phenotypes and attempted replication in three independent Hispanic/Latino cohorts.

- Sex-stratified analyses were performed, a binary trait indicating probable depression was analyzed, and 3 trans-ethnic analyses were done. The 3 phenotypes exhibited significant heritability in the total sample. No SNPs were genome-wide significant in analyses of the 3 phenotypes or the binary indicator of probable depression. Sex-stratified analyses identified 7 genome-wide significant SNPs (1 in females; 6 in males), although none were supported through replication. Four out of 24 loci identified in prior GWAS were nominally associated. No evidence of overlap in genetic risk factors across ancestry groups was found, although this may have been due to low power.
4. Ratanatharathorn, A., Boks, M. P., Maihofer, A. X., Aiello, A. E., Amstadter, A. B., Ashley-Koch, A. E., Baker, D.G., Beckham, J. C., Bromet, E., Dennis, M., Garrett, M. E., Geuze, E., Guffanti, G., Hauser, M. A., Kilaru, V., Kimbrel, N. A., Koenen, K. C., Kuan, P. F., Logue, M. W., Luft, B. J., Miller, M.W., Mitchell, C., Nugent, N.R., Ressler, K. J., Rutten, B.P.F., Stein, M.B., Vermetten, E., Vinkers, C.H., Youssef, N. A., VA Mid-Atlantic MIRECC Workgroup, PGC PTSD Epigenetics Workgroup, Uddin, M., Nievergelt, C. M., Smith, A.K. Epigenome-wide association of PTSD from heterogeneous cohorts with a common multi-site analysis pipeline. (2017). *Am J Med Genet B Neuropsychiatr Genet.* 174(6), 619-630. doi: 10.1002/ajmg.b.32568.
- Evidence suggests that epigenetic mechanisms such as DNA methylation play a role in stress regulation and in the etiologic basis of stress related disorders such as PTSD. This study describes the purpose and methods of an international consortium developed to study the role of epigenetics in PTSD.
  - Based on the PGC, this study brought together investigators representing 7 cohorts with a collective sample size of N = 1147 that included detailed information on trauma exposure, PTSD symptoms, and genome-wide DNA methylation data. The objective was to increase the analytical sample size by pooling data and combining expertise so that DNA methylation patterns associated with PTSD can be identified. Several quality control and analytical pipelines were evaluated for their control of genomic inflation and technical artifacts with a joint analysis procedure established to derive comparable data over the cohorts for meta-analysis.
  - The study proposed methods to deal with ancestry population stratification and type I error inflation, and discussed advantages and disadvantages of applying robust error estimates.

- The study reported results from an epigenome-wide association study (EWAS) of age, which is a well-characterized phenotype with known epigenetic associations. While EWAS is highly complex and subject to similar challenges as genome-wide association studies (GWAS), the study demonstrated that an epigenetic meta-analysis with a relatively modest sample size can be well-powered to identify epigenetic associations. The pipeline can be used as a framework for consortium efforts for EWAS.
5. Wang, Y., Karstoft, K. I., Nievergelt, C. M., Maihofer, A. X., Stein, M. B., Ursano, R. J., Bybjerg-Grauholm, J., Baekvad-Hansen, M., Hugaard, D. M., Andreassen, O. A., Werge, T., Thompson, W. K., & Andersen, S. B. (2019). Post-traumatic stress following military deployment: Genetic associations and cross-disorder genetic correlations. *J Affect Disord*, 252, 350-357. doi:10.1016/j.jad.2019.04.070
- Post-traumatic stress disorder (PTSD) is a complex psychiatric disorder that occurs with relatively high frequency after deployment to warzones (~10%). While twin studies have estimated the heritability to be up to 40%, indicating a considerable genetic component in the etiology, the biological mechanisms underlying risk and development of PTSD remain unknown.
  - This genome-wide association study (GWAS; N = 2,481) was conducted to identify genome regions that associate with PTSD in a highly homogenous, trauma-exposed sample of Danish soldiers deployed to war and conflict zones. Integrated analyses were performed with gene-expression and chromatin-contact datasets to prioritize genes. Other large GWAS (N>300,000) were leveraged to investigate genetic correlations between PTSD and other psychiatric disorders and traits.
  - Study discovered, but did not replicate, one region, 4q31, close to the IL15 gene, which is genome-wide significantly associated with PTSD. Study demonstrated that gene-set enrichment, polygenic risk score and genetic correlation analyses show consistent and significant genetic correlations between PTSD and depression, insomnia and schizophrenia. The limited sample size, the lack of replication, and the PTSD case definition by questionnaire are limitations to the study.
  - The results suggest that genetic perturbations of inflammatory response may contribute to the risk of PTSD. In addition, shared genetic components contribute to observed correlations between PTSD and depression, insomnia and schizophrenia.

6. Smith, A. K., Ratanatharathorn, A., Maihofer, A. X., Naviaux, R. K., Aiello, A. E., Amstadter, A. B., Ashley-Koch, A. E., Baker, D. G., Beckham, J. C., Boks, M. P., Bromet, E., Dennis, M., Galea, S., Garrett, M. E., Geuze, E., Guffanti, G., Hauser, M. A., Katrinli, S., Kilaru, V., Kessler, R. C., ... Nievergelt, C. M. (2020). Epigenome-wide meta-analysis of PTSD across 10 military and civilian cohorts identifies methylation changes in AHRR. *Nature Communications*, 11(1), 5965. <https://doi.org/10.1038/s41467-020-19615-x>

- Epigenetic differences may help to distinguish between PTSD cases and trauma-exposed controls. This study is the largest DNA methylation meta-analysis of PTSD to date.
- Ten military and civilian cohorts contributed blood-derived DNA methylation data from 1,896 PTSD cases and trauma-exposed controls. Four CpG sites within the arylhydrocarbon receptor repressor (AHRR) were associated with PTSD after adjustment for multiple comparisons, with lower DNA methylation in PTSD cases relative to controls.
- Although AHRR methylation is known to associate with smoking, the AHRR association with PTSD was most pronounced in non-smokers, suggesting the result was independent of smoking status. Evaluation of metabolomics data reveals that AHRR methylation is associated with kynurenine levels, which are lower among subjects with PTSD.
- This study supports epigenetic differences in those with PTSD and suggests a role for decreased kynurenine as a contributor to immune dysregulation in PTSD.

## **STARRS-RELATED PUBLICATIONS:**

The following are STARRS-related publications. These publications include members of the STARRS Research Team as co-authors, except where noted with an asterisk. Some of these publications summarize or review previously published STARRS findings and others present new findings.

1. Gonzalez, O. I., Naifeh, J. A., Mash, H. H. (2018, June). Interpersonal Violence and Suicide Risk Among U.S. Army Soldiers. *ISTSS Stress Points*, 32(3). Retrieved from <http://sherwood-istss.informz.net/admin31/content/template.asp?sid=60943&brandid=4463&uid=1044618441&mi=7664760&mfqid=40875668&ptid=&ps=60943>
2. Naifeh, J. A., Mash, H. B. H., Stein, M. B., Fullerton, C. S., Kessler, R. C., & Ursano, R. J. (2018). The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS): Progress toward understanding suicide among soldiers. *Mol Psychiatry*, 24, 34-48. doi:10.1038/s41380-018-0197-z.
3. Levey, D. F., Polimanti, R., Cheng, Z., Zhou, H., Nunez, Y. Z., Jain, S., He, F., Sun, X., Ursano, R. J., Kessler, R. C., Smoller, J. W., Stein, M. B., Kranzler, H. R., & Gelernter, J. (2019). Genetic associations with suicide attempt severity and genetic overlap with major depression. *Transl Psychiatry*, 9(1), 22. doi:10.1038/s41398-018-0340-2
4. Karlsson Linner, R., Biroli, P., Kong, E., Meddens, S. F. W., Wedow, R., Fontana, M. A., Lebreton, M., Tino, S. P., Abdellaoui, A., Hammerschlad, A. R., Nivard, M. G., Okbay, A., Rietveld, C. A., Timshel, P. N., Trzaskowski, M., Vlaming, R. Zund, C. L., Bao, Y., Buzdugan, L., Caplin, A. H., Chen, C. Y., Eibich, P., Fontanillas, P., Gonzalez, J. R., Joshi, P. K., Karhunen, V., Kleinman, A., Levin, R. Z., Lill, C. M., Meddens, G. A., Muntain, G., Sanchez-Roige, S., Rooij, F. J. V., Taskesen, E., Wu, Y., Zhang, F. I., Auton, A., Boardman, J. D., Clark, D. W., Conlin, A., Dolan, C. C., Fischbacher, U., Groenen, P. J. F., Harris, K. M., Hasler, G., Hofman, A., Ikram, M. A., Jain, S., Karlsson, R., Kessler, R. C., Kooyman, M., MacKillop, J., Mannikko, M., Morcillo-Suarez, C., McQueen, M. B., Schmidt, K. M., Smart, M. C., Sutter, M., Thurik, A. R., Uitterlinden, A. G., White, J., Wit, H., Yang, J., Betram, L., Boomsma, D. I., Esko, T., Fehr, E., Hinds, D. A., Johannesson, M., Kumari, M., Laibson, D., Magnusson, P. K. E., Myer, M. N., Navarro, A., Palmer, A. A., Pers, T. H., Posthuma, D., Schunk, D., Stein, M. B., Svento, R., Tiemeier, H., Timmers, P. R. H. J., Turley, P., Ursano, R. J., Wagner, G. G., Wilson, J. F., Gratten, J., Lee, J. J., Cesarini, D., Benjamin, D. J., Koellinger, P. D., & Beauchamp, J. P. (2019). Genome-wide association analyses of risk tolerance and risky behaviors in over 1 million individuals identify hundreds of loci and shared genetic influences. *Nat Genet*, 51, 245-257. doi:10.1038/s41588-018-0309-3.
5. Kessler, R. C., Bossarte, R. M., Luedtke, A., Zaslavsky, A. M., & Zubizarreta, J. R. (2019). Suicide prediction models: A critical review of recent research with recommendations for the way forward. *Mol Psychiatry*. doi:10.1038/s41380-019-0531-0.

6. \* Curley, J. M., Penix, E. A., Srinivasan, J., Sarmiento, D. M., McFarling, L. H., Newman, J. B., & Wheeler, L. A. (2019). Development of the U.S. Army's Suicide Prevention Leadership Tool: The Behavioral Health Readiness and Suicide Risk Reduction Review (R4). *Mil Med*. doi:10.1093/milmed/usz380
7. \* Duncan, J. M., Reed-Fitzke, K., Ferraro, A. J., Wojciak, A. S., Smith, K. M., Sánchez, J. (2020). Identifying Risk and Resilience Factors Associated With the Likelihood of Seeking Mental Health Care Among U.S. Army Soldiers-in-Training. *Mil Med*, Feb 20, pii: usz483
8. Qiu, H., Carone, M., Sadikova, E., Petukhova, M., Kessler, R. C., Luedtke, A. (2020). Optimal Individualized Decision Rules Using Instrumental Variable Methods. *Journal of the American Statistical Association*, May 12
9. Chu, C., Wilks, C. R., Zuromski, K. L., Bernecker, S. L., King, A., Gutierrez, P. M., Joiner, T. E., Nock, M. K., Ursano, R.J., Kessler, R. C. (2020). Psychological Problems among 12th-Grade Students Predicting Military Enlistment: Findings from the Monitoring the Future Survey. *Psychiatry*, 83:244–258