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Study to Assess Risk and Resilience in Servicemembers - Longitudinal Study

Study to Assess Risk and Resilience in Servicemembers

Army STARRS to STARRS-LS

Co-Principal Investigators:

MD (USUHS)

MD, MPH (UCSD)

and

Site PI's: PhD (Harvard) & PhD (UM) on behalf of the Army STARRS & STARRS-LS Research Team

May 13, 2016

Award Number: USUHS Grant HU-0001-15-2-0004

Period of Performance: 2015 to 2020 (5 years)

Award Amount: $30.1 million

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Transition: Army STARRS to STARRS-LS

STARRS-LS: 5-year follow-up project to continue using Army STARRS data and platform to discover additional findings for Army and DoD

- Funded by DoD: OASD (HA)
- Additional emphasis on subgroups of interest to DoD
- Army Analytics Group & Army Public Health Center (Provisional) will continue support
- Building bridges with other departments/studies (VA, MSRC, others)
- Work to be done:
  - Enhance 2004-2009 HADS to include 2010-2015 data & extend HADS analyses
  - Continue analyses of other Army STARRS datasets
  - Longitudinal follow-up & data collection (>72K AAS, NSS, PPDS participants)
  - Maintain Army STARRS data in enclave
  - Maintain Army STARRS biospecimens in biorepository (>147,000 vials)

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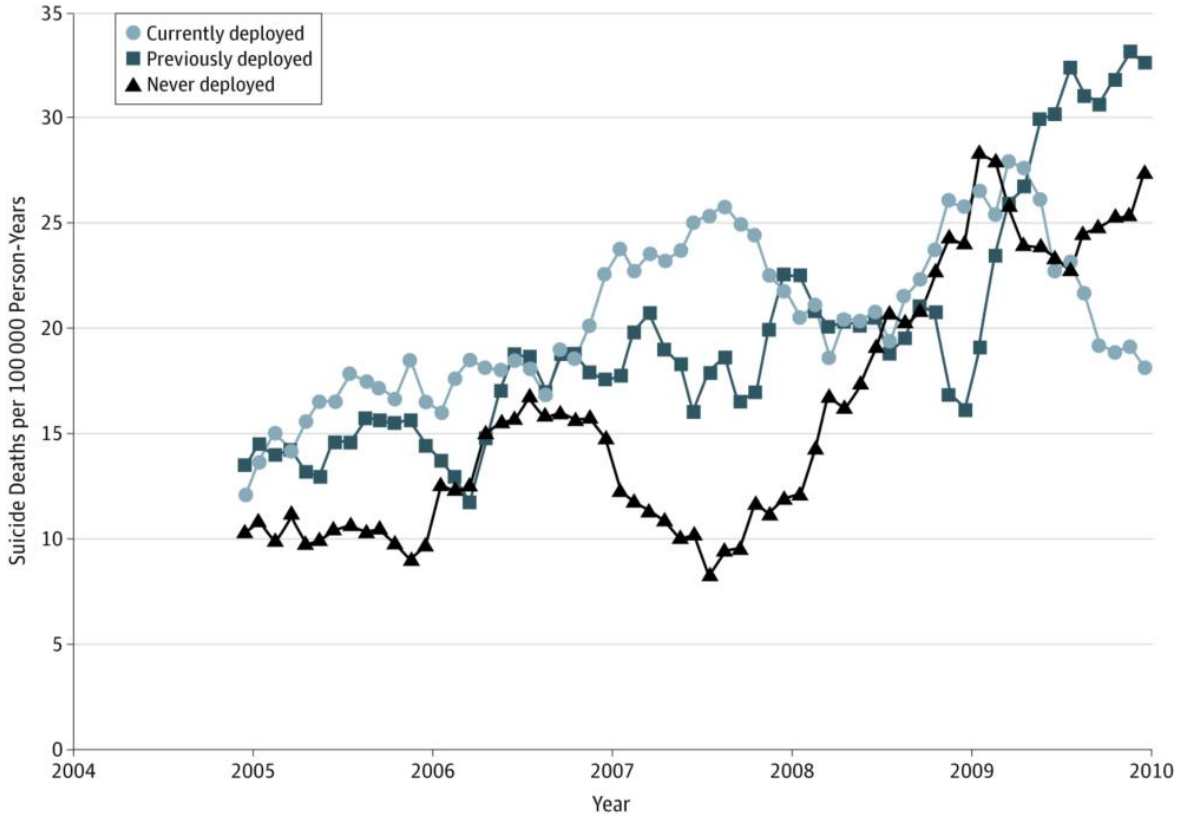
US Army Suicide Deaths: Rolling 12 month average by Deployment Status



Predictors of Suicide and Accident Death: JAMA Psychiatry. 2014;71(5):493-503. doi:10.1001/jamapsychiatry.2013.4417

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Approach to Producing Actionable Findings

Concentration of Risk

- Who (e.g., MOS, rank, demographics, mental disorders)
- When (e.g., time in service, deployment status, time pre/post deployment)
- Where (e.g., installations, training, combat zones, transitioning)

Risk variables

- Identify risk sub-groups (who, when, where) so Army can consider programs to target for intervention

Neurocognitive

- Use neurocognitive tests to identify those at risk and possible neurocognitive functioning associations with suicidal behavior

Biomarkers

- Identify biomarkers for those at risk and determine possible neurobiologic mechanisms

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8 Army STARRS Studies Completed

1	Historical Admin. Data Study (HADS)	• >1.6 million active duty Soldiers from 2004 to 2009 • Integrated >1.1 billion de-identified records (from 38 Army/DoD sources)
2	New Soldier Study (NSS)	• 55,814 Soldiers participated in survey (at 3 sites) • 34,986 Soldiers provided a blood sample
3a	All Army Study (AAS)	• 32,272 Soldiers participated in survey (at >50 sites CONUS & OCONUS)
3b	AAS In-Theater (in Kuwait)	• "Outbound" & "inbound" Soldiers during R&R processing in Kuwait • 8,938 Soldiers participated in survey
4	Pre/Post Deployment Study (PPDS)	Longitudinal study with 4 waves of data collection (4 time-points) at 3 sites • 1 mo pre-deployment (T0): 9,488 Soldiers participated; 8,090 gave blood • 1 mo post-deployment (T1): 10,116 Soldiers participated; 8,822 gave blood • 3 mos post-deployment (T2): 9,193 Soldiers participated • 9 mos post-deployment (T3): 6,977 Soldiers participated
5	SHOS-A (case-control)	• Interviewed in-patient suicide attempters (cases) at 5 sites & controls • 561 Soldiers enrolled (186 cases, 375 controls) & 296 blood samples
6	SHOS-B (case-control)	• Interviewed Army supervisors & next-of-kin of suicide cases & controls • 603 interviews completed for 150 cases & 276 controls
7	Criminal Investigation Division Study (CID)	• Systematic review & abstraction of Army death reports from 2005 to 2009 • Reviewed, abstracted, thematically-coded 1,311 CID case files
8	Clinical Reappraisal Study (CRS)	• To calibrate clinical survey measures used in AAS and NSS • Conducted clinical interviews with 460 Soldiers

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Data Collection Summary: Soldiers, Surveys, Biosamples

For Studies with Data Collection from Soldiers (HADS, CID, CRS not included)

Studies		Number of Soldiers Who Participated*	Number of Surveys Collected	Number of Biosamples		
				Soldiers Who Provided Blood	Blood Tubes Collected	Vials in Frozen Storage
Cohort Studies						
NSS (2 survey sessions/Soldier)		55,814	111,628	34,986	34,986	37,477
AAS (including Guard & Reserve)		32,272	32,272	-	-	-
AAS in-theater (Kuwait)		8,938	8,938	-	-	-
PPDS	Pre-deployment Time 0	10,116	9,488	8,090	23,791	53,966
	Post-deployment Time 1		10,116	8,822	17,542	55,136
	Post-deployment Time 2		9,193	-	-	-
	Post-deployment Time 3		6,977	-	-	-
Total Participants in Cohort Studies		107,140				
Case-Control Studies						
SHOS-A		186	756	296	592	873
SHOS-B		150	603	-	-	-
Total for All Studies		107,476	189,971	52,194	76,911	147,452

*Participation is defined as starting a survey. For SHOS-A and SHOS-B, number of participants includes only cases (because controls are already counted in AAS) but number of surveys includes cases and controls. For SHOS-B cases (deceased) and controls (living), surveys were administered to Army supervisors and/or next-of-kin.

NOTE: NSS blood collection started 6 months after data collection began and about 80% of Soldiers who were asked gave blood.

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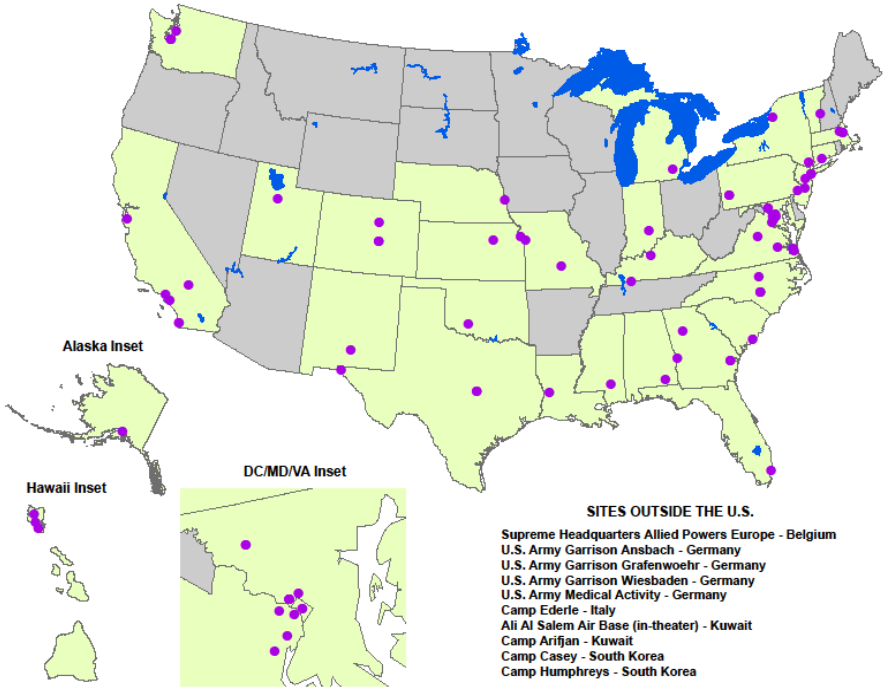
Army STARRS Sites and Biomarker Assays Performed

Army STARRS Sites: Principal Investigators, Other Investigators, Scientific Advisory Board Members, Data Collection & Processing, and Laboratories.



Biomarker Assays	# Performed
Genotyping arrays for GWAS	19,070
Other genetic assays: 5HTTLPR	1,462
RNA sequencing	420
DNA Methylation	480
Telomere length	992
Ultrasensitive IL-6	240
Metabolomics	480
TBI Plasma Tau	240
Micro RNA sequencing	80
Proteomics	288
Inflammatory marker panel	719
TOTAL ASSAYS	**24,471**

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Dissemination of Findings

Publications/Papers

- 29 papers published
- 6 papers accepted for publication (in press)
- 9 papers submitted (waiting for decision)
- 32 papers under development (in process)

Briefings to Senior Army Leadership

- Research team conducted 13 in-person briefings of findings

Presentations

- Research team made more than 100 presentations

Website

- Publications, press releases, media reports posted on website

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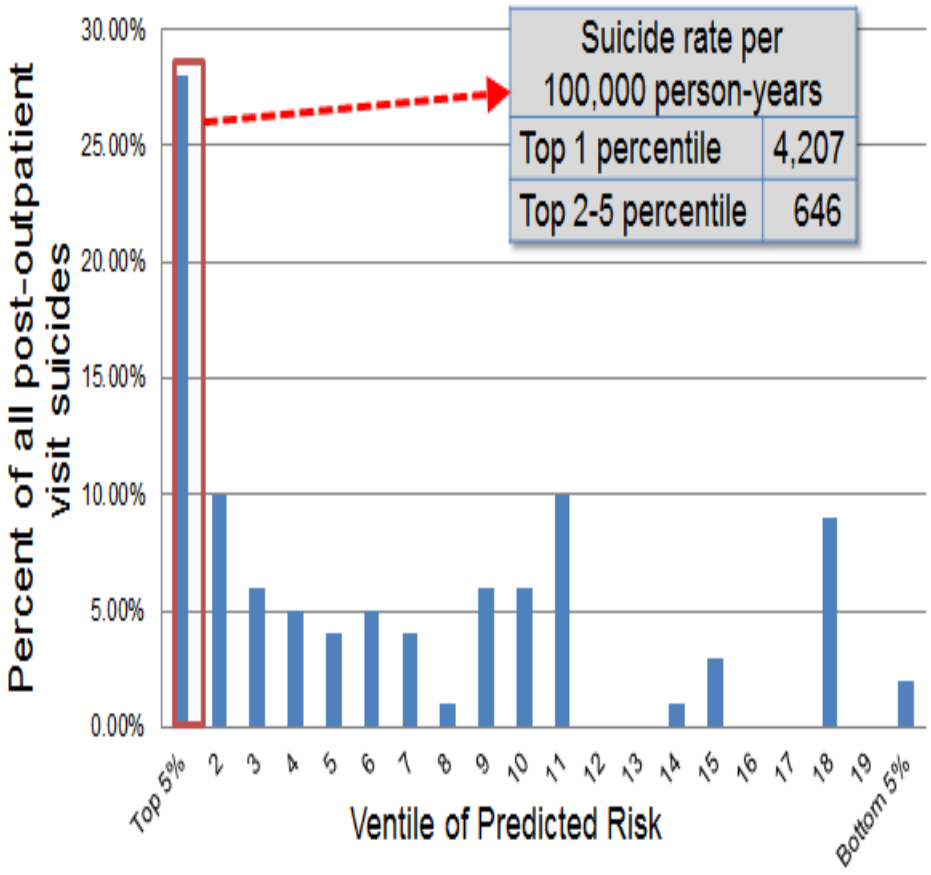
Predicting Suicides after Psychiatric Hospitalization (HADS 2004-2009)

- Sixty-eight soldiers died by suicide within 12 months of hospital discharge (12.0% of all U.S. Army suicides), 263.9 suicides per 100,000 person-years
- The strongest predictors included sociodemographics: male ,late age of enlistment, criminal offenses (verbal violence and weapons possession), prior suicidality, aspects of prior psychiatri 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 unintentional injury deaths, suicide attempts, and subsequent hospitalizations). Kessler, et al. JAMA Psychiatry, 2015



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Predicting Non-familial Major Physical Violent Crime Perpetration in the Army (HADS 2004-2009)

- 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 Soldiers committed a major physical violent crime (murder-manslaughter, kidnapping, aggravated arson, aggravated assault, robbery) 2004-2009
- **The 5% of Soldiers classified by model as having highest predicted risk accounted for 36.4% of all major physical violent crimes committed by men (14.7/1,000 person-years), and 33.1% by women (6.1/1,000 person-years).**
- Model applied to 2011-2013 cohort (validation sample) - **5% of Soldiers with highest predicted risk accounted for 50.5% of all major physical violent crimes.**
- Key predictors: indicators of disadvantaged socio-economic status, early career stage, prior crime, mental disorder treatment.

Rosellini, et al., Psychological Medicine, 2015

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Mental Health Treatment among Soldiers with Current Mental Disorders (AAS 2011)

- Includes a representative sample of 5,428 non-deployed Regular Army soldiers who completed a self-administered questionnaire (SAQ).
- SAQ includes prevalence & treatment of current DSM-IV internalizing (anxiety, mood) & externalizing (disruptive behavior, substance) mental disorders.
- **21.3% of soldiers with any current disorder reported current treatment**.
- 7 significant predictors of being in treatment were identified: 4 indicators of psychopathology (bipolar disorder, panic disorder, post-traumatic stress disorder, 8+ months duration of disorder); 2 sociodemographics (history of marriage, not being non-Hispanic Black). The final predictor was history of deployment.
- Treatment rates varied from 4.7 to 71.5% depending on how many positive predictors the soldier had. The vast majority had a low number of these predictors.
- **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**.

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Women entering the Army (New Soldier Study 2011-2012)

- Women entering the Army reported higher lifetime rates than men of nearly all mental health disorders:
  - Any mental disorder: 47.9% women vs. 44.8% men
  - In particular PTSD (17.9% vs. 11.5% men) and depression (11.2% vs. 7.2% men)
- **Women enter the Army with more life stressors/disruptions in the previous year than men**
  - Betrayal by someone close (19.2% vs. 12.4% men)
  - Argument/break-up with friend/family (19.3% vs. 12.8% men)
  - Very severe/severe financial problem (18.9% vs. 13.5% men)
  - 3 or more very severe/severe life stressors (18.4% vs. 3.3% men)
- Women reported substantially more prior emotional abuse at home than men (16.9% vs. 10.8% men)
- **The reason for enlistment most often rated "very important" among women was "Do something you can be proud of" (60.6% vs. 53.2% men)**

NSS "Banner Book" 2014

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Occupational Differences in Army Suicide Rates (HADS 2004-2009, Enlisted Regular Army)

- The overall Army suicide rate was 20.1/100,000 person-years
- There was a wide range of MOS-specific group suicide rates
  - Combat engineer 38.2/100,000 person-years
  - Infantry 37.2/100,000 person-years
  - Admin support 13.1/100,000 person-years
  - Intelligence 11.7/100,000 person-years
- Infantry (11B/C/H/X/Z) was the only large MOS group with consistently elevated suicide rates compared to the Army-wide average
- **The suicide rate of all MOS groups varied by deployment status. Whereas the suicide rate for most MOS groups was significantly *higher* while deployed, it decreased for a few MOS groups, most notably the infantry (not due to differential deployment by PreDep MHDx)**

Kessler, et al., Psychological Medicine, 2015

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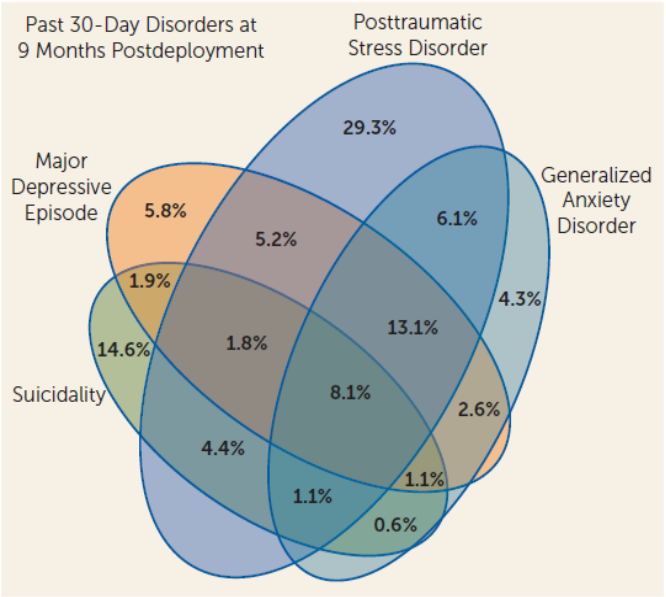
Longitudinal Evaluation of the Effect of Deployment-acquired TBI on Posttraumatic Stress and Related Disorders (PPDS 2012-2013)

- Prospective, longitudinal survey in 3 Brigade Combat Teams (n=4,645 Soldiers)
- Data were collected at 4 time points (1–2 months pre-deployment, 1 month post-deployment, 3 months post-deployment, and 9 months post-deployment)
- **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**

FIGURE 2. Comorbidity of Disorders Among Soldiers Classified at T3 (9 Months Postdeployment) as Experiencing Major Depressive Episode, Posttraumatic Stress Disorder, Generalized Anxiety Disorder, or Suicidality in the Past 30 Days[a]



[a] Prevalence of any of these four outcomes at T3 was 16.8%.

Stein, et al., American Journal of Psychiatry, 2015

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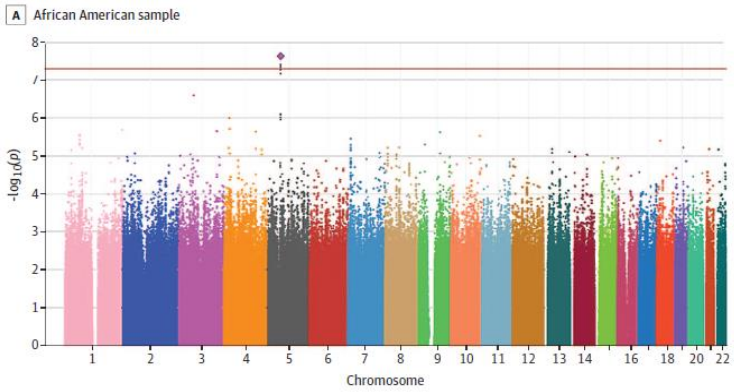
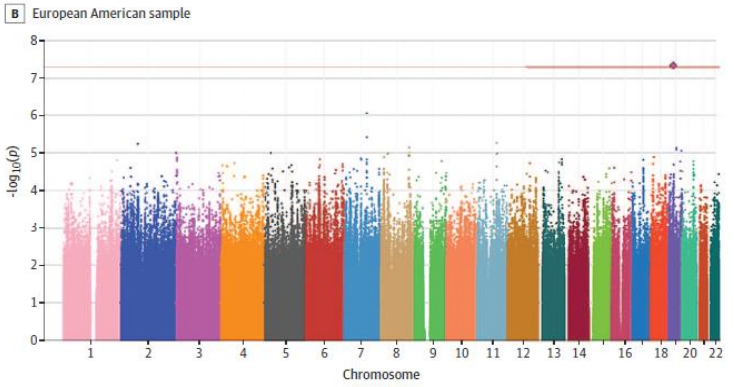
Genomewide Association Studies of PTSD (NSS and PPDS)





- **Largest GWAS of PTSD to date**.
- Two genome wide significant single nucleotide polymorphisms (SNPs) were found in association with PTSD for African American (left panel) and European American (right panel) Soldiers, respectively.
- The SNP in the African American sample is in a gene, **ANKRD55, known to be associated with a variety of inflammatory and immune disorders.**
  - The study also showed significant pleiotropy (i.e., genes affecting multiple traits) between PTSD and rheumatoid arthritis and psoriasis.
  - Points to a possible biological association between PTSD and these disorders, and consistent with a possible role for inflammatory processes in PTSD.

Stein, et al. JAMA Psychiatry (in press)

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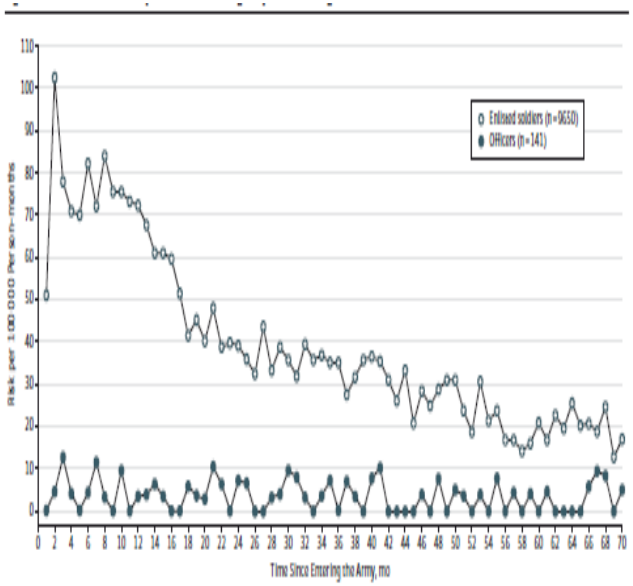
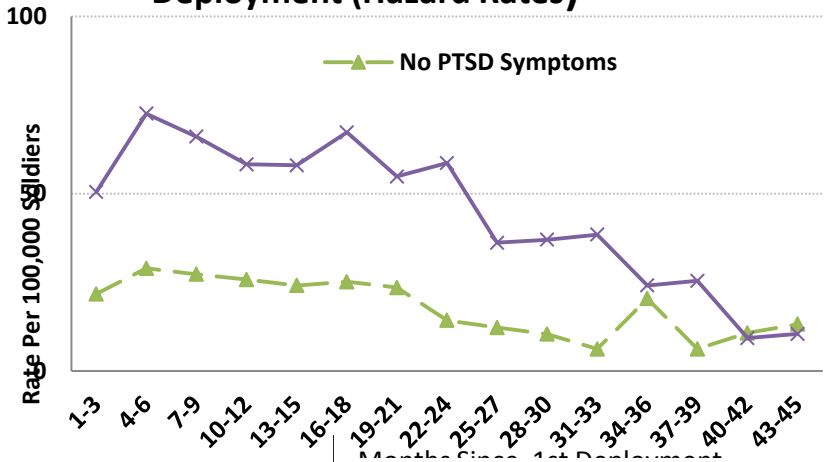
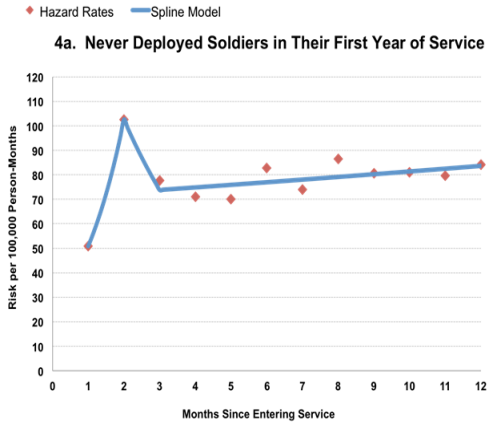
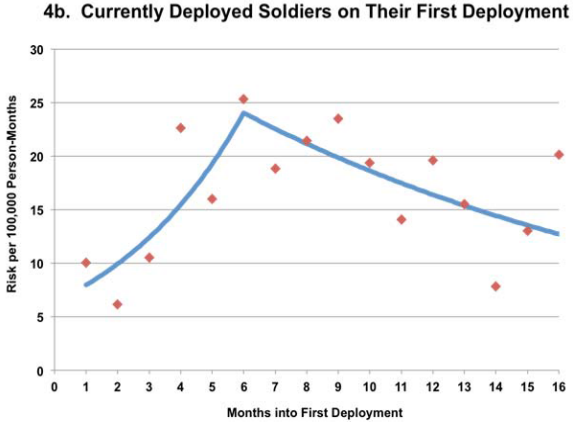
Suicide Attempt Risk among Regular Army Enlisted Soldiers (HADS 2004-2009)

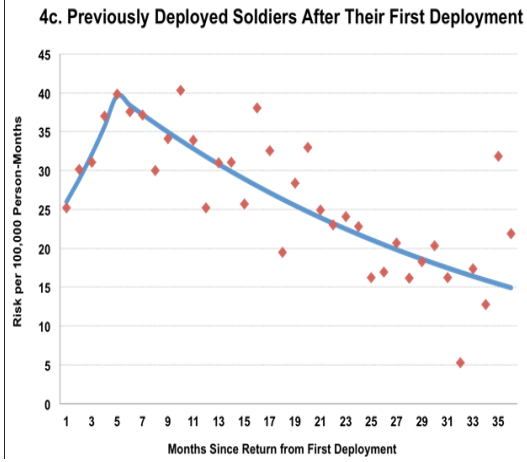


With and Without PTSD Sxs Fol 1st 1st Deployment (Hazard Rates)









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BACK-UP

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Study to Assess Risk and Resilience in Servicemembers - Longitudinal Study

PDHA/PDHRA: Risk of Suicide Attempt and PTSD Symptoms (HADS 2004-2009, Regular Army)

Deployment Health Assessment - PTSD

PTSD Symptoms*	Likelihood of Suicide Attempt Controlling for career Time Odds Ratio (95% Confidence Interval)[w]								
	Entire Sample			≤4 Years of Service			>4 Years of Service		
	OR	95% CI	Rate	OR	95% CI	Rate	OR	95% CI	Rate
Following 1st Deployment									
No PTSD Symptoms	[Reference]		322.1			540.1			156.8
Missing	1.1	(1.0,1.2)	243.6	1.1	(0.9,1.2)	494.9	1.3	(1.0,1.6)*	126.7
Early Symptoms of PTSD	1.4	(1.1,1.8)*	530.5	1.2	(0.9,1.7)	716.0	2.0	(1.2,3.2)*	343.3
Late Symptoms of PTSD	2.0	(1.6,2.4)*	826.2	2.0	(1.6,2.5)*	1274.1	2.0	(1.4,3.0)*	410.3
Early and Late Symptoms of PTSD	2.5	(2.0,3.1)*	966.6	2.4	(1.8,3.1)*	1416.5	2.9	(2.0,4.3)*	601.5

*p < .05

[w]. Estimates are based on a probability sample of person-month records that are weighted to reflect the total army population.
*PTSD defined by DoD criteria of 2 or more out of 4 items
Odds Ratios (OR) were adjusted for historical time, gender, age at entry to Army service, education levels, race, marital status, and rank.
Cases (n=2152); controls (n=45,475)

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PDHA/PDHRA: Risk of Suicide Attempt and Symptoms of Depression (HADS 2004-2009, Regular Army)

Deployment Health Assessment - Depression

Depression Symptoms*	Likelihood of Suicide Attempt Controlling for Career Time Odds Ratio (95% Confidence Interval)[w]								
	Entire Sample			≤4 Years of Service			>4 Years of Service		
	OR	95% CI	Rate	OR	95% CI	Rate	OR	95% CI	Rate
Following 1st Deployment									
No Symptoms of Depression	[Reference]		239.7			432.7			102.5
Missing	1.4	(1.2,1.6)*	248.8	1.3	(1.1,1.5)*	503.3	1.8	(1.4,2.3)*	127.9
Early Symptoms of Depression (Some)	1.4	(1.0,1.9)*	398.2	1.4	(1.0,2.0)	678.9	1.4	(0.7,2.5)	177.8
Early Symptoms of Depression (A lot)	2.7	(1.9,3.8)*	986.5	2.5	(1.6,3.7)*	1342.5	3.4	(1.8,6.4)*	589.0
Late Symptoms of Depression (Some)	2.2	(1.8,2.7)*	664.0	2.0	(1.6,2.5)*	1021.6	2.9	(2.4,3.0)*	369.3
Early And Late Symptoms of Depression (Some)	2.3	(1.8,3.0)*	708.2	1.7	(1.2,2.4)*	822.2	4.1	(2.7,6.2)*	606.8
Late Symptoms of Depression (A lot)	6.3	(4.8,8.3)*	2461.2	5.5	(4.0.7.6)*	3339.5	8.9	(5.3,15.0)*	1478.7
Early And Late Symptoms of Depression (A lot)	10.9	(6.8,17.7)*	3986.7	8.8	(4.8,16.2)*	3655.5	15.7	(6.9,35.5)*	4648.6

*p < .05

[w]. Estimates are based on a probability sample of person-month records that are weighted to reflect the total army population.

*Depression defined by 'feeling down, depressed, or hopeless' item

Odds Ratios (OR) were adjusted for historical time, gender, age at entry to Army service, education levels, race, marital status, and rank.

Cases (n=2152); controls (n=45,475)

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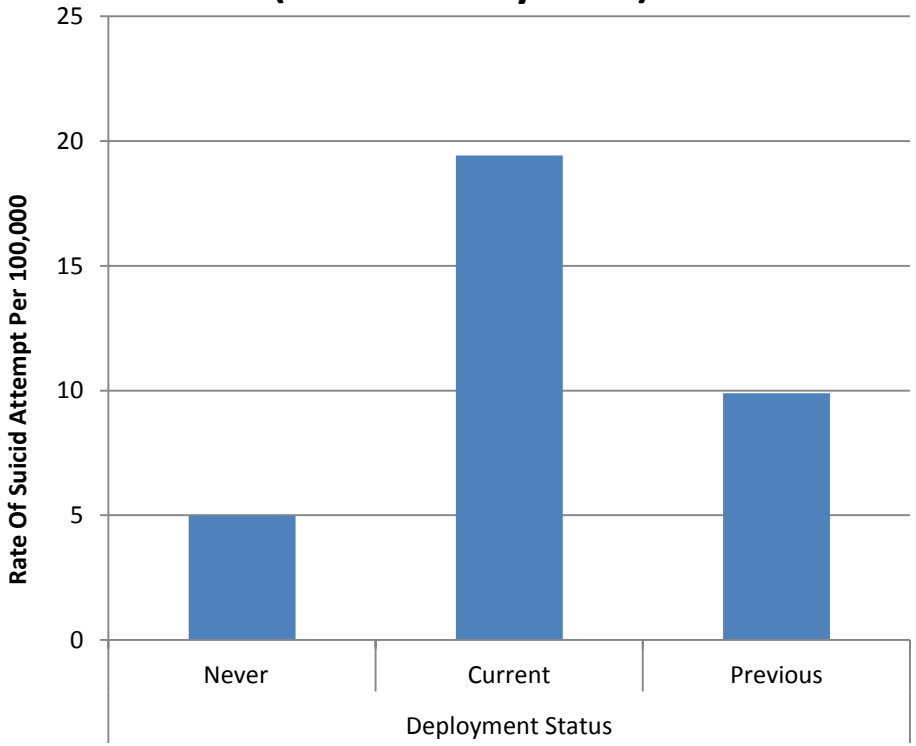
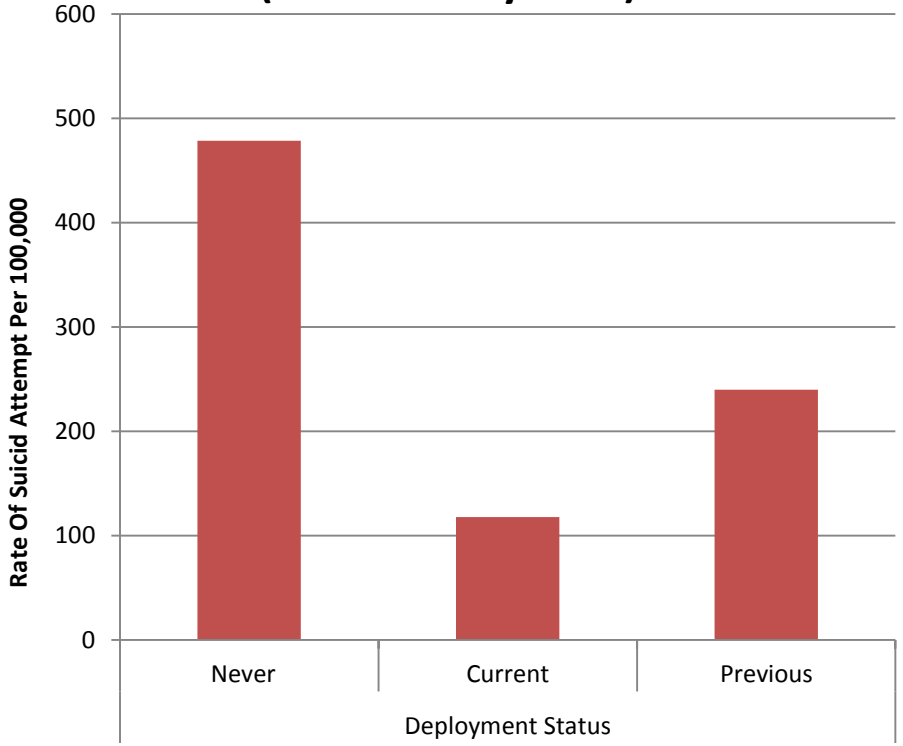
Method of Suicide Attempt By Deployment Status (HADS 2004-2009, Regular Enlisted Army)

Method of Suicide Attempt: Firearm (Crude Yearly Rate)



Method of Suicide Attempt: Other (Crude Yearly Rate)



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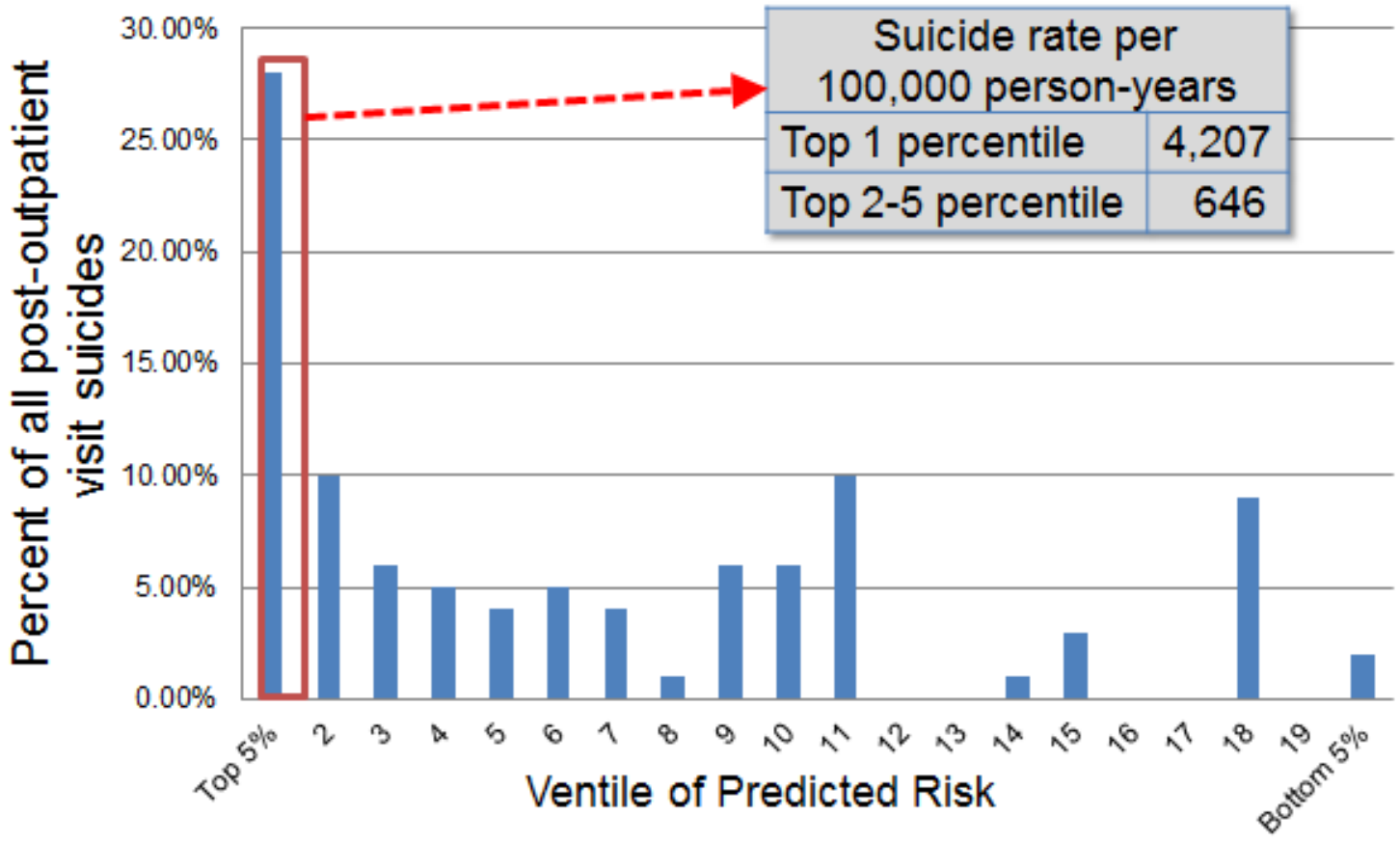
Concentration of Risk of Post-Outpatient Suicides for Non-deployed Males Within 5 Weeks after a Mental Health Visit (HADS 2004-2009, Regular Army)



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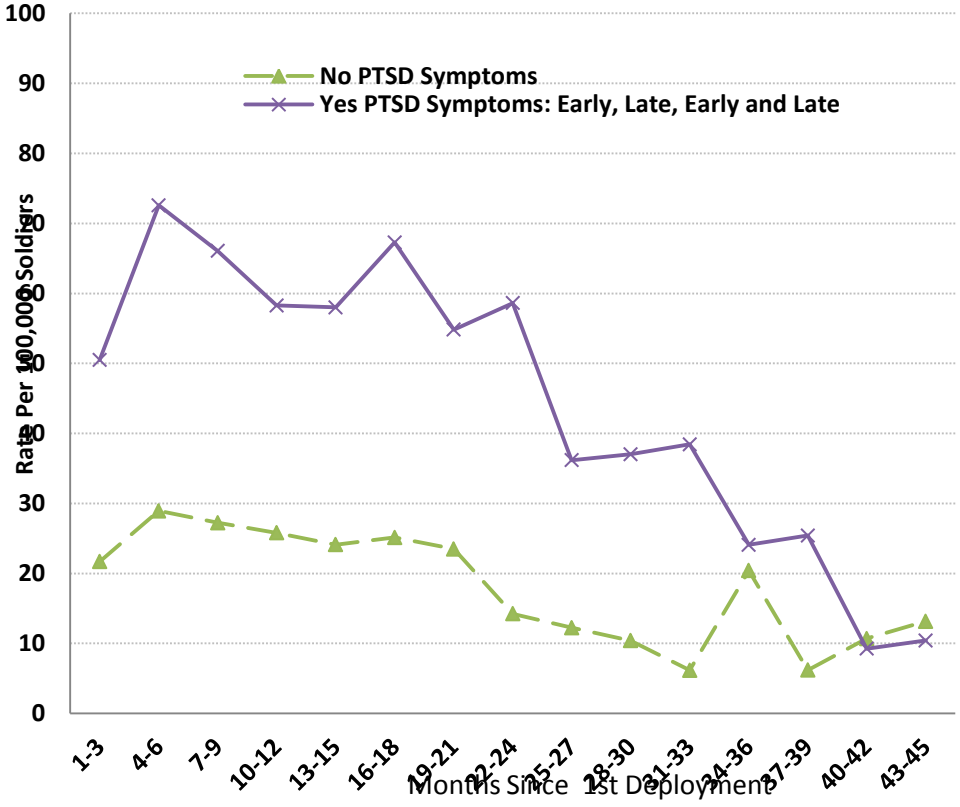
Risk of Suicide Attempt (HADS 2004-2009, Regular Army)

Suicide Attempt Rates For Soldiers With and Without PTSD Sxs Following First 1st Deployment (Hazard Rates)



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Occupational Differences in Army Suicide Rates (HADS 2004-2009, Enlisted Regular Army)

- The suicide rate of all MOS groups varied by deployment status. Whereas the suicide rate for most MOS groups was significantly *higher* while deployed, it decreased for a few MOS groups, most notably the infantry
  - Never deployed infantry 41.0/100,000 person-years
  - While deployed infantry 30.0/100,000 person-years
  - Previously deployed infantry 39.4/100,000 person-years

- This pattern was not due to a "differential healthy warrior effect," i.e., Infantry with mental health problems were not more likely to be held back from deploying than Soldiers in other MOSs with similar problems

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Does deployment cause suicide?

- Recent MCS and T2 reports find deployment history unrelated to subsequent suicide.
- Does this mean deployment does not cause suicide?
- The MOS analysis shows things are more complex than this.
- Selection biases exist into MOS, early attrition, first-term deployment/eligible, and re-enlistment
- Can causal inferences about effects of deployment be made despite these complexities?
- Our plans for addressing this question:
  - Approximating an experiment by excluding ineligibles;
  - Conditional independence of assignment to a first duty assignment in the part of the ARFORGEN cycle that will deploy within the soldier's first term;
  - Modeling selection bias and loss to follow-up;
  - Double-robust estimation (targeted maximum-likelihood).

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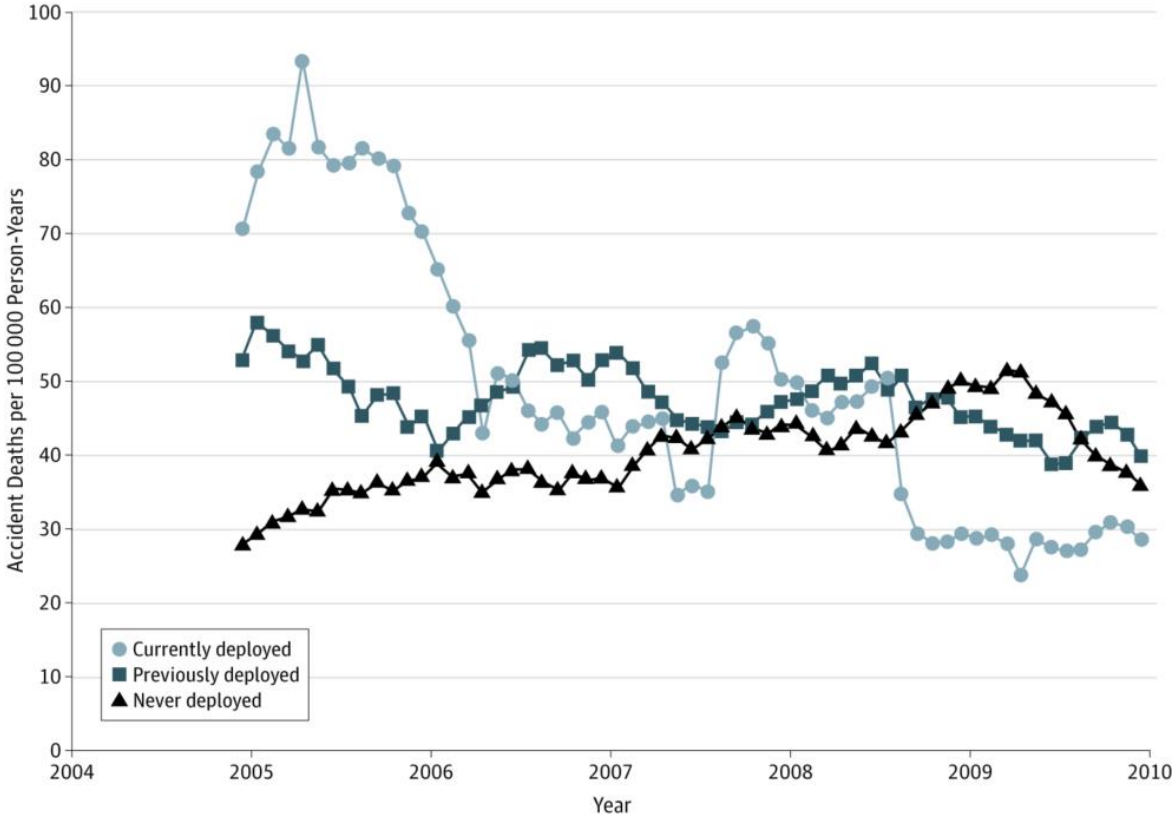
Accident Deaths by Deployment Status



Accident Deaths per 100 000 Person-Years of Active Duty Army ServiceShown are Regular Army 12-month moving averages. Each line represents a 12-month moving average (ie, each respective dot reports the rate for the prior 12-month period).

Predictors of Accident Death JAMA Psychiatry. 2014;71(5):493-503. doi:10.1001/jamapsychiatry.2013.4417

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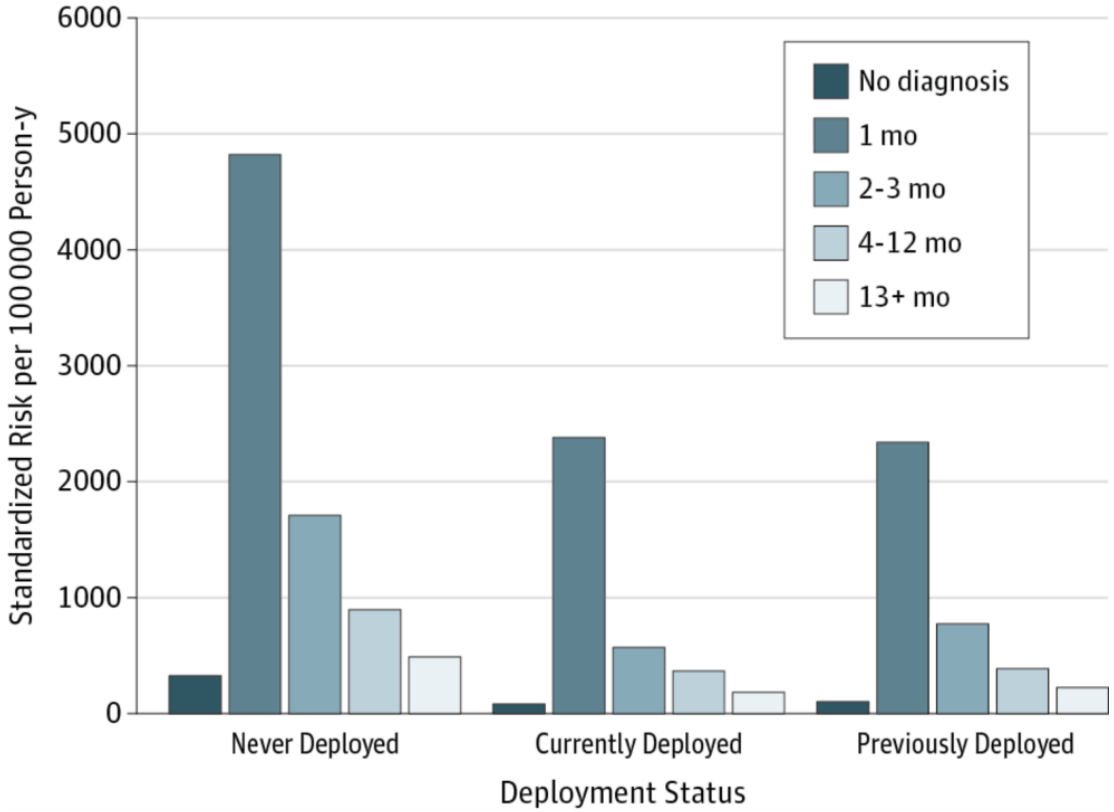
STARRS-LS

Study to Assess Risk and Resilience in Servicemembers - Longitudinal Study

Suicide Attempts, Deployment Status and Recency of MHDx



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