

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

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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**, 200 veterans will be randomized into one of four different THC:CBD dose conditions (High THC:High CBD; High THC: Low CBD; Low THC:High CBD, and Low THC:Low CBD) for a 12-week treatment phase. In **Study 2**, 150 veterans will be randomized into *one of three groups*: a control group (n=50) that receives cannabis that is closely matched to their usual product (up to maximum of 25% THC); (2) a THC reduction group (n=50), tailored across three THC concentrations (5%, 10%, or 15% THC) that are approximately 50% lower than the products they currently use; and (3) a THC reduction + 1:1 CBD group (n=50), also including tailored THC concentrations as in Group 2 but with CBD added in a 1:1 THC:CBD ratio. **Both studies** involve assessments weekly and bi-weekly throughout a 12-week treatment phase, and at 3- (post-treatment), 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 THC and CBD levels 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 and have been submitted to WSU IRB for approval.

- **Project Progress**

During this period we continued our communication with Veterans organizations and have been invited to meet with the behavioral health treatment team at the Detroit VA to recruit participants. We are also in continued contact with the Ann Arbor Veteran Affairs Administration to discuss recruitment efforts. We continued to reach out to veteran organizations through Facebook and contacted coordinators from other veteran organizations to keep them apprised of our readiness to recruit. We distributed IRB-approved study flyers and informational brochures to these and similar organizations (Southwest Solutions and Piquette Square) weekly and posted flyers around the Wayne State medical campus. Our recruitment team is working with Wayne State University Veteran organizations, including the Office of Military & Veterans Academic Excellence, where we have also distributed flyers. Advertisements have also been posted on social media and other

advertising platforms such as Facebook and Craigslist weekly. We update our project website (www.warriorCARE.net) regularly. We have screened several potential participants through this source. Our studies are also listed on ClinicalTrials.gov, which provides contact information, as well.

Our full-time recruiter continues to seek out 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, conducting initial screening interviews and schedule in-person screening. We are maintaining a waitlist of Veterans who express interest in participating, ensuring we can ramp up recruitment quickly once all regulatory requirements are completed.

We continue to check in with DEA-approved cannabis suppliers to monitor when cannabis product will be available for purchase. In the meantime, we began the Import/Export process with the Office of Medical Cannabis (OMC) in the Ministry of Health (Netherlands), which has the products we need (i.e., the THC:CBD ratios) currently available. We submitted initial paperwork to order cannabis from the OMC and are in the process of applying for an import license and obtaining DEA approval for shipment.

We have started coordinating with the Supplemental Brain Imaging Study team to integrate the MRI protocol into Study 1.

Finally, we moved into the new space provided by the Department of Psychiatry and Behavioral Neurosciences that was allocated to our research lab to significantly expand and re-organize. The Substance Abuse Research Division (SARD), which will administer all Wayne State University Veteran Marijuana Research Grants, now has 4 new participant testing and interview rooms, a new phlebotomy and biological sample storage room, and a new physiological testing room dedicated to these studies. We have begun expansion that adds office space for 5 new research assistants, 2 new research coordinators, 4 new Postdoctoral Fellows, 10-12 'hot desk' workstations for students and research volunteers, and a new conference room. The SARD now occupies an entire floor in the Tolan Park Medical Building located in Detroit, MI and will serve as the largest clinical cannabis research laboratory in Michigan (and possibly the country). The conversion of a conference room to a comfortable waiting room for caretakers and family members who accompany Veterans on their lab study days has been completed. Study days can be long and we wish to provide a comfortable and welcoming space, with reading areas, workspaces, and TV/lounge area for Veterans and their family members or caretakers. The "Living Room", a calming room/safe space for participants who may experience emotional distress during study procedures, has been set up, as well.

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

The move and expansion into the Warrior CARE suite is almost complete.

The mobile pharmacology van is ready for us to take delivery. This van will allow us to deliver cannabis doses and conduct assessments at participant's homes which will be more convenient for veterans who may have transportation/mobility issues.

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

Because the procedural changes made to Study 2 require approval by our university IRB, we have stopped enrolling participants into the study while we await IRB approval. However, there has been a great deal of interest in the research projects and we are continuing telephone screening. Currently we have more than 20 Veterans who have agreed to be contacted when we have received IRB approval. Currently our IRB office is experiencing delays due to being short-staffed and because the lifting of COVID-related restrictions has resulted in a larger than normal number of research protocol applications. This situation should improve soon as they hire additional personnel.

We continue to be in contact with two DEA Schedule I cannabis growers, to monitor the availability of their cannabis products. FDA IND applications have been prepared for both companies so we can submit them as soon as a grower indicates a product is ready for release. We also began the import/export process to obtain cannabis from an overseas cannabis grower as other US cannabis researchers are currently doing as we await the US supply.

While we await IRB approval for protocol changes and for DEA-approved research cannabis products to become available, we have significantly reduced salary support for research staff members who will resume their duties once the projects are fully underway.

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.

**Wayne State University: Veteran Marijuana Research 2021 Grant
Title: Investigating the Impact of Cannabinoids on Veterans’ Behavioral Health**

CATEGORY	TOTAL BUDGET	Expenses- thru 12/31/22	% of Budget Spent
Personnel/Fringe	3,925,223	782,535	
Equipment	129,404	12,398	
Supplies/Other	2,282,480	26,877	
Computers	45,575	9,321	
Travel	-	-	
DIRECT TOTALS	6,382,682	831,131	14.01%
Indirect Costs- 10%	638,268	83,113	
BUDGET TOTALS	7,020,950	793,180	14.01%

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,



Leslie H. Lundahl, PhD
Lead/Contact Principal Investigator

January 15, 2023