MEDICAMENT

MEDICAL MARIJUANA RESEARCH NEWSLETTER

FALL 2021

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 2021 issue of MEDICAMENT:

Consortium for Medical Marijuana Clinical Outcomes Research

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

CANNABIS CLINICAL OUTCOMES RESEARCH CONFERENCE (CCORC)

Recordings and Continuing Medical Education (CME) credits are still available through May 3, 2022

Did you miss the 2021 Cannabis Clinical Outcomes Research Conference (CCORC)?

The presentations were recorded and posted to the conference website along with the poster presentations and program details. Recordings will be available online for six months to registrants.

To access recordings, visit CCORC Conference Home and use the password you received in your confirmed registration email.

You can still register and receive CME credit until May 2022. To register, visit UF CME Office.

STAY IN TOUCH FOR CCORC UPDATES

RESEARCH GRANTS PROGRAM

Upcoming Call for Proposals: 2022 Grants Program

The 2022 Request for Proposals (RFP) will be released soon.

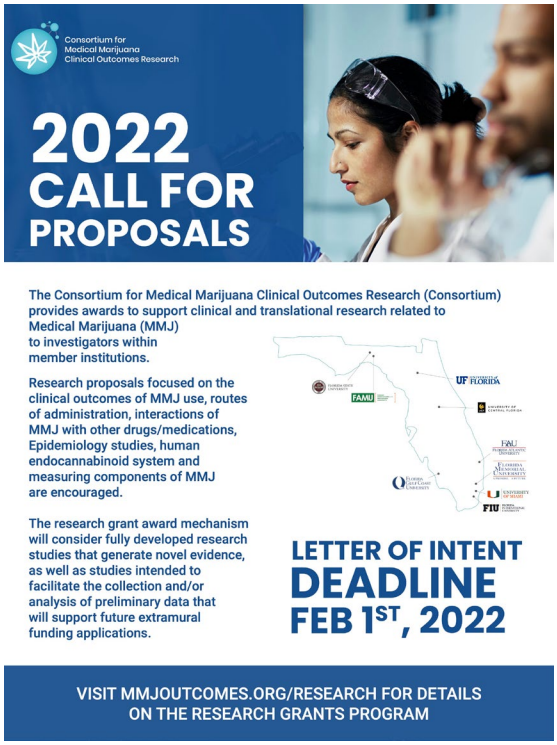
The deadline for the required Letter of Intent (LOI) will be February 1st, 2022.

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, routes of administration, interactions of MMJ with other drugs/medications, Epidemiology studies, human endocannabinoid system and measuring components of MMJ are encouraged.

Would you like to be notified when the new RFP is released?

Complete the interest form with your full name and email.



2021 Research Grant Awardees Release Project Narratives and Anticipated Impact

In June 2021, the Consortium awarded 11 grants to researchers from 5 member institutions for our third research grants cycle.

The 2021 awardees, their affiliations, along with the project narratives and anticipated impact of their proposed research, are presented below.

Acceptance of and access to medical marijuana and CBD as palliative care and hospice treatments for nursing home patients
PI: Jennifer Attonito, PhD
Florida Atlantic University

Project narrative: Cannabis products, including Medical Marijuana (MMJ) have been found effective to improve multiple symptoms that are commonly observed among nursing home patients.

This study will examine Florida nursing home clinicians' knowledge of MMJ effects, contraindications, dosing, and prescribing/procuring processes; attitudes, and beliefs surrounding use of MMJ for their patients; barriers to accessing MMJ as a treatment; and regional, institutional, and economic factors

that may be linked to variations in MMJ access in this setting.

In addition, structured interviews of patients/caregivers will be conducted to explore their understanding of the process for accessing and perceived outcomes of utilizing MMJ for their conditions and symptoms.

Anticipated impact: MMJ is rarely utilized as a therapy in long-term care settings where patients might find symptom relief from these products.

This study creates a base of knowledge around MMJ knowledge, utilization, access, and acceptance around MMJ among nursing home clinicians and patients.

Outcomes will provide a foundation for larger scale research that will further elucidate barriers to access to MMJ and test interventions for improving knowledge and access for patients, clinicians, and caregivers. The long-term objective is to translate research findings to clinical guidelines, standardized treatment protocols, and policies related to the use of MMJ in nursing homes.

Characterizing adverse drug events reports involving cannabis and cannabinoid
PI: Joshua Brown, PharmD, PhD, MS
University of Florida

Project narrative: This project aims to understand the impact cannabis and cannabinoids have on adverse drug events and the contribution of drug interactions to this risk.

We will identify common serious adverse events associated with cannabis use and conduct reviews of case reports to understand the causes and contributions to these events.

Anticipated Impact: This study aims to bring more attention to adverse effects of cannabis and to identify contributing factors, such as drug interactions or underlying health conditions.

Output from this project will help set priorities for future research in adverse drug events and drug interactions with cannabis and will provide novel evidence to patients and physicians to make better decisions when using medical cannabis.

Investigating cannabidiol anti-headache actions through PPAR signaling
PI: Andrea Cippitelli, PhD
Florida Atlantic University

Project narrative: This project aims at identifying a specific mechanism that mediates the observed anti-headache properties of cannabidiol (CBD) and evaluating the effects of a new class of compounds that promote peroxisome proliferating-activated receptors (PPAR) activity, or concurrently affect PPAR and cannabinoid-like activity, in the complex migraine symptomatology.

Anticipated impact: Migraine is a debilitating disease lacking successful treatment options. Cannabidiol (CBD) appears to play a role in reducing head

pain but the mechanism through which this effect occurs is unknown.

This research will tell us whether activation of a group of receptor proteins called PPARs by CBD is responsible for relieving the pain associated with migraine and whether a new class of compounds with CBD-like activities can serve as a novel and effective treatment for migraines.

Cannabinoid modulation of neuroinflammation in a pre-clinical animal model of anorexia nervosa
PI: Lisa Eckel, PhD
Florida State University

Project narrative: Anorexia nervosa (AN) is a serious psychiatric illness with poor treatment outcomes.

Our work examines the endocannabinoid system (ECS) as a novel therapeutic target for AN, based on the critical role it plays in regulating food intake, energy expenditure, and reward processing, all of which are dysregulated in AN.

Our study uses a pre-clinical animal model of AN to (i) investigate whether progressive weight loss promotes inflammation in brain areas that regulate food intake and (ii) test the therapeutic potential of cannabinoid-based medications in restoring normal immune function, improving appetite, and attenuating weight loss.

Anticipated Impact: This pre-clinical study investigating the therapeutic potential of cannabinoid drugs in alleviating AN symptoms in rodents offers a translational model for the development of new cannabinoid-based pharmacotherapies, including the use of medical marijuana, that would help to ease the high personal and societal costs of AN.

The role of endocannabinoids and cannabinoids in the clearance of bacterial infections and macrophage polarization
PI: Mariola Edelmann, PhD
University of Florida

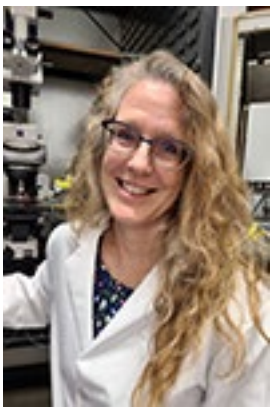
Project narrative: In this proposal, we will uncover the function of immunometabolism in infectious disease and design new therapeutic approaches using cannabinoids by creating the framework supporting novel antimicrobial compound discovery.

We will test cannabinoids in the preclinical study as candidates for host-directed therapies controlling bacterial clearance that stimulate the host defense mechanism and limit gastrointestinal inflammation.

Anticipated Impact: At the completion of the proposed research, we will determine the mechanisms by which endocannabinoids regulate innate immune response in infections with Gram-negative Salmonella and identify novel cannabinoids priming the host survival during this infection.

The mechanism-based understanding of the lipid homeostasis in infection with Salmonella will provide a framework for the future development of specific cannabinoid-based therapeutic

applications in the treatment of Gram-negative infections and inflammatory conditions caused by these infections.



Early Developmental Mechanisms of Action for Cannabidiol (CBD) in a Mouse Model of Anxiety
PI: Debra Fadool, PhD
Florida State University

Project narrative: CBD is a nonpsychoactive ingredient of cannabis that has demonstrated changes in anxiety, chronic pain, sleep, and prevention of substance abuse in mouse and human subjects.

We are using a newly found mouse model that exhibits anxiety and attention deficit to examine behavioral intervention of chronic CBD therapy during gestation and perinatal life (two weeks prior to pregnancy, during fetal development, and during lactation).

We want to understand if CBD fetal exposure affects brain development and may persist to reflect changes in anxiety as an adult.

Anticipated impact: Investigators can either induce anxiety by adding a stressor ("state" anxiety), or use a mouse model whereby the "trait" anxiety does not vary over time.

Because CBD is not addictive, it has high therapeutic potential for chronic treatments and the use of the latter model affords an advantageous tool to explore reduction or elimination of anxiety- or ADHD-associated behaviors.

This gestational and perinatal study will develop a preclinical tool for probing the neuronal excitability, brain development (neural imaging), and anxiety and attention deficit behaviors that may accompany CBD, fetal-exposed mice that are then raised to early adults.

CBD-induced biomarkers of inflammation reduction in people living with HIV at the single cell level
PI: Simone Marini, PhD
University of Florida

Project narrative: People living with HIV (PLWH) are affected by comorbidities, including myocardial infarction and cancer, typically occurring earlier than in healthy individuals.

These comorbidities appear to be strongly related to chronic inflammation, a condition characterizing PLWH. Cannabidiol (CBD) is known for its anti-inflammatory properties, however, the molecular mechanisms used to alter inflammation poorly understood. We propose to study the effects of CBD on inflammation in PLWH to understand the molecular role of different cells involved in the inflammation process.

Anticipated Impact: Showing the mechanisms of CBD in curbing chronic inflammation in PLWH could help reducing or resolving inflammation-related comorbidities that currently affect PLWH.

Evaluation of Minor Cannabinoids loaded Exosomes in Chronic Diabetic Neuropathy
PI: Mandip Sachdeva, PhD
Florida A&M University

Project narrative: Diabetic Peripheral Neuropathy (DPN) is the major clinical manifestations of diabetes and affects 50-70% of the diabetic population despite with the limited treatment options.

Recently, we have optimized loading cannabinoids in extracellular vesicles derived from human umbilical cord derived stem cells/stromal cells (hUCMSCs-EVs) grown in PBS-vertical wheel (PBS-VW) bioreactors and our formulations have shown excellent role in offering neuroprotection against chemotherapy induced neuropathy.

Based on these results, we will now be studying the effects of CBD/CBG/THCV loaded EVs either alone or in combination against diabetic pain.

Anticipated impact: This study will provide insights about the therapeutic potential of minor cannabinoids (CBD, CBG & THCV) loaded exosomes in alleviating experimental DPN.

This study would also suggest the beneficial effects of using exosomes derived from neural stem cells/hUCMSCs as novel drug carriers for therapy of painful DPN.

Alleviation of phantom limb pain in a rat model by treatment with components of Cannabis
PI: Jacqueline Sagen, PhD, MBA
University of Miami

Project narrative: Phantom limb pain is a frequent and debilitating consequence of medically-required amputation and is poorly managed by currently available therapies.

The most frequently reported use of medical marijuana is for pain relief, and may be particularly indicated for treatment of complex chronic pain syndromes like phantom limb pain due to the wealth of cannabinoid compounds and terpenes acting via distinct complementary mechanisms.

The goal of the study is to evaluate the potential beneficial effects of major Cannabis components and their combination in preventing and reducing phantom limb pain using a preclinical rodent model.

Analgesic dose-ranging, side effects, and effects on reducing opioid use will be tested to provide the foundation for further development of medical marijuana in the treatment of this debilitating chronic neuropathic pain syndrome.

Anticipated Impact: There is a compelling need for improved treatment options for chronic pain patients through the identification of new and potent therapeutics.

Solid preclinical evidence supporting the use of Cannabis-derived compounds for management of challenging neuropathic pain syndromes such as phantom limb pain is lacking.

The study will address this knowledge gap to provide needed preclinical evidence in guiding policy decision-making on the medical use of marijuana for the clinical management of complex neuropathic pain syndromes.

Translational examination of the pharmacological interactions of medical marijuana with neuropathic pain analgesics in both young and older adults
PI: Jenny Wilkerson, PhD
University of Florida

Project narrative: This work will directly address the Consortium's charge to investigate drug-drug interactions with medical marijuana.

Specifically, we will conduct a multi-disciplinary study moving from bedside to bench and back to bedside to understand what happens in the real-world, fill gaps in knowledge using animal models, and conclude with recommendations for best practices.

Anticipated impact: Output from this study aims to inform combination therapy for a debilitating pain condition and to make recommendations to physicians regarding appropriate therapy.

Our stratification by young and older adults will be further informative to reducing potentially high-risk prescribing among vulnerable populations.

The Effect of Delta-9-tetrahydrocannabinol (THC) on Intestinal Inflammation and Fibrosis in Experimental Crohn's disease
PI: Ellen Zimmermann, MD
University of Florida

Project narrative: Crohn's disease (CD) causes intestinal inflammation that leads to fibrotic strictures that often require surgical resection. Cannabinoids improve symptoms of CD and have become a popular adjunct to traditional immunosuppressive therapy.

Surprisingly little is known about how cannabinoids work in CD and whether they effect intestinal inflammation or fibrosis. If cannabinoids improve fibrosis in our CD patients it would be a great benefit. However, a major adverse effect could result if patients using cannabinoids to calm their GI symptoms increased the fibrosis in their gut leading to surgery.

Our aim is to study the most abundant psychoactive substance in cannabis, delta-9-tetrahydrocannabinol (THC), in an animal model of CD and in cultured human tissue to lend insight into their mechanism of action and safety. Our outcome measures are standard histologic

and molecular measures of inflammation and fibrosis that are used in therapeutic trials in CD.

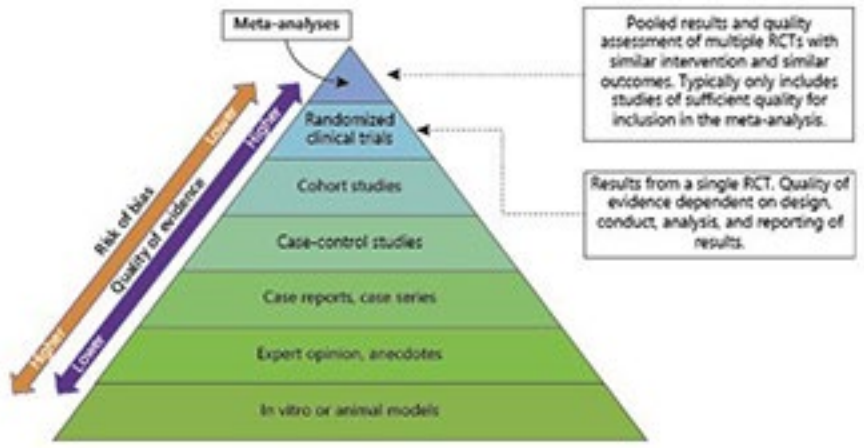
Anticipated Impact: The impact of our studies is to better understand how cannabinoids work for Crohn's disease and to have more confidence in their safety.

A better understanding of the mechanism of action could lead to the development of more effective therapies for these difficult diseases.

EVIDENCE AND RESEARCH ANNOUNCEMENTS

Evidence on medical marijuana safety and effectiveness: Read with Caution

The Consortium leads for evidence and for MEMORY, Dr. Amie Goodin and Dr. Joshua Brown, published a commentary on the rigor of studies evaluating the safety and effectiveness of medical marijuana in the Consortium's *Evidence in Context* Series: *High Risk of Bias in Medical Cannabis and Cannabinoid Clinical Trials Dictates the Need for Cautious Interpretation*.



RCTs are generally considered the "gold standard" of evidence and commonly inform clinical guidelines, lead to the approval of new drugs, and are often disseminated to the public through media coverage.

The use of meta-analyses serves to combine the evidence from multiple trials while providing an objective, systematic quality assessment of these studies.

Several meta-analyses illustrate the low quality and poor rigor of studies that support the effectiveness of medical marijuana. Readers of the primary literature need to be aware of the impact of problems in study design and analysis when interpreting the results.

Read the full article.

3-7% of Pregnant Women in the USA Report Using MMJ During Pregnancy

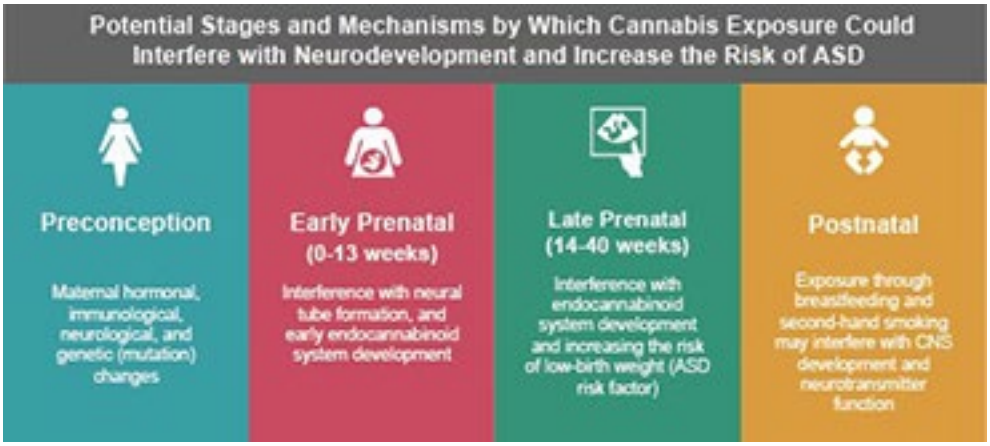
Since the early 2000s, cannabis use during pregnancy has doubled.

The Substance Abuse and Mental Health Services Administration found that 3-7% of pregnant women in the USA reported medical marijuana use during pregnancy, specifically for nausea and vomiting symptoms.

In a recent research letter, published in Nature, the authors examined the association between

prenatal maternal cannabis use and the risk of neurodevelopmental disorders, specifically autism spectrum disorder (ASD).

The Consortium discusses the rigor of this study and the need for similar studies that address medical marijuana and maternal and child health in this new addition to our *Evidence in Context* Series: *Perinatal Cannabis Exposures and Autism Spectrum Disorders*.



Read the full article.

What about a Standardized Cannabis Unit?

One of the largest challenges for cannabis research is the standardization of cannabis dose.

In this article of our *Evidence in Context* Series: *Much Ado about Dosing*, the Consortium assesses the needs and challenges of defining a standardized cannabis unit.

A recent review of medical cannabis clinical research in the USA showed significant variability in the dose, route of administration, and THC/CBD content of cannabis products studied.

Such variability limits the ability to compare and summarize study findings as well as the ability to formulate recommendations for use in clinical practice.

Researchers have proposed a “Standard THC Unit” of 5 mg based on the premise that THC is the principal constituent responsible for the psychoactive effects of cannabis.

Read the full article.

Consortium Members present at the Research Society on Marijuana

Consortium members presented their research at the 5th Annual Meeting of the Research Society on Marijuana (RsMJ) on July 23, 2021.

The Research Society on Marijuana (RSMj) is a network of scientists with the goal to promote understanding through research of the consequences and assessment of marijuana use and the treatment of conditions including cannabis use disorder.

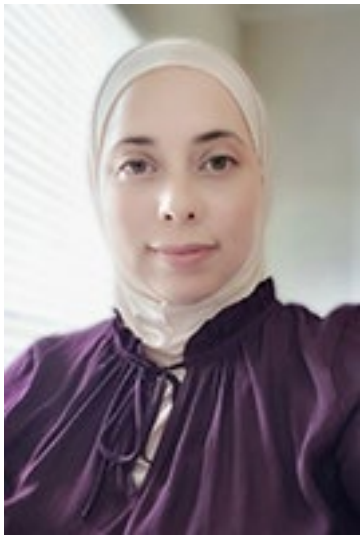
RSMj fosters multidisciplinary research from biomedical, psychosocial, clinical, and socioeconomic approaches and conduct basic, translational, and applied research.

Read the full article and view presentations. The following were poster presentations:

Reasons for Marijuana Use and Its Perceived Effectiveness in Therapeutic and Recreational Marijuana Users Among People Living with HIV in Florida
*Sajdeya R.**; Joseph, V.; Stetten, N.; Ibañez, G.; *Wang, Y.*; Powell, L.; Somboonwit, C.; Corsi, K.; *Cook, R.*

Legalization of "smokable" medical marijuana was associated with significantly increased THC use per certified patient in the Florida medical marijuana program: An interrupted time series analysis
Jugl, S.; Sajdeya, R.; Cook, R.L.; Brown, J.D.; Winterstein, A.G.; Goodin, A.J.*

Ruba Sajdeya, MD awarded the 2021 AHSR Early Career Investigator Award



Ruba Sajdeya, MD, a research assistant in the Consortium and graduate student received the 2021 Addiction Health Services Research Conference (AHSR) Early Career Investigator Award for her abstract poster submission, "Free-text searching algorithms to identify patients using cannabis in electronic health records: A rapid literature review".

Her research is related to improving cannabis use assessment and documentation in healthcare and utilizing free-text searching algorithm to identify patients who use cannabis from electronic health records to improve cannabis-related health outcomes research. Co-authors of Ruba's research are Sebastian Jugl, BPharm, RPh; Amie Goodin, PhD; and Robert Cook, MD, MPH.

Ruba joins five other early career investigator awardees who will present their work at the conference on October 14 and 15.

Physicians indicate their clinical practices rely on a blend of research and anecdotal information

Between June and October 2020, the Consortium conducted a cross-sectional state-wide survey of registered medical marijuana physicians in Florida. The survey aimed to understand training needs, prescribing practices, and desired research priorities.

Ruba Sajdeya, MD, a research assistant in the Consortium and graduate student, analyzed data from the state-wide survey and co-authored an article in the Journal of Primary Care & Community Health, titled "Practice Patterns and Training Needs Among Physicians Certifying Patients for Medical Marijuana in Florida".

Physicians indicated their clinical practice relies on a blend of research and anecdotal information sources.

Physicians report clinical factors influencing their recommendations to patients, but treatment plans vary substantially and rely on experimental approaches.

Read the full article.

MEDICAL MARIJUANA & ME

Coming late 2021: Medical Marijuana and Me (M^3)

Launched by the Consortium, ***Medical Marijuana and Me (M^3): A Statewide Study to Characterize Experiences and Clinical Outcomes of Medical Marijuana Patients in Florida*** will begin recruitment in late 2021.

Medical Marijuana and Me will be the first large patient cohort in Florida that is followed to understand patient experience with medical marijuana. M^3 aims to:

- collect patient-centered data, focusing on the most common health conditions, to characterize the experiences and clinical outcomes among a diverse and representative group of medical marijuana (MMJ) users in Florida.
- support high-quality, impactful research that can inform state policy, clinician practice and patient outcomes related to MMJ.
- provide access to data and recruitment infrastructure for consortium researchers to support pilot studies, papers, and grant proposals.

The Consortium plans to recruit at least 1,000 adult participants to complete a sequence of surveys about their general health, use and experiences with medical marijuana and related health outcomes.

More details about the M^3 coming soon!

GET INVOLVED IN RESEARCH

Using or considering using medical marijuana in Florida and interested in research study participation? Join the MMJ Registry

The Consortium maintains a registry of patients who are interested in being contacted to participate in medical marijuana studies.

Any current or future medical marijuana user in Florida can register their interest in participating in research.

By joining the MMJ Registry, you will help us with recruitment of patients for research studies and contribute to our understanding of the clinical benefits and side effects of medical marijuana.

JOIN THE MMJ REGISTRY

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

Have news or feedback to share? Let us know!

Share your Consortium-related research and news through our submission form.

Share your comments on our newsletter through our feedback form.

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Consortium for Medical Marijuana Clinical Outcomes Research