Commentary on "The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS)"

Army STARRS: A Framingham-Like Study of Psychological Health Risk Factors in Soldiers

Kerry J. Ressler and Eric B. Schoomaker

Although historically the Army suicide rate has been significantly lower than the civilian rate, in 2004, the suicide and accidental death rates began trending upward. By 2008, the Army suicide rate had risen above the national average (20.2 per 100,000). In 2009, 160 active duty Soldiers took their lives, making suicide the third leading cause of death among the Army population. If accidental death, frequently the result of high-risk behavior, is included, then more Soldiers died by their own actions than in combat in 2009. The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) was thus created in 2009 to begin to address these problems. The Army STARRS project is a large consortium of seven different studies to develop data-driven methods for mitigating or preventing suicide behaviors and improving the overall mental health and behavioral functioning of Army Soldiers during and after their Army service. The first research articles from the Army STARRS project were published in late 2013 and early 2014. This work has already begun to outline important facets of risk in the military, and it is helping to drive an empirically derived approach to improvements in understanding mental disorders and risk behavior and to improve prevention and support of mental health and resilience. The Framingham Heart

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Kerry J. Ressler, MD, PhD, is Professor and Investigator, Howard Hughes Medical Institute, Emory University, Atlanta, Georgia. *Eric Schoomaker, MD, PhD, Lieutenant General, U.S. Army (Retired)*, is Scholar-in-Residence and Distinguished Professor of Military and Emergency Medicine, Former U.S. Army Surgeon General and Commanding General, U.S. Army Medical Command, Uniformed Services University of the Health Sciences, Bethesda, Maryland.

Address correspondence to Kerry J. Ressler, Yerkes Research Center, Emory University, 954 Gatewood Rd. NE, Atlanta, GA 30329. E-mail: kressle@emory.edu

Study, started in the 1940s, marked a watershed event in utilizing large cross-sectional and prospective longitudinal collaborative research to identify and understand risk factors for cardiovascular disease. The Army STARRS project, through its collaborative, prospective, and robust innovative design and implementation, may provide the beginning of a similar scientific cohort in mental disorders. The work of this project will help understand biological and psychological aspects of military service, including those leading to suicide. When coupled with timely feedback to Army leadership, it permits near real-time steps to diagnose, mitigate, and manage emerging mental health issues and the root causes of risk and resilience in Army Soldiers, with potential impact extending across many traumatized populations—not unlike a parallel process that has markedly improved survival and recovery from physical combat wounds.

In 1948, the largest to date planned epidemiological and biological prospective study of heart disease was initiated with a group of ~5200 adult subjects from Framingham, Massachusetts. Since that time, this ongoing collaborative project has enrolled three generations of subjects in one of the largest, most famous, and most impactful studies in human history targeted toward the understanding of a medical problem. Prior to the initiation of what became known as "The Framingham Heart Study," almost nothing was known about the epidemiology of hypertensive or arteriosclerotic cardiovascular disease (Mahmood, Levy, Vasan, & Wang, 2014). Much of our now-common knowledge concerning heart disease, such as the effects of diet, cigarette smoking, exercise, and common medications such as aspirin, is based on this groundbreaking longitudinal study. Furthermore, our current understanding of the impact of elevated blood pressure and cholesterol risk on stroke and heart disease is the direct result of this work. Most recently, work with large-scale genomic approaches to understanding cardiovascular and stroke risk have led to this study being considered a gold standard for cardiovascular genetic epidemiology (Jaquish, 2007).

The Framingham Heart Study was groundbreaking and critical for a number of reasons, among the most important of which was the realization that understanding complex disorders such as cardiovascular illness requires access to very large, collaborative datasets and highlighted the importance of understanding the effects of environmental risk intersecting with biological processes and the power of prospective, longitudinal studies in addressing these complex problems.

Notably, the problems currently faced in the arena of mental health are very similar to those faced in cardiovascular medicine in the mid-20th century. The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) was created in 2009 to address these problems in our military populations. The past 5 years of data collection and analyses are beginning to come to fruition, with three very recent articles published online in March 2014 in *JAMA Psychiatry,* one published online in *Psychological Medicine*, one in *Psychiatry* (this issue), and four recently published articles in the *International Journal of Methods in Psychiatric Research* (Gilman et al. 2014; Heeringa et al., 2013; Kessler, Colpe, et al., 2013; Kessler, Heeringa, et al., 2013; Kessler, Santiago, et al., 2013; Kessler et al., 2014; Nock et al., 2014; Schoenbaum et al., 2014; Ursano et al., 2014). This commentary will serve to provide the background and context to the Army STARRS project, as well as to briefly review the recently published findings and address future directions of this critical, Framingham-like study of mental health outcomes in the military.

THE NEED FOR A LARGE-SCALE STUDY OF MENTAL HEALTH RISK IN THE MILITARY

The ultimate goal of the Army STARRS project is to develop data-driven methods for mitigating or preventing suicide-related behaviors and improving the overall mental health and behavioral functioning of Army Soldiers during and after their Army service. Before we further review the individual studies that make up the project, we will explore the increasingly difficult nature of the problem and why such a large, multi-institutional, multi-programmatic approach was urgently needed to approach the current challenges.

Physical, Emotional, and Social Challenges of Current Military Conflict

The U.S. military in the 2000s found itself in a situation unlike any previously faced in the modern era. It was engaged in armed conflict simultaneously in two theaters, Iraq and Afghanistan. Furthermore, the military is made of an all-volunteer force, with a heavy reliance upon the National Guard and Reserves. This is in contrast to prior large engagements (World War I, World War II, Vietnam), where a cross-sectional draft, despite its inherent problems, generally resulted in single tours of duty and at times more clear expectations of what was in store for new soldiers. From a military strategy perspective, these new theaters of war often have a discontinuous battlefield without a "front" or "rear." In addition, the enemy has engaged in "asymmetrical" combat, i.e., avoiding the use of force on force but relying upon improvised explosive devices (IEDs) and other forms of indirect violence, attacks on civilian populations, and other methods unlike those operational tactics faced in the First Gulf War or trained for in five decades of the Cold War, leading to novel roles for traditional combat Soldiers and support troops. Weapons that produce blast injuries often cause comorbid conditions such as concussions and other forms of traumatic brain injuries, which exacerbate and confound psychological injuries. Furthermore, Soldiers in more recent theaters have been subject to often lengthy deployments with short "dwell" at home between successive combat tours. A final component that is relatively new in the current era is a higher prevalence of married military families, providing on the one hand increased social support, but on the other, increased complexity in families separated for long periods of time. Thus, although the military and Veterans Administration have been more prepared than ever in history to address and treat mental health issues, and to support mental well-being, progress in these areas has been offset by many new challenges leading to ongoing sequelae of stress and trauma both in the war theater and at home.

Success of Advanced Approaches to Treating and Healing Physical Wounds

The past two decades have witnessed unprecedented progress in battlefield medicine and rehabilitation. This has had a tremendous impact on physical survival of our Soldiers; unfortunately, our mental health interventions and rehabilitations haven't necessarily kept up with the pace of progress. In contrast to struggles with psychological or behavioral health issues, many advances in battlefield care, evacuation, recovery, and rehabilitation for combat wounds have ensued since the last major U.S. military action and these most current theaters of war. Incremental improvements in survival from combat wounds, deployment injuries, and illnesses have been seen. These improvements have been brought about by improved Soldier protection, better training for medics and other first responders on the battlefield, tactical (intra-theater) and strategic (battlefield to home) evacuation, as well as improved re-

covery and rehabilitation treatment. Together, this approach of "focused empiricism" has led to unprecedented survival from even grievous wounds.

These efforts to improve clinical outcomes through the consistent and standardized collection of data on wounds, interventions at all levels of treatment, and evacuation across the continuum of care and rehabilitation provided actionable information that could be applied and further examined for its impact on the effectiveness of care. Notably, the use of a database of combat wounds and treatment from the point of injury to rehab centers, the Joint Trauma System, has been particularly efficacious (Hetz, 2006).

These advances have led to two divergent outcomes in relation to mental health. First, Soldiers who would have never survived in previous eras are now surviving following severe trauma exposure, which is to be greatly celebrated. However, the mental health impact and need for improved prevention, treatment, and intervention related to survival from these severe injuries and trauma exposures have brought about significant new challenges. Second, the widely implemented standardized collection of data as outlined above for combat wounds and physical traumas is increasingly recognized as a successful model—such that if similar broad-based, empirical data collection in the mental health arena could be performed, a similar level of success may be achieved.

Rise in Suicides, Alcohol, and Drug Addiction

Suicide is among the leading causes of death worldwide (Goldsmith, Pellmar, Kleinman, & Bunney, 2002; Nock et al., 2008). Historically, the suicide rate among U.S. Army soldiers has been below the general population rate. Notably, the Army suicide rate has increased dramatically recently, while the civilian rate has remained stable (Nock et al., 2013). This increase in suicide has been paralleled by increases in suicidal behavior, as well as addiction and other negative mental health outcomes. It remains unclear why these patterns of risk have increased. Several recent studies have examined patterns and correlates of Army suicides to increase understanding of risk factors (Bachynski et al., 2012; Haney et al., 2012), but they have not carefully examined pre- versus post-enlistment risk factors.

Overall this observed rise in suicides, alcohol, and drug addiction in the mid-2000s led to a need for a system parallel to the newly implemented physical trauma data collection to apply useful information against the underlying psychological issues facing Soldiers and families. In recent wars, the Army launched a series of very informative in-theater data collections and analyses of factors leading to mental health problems resulting from deployment, deployment length, combat exposure, dwell time between deployments, and similar factors. This set of projects is referred to as "The Mental Health Advisory Team" (MHAT) studies. Although extraordinarily useful, these studies were unable to gain a comprehensive view of mental health problems across the entire Army, including the onset of a Soldier's enlistment and training. Furthermore, it was difficult from these data to assess stresses or behavioral health problems encountered prior to service and prior to deployment, and the aim was not specifically to explicate suicide by focusing on attempted and completed suicides. Nor was there an opportunity to collect biological samples to study correlates or predictors of behavioral problems. Therefore, other approaches needed to be rolled out to address this urgent mental health need.

One of the approaches undertaken was the Millennium Cohort Study (Leard-Mann et al., 2013; Riddle et al., 2007; Smith et al., 2007). This study was particularly valuable in the sample size examined (tens of thousands of U.S. service members) and scope of the questions addressed. One aspect of the Millennium Study is that it includes all service members, with at least half of the service members being Sailors and Airmen.

Given the very different components of deployment context and trauma exposure, it is expected that the physical and mental health risks faced by Army Soldiers could be markedly different from those faced by Navy and Air Force service members. Another recent important initiative was the Vice Chief of Staff of the Army's Health Promotion, Risk Reduction, Suicide Prevention Task Force, which outlines much of the state-of-the-problem and begins to set out a strategy for solutions and interventions (Army Mental Health Advisory Team, 2010). Notably, it was clear by 2008–2009 that a large, empirically focused approach, targeting Army Soldiers, was needed to have the type of impact in mental health as had been seen with similar targeted approaches in physical health.

GENESIS AND MISSION OF ARMY STARRS

To address all of the above, the Secretary of the Army sought an external examination from leading experts on the biology, epidemiology, and clinical behaviors leading to suicide and comorbid factors. The funding for this initiative was provided by the Department of the Army ($50 million) with supplemental funds ($15 million) from the National Institute of Mental Health (NIMH), competitively awarded under the NIH Cooperative Agreement U01MH87981. The research team is examining mental health, psychological resilience, suicide risk, suicide-related behaviors, and suicide deaths in the Army with the goal of understanding the modifiable risk and protective factors for suicidal behaviors in Soldiers. The ultimate goal of the project is to develop data-driven methods for mitigating or preventing suicide behaviors and improving the overall mental health and behavioral functioning of Army Soldiers during and after their Army service.

Among the most specific tasks is the goal of identifying salient risk and protective factors in Army Soldiers. The hope is to thus provide mental health and well-being prevention and interventions that are in parallel with successful efforts to improve survival and ultimate clinical outcome from care of combat wounds, injuries, and illnesses. Additionally, the intention is to inform development and testing of empirically derived interventions for Army Soldiers and to rapidly deliver "actionable" findings to Army command.

Additional goals include the establishment of Army cohorts for future follow-up studies and continued benefit to the Army and uniformed Services, as well as to civilian patients. Together these approaches would set the conditions for a Framingham-like study with impact on insights into the genesis and management of mental health problems, as the Framingham studies have shed light on the etiology and management of atherosclerotic heart disease.

Elements of Army STARRS

The Army STARRS is being conducted by a consortium of investigators—from the Uniformed Services University of the Health Sciences, the University of California, San Diego, Harvard Medical School, and the University of Michigan—in collaboration with the National Institutes of Mental Health. The co-principal investigators (PIs) include Robert Ursano, MD (Uniformed Services University of the Health Sciences), and Murray Stein, MD, MPH (University of California, San Diego), with site PIs Ron Kessler, PhD (Harvard Medical School), and Steve Heeringa, PhD (University of Michigan), and NIMH collaborating scientists Lisa Colpe, PhD, and Michael Schoenbaum, PhD. The Army STARRS in-theater research was conducted under a protocol reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Institutional Review Board and in accordance with the approved protocol.

Of note, the Army STARRS is not a single study but seven closely related stud-

ies targeting different cohorts of Soldiers. It includes both cross-sectional and longitudinal designs, as well as in-depth examinations of Soldiers and families with surveys of attempted or completed suicide. The project relies upon combining demographic and other service-related characteristics, exposures, and experiences from approximately 40 non-classified administrative databases and direct survey data of Soldiers and families. Finally, a subset of the STARRS projects includes the most cutting-edge approaches to understanding blood-based biomarkers, including protein, genetic, and epigenetic mechanistic markers of risk and resilience. Below we provide a brief overview of each of the studies within the STARRS project.

Historical Administrative Data Study (HADS). This includes a cohort of more than 1.6 million active duty Soldiers from 2004 to 2009. Furthermore, the researchers are examining more than 1.1 billion de-identified Army/Department of Defense records. This large epidemiological sampling is unsurpassed, and one of the first reports of these data (Schoenbaum et al., 2014) examined records from nearly a million Soldiers. As outlined below, the data suggest that the suicide rate rose between 2004 and 2009 among never deployed and currently and previously deployed Regular Army soldiers and that predictors of Army suicides are largely similar to those for civilians, although some are distinct to Army service.

New Soldier Study (NSS). This cohort contains approximately 50,000 soldiers examined during their pre-deployment reception week at three sites: Forts Jackson, Benning, and Leonard Wood. These data collections provide for a very in-depth (and confidential) survey collection including past and current risk and resilience factors related to mental health outcomes, as well as a large amount of biological data collection to help identify blood-based biomarkers associated with risk and resilience.

All Army Study (AAS). This study includes a cohort of approximately 40,000 Soldiers from across the entire Army from more than 50 sites, including those both within and outside of the continental U.S. The study also comprises an in-theater sample that was interviewed during a Rest and Recovery visit in Kuwait. This cohort provides the sample set for two of the recent *JAMA Psychiatry* articles (Kessler et al., 2014; Nock et al., 2014), which outline prevalence and correlates of mental disorders and suicidal behavior among this cohort of soldiers.

Clinical Reappraisal Study (CRS). This smaller study covers 460 Soldiers who are very rigorously interviewed, assessed, and phenotyped to calibrate measures used in the AAS and NSS outlined above.

Soldier Health Outcomes Study A (SHOS-A). This is a case-control study of ~185 suicide attempters (cases) admitted at Walter Reed Army Medical Center and National Military Medical Center in Washington, D.C., as well as medical facilities at Joint Base Lewis-McChord (JBLM), Washington State; Ft. Bragg, North Carolina; Ft. Stewart, Georgia; and Ft. Hood, Texas, during and prior to the study period. Controls for these cases are selected from the All Army Study. This series of very deeply characterized cases will provide among the most in-depth study of suicidal behavior to date across a military or civilian population.

Soldier Health Outcomes Study B (SHOS-B). The main difference between the SHOS-A and SHOS-B is that this study focuses on ~150 completed suicides, performing 360-degree style interviews of informants (Army supervisors and relatives) of the completed suicide cases. A parallel set of well-matched (surviving) controls was identified from the All Army Study, and a similar set of interviews was performed across the informants of these controls for comparison. Complementing the SHOS-A study, this will provide the most comprehensive dataset of

post-mortem interviews for completed suicides and matched controls.

Pre/Post Deployment Study (PPDS). This is comprised of a longitudinal study of approximately 10,000 Soldiers in three Brigade Combat Teams (Ft. Bragg, Ft. Carson, JBLM). This very intensive study involves data collection at four different time points: < 1 month before deployment (pre-deployment survey and blood), followed by collections at < 1 month, 3 months, and 9 months after deployment (survey at all three post-deployment time points, blood at first post-deployment time point). While it is extremely time- and staff-intensive to collect this amount of prospective, longitudinal data, the PPDS has the promise of providing the most powerful and robust database of longitudinal and predictive risk factors to date, examining risk and resilience and the development of mental disorders over time, spanning historical, environmental, psychological, and biological datasets.

EARLY FINDINGS AND PUBLICATIONS

Four 2013 methodological reports were recently published in the *International Journal of Methods in Psychiatric Research*. Two of these articles focused on the design and implementation of the Army STARRS data collection procedures (Heeringa et al., 2013; Kessler, Colpe, et al., 2013). The next study focused on the potential impact of sample bias and methods to apply statistical weighting accordingly, with such large epidemiological samples of this nature (Kessler, Heeringa, et al., 2013). The last study of this series was performed to evaluate concordance of *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (*DSM-IV*; American Psychological Association, 1994), diagnoses based on the Composite International Diagnostic Interview Screening Scales (CIDI-SC) and post-traumatic stress disorder (PTSD) checklist (PCL), with diagnoses based on independent clinical reappraisal interviews (Kessler, Santiago, et al., 2013). Good individual-level concordance was found between CIDI-SC/PCL and Structured Clinical Interview for *DMS-IV* (SCID) diagnoses at these thresholds. However, concordance was even higher for continuous than dichotomous screening scale scores, suggesting that continuous/spectrum measures of predicted probabilities of clinical diagnoses are an important complement to dichotomous diagnostic variables.

Three recent publications in *JAMA Psychiatry* detail the first associations between epidemiological data and risks for mental disorders from the project. Matt Nock and colleagues examined one of the most pressing questions for the project: evaluating prevalence and correlates of suicidal behavior from Army STARRS (Nock et al., 2014). They used an All Army Study, non-deployed Soldier cohort of 5428 subjects to understand and identify rates of suicide-related risk factors and behaviors. They found that the lifetime prevalence estimates of suicidal ideation, suicide plans, and suicide attempts are 13.9%, 5.3%, and 2.4%, respectively. Most reported cases had pre-enlistment onsets, yet pre-enlistment onset rates were lower than in a prior national civilian survey, whereas post-enlistment onsets of ideation and plans were higher, and post-enlistment first attempts were equivalent to civilian rates. Most ideators reported onsets of plans and attempts occurring within the year of onset of ideation. Additional risk factors included female sex and being married. Pre-enlistment panic disorder, PTSD, depression, and intermittent explosive disorder were all predictors of post-enlistment suicide attempts. The authors argue that the finding that one-third of post-enlistment suicide attempts are associated with pre-enlistment mental disorders suggests that pre-enlistment mental disorders are important targets for early screening and intervention.

The study led by Ron Kessler, PhD, examined the 30-day prevalence of *DSM-IV*

mental disorders among nondeployed Soldiers (Kessler et al., 2014). This analysis used the same AAS cohort as the above study, with the goal of estimating the proportions of mental disorders among nondeployed Soldiers with first onset prior to enlistment. They further investigated the differential effect of pre- versus post-enlistment disorder onset in impairing function. Surprisingly, a total of 25% of respondents met criteria for any disorder and 11% for multiple disorders; 77% of cases reported pre-enlistment age at onset of at least one disorder. Controlling for sociodemographic and Army career correlates, 30-day disorders with pre- and post-enlistment onset both significantly predicted severe role impairment. Notably, pre-enlistment disorders were more consistently powerful predictors. The authors conclude that 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.

The final study of this recent trio in *JAMA Psychiatry*, led by Michael Schoenbaum, investigated the predictors of completed suicide and accidental death from the HADS dataset (Schoenbaum et al., 2014). This study examined death by suicide or accident from a database of nearly one million Soldiers. They found that the suicide rate rose between 2004 and 2009 among all three deployment categories of Regular Army Soldiers: those never deployed, those currently and those previously deployed. Increased suicide risk was associated with male sex, 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. The authors concluded that predictors of Army suicides were largely similar to those reported elsewhere for civilians, although some predictors distinct to Army service need follow-up. They surmise that the finding of a trend in suicide risk among never-deployed soldiers over time argues against the view that exposure to combat-related trauma is the exclusive cause of the increase in Army suicides.

As argued by Matt Friedman, MD, PhD, from the U.S. National Center for PTSD (Friedman, 2014), this is a groundbreaking series of studies from the Army STARRS initiative, and these first articles only begin to address the problems facing us. But several points can be made: (1) Only a relatively small number of soldiers account disproportionally for the suicidal, addictive, and other behaviors associated with mental disorders, and improved programmatic focus on early identification and intervention could go a long way. (2) Externalizing disorders including addiction and a subset of subjects with PTSD account disproportionally for suicidal behavior. (3) The rate of suicidal behavior among never-deployed soldiers is alarming and suggests that better identification and intervention up front may provide robust prevention approaches. And (4), the surprising finding of higher suicidal risk among married versus never-married soldiers is in contrast to the civilian situation and suggests that further targeting family support in the military may provide a critical point of intervention.

CONCLUSIONS AND FUTURE DIRECTIONS

The Army STARRS project is only just beginning to provide the fruits of multiple years of effort on behalf of large teams of investigators and on-the-ground researchers. However, this work is paying off, and there are hopeful prospects for future advances in understanding etiology and providing potential interventions. Such advances promise to lessen the burden of psychological stressors and avert mental health problems associated with military service and war. Future work needs to examine the applicability of these findings to broader populations beyond the military, including civilians in stressful roles as first responders, law enforcement, and victims of natural and manmade disasters, as

well as victims of violent crimes and terrorism.

Additionally, ongoing work across the Army STARRS Projects is examining biological, genetic, and neuroimaging correlates of PTSD, traumatic brain injury, and other trauma-related sequelae including addiction, violence, and other high-risk behavior. Additional future work is focused on resilience and how training resilience and mental well-being might be incorporated into prevention of trauma-related disorders. The enormously rich database and unprecedented cooperation among the participating Army, NIH, and academic investigators and supporters have led to the development of this Framingham-like study to address mental disorders as well as mental health and resilience in our Soldiers. This work will undoubtedly provide fundamental insights into the environmental, psychological, biological, and epigenetic variables underlying mental health disorders, including suicide. With hope, advances in mental health will soon follow the recent path of progress in physical medicine, such that the entire individual—both body and mind—will benefit from these prevention and intervention efforts.

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