

Wayne State Warriors Marijuana Clinical Research Program: Investigating the Impact of Cannabinoids on Veterans' Behavioral Health

Leslie H. Lundahl, PhD, Lead Principal Investigator
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Project Aims:

In this randomized, controlled clinical trial we are recruiting veterans with PTSD who report using cannabis. **We are conducting two studies that are complementary and linked via their aims and methodology.** In **Study 1**, a minimum of 200 veterans will be randomized into one of four different THC:CBD dose conditions (THC; CBD; THC+CBD, and placebo) for a 12-week treatment phase. In **Study 2**, 150 veterans will be randomized into *one of two groups*: a THC reduction group (n=75), tailored across THC products that are approximately 50% lower in THC than the products participants currently use; or a THC reduction + 1:1 THC:CBD group (n=75), also including tailored THC concentrations as in the first group but with CBD added in a 1:1 THC:CBD ratio. Within each Study 2 treatment group, participants will be randomly assigned on a 1:1 basis to either start the 12-week treatment after a 2-week baseline or a 6-week baseline so we can examine participant naturalistic cannabis use before introducing the new product. **Both studies** involve assessments weekly and bi-weekly throughout a 12-week treatment phase, and at 3-, 6-, 9, and 12-months post-baseline. **Primary outcomes** include clinical assessments of PTSD symptom severity, mood and anxiety symptoms, and suicidality. **Secondary measures** include (1) neurocognitive function; (2) overall health, sleep quality, pain, healthcare utilization, and quality of life; (3) individual differences in fear learning and extinction associated with PTSD symptom severity; (4) saliva for DNA analysis to examine genetic and epigenetic markers associated with the endocannabinoid system; and, (5) urine, blood, and saliva samples to quantify levels of endocannabinoids and their metabolites (e.g., anandamide [AEA] and 2-AG), as well as THC and CBD and their metabolites, to examine whether these levels vary as a function of THC:CBD dose mixtures and differentially affect outcomes. Data will be analyzed to determine which dose conditions might be associated with the outcome measures. These data will be used to (1) develop a predictive algorithm that will help determine personalized profiles of patients who may be at increased risk for suicide; and, (2) develop a profile of who might most benefit from cannabinoid therapeutics.

1). Project Milestones

Study 1 and Study 2 Protocols have been revised and finalized in accordance with discussion with CRA/LARA.

- **Project Progress**

We continue to update our project website (www.warriorCARE.net) regularly. Study 1 is listed on ClinicalTrials.gov, which also provides contact information to enhance referral efforts. Study 2 is in the process of being listed.

Our recruiter continues to maintain contact with Veteran-related organizations we can approach for referrals and events like job fairs, where we can rent exhibition booths for our research staff to answer questions, provide information, conduct initial screening interviews and schedule in-person screening. We also continue to check in with the Veterans on our waitlist, ensuring we can ramp up recruitment quickly once all regulatory requirements are completed. There are two local Veterans Health Fair events in Feb/March 2025 that we will attend.

We have hired and on-boarded one new research staff member who is engaged in study start-up activities, and she will transition to recruitment and data collection once recruitment begins.

The Pharmacology Lab Van has been fully outfitted by Base Camp Van Company and is ready to be deployed for recruitment start up.

As noted in our Q3 report, we submitted our FDA IND application in late June 2024 and received an IND number for the cannabis formulations needed for the trial. However, FDA placed this protocol on a Clinical Hold which prevented us from starting the trial at that time. We submitted our full response to the identified issues, responded to several rounds of requests for additional information, and made both required and recommended changes in the protocol. At present the only remaining issue is the use of our proposed blended cannabis batch (1:1 ratio of THC:CBD) for which FDA is requiring a Certificate of Analysis (CoA). The manufacturer is currently conducting the tests required to issue the CoA and once we receive it we will submit it to FDA with a Complete Hold Response. All protocol changes will be submitted for approval by the WSU IRB, as well.

The DEA Schedule I Protocols will be submitted to the DEA for approval as soon as the clinical hold is lifted and we have IRB approval of any required protocol changes.

• Noteworthy Accomplishments – Identify and describe any milestones reached or noteworthy accomplishments completed during the period.

We received IRB approval for the one-year continuation of both Study 1 (CBH) and Study 2 (TRS) protocol. We are also continuing our ongoing edits of regulatory documentation, including updating our clinicaltrial.gov entries for these projects and amending our IRB Protocols as we make FDA-required protocol changes.

The set up of REDCap data capture for data collection and participant monitoring for Study 1 is complete. Study 2 set up has begun.

Research staff members are continuing to train on all procedures and prepare protocols for all procedures.

All WSU IRB approvals are up-to-date.

2). Delays – Brief description of problems or delays, real or anticipated, which should be brought to the attention of the Grant Administrator.

Until we begin recruitment operations, we continue to operate under reduced salary support for research staff members.

3). Statement concerning any significant deviation from previously agreed-upon Statement of Work.

N/A

4). Financial expenditures of grant money and other contributions to the project, in-kind and/or direct funding.

All financial information is being provided through Wayne State University Sponsored Programs Administration and is being sent under separate cover.

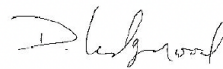
Attachments and Other Materials – Provide project materials developed and implemented during the reporting period (e.g. newspaper articles, newspaper advertisements, forms, brochures, announcements, studies, reports, analyses, audits, etc.).”

N/A

Respectfully submitted,



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