

MEDICAMENT

MEDICAL MARIJUANA RESEARCH NEWSLETTER



FALL 2023

**WELCOME TO
MEDICAMENT,**
the Consortium for Medical
Marijuana Clinical Outcomes
Research's quarterly newsletter.

The Consortium, founded by
the State of Florida, conducts,
disseminates, and supports
research on the use and effects
of medical marijuana on patient
outcomes.

*In the Fall 2023 issue of
MEDICAMENT:*

- Cannabis Clinical Outcomes
Research Conference
(CCORC)
- Research Grants Program
- New Consortium Members
- Get Involved in Research



Consortium for
Medical Marijuana
Clinical Outcomes Research

To learn more about the
Consortium and our programs,
visit us at mmjoutcomes.org.

SAVE THE DATE: CANNABIS CLINICAL OUTCOMES RESEARCH CONFERENCE (CCORC) 2024



CCORC 2023 Summary Available Now

Did you miss CCORC 2023?

[Read the summary brochure here >](#)

CCORC 2023 Proceedings and Abstracts Published

The proceedings and abstracts for CCORC 2022 have been
published in *Medical Cannabis and Cannabinoids*, the official
journal of the Consortium.

[Read CCORC 2023 proceedings here >](#)

[Read CCORC 2023 abstracts here >](#)

STAY IN TOUCH FOR CCORC UPDATES AT
ccorc.mmjoutcomes.org

RESEARCH GRANTS PROGRAM

Upcoming Request for Proposals: 2024 Grants Program



Consortium for Medical Marijuana Clinical Outcomes Research

COMING SOON

2024 REQUEST FOR PROPOSALS

The Consortium for Medical Marijuana Clinical Outcomes Research (Consortium) provides awards to support clinical and translational research related to Medical Marijuana (MMJ) to investigators within member institutions.

Research proposals focused on the clinical outcomes of MMJ use, effect of MMJ use in reducing opioid dependence, routes of administration, interactions of MMJ with other drugs/medications, epidemiology research, and evaluating components of MMJ/cannabis are encouraged.

The research grant award mechanism will consider fully developed research studies that generate novel evidence, as well as studies intended to facilitate the collection and/or analysis of preliminary data that will support future extramural funding applications.



LETTER OF INTENT DEADLINE FEB 1ST, 2024

VISIT [MMJOUTCOMES.ORG/RESEARCH](https://mmjoutcomes.org/research) FOR DETAILS ON THE RESEARCH GRANTS PROGRAM

2023 Research Grant Awardees Release Project Narratives & Anticipated Impact

Six new awards along with two Level-2 renewals were made in the 2023 Grants Program. These represent researchers from three Consortium-member institutions.

The 2023 awardees, their affiliations, along with the project narratives and anticipated impact of their proposed research, are presented below.



Cannabinoid Treatment for Reducing Chemotherapy-Induced Cachexia and Neuropathic Pain in a Pre-Clinical Rodent Model

PI: Lisa Eckel, PhD
Florida State University

Project narrative: Cachexia is a multi-faceted wasting syndrome characterized by anorexia, weight loss, and skeletal muscle atrophy. It is a common side effect in advanced cancer patients receiving chemotherapy. In addition to exacerbating cachexia, cytotoxic chemotherapies can damage sensory fibers through inflammatory processes, resulting in peripheral neuropathies and chronic pain. Our research will examine the effects of multiple cannabinoids, including cannabidiol (CBD) and cannabigerol (CBG), in alleviating anorexia, loss of adipose and lean tissue mass, inflammation, and allodynia in a rodent model of cisplatin-induced cachexia.

Anticipated impact: Chemotherapy-induced cachexia and neuropathic pain are not well managed under current treatment protocols, which are typically limited to managing nausea. Cannabinoid based treatments, including CBD and CGD offer a novel therapeutic option for chemotherapy-induced cachexia and represent a viable alternative to opioids for chronic, neuropathic pain management with less dependence liability. Outcomes of the proposed studies have significant implications for informing medical practice related to treating cachexia and chronic neuropathic pain and thus improving the quality of life for patients with advanced cancer diagnoses.



Impacts of Medical Marijuana Use on Inflammasome Activation and Breast Cancer Clinical Outcomes

PI: Jennifer J. Hu, PhD
University of Miami

Project narrative: Breast cancer is the most frequently diagnosed cancer and the second leading cause of cancer death in American women. A recent survey reported that 42% of breast cancer patients used Medical Marijuana (MMJ) to manage treatment-related symptoms. Although MMJ is generally considered safe and well-tolerated in cancer patients, there are potential adverse effects and conflicting reports of interactions with cancer therapies on clinical outcomes.

Therefore, we propose a prospective cohort study of a diverse breast cancer population (50% minorities) to assess the impacts of MMJ on clinical outcomes and quality of life.

Anticipated impact: Our research will bridge critical scientific knowledge gaps regarding the benefits and harms of MMJ in breast cancer patients during and after treatments, whether inflammasome/inflammatory biomarkers mediate the benefits and harms of MMJ in breast cancer therapies and other medications used, and the impact of MMJ characteristics on the benefits and harms and biomarkers. The outcomes will support future validation studies and ultimately impact decision-making when physicians/patients consider MMJ for improving QOL and enhancing clinical outcomes.



Development of Cannabinoid Treatments to Ameliorate Methamphetamine Use Disorder

PI: Habibeh Khoshbouei, PhD, PharmD
University of Florida

Project narrative: Increasing efforts are made to develop treatments for methamphetamine use disorder. For instance, agonist replacement medications such as oral dosage forms of d-amphetamine and methylphenidate have shown promise in reducing methamphetamine relapse by increasing basal dopamine levels, but they have abuse potential. Alternatively, the endocannabinoid system modulates the activity of dopaminergic neurons through other mechanism(s).

The CB1R agonist Δ9-Tetrahydrocannabinol (THC) increases firing activity of dopamine neurons and enhances dopamine synthesis. Although interactions between cannabinoid receptors and increased dopamine transmission are reported, their properties for methamphetamine relapse have been scarcely investigated. This study assesses the hypothesis that in freely behaving mice, THC reduces methamphetamine regulation of VTA dopamine neurons and striatal dopamine transmission.

Anticipated Impact: The results are two-fold: revealing THC regulation of VTA dopamine neuronal activity, striatal dopamine release, their correlation with behavioral responses, and their contribution to methamphetamine reinstatement. We predict THC could increase VTA dopamine neuronal activity that increases striatal dopamine levels that potentially facilitate drug extinction and reduce drug reinstatement.



A Pilot Double-Blind Placebo-Controlled, Randomized, Safety, Efficacy, and Acceptability Trial of a Hemp-Derived Cannabidiol Extract for the treatment of Anxiety

PI: Catalina Lopez-Quintero, MD, PhD
University of Florida

Project narrative: Approximately one-third of Americans will experience an anxiety disorder at some point in their lifetime. Anxiety is primarily treated with antidepressants or benzodiazepines, but unfortunately, many patients report a partial response or cannot tolerate the side effects of these medications. The therapeutic potential of various compounds derived from the Cannabis sativa

plant has generated considerable interest, particularly for managing neuropsychiatric disorders that have limited treatment options. Animal and small-scale human studies have demonstrated CBD's anxiolytic, antidepressant, panicolytic, and anticomulsive actions, however, more research is needed to investigate the mechanisms of action and determine whether these products represent a safe and effective option for the treatment of anxiety. To close this research gap, we will conduct a 1:1 randomized, double-blind, 4-week pilot clinical trial to investigate the dosing, safety, tolerability, efficacy, and acceptability of a hemp-derived CBD extract compared with placebo among 30 study participants (15 per treatment group).

Anticipated Impact: As the use of medical cannabis for anxiety continues to increase in Florida and the US, without sufficient research supporting its use, there is a pressing need to elucidate the mechanisms of action for CBD and other minor cannabinoid products and determine their potential as a therapeutic resource for anxiety treatment. CBD has demonstrated a promising profile for the treatment of anxiety, exhibiting anxiolytic, panicolytic, and anticomulsive effects. CBD may offer an alternative option for the approximately 30% of individuals with anxiety who are unresponsive to conventional treatments.



The Influence of Cannabis Smoke Condensate on Drug Metabolizing Enzymes in the Human Lung

PI: John S. Markowitz, PharmD
University of Florida

Project narrative: Drug-drug interactions (DDIs) are a major cause of medication-associated morbidity and mortality. Conventional medications undergo a rigorous assessment for DDI liability per specific FDA guidelines while medical cannabis (MC) has undergone no systematic DDI evaluation and information is highly limited. Cannabis flower, the most widely utilized form of MC in Florida and the US, contains > 400 phytoconstituents including > 100 cannabinoids.

However, following combustion (i.e., smoking) hundreds of additional compounds are formed such that ultimately the lungs are exposed to thousands of compounds in MC smoke. Importantly, the lung contains many of the same drug-metabolizing enzymes as the liver, and their disruption is anticipated to impair the metabolism of inhaled therapeutics and the normal physiological functioning of lung drug-metabolizing enzymes (DMEs) in detoxification from environmental exposures. The influence of smoked MC on drug metabolism occurring in the lung is essentially unknown. Current regulatory and legal constraints highly limit research studies of smoked cannabis. We are incorporating a highly novel in vitro approach to assessing this issue via the production and use of cannabis smoke condensate (CSC) as a highly representative mixture to assess the influence of MC smoking on DMEs utilizing human lung microsomes. Furthermore, we will assess the influence of CSC on the metabolism of the commonly used inhaled corticosteroid for asthma, beclomethasone.

Anticipated impact: Qualifying conditions and disorders for medical cannabis in Florida are chronic in nature and multiple conventional medications are often prescribed concurrently with cannabis posing risks for the occurrence of detrimental drug interactions. The vast majority of dispensed MC in FL is in the form of smoked cannabis flower. There is essentially no information on the influence of cannabis smoke on drug-metabolizing enzymes in the human lung. Inhibition of their activity could significantly impair the effectiveness of pulmonary therapeutics. Study results could have direct implications for presently marketed inhaled therapeutics such as the steroid beclomethasone and potential and COVID-19 therapeutics presently under clinical development. Results from these studies will provide the first information, and perhaps guidance on the influence of smoked medical cannabis on drug metabolism, and help guide the selection of MC formulations and administration routes (e.g. oral vs smoking) in individual patients.



Comparative evaluation of cannabinoids and opioids for treating chronic pain in aged subjects

PI: Niall Murphy, PhD
University of Florida

Project narrative: Treating chronic pain in the elderly is challenging due to a poor understanding of how advanced age affects physiology and drug action. In this project, we will test the analgesic potency of marijuana constituents in aged animals, seeking evidence that cannabidiol (CBD) particularly may present itself as a safer alternative to other analgesics, e.g., opioids, for treating pain in the elderly.

Anticipated Impact: Finding safe and efficacious analgesics for treating pain in the elderly is a high priority, particularly given the rise in aged populations. Results from the current study aim to address

this need by seeking evidence to support using marijuana constituents as an alternative and safer pain treatment for the elderly.



Evaluation of immunomodulatory effects of chronic medicinal marijuana use and its routes of administration (smoking versus vaping) on the cerebral metabolism, morphology, dopamine (via neuromelanin MRI), and neural circuits of the whole-brain, and pain in young adults living with- and without-HIV

PI: Varan Govind, PhD
University of Miami

Project narrative: More than 50% of HIV-positive individuals use marijuana for alleviating the adverse effects of HIV infection and its medication. Inhalation is the most widely used consumption method for marijuana products and these are available in many forms or formulations such as joints, blunts, vape oil cartridges, and other forms. The beneficial and harmful compounds in these marijuana-based products vary widely across the cannabis plant strains and the parts thereof used, forms/formulations used, routes of administration, and intake durations. Consequently, marijuana users experience conflicting or mixed health outcomes. This study proposes to evaluate the effects of chronic marijuana use and routes of its administration on the brain, inflammation, immune function, pain, and behavioral functions in HIV+ individuals.

Anticipated impact: People living with HIV use medical or recreational marijuana for alleviating adverse effects of HIV infection and its medication such as neuropathic pain, anxiety, depression, and cognitive dysfunction among many others. Specifically, this proposal will evaluate effects of chronic marijuana use and its routes of administration on the brain, systemic inflammation, immune activation, neuropathic pain, and behavioral measures in HIV-positive individuals. We anticipate that this study will provide preliminary data for assessing the impact of the form, dose and route of cannabis administration on the systemic inflammation and immune activation, brain metabolism and tissue structure, and interactions between the systemic and central nervous system (CNS) measures. This will form an important first step for designing cannabis-based systematic interventional studies to ameliorate specific conditions in HIV-positive individuals.



Quantitative assessment of complex drug-drug interaction networks involving medical cannabis products in special populations

PI: Rodrigo Cristofolletti, PhD
University of Florida

Project narrative: Patients receiving medical cannabis are likely to be taking other concomitant drugs and thus, risks related to Drug-Drug Interactions (DDIs) should be carefully assessed. An emerging body of evidence from *in vitro* studies has predicted inhibitory effects of cannabinoids on several drug metabolizing enzymes. However, clinical studies designed to assess DDIs involving major cannabinoids are scarce in the literature, partially due to the small number of

approved cannabinoid products by the Food and Drug Administration, the high costs associated with performance of confirmatory clinical DDI trials, and legal and ethical issues surrounding medical cannabis use. We will apply modern *in silico* modeling techniques to estimate DDI risks related to cannabinoids.

Anticipated Impact: Qualifying conditions to get access to medical cannabis in Florida are common is both their chronicity and the lack of fully effective therapeutics to treat them. Thus, multiple

medications are frequently prescribed concurrently (i.e. polypharmacy), and many of these agents will continue to be used concomitantly with medical cannabis. Such practices pose unknown risks for potential DDIs. Our research project aims to identify and mitigate the risks of DDIs involving medical cannabis in these complex patients.

Q&A: GET TO KNOW OUR NEWEST TEAM MEMBERS

The Consortium welcomes two new members, Dr. Mahmud Hasan and Sophie Maloney.



Dr. Md Mahmudul Hasan

Assistant Director, MEMORY

Welcome to the Consortium, Dr. Hasan! Can you give us a brief description of your background before you joined the consortium?

I am an assistant professor in the Department of Pharmaceutical Outcomes and Policy (POP), and the department of Information Systems and Operations Management (ISOM) at the University of Florida. Prior to joining UF I worked as an Oak Ridge Institute for Science and Education (ORISE) Postdoctoral Fellow of Drug Safety and Artificial Intelligence Methods in the Center for Drug Evaluation and Research (CDER) at the United States Food and Drug Administration (FDA).

Many of the research projects I've worked on address critical issues surrounding substance use disorder, in particular, opioid use disorder and opioid overdose epidemic.

You joined the University of Florida as part of the university's AI initiative, can you explain how your work utilizes artificial intelligence for drug evaluation and research?

I conduct data-driven interdisciplinary research in pharmaceutical outcomes and health service utilization with a focus on substance use and mental health disorder, opioid related adverse drug events, and chronic diseases. From a methodological standpoint, I leverage advanced data science, in particular Artificial Intelligence (AI)/Machine Learning (ML), statistical modeling, and management science techniques.

Outside of AI, what perspectives and/or expertise do you bring to the Consortium?

I will contribute to the consortium using my research experience in medication adherence and opioid related adverse health outcomes. I also aim to utilize my extensive experience working with large-scale longitudinal healthcare databases including administrative claims, hospital discharge, and EHR data to potentially enrich the consortium's unique research data repository known as the Medical Marijuana Clinical Research Repository (MEMORY).

What aspects of medical marijuana clinical outcomes research particularly interests you?

I'm interested in medical marijuana clinical outcomes research primarily because of many unknowns, finding the answer of which could potentially enhance the safety and effectiveness of this emerging treatment for certain severe clinical conditions. I also understand the critical need to study the utilization of medical marijuana and associated adverse health outcomes and believes there exists a unique opportunity to apply AI/ML to fill that gap.

What projects will you be working on with the Consortium? What do you hope to achieve through these projects?

I will primarily devote my expertise to enhancing MEMORY’s strength by designing the process for linking OMMU registry data to Florida Medicaid data managed by Florida Agency for Healthcare Administration (AHCA). This interlinked database will be a unique resource and will potentially open many opportunities to conduct a handful of retrospective observational studies on the safety and effectiveness of medical marijuana for approved clinical conditions. In addition, I am interested in studying the patterns of medical marijuana-related adverse health outcomes and further developing fair and trustworthy AI models that can potentially assist clinicians to predict and identify patients at high risk of such adverse outcomes. Such a prediction model can be translated into a clinical decision support tool that can help physicians in prescribing medical marijuana in an informed and judicious manner.



Sophie Maloney

Research Coordinator, Clinical Core

Welcome to the Consortium, Sophie! Can you give us a brief description of your background before you joined the consortium?

Thank you for the warm welcome! Prior to joining the consortium, I attended the University of Florida and received a Bachelor of Arts in Sociology. Shortly after graduation, I began working with the Alachua County Department of Health. I was a case manager for low-income and uninsured Alachua county residents and helped them receive free specialty care, dental, and mammograms. I would also help run dental clinics for these individuals during this time.

You’re currently pursuing your Master of Public Health, specializing in epidemiology. What interested you in pursuing an advanced degree in this field?

My interest in epidemiology really hit me after a series of cancer diagnoses within not only my immediate family, but my extended family as well. I became curious of certain risk factors that could play into developing cancer, as well as wondering how many people were going through cancer treatment. This then expanded to becoming interested in not only chronic diseases like cancer, but also infectious and viral diseases. At the same time, I was taking an interest in the inter-workings of society as well as the relationships that form between people. During undergrad, I was able to find that through epidemiology I can merge these two interests.

What aspects of medical marijuana clinical outcomes research particularly interests you?

The aspects that interest me are seeing the effects that medical marijuana can have on cancer patients and those living with chronic illnesses/diseases. I am also interested in seeing how/if stigma surrounding medical marijuana use affects the sample population.

What projects are you most interested in working on at the Consortium? What do you hope to accomplish?

The projects that I am most interested in working on at the Consortium are expansive. I have never worked in research before, so I am excited to learn all I can! More specifically, I would like to work on some papers as well as get a better grasp on data analysis in a real-world application.

GET INVOLVED IN RESEARCH

CARMMA: Changing the way we collaborate across the state of Florida

The [Connect and Advance Research for Medical Marijuana Analysis \(CARMMA\) Database](#) is accessible to researchers, physicians, and industry collaborators.

We believe collaborations bring research advancements. The CARMMA Database connects researchers, clinicians, and industry to foster medical marijuana research.

Anyone interested in engaging in medical marijuana research is invited to register in CARMMA to find collaborators.

JOIN THE CARMMA DATABASE



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