

AWARD NUMBER:
W81XWH-12-2-0094

TITLE:
Prazosin Augmentation of Outpatient Treatment of Alcohol Use
Disorders in Active Duty Soldiers with and without PTSD

PRINCIPAL INVESTIGATOR:
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14. ABSTRACT This project is a 12-week randomized controlled trial (RCT) of prazosin for AUD in 200 OIF/OEF soldiers both with and without comorbid PTSD enrolled in the Alcohol and Substance Abuse Program (ASAP) at Madigan Health Care System/Joint Base Lewis McChord. The aims of this trial are 1) to determine prazosin's efficacy for AUD in OIF/OEF soldiers participating in outpatient AUD treatment and 2) to determine if the presence of PTSD affects prazosin efficacy for AUD. In the first year of the study, the protocol was extensively review and recently approved by the VA Puget Sound IRB. This approval was necessary before the Madigan IRB would review the protocol. Madigan IRB has now accepted the study's application and we anticipate their approval by end of November 2013; this would allow an early December 2013 start of participant randomization.					
15. SUBJECT TERMS Nothing Listed					
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This project is a 12-week randomized controlled trial (RCT) of prazosin for alcohol use disorders (AUD) in 200 OIF/OEF soldiers both with and without comorbid PTSD enrolled in the Alcohol and Substance Abuse Program (ASAP) at Madigan Health Care System/Joint Base Lewis McChord. The aims of this trial are 1) to determine prazosin's efficacy for AUD in OIF/OEF soldiers participating in outpatient AUD treatment and 2) to determine if the presence of PTSD affects prazosin efficacy for AUD.

AUD are major causes of behavioral, medical, family, and occupational morbidity in Soldiers returning from OIF and OEF deployment(s). Developing an effective, well-tolerated (and inexpensive) pharmacologic treatment for AUD will directly benefit Soldiers' function and quality of life.

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1. INTRODUCTION:

Alcohol use disorder (AUD) is a common debilitating problem in active duty Service Members and is a frequent comorbidity of posttraumatic stress disorder (PTSD). Our pilot placebo-controlled trial of prazosin in alcohol dependent civilian men seeking abstinence demonstrated significant prazosin efficacy for reducing alcohol drinking.

This project is a 12-week randomized controlled trial (RCT) of prazosin for AUD in active duty soldiers both with and without comorbid PTSD enrolled in the Alcohol and Substance Abuse Program (ASAP) at Madigan HCS/Joint Base Lewis McChord. The aims of this trial are 1) to determine prazosin's efficacy for AUD in OIF/OEF soldiers participating in outpatient AUD treatment and 2) to determine if the presence of PTSD affects prazosin efficacy for AUD. Primary outcome measures will be the Timeline Followback (TLFB) and the Penn Alcohol Craving Scale (PACS) scores. Soldiers completing the 12-week double-blind placebo controlled prazosin RCT will then enter an open label prazosin phase for an additional 12 weeks to allow those randomized to placebo in the RCT phase the opportunity to receive active prazosin treatment. It also will provide observational data regarding the long term durability of prazosin effect on AUD in those randomized to prazosin in the RCT.

2. KEYWORDS:

alcohol use disorder, prazosin, Service Member, PTSD, treatment, randomized controlled trial

3. OVERALL PROJECT SUMMARY:

Complete regulatory approval was received on January 15, 2015, at which time participant recruitment commenced. As of October 6, 2016, we have recruited 244 servicemembers for participation in the study. We have consented 114 servicemembers participating in the JBLM ASAP. Following screening evaluations, 78 servicemembers who met all inclusion and exclusion criteria have been randomized.

Although the recruitment rate has been very good, the long regulatory approval delay (resulting from needing in series IRB approvals first from the VA and subsequently from a Madigan IRB slowed by the Congressional Sequestration) has shortened our time period for completing the study. Therefore, we have further increase recruitment by opening the study to Service Members who are enrolled in ASAP but have not been deployed to combat operations. When the study was first conceived (during our successful RCT of prazosin for combat PTSD in active duty Service Members) the majority of Service Members in garrison at JBLM as well as the majority of those in ASAP for AUD treatment had returned from deployments to Afghanistan and/or Iraq. With the end of OEF deployments, 2/3 of Service Members in Madigan ASAP have not been deployed. As another measure to reach recruitment goals we have recently submitted a formal request for an extension without funding in order to facilitate study completion. The extra 12 months will allow the necessary time to recruit and complete study goals.

4. KEY RESEARCH ACCOMPLISHMENTS:

1. Completed regulatory approval (3 IRBs).
2. Robust recruitment and randomization is underway.

5. CONCLUSION:

Nothing to report.

6. PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

Raskind, MA. Prazosin Augmentation of Outpatient Treatment of AUD in Active Duty Soldiers with and without PTSD. Presented at Joint Army/NIH Substance Abuse IP – September 29-October 1, 2015, Fort Detrick, MD

Presented at National Institute of Alcohol Abuse and Alcoholism Special Symposium at American Psychiatric Association Annual meeting, Toronto, May, 2015

7. INVENTIONS, PATENTS AND LICENSES:

Nothing to report.

8. REPORTABLE OUTCOMES:

Developed administrative and VA/DoD collaborative methodology to perform this first ever randomized controlled trial of a pharmacologic treatment for alcohol use disorder in active duty Service Members..

9. OTHER ACHIEVEMENTS:

Nothing to report.

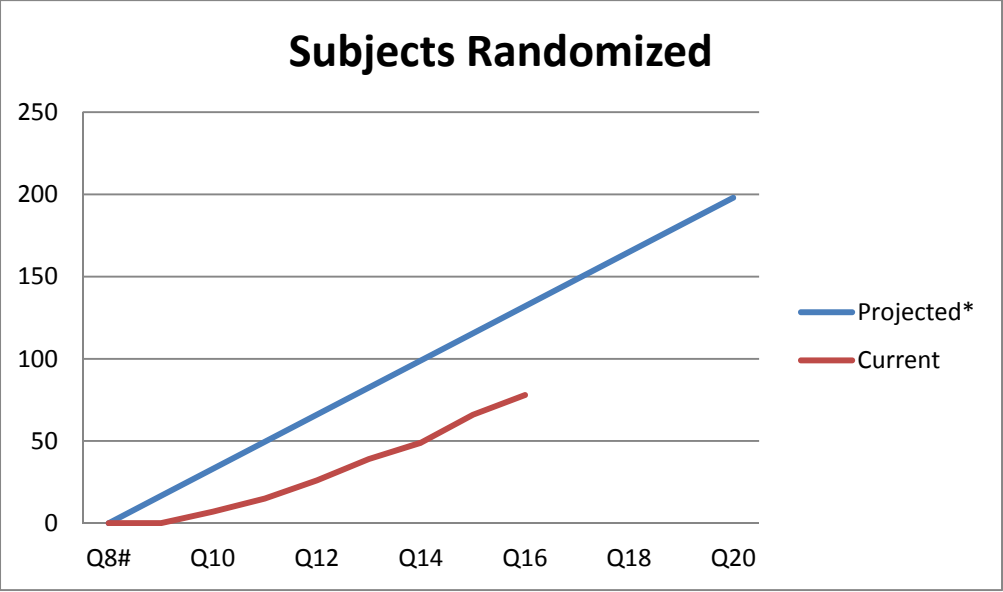
10. REFERENCES:

1. Simpson TL, Saxon AJ, Meredith CW, Malte CA, McBride B, Ferguson LC, et al. A pilot trial of the alpha-1 adrenergic antagonist, prazosin, for alcohol dependence. Alcohol Clin Exp Res. 2009;33(2):255-263.

11. APPENDICES:

Randomization Chart

QUAD CHART: Please see attached.



Prazosin Augmentation of Outpatient Treatment of Alcohol Use Disorders in Active Duty Soldiers with and without PTSD

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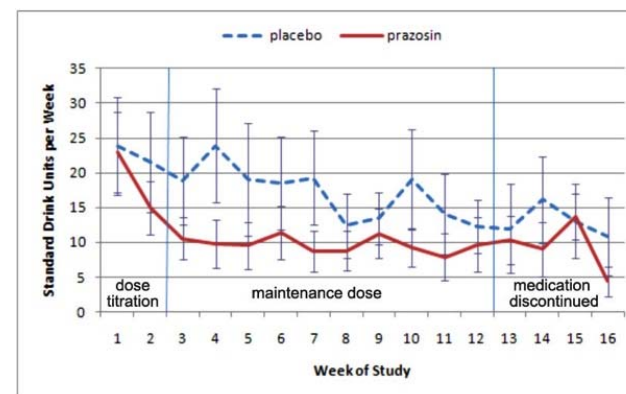


PI: Murray Raskind, MD, VAPSHCS **Org:** Seattle Institute for Biomedical and Clinical Research **Award Amount:** \$1,400,000

Aims / Approach

We will conduct a 12-week RCT of prazosin for alcohol use disorders AUD in soldiers with and without comorbid PTSD to determine prazosin's efficacy for AUD in OIF/OEF soldiers participating in outpatient AUD treatment and to determine if the presence of PTSD affects prazosin efficacy for AUD. . Soldiers completing the 12 week double blind placebo controlled prazosin RCT will then enter an open label prazosin phase for an additional 12 weeks to allow those randomized to placebo in the RCT phase to receive active prazosin treatment. This also will provide observational data regarding the long term durability of prazosin effect on AUD in those randomized to prazosin in the RCT, and the response to initiation in soldiers originally randomized to placebo. Primary outcome measures will be the Timeline Followback (TLFB) and the Penn Alcohol Craving Scale (PACS) scores.

Preliminary Data: Prazosin reduces alcohol consumption in non-PTSD alcohol dependent persons (n=41) seeking abstinence (ongoing NIAAA funded trial at VA Puget Sound).



Timeline and Cost

Activities	Year 1	Year 2	Year 3	Year 4	Ext.
Regulatory Approvals	■	■	■	■	■
Preparatory Tasks	■	■	■	■	■
Subject Recruitment			■	■	■
Enter / Clean Study Data			■	■	■
Data Analysis				■	■
Write and submit results					■
Estimated Budget (\$K)	\$351	\$352	\$300	\$260	\$137

Period of Performance: 09/15/12-10/14/16 / Updated: 10/14/16

Goals/Milestones

☒ ☒ **Regulatory Approvals and Preparatory Tasks**

Completed / In progress

☒ ☐ **Recruitment and Retention Efforts**

☒ ☒ **Recruit and Randomize 30 Subjects**

☒ ☒ **Recruit and Randomize 100 Subjects**

☒ ☐ **Recruit and Randomize 175 Subjects**

☐ ☐ **Recruit and Randomize 200 Subjects**

☐ ☐ **Enter and clean study data** – Not yet initiated

☐ ☐ **Analyses and Evaluation** – Not yet initiated

☐ ☐ **Publish Results** – Not yet initiated

Comments/Challenges/Issues/Concerns – None at this time.

Budget Expenditure to date

Projected Expenditure:\$1,263,000 Actual Expenditure:\$1,268,200