

ABSTRACT

Title: Antidepressants and the risk of self-harm and unintentional injury among younger veterans

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Background: Suicide and deaths resulting from motor vehicle crashes are the two leading causes of non-hostile death among active duty military personnel. Recently, epidemiological studies have raised questions about whether some classes of antidepressants may increase the risk of these injuries, especially in the early stages of a person's use and among younger-aged cohorts. It is presently unknown whether some antidepressant preparations are safer than others with respect to self-harm and transportation-related injury among active duty military personnel. This issue is highly relevant today since, for the first time in military history, a large number of U.S. combat troops are taking daily doses of antidepressants. For example, data contained in the Army's fifth Mental Health Advisory Team report indicate that about 6% of combat troops in Iraq and 9% of those in Afghanistan are taking prescription antidepressants.

Objective/Hypothesis: This proposal will assess whether some antidepressant classes (e.g., selective serotonin reuptake inhibitors), compared to other antidepressant classes (e.g., tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors), are associated with a disproportionately lower risk of fatal and non-fatal injury due to suicidal behavior and motor vehicle crashes. We will examine when, relative to initiating antidepressant therapy, the risk of suicide and motor vehicle related injury is greatest and identify clinical and policy relevant factors that may modify risk (e.g., PTSD, combat-related injuries, comorbidity, and comedication). Representative hypotheses to be tested include 1) selective serotonin reuptake inhibitors (SSRIs) are associated with a higher risk of completed suicide than are tricyclic antidepressants (TCAs) or serotonin-norepinephrine reuptake inhibitors (SNRIs) during the first month of therapy but not thereafter, 2) the risk of injury resulting from motor vehicle crashes will be higher among users of TCA antidepressants compared to SSRI antidepressants, and 3) hazard ratios will be a) greatest immediately after initiating therapy, b) dose related, and c) modified by patient characteristics such as age, comorbidity, and comedication.

Specific Aims: To determine whether some antidepressant classes (e.g., SSRIs), compared to other antidepressant classes (e.g., SNRIs) are associated with a disproportionately high risk of completed suicide, intentional self harm and fatal and non-fatal motor vehicle-related injury among a cohort of veterans 50 years of age and younger with depression and/or PTSD. Our primary comparisons will be between recent initiators of SSRI vs. TCA vs. SNRI antidepressants. For all these outcomes we will examine the time-varying nature of the risk associated with antidepressant use and identify effect modifiers (e.g., PTSD, generalized anxiety disorder, combat related injuries, comorbidity, and comedication).

Study Design: The proposed study will use the Department of Veterans Affairs' large health care utilization data base linked to National Death Index files and appropriate pharmacoepidemiologic methods to assess the relationship between initiating antidepressant therapy (our exposure of interest) and our outcomes of interest: the risk of suicide, non-fatal intentional self-harm, and mortality and morbidity due to motor vehicle crashes. The study population consists of veterans 50 years of age and younger who received care within the Veterans Affairs Healthcare (VHA) system, 1999-2009. Two parallel cohort studies are

proposed, one for fatal injuries and one for non-fatal injuries. The major antidepressant classes we will compare to one another are the selective serotonin reuptake inhibitors (SSRIs), the tricyclic antidepressants (TCAs), and the serotonin-norepinephrine reuptake inhibitors (SNRIs).

Relevance: Our aims have direct military relevance. Each aim seeks to generate clinical and policy relevant empirical evidence regarding the major risks, benefits and overall effectiveness of the most common form of treatment (i.e., antidepressants) given to soldiers and veterans who are depressed and frequently to soldiers and veterans with PTSD even in the absence of depressive disorders. Our outcomes focus on the two leading causes of non-hostile death among active duty military in the current combat theaters (i.e., suicide and motor vehicle crashes), as well as their non-fatal analogues (i.e., suicide attempts and non-fatal motor vehicle crashes). Our objectives are directly relevant to military clinicians who must balance the risks and benefits of treating soldiers who are at risk of suicide and to policy makers within the DoD who are attempting to strengthen the empirical foundation for interventions to prevent suicide among active duty soldiers and soldiers recently separated from active duty.