The Pharma Loaded US Soldier
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What is the total load on America's soldiers? Since 2001, the modern combatant has endured numerous deployments overseas to Afghanistan and Iraq after a decade of relative peace following the Persian Gulf War in 1990. Across all services, members have engaged in traumatic combat situations with enemy, friendly, and civilian casualties resulting in 13% of OIF/OEF veterans diagnosed with PTSD.[1] US military members are routinely taking up to 19 prescription medications to enhance performance and reduce stress. Military personnel have returned from dangerous deployments to face both public scrutiny about disputed wars and personal struggles with recollections of harrowing ordeals. They encounter barriers to therapeutic interventions, with a priority given to pharmacotherapy. The collateral damage is that 20 veterans die by suicide every day in the US, when current active duty, reserve members, and the National Guard are included. This paper will examine the research for toxic indications in PTSD and postulate on causal factors for military suicides.

Military Suicide Data

The 2018 Department of Defense Suicide Report (DoDSER 2018) details 325 active duty suicides with an additional 1,375 suicide attempts by 1,219 unique individuals. The reserve component reported 81 suicides and the National Guard reported 135 suicides. The 2019 National Veterans Suicide Prevention Annual Report summarizes 6,139 veteran suicides in 2019. Veteran suicides have been increasing annually since 2006. The number of veteran suicides has exceeded 6,000 annually from 2008 to 2017. Military members and veterans have a higher risk of suicide than their civilian counterparts. Veterans ages 18-34 having the highest suicide rate among all military subgroups with an increase of 76% from 2005 to 2017.

Table 1. Population by Rate of Suicide

Population	Rate of Suicide
US Active Duty Military	24.8 per 100,000 (2018)
US Reserve Military	22.9 per 100,000 (2018)
US National Guard	30.6 per 100,000 (2018)
US Civilians age 17-59	18.2 per 100,000 (2018)
US Veterans	27.7 per 100,000 (2017)
US Veterans age 18-34	44.5 per 100,000 (2017)

The two aforementioned reports have detailed the frequency, demographics, event characteristics, basic health information, contextual factors or stressors with each military suicide. These reports are intended for surveillance only and do not provide any analysis of causation.

Number of Deployments

DoDSER 2018 reports that 47% of active duty suicides had zero deployments. The 2019 Veterans Suicide Prevention Annual Report indicates that 919 suicides were from never federally activated reserve units and National Guard. Hazardous duty is a co-factor in PTSD and suicides, but this high rate of military members who have never deployed indicates other potentially non-trauma factors are contributing.

General Health Deterioration

48% of active duty soldiers had visited a Medical Treatment Facility in the 90 days prior to death for general health, not mental health and not substance abuse. Physical health deteriorates with PTSD and should be included as a signal for suicide risk screening.

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[1] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

"*Decline in overall health over time may be associated with PTSD. Iraq and Afghanistan veterans of both sexes (n = 72,567) with PTSD had increased cardiovascular risk factors including tobacco use, hypertension, dyslipidemia, obesity, and diabetes compared with controls without a mental disorder (Cohen, Marmar, Ren, Bertenthal, & Seal, 2009) (refer to Table 3). Each increase in level of combat-related PTSD symptoms was associated with increased cardiovascular disease for angina, nonfatal myocardial infarction, and fatal coronary heart disease in the Normative Health Study (Kubzansky, Koenen, Spiro, Vokonas, & Sparrow, 2007). U.S. veterans 55 years and older (n = 181,093) were twice as likely to develop dementia with PTSD, even without substance use disorders and depression, compared with those without PTSD (Yaffe et al., 2010). Association of PTSD with physical disease is not limited to slowly evolving geriatric manifestations. Early onset of hypertensive, circulatory, digestive, nervous, and musculoskeletal system disease was also documented in young U.S. veterans (n = 4,416) with PTSD within the first 5 years post-deployment (Anderson, Wade, Possemato, & Ouimette, 2010).*" [2]

"*Many genes associated with the immune system defense are inactive in those with PTSD (n = 23) leaving them more vulnerable to disease development compared with controls without trauma (n = 97) (Uddin et al., 2010). Poor health outcomes associated with mental health disorders may also contribute to prolonged suicide risk in veterans despite treatment (Valenstein et al., 2009).*" [3]

Age Risk

Veterans age 18-34 have the highest suicide rates at 45 per 100,000, while veterans age 55-74 had the lowest suicide rate at 27 per 100,000. Younger veterans have a greater risk, which should be investigated for an exposure(s) that older veterans do not have.

The increasing trend of military suicides in the US began in 2006 and is temporally correlated with the Pentagon's 2006 policy that permitted and encouraged SSRI medications, discussed in *America's Medicated Army*.

"*It wasn't until November 2006 that the Pentagon set a uniform policy for all the services. But the curious thing about it was that it didn't mention the new antidepressants. Instead, it simply barred troops from taking older drugs, including "lithium, anticonvulsants and antipsychotics." The goal, a participant in crafting the policy said, was to give SSRIs a "green light" without saying so. Last July, a paper published by three military psychiatrists in Military Medicine, the independent journal of the Association of Military Surgeons of the United States, urged military doctors headed for Afghanistan and Iraq to "request a considerable quantity of the SSRI they are most comfortable prescribing" for the "treatment of new-onset depressive disorders" once in the war zones. The medications, the doctors concluded, help "to 'conserve the fighting strength,'" the motto of the Army Medical Corps.*" [4]

Number of Prescription Drugs

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[2] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

[3] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

[4] Thompson, M. (2008, June 16). America's Medicated Army. *Time*, *171*(24), 38

A Veteran Affairs study of 157 veterans with PTSD reported veterans' medical records documented a mean use of 6.4 ± 3.8 prescribed drugs with a maximum of 19 prescribed drugs.[5] These drugs were from the following 17 categories: anti-depressants, anti-psychotics, anxiolytics, hypnotics, mood stabilizers, stimulants, anti-cholinergics, anti-convulsants, anti-hypertensives, diuretics, cardiovascular drugs, diabetes drugs, dyslipidemia drugs, analgesics, anti-inflammatory drugs, gastrointestinal drugs, and narcotics.

Military members are at risk of cascading prescriptions due to treatment from numerous doctors over their careers. They are not likely to have one primary doctor reviewing their medical file for drug interaction or cumulative effect. Veterans are especially at risk of cascading prescriptions. As people get older, they become more sensitive to drugs, as medications stay in the body longer due to less muscle, the liver and kidney do not process medications as effectively, and medications become more concentrated.

Stimulants and PTSD

Prescription Stimulants and PTSD Among U.S. Military Service Members reported the risk of PTSD was significantly higher in military personnel who were prescribed stimulants than those who did not. The risk of PTSD was significantly higher as the number of prescription stimulants increased and the cumulative days of use increased.[6]

Among 25,971 military personnel, with "incident PTSD" defined as those who did not have a history of PTSD at baseline and developed new-onset PTSD, stimulants contribute to new-onset PTSD.

> *"We found an association between prescription stimulant use and incident PTSD. Even though only a small percentage of our sample were prescribed stimulants, our findings suggest that stimulants may be a contributing factor for incident PTSD. The use of stimulants is known to increase norepinephrine levels in the brain and previous research has demonstrated that increased noradrenergic levels at the time of a traumatic event create more vivid, long-lasting memories and fear of the event, which increase the risk of developing PTSD* (*Debiec et al., 2011).*"[7]

Polypharmacy screening

Blanchfield Army Community Hospital (BACH) Polypharmacy Clinic reports "The increased use of central nervous system depressants (CNSD) and psychotropics are one of the many factors that contribute to suicidal behavior in soldiers."[8] Fort Campbell reported polypharmacy (chronic use of 5 or more drugs) ranged from 2.2% to 7.6% of soldiers for each brigade, after screening out soldiers using polypharmacy short-term for surgery medications.

> "*A pharmacy-led team established the Polypharmacy Clinic (PC) at Blanchfield Army Community Hospital. Of the 3,999 soldiers assigned, 540 (13.5%) met the initial screening criteria. Success of the pilot program led to the mandatory screening of all other Fort Campbell, Kentucky, brigades. During the first 12 months, 895 soldiers were seen by a clinical pharmacist, and 1,574 interventions were documented. Significant interventions included medication added (121), medication changed (258), medication stopped (164), lab monitoring recommended (172), adverse reaction mitigated (41), therapeutic duplication prevented (61), and drug-drug interaction identified (93).*

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[5] Vieweg, W. V. R., Julius, D. A., Bates, J., Quinn, J. F., Fernandez, A., Hasnain, M., & Pandurangi, A. K. (2007). Posttraumatic stress disorder as a risk factor for obesity among male military veterans. *Acta Psychiatrica Scandinavica*, *116*(6), 483–487. https://doi.org/10.1111/j.1600-0447.2007.01071.

[6] Crum-Cianflone, Nancy et al. (2015). Prescription Stimulants and PTSD Among U. S. Military Service Members. *Defense & Aerospace Week*, 154.

[7] Crum-Cianflone, Nancy et al. (2015). Prescription Stimulants and PTSD Among U. S. Military Service Members. *Defense & Aerospace Week*, 154.

[8] Ridderoff, Kevin et al. (2015). Blanchfield Army Community Hospital Polypharmacy Clinic. *J Manag Care Pharm.* 21(1):8-11.

Additionally, 55 soldiers were recommended for temporary duty profiles based on their adverse drug effects. Ten soldiers were recommended for enhanced controlled substance monitoring." [9]

895 soldiers were potentially saved from polypharmacy adverse reactions. Despite the Office of the Surgeon General directing this unprecedented polypharmacy screening pilot program at Fort Campbell, the extent to which this successful program was adopted by all military duty stations or continued beyond 2013 is unknown. *The 2018 VA Office of Mental Health and Suicide Prevention Guidebook* does not list polypharmacy screening as an intervention. The VA only targets one prescription drug, opioids, in the Substance Abuse Disorder program. The VA assisted 10,500 veterans in 2017 with opioid substitution.[10]

Pain Medications and Risk

The Army's Health Promotion, Risk Reduction, and Suicide Prevention Report (2010) reports that 14% of the force is taking an opiate medication, often in addition to prescriptions for depression and anxiety. Research of pain medication and PTSD has found "Those with PTSD had significantly higher use of analgesic medication (both opiate and non-opiate), as compared with non-PTSD patients. PTSD symptoms, as measured by the Posttraumatic Symptom Scale, were significantly higher in subjects who were prescribed analgesics."[11] Among veterans, suicide rates were highest VHA patients diagnosed with opioid use disorder.

SSRI Medications in PTSD

SSRI medications have become the first line of response to mental health disorders, with mixed results in research that is influenced by the source of the research, often the pharmaceutical companies.

"…the Institute of Medicine (IOM) (2008) found inadequate evidence to support efficacy of pharmacotherapy and cited bias from dependence on funding by pharmaceutical manufacturers for most studies. Half of the 14 studies from 1980 to June 2007 demonstrated no benefit for PTSD from SSRIs." [12]

In PTSD research, SSRI medications such as paroxetine and sertraline have demonstrated only moderate efficacy with a 53-60% response rate compared to placebos with a 32-38% response rate. [13] However, these medications have not demonstrated efficacy in combat-related PTSD with the following outcomes: no significant improvement over placebos, side effects, and failure to improve hyperarousal.

"*However, in contrast to the studies that demonstrated efficacy for SSRIs in PTSD, clinical studies for combat-related PTSD, involving veterans seeking treatment in*

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[9] Ridderoff, Kevin et al. (2015). Blanchfield Army Community Hospital Polypharmacy Clinic. *J Manag Care Pharm.* 21(1):8-11.

[10] Veterans Health Administration (2018). VA Office of Mental Health and Suicide Prevention Guidebook. Washington, DC.

[11] Schwartz, Ann et al. (2006). Pain Medication Use Among Patients With Posttraumatic Stress Disorder**.** *Psychosomatics*. 47(2): 136–142. doi:10.1176/appi.psy.47.2.136.

[12] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

[13] Kelmendi, B., Adams, T. G., Yarnell, S., Southwick, S., Abdallah, C. G., & Krystal, J. H. (2016). PTSD: from neurobiology to pharmacological treatments. *European Journal of Psychotraumatology*, *7*, 1–N.PAG. https://doi.org/10.3402/ejpt.v7.31858

Department of Veterans Affairs (VA) hospital, have shown mixed results. In a double-blind placebo-controlled 10-week study of 42 military veterans with combat-induced PTSD, sertraline resulted only in non-statistically significant improvement (Zohar et al., 2002). In another double-blind placebo-controlled study, 12 weeks of flexible doses of sertraline (25--200 mg/day) did not demonstrate to be efficacious in the treatment of PTSD in 196 patients recruited from 10 different VA medical centers (Friedman, Marmar, Baker, Sikes, & Farfel, 2007). Given these findings, unsurprisingly, recent guidelines on the treatment of PTSD question the recommendation of SSRIs for veterans with combat-related PTSD (Benedek, Friedman, Zatzick, & Ursano, 2009)." [14]

Anti-depressant Medications in PTSD

Anti-depressants (MAOIs,TCAs, SNRIs, NDRIs) are the most commonly prescribed medications for the treatment of PTSD but the shortcomings include low remission rates of 30%, non-responders, residual symptoms, and long term side effects such as changes in appetite and weight, gastrointestinal disturbances, and loss of sexual drive.

"*The first double-blind placebo-controlled trial of anti-depressants [phenelzine, a monoamine oxidase inhibitor, and imipramine, a tricyclic antidepressant] showed both medications to be superior to placebo in patients with PTSD (Frank, Kosten, Giller, & Dan, 1988). However, due to the side effects associated with these classes of antidepressants, they are less commonly prescribed in clinical practice. In a 12-week double-blind study, extended-release (ER) venlafaxine, a serotonin norepinephrine reuptake inhibitor (SNRI), as well as sertraline was performed in patients with PTSD (Davidson et al., 2006). A total of 538 subjects were randomly assigned to receive venlafaxine ER, sertraline, or placebo. Of the 350 who completed the study, remission rates were 30.2% for venlafaxine ER (PB0.05 vs. placebo), 24.3% for sertraline, and 19.6% for placebo. In another study, 6 months of flexible doses of venlafaxine ER resulted in greater rates of remission (50.9%) compared with placebo (37.5%) (Davidson et al., 2006). In both studies, venlafaxine ER failed to improve hyperarousal symptoms."* [15]

Some anti-depressants have not proven better than placebos in veterans with PTSD.

"*No difference was found between placebo (n = 26) and fluoxetine (n = 26) in veterans with PTSD (van der Kolk et al., 2007) and placebo (n = 83) and sertaline (n = 86) in veterans with PTSD (Friedman, Marmar, Baker, Sikes, & Farfel, 2007).*" [16]

Venlafaxine and other anti-depressants can increase the risk of suicide in adolescents. This has dire implications for young military members.

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[14] Kelmendi, B., Adams, T. G., Yarnell, S., Southwick, S., Abdallah, C. G., & Krystal, J. H. (2016). PTSD: from neurobiology to pharmacological treatments. *European Journal of Psychotraumatology*, *7*, 1–N.PAG. https://doi.org/10.3402/ejpt.v7.31858

[15] Kelmendi, B., Adams, T. G., Yarnell, S., Southwick, S., Abdallah, C. G., & Krystal, J. H. (2016). PTSD: from neurobiology to pharmacological treatments. *European Journal of Psychotraumatology*, *7*, 1–N.PAG. https://doi.org/10.3402/ejpt.v7.31858

[16] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

"…use of the serotonin–norepinephrine reuptake inhibitor, venlafaxine, with benzodiazepines in SSRI resistant depression in adolescents (n = 334) was associated with a higher rate of suicide and suicide attempts (Brent et al., 2009). [17]

Sleep medications are also commonly prescribed adjunctive medications for night terrors in PTSD. In a 15-week trial of 46 active duty members who had acquired PTSD from combat in Iraq and Afghanistan, a Prazosin treatment group showed reduced trauma nightmares, improved sleep quality, and improved global functioning in the treatment group compared to the placebo group. [18] Adverse effects included syncope, lightheadedness, nasal congestion, palpitations, drowsiness, muscle weakness, and headaches. The 15-week length of this trial does not provide insightful precautions on the long-term side effects in duration, frequency, and severity. 20 of the participants were concurrently taking SSRI medications, which have demonstrated in studies to degrade sleep in efficiency, time, continuity, depth, and wave. This is an example of cascading prescriptions, when a patient who has sleep deprivation side effects from SSRIs is prescribed a sleep inducing NDRI medication to counteract a drug side effect.

GABAergics drugs and PTSD

GABAergic drugs are widely prescribed and yet trials have indicated low efficacy with side effects, tolerance issues, addictive potential, as well as adverse effects on neurocognitive functioning.

"*Benzodiazepines are a very popular form of treatment for PTSD, but their use is in decline (Lund, Bernardy, Alexander, & Friedman, 2012) due to addictive potential. While helpful for insomnia and anxiety (Lund et al., 2012), benzodiazepines are not effective for avoidance and dissociation (Viola et al., 1997), impair fear extinction (Rothbaum et al., 2014), and can reduce the effectiveness of exposure therapy (van Minnen, Arntz, & Keijsers, 2002). The 2010 VA/DoD Clinical Practice Guideline discouraged the use of benzodiazepines for the treatment of both acute stress disorder and PTSD, citing evidence that risks outweigh benefits and that benzodiazepines might worsen recovery from trauma (VA/DoD, 2010). Eszopiclone--a high affinity GABA-A receptor agonist-- has been shown to significantly improve sleep disturbance associated with PTSD (Pollack, Jensen, Simon, Kaufman, & Renshaw, 2008). GABAergic anticonvulsants are also often prescribed for PTSD-related symptoms, but results have not been uniform. One large placebo-controlled study of tiagabine found no significant effect of the drug on PTSD, depression, or functional impairment (Davidson, Brady, Mellman, Stein, & Pollack, 2007). Divalproex was similarly shown to have no significant effect on PTSD symptoms (Hamner et al., 2009). In a small international trial, topiramate was reported to significantly reduce PTSD symptoms (Yeh et al., 2011), but these results have yet to be replicated.*" [19]

Of the GABA targeting drugs summarized above that showed efficacy in PTSD research, Eszopiclone (Lunesta by brand name) has shown to improve sleep disturbance while creating substantially more health risks for the patient. Side effects include headache, dry mouth, rash, itching, frequent urination, peripheral edema, dizziness, impaired coordination, and daytime drowsiness. Severe side effects include depression, suicidal thoughts, hallucinations, confusion, abnormal thinking, sleep driving and sleep walking, agitation, aggressive behavior, depersonalization, and amnesia. Eszopiclone is classified as a non-BZD sedative hypnotic and decreasing dose can result in withdrawal. Prescribing an

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[17] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

[18] Raskind, M. et al. (2013) A Trial of Prazosin for Combat Trauma PTSD With Nightmares in Active-Duty Soldiers Returned From Iraq and Afghanistan. *The American Journal of Psychiatry*, 170 (9), 1003-1010.

[19] Kelmendi, B., Adams, T. G., Yarnell, S., Southwick, S., Abdallah, C. G., & Krystal, J. H. (2016). PTSD: from neurobiology to pharmacological treatments. *European Journal of Psychotraumatology*, *7*, 1–N.PAG. https://doi.org/10.3402/ejpt.v7.31858

addictive drug with suicidal ideation as a side effect to a patient with PTSD is irresponsible and yet common.

Topiramate (Topamax by brand name) is anti-convulsant drug created for seizures, but used off-label for migraines, bipolar, obesity, and alcoholism. It is also prescribed to counter the weight gain from the side effects of anti-psychotic drugs. Despite having serious adverse effects of suicide and encephalopathy, Topiramate is listed in the *VA/DOD 2015 Clinical Practice Guideline for the Management of Substance Use Disorders* as a "strong" recommendation.

Alternative Medications for PTSD

Emerging research shows that ocytocin, a hormone, and cannabis, a plant derived medication, are promising adjunctive medications to therapy without the adverse side effects of anti-depressant medications.

> "[Ocytocin] is well known for its pro-social effects and anxiolytic properties and it has been suggested as promising psychological intervention to enhance treatment response in PTSD (Olff et al., 2014)." [20]

> "One un-controlled, cross-sectional, retrospective self-report study found that individuals with significant posttraumatic stress symptoms reported that their symptoms were 75% less severe when they were using cannabis compared with when they were not (Greer, Grob, & Halberstadt, 2014). Cannabis has been reported to be particularly helpful to persons with severe traumatic intrusions (Bonn-Miller, Boden, Bucossi, & Babson, 2014) and has been shown to help manage hyperarousal symptoms (Bremner et al., 1996)." [21]

Therapies for PTSD

Cognitive Behavioral Therapy (CBT) and Cognitive Processing Therapy (CPT) are two of the most effective therapies for PTSD and have demonstrated higher remission rates in PTSD than pharmaceutical medications.

> "*CBT usually involves prolonged exposure, repeatedly recalling a traumatic event until emotional response tapers to allow cognitive confrontation of the trauma. Two additional forms of CBT commonly used are cognitive restructuring, the process of verbalizing, challenging, and replacing erroneous thoughts with balanced ones; and stress inoculation training, a process of reducing anxiety and enhancing coping skills*." [22]

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[20] Kelmendi, B., Adams, T. G., Yarnell, S., Southwick, S., Abdallah, C. G., & Krystal, J. H. (2016). PTSD: from neurobiology to pharmacological treatments. *European Journal of Psychotraumatology*, *7*, 1–N.PAG. https://doi.org/10.3402/ejpt.v7.31858

[21] Kelmendi, B., Adams, T. G., Yarnell, S., Southwick, S., Abdallah, C. G., & Krystal, J. H. (2016). PTSD: from neurobiology to pharmacological treatments. *European Journal of Psychotraumatology*, *7*, 1–N.PAG. https://doi.org/10.3402/ejpt.v7.31858

[22] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

Prolonged exposure (PE) sessions promote confronting traumatic memories to replace maladaptive avoidance behaviors and PE sessions have resulted in complete remission of combat induced PTSD symptoms and lesser likelihood of taking anti-psychotic drugs.

> "*Prolonged exposure is recommended as most beneficial even with variance in frequency and number of sessions for veterans with combat-induced PTSD (Benedek et al., 2009). U.S. female veterans (n = 277) and active duty personnel (n = 7) treated with 10 sessions of prolonged exposure treatment were more likely to no longer meet PTSD criteria (OR 1.80, 95% CI = 1.10–2.96) and to achieve total remission of PTSD symptoms (OR 2.43, 95% CI = 1.10–5.37) than those treated with present-centered therapy; the present-centered group was also more likely to be taking an antipsychotic at post-treatment (p = .03) (Schnurr, Friedman, & Engel, 2007)."* [23]

Cognitive Processing Therapy helps patients modify maladaptive emotions about traumatic experiences and demonstrates efficacy in 40% of patients with remission of PTSD diagnosis criteria and 50% of clients with reduction in PTSD symptoms.

> "*Significant improvement in PTSD, depression, and Cognitive Distortion Scales for self-criticism, self-blame, helplessness, hopelessness, and preoccupation with danger occurred following 7 weeks of intensive CPT therapy (p < .001 all) in a pretest and posttest study of U.S. veterans (n = 99) in a residential PTSD program (Owens, Chard, & Cox, 2008). Com- pared with U.S. Vietnam veterans (n = 50) with similar clinician assessed pretreatment PTSD scores, OIF/OEF veterans (n = 51) demonstrated significantly lower clinician assessed posttreatment PTSD scores (p < .001), even though they attended significantly fewer CPT sessions (p < .01) (Chard, Schumm, Owens, & Cottingham, 2010). Youth and early treatment may make a difference in treatment efficacy. Even more encouraging, 90% of U.S. veterans (6 women, 54 men) assigned to a 12-session cognitive processing therapy (CPT) composed of cognitive and exposure components showed significant improvement despite long-term PTSD- related disability (40% no longer met PTSD criteria and 50% had reliable reduction in PTSD symptoms; p < .001 both) (Monson et al., 2006)."* [24]

The VA mental health staff offers members both Prolonged Exposure and Cognitive Processing Therapy. The VA also offers medication treatments that may be indicated for a variety of PTSD conditions. There is likely a treatment preference among patients for prescription drugs over evidence-based therapy because of the perceived response effort. Prescription drugs may not be perceived as requiring time off from duty or work, while therapy sessions require lengthy sessions and weekly appointments. However, the daily maintenance of taking numerous prescription drugs and monthly follow-up appointments also require effort and time off from duty and work. Therapies which have demonstrated 100% remission of PTSD symptoms with 10-12 weeks of sessions should be compared to a lifetime of prescription drug maintenance with at most a 60% remission of PTSD symptoms, and with an additional burden of cascading prescriptions and deteriorating physical health. The idea that prescription drug therapy is a quick fix is also negated by the fact that most drugs prescribed for PTSD take weeks to months of use to provide medicinal effects. Stigma of counseling and lack of trained therapists are also barriers to therapy.

Military Guidelines and Clinical Practices Over Time

In 2004, the FDA published two public health advisories warning the public that SSRI medications doubled the risk of suicide risk for both children and young adults ages 18-24, and yet the 2006 Pentagon

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[23] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

[24] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

medication guidelines for depressive disorders allowed widespread prescriptions of SSRI medications that may be contributing to the highest rate of suicide among veterans age 18-34 at 44.5 per 100,000.

> "*Because of concerns about reported cases of suicide in association with the newer antidepressants, the FDA required a re-evaluation of all prior double blind placebo controlled clinical trials conducted on children and youth conducted during the FDA approval process [33]. The selective serotonin reuptake inhibitor (SSRI) antidepressants were re-evaluated including fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft), citalopram (Celexa) and escitalopram (Lexapro). In reports issued by the FDA (e.g. [26]) four other potentially stimulating antidepressants were found to produce similar adverse behavioral and mental effects and were included in the group: venlafaxine (Effexor), mirtazapine (Remeron), bupropion (Wellbutrin or Zyban) and nefazodone (Serzone). The meta-analysis found that the risk of suicidal ideation and behaviors was doubled for children and youth taking the antidepressants compared to placebo (4% versus 2%) [25]*" [25]

In 2008, the IOM reported evidence was adequate for the efficacy of exposure-based therapy but inadequate for other psychotherapy or pharmacotherapy treatments. In 2009, the APA reversed its recommendation for prescribing SSRIs for combat-related PTSD and supported exposure-based therapy.

> "*The American Psychiatric Association's Guideline Watch was issued in 2009, updating rigorous studies published in 2004–2009 on PTSD treatment (Benedek et al., 2009). Evidence supported the efficacy of exposure-based psychotherapy. Contrary to previous clinical practice, routinely prescribing SSRIs with combat-related PTSD was not recommended."* [26]

The VA/DoD publish conflicting guidelines on treatment preference for PTSD in 2010 and 2011.

> "*According to early Department of Veterans Affairs and Department of Defense (VA/DoD) guidelines for Iraq War, a 12-week trial with a SSRI was strongly recommended as first-line treatment for PTSD, and CBT was only suggested (Kudler & Ruzek, 2010)… VA/DoD guidelines release in January 2011 recommend psychotherapy with exposure and/or cognitive restructuring for significant benefit and cite pharmacotherapy as proving either unknown (antidepressants, anticonvulsants, atypical antipsychotics, prazosin, propranolol, and imipramine) or no benefit (benzodiazepines and typical antipsychotics) (Management of Post-traumatic Stress Working Group, 2010).*" [27]

In the past twenty years from 2000-2019, the UK armed forces directed different treatment priorities for PTSD than the US which resulted in a significantly better outcome. In 2005, the UK guidelines for PTSD recommended implementing trauma-focused CBT therapy first, and only using an

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[25] Breggin, P. R. (2010). Antidepressant-induced suicide, violence and mania: Risks for military personnel. *International Journal of Risk & Safety in Medicine*, *22*(3), 149–157. https://doi.org/10.3233/jrs-2010-050

[26] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

[27] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

SSRI if CBT therapy was not sufficient.[28] Conversely, in 2006, the US Pentagon medication policy encouraged a preference for SSRIs medications in PTSD. The UK's treatment preference has correlated with a 2018 rate of 11 per 100,000 suicides in the active armed forces. [29] The US's treatment preference for SSRI's has correlated with a significantly higher 2018 rate of 24.8 per 100,000 suicides in active duty members. The UK and US have similar 2018 rates of suicide in civilians ages 17-59 at 20 per 100,000 in the UK and 18.2 per 100,000 in the US. Among veterans, the UK's unofficial data in the press reports a much lower number of suicides at 75 veteran suicides in 2018,[30] while the US VA/DoD officially reported 6,139 veteran suicides in 2017. The UK Department of Defence reports that military member suicide is a rare event with a total of 306 suicides in the armed forces from 2000-2019,[31] and subsequently the UK does not have a veteran suicide tracking system. As of 2020, the research and data suggest that the US military suicide rate associated with PTSD has been highly exacerbated by a 15-year delay in implementing guidelines across both active duty members and veterans that prioritize evidence-based CBT therapy over pharmaceutical medications.

Causation

In 2010, the US Army announced its hypothesis on the epidemic of suicides summarized below as due to the frenetic pace of Army life.

> "*At first glance, there seemed to be a simple explanation for the increase in suicides: Soldiers were returning from a prolonged, violent war traumatized by their experiences, and some of them took their own lives. While logical, this explanation turned out to be oversimplified. When the Army's Health Promotion, Risk Reduction and Suicide Prevention Task Force studied cases of suicide, it found that most soldiers who had taken their own lives had deployed only once to Iraq, or not at all, and that deployment-related mental-health troubles didn't necessarily correlate with suicides. Instead, the committee found that the pace of Army life, particularly during wartime, produced a hectic stream of trainings, deployments, job changes and relocations that placed soldiers under more stress than their civilian peers but that soldiers most often took their lives for the same reasons that civilians did: failed relationships; careers imperiled by legal trouble or injury; mounting debts; or unmanageable depression, anxiety or substance abuse.*" [32]

While Army pace of life may be a contributing factor to suicides in active duty members, it cannot explain the unacceptably high rate of suicides among veterans. It is also neglectful to mention substance abuse as a factor in military suicides without analysis of the number of prescription medications that veterans consume on a daily basis for long term effect. Military personnel are routinely prescribed

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[28] Lee, E. A. D. (2012). Complex Contribution of Combat-Related Post-Traumatic Stress Disorder to Veteran Suicide: Facing an Increasing Challenge. *Perspectives in Psychiatric Care*, *2*, 108.

[29] Ministry of Defence (2020). Suicides in the UK Regular Armed Forces: Annual Summary and Trends Over Time 1 January 1984 to 31 December 2019.

[30] Roberts, Joe. (2019). "Veteran suicide is a 'hidden epidemic and the government is ignoring it.'" *Metro*. https://metro.co.uk/2019/05/14/veteran-suicide-hidden-epidemic-government-ignoring-9525180/

[31] Ministry of Defence (2020). Suicides in the UK Regular Armed Forces: Annual Summary and Trends Over Time 1 January 1984 to 31 December 2019.

[32] Kiernan, David (2019). "What the military can teach us about preventing suicide." *Washington Post*. https://www.washingtonpost.com/outlook/2019/03/13/what-military-can-teach-us-about-preventing-suicide/

numerous medications with Black Box warnings for suicidal ideation, mania, psychosis, violent behavior, delusions, hallucinations, and psychotic behaviors. Many of these drugs are addictive and prescribed without a plan to wean off dependency. Instead the needed therapeutic dose will increase over time. New soldiers anecdotally report being prescribed medications for the expected stress of Basic Training, which will begin the cascading prescriptions for deployment induced trauma and pain from injuries, and will cumulate with additional prescriptions as veterans for deteriorating physical health associated with unresolved PTSD symptoms. The total pharmaceutical load on the modern US soldier will continue to result in over 6,000 veteran suicides per year until polypharmacy screening and mitigation is implemented and prioritized at every Veterans Health Administration program. This recommendation also has implications for the mental health epidemic for the civilian population in America.