

# Screening for Schizophrenia in Recruits, Active Duty Soldiers and Veterans: Can we do a Better Job?

Mark B Detweiler<sup>1-3,†</sup>, Amara S Chudhary<sup>4-6</sup>, Pamela F Murphy<sup>3,7</sup>

## Abstract

The United States military continues to have difficulty maintaining the number of troops they need to accomplish their global military missions. The United States military medical service has been struggling with methods of identifying mental disorders, including schizophrenia, during recruitment and, if possible, no later than basic training. From World War I, the United States military medical service has continually worked to improve their ability to evaluate military recruits with prodromal or mild schizophrenia symptoms at enlistment or early in their training in order to limit military and personal disruptions during active duty and especially during deployment to combat theaters. It is known that the longer the recruit progresses through training to active duty, the greater the disruption for the military command when schizophrenia is diagnosed and the soldier is withdrawn from active duty. In particular, the diagnosis of combat troops with schizophrenia results in key military unit members being withdrawn from their combat team. This results in short-term and long-term problems for the military command and its mission, in addition to the career and lifetime quality of life changes for the soldier. The economic burden to the United States military and the United States Government continues for the lifetime of the soldier who has been diagnosed with schizophrenia at any point during their training which leads to lifetime service connected disability. We review the history of the United States armed forces medical service and its efforts to minimize the number of recruits from entering the military and becoming active duty before being diagnosed with schizophrenia. A more aggressive screening protocol for schizophrenia based on existing tests and technology is presented.

## Keywords

Schizophrenia, Disability, Screening, Military, Recruits, Veterans

#### Introduction

"In a war in which PTSD (post-traumatic stress disorder) and TBI (traumatic brain injury) are of great concern, it can be easy to forget that young adults beginning military service are often at an age where schizophrenia symptoms first become apparent" [1]. For many veterans the diagnosis of schizophrenia spectrum and other psychotic disorders is the end-point of their productive military and often their avocational lives. DSM-5 [2] describes schizophrenia spectrum

<sup>7</sup>Ashford University, College of Health, Human Services, and Science, Psychology Program, San Diego, California, USA

<sup>+</sup>Author for correspondence: Mark B. Detweiler MD (116A7), Veterans Affairs Medical Center, 1970 Roanoke Boulevard, Salem, Virginia, 24153, USA. Phone: 540-982-2463, ext: 1652, Fax: 540-982-1080, email: mark.detweiler1@va.gov

<sup>&</sup>lt;sup>1</sup>Staff Psychiatrist, Salem Veterans Affairs Medical Center, Salem, Virginia, USA

<sup>&</sup>lt;sup>2</sup>Professor, Edward Via College of Osteopathic Medicine, Department of Psychiatry, Blacksburg, Virginia, USA

<sup>&</sup>lt;sup>3</sup>Geriatric Research Group, Salem Veterans Affairs Medical Center, Salem, Virginia, USA

<sup>&</sup>lt;sup>4</sup>Staff Psychiatrist, Patrick B. Harris Psychiatric Hospital 130 Highway 252. Anderson, South Carolina, USA

<sup>&</sup>lt;sup>5</sup>Clinical Assistant Professor, University of South Carolina Greenville, South Carolina, USA

<sup>&</sup>lt;sup>6</sup>Assistant Professor Edward Via College of Osteopathic Medicine Carolina campus, Spartanburg, South Carolina, USA

and other psychotic disorders as including: delusional disorder; brief psychotic disorder; schizophreniform disorder; schizophrenia; schizoaffective disorder; substance/medication induced psychotic disorder; psychotic disorder due to another medical condition; catatonia; other specified schizophrenia spectrum and other psychotic disorders; and unspecified schizophrenia spectrum and other psychotic disorders. These disorders in general are defined as having abnormalities in five delusional domains: hallucinations; disorganized thinking and speech; grossly disorganized or abnormal motor behavior; and negative symptoms [2]. Symptoms of schizophrenia most often render active duty soldiers incapable of meeting their duty requirements and leads to a medical discharge and lifetime payments from the United States military for their disability. In this paper, the single word "schizophrenia" will be used to include all the signs and symptoms related to schizophrenia spectrum and other psychotic disorders.

Schizophrenia is one of the top 25 disabling diseases in the world [3]. For young men and women who wish to have careers in the United States armed forces, schizophrenia will usually end their dreams and aspirations for a career in the military and/or a productive and satisfying life [4]. The disease removes soldiers from active duty and creates a monetary and medical burden for the United States military and the United States economy [5]. It is noteworthy that in 2002, the estimated total cost of schizophrenia in the United States was \$62.7 billion [6]. In 2007, veterans with mental health diagnoses accounted for 15 percent of the Veterans Affairs (VA) patients; however, their care consumed 33 percent of the total Veterans Health Administration (VHA) medical costs [7]. Recently, more than one-third of Veterans returning from Iraq or Afghanistan that have entered the VHA have been diagnosed with mental health disorders including schizophrenia, PTSD, depression and bipolar disorder. Consequently, the VHA has been funding more than 20 projects to improve the treatment and decrease schizophrenia morbidity [8].

Although there is a growing body of evidence describing the neuroanatomical and functional alterations of schizophrenia, research is ongoing [9-12]. The evolving understanding of the genetic mechanisms of schizophrenia supports the need for early diagnosis in the prodromal stages [13]. Clinical symptoms of schizophrenia reflect the results of the manifestation of interacting genetic

and environmental (epigenetic) factors in concert with ongoing heterogeneous neurobiological processes [11]. Genetic factors begin to alter early neural development and continue a cascade of detrimental processes during pre- and perinatal development [14,15]. The Schizophrenia Working Group of the Psychiatric Genomic Consortium has identified 108 chromosomal sites with inherited variations in the genetic code linked to schizophrenia [16].

Two of the schizophrenia susceptibility genes involved in the cognitive disruptions of schizophrenia that have been identified are catechol-o-methyltransferase (COMT) and glutamate metabotropic receptor 3 (GRM3) [17]. Alterations of COMT appear to disrupt cortical dopamine signaling resulting in altered variable neural strategies for working memory and altered patterns of intra-cortical functional correlations. Working memory is impacted by the interaction of GRM3 and COMT. Genetic analysis suggests that GRM3 influences synaptic glutamate levels in addition to cooperating with COMT leading to cortical genetic alterations responsible for the declining logic of the neural circuits involved in memory and behavior [17,18].

One recent important genetic finding is the role of gene C4 on chromosome 6 in schizophrenia. It is reported that the degree of activation of gene C4 on chromosome 6 controls the severity of excessive neural pruning in the early stages of the disease. In the brains of adolescents at risk for the schizophrenia, the excessive pruning of the maturing brain interconnections manifests clinically as the positive and negative symptoms of schizophrenia with concurrent cognitive and functional deficits [19,20]. Also, larger cortical networks are employed with interplay between reduced signal-to-noise components and the recruitment of compensatory networks [17]. Dopamine release disruption from the nucleus accumbens, prefrontal cortex (PFC) and other brain structures are involved in the impairment of cognition as reduced dopamine impairs memory imprinting with concurrent degradation of memory [21,22].

It is notable that the severe biopsychosocial morbidity of schizophrenia is relatively treatment refractory [23]. Once the C4A gene on chromosome 6 is activated, science has not yet found a method to turn off the excessive pruning that diminishes brain reserve and results in smaller brains than for the general population [24,25]. Disease progression in schizophrenia is principally the result of structural brain changes that can be imaged as neuro anatomical disruption emerges from its relatively early dormant stages to more advanced stages eventually leading to clinically observable signs and symptoms [26]. Many individuals, especially the highest risk group for developing schizophrenia, have significant executive control impairment in the PFC that can be imaged and also assessed with face to face testing [13,17,22,27]. These findings highlight the fact that the genomic [28], anatomical and cognitive deficits of schizophrenia can be detected before the common clinical presentation deficits are recognized [29]. For example, functional magnetic resonance imaging (fMRI) yields digitally enhanced color images of brain function, depicting localized changes in blood flow and oxygenation that allow digital imaging of various functional levels of localized brain areas. fMRI and electroencephalography studies have detected changes in the PFC. When healthy persons make executive decisions which occur in the PFC, fMRI reveals activation of frontal and mid-brain regions that are marginally or not activated in persons with schizophrenia [29].

The clinical manifestations of the genetically driven process of schizophrenia are most frequently first seen in young males, e.g., 18-22 years of age [1]. This debilitating mental illness incurs a high cost for the United States military, the United States Government in health care costs and a in substantial burden for veterans, their families and society. Perhaps what is missed in the discussion of veterans with schizophrenia is the fact that the joint medical services of the United States armed forces have been struggling to reduce the number of recruits with nascent or ongoing mental disabilities from entering boot camp and active duty since World War I (WWI). Thus, the objective of the United States armed forces medical services of decreasing the percentage of soldiers with schizophrenia and also of reducing the long term morbidity and early death rate of veterans with schizophrenia has been an ongoing project for approximately 90 years [30].

It is estimated that one of every 4 active duty soldiers demonstrates signs of a mental health condition [31-33]. In 1997, the United States Congress mandated that the military screen all troops scheduled to be deployed for mental health problems. However, Pentagon statistics indicate that fewer than 1 in 300 service members were referred to a mental health professional before being deployed to Iraq as of October 2005. United States Army mental health expert Dr. Elspeth Ritchie has noted that some soldiers with mental health problems are often returned to combat theaters due to an underlying troop shortage [34].

When an active or reserve duty soldier is diagnosed with schizophrenia that reaches clinical criteria, the soldier is lost as a contributing component of their military unit with the need to find and train a replacement soldier. This is less disturbing to a military unit in garrison when compared to a deployed combat unit. In these situations, both the soldier suspected of having schizophrenia and the military unit lose. For example, veterans with schizophrenia have elevated rates of non-cancer pain (arthritis, back pain, chronic pain, migraine, headache, psychogenic and neuropathic) and are more likely to die as hospital inpatients when compared to veterans without schizophrenia [35,36]. Of note, it is well known that veterans with schizophrenia 40 years of age and older have better daily functioning, health-related quality of life, cognitive performance, and less substance abuse compared to nonveterans with schizophrenia [5]. based on the lifetime care given to veterans in the VHA [37].

A significant question for the United States armed forces and the United States Government is what new strategies can be implemented to reduce the diagnoses of schizophrenia among US armed forces recruits, active duty soldiers and veterans? For today's cohort of veterans from the Vietnam era to the Iraq and Afghanistan combat theaters, the repercussions of schizophrenia have been life altering, often with permanent and progressive reductions in quality of life [11,38,39]. As clinicians who have worked with active duty soldiers, reserve duty soldiers and veterans with the diagnosis of schizophrenia, in this paper we suggest an improved schizophrenia screening protocol to be employed for pre- and post-enlistment, including the identification of schizophrenia among combat troops being evaluated for PTSD in the battle field or after returning to garrison in addition to veterans entering the VA medical system.

Limited insight into the biological mechanisms of schizophrenia has fostered only a few consensus treatment strategies based on incomplete research. Presently, there is the risk of a worsening prognosis over the lifetime of veterans once schizophrenia and its variants are identified [10,11]. Many veterans and nonveterans do not significantly improve with treatment, even if clinicians follow guidelines for current multimodal treatment approaches for schizophrenia [10,40,41]. Treatment resistant patients are commonly managed with multiple medications for schizophrenia with less than ideal outcomes [10,11,42-44].

The United States Military medical services have acknowledged that since WWI, the early diagnosis of mental illness, including schizophrenia, prior to the recruits reaching active training is a difficult problem. Military recruits with a genetic predisposition and epigenetic enhancers for schizophrenia such as childhood abuse, neglect and the use of street drugs prior to or during their military service, risk having an earlier schizophrenia onset when coupled with the stress of military training and active duty. Complicating this situation, in order to avoid detection and removal from active duty and probable military discharge, once entered into the military and on active duty, it is uncommon for soldiers to voluntarily admit to symptoms of depression, odd or bizarre thoughts, paranoia or hallucinations until they are relatively incapacitated [45,46]. Moreover, given the challenge of meeting recruiting and active duty preparedness requirements, the needs of the military mission objectives are sometimes viewed by commanders as superseding the soldiers' personal needs. It has been reported that United States military troops with significant psychological problems have been sent to Iraq or kept in combat even though the responsible commanders and medical staff have been aware of signs of mental illness [36]. Such problems complicate the diagnosis of schizophrenia in the military arena.

Soldiers diagnosed with major or severe depression can be stabilized and returned to duty [47]. In contrast, once diagnosed with schizophrenia, soldiers rarely return to active duty after assessment and treatment in a military hospital. A majority of soldiers diagnosed with psychosis, bipolar disorder or schizophrenia will receive a medical discharge. Subsequently, they will receive payments from the United States Government for their schizophrenia service connected disability, usually for the remainder of their lives.

The United States military medical services have a long history of mental health screening dating from post WWI. Salmon proposed that

general practitioners receive better education in the principles of psychiatry with the goal of improving the screening of young persons who are under their care and who may choose to enlist in the United States armed services [48,49]. Following World War II (WWII) psychiatrists argued that attention should shift from problems of the abnormal mind in normal times to problems of the normal mind in abnormal times [50]. United States military psychiatrists have played a major role in attempting to reduce the debilitating impact of psychiatric syndromes on military preparedness. Psychoanalyst Harry Stack Sullivan, who was a consultant to the Selective Service System in the 1940s, had the goal of developing a screening program to exclude all recruits suffering mental illness and maladjustment syndromes [51,52].

The same goal of reducing the number of military recruits with psychiatric disabilities was addressed by Britain in 1942 during WW II. In Britain, all armed forces recruits from 1942 onwards have received a twenty-minute version of the Standard Progressive Matrices (SPM) [53,54] to estimate abstract reasoning and non-verbal fluid intelligence [54]. Although not a screen for mental illnesses, this screen was adopted by other national military medical services to screen for intellectual capacity helpful for MOS assignments. It is significant that lower scores on the Raven Progressive Matrices test assist in separating persons with schizophrenia risk when compared to controls [55], suggesting that the Raven Progressive Matrices test may be employed as a secondary screening test for schizophrenia [53,54].

It can be posited that the multiple decades of developing screening protocols by the United States armed forces medical services for schizophrenia among recruits and active duty soldiers have not achieved expectations identified since World War I. Also, the effects of treatment for mental illnesses such as PTSD and other psychiatric diagnoses in combat theaters are unclear, and the results of treatment for chronic postwar syndromes are mixed [27,56-58]. After the Persian Gulf War, a number of military physicians made innovative proposals for a population-based approach, anchored in primary care instead of specialty-based care medical model. This approach appears to hold the most promise for the future according to some authors [57].

Presently, the United States Army uses only

educational achievement, cognitive testing and a cursory psychiatric screening for mental illnesses. Confidential surveys and interviews with 5,428 soldiers at Army bases in the United States revealed that 20 percent of these soldiers had a mental illness (e.g., depression, panic disorder, intermittent explosive disorder, ADHD, substance use disorder) prior to enlisting in the Army. Of these soldiers, over eight percent had pre-enlistment suicidal ideations and more than one percent had prior suicide attempts. Notably, both soldiers who had been deployed and those with no history of deployment reported higher rates of attention deficit hyperactivity disorder (ADHD), intermittent explosive disorder, PTSD and substance use disorder than recorded among civilians [31-33,58]. These data support the argument that the proficiency of recent United States military medical services screens of recruits and active duty soldiers for mental illnesses including schizophrenia is less than ideal.

Lieutenant Colonel Joseph Candelario, retired former Battalion Surgeon of the United States Army Warrior Transition Clinic, Womack Army Medical Center at Fort Bragg, North Carolina, has commented that he had advocated for many years that the United States Army could do a better job of prescreening recruits "in an effort to save hundreds of millions of dollars" for the treatment of mental illness during and after military service. He has suggested that the United States Army should screen recruits the same way the Army Special Forces soldiers are screened prior to allowing them into the Special Operations Command. The screening used for the Special Operations Command is expensive, but necessary due to the level of importance of the Special Forces operations and missions. The question is, if the United States Military medical services allocated resources for better mental health screening for all recruits prior to enlistment or during basic training, how much money could be saved versus the costs associated with losing soldiers from active duty units followed by treatment in military medical units and eventually treating veterans with service-connected mental health disabilities for their lifetime after being released from active duty? Lieutenant Colonel Candelario posits that it would be financially beneficial to screen out potentially debilitating mental illnesses prior to enlistment. He notes that this would significantly reduce the disruption of operations that the

United States Army commanders face during the process of removing soldiers with mental illness from their command units. Lieutenant Colonel Candelario also notes that even more disruptive to United States military forces are the problems that can compromise the mission of United States combat operations with the discovery of incapacitating mental illness in deployed soldiers with an essential MOS in a combat theater [59].

During early training, the United States Navy and Air Force employ a fourth assessment in addition to those assessment measures used by the United States Army. While it has been proposed that having a high school diploma or 1-2 years of college in addition to the rigors of basic training, may be the best screening techniques, the effectiveness of these measures in the early identification of schizophrenia are unknown [30]. As part of the 2015 defense budget, the House of Representatives proposed a bill ordering the National Institutes of Health to create a universal mental health evaluation for potential recruits that would screen for past suicide attempts and psychiatric disorders. The main focus was to reduce the number of suicide attempts and completions; it was not specifically focused on decreasing schizophrenia in the military ranks [60]).

It has been proposed that diagnosing schizophrenia in combat soldiers during the early stages of schizophrenia may be more effective than later therapeutic interventions in the more advanced disease stages as seen in some young military soldiers and veterans [61,62]. In the most recent combat theaters, the prevalence of PTSD has been relatively similar: 11-20 percent in a given year for Operations Iraqi Freedom (OIF) and Enduring Freedom (OEF); 12 percent in a given year for the Persian Gulf intervention (Desert Storm); and 15 percent in a given year for the Vietnam military action. It is estimated that about 30 percent of Vietnam Veterans will have had PTSD in their lifetime [63]. It is now understood that PTSD may mask the early stages of comorbid schizophrenia. During the Iraq and Afghanistan conflicts, there has been a problem diagnosing schizophrenia among active duty and reserve duty soldiers in active combat as PTSD has some symptoms that are also commonly found in schizophrenia [74]. In part this is due to the fact that the primary objective of the United States armed forces medical services has been to identify PTSD at its earliest stages to reduce morbidity [64]. Therefore, it would be helpful to

have a more aggressive and consistent screening protocol for schizophrenia to accompany every PTSD screen in active duty soldiers. If comorbid schizophrenia is missed or the diagnosis delayed, the underlying schizophrenia most often progresses and worsens the prognosis [37,62].

Based on ongoing medical and psychiatric problems in the United States military, new diagnostic protocols for recruits and active unit soldieries would be beneficial for both the military and the individuals involved. A literature search revealed some suggestions for a more proactive serial screening protocol for schizophrenia in men and women who wish to join the United States armed forces, active duty soldiers, and also for veterans entering the VAMC (Table 1). Such a suggested protocol would utilize existing, relatively brief (between 10 and 45 minutes) and easily manually scored screening tools. For example, the Prodromal Questionnaire Brief Version (PQ-B) could be administered at the lowest threshold of suspected schizophrenia [64,65]. A positive screen could be followed by a test for a biological markers of schizophrenia such as the single nucleotide polymorphism (SNP) in the gene SLC1A1 on chromosome 9p24, encoding the neuronal glutamate transporter EAAC1 [65] (Table 2).

We propose a multistep program screening protocol for schizophrenia from pre-enlistment, during active duty and for veterans entering VHA. It is suggested that a short screen for schizophrenia be initiated at: (A) pre-enlistment at Armed Forces Recruiting Stations; (B) during boot camp; (C) prior to MOS training graduation; (D) during active duty when screening for PTSD in combat or post-combat; (E) at admission to Veterans Affairs Medical Centers (Table 1).

The screening for schizophrenia should begin prior to enlistment. Once a person seeking to enlist in the Armed Forces presents at a recruiting station, they should be asked to have their primary care physician screen for: drug use (with urine drug screen) within 1-2 months of presentation; their mental health history; and their family's mental illness history. Perhaps the most important elements of this history would include a history of schizophrenia, schizoaffective disorder, bipolar disorder, depression, mania, or schizophreniform disorder. For the primary care provider, such an evaluation has been made progressively easier due to advanced technology involving electronic medical records which permits rapid review of an individual's

medical history. This technology has been available at Veterans Affairs Medical Centers for approximately two decades and is expected to spread to most hospitals and eventually to a nationwide linked electronic medical record system [66]. This primary care report would then be taken to the recruiting station to qualify the individual for the next step of joining the United States military.

If the past medical record review meets satisfactory criteria, the individual would be administered PO-B which can differentiate between persons with the prodromal schizophrenia and the more advanced forms characterized by psychotic features [64]. The PQ-B would be administered by the recruiter, or better, by a United States military screening center that serves all the military service recruiting stations regionally. If the PQ-B is positive, the prospective recruits would have to have be screened for a biological marker of single nucleotide polymorphism (SNP) in the gene SLC1A1 on chromosome 9p24, encoding the neuronal glutamate transporter EAAC1 [14,65]. If positive, the person would not qualify for admission to the military and the testing results would be part of the military's electronic records regarding potential recruits. Once the recruit has a confirmatory schizophrenia examination, no Government/military money or time should be allocated for their future recruitment or assessment.

If the recruit progresses to basic training, a major effort needs to be implemented to minimize the possibility of having a recruit graduate from basic training or MOS training with underlying schizophrenia. Therefore, it is proposed that during basic training and prior to MOS school graduation, all soldiers would receive the Raven Progressive Matrices test 20 minute version as a preliminary rapid screen for schizophrenia [53,54]. This test is helpful as some astute individuals who fear that they have a mental illness will probably not understand that this is an indirect screen for schizophrenia and other mental disorders. This would be followed by the PQ-B [64] along with the Brief Cognitive Assessment Tool for Schizophrenia [67]. If positive, the screen for the biological marker of the single nucleotide polymorphism (SNP) in the gene SLC1A1 on chromosome 9p24, encoding the neuronal glutamate transporter EAAC1b would follow.

Once the soldier has graduated from their MOS school and transferred to their duty station, any signs of altered mental status particularly

## Screening for Schizophrenia in Recruits, Active Duty Soldiers and Veterans: Can we do a Better Job? Research

A.	Pre-enlistment: Armed Forces Recruiting Stations, Schools, Medical Offices					
l.	Urine drug screen.					
2.	Personal and Electronic record review of family history for mental illnesses such as schizophrenia, schizoaffective disorder, bipolar disorder, Depression, mania, or schizophreniform disorder.					
3.	If positive: Prodromal Questionnaire Brief Version.					
<b>1</b> .	If positive, utilize a confirmatory biological marker: Screen for biological marker of single nucleotide polymorphism (SNP) in the gene SLC1A1 on chromosome 9p24, encoding the neuronal glutamate transporter EAAC1.					
3.	Military : During basic training and prior to military occupational specialty school graduation, prior to first active station assignment					
l.	Indirect screen: Raven Progressive Matrices test ;					
2.	Prodromal Questionnaire Brief Version and the Brief Cognitive Assessment Tool for Schizophrenia;					
3.	If positive: DSM 5 diagnostic examination;					
ŀ.	If positive: Screen for biological marker of single nucleotide polymorphism (SNP) in the gene SLC1A1 on chromosome 9p24, encoding the neuronal glutamate transporter EAAC1.					
2.	Diagnosis of PTSD in combat or post- combat					
	As part of the differential diagnosis assessment: Prodromal Questionnaire Brief Version.					
	If positive and needs a biological marker confirmation: Screen for biological marker of single nucleotide polymorphism (SNP) in the gene SLC1A1 or chromosome 9p24, encoding the neuronal glutamate transporter EAAC1					
).	Veterans Affairs Medical Center					
or	all veterans on admission					
	In Primary care Intake: Prodromal Questionnaire Brief Version.					
	If positive: consult psychiatry to perform schizophrenia screening protocol:					
)	Screen for a individual signs and symptoms of PTSD;					
)	Screening for family history for mental illnesses such as schizophrenia, schizoaffective disorder, bipolar disorder, Depression, mania, or schizophren form disorder;					
)	Exclusion of other metabolic or psychiatric disorders that are presenting symptoms mistaken for schizophrenia DSM 5 diagnostic examination.					
)	To assess the key cognitive demains relevant to schizophrenia: Measurement and Treatment Research to Improve Cognition in Schizophrenia (MA- TRICS).					

paranoia and delusional disorders should be evaluated with the PQ-B. The PQ-B should be used aggressively during active duty at the lowest threshold of schizophrenia symptomatology in garrison. This is most critical when an active duty soldier is being evaluated for PTSD in a combat theater [37,62].

At admission to the Veterans Affairs Medical Centers, during primary care team admissions, all veterans should be screened for schizophrenia by clinical technicians, nurses or social workers utilizing the PQ-B. If positive, the veteran would have a consult to psychiatry. Psychiatry would perform the routine schizophrenia screen utilizing DSM 5 diagnostic criteria. All other biologic and psychiatric disorders which could present with signs and symptoms similar to schizophrenia would need to be ruled out. A positive result would benefit from an assessment of the key cognitive domains relevant to schizophrenia using the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) assessment tool [68]. This assessment will enable the treatment team to better meet the needs of the veteran for intermediate and future care.

#### Conclusions

Many young soldiers experience their prodromal and early manifestations of schizophrenia prior to enlistment or after joining the United States armed forces. The schizophrenia often goes undetected clinically until during or after basic training. The diagnosis of schizophrenia spectrum and other psychotic disorders most often ends the soldiers' military careers prematurely. The result is a substantial financial burden for the United States military and for the individual. Studies suggest that schizophrenia is under diagnosed prior to enlistment, during active duty, particularly in combat theaters. A more efficient screening process for schizophrenia would reduce the number of military recruits with nascent schizophrenia reaching active duty where a diagnosis of schizophrenia reduces the ability of United States Armed Forces to meet their mission expectations and goals.

The benefits of better screening would include reducing the number of recruits with schizophrenia reaching active duty and early diagnosis and treatment for the individuals diagnosed with schizophrenia. It is proposed that the potential cost savings of a more comprehensive screening protocol for schizophrenia for the United States armed forces and the United States Government may outweigh the cost of losing soldiers from active duty and paying them lifetime service connected schizophrenia disability payments each month until their death.

Test	Administration time	Description	Objective 1	Objective 2	Objective 3
Primary Care Physician and/or Psychologist or Psychiatrist	Results to be taken to the military recruiter	Psychological assessment from electronic medical records of recruit	Recruit psychological history	Family psychological history	Include urine drug screen withir the last 2 months
Raven's Standard Progressive Matrices (53,54)	Untimed, individual or group: 20-45 minutes	60-item test: 5 sets of visual geometric designs with a missing piece of 12 items each; increasing difficulty within each set	Non-verbal estimate of fluid intelligence	Ability to think clearly	Observation skills
Prodromal Questionnaire Brief Version (64)	5 – 10 minutes	16 self-reported true/false items that screen for the risk of psychosis	9 items assess perceptual abnormalities and hallucinations	5 items assess unusual thought content, delusional ideas, paranoia	2 items assess negative symptoms
Brief Cognitive Assessment Tool for Schizophrenia (67)	15 minutes	3 tests commonly included in comprehensive cognitive batteries administered to patients with schizophrenia	Verbal fluency	Trails A and B	Hopkins Verbal Learning Test
Single nucleotide polymorphism (SNP) in the gene SLC1A1 on chromosome 9p24 (65)		Association of schizophrenia with glutamate transporter genes with the glutamate receptor genes	Association of schizophrenia with a genotype of SNP4	Glutamate transporter genes SLC1A6 encoding the glutamate transporters EAAT4	
MATRICS Consensus Cognitive Battery (68)	60 to 90 minutes	10 tests that measure 7 cognitive domains	Brief evaluation of key cognitive domains relevant to schizophrenia and related disorders	Speed of processing; attention/vigilance; working memory; verbal learning	Visual learning; reasoning and problem solving; social cognition

Schizophrenia in US Armed Forces Recruits, Active Duty Soldiers and Veterans.

#### References

- 1. Young Adults Often Begin Military Service at an Age When Schizophrenia Symptoms Begin to Manifest. US Medicine (2009).
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5<sup>th</sup> ed). Washington, DC (2013).
- Chong HY, Teoh SL, Wu DB, et al. Global economic burden of schizophrenia: a systematic review. *Neuropsychiatr .Dis. Treat* 12(1), 357-373 (2016).
- Soldiers with Injuries, Schizophrenia, PTSD, and Brain Trauma are Left in Neglect. Schizophrenia.com (2007).
- Thorp SR, Sones HM, Danielle Glorioso D, et al. Older Patients With Schizophrenia: Does Military Veteran Status Matter? Am. J. Geriatr. Psychiatry 20(3), 248-256 (2012).
- 6. McEvoy JP. The costs of schizophrenia. J. *Clin. Psychiatry* 68(Suppl 14), 4-7 (2007).
- Watkins KE, Pincus HA, Smith B, et al. Veterans Health Administration Mental Health Program Evaluation: Capstone Report, Santa Monica, Calif.: RAND Corporation, TR-956-VHA (2011).

- Mental Health: Schizophrenia. Health Services Research & Development. US Department of Veterans Affairs (2016).
- Bottas A, Cooke RG, Richter MA. Comorbidity and pathophysiology of obsessive-compulsive disorder in schizophrenia: is there evidence for a schizo-obsessive subtype of schizophrenia? J. Psychiatry. Neurosci 30(3), 187-193 (2005).
- 10. Zink M, Englisch S, Meyer-Lindenberg A. Polypharmacy in schizophrenia. *Curr. Opin. Psych* 23(2), 103-111 (2010).
- 11. Zink M. Comorbid Obsessive-Compulsive Symptoms in Schizophrenia: Insight into Pathomechanisms Facilitates Treatment. *Adv. Med* 42(1), 28-38 (2014).
- Attademo L, Bernardini F, Quartesan R. Schizo-Obsessive Disorder: A Brief Report of Neuroimaging Findings. *Psychopathology* 49(1), 1-4 (2016).
- 13. Klosterkötter J, Hellmich M, Steinmeyer EM, et al. Diagnosing Schizophrenia in the Initial Prodromal Phase. Arch. Gen. Psychiatry 58(2), 158-164 (2001).
- 14. Jakob H, Beckmann H. Prenatal

developmental disturbances in the limbic allocortex in schizophrenics. J. Neu. Trans 65(3-4), 303-326 (1986).

- Raedler TJ, Knable MB, Weinberger DR. Schizophrenia as a developmental disorder of the cerebral cortex. *Curr. Opin. Neurobiol* 8(1), 157-161 (1998).
- Schizophrenia's genetic skyline rising. Suspect common variants soar from 30 to 108 – NIH-funded study. National Institute of Health (2014).
- Tan HY, Callicott JH, Weinberger DR. Dysfunctional and Compensatory Prefrontal Cortical Systems, Genes and the Pathogenesis of Schizophrenia. *Cereb. Cortex* 17(suppl 1), i171-i181 (2007).
- Luo L, Callaway EM, Svoboda K. Genetic Dissection of Neural Circuits. *Neuron* 57(5), 634-660 (2008).
- Emsley R, Chiliza B, Asmal L. The evidence for illness progression after relapse in schizophrenia. *Schizophr. Res* 148(1-3), 117-121 (2014).
- 20. Sekar A, Biala AR, de Rivera H, D, *et al*. Schizophrenia risk from complex

Screening for Schizophrenia in Recruits, Active Duty Soldiers and Veterans: Can we do a Better Job? Research

variation of complement component. *Nature* 530(7589), 177–183 (2016).

- 21. Wise RA. Dopamine, learning and motivation. *Nat. Rev. Neurosci* 5(6), 483-494 (2004).
- 22. Slifstein M, van de Giessen E, Van Snellenberg J, et al. Deficits in prefrontal cortical and extrastriatal dopamine release in schizophrenia: a positron emission tomographic functional magnetic resonance imaging study. JAMA. Psychiatry 72(4), 316-324 (2015).
- Bushe CJ, Taylor M, Haukka J. Mortality in schizophrenia: a measurable clinical endpoint. *J. Psychopharmacol* 24(4 supplement), 17-25 (2010).
- 24. Stern Y. The Concept of Cognitive Reserve: A Catalyst for Research. J. Clin. Exp. Neuropsychol 25(5), 589-593 (2003).
- Keshavan MK, Eack SM, Wojtalik JA, et al. A Broad Cortical Reserve Accelerates Response to Cognitive Enhancement Therapy in Early Course Schizophrenia. Schizophr. Res 130(1-3), 123-129 (2011).
- 26. Pol H, Oak S. War & Military Mental Health, The US Psychiatric Response in the 20th Century. *Am. J. Public. Health* 97(12), 2132-2142 (2007).
- 27. Vollmer-Larsen A, Handest P, Parnas. Reliability of measuring anomalous experience: the Bonn Scale for the Assessment of Basic Symptoms. *Psychopathology* 40(1), 345-348 (2007).
- O'Donovan, Ripke S, Neale BM, et al. Biological insights from 108 schizophrenia-associated genetic loci. Nature 511(7510), 421-427 (2014).
- 29. University of North Carolina School of Medicine. Brain Imaging Study May Hold Clues To Onset Of Schizophrenia In People At High Risk. Science Daily (2005).
- Cardona RA, Ritchie EC. U.S. military enlisted accession mental health screening: history and current practice. *Mil. Med* 172(1), 31-35 (2007).
- 31. Nock MK, Stein MB, Heeringa SG, et al. Prevalence and Correlates of Suicidal Behavior among Soldiers: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). JAMA. Psychiatry 71(5), 514-522 (2014).
- 32. Kessler RC, Heeringa SG, Stein MB, et al. Thirty-Day Prevalence of DSM-IV Mental Disorders Among Nondeployed Soldiers in the US Army: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). JAMA. Psychiatry 71(5), 504-513 (2014).
- 33. Schoenbaum M, Kessler RC, Gilman SE, et al. Predictors of Suicide and Accident Death in the Army Study to Assess Risk and Resilience in Service members (Army STARRS): Results from the Army Study to Assess Risk and

Resilience in Service members (Army STARRS). JAMA. Psychiatry 71(5), 493-503 (2014).

- 34. Military Ignores Mental Illness. Today in the Military (2006).
- Copeland LA, Zeber JE, Rosenheck RA, et al. Unforeseen inpatient mortality among veterans with schizophrenia. *Med. Care* 44(2), 110-116 (2006).
- 36. Birgenheir DG, Ilgen MA, Bohnert AA, et al. Pain conditions among veterans with schizophrenia or bipolar disorder. Gen. Hosp. Psychiatry 35(5), 480-484 (2013).
- Boyle AM. Making the Diagnosis: PTSD with Psychosis, Schizophrenia or Both? U.S. Medicine, Department of Veterans Affairs (2016).
- 38. Glick ID, Poyurovsky M, Ivanova O, et al. Aripiprazole in schizophrenia patients with comorbid obsessive-compulsive symptoms: an open-label study of 15 patients. J. Clin. Psychiatry 69(12), 1856-1859 (2008).
- Poyurovsky M, Weizman A, Weizman R. Obsessive-compulsive disorder in schizophrenia: clinical characteristics and treatment. *CNS. Drugs* 18(14), 989-1010 (2004).
- 40. Hasan A, Falkai P, Wobrock T, *et al.* World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Schizophrenia, Part 2: update 2012 on the long-term treatment of schizophrenia and management of antipsychotic-induced side effects. *World. J. Biol. Psych* 14(1), 2-44 (2013).
- 41. Hargreaves S. NICE guidelines address social aspect of schizophrenia. *BMJ* 326(7391), 679 (2003).
- 42. Bloch MH, Landeros-Weisenberger A, Kelmendi B, et al. A systematic review: antipsychotic augmentation with treatment refractory obsessive-compulsive disorder. *Molecular. Psych* 11(7), 622-632 (2006).
- 43. Fineberg NA, Gale TM, Sivakumaran T. A review of antipsychotics in the treatment of obsessive compulsive disorder. *J. Psychopharmacology* 20(1), 97-103 (2006).
- 44. Dold M, Aigner M, Lanzenberger R, et al. Efficacy of antipsychotic augmentation therapy in treatment-resistant obsessivecompulsive disorder a meta-analysis of double-blind, randomised, placebocontrolled trials. Fortschritte. Der. Neurologie. Psychiatrie 79(8), 453-466 (2011).
- 45. Friedman MJ. Acknowledging the Psychiatric Cost of War. *New. Eng. J. Med* 351(1), 75-77 (2004).
- 46. Difficulties in Detecting Schizophrenia Can Have Serious Consequences in Military Setting. (2011)
- 47. Lehmann C. Military Psychiatrists Must Determine If Soldiers Can Return to Duty.

Psychiatric. News (2005)

- 48. Salmon TW. The Insane Veteran and a Nation's Honor. American Legion Weekly (1921).
- 49. Bailey P. Detection and Elimination of Individuals with Nervous or Mental Disease: Principles Underlying Neuropsychiatric Examinations, in Neuropsychiatry, ed. Pearce Bailey, Frankwood E. Williams, and Paul O. Komora, The Medical Department of the United States Army in the World War; Washington, DC: US Government Printing Office (1929).
- Farrell MJ, Appel JW. Current Trends in Military Neuropsychiatry. Am. J. Psychiatry 101(1), 19 (1944).
- 51. Sullivan HS. Psychiatry and the National Defense. *Psychiatry* 4(1), 201-217 (1941).
- 52. Sullivan HS. Mental Hygiene and National Defense: A Year of Selective-Service Psychiatry. *Ment. Hygiene* 26(1), 7-14 (1942).
- 53. Flynn JR. Massive IQ Gains in 14 Nations: What IQ Tests Really Measure? *Psychol. Bull* 101(2), 171-191 (1987).
- 54. Bilker WB, Hansen JA, Brensinger CM, *et al.* Development of abbreviated nine-item forms of the Raven's standard progressive matrices test. *Assessment* 19(3), 354-369 (2012).
- 55. Gheorge MD, Baloescu A, Grigorescu G. Premorbid cognitive and behavioral functioning in military recruits experiencing the first episode of psychosis. *CNS. Spectr* 9(8), 604-606 (2004).
- 56. Hoge CW, Castro CA, Messer SC, *et al*. Combat Duty in Iraq and Afghanistan, Mental Health Problems, and Barriers to Care. *N. Engl. J. Med* 351(1), 13-22 (2004).
- 57. Pol HEH, Kahn RS. What Happens After the First Episode? A Review of Progressive Brain Changes in Chronically III Patients with Schizophrenia. *Schizoph. Bull* 34(2), 354-366 (2008).
- 58. Adams RS, Larson M, Corrigan JD, et al. Frequent Binge Drinking After Combat-Acquired Traumatic Brain Injury Among Active Duty Military Personnel with a Past Year Combat Deployment. J. Head. Trauma. Rehabil 27(5), 349-60 (2012).
- 59. Candelario J. Interview with Lieutenant Colonel retired former head of the US Army Warrior Transition Medical Center at Fort Bragg, North Carolina, Veterans Affairs Medical Center, Salem, Virginia (2016).
- 60. Tritten TJ. House passes new mental health screening for recruits. Stars and Stripes (2014).
- 61. Insel TR. Rethinking schizophrenia. *Nature* 468(7321), 187-193 (2010).
- 62. O'Conghaile A. DeLisi LE. Distinguishing Schizophrenia from Post-Traumatic Stress Disorder with Psychosis. *Curr. Opin. Psychiatry*

28(3), 249-255 (2015).

- 63. How common is PTSD. National Center for PTSD. U.S. Department of Veterans Affairs.
- 64. Loewy RL, Pearson R, Vinogradov S, *et al.* Psychosis risk screening with the Prodromal Questionnaire — Brief Version (PQ-B). *Schizophr. Res* 129(1), 42-46 (2011).
- 65. Cacabelos R, Martinez-Bouza R. Genomics

and Pharmacogenomics of Schizophrenia. *CNS. Neurosci & Therap* 17(5), 541-565 (2011).

- 66. Hsiao CJ, Hing E, Ashman J. Trends in electronic health record system use among office-based physicians: United States, 2007-2012. Natl. Health. Stat. Report 20(75), 1-18 (2014).
- 67. Cuesta MJ, Basterra V, Sanchez-Torres A, et

*al.* Controversies surrounding the diagnosis of schizophrenia and other psychoses. *Expert. Rev. Neurother* 9(10), 1475-1486 (2009).

68. Nuechterlein KH, Green MF, Kern RS, *et al.* The MATRICS Consensus Cognitive Battery, Part 1: Test Selection, Reliability, and Validity. *Am. J. Psychiatry* 165(2), 203-213 (2008).