Consortium for Medical Marijuana Clinical Outcomes Research

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Prepared by the Consortium for Medical Marijuana
Clinical Outcomes Research

For more information about the Consortium visit: *www.mmjoutcomes.org*

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EXECUTIVE SUMMARY

Since passing of the Compassionate Use Act in 2014, Florida citizens have had access to marijuana and marijuana products for the treatment of certain debilitating conditions. While medical marijuana (MMJ) may improve health outcomes, evidence to support its effectiveness for the treatment of most conditions is scarce and there are significant safety concerns related to cognitive effects, risk of accidents, interactions with other medications, psychosis, and addiction. Moreover, cannabis varies in terms of its components and mode of administration, but there is limited research to elude which types, doses and delivery methods provide the optimal risk-benefit. This substantial need for research stands in stark contrast to the available infrastructure to support such work and to the rapid uptake of medical marijuana. **As of January 14th, 2022, the number of Floridians licensed to use MMJ has grown by more than 20% compared to last year, to a total of 661,496 individuals.**

The following report details activities of the Consortium for Medical Marijuana Clinical Outcomes Research completed during the third year of its existence (July 2021 – Feb 1, 2022). The first and second annual reports were submitted on February 15th in 2020 and 2021 and are available at *https://mmjoutcomes.org/our-consortium/annualreport/*. An overview of Consortium activities was also provided to the Florida House Professions and Public Health Subcommittee in November 2021 and is available for review on the Florida channel: *https://thefloridachannel.org/videos/11-3-21-house-professions-public-health-subcommittee/* (presentation starts at 46:00).

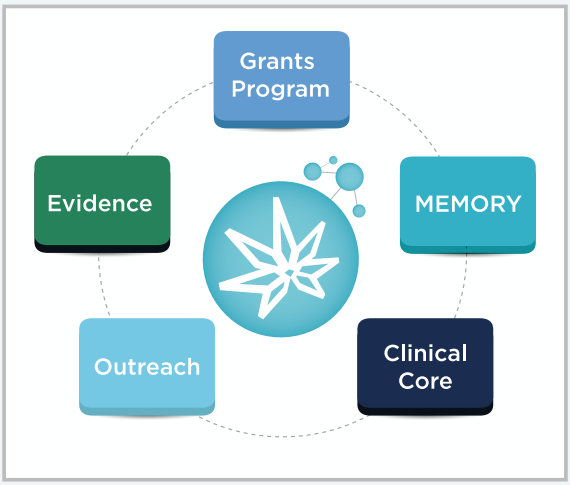
HIGHLIGHTS OF CONSORTIUM RESEARCH FINDINGS

New to this report is a section on research findings produced by Consortium core faculty and grant awardees in the past year. Some key messages are summarized below, and further detail is provided in the body of this report.

- Each week Florida dispensaries supply 200kg THC per week in non-smokable products and more than 400-700kg THC if smokable products with THC content between 10-20% are also considered.
- For non-smokable products, the weekly dispensed amount of THC per total number of MMJ cardholders remained stable over the past 3 years. When including smokable products, there was a 2.4 increase in weekly dispensed THC over the same period, from 279mg to 673mg (assuming 10% THC content in smokables).
- Physicians authorized to certify patients for MMJ and treatment centers are concentrated in urban regions. This concentration results in disproportionately lower access to MMJ for Floridians living in regions with more social deprivation.
- During the first year of the MMJ program in FL, early adopters were mainly patients with muscoloskeletal conditions , chronic pain and mental health disorders. One in four reported use of prescription opioids. Among older early adopters, 45% reported concomitant use of at least one medication with sedating effects.
- Nearly one half of users of federally approved CBD products reported adverse effects, including elevated liver enzymes, sedation, sleep disturbances, infection and anemia. Given CBD effects on drug metabolism and excretion, the potential for drug interactions is high.
- Compared to MMJ cardholders, adults who obtain marijuana from other sources reported lower educational achievement and less income. While expenditures for marijuana were similar, cardholders used a broader array and more CBD-dominant products. Cardholders reported more pain, suicidal ideation, and PTSD.

CONSORTIUM RESEARCH PROGRAM

The Consortium research program rests on five pillars aimed at supporting the Consortium mission to foster medical marijuana clinical outcomes research including: **A Grants Program**, a unique research data repository known as the **MEdical Marijuana Clinical Outcomes RepositorY (MEMORY)**, a **Clinical Research Core**, an **Evidence Core** and an **Outreach Program**. Following is a brief overview of the purpose and accomplishments for each pillar.



Grants Program

Launched in September 2019, the Consortium grant program has since completed three award cycles and initiated its fourth cycle. During the first three grant cycles, 85 research proposals were received and ~$2M have been awarded to 30 researchers from 7 Consortium member institutions. Research outcomes and health conditions addressed in these proposals include neuropathy and pain of various origins, anxiety, cancer, PTSD, drug interactions, pattern and motivation for MMJ use and access to MMJ, adverse drug events among others.

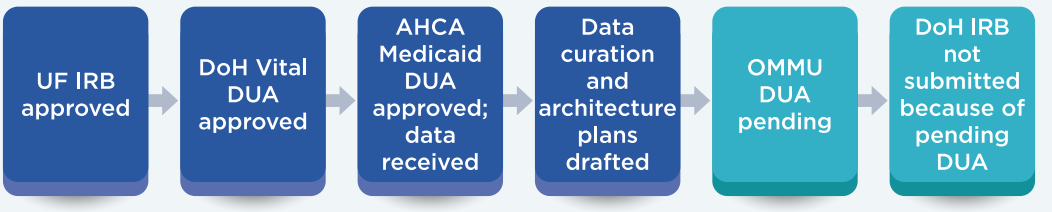
With little more than 2 years after the first grants were awarded and despite the COVID-19 pandemic, grant awardees have generated important evidence. Research findings were presented at scientific meetings and in 25 peer-reviewed publications, and the new data have served as the basis for 1 patent and 14 new extramural grant applications, two of which have been awarded. Noteworthy, 50 trainees including 12 from under-represented minorities have been involved in the funded research grants and two new courses have been developed, one of which is approved by the state university system, supporting the development of MMJ research capacity in the state.

MEMORY

The growing use of MMJ in Florida offers a unique opportunity for real-world evaluations of MMJ outcomes, that can help overcome the slow uptake of randomized clinical trials. MEMORY has been conceived to establish the infrastructure for real-world MMJ clinical outcomes evaluations similar to those employed by the FDA to evaluate and monitor the risk-benefit of approved prescription medications. To ensure comprehensive longitudinal follow-up to capture relevant health outcomes and availability of control groups, the Consortium aims to link the Office of Medical Marijuana Use (OMMU) Medical Marijuana Use Registry (MMUR) with other clinical databases commonly used for outcomes

research, to create a robust research-ready repository. Linkage to clinical databases including pharmacy dispensing records will allow establishment of control groups to facilitate comparisons of outcomes among patients who have initiated MMJ and patients with similar conditions and health history who are relying on conventional therapeutic approaches. Pending relevant approvals, the Consortium plans to make a de-identified version of the repository available to Consortium researchers, thus providing state-wide infrastructure for real-world clinical outcomes research.

Regulatory approvals including Data Usage Agreements (DUAs) for the access to identifiable Medicaid claims data from the Agency for Healthcare Administration (AHCA) and vital statistics data from the Department of Health (DoH) Vital Statistics Office have been obtained. Approvals from the Department of Health OMMU to access the MMUR are still pending. The MEMORY data science team has completed development of the data architecture and the data dictionary that will define variables after final data acquisition.



During this fiscal year, OMMU did grant the Consortium access to a de-identified version of MMUR data that uses a range of predefined queries. The Consortium has begun exploring the data that can be retrieved with these query options, which has further informed the development of the MEMORY data architecture and has facilitated analyses of MMJ utilization pattern at the population level, which are included in this report. Analyses of physician-reported adverse reactions and changes in the use of controlled substances are ongoing.

Clinical Research Core

The Clinical Research Core was established to complement MEMORY, and provide infrastructure support for prospective studies (including randomized controlled trials). To facilitate such studies, a MMJ patient contact registry to support recruitment into research studies has been rolled out statewide, with a registry portal on the consortium website. To date, 476 individuals who are using or are planning to use MMJ have registered. Providers and industry partners are now listed in the online *Connect and Advance Research for Medical Marijuana for Analysis* (CARMMA) database.

The Consortium also completed planning of the launch of **Medical Marijuana and me (M^3)**, the first large MMJ patient cohort in Florida, and one of the first in the United States with an enrollment goal of 1000 patients. Enrollees will be asked to complete a sequence of surveys about their general health, use and experiences with MMJ and related health outcomes. Targeted research areas that M^3 will contribute to include pattern and determinants of MMJ use, outcome trajectories, adverse effects, concurrent prescription medication and other substance use, and MMJ drug interactions. M^3 design has been guided by a scientific planning committee consisting of 11 members, including six researchers from consortium member universities, four MMJ physicians, and one MMJ patient representative.

Outreach

The Consortium's outreach activities are directed towards patients, providers, researchers, and industry, to maximize participation in research, and keep these stakeholders abreast of the latest research findings. In addition to its website and quarterly newsletter, the Consortium enhanced its outreach activities with a new researcher spotlight video series and by hosting the inaugural annual Cannabis Clinical Outcomes Research Conference (CCORC).

The first **CCORC** was hosted virtually on April 8th and 9th, 2021 and featured keynote addresses by three national level experts in the field of cannabis research, three panel discussions, as well as poster presentations, networking sessions, and an exhibitor hall. **CCORC 2021 drew over 225 registrants from across 31 U.S. states and five countries** (Germany, Italy, Mexico, United Kingdom, and United States). Most attendees were researchers followed by physicians, students, industry representatives and others.

Evidence Core

The evidence core focuses on the synthesis and dissemination of scientific evidence for researchers, providers and patients. Evidence core activities include publication of its Evidence in Context series and Patient Info Sheets, provision of scientific expertise as needed, and development of evidence reviews to inform the Consortium research priorities.

The first collection of **Patient Info Sheets** includes three entries in the Medical Marijuana 101 series: 1) The Medical Marijuana Program in Florida: History and Definitions, 2) Explanation of Common Terms, 3) An Introduction to the Endocannabinoid System (ECS). The purpose of these info sheets is to provide unbiased, evidence-based and up-to-date information about important topics on MMJ clinical outcomes for all members of the public. These info sheets are accessible on the Consortium website and disseminated by the Consortium in collaboration with the Florida A&M University's (FAMU) Medical Marijuana Education and Research Initiative (MMERI).

The **Evidence in Context** series addresses needs for rapid distillation and appraisal of emerging evidence in the form of brief, plain-language commentaries. These articles are available in the scientific journal *Medical Cannabis and Cannabinoids* and on the Consortium website and both publication platforms are fully accessible to all members of the public. To date, the journal has published four articles within this series accessible at *https://mmjoutcomes.org/evidence/evidence-in-context/*. No such resource was previously available specifically for MMJ.

CONSORTIUM RESEARCH PLAN 2022-2023

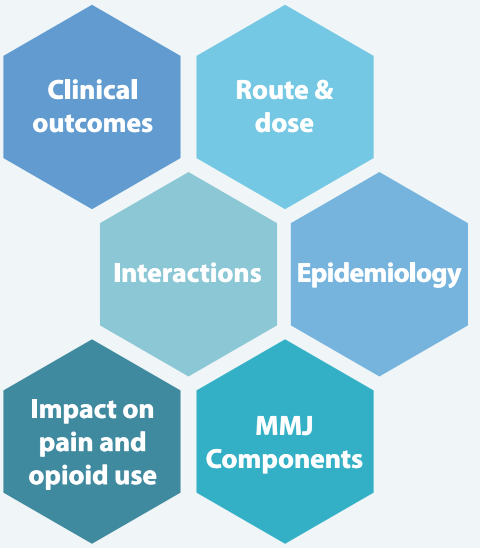
In the coming year, the Consortium will continue its efforts towards facilitating and conducting research that informs clinical care and policy within the five original Consortium research program pillars: the Grants program, MEMORY, the Clinical Core, Outreach, and the Evidence Core activities. Modifications of the Consortium research plan were informed by interactions with the Florida House Subcommittee on Professions and Public Health and the Office of Medical Marijuana Use at the Department of Health. Key needs for research that were emphasized are:

- Accelerate the generation of conclusive evidence on effects of MMJ use including both risk and benefit with priority to studies in humans with direct value to support clinical and regulatory decisions
- Conduct evaluations of dosing, in particular research on high potency THC
- Conduct epidemiologic studies on utilization pattern, patient demographics and accessibility of MMJ across diverse groups
- Prioritize research on the effects of MMJ use in reducing opioid dependency

The following describes the Consortium Research Plan for fiscal year 2023.

Grants Program

Review of the grants program progress and funding priorities over the past two years highlighted two areas for enhancement, both focused on emphasizing the Consortium's support of clinical research. First, the new grant funding program has been restructured to support two studies at $130,000 over a total of two years. An additional fund for one-year projects as offered previously has been retained. Second, the Consortium Board revised its research priorities to emphasize the focus on clinical research, the impact of MMJ on pain management and opioid use and expanded the scope of its epidemiologic research priority.



2022 Research Priorities

The Consortium has launched its fourth grants cycle in December 2021 with release of its *Request for Proposals* and updated research priorities. The intent is to complete the application reviews by the end of the fiscal year to expedite funding of prioritized proposals, upon approval of the FY 2023 Consortium budget.

MEMORY

With the new provision of access to a de-identified version of the OMMU Medical Marijuana Use Registry, the Consortium has been given the ability to evaluate utilization pattern and certain physician-reported outcomes. Analyses of these data have commenced and will be expanded over the next year. Pending provision of identifiable data for linkage to other health outcomes databases, plans for MEMORY development remain unchanged for fiscal year 2023. As envisioned, MEMORY will then serve in two key capacities: for controlled studies on MMJ effectiveness and safety, and for active surveillance to capture emerging safety issues among MMJ users.

Clinical Core

Goals for the Clinical Core include continued expansion of the Consortium infrastructure to support patient recruitment into prospective research studies via its patient contact registry and CARMMA database of collaborating physicians, researchers and industry. The Consortium will launch its Medical Marijuana and Me (M3) patient cohort in early 2022 with the goal to evaluate detail on MMJ use and patient-reported outcomes. The Clinical Core will also continue to work on guidance for investigators on regulatory issues involving use of MMJ in research studies. This will include guidance on DEA licensure and other relevant state and federal regulations.

Outreach

Following up on the success of our inaugural Cannabis Clinical Outcomes Research Conference (CCORC), the Consortium plans to hold its second annual CCORC in May 2022. Other outreach activities through the Consortium website, its quarterly newsletter and participation in scientific conferences will continue. The newly added Researcher Spotlight Series will be developed further to promote Consortium activities and disseminate research outcomes.

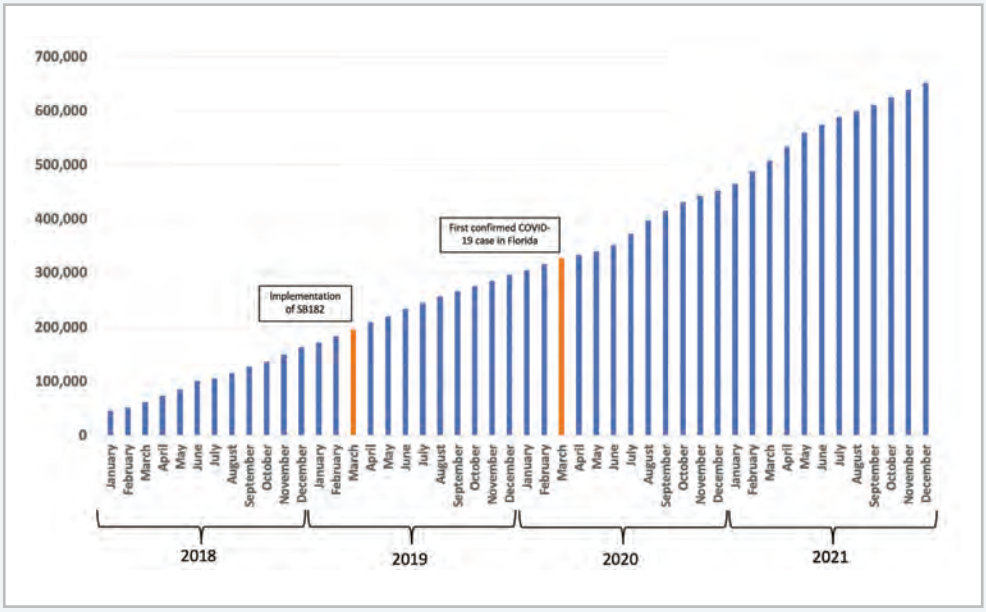
Evidence Core

The Consortium will build upon the two new activities introduced in the previous year including publication of the Evidence in context series and patient info sheets. The Consortium considers the emerging evidence reviews and info sheets an important contribution to the availability of unbiased up-to-date evidence on MMJ and instrumental in its communication with providers and patients.

The Consortium board core faculty and staff look forward to continuing this critical work to support the Florida Medical Marijuana program's primary goal to improve the health of Florida citizens. The Consortium addresses an urgent and critical need in this regard in providing patients, providers and regulators the necessary evidence on the safe and effective use of MMJ.

INTRODUCTION

Beginning with the Compassionate Use Act passed in 2014 and followed by several amendments, Florida law allows the use of marijuana for the treatment of certain debilitating conditions. Persons seeking medical marijuana (MMJ) may suffer from serious health conditions and symptoms, which may not be completely alleviated with approved medications. While there is some promise that MMJ may improve certain health outcomes, evidence in support of its effectiveness for treatment of most conditions is lacking and there are significant safety concerns related to cognitive effects, risk of accidents, interactions with other medications, psychosis, and addiction. Moreover, marijuana products vary in terms of specific components and mode of administration, but little is known about what components, doses and delivery methods provide the optimal risk-benefit. **There is a substantial and urgent need to understand how MMJ impacts health to guide both policy and clinical decision-making. But due to the complex legal restrictions, the research infrastructure to support MMJ evaluations is lagging far behind the rapid uptake of MMJ in the state. As of January 14th, 2022, the number of Floridians licensed to use medical marijuana has grown by more than 20% compared to last year, to a total of 661,496 individuals.**



Increase in certified medical marijuana patients in Florida, 2018 - 2021

To address the need for rigorous evidence on the safety and effectiveness of MMJ for the various patient populations who are seeking certification for use, the state legislature introduced Section 1004.4351, Florida Statutes, to establish the Consortium of Medical Marijuana Clinical Outcomes Research to conduct, disseminate and support rigorous scientific research on the clinical outcomes of medical marijuana use. In July 2019, the Florida State University System Board of Governors, following a competitive request for proposals, designated the University of Florida as the lead university of the Consortium. Eight additional universities have joined the Consortium to-date.

Consortium member universities

Consortium responsibilities as defined in the charter and consistent with statute include:

- Conduct rigorous scientific research
- Disseminate research
- Guide statewide policy on ordering and dosing practices for the medical use of marijuana.

The Consortium of Medical Marijuana Clinical Outcomes Research presents its third Annual Report on its accomplishments in research and outreach, and future plans.

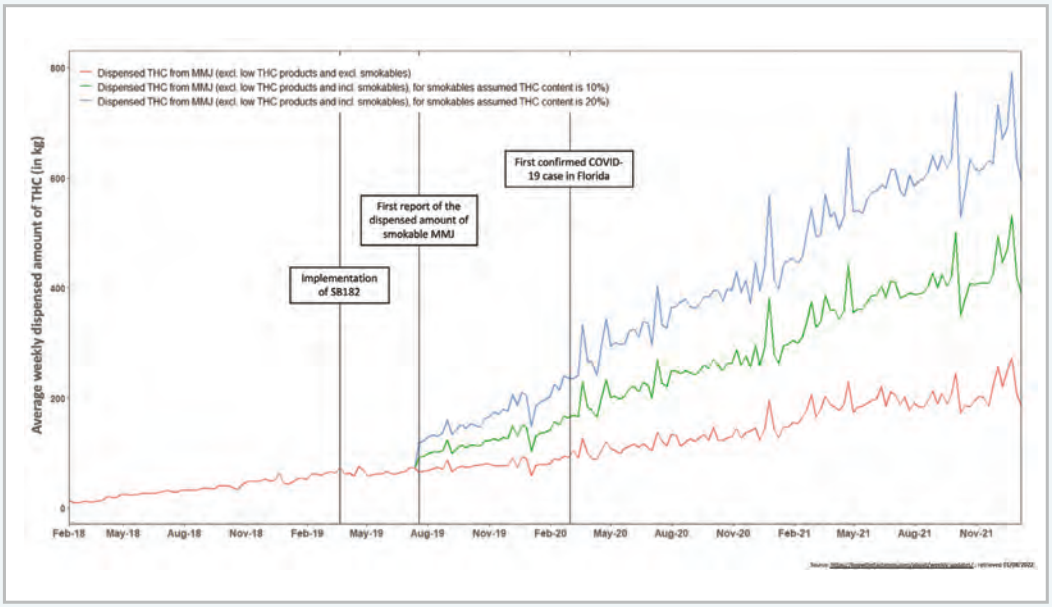
HIGHLIGHTS OF CONSORTIUM RESEARCH FINDINGS

Over the past 3 years, the Consortium has generated research on the use, mechanisms of action, and clinical outcomes of MMJ. The following highlights key findings with relevance to regulatory and clinical decisions involving the use of MMJ for the treatment of debilitating conditions.

MEDICAL MARIJUANA UTILIZATION

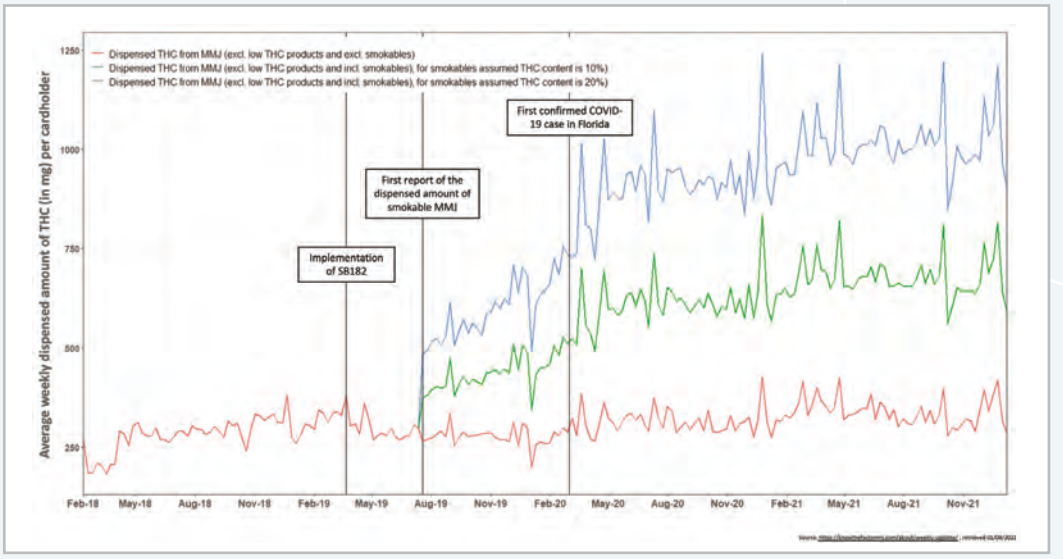
MMUR Analyses

Consistent with the growth of certified MMJ users is the growth in the total dispensed amount in the state, now totaling more than 200kg THC per week dispensed in non-smokable products, and between more than 400 and 700kg if smokable products are included, assuming a THC content between 10-20%, respectively.



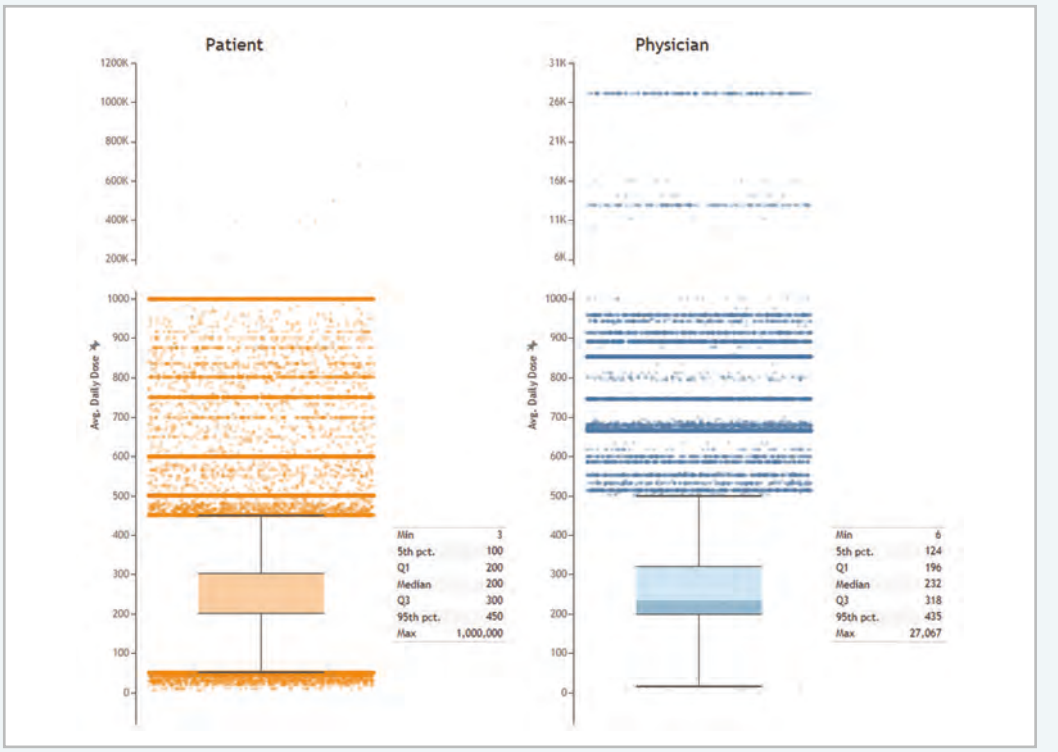
Weekly dispensed amount of THC in medical marijuana including or excluding smokables in Florida, February 2018 – January 2022

For non-smokable products, the average weekly dispensed amount of THC per total number of cardholders in a given week remained fairly consistent when comparing 2018 to 2021, with a 1.2-fold increase from a weekly average of 279mg in 2018 to 338mg in 2021. In comparison, when including smokable products, assuming 10% THC content, there was a 2.4-fold increase in the average weekly dispensed amount of THC per cardholder over the same period, from 279mg to 673mg in 2021. Including smokable and non-smokable products and assuming a THC content of 20 % in smokables, this increase was 3.6-fold.



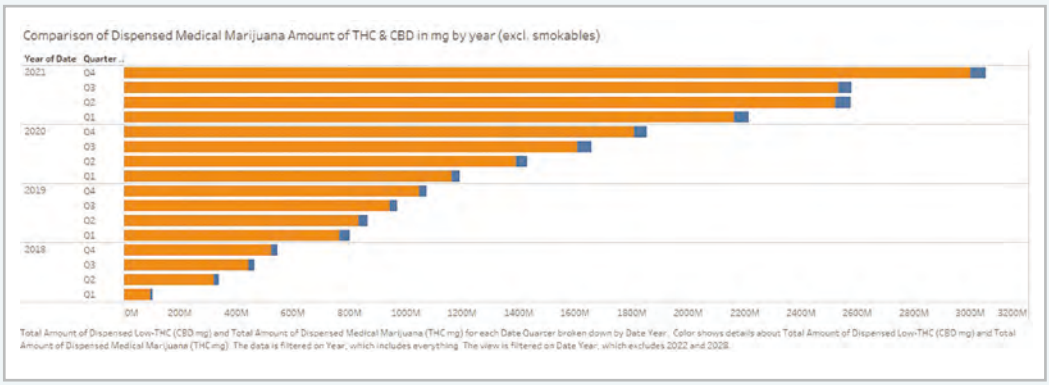
Weekly dispensed amount of THC in medical marijuana including or excluding smokables per total number of cardholders in Florida, February 2018 – January 2022

The median daily dose of THC for which patients were certified in November 2021 was 200mg. About 5% of patients were certified for a dose of 100mg or less while another 5% was certified for doses that exceeded 450mg. Averaging the doses for which patients were certified at the physician level, we note a median of 232mg. About 5% of physicians averaged 124mg or less in the daily amount of THC for which they patients for certified, while another 5% average 435mg or more.



Certified amount of THC (in mg) per day in November 2021: distribution among certified patients and certifying physicians

Note that in summarizing daily doses, the available MMUR report does not distinguish between the active ingredient, i.e., whether a patient was certified for THC when receiving a marijuana product or for CBD when receiving a low-THC product is not distinguishable. However, because the proportion of low-THC products that are dispensed is minimal, the dose distributions presented here reflect THC.

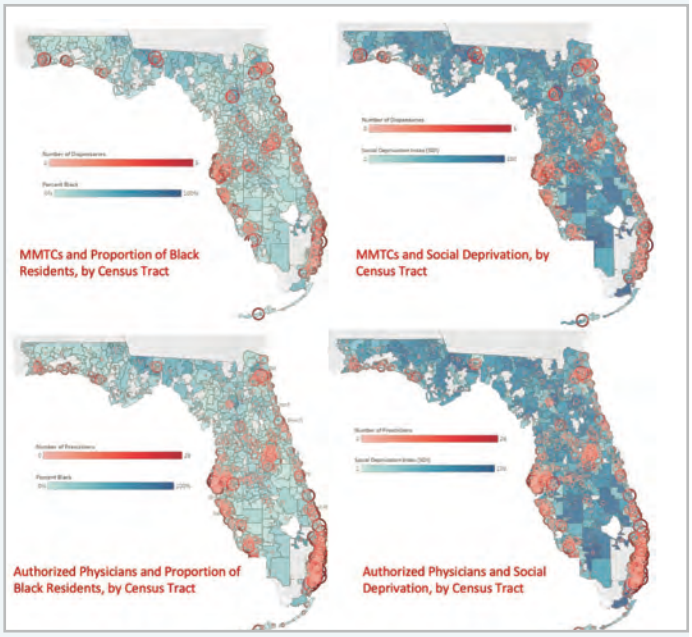


Dispensed mg THC in marijuana products excluding smokables (orange) and CBD in low-THC products

This work was completed by Consortium core faculty Drs. Brown and Winterstein and the Consortium MEMORY data science team.

Community-Level Factors and Medical Marijuana Prescriber Authorizations in Florida

MMJ authorized physicians and MMJ treatment centers (MMTCs) are concentrated in distinct regions throughout Florida. Not surprisingly, physicians that can certify patients for MMJ use and MMTCs are concentrated in urban regions due to higher population density. This concentration results in disproportionately lower access to MMJ for Floridians living in regions with more social deprivation (i.e., lower income and less access to healthcare services), located in northern and central rural regions.



Geographic distribution of MMJ certifying physicians and treatment centers by social deprivation index and proportion of citizens who are black

This work was completed by Consortium core faculty and presented at the first Consortium Research Conference CCORC in May 2021: Amie J Goodin, Yun Shen, Michael Maguire, Joshua Brown. Community-Level Factors Associated with Medical Marijuana Prescriber Authorizations in Florida.

Clinical Conditions and Prescription Drug Utilization Among Early Medical Marijuana Registrants in Florida

Initial legalization of MMJ in Florida required providers to submit initial and follow-up treatment plan forms to the University of Florida to support research on MMJ safety and efficacy. This study analyzed all treatment plans submitted between program inception (August 2016) through July 2017. The 7,548 new registrants were mostly white (83.7%), had a mean age of 52.3 years and were assessed by the provider as at least moderately ill (79.6%). Musculoskeletal and spasticity-related conditions (44.8%), chronic pain (41.9%), and mental health disorders (17.0%) were the most frequent medical complaints for seeking MMJ treatment. One in four (25.9%) patients reported use of prescription opioids and over one-fifth of patients frequently utilized at least one psychotropic medication as well as cardiovascular agents.

		Cannabis type ordered			
Medication class†, n (%)	**Total (N = 7,548)**	**Low-THC cannabis (n = 3,222)**	**Medical cannabis (MC) (n = 2,600)**	**Both (LTHC+MC) (n = 1,636)**	**p value‡**
# of medications per patient, *m* (SD), IQR	2.16 (2.4), 0-3	2.47 (2.4), 1-4	1.78 (2.3), 0-3	2.18 (2.4), 0-4	<.0001
Psychiatric medications					
Antidepressants	1,684 (22.6)	814 (25.3)	474 (18.2)	396 (24.2)	<.0001
Anxiolytics/benzodiaze-pines	1,721 (23.1)	839 (26.0)	481 (18.5)	401 (24.5)	<.0001
Hypnotics/sedatives	443 (5.9)	223 (6.9)	104 (4.0)	116 (7.1)	<.0001
Antipsychotics	270 (3.6)	113 (3.5)	105 (4.0)	52 (3.2)	0.1874
Stimulants	266 (3.6)	123 (3.8)	76 (2.9)	67 (4.1)	0.1922
Mood stabilizers	121 (1.6)	62 (1.9)	37 (1.4)	37 (1.4)	0.1943
Pain medications					
Opioids±	1,929 (25.9)	1,108 (34.4)	519 (20.0)	302 (18.5)	<.0001
Non-opioid analgesics	1,299 (17.4)	620 (19.2)	409 (15.7)	270 (16.5)	0.0020
Musculoskeletal medications					
Skeletal muscle relaxants	1,079 (14.5)	585 (18.2)	302 (11.6)	192 (11.7)	<.0001
Other musculoskeletal agents††	195 (2.6)	87 (2.7)	54 (2.1)	54 (3.3)	0.0481
Neurological medications					
Anticonvulsants	1,285 (17.2)	708 (22.0)	327 (12.6)	250 (15.3)	<.0001
Anti-Parkinson	180 (2.4)	99 (3.1)	44 (1.7)	32 (2.3)	0.0133
Other neurological agents±±	111 (1.5)	61 (1.9)	29 (1.1)	21 (1.3)	0.0381
Other classes					
Cardiovascular agents	1,525 (20.5)	694 (21.5)	447 (17.2)	384 (23.5)	<.0001
Hormonal agents & steroids	807 (10.8)	370 (11.5)	237 (9.1)	200 (12.2)	0.0018
Others incl. OTC medications	747 (7.5)	233 (7.2)	181 (7.0)	148 (9.1)	0.0557
Antiemetics	345 (4.6)	181 (5.6)	92 (3.5)	72 (4.4)	0.0020
Antidiabetic agents	340 (4.6)	149 (4.6)	100 (3.9)	91 (5.6	0.0325
Other GI agents	317 (4.3)	153 (4.8)	91 (3.5)	73 (4.5)	0.0566
Genitourinary agents	299 (4.0)	130 (4.0)	101 (3.9)	68 (4.2)	0.9037
Vitamins & supplements	262 (3.5)	124 (3.9)	77 (3.0)	61 (3.7)	0.1631
Respiratory agents	253 (3.4)	121 (3.8)	68 (2.6)	64 (3.9)	0.0243
Chemotherapeutic agents	145 (1.9)	56 (1.7)	50 (1.9)	39 (2.4)	0.3037
Hematologic agents	142 (1.9)	65 (2.0)	35 (1.4)	42 (2.6)	0.0149
Autoimmune agents	111 (1.5)	44 (1.4	31 (1.2)	36 (2.2)	0.0230
Antivirals incl. HIV medications	114 (1.5)	41 (1.3)	37 (1.4)	36 (2.2)	0.3240
Anti-infective agents	98 (1.3)	36 (1.1)	31 (1.2)	31 (1.9)	0.0635
Ophthalmic & glaucoma medications	58 (0.8)	28 (0.9)	19 (0.7)	11 (0.7)	0.719

This work was completed by Consortium core faculty and published in: Costales B, van Boemmel-Wegmann S, Winterstein A, Segal R. Clinical Conditions and Prescription Drug Utilization among Early Medical Marijuana Registrants in Florida. J Psychoactive Drugs. 2021 Jul-Aug;53(3):185-194.

Characteristics of Older Adults Who Were Early Adopters of Medical Cannabis in the Florida Medical Marijuana Use Registry

Of the state's 7548 registered MMJ users between August 2016 and July 2017, 4447 (58.9%) were older adults. Patients utilized cannabidiol (CBD)-only preparations (45%), preparations that had both tetrahydrocannabinol (THC) and CBD (33.3%) or were recorded to use both CBD-only and THC + CBD products (21.7%). The chief complaints indicating medical cannabis treatment were musculoskeletal disorders and spasms (48.4%) and chronic pain (45.4%). Among other prescription medications, patients utilized antidepressants (23.8%), anxiolytics and benzodiazepines (23.5%), opioids (28.6%), and cardiovascular agents (27.9%). Among all drug classes with potential sedating effects, 44.8% of the cohort were exposed to at least one. Patients with follow-up visits (27.5%) exhibited marked improvement as assessed by the authorizing physicians. However, the patient registry lacked detailed records and linkable information to other data resources to achieve complete follow up to assess safety or efficacy.

		Age Group		
Characteristic, n (%)	Total (N = 4,447)	**50-64 years (n = 2,662)**	**65-74 years (n = 1,238)**	**75+ years (n = 547)**
Age, m (SD)	63.4 (9.17)	57.3 (4.17)	68.8 (2.71)	80.9 (5.37)
Race				
White	3,893 (87.5)	2,290 (86.0)	1,115 (90.1)	488 (89.2)
Black	157 (3.5)	118 (4.4)	29 (2.3)	***
Hispanic, Latino or Spanish	203 (4.6)	121 (4.6)	52 (4.2)	30 (5.5)
Other/Unknown‡	194 (4.4)	133 (5.0)	42 (3.4)	19 (3.5)
Patient Condition Assessed by Provider				
Normal, not at all ill	195 (4.4)	111 (4.1)	61 (4.9)	23 (4.2)
Borderline ill	99 (2.2)	59 (2.2)	20 (1.6)	20 (3.7)
Mildly ill	588 (13.2)	359 (13.5)	167 (13.5)	62 (11.3)
Moderately ill	1,909 (42.9)	1,150 (43.2)	512 (41.4)	247 (45.1)
Markedly ill	1,156 (26.0)	715 (26.9)	317 (25.6)	124 (22.7)
Severely ill	412 (9.3)	224 (8.4)	130 (10.5)	58 (10.6)
Among the most ex-tremely ill	88 (2.0)	44 (1.7)	31 (2.5)	13 (2.4)
Alcohol	628 (14.1)	406 (15.3)	160 (12.9)	62 (11.3)
Smoking	444 (10.0)	323 (12.1)	202 (8.2)	20 (3.7)
Illicit drugs	162 (3.6)	118 (4.4)	42 (3.4)	***
Cannabis Type Ordered±				
Medical cannabis	1,481 (33.3)	926 (34.8)	409 (33.1)	146 (26.7)
Low-THC cannabis	2,000 (45.0)	1,172 (44.0)	534 (43.1)	294 (53.7)
Both low-THC & medical cannabis	966 (21.7)	564 (21.2)	295 (23.8)	107 (19.6)
Planned Order Duration				
< 1 month	469 (10.6)	288 (10.8)	110 (8.9)	71 (13.0)
1-3 months	1,919 (43.2)	1,209 (45.4)	515 (41.6)	195 (35.7)
3-12 months	382 (8.6)	238 (8.9)	109 (8.8)	35 (6.4)
> 12 months or indefinitely	1,343 (30.2)	739 (27.8)	406 (32.8)	198 (36.2)
Not specified	334 (7.5)	188 (7.1)	98 (7.9)	48 (8.8)

‡Includes Asian, Native Hawaiian, Pacific Islander, American Indian, or Alaska Native

±Medical cannabis not explicitly defined by Florida law; *Low-THC cannabis* defined by Florida law as "containing no more than 0.8 percent of tetrahydrocannabinol (THC) and at least 10 per-cent of cannabidiol (CBD)"

*** cell count ≤10

Characteristics of Florida medical marijuana registry patients at the initial treatment visit by cannabis type ordered.

Chief complaint, n (%)	Total (N = 7,548)	Age Group 50-64 years (n = 2,662)	65-74 years (n = 1,238)	75+ years (n = 547)
Musculoskeletal disorders & spasms	2,154 (48.4)	1,348 (50.6)	534 (43.1)	272 (49.7.)
Cancer	691 (15.5)	350 (13.2)	235 (19.0)	106 (19.4)
Epilepsy or seizures	130 (2.9)	93 (3.5)	30 (2.4)	***
Glaucoma	87 (2.0)	41 (1.5)	30 (2.4)	16 (2.9)
Autoimmune disorders±	142 (3.2)	104 (3.9)	29 (2.3)	***
Post-traumatic stress disorder (PTSD)	444 (10.0)	298 (11.2)	136 (11.0)	***
Amyotrophic lateral sclerosis (ALS)	24 (0.5)	***	***	***
Crohn's disease	52 (1.2)	33 (1.2)	15 (1.2)	***
Parkinson's disease	201 (4.5)	51 (1.9)	92 (7.4)	58 (10.6)
Multiple sclerosis (MS)	121 (2.7)	83 (3.1)	30 (2.4)	***
Chronic pain	2,019 (45.4)	1,242 (46.7)	520 (42.0)	257 (47.0)
Back, spine, or neck conditions	696 (15.7)	475 (17.8)	147 (11.9)	74 (13.5)
Major brain & head injuries	149 (3.4)	110 (4.1)	31 (2.5)	***
Gastrointestinal conditions	225 (5.1)	137 (5.2)	69 (5.6)	19 (3.5)
Headaches or migraines	461 (10.4)	318 (12.0)	93 (7.5)	50 (9.1)
Nervous system & neurological disorders	486 (10.9)	269 (10.1)	123 (9.9)	94 (17.2)
Psychological disorders (excl. PTSD)	589 (13.2)	376 (14.1)	158 (12.8)	55 (10.1)
Sleep disorders	310 (7.0)	199 (7.5)	82 (6.6)	29 (5.3)
Others	35 (0.8)	***	***	***

MC = medical cannabis; LTHC+MC = both low-THC and medical cannabis
†Chief complaints are not mutually exclusive; more than one condition per patient possible
±Including HIV/AIDS; excluding MS and Crohn's disease
*** low cell count < 11

Characteristics of Florida medical marijuana registry patients at the initial treatment visit by cannabis type ordered.

This work was completed by Consortium core faculty and is published in: Brown JD, Costales B, van Boemmel-Wegmann S, Goodin AJ, Segal R, Winterstein AG. Characteristics of Older Adults Who Were Early Adopters of Medical Cannabis in the Florida Medical Marijuana Use Registry. Journal of Clinical Medicine. 2020; 9(4):1166. https://doi.org/10.3390/jcm9041166

Florida Young Adult Cannabis Study (patient users vs. non-patient users)

The Florida Young Adult Cannabis Study included young adults aged 18 to 34, who had used cannabis products at least three times in the past 90-days and were residents of the state of Florida during the previous 12-months. Participation in the study was voluntary and anonymous and included 900 individuals who submitted complete survey data. Respondents were classified as a patient user if they had a MMJ registry card in the state of Florida. The sample consisted of 415 patient users (46.11%) and 485 non-patient users (53.89%). Interestingly, about 31% of non-patient users identified their cannabis use as being for primarily or exclusively self-treatment motives, while only 13% of patient users identified their cannabis use being for primarily or exclusively for recreational motives.

	Non-patient User	Patient User
Age (mean)	**24.91**	**25.75**
Sex		
Female	**65.98%**	52.29%
Male	31.13%	**42.65%**
Race/Ethnicity		
White	44.74%	44.58%
Black	23.92%	27.23%
Hispanic	20.41%	18.55%
Multiracial	**8.25%**	4.10%
Sexual Identity		
Heterosexual	70.10%	75.90%
Gay or Lesbian	5.77%	6.99%
Bisexual	**19.79%**	14.46%
Educational Attainment		
Less than High School	**6.60%**	2.41%
Completed High School	**31.13%**	22.65%
Some College	44.95%	40.24%
College Graduate	17.32%	**34.70%**
Income < $25,000	**43.30%**	29.40%
Employed	63.92%	**82.17%**
Has Health Insurance	68.45%	**82.65%**

Patient users were slightly older than non-patient users and more likely male. Respondents who dropped out of school and those who finished high school but did not go on to college were more likely to be non-patient users, while college graduates were more likely to be patient users. Respondents with an income below $25,000 were more likely to be non-patient users. Finally, respondents who were employed or had health insurance were more likely to be patient users.

Participants were asked to report all the various forms of cannabis they had used in the past 90-days, with patient users being more likely to report almost all forms compared to non-patient users. Patient users were also more likely to report microdosing cannabis 76.9% versus 57.7%), and be CBD-dominant cannabis users (64.6% versus 37.3%).

Patient users were more likely to report several health-related conditions compared to non-patient users, including pain interfering in their day-to-day activities and increased thoughts of suicide. Patient users were also more likely to be diagnosed with PTSD and report avoiding situations, having dreams, or feeling guilty related to PTSD. Patient users were also more likely to test positive and be hospitalized for COVID-19, as well as having access to medical care or medications being limited to the COVID-19 pandemic. However, non-patient users reported that the COVID-19 pandemic had a worse impact on their mental health (e.g., anxiety, depression, irritability, loneliness) than patient users.

	Non-patient User	Patient User
Experience pain	79.79%	81.69%
Pain interferes	72.37%	**82.89%**
Suicidal Ideation	22.68%	**42.41%**
Primary Care PTSD		
Felt numb/detached	43.71%	41.69%
Avoid situations	38.14%	**46.02%**
Had Nightmares	32.16%	**45.54%**
Felt guilty/blamed self	33.20%	**42.41%**
Constantly on guard	35.05%	38.55%
Diagnosed with PTSD	21.24%	**41.45%**
COVID-19		
Tested positive	10.93%	**22.89%**
Hospitalized	3.09%	**18.07%**
Access to medical care	13.61%	**27.71%**
Access to medications	9.69%	**24.34%**
Health-Related Issues		
Anxiety	**57.32%**	47.23%
Depressed mood/sadness	**52.99%**	43.61%
Difficulty with sleep	47.22%	42.89%
Irritability	**48.25%**	41.69%
Loneliness	**48.04%**	40.72%
Less motivated to connect	**47.36%**	38.80%
Appetite changes	**44.54%**	37.83%
More physically active	41.03%	39.52%
Trouble coping	41.86%	36.14%
Hopelessness	41.65%	35.90%
Restlessness	40.41%	34.46%
Trouble concentrating	38.76%	35.42%
Feeling of helplessness	36.29%	34.46%
Increased fatigue	34.43%	31.33%
Breathing difficulties	17.11%	**22.65%**

This work was completed by Consortium grant awardee Jason Ford, PhD, from the University of Central Florida.

CANNABIS DRUG INTERACTIONS

Potential Adverse Drug Events (ADE) and Interactions with Cannabis

THC has demonstrated the capability to produce clinically relevant interactions as an inhibitor of CYP3A4, CYP2C9, CYP2C19, CYP2D6, and carboxylesterase-1. Many common medications interact with these enzymes, but evidence on the clinical relevance of these interactions is lacking.

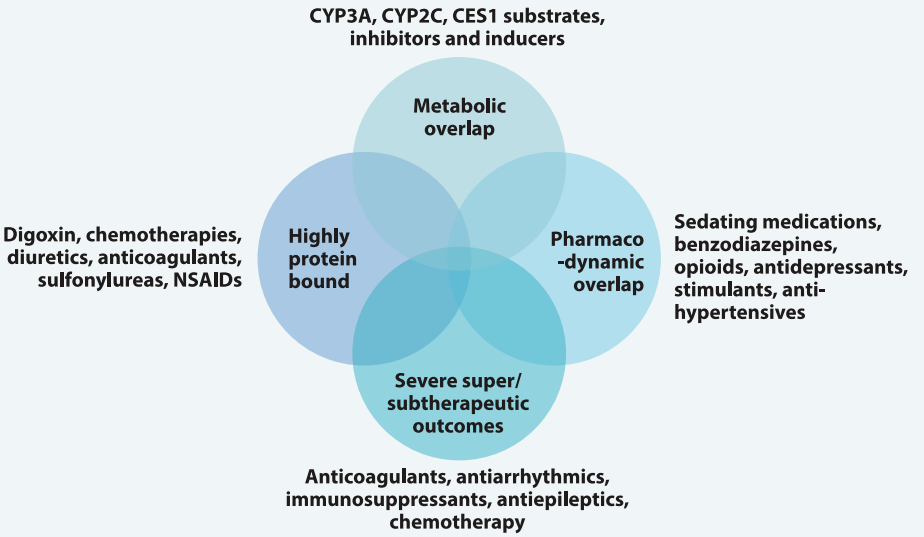
Based on our review of federally approved products containing CBD, we found that nearly one-half of CBD users experienced adverse effects, which displayed a general dose-response relationship. Common adverse effects include transaminase elevations, sedation, sleep disturbances, infection, and anemia. Given CBD effects on common biological targets implicated in drug metabolism (e.g., CYP3A4/2C19) and excretion (e.g., P-glycoprotein), the potential for drug-drug interactions (DDIs) with commonly used medication is high. General clinical recommendations of reducing substrate doses, monitoring for ADEs, and finding alternative therapy should be considered, especially in medically complex patients. CBD is implicated as both a victim and perpetrator of DDIs and has its own ADE profile. These effects should be considered in the risk-benefit assessment of CBD therapy and patients and consumers made aware of potential safety issues with CBD use.

Metabolic Drug-Drug Interactions Between Cannabidiol and Enzyme Substrates, Inhibitors, or Inducers

Enzyme	Medication Examples	Effect/Recommendation
CYP3A4 substrates	Immunosuppressants, chemotherapeutics, antidepressants, antipsychotics, opioids, benzodiazepines, z-hypnotics, statins, calcium channel blockers, others	↑ side effects related to substrate. Avoid coadministration, reduce substrate dose, monitor for adverse effects and toxicity. Avoid prescribing cascade with new treatment for side effects.
CYP3A4 inhibitors	***Strong:*** protease inhibitors, ketoconazole, loperamide, nefazodone ***Moderate:*** amiodarone, verapamil, cimetidine, aprepitant, imatinib	↑ CBD bioavailabilty, possible ↑ adverse effects. Reduce CBD dose.
CYP3A4 inducers	***Strong:*** enzalutamide, phenytoin ***Moderate:*** carbamazepine, topiramate, phenobarbital, rifampicin, efavirenz, pioglitazone	↓ CBD bioavailability, possible ↓ in effectiveness. Increase CBD dose.
CYP2C19 substrates	Antidepressants, antiepileptics, proton pump inhibitors, clopidogrel, propranolol, carisoprodol, cyclophosphamide, warfarin	↑ side effects related to substrate. Avoid coadministration, reduce substrate dose, monitor for adverse effects and toxicity. Avoid prescribing cascade with new treatment for side effects.
CYP2C19 inhibitors	***Strong:*** fluvoxamine, fluoxetine ***Other:*** proton pump inhibitors, cimetidine, ketoconazole, clopidogrel, fluconazole, efavirenz	↑ CBD bioavailabilty, possible ↑ adverse effects. Reduce CBD dose
CYP2C19 inducers	Rifampin, carbamazepine, phenobarbital, phenytoin, St. John's Wort	↓ CBD bioavailability, possible ↓ in effectiveness. Increase CBD dose.
CYP2C8/9 substrates	Rosiglitazone, burprenorphine, montelukast, celecoxib, sulfonylureas, losartan, naproxen, phenobarbital, phenytoin, rosuvastatin, valsartan, warfarin	↑ side effects related to substrate. Avoid coadministration, reduce substrate dose, monitor for adverse effects and toxicity. Avoid prescribing cascade with new treatment for side effects.

Drug-Drug Interactions Between Cannabidiol and Secondary Metabolism or Transport Proteins		
Enzyme	**Medications**	**Effect/Recommendation**
UGT1A9	Regorafenib, acetaminophen, canaglifozin, sorafenib, irinotecan, propofol, mycophenolate, valproic acid, haloperidol, ibuprofen, dabigatran, dapagliflozin, others.	↑ side effects related to substrate. Avoid coadministration, reduce substrate dose, monitor for adverse effects and toxicity.
UGT2B7	Hydromorphone, losartan, ibuprofen, naproxen, ezetimibe, lovastatin, simvastatin, carbamazepine, valproate, others.	
BCRP	Glyburide, imatinib, methotrexate, mitoxantrone, nitrofurantoin, prazosin, statins, dipyridamole	
BSEP	Paclitaxel, digoxin, statins, telmisartan, glyburide, ketoconazole, rosiglitazone, celecoxib	
UGT = uridine 5'-diphospho-glucoronosyltransferase BCRP = breast cancer resistance protein BSEP = bile salt export pump		

Considering additional pathways for interactions (beyond those mediated through metabolizing enzymes) such as protein binding or overlapping effect profiles as well as the severity of the potential adverse effect might provide a rational approach to avoiding certain combinations of cannabis with prescription drugs.



Key characteristics contributing to drug-drug interactions with cannabinoids and example medications. Medications with 2 or more categories of overlap should be used with caution, as these could lead to severe acute outcomes. CYP- Cytochrome P450; CES1- Carboxylesterase 1; NSAID- Non-steroidal anti-inflammatory drugs

The work was completed by Consortium core faculty and is published in:

Brown JD, Winterstein AG. Potential adverse drug events and drug-drug interactions with medical and consumer cannabidiol use. J Clin Med 2019;8(7):989.

Brown JD, Rivera Rivera KJ, Hernandez LYC, Doenges MR, Auchey I, Pham T, Goodin AJ. Natural and Synthetic Cannabinoids: Pharmacology, Uses, Adverse Drug Events, and Drug Interactions. J Clin Pharmacol. 2021;61 Suppl 2:S37-S52.

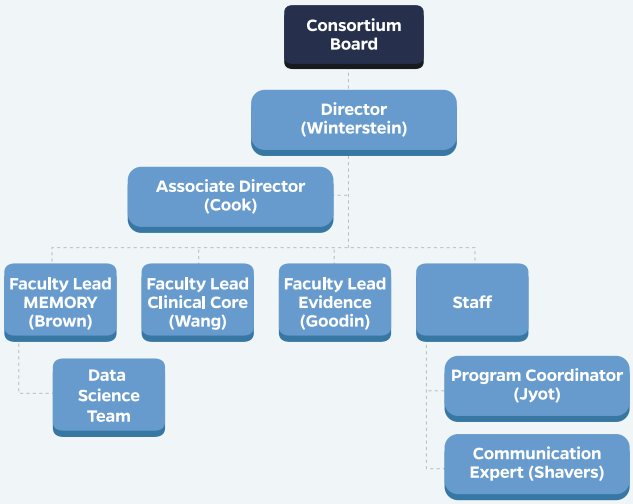
CONSORTIUM LEADERSHIP AND ADMINISTRATIVE STRUCTURE

The Consortium of Medical Marijuana Clinical Outcomes Research is open to all public and private universities in Florida. The Consortium is directed by the Medical Marijuana Research Board, which is composed of representatives from each participating university. Board members represent a variety of scientific and medical fields as required per statute. Profiles of the Consortium Board members are available in the Appendix.

CONSORTIUM FOR MEDICAL MARIJUANA CLINICAL OUTCOMES RESEARCH BOARD	
BOARD MEMBER	**INSTITUTION**
William Anderson, PhD (Chair)	Florida International University
Martha S. Rosenthal, PhD (Vice Chair)	Florida Gulf Coast University
Ximena Levy, PhD	Florida Atlantic University
Roger B. Fillingim, PhD	University of Florida
Jacqueline Sagen, PhD	University of Miami
Timothy Gilbertson, PhD	University of Central Florida
Eric H. Holmes, PhD	Florida State University
Charles Weatherford. PhD	Florida A&M University
Max. C. E. Orezzoli, PhD	Florida Memorial University

Pursuant to statute, the board appointed Almut G Winterstein, RPh, PhD, FISPE, Distinguished Professor and Dr. Robert and Barbara Crisafi Chair in Pharmaceutical Outcomes and Policy and Director of the Center for Drug Evaluations and Safety (CoDES) at UF as its director. Dr. Winterstein leads the development of MEMORY, the Consortium research data repository, administers the grants program, and oversees Consortium administration as defined by statute. She is supported by Dr. Robert Cook, MD, MPH, professor of Epidemiology and Internal Medicine and director of the Southern HIV and Alcohol Research Consortium (SHARC) Center for Translational HIV Research. Dr. Cook has assumed responsibility for developing the Clinical Research Core and leads the statewide MMJ Provider Partners Group.

They are supported by a faculty lead for MEMORY, the Clinical Research Core, and the Evidence Core, which is supported by a national scientific expert group. Program staff include a program coordinator and a communication expert who leads outreach activities, in addition to a data science team. Taking advantage of its academic base, Consortium leadership involves several trainees in Consortium activities. Profiles of the Consortium leadership and staff are available in the Appendix.



Consortium Administrative Structure

BOARD MEETINGS

Since its inception, the board has met eleven times between August 2019 and Feb 1, 2022. Key accomplishments and decisions at the board meetings are summarized in the following section and complete meeting minutes are available on the Consortium website at *https://mmjoutcomes.org/our-consortium/board-meetings/*

JUNE 3, 2021

- During the web-based meeting two new Board Members joined the Consortium board- Dr. Ximena Levy of Florida Atlantic University (FAU) and Dr. Charles Weatherford from Florida A&M University (FAMU) replacing Dr. Daniel Flynn (FAU) and Dr. Cynthia Hughes-Harris (FAMU).
- The board finalized the selection of research proposals for the 2021 grants funding cycle.

SEPTEMBER 3, 2021

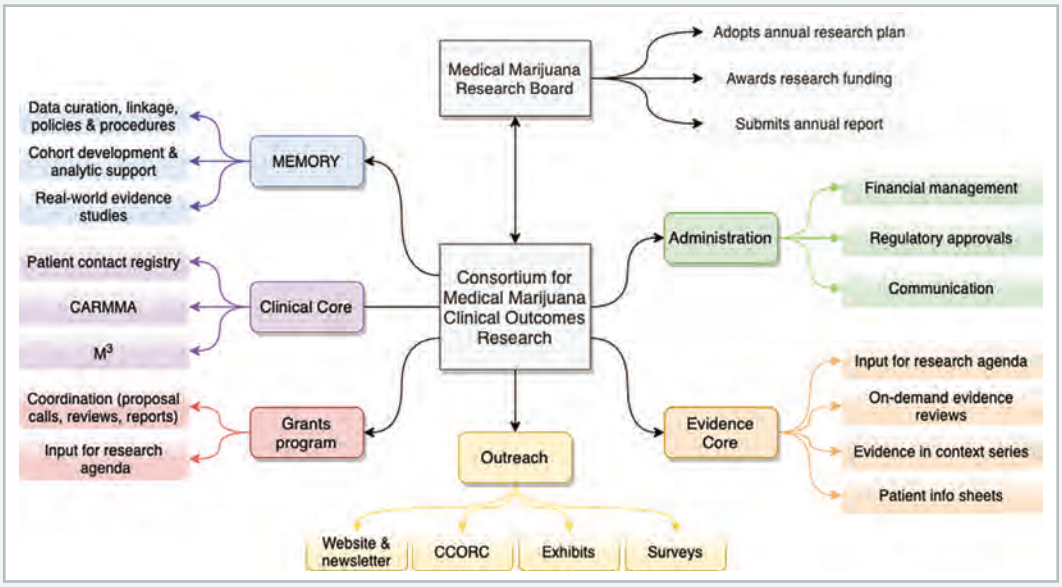
- Dr. Jacqueline Sagen from University of Miami was introduced as a new Board Member, in place of outgoing member Dr. Dalton Dietrich.
- The board approved the FY22 budget including new support for Medical Marijuana and Me (M3), a prospective study of medical marijuana patients.
- Board members approved the plans for the second conference of the consortium to be held in May 2022 in Orlando.

DECEMBER 6, 2021

- The board approved the proposed plans for the 2022 research grants program, including an updated list of research priorities and a new level of funding for clinical research proposals.

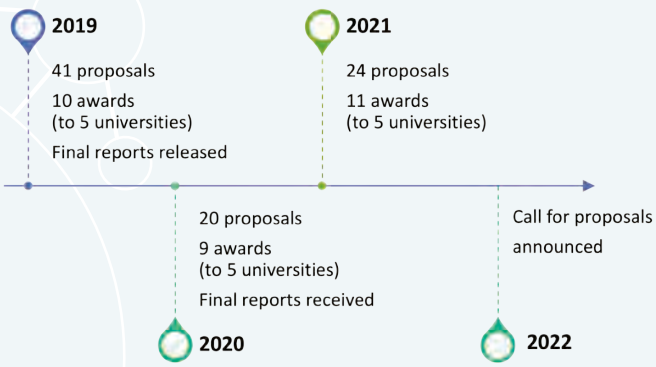
CONSORTIUM ACTIVITIES IN FY 2022

Central to the Consortium is its mission to foster clinical outcomes research on MMJ across the state. Five pillars constitute the Consortium Research Program: A Grants Program, the MEdical Marijuana Clinical Outcomes RepositorY (MEMORY), a Clinical Research Core, Outreach activities and an Evidence Core. Consistent with its charter, the Consortium has engaged scientists with relevant research programs to participate in the Consortium and foster research collaborations to accelerate the development of evidence on MMJ clinical outcomes. The following sections provide a description of each of the Consortium functions and a detailed progress report.

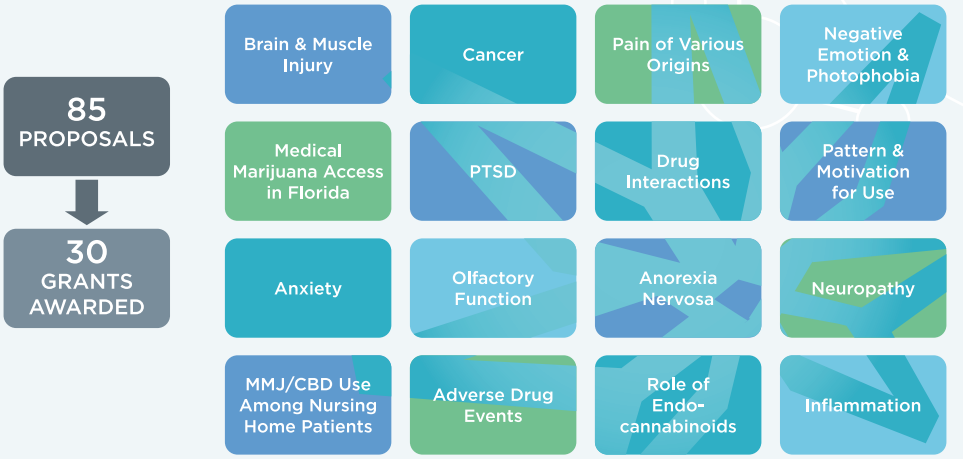


GRANTS PROGRAM

Each year, the Consortium offers a Research Grants Program, open to all members of the Consortium and teaching nursing homes. The research focus of the grants program is prioritized based on statutory guidance and the annual Consortium research agenda to ensure optimal fund utilization. Applications are reviewed by external reviewers, recruited from out-of-state, using NIH review criteria. Final grant awards are made by the Medical Marijuana Research board based on study quality, impact and relevance to the Consortium research priorities. Calls for proposals are disseminated by each board member within their university systems and through the Consortium website, newsletter, and listservs. We have completed the 2019 and 2020 grant program cycles, are mid-way through the 2021 grant program cycle and have launched the 2022 grant cycle.



The Consortium Grants Program, awarded 10 grants to faculty from 5 Consortium member institutions in 2019, 9 to faculty in 5 universities in 2020 and 11 to faculty of 5 universities in 2021. The awards, totaling close to $2 million cover a broad range of focus areas consistent with Consortium research priorities.



Consortium Grants Program: >$1.97 Million Awarded

Research outcomes and health conditions addressed in these proposals include a variety of clinical conditions such as neuropathy and pain of various origins, anxiety, cancer, and PTSD, drug interactions, pattern and motivation for MMJ use, adverse events, palliative care and MMJ access in Florida. A summary of findings of the completed studies of the 2019 and 2020 grant cycles and an overview of ongoing studies from the 2021 grants cycle are presented as follows.

Summaries for Studies Completed During the 2019 and 2020 Grant Cycles

PI: HASSAN AZARI, PHD
University of Florida

Study Title: Hemp derived extracellular vesicles (EVs) for the treatment of glioblastoma

Study Summary: Hemp EVs are nanoparticles that are naturally available in the hemp plant. We isolated and analyzed their cannabinoid content and potential therapeutic benefits in controlling tumor cell proliferation, death and invasion in human and murine glioblastoma (GBM) in tissue culture and in animal models. Hemp EVs effectively reduced GBM cell proliferation and invasion in tissue culture. Interestingly, intranasal delivery of hemp EVs into the brain tumor bed significantly delayed tumor growth and increased animal survival in an immunocompetent murine glioma model (KR-158-luc) but not in human L0 GBM xenotransplant (immunocompromised) model. With respect to the effects of hemp EVs on temozolomide (TMZ) chemotherapy, our results showed that hemp EVs might increase TMZ cytotoxic effects. Using hemp EVs together with TMZ therapy in animal model of GBM did not show any further benefits in reducing tumor growth or increasing animal survival. Measuring the amount of CBD-A in tumor bed showed that CBD-A concentration delivered via hemp EVs was much lower than the amount required to have a direct anti-tumor effect. Moreover, we found that cannabigerloic acid (CBG-A, the least abundant cannabinoid in our hemp EVs) accumulates in brain tumor tissue overtime. Overall, feasibility for large scale production, efficacious delivery of hemp EVs to the brain via the non-invasive intranasal route, possible anti-inflammatory effects of hemp EVs, and the increase in the survival of GBM tumor bearing animals, hold a great promise for future clinical utility of the hemp EVs. Patent Filed — US Provisional application for: Cannabinoid containing plant derived extracellular vesicles and therapeutic methods using the same

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PI: PAUL BORSA, PHD
University of Florida

Study Title: Efficacy of a controlled short-term trial of CBD ingestion on reducing symptomatic response and facilitating recovery after induced muscle injury

Study Summary: Many physically active Americans have reported pain-relieving effects of cannabidiol (CBD) that can reduce or eliminate use of nonsteroidal anti-inflammatory drugs (NSAIDs). Currently its biological and therapeutic effects have not been explained, and clinical research in humans regarding its effectiveness is urgently needed. We have secured Investigational New Drug (IND) status for our investigational product from the US Food & Drug Administration (FDA) Center for Drug Evaluation and Research (CDER). Our IND approved investigational product has been manufactured and processed through a Florida-based CBD company, which has agreed to source our hemp-derived CBD for the project as well as for future studies. Patient recruitment has commenced after initial delays due to the pandemic. Data from this study will help shape future grant applications on identifying an efficacious dose range of CBD, as well as determining the cellular and molecular mechanisms that contribute to symptom resolution and recovery.

PI: HELEN BRAMLETT, PHD
University of Miami

Study Title: Therapeutic dosing of a cannabinoid (CBD) after mild and moderate brain injury for translation to the clinic

Study Summary: Cannabidiol (CBD) has been shown to have anti-inflammatory, neuroprotective effects and its administration may be a therapeutic strategy in the treatment of traumatic brain injury (TBI). We observed several interesting trends with CBD treatment after TBI. We found that oral consumption of CBD may have reduced inflammation, protected vulnerable brain regions, and reversed certain memory and sensorimotor deficits that are observed after brain injury. The appearance of reduced microglia reactivity led us to believe that a higher oral dose may be more efficacious in reversing neuropathological sequelae. Further investigation is needed to fully evaluate CBD as a therapeutic avenue in TBI.

PI: JOSHUA BROWN, PHARMD, MS, PHD
University of Florida

Study Title: Characterizing community and physician-level factors associated with medical marijuana prescriber registration and patient access

Study Summary: This project created a dynamic data visualization tool and linkable database to cross-reference cannabis-licensed physician practices, cannabis dispensary locations, and community-level and physician-level indicators of access and health. We found that authorized physicians, overall and for select specialties, prescribed more opioids and more benzodiazepines than non-authorized physicians of the same specialty. Overlay of physician prescribing, practice location, dispensary locations, and other community-level measures revealed that, during the study period, there was lack of medical cannabis access in rural areas as compared with more densely populated areas in Florida. Additionally, we documented a strong correlation between cannabis access and utilization of opioids.

PI: ANDREA CIPPITELLI, PHD
Florida Atlantic University

Study Title: Cannabidiol: A potential treatment for migraine-like pain, negative emotion and Photophobia

Study Summary: Migraine is a complex condition characterized by the tendency to have headache with sensory disturbances and comorbid anxiety and depression. Our calcitonin gene-related peptide (CGRP) migraine model) in mice revealed that CGRP-induced cephalic allodynia is successfully blocked

by CBD treatment (30 mg/kg, ip) both in male and female C57BL/6J mice. We also observed reliable photosensitivity both in male and female mice, but CBD pretreatment was not effective in blocking CGRP-induced photophobia. CGRP produced anxiogenic-like activity only in male mice, an effect reversed by CBD. Collectively, our results suggest that CBD is effective in relieving migraine-like pain and anxiety comorbid to headache pain but fails in providing protection from other symptoms experienced by migraineurs such as photophobia.

PI: LISA ECKEL, PHD
Florida State University

Study Title: Cannabinoid medication for treatment of a pre-clinical model of anorexia nervosa

Study Summary: Anorexia nervosa (AN) is a serious psychiatric illness that disproportionately affects young women during adolescence and early adulthood. Clinical practice shows that this eating disorder is treatment resistant, relapse rates are high, and full recovery occurs in less than half of AN patients. While various forms of THC, including medical marijuana, have been shown to improve appetite in patients with cancer and HIV infection, the therapeutic potential of THC in alleviating AN symptoms has received relatively little attention.

In our rodent model of AN called activity-based anorexia (ABA), we found that female rats receiving THC lost less body weight and displayed increased survivability in the ABA paradigm, relative to vehicle-treated rats. Interestingly, THC's ability to attenuate weight loss in rats with ABA was due to decreases in exercise (running wheel activity) and metabolic energy expenditure. We were surprised to find that THC did not increase food intake in rats with ABA, but believe this may be related to the short duration of food access in the current study.

PI: DEBRA FADOOL, PHD
Florida State University

Study Title: Mechanisms of Action for Cannabidiol in a Mouse Model of Anxiety

Study Summary: Given the over-the-counter accessibility of CBD and the fact that anxiety disorders are the most common type of mental illness in the United States, our objective was to assess the therapeutic potential of CBD for the treatment of anxiety, attention deficit, and ingestive disorders. Our data demonstrate that acutely administered CBD decreases obsessive compulsive-like behaviors in male mice but has no effect in female mice. In terms of anxiety, wildtype female mice are responsive to a low dose of 10 mg/kg CBD and unresponsive to a high dose (20 mg/kg), whereas males required a higher dose to observe a significant reduction in anxiety-like behaviors. Interestingly, in the Kv1.3-/- mice that are naturally more anxious, acutely administered CBD was anxiogenic (anxiety generating or producing) – it caused the mice to increase their anxiety-like behaviors rather than mitigating them.

PI: JASON FORD, PHD
University of Central Florida

Study Title: Patterns, Motives, and Risks Associated with Marijuana Use: A Comparison of Medical Marijuana Patients and Non-Patient Marijuana Users in Florida

Study Summary: The Florida Young Adult Cannabis Study (FYACS) is a study of young adult cannabis users, aged 18 to 34, in the state of Florida. Our findings show that medical cannabis patients (MCPs) are older, more likely to be male, and more likely to be a college graduate, employed, and have health insurance. Non-patient cannabis users (NPUs) reported initiating regular cannabis use at a younger age and consuming cannabis products more frequently. MCPs used edible forms of cannabis more often and are also more likely to indicate microdosing or CBD-dominant use. Finally, MCPs are more likely to report health-related problems (e.g., pain, suicidal ideation).

We also found that MCPs have higher rates of other substance use and are also more likely to indicate cannabis substitution (i.e., stopping/reducing use of another drug and using cannabis in its place). MCPs are more likely to indicate that they operated a watercraft under the influence of cannabis. Finally, we found evidence of cannabis diversion from dispensaries as both MCP and NPU reported buying/receiving cannabis from someone (e.g., dealer, friend, or family) who originally obtained the cannabis at a dispensary.

MCPs are more likely to report testing positive for COVID-19, being hospitalized due to COVID-19, and having access to medical care or medications impacted due to COVID-19. Conversely, the COVID-19 pandemic appears to have a more negative effect on the mental health of NPUs as they are more likely to indicate anxiety, depression, and feelings of loneliness. MCPs reported increased access to cannabis via non-dispensary sources due to COVID-19. Finally, MCP reported being more likely to practice "social distancing" than NPUs.

Interestingly, about 30% of NPU identify using cannabis for exclusively or primarily medical reasons.

PI: GREGORY MANUS, PHD
Florida Golf Coast University

Study Title: Rapid identification and quantification of heavy metals and microplastics in CBD oil

Study Summary: The goal of this project was to develop reliable, rapid, inexpensive techniques for the determination of key contaminants within the cannabis plant. For the purposes of this study we collected 25 different CBD oil samples from 15 different vendors across the country. Analysis showed that heavy metals were not present in the samples within the detection limits of the WDXRF instrument. However, analysis did identify the presence of trace amounts of silicon in at least 12 of the 25 samples measured. Presumably, due to the low concentrations of microplastics in the samples, no characteristic endothermic phase transition temperatures were observed for the samples.

PI: JOHN MARKOWITZ, PHD
University of Florida

Study Title: An Assessment of the Drug Interaction Potential Between Oral Cannabidiol (Epidiolex®) and the CES1 Substrate Methylphenidate in Healthy Volunteers

Study Summary: The use of MMJ includes the potential risk for potential drug-drug interactions (DDIs). This study assessed whether cannabidiol (CBD) could significantly inhibit the activity of the major hepatic enzyme carboxylesterase 1 (CES1), potentially resulting in significant drug-drug interactions (DDIs) with drugs dependent on CES1 for clearance. In our open-label, placebo-controlled, crossover pharmacokinetic (PK) study in 12 healthy subjects, we assessed the influence of CBD (administered as Epidiolex®) on the disposition of the known CES1 substrate methylphenidate (MPH; Ritalin®). We noted an increase in area under the plasma concentration curve (AUCtotal) of MPH in 8 of the 12 subjects. The maximum increase of AUCtotal with coadministration of CBD reached 1.49-fold concentrations over control (placebo). Coadministration of MPH with CBD also resulted in an increased maximum plasma concentration (Cmax), in 8 of the 12 subjects with a maximum increase of a 2-fold concentration in a single subject. There was also an increased half-life (t1/2) in 6 subjects with the maximum 1.48-fold. However, when the mean MPH values for all 12 subjects were examined with and without CBD concurrent use, calculated GMRs suggested the two conditions were approximately bioequivalent i.e., suggesting a significant DDI did not occur.

PI: DAVID NEWMAN, PHD
Florida Atlantic University

Study Title: Assessing and Supporting Effective and Safe Use of Medical Marijuana for Older Adults with Chronic Pain

Study Summary: This study recruited 131 MMJ participants to obtain information on patterns of use, safety concerns, education, and MMJ's effectiveness in reducing pain. The overall finding indicated that there were some side effects, with the largest side effect being an in increased appetite (22.3%). This was followed by change in lethargy (14.0%), elevated mood changes (12.4%), lack of concentration (11.6%) and dizziness (9.1%). There was a statistically significant decrease in reported pain from prior to after MMJ use, with an average decrease of 52.7% in total pain. Participants reported that most of the education comes from the MMJ provider (52%) with an average education time lasting less than 20 minutes.

PI: MANDIP SINGH SACHDEVA, PHD
Florida A&M University

Study Title: Hyaluronic acid functionalized, Cannabidiol-loaded Mesenchymal Stem Cells (MSC)-Derived Exosomes for Drug Resistant Cancers

Study Summary: About 10-14 % of all breast cancers are triple negative (TNBC), which represents an important clinical challenge, as these tumors often develop resistance to conventional chemotherapeutics. While cannabidiol (CBD) may have favorable effects, poor solubility and increased metabolism by cytochromes P450 enzymes limit the bioavailability of CBD. We formulated exosomes derived from hUCMSCs with CBD. CBD Exosomes significantly decreased the proliferation of MDA-MB-231 and MDA-MB-468 cells. We further functionalized these exosomes by using Hyaluronic acid (HA) and it was observed that these exosomes significantly decreased the proliferation of MDA-MB-468 cells with significant increase in G1 phase cell cycle arrest when compared to CBD alone at similar doses.

PI: MANDIP SINGH SACHDEVA, PHD
Florida A&M University

Study Title: Preclinical evaluation of exosomal cannabinoid formulations in chemotherapy induced peripheral Neuropathy

Study Summary: Paclitaxel (PTX) is widely used for Triple negative breast cancer (TNBC) and PTX-induced peripheral neuropathy (PIPN) is a major clinical concern for patients. We evaluated the effects of CBD exosomes in PTX induced neuropathic mice. CBD and CBD-exosomes treatments significantly displayed improvement in neurobehavior of paclitaxel induced neuropathic animals. In our animal model, thermal and mechanical sensitivity was considerably reduced after 6 weeks in PTX induced neuropathic animals when compared to control animals. The decrease in tail flick and paw withdrawal latencies (parameters to assess neuropathy) with hot stimulus and IR radiation respectively were significantly reversed when treated with CBD and CBD-exosomes.

PI: JACQUELINE SAGEN, MBA, PHD
University of Miami

Study Title: Evaluation of medical marijuana for the treatment of chronic spinal cord injury pain using a rat central neuropathic pain model

Study Summary: Although the most frequently reported use of MMJ is for pain relief, there has been a paucity of preclinical studies evaluating the effects of cannabis in chronic pain models. Chronic pain following spinal cord injury (SCI) occurs in a majority of patients and can be so severe that it is their top quality of life concern. The chronic SCI pain-reducing effects of CBD and beta-caryophyllen (BCP) were evaluated using a battery of behavioral tests for neuropathic SCI pain in both male and female rats with clip compression spinal injury. Results showed that the CBD/BCP combination synergistically reduced cold allodynia in both male and female rats with chronic SCI neuropathic pain. The combination produced additive effects in reducing tactile allodynia.

PI: DOUGLAS STORACE, PHD
Florida State University

Study Title: The influence of cannabinoid receptors on olfactory function

Study Summary: Cannabinoids play an important therapeutic role in the stimulation of appetite. One potential mechanism underlying these changes in food-seeking behavior is the modulation of sensory input. The current study uses a combination of functional imaging and behavioral assays to determine how cannabinoid receptor modulation alters olfactory sensory input and perception.

We determined the impact of both exogenous and endogenous cannabinoids on olfactory sensitivity in mice. The infusion of WIN 55212 (CB1 receptor agonist) directly to the olfactory bulb caused a decrease in sensitivity while an intraperitoneal injection of the same drug caused no change in sensitivity. We also found that the infusion of a CB1 receptor antagonist directly into the olfactory bulb had no effect on sensitivity. This result challenges the current theory regarding the effect of cannabinoids on olfactory perception in the mouse and highlight some potential similarities with humans.

PI: KRISHNA VADDIPARTI, MSW, MPE, PHD
University of Florida

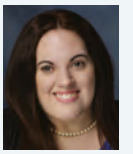
Study Title: A feasibility study of real-time monitoring of posttraumatic stress disorder related sleep disturbances and other symptoms among patients on medical marijuana

Study Summary: The goal of this pilot grant is to evaluate the feasibility of recruiting and retaining patients with PTSD on MMJ in a prospective study and examine in real-time how MMJ affects PTSD related sleep disturbances and recovery from PTSD symptoms and distress, using Ecological Momentary Assessment (EMA) delivered via smartphone and surveys. To test our hypothesis, we recruited 15 patients with confirmed PTSD seeking to start MMJ for their PTSD symptoms from cannabis clinics in North-Central Florida and assessed them at different phases of MMJ treatment. This pilot study confirmed that patients with PTSD on MMJ could be recruited and retained in longitudinal real-time monitoring research. Our preliminary analysis also suggests that there might be improvements in sleep and mental health well-being, and decreases in PTSD symptoms and nightmares.

PI: ROBERTO VINCIS, PHD
Florida State University

Study Title: Endocannabinoid mechanism in the neural processing of food-predicting sensory cues

Study Summary: In recent years, the endocannabinoid system (ECS) has emerged as one of the most important neuromodulatory systems involved in the regulation of food intake, gathering significant attention as a promising therapeutic target in eating disorders. We investigated the role of cannabinoid modulation of the mouse Insular Cortex (IC), a cortical area known to process motivationally salient stimuli associated with food reward cues and driving food-oriented behaviors. Due to the Covid pandemic and the complicated nature of the experiments itself, experiments are not yet completed.



PI: JENNY L WILKERSON, PHD
University of Florida

Study Title: Marijuana-derived terpenes for the treatment of chemotherapy-induced pain

Study Summary: Paclitaxel, commonly used to treat breast, lung and other cancers, can also produce persistent and debilitating side effects such as chemotherapy induced peripheral neuropathy (CIPN). Anecdotal reports suggest marijuana may be an effective analgesic. We examined the ability of a subset of terpenes found in marijuana and found that eah terpene reversed pain-related behavior in paclitaxel-treated mice. Cannabis-based terpenes possess a pharmacological profile that may yield new efficacious analgesics.

PI: ALI M. YURASEK, PHD
University of Florida

Study Title: The Relationship between State Medical Marijuana Laws, Substance Use and Mental Health Disorder Diagnoses, and Associated Health Care Costs

Study Summary: Despite the potential of MMJ to assist with mental health conditions, marijuana use is also associated with increased participation in substance use treatment and risk for the development of psychosis and mood-related disorders. Yet, whether the passage of MMJ laws is associated with changes in substance use, mental health diagnoses or healthcare costs remains unclear. Our preliminary analyses examined the treatment costs associated with 8 different mental health disorder diagnosis in 2012, including Opioid Use Disorder (OUD), Cannabis Use Disorder (CUD), Alcohol Use Disorder (AUD), Post-Traumatic Stress (PTSD) related disorders, Anxiety Disorders (AD), Depressive Disorders (DD), Psychosis related disorders (PD), and Sleep Disorders (SD). In 2012, states that passed MMJ laws had higher rates of OUD, CUD, AUD, PTSD, DD, and PD than those that did not yet pass MMJ laws. Similarly, the healthcare costs were significantly higher across all disorders examined in states with MMJ laws compared to those without MMJ laws.

Ongoing Studies from the 2021 Grants Cycle

PI: JENNIFER ATTONITO, PHD
Florida Atlantic University

Study Title: Acceptance of and access to medical marijuana and CBD as a palliative care and hospice treatments for nursing home patients

Project Narrative: Cannabis products may be effective to improve 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. This study creates knowledge around MMJ utilization, access, and acceptance among nursing home clinicians and patients. 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.

PI: JOSHUA BROWN, PHARMD, PHD, MS
University of Florida

Study Title: Characterizing adverse drug events reports involving cannabis and cannabinoid

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: 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.

PI: JOSHUA BROWN, PHARMD, MS, PHD
University of Florida

Study Title: Translational examination of the pharmacological interactions of medical marijuana with neuropathic pain analgesics in both young and older adults

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.

PI: ANDREA CIPPITELLI, PHD
Florida Atlantic University

Study Title: Investigating cannabidiol anti-headache actions through PPAR signaling

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.

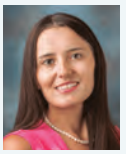
Anticipated Impact: Migraine is a debilitating disease lacking successful treatment options. Cannabidiol (CBD) appears to play a role in reducing head pain but the mechanism through which this effect occurs is unknown. This research will tell us whether activation of a group of receptor proteins called 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.

PI: LISA ECKEL, PHD
Florida State University

Study Title: Cannabinoid modulation of neuroinflammation in a pre-clinical animal model of anorexia nervosa

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.



PI: MARIOLA EDELMANN, PHD
University of Florida

Study Title: The role of endocannabinoids and cannabinoids in the clearance of bacterial infections and macrophage polarization

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: 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.

PI: DEBRA FADOOL, PHD
Florida State University

Study Title: Early Developmental Mechanisms of Action for Cannabidiol (CBD) in a Mouse Model of Anxiety

Project Narrative: CBD 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: 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.

PI: SIMONE MARINI, PHD
University of Florida

Study Title: CBD-induced biomarkers of inflammation reduction in people living with HIV at the single cell level

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.

PI: MANDIP SINGH SACHDEVA, PHD
Florida A&M University

Study Title: Evaluation of Minor Cannabinoids loaded Exosomes in Chronic Diabetic Neuropathy

Project Narrative: Diabetic Peripheral Neuropathy (DPN) is the major clinical manifestation of diabetes and has limited treatment options. Recently, we have optimized loading cannabinoids in extracellular vesicles from human umbilical cord derived stem cells/ stromal cells (hUCMSCs-EVs) grown in PBS-vertical wheel (PBS-VW) bioreactors. We will now study 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.

PI: JACQUELINE SAGEN, PHD, MBA
University of Miami

Study Title: Alleviation of phantom limb pain in a rat model by treatment with components of Cannabis

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. 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.

PI: ELLEN ZIMMERMANN, MD
University of Florida

Study Title: The Effect of Delta-9-tetrahydrocannabinol (THC) on Intestinal Inflammation and Fibrosis in Experimental Crohn's disease

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 affect 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.

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.

MMJ CLINICAL OUTCOMES RESEARCH DATA REPOSITORY (MEMORY)

The growing uptake of MMJ in Florida offers a unique opportunity for real-world evaluations of MMJ outcomes that can help overcome the slow uptake of randomized clinical trials and provide timely evidence on MMJ risk benefit. MEMORY has been conceived to establish the infrastructure for real-world MMJ clinical outcomes evaluations similar to those employed by the FDA to evaluate and monitor the risk-benefit of prescription medications.

MEMORY will support:

- **controlled studies** on MMJ effectiveness and safety
- **active surveillance** to capture emerging safety issues involving individual products or generalized effects among MMJ users
- **MMJ utilization studies** on MMJ access and utilization pattern across Floridians

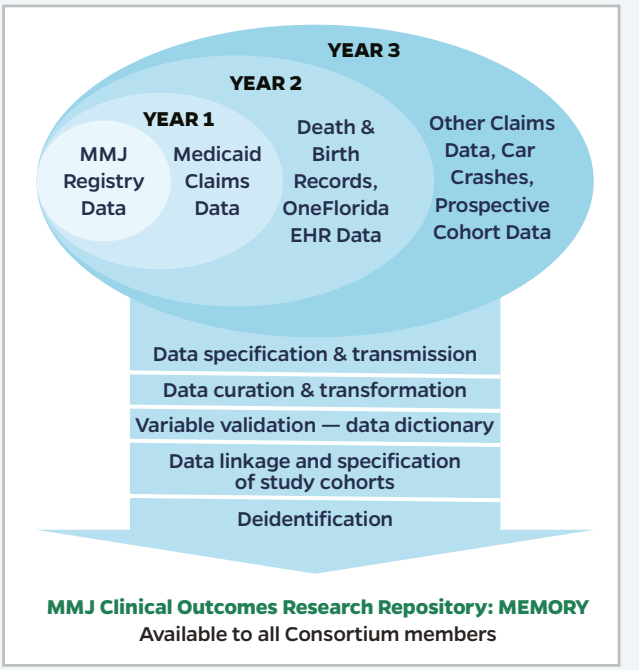
To ensure comprehensive longitudinal follow-up to capture relevant health outcomes and availability of control groups, the Consortium aims to link the Office of Medical Marijuana Use (OMMU) Medical Marijuana Use Registry (MMUR) with other clinical databases commonly used for outcomes research to create a robust research-ready repository. The planned linkages will optimize detail on MMJ use (type, dose, route, from the MMUR) and detail on patient health history, other treatments and outcomes (from linked clinical encounter data), and facilitate controlled longitudinal studies on safety and effectiveness outcomes. Importantly, via linkage to other clinical databases including pharmacy dispensing records, we will be able to establish control groups to facilitate comparisons of outcomes among patients who have initiated MMJ and patients with similar conditions and health history who are relying on conventional therapeutic approaches alone.

Pending relevant approvals, the Consortium plans to make a de-identified version of the repository available to Consortium researchers, thus providing state-wide infrastructure for real-world clinical outcomes research.

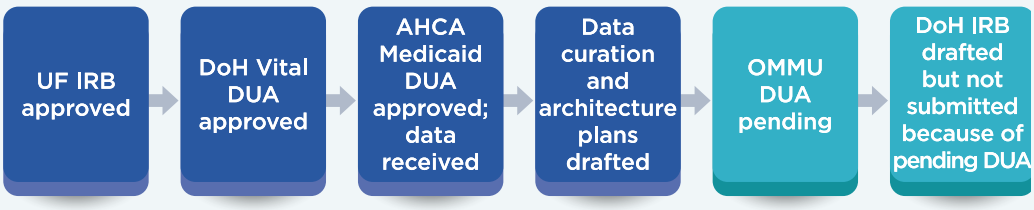
Memory Development — Progress Towards Core Milestones

MEMORY development involves several milestones including:

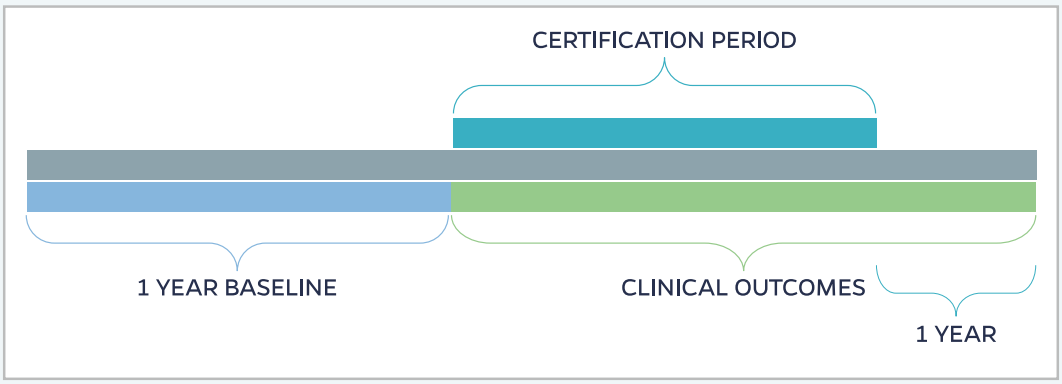
- Regulatory approvals
- Data acquisition, curation and linkage, resulting in a well-documented longitudinal database of patients who initiated MMJ and adequate control groups who have not (yet) initiated MMJ,
- Provision of adequate study cohort data for researchers along with analytical support, and
- Policies and procedures to access and use the data.



Regulatory approvals for the access to identifiable Medicaid claims data from the Agency for Healthcare Administration (AHCA) and vital statistics data from the Department of Health Vital Statistics Offices have been obtained. Approvals from the Department of Health OMMU to access the MMUR is still pending. The University of Florida Institutional Review Board (IRB) has approved the development of MEMORY and related research aims and methods, contingent upon receipt of the signed MMUR data user agreement (DUA). The same submission has been prepared for the Department of Health IRB, but submission is pending the approved MMUR DUA.



The MEMORY data science team has developed the data architecture and the data dictionary that will define variables after final data acquisition. The data dictionary contains specifications for all variables that are accessible to Consortium researchers within a de-identified longitudinal dataset. The data architecture has been specified to include cohorts of MMJ initiators whose MMJ utilization data is overlaid with healthcare utilization and outcomes data from claims and vital data. Control cohorts are customized and matched based on MMJ patients' study entry.



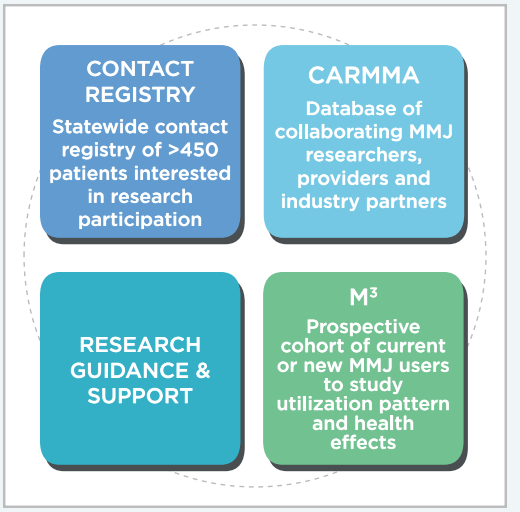
Memory Research Findings

During this fiscal year, OMMU did grant the Consortium access to a de-identified version of MMUR data that provides access to certain predefined queries. The Consortium has begun exploring these data, which has informed the development of the planned MEMORY data architecture and facilitated analyses of MMJ utilization pattern at the population level, which are featured in this report. Analyses of physician-reported adverse reactions and changes in the use of controlled substances are ongoing.

CLINICAL RESEARCH CORE

The Clinical Research Core establishes infrastructure support for prospective studies including randomized controlled trials, involving collection of new data such as patient-reported outcomes. Support services in collaboration with the Clinical and Translational Science Institutes (CTSIs) at UF, the University of Miami and Florida State University, include assistance with patient recruitment, data collection or analysis, clinical research study design, support with regulatory issues (with FDA or DEA), and access to laboratory experts for product analysis.

The Clinical Core also provides three specific resources to support clinical outcomes research: its Patient Contact Registry, the "medical marijuana and me M3" Patient Cohort, and a database of research collaborators (CARMMA).



MMJ Contact Registry

The **MMJ contact registry** facilitates patient recruitment for future research on MMJ clinical outcomes. The registry was approved by the University of Florida IRB in November 2020. As of January 2022, 476 current or prospective MMJ users across the state are enrolled in the contact registry. Clinics participating in recruitment and the geographic location of enrolled patients is similar to the current geographic distribution of MMJ clinics and dispensaries.

The mean age of registrants is 44 years, with slightly larger representation of female patients (55.2% female, 43.0% male, 0.4% transgender, 1.1% non-binary). The race/ethnicity distribution of the patients is 80.8% White, 10.2% Black, 4.2% Multiracial, 1.8% American Indian or Alaska Native, 0.4% Asian, 0.4% Native Hawaiian or Other Pacific Islander, and 12.7% Hispanic/Latino. Participants identified the following five health conditions as their main reason for using or starting the use of medical marijuana: anxiety (79.6%), chronic pain (67.6%), depression (61.6%), insomnia (52.2%), and post-traumatic stress disorder (PTSD) (41.6%).

Medical Marijuana & Me (M^3)

During 2021, the Consortium launched Medical Marijuana & Me (M^3), the first large MMJ patient cohort in Florida, and one of the first in the United States. M3will provide detailed patient-reported data to enhance our understanding of patient experiences with MMJ. The strategic goals for Medical Marijuana & Me are 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 MMJ users in Florida.
- provide access to data and recruitment infrastructure for consortium researchers to support pilot studies, papers, and grant proposals.
- support high-quality, impactful research that can inform state policy, clinician practice and patients.

Starting early 2022, the Consortium will begin recruitment of at least 1,000 adult patients (500 new MMJ users and 500 current MMJ users) to complete a sequence of surveys about their general health, use and experiences with MMJ and related health outcomes.

M3aims to answer the following eight research aims.

1. **Persistence of MMJ use** — quantify persistence of among MMJ initiators at 3 months and 9 months after initiation and identify reasons for discontinuation.
2. **Outcome trajectories** — among MMJ initiators, describe outcome trajectories for the most commonly cited primary reasons for MMJ use (e.g., pain, anxiety, insomnia, and PTSD), and determine factors associated with differences in trajectories.
3. **Preferred MMJ uses** — describe the specific modes of MMJ consumption, dosing, and frequency of use that patients report to be "most effective" and describe patient characteristics associated with these preferences.
4. **MMJ utilization pattern** — describe the change in products, modes of consumption, and dosing over time.
5. **Adverse effects** — characterize the types of adverse effects and identify the specific products and patient characteristics associated with different types of side effects from MMJ, including symptoms of a cannabis use disorder.
6. **Other substance use** — among MMJ initiators document the use of alcohol, tobacco, and other substances.
7. **Concurrent use of prescription medications** — among MMJ initiators describe the concurrent use of prescription medications for the treatment of mental health conditions and factors associated with changes in prescription medication/substance use after initiating MMJ.
8. **MMJ drug interactions** — characterize concomitant medication use and assess the potential risk for drug interactions with medical marijuana.

M3design has been guided by a scientific planning committee consisting of 11 members, including six researchers from consortium member universities, four MMJ physicians, and one MMJ patient representative.

SCIENTIFIC PLANNING COMMITTEE MEMBERS — M³ (MMJ PATIENT COHORT)		
PARTICIPANT	**INSTITUTION**	**ROLE ON PLANNING GROUP**
George Burgess	University of Florida	MMJ Patient Liaison
John Crump, MD	Releafe Now	Certified MMJ Provider
Justin Davis, MD	Florida Marijuana Doctors	Certified MMJ Provider
Jason Ford, PhD	University of Central Florida	MMJ Researcher
Raul Gonzalez, PhD	Florida International University	MMJ Researcher
Patricia Green-Powell, PhD	Florida A&M University	MMJ Researcher
Dushyantha Jayaweera, MD	University of Miami	MMJ Researcher
Jonathon Quinonez, DO	CannaMD	Certified MMJ Provider
Martha Rosenthal, PhD	Florida Gulf Coast University	MMJ Researcher
Denise Vidot, PhD	University of Miami	MMJ Researcher
Michelle Weiner, DO, MPH	Spine Wellness America	Certified MMJ Provider

CARMMA

The Consortium launched the Connect and Advance Research for Medical Marijuana Analysis (CARMMA) Database to connect researchers, physicians, and industry collaborators with the goal to increase and accelerate MMJ research. Researchers, physicians, and industry collaborators can add their contact information and connect with other researchers, physicians, and industry collaborators at any time. As of January 2022, CARMMA has 21 researchers, five physicians, and two industry collaborators and can be accessed at *https://mmjoutcomes.org/collaborate/carmma/*.

OUTREACH

The Consortium's outreach activities are directed towards patients, providers, researchers, and industry, to maximize participation in research and keep these stakeholders abreast of the latest research findings.

In addition to its website and newsletter, the Consortium enhanced its outreach activities with a new researcher spotlight video series and by hosting the inaugural annual Cannabis Clinical Outcomes Research Conference (CCORC).

Researcher Spotlight Series

In Fall 2021, the Consortium commenced the Researcher Spotlight Series, a video series showcasing Consortium researchers. The Spotlight series intends to disseminate Consortium research and raise awareness about Consortium work and the importance of the scientific process in evaluating MMJ outcomes.

The videos will include an overview of the researcher's project, methodological approaches, clinical relevance, and current/expected results. The first two spotlight videos will feature Dr. John Markowitz and Dr. Paul Borsa and are expected to be released in Feb 2022.

Website

The Consortium continues to expand its website (*https://mmjoutcomes.org/*) to disseminate information to researchers, member institutions, physicians/providers, patients, and the public. The website provides a comprehensive and interactive hub for the grants program, research updates, and Consortium news. Since its launch in October 2019, more than 7,338 web-users have visited the new website. The Consortium has started to optimize its website utility to ensure all content is accessible from mobile devices.

Newsletter

As part of the communication and outreach plan, the Consortium distributes quarterly newsletters via email to researchers, physicians/providers, and individuals interested in MMJ research.

The newsletter includes updates on Consortium activities and ongoing research. For recognition, the Consortium branded the newsletter as **MEDICAMENT**, which stands for **MEDICA**l **M**arijuana r**E**search **N**ewsle**T**ter. A total of 735 individuals have signed up for the newsletter as of December 2021.

The Consortium has published nine issues of MEDICAMENT, one every quarter, available at *https://mmjoutcomes.org/newsletter.*

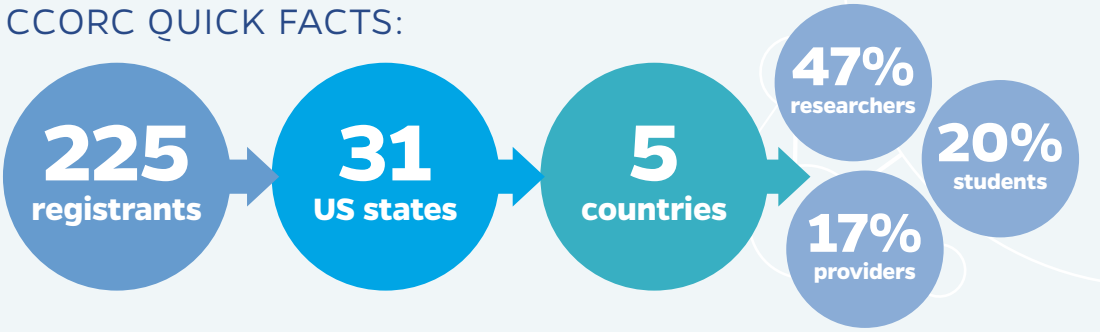
Cannabis Clinical Outcomes Research Conference (CCORC)

In 2021, the Consortium for Medical Marijuana Clinical Outcomes Research launched its annual Cannabis Clinical Outcomes Research Conference (CCORC), a research-centric meeting, open to patients and providers, to share research findings, disseminate the latest evidence on the health effects of marijuana, and stimulate research collaborations throughout the state and nationally.

The objectives of CCORC are:

- Dissemination of research findings on medical cannabis use, efficacy, safety, and other relevant outcomes
- Provide a venue for clinical and research educational opportunities related to medical cannabis
- Foster research collaboration, and stakeholder engagement, between Consortium member institutions and beyond

CCORC QUICK FACTS:



CCORC 2021

On April 8th and 9th, 2021, the Consortium virtually hosted the inaugural Cannabis Clinical Outcomes Research Conference (CCORC). CCORC 2021 was made possible by the hard work of two committees, the CCORC Organizing committee and the Scientific Program Committee, where committee membership is recruited from all Consortium member institutions.

The committees helped successfully plan and execute the CCORC 2021 agenda, which included keynote addresses by three national level experts in the field of cannabis research, three panel discussions, as well as poster presentations, networking sessions, and an exhibitor hall.

The three eminent keynote speakers all served on the National Academy of Science panel that synthesized the evidence on marijuana effectiveness and safety in 2017. **Dr. Ziva Cooper**'s research focuses on preclinical and clinical studies on the behavioral and physiologic effects of psychoactive drugs, including cannabis and opioids. Her current research involves understanding the neurobiological, pharmacological, and behavioral variables that influence both the abuse liability and therapeutic potential of cannabinoids and opioids. **Dr. Donald Abrams** has conducted numerous clinical trials investigating complementary therapies in patients with HIV, including therapeutic touch, traditional Chinese medicine interventions, medical marijuana, medicinal mushrooms, and distant healing. **Dr. Lorraine Collins**' research interests include cognitive and behavioral approaches to the conceptualization, prevention, and treatment of addictive behaviors, particularly among emerging and young adults.

A total of 35 abstracts were accepted for presentation following peer review and are published in the scientific journal Medical Cannabis & Cannabinoids.

CCORC 2021 drew over 225 registrants from across 31 U.S. states and five countries (Germany, Italy, Mexico, United Kingdom, and United States). Majority of the attendees were researchers followed by physicians, students, industry representatives and others.

PROGRAM

AT A GLANCE

April 8, 2021

TIME EDT (PDT)	EVENT
12:00-12:30pm (9:00-9:30am)	**Day 1 Welcome Address** Dr. Roger Fillingim Chair, Consortium for Medical Marijuana Clinical Outcomes Research Board Dr. Almut Winterstein Director, Consortium for Medical Marijuana Clinical Outcomes Research Dr. Amie Goodin Program Chair, CCORC Faculty Lead - Evidence, Consortium for Medical Marijuana Clinical Outcomes Research
12:30-1:30pm (9:30-10:30am)	**Keynote: Cannabis Science vs. Policies: Reconciling the Disconnect *** Dr. Lorraine Collins University at Buffalo
1:30-2:00pm (10:30-11:00am)	**Poster Session: Cannabis and Cannabinoids for Pain and Anxiety-Related Conditions**
2:00-2:30pm (11:00-11:30am)	**Keynote: Clinical Trials of Cannabis in Cancer and Sickle Cell Pain: 'Not as Easy as It Looks!' *** Dr. Donald Abrams University of California, San Francisco
2:30-3:30pm (11:30am-12:30pm)	**Panel: Research and Regulatory Barriers *** Dr. Shanna Babalonis University of Kentucky Dr. Chinazo Cunningham Albert Einstein College of Medicine Dr. Lance McMahon University of Florida Dr. Jacqueline Sagen University of Miami Dr. Donald Abrams University of California, San Francisco
3:30-4:30pm (12:30-1:30pm)	**Poster Session: Education, Practices and Safety** **Networking Session**
Continuous	**Exhibition hall, forums, and poster breakout rooms**

April 9, 2021

TIME EDT (PDT)	EVENT
12:00-12:30pm (9:00-9:30am)	**Day 2 Welcome Florida Director of Cannabis, "The Future of Cannabis Research in Florida"** Holly Bell Florida Department of Agriculture and Consumer Services Dr. Robert Cook Associate Director, Consortium for Medical Marijuana Clinical Outcomes Research Dr. Amie Goodin Program Chair, CCORC Faculty Lead - Evidence, Consortium for Medical Marijuana Clinical Outcomes Research
12:30-1:30pm (9:30-10:30am)	**Keynote: Controlled Human Studies Investigating Cannabis Constituents for Pain: A Translational Perspective *** Dr. Ziva Cooper University of California, Los Angeles
1:30-2:00pm (10:30-11:00am)	**Poster Session: Cannabis Use Patterns and Behavior**
2:00-3:00pm (11:00am-12:00pm)	**Panel: Oral Presentations of Top Abstracts *** Dr. Yan Wang University of Florida Dr. Robert Cook University of Florida Dr. Hassan Azari University of Florida Krystal Hemingway Florida State University
3:00-3:30pm (12:00-12:30pm)	**Poster Session: Cannabis as a Novel Therapeutic**
3:30-4:30pm (12:30-1:30pm)	**Networking Session** **Closing; Board Reception**
Continuous	**Exhibition hall, forums, and poster breakout rooms**

** Eligible for CME credit. Please check http://ccorc.mmjoutcomes.org/cme-credit/ for details.*

The University of Florida College of Medicine designates this live activity for a maximum of 3.5 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity. The University of Florida College of Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

PROGRAM

Proceedings of CCORC 2021 are published in: Goodin AJ, Wilson DL, Cook RL, Wang Y, Brown J, Winterstein AG. Proceedings of the 2021 Cannabis Clinical Outcomes Research Conference. Med Cannabis Cannabinoids 2021;4:143-146.

CCORC 2022

The Consortium is planning the second Cannabis Clinical Outcomes Research Conference (CCORC) to be held on May 19th and 20th, 2022 in Orlando, Florida. To accommodate constraints that might be imposed by the pandemic and to maximize outreach, CCORC 2022 will be a hybrid event, with both in-person and virtual options. A scientific program committee with participation from consortium member institutions advises the organizing committee on conference themes and scientific content.

The CCORC save-the-date announcements and call for abstracts have been widely disseminated.

EVIDENCE CORE

The evidence core focuses on the synthesis and dissemination of scientific evidence for researchers, providers and patients. Evidence core activities include publication of its Evidence in Context series and patient info sheets, provision of scientific expertise as needed by Consortium researchers, clinicians, policy-makers and other stakeholders and development of evidence reviews to inform the Consortium research priorities.

Patient Info Sheets

The Evidence core has launched a new collection of patient info sheets with initial focus on three entries in the "Medical Marijuana 101 series":

1) The Medical Marijuana Program in Florida: History and Definitions,

2) Explanation of Common Terms,

3) An Introduction to the Endocannabinoid System (ECS).

The purpose of these info sheets is to provide unbiased, evidence-based and up-to-date information about important topics on MMJ clinical outcomes in a format that is clear and concise for all members of the public. A series on common medications that may interact with cannabis, and a series on the effectiveness and safety of MMJ for currently approved conditions is in development. These info sheets are accessible on the Consortium website and disseminated by the Consortium in collaboration with the Florida A&M University (FAMU)'s Medical Marijuana Education and Research Initiative (MMERI).

MEDICAL MARIJUANA PROGRAM IN FLORIDA: HISTORY AND DEFINITIONS

EDUCATIONAL SERIES:
MEDICAL MARIJUANA 101

Updated September 2021

In 2016, Florida implemented the Compassionate Medical Use Act, also known as Amendment 2. This allows patients with a qualifying condition to use medical marijuana after receiving certification from an authorized medical marijuana physician.

OMMU

Established by the Florida Department of Health, the Office for Medical Marijuana Use (OMMU) is charged with writing and implementing the Department of Health's rules for medical marijuana; overseeing the statewide Medical Marijuana Use Registry; licensing Florida businesses to cultivate, process and dispense medical marijuana; and certifying marijuana testing laboratories.

MMUR

The Medical Marijuana Use Registry (MMUR) is a secure, electronic, online database for the registration of qualified physicians and patients and their orders.

It is accessible by patients, qualified physicians, law enforcement, medical marijuana treatment center staff and Office of Medical Marijuana Use staff.

MMTCs

Often called dispensaries, licensed Medical Marijuana Treatment Centers (MMTCs) are the only businesses in Florida authorized to dispense medical marijuana and low-THC cannabis to qualified patients and caregivers.

CERTIFYING PHYSICIAN

A physician who is authorized to order low-THC cannabis, medical marijuana or cannabis delivery devices for qualifying patients. *A list of certifying physicians can be located at knowthefactsmmj.com.*

CONDITIONS

To be eligible for medical marijuana in Florida, you must have one of the following qualifying medical conditions or symptoms:

- Cancer
- Epilepsy
- Glaucoma
- HIV/AIDS
- Post-Traumatic Stress Disorder (PTSD)
- Amyotrophic Lateral Sclerosis (ALS)
- Crohn's Disease
- Multiple Sclerosis (MS)
- Parkinson's Disease
- Medical condition comparable to those listed
- Terminal condition diagnosed by a physician other than the qualified physician issuing the physician certification
- Chronic nonmalignant pain caused by a qualifying medical condition or that originates from a qualifying medical condition and persists beyond the usual course of that qualifying medical condition

To learn more, please visit the Office of Medical Marijuana Use (OMMU) at knowthefactsmmj.com

Consortium for Medical Marijuana Clinical Outcomes Research

For more information, please visit the Consortium for Medical Marijuana Clinical Outcomes Research at mmjoutcomes.org.

Please note: this document is for informational purposes only, but is not medical or legal advice and should not be used to make healthcare decisions. Please consult your healthcare provider to find out what treatment options are available for you.

EXPLANATION OF COMMON TERMS

EDUCATIONAL SERIES:
MEDICAL MARIJUANA 101

Updated May 2021

While research is not conclusive about the benefits and risk of medical marijuana, it is helpful to understand what makes up marijuana and what compounds are believed to affect health. This information sheet is intended to provide an explanation of common terms that describe marijuana plants and some components of these plants.

CANNABIS

Cannabis is the plant used to create hemp and marijuana products. There are three common cannabis plant species:

Sativa
Tall plant, narrow leaves

Indica
Bushy plant, broad leaves

Ruderalis
Short plant, varied leaves

HEMP

Hemp plants are cannabis species.

Hemp products, however, contain a small amount of the chemical known as "THC" (less than 0.3% THC), which means hemp products are unlikely to have psychoactive effects. Hemp products can be cultivated and sold as of 2018 according to the Federal Agricultural Act.

MARIJUANA

Marijuana is another word for the cannabis plant.

Marijuana products contain more THC (greater than 0.3% THC) than hemp, and are only legally available through Medical Marijuana Treatment Centers (MMTCs) in Florida.

CANNABINOIDS

Marijuana contains at least 120 compounds called cannabinoids that cause euphoric feelings or psychoactive effects.

The two most common cannabinoids are cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC).

CBD

CBD is a cannabinoid that causes blissful feelings and may reduce certain types of inflammation (swelling).

It is believed to cause a "calm" feeling.

THC

THC is a cannabinoid that causes both blissful feelings and psychoactive effects.

It is believed to cause a "high" feeling.

TERPENES

Marijuana contains compounds called terpenes that produce a distinctive marijuana odor, as well as therapeutic smells like lavender and peppermint.

It is currently unknown if terpenes play a role in health effects.

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Consortium for Medical Marijuana Clinical Outcomes Research

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AN INTRODUCTION TO THE ENDOCANNABINOID SYSTEM (ECS)

EDUCATIONAL SERIES:
MEDICAL MARIJUANA 101

Updated May 2021

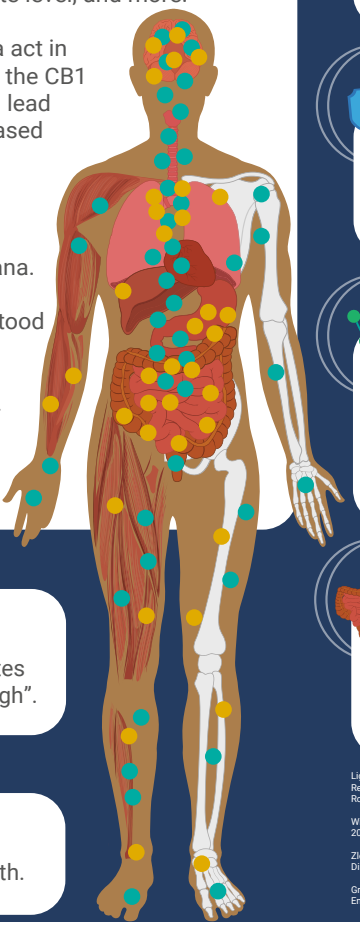
Your body naturally creates substances called endocannabinoids, and some of these are similar to the cannabinoids found in marijuana.

The body's ECS sends "signals" (endocannabinoids) to "receivers" (CB1 and CB2 receptors) to help balance your body's sleep cycle, appetite level, and more.

The cannabinoids in marijuana act in a similar way by connecting to the CB1 and CB2 "receivers" which can lead to different effects (e.g., increased appetite, changes in mood). But cannabinoids in marijuana are not identical to human cannabinoids and they are not the only component of marijuana.

It is not yet completely understood whether and how medical marijuana may help with a number of medical conditions.

- CB1 receptors
- CB2 receptors



CENTRAL NERVOUS SYSTEM

Supports the brain and central nervous system including increasing memory.

IMMUNE SYSTEM

Affects the immune system to reduce inflammation.

HORMONES

Balances hormones that support metabolism, reproduction, and stress levels.

MUSCLES

Helps control blood sugar. Creates a feeling similar to a "runner's high".

BONES

Supports bone mass and strength.

DIGESTING FOOD

Helps control irritation and inflammation in your digestive system.

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Consortium for Medical Marijuana Clinical Outcomes Research

For more information, please visit the Consortium for Medical Marijuana Clinical Outcomes Research at mmjoutcomes.org.

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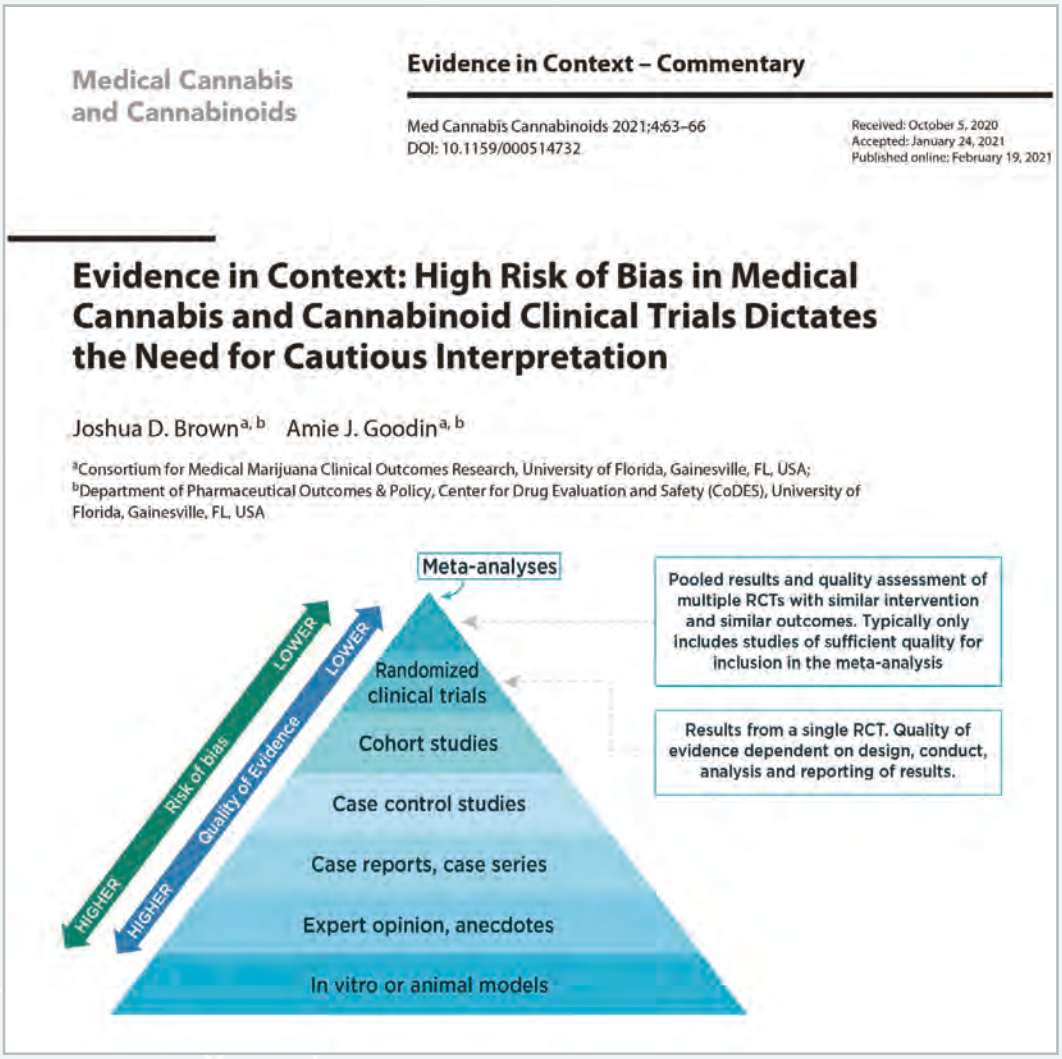
Evidence in Context Series

The evidence base for medical cannabis and cannabinoids continues to evolve rapidly while researchers, healthcare providers, and patient communities remain in need of clear translation of study findings to future or current implications for clinical practice. The "Evidence in Context" series addresses these needs for rapid distillation and appraisal in the form of brief, plain-language commentaries. These articles are available in the scientific journal Medical Cannabis and Cannabinoids and on the Consortium websites and both of these publication platforms are fully accessible to all members of the public, as the journal uses an open-access publishing format. To date, the journal has published four articles within this series accessible at *https://mmjoutcomes.org/evidence/evidence-in-context/* and in linked to in the Bibliography section. No such resource was previously available specifically for MMJ.



Medical Cannabis and Cannabinoids

Evidence in Context – Commentary

Med Cannabis Cannabinoids 2021;4:63–66
DOI: 10.1159/000514732

Received: October 5, 2020
Accepted: January 24, 2021
Published online: February 19, 2021

Evidence in Context: High Risk of Bias in Medical Cannabis and Cannabinoid Clinical Trials Dictates the Need for Cautious Interpretation

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Medical Cannabis and Cannabinoids

Evidence in Context – Commentary

Med Cannabis Cannabinoids 2021;4:121–124
DOI: 10.1159/000517154

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Accepted: May 10, 2021
Published online: June 17, 2021

Much Ado about Dosing: The Needs and Challenges of Defining a Standardized Cannabis Unit

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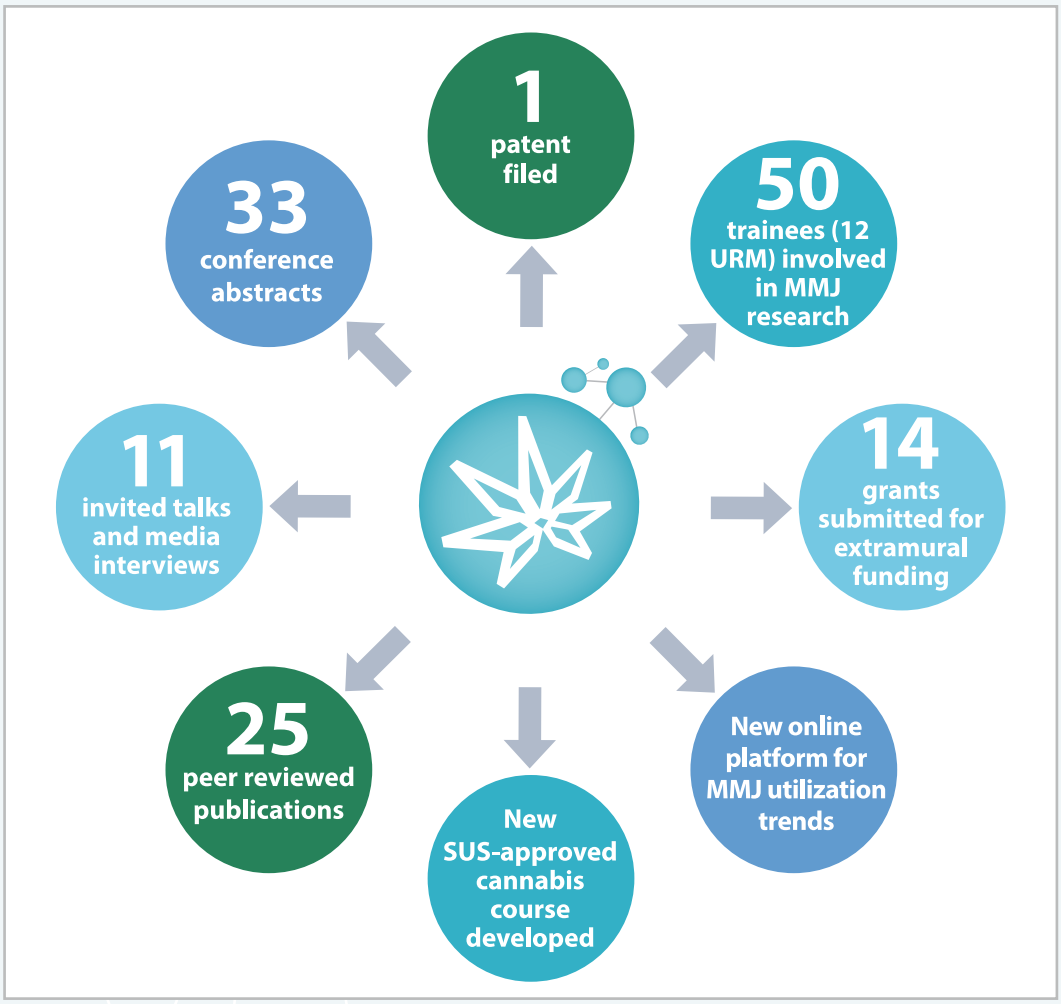
[a]Consortium for Medical Marijuana Clinical Outcomes Research, University of Florida, Gainesville, FL, USA; [b]Department of Pharmaceutical Outcomes & Policy, Center for Drug Evaluation and Safety (CoDES), University of Florida, Gainesville, FL, USA; [c]Department of Epidemiology, University of Florida, Gainesville, FL, USA

Key Points

- A definition of a standardized cannabis unit is needed to accelerate research in medical cannabis and enable safe and effective use of medical cannabis products.
- A standardized cannabis unit should incorporate several factors, such as plant-related aspects (e.g., varied cannabinoid concentrations in *Cannabis sativa*) and product attributes, such as different administration routes and cannibinoid concentrations. Furthermore, different intentions for the use and desired subjective effects also influence the dose needed for the intended effect.
- Many barriers remain in defining a standardized unit for cannabis (e.g., different delivered doses and pharmacokinetics depending on the administration route) and pathophysiological factors that can impact the response to the therapy or side-effect profile.
- A recent proposal for a standardized tetrahydrocannabinol (THC) unit by Freeman and Lorenzetti, which defines a "Standard THC Unit" of 5 mg THC, presents a sophisticated approach to support safe, nonmedical cannabis consumption within the same administration route. However, this approach may be limited when considering medical cannabis products, given a need to track efficacy and safety, a variety of products available, and the need to understand the composition of other cannabinoids.
- Further efforts in developing a standardized cannabis unit are needed to capture the medical cannabis perspective, possibly including the antagonizing effect of cannabidiol on THC, the role of the entourage effect, and the relationship between pharmacokinetic profiles and therapeutic effects of cannabis constituents.

SUMMARY OF CONSORTIUM RESEARCH PRODUCTIVITY

Over the only 2.5 years of its existence, Consortium core faculty and Consortium grant awardees have generated 25 published manuscripts in peer-reviewed journals, and the new data has already served as the basis for 1 patent and 14 new extramural grant applications, two of which were awarded. Noteworthy, 50 trainees including 12 from underrepresented minorities have been involved in the funded research grants and two new courses have been developed, one of which is SUS approved, supporting the development of MMJ research capacity in the state.



Early Outputs of the Consortium Research Program

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25. **Wilkerson JL**, Bilbrey JA, Felix JS, Makriyannis A, McMahon LR. Untapped endocannabinoid pharmacological targets: Pipe dream or pipeline? Pharmacol Biochem Behav. 2021 Jul;206:173192. doi: *10.1016/j.pbb.2021.173192*, Epub 2021 Apr 29. PMID: 33932409..

EXTRAMURAL GRANTS SUBMITTED BY CONSORTIUM FACULTY AND GRANT AWARDEES

Lead principal investigator, funding agency, title

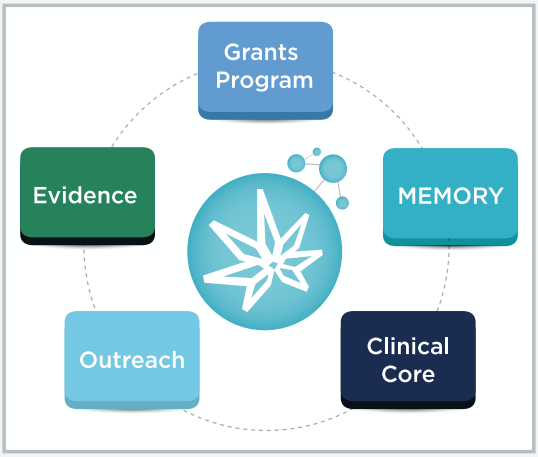
- **Hassan Azari,** NIH, Acidic cannabinoids for the treatment of high-grade glioma
- **Hassan Azari**, DOD, Cannabinoids Acidic for the treatment of Glioblastoma
- **Hassan Azari,** The Florida Center for Brain Tumor research (FCBTR), Effects of cannabigerolic acid containing hemp NPs on glioma tumor progression
- **Joshua Brown,** NIA, Cannabis use and adverse drug events in older adults
- **Mariola Edelmann**, NIH, The regulatory functions of the endocannabinoid system in the innate immune responses against Gram-negative pathogens
- **Nicole Ennis, Sherrilene Classen,** NIDA, Medical Marijuana Use and Driving Performance: A Test of Psychomotor Functioning in Adults 50 and Older. **Funded for $205,662 from 09/15/2020 – 09/14/2022.**
- **Amie Goodin, NIDA,** Medication use trajectories for opioid use disorders among pregnant women and resulting neonatal outcomes
- **Mandip Sachdeva,** James and Esther King Foundation, Role of Exosomal Formulations of CDB for Treatment of Cancer-related Peripheral Neuropathy
- **Mandip Sachdeva**, NIH, Preclinical evaluation of minor cannabinoids in chemotherapy induced peripheral Neuropathy
- **Jacqueline Sagen**, NCCIH, Combination analgesic evaluation of minor cannabinoids and terpenes with exercise in chronic spinal cord injury pain
- **Douglas Storace**, NIDCD, Defining the role(s) of the olfactory bulb in adaptation
- **Yan Wang,** NIA, Real-Time and Long-Term Effects of Medical Marijuana on Older Adults: A Prospective Cohort Study. **Funded for $2,940,426 from 2/15/2022-11/30/2026**
- **Jenny Wilkerson,** NCCIH, Terpenes and minor cannabinoids as novel analgesics
- **Jenny Wilkerson,** NIDA, Terpenes and minor cannabinoids as novel analgesics

MEDIA COVERAGE

- **Dr. Joshua Brown**, Can weed protect you from COVID? (*slate.com*)
- **Dr. Joshua Brown**, Are THC and CBD actually safe for everyone? Renee Consorte, July 27, 2021. Medium. *https://perma.cc/LCD7-PAHA*
- **Dr. Jenny Wilkerson**, How Cannabis-Based Therapeutics Could Help Fight COVID Inflammation, Medscape, *https:// www.medscape.com/viewarticle/940265*

CONSORTIUM RESEARCH PLAN 2022-2023

Since its inception in July 2019, the Consortium has made great strides towards facilitating and conducting research that informs clinical care and policy about the medical use of marijuana. In the coming year, the Consortium will continue these efforts within the five original Consortium research program pillars: the Grants program, MEMORY, the Clinical Core, Outreach, and the Evidence Core activities. The specific goals and plans for each pillar have been updated and are described below.



Modifications of the Consortium research plan were informed by interactions with the Florida House Subcommittee on Professions and Public Health and by increasing exchange with the Office of Medical Marijuana Use at the Department of Health. For a recording of the Consortium's presentation at the House Subcommittee in November 2021, see *https://thefloridachannel.org/videos/11-3-21-house-professions-public-health-subcommittee/* — starting at 46:00. Key needs for research that were emphasized by these interactions were:

- Accelerate the generation of conclusive evidence on effects of MMJ use including both risk and benefit with priority to studies in humans with direct value to support clinical and regulatory decisions
- Conduct granular evaluations of dosing, in particular research on high potency THC
- Conduct epidemiologic studies on utilization pattern, patient demographics and accessibility of MMJ across diverse groups
- Prioritize research on the effects of MMJ use in reducing opioid dependency

The following describes the Consortium Research Plan for fiscal year 2023.

GRANTS PROGRAM

Review of the grants program progress and funding priorities over the past two years highlighted two opportunities for enhancement, both focused on emphasizing the Consortium's support of clinical research with direct application to treatment and/or regulatory decisions to optimize the state's medical marijuana program's public health benefit. First, the Consortium's ability to support larger clinical research studies has been limited by its funding structure, which establishes a budget on an annual basis. While funding for studies exceeding one year is dependent on state appropriations, the board is

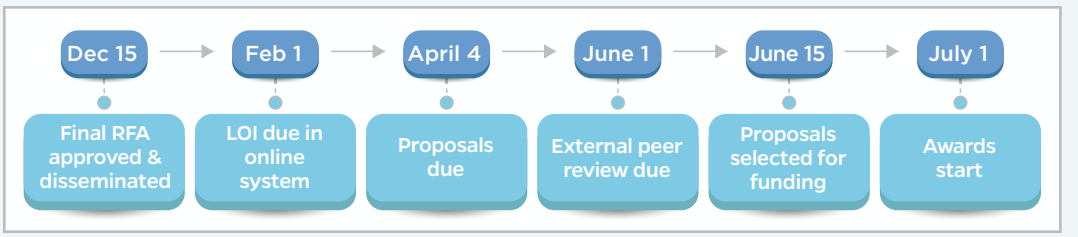
committed to support studies with longer duration such as those requiring time for patient recruitment. The new grant funding program has therefore been restructured to support two studies at $130,000 over a total of two years, where the second-year funding is committed if intermediate research goals for the first year have been accomplishment and adequate funding is available. An additional fund for one-year projects as offered previously has been retained.

Second, the Consortium Board revised its research priorities to emphasize the focus on clinical research, the impact of MMJ on pain management and opioid use, and expanded the scope of its epidemiologic research priority.

Consortium Research Priorities 2022

1. **Clinical Outcomes of Medical Marijuana use:** with priority granted to studies in humans investigating efficacy and safety, for the treatment of qualifying conditions.
2. **Effect of MMJ in reducing opioid dependence:** Human subjects research on the effectiveness of MMJ as an analgesic/adjuvant in pain management and in reducing opioid use.
3. **Route of Administration:** effect of dosing and routes of medical marijuana on efficacy and safety; of particular interest are studies that evaluate effects of smoking and vaping.
4. **Interactions of Medical Marijuana with other drugs/medications:**
   - with focus on medications that are commonly used by patients who seek MMJ treatment
   - impact of polysubstance use, including interactions with alcohol, tobacco, benzodiazepines, and prescription and nonprescription opioids
5. **Epidemiologic research:** trends for cannabis use and cannabis use disorder (CUD), including new products, patterns of use, and reasons for use in different populations, and medical and socioeconomic disparities in the access to and outcomes of MMJ across diverse communities.
6. **Evaluating components of medical marijuana/cannabis: and contrast their clinical outcomes:**
   - comparing different components of medical marijuana (e.g. different terpenes)
   - research on different potency levels of THC products (e.g. >10% vs <10% THC)
   - standards for measuring cannabis dose, intoxication, and impairment

The Consortium has launched its fourth grants cycle in December 2021 with release of its Request for Proposals and updated research priorities. The intent is to complete the application reviews by the end of the fiscal year to expedite funding of prioritized proposals, upon approval of the FY 2023 Consortium budget.



MEMORY

With the new access to a de-identified version of the OMMU Medical Marijuana Use Registry, the Consortium has been given the ability to evaluate utilization pattern and certain physician-reported outcomes. Analyses of these data has commenced and will be expanded over the next year. Pending provision of identifiable data for linkage to other health outcomes databases, plans for MEMORY development remain unchanged for fiscal year 2023. As envisioned, MEMORY will then serve in two capacities: for controlled studies on MMJ effectiveness and safety and for active surveillance to capture emerging safety issues among MMJ users. The former will employ rigorous study designs including control groups of patients who do not use MMJ but have similar health conditions, while the latter follows MMJ users to capture signals of unexpected adverse events that may be associated with a particular marijuana product.

CLINICAL CORE

Goals for the Clinical Core include continued expansion of the Consortium infrastructure to support patient recruitment into prospective research studies via its patient contact registry and CARMMA database of collaborating physicians, researchers and industry. The Consortium will launch its Medical Marijuana and Me (M3), patient cohort in early 2022 with the goal to evaluate detail on MMJ use and patient-reported outcomes. The Consortium hopes to establish a patient recruitment mechanism that has proven effective and that can be provided to investigators from all Consortium institutions to accelerate and enhance conduct of clinical outcomes studies. Data sharing policies and procedures will be finalized. A proven patient recruitment platform is also critical for extramural grant applications (e.g., to NIH) to further expand the consortium's research program. The Clinical Core will also continue to work on guidance for investigators on regulatory issues involving use of MMJ in research studies. This will include guidance on DEA licensure and other relevant state and federal regulations.

OUTREACH

Following up on the success of our inaugural Cannabis Clinical Outcomes Research Conference (CCORC), the Consortium plans to hold its second annual CCORC in summer 2022. Other outreach activities through the Consortium website, its quarterly newsletter and participation in scientific conferences will continue. The newly added Researcher Spotlight Series will be developed further to promote Consortium activities and disseminate research outcomes.

EVIDENCE CORE

The Consortium will build upon the two new activities introduced in the previous year including publication of the Evidence in context series and patient info sheets. The Consortium considers the emerging evidence reviews and info sheets an important contribution to the availability of unbiased up-to-date evidence on MMJ and instrumental in its communication with providers and patients.

The board and Consortium faculty and staff would like to conclude this report by expressing strong continuing support and enthusiasm to advance the Consortium research program. The Consortium addresses an urgent and critical need to provide patients, providers and regulators the necessary evidence on the safe and effective use of MMJ. The medical use of marijuana must be guided by the same level of scientific evidence that is available for prescription medications and MMJ products should be monitored with similar surveillance methods. The Consortium is devoted to establishing both.

APPENDIX

THE CONSORTIUM FOR MEDICAL MARIJUANA CLINICAL OUTCOMES RESEARCH BOARD

WILLIAM (BILL) ANDERSON, PH.D.

Associate Vice President of Research; Florida International University

Chair of the Consortium Board

Associate Vice President William (Bill) Anderson leads initiatives that expand FIU's efforts in research development for faculty, doctoral students and postdoctoral scholars. Additional areas of leadership focus include research labs, core facilities, research integrity, and laboratory safety, among others. Dr. Anderson joined FIU in 2000 as Assistant Professor and has risen to the rank of Professor. Administratively, he has served as Chair of the Department of Earth & Environment and Associate Dean of Faculty in the College of Arts, Sciences & Education where he most recently served as the Vice Dean.

He received a doctorate of Natural Sciences from the Swiss Federal Institute of Technology (ETH-Zentrum), a M.S. in Geology from Syracuse University and a B.A. in Geology from the University of Kansas. His research has been published in top tier journals; he has presented in national and international conferences; and he has received funding from the NSF, the American Chemical Society, and the U.S. Department of the Interior, among others.

ROGER B. FILLINGIM, PH.D.

Distinguished Professor; Director, University of Florida, Pain Research and Intervention Center of Excellence (PRICE); University of Florida

Roger B. Fillingim, Ph.D., a Clinical Psychologist, is Distinguished Professor in the University of Florida College of Dentistry and Director of the UF Pain Research & Intervention Center of Excellence. Dr. Fillingim maintains an active research program investigating individual differences in pain.

He has been continuously NIH-funded since 1994, and his current grants include a MERIT Award from the National Institute on Aging, which investigates biological and psychosocial factors contributing to ethnic group differences in osteoarthritis pain. He also serves as Director of the UF Center for Advancing Minority Pain and Aging Science. He has published more than 300 scientific articles and is a frequent speaker at national and international conferences. He served as President of the American Pain Society from 2012-2014, served as Co-Chair of the Federal Pain Research Strategy Disparities Workgroup, and is currently a member of the US Department of Health and Human Services Interagency Pain Research Coordinating Committee. He has received several awards, including a University of Florida Term Professorship, as well as the Fordyce Clinical Investigator Award and the Distinguished Service Award, both from the American Pain Society.

TIMOTHY A. GILBERTSON, PH.D.

Professor of Medicine; University of Central Florida

Timothy A. Gilbertson is a Professor of Medicine in the Department of Internal Medicine at the University of Central Florida, College of Medicine. He received his Ph.D. in Neurobiology from the University of California-Davis in 1991 and his postdoctoral training at Colorado State University from 1991-1993.

He has served as Chairman of the National Institutes of Health Communication Disorders Review Committee at the National Institute of Deafness and other Communication Disorders and as Chairperson of the Health and Scientific Advisory Board and on the Board of Directors of the Institute of Public Health and Water Research. From 2007-2011 he served as the Director for the Center for Advanced Nutrition at Utah State University. His research focuses on how the body recognizes and responds to nutrients and how this process is tuned to the underlying nutritional needs of an organism. This has implications ranging from basic mechanisms for taste transduction and the design of taste mimetics to post-ingestive nutrient chemoreception and the control of food intake, dietary-induced obesity and diabetes.

His laboratory was the first to elucidate the mechanisms underlying the taste of both fat and sour and has been the first to show unequivocally that nutrient recognition in the peripheral taste system is modulated by diet and disease. Dr. Gilbertson has generated well in excess of $7 million in extramural funding, published over 70 research articles including in Science, PNAS, The Journal of Neuroscience and Neuron and received the Ajinomoto Award for Outstanding Research in Gustation and the Outstanding Graduate Mentor Award from Utah State University. He has served as advisor and mentor for 25 graduate students, 9 postdoctoral fellows and several visiting professors.

ERIC H. HOLMES, PH.D.

Assistant Vice President for Research; Florida State University

Eric Holmes has a PhD in Biochemistry from the University of California, Davis. Since 2013 he has been an Assistant Vice President for Research in the FSU Office of the Vice President for Research. He currently also serves as the Interim Director for the FSU Office of Human Subjects. Prior to joining FSU, he was Director of Research at the University of Hawaii's John A. Burns School of Medicine.

Dr. Holmes has a long track record of directing NIH-funded research in biochemical oncology. He is an author of approximately 100 research publications and is an inventor on over 30 issued US and foreign patents. Dr. Holmes has also worked in the Biotech industry in development-stage pharmaceutical companies located in the Pacific Northwest focused on antibody therapy and drug delivery technologies, and has designed and managed clinical trials related to the development of these technologies.

XIMENA LEVY, MD, MPH

Director of Clinical Research, Florida Agricultural University

Dr. Levy is the Director of Clinical Research at FAU and oversees the Clinical Research Unit. Dr. Levy received her Medical Doctor degree from Universidad Javeriana (Colombia) and holds an MPH degree from T.H Chan Harvard School of Public Health. She holds a secondary appointment as Research Professor in the Charles E. Schmidt College of Medicine at FAU.

She is a clinical researcher trained by NIH/Fogarty Center at the University of Miami, and in the Brigham and Women's Hospital in Clinical Research Methods. Dr. Levy was the program coordinator of NIH and FDOH funded projects involving HIV subjects from minority populations at Florida International University and was the Director of the Human Research Protection Program at FAU before moving to her current position.

Dr. Levy's career is focused on providing leadership and guidance in the development and oversight of research and value-based care projects, responsible conduct of research, protection of human subjects, and social responsibility. Through her current role at Florida Atlantic University, she promotes research collaborations, translational sciences, clinical outcomes research, and ethical conduct of research. Her research interests are substance use disorders, mental health, and health services research.

MAX C. E. OREZZOLI, PH.D.

Assistant Professor of Sociology (Medical); Florida Memorial University

Max C. E. Orezzoli, Ph.D. is an Assistant Professor of Sociology (Medical) specializing in health and quantitative analysis at Florida Memorial University. Dr. Orezzoli has 15 years of experience in minority health disparities research focusing on Substance Use Disorder (SUD), including marijuana use, nutrition, and HIV research, and how these areas intersect.

His expertise and research interests are centered on transdisciplinary and translational public health and Community Based Participatory Research (CBPR) interventions that positively impact the health of underrepresented communities regionally, nationally and internationally. Dr. Orezzoli is bilingual and fluent in Spanish. He has extensive experience in formative and summative program evaluation using quantitative and qualitative methods, which are regionally and culturally appropriate. He has served as an evaluator on several Substance Abuse and Mental Health Services Administration (SAMHSA) grants addressing SUD in Hispanic, black, and Native American communities. Dr. Orezzoli serves as the Co-chair of the Institutional Review Board (IRB) at Florida Memorial University.

MARTHA S. ROSENTHAL, PH.D.

Professor of Neuroscience/Physiology; Director of the Cannabis Research, Education, and Workforce initiative; Florida Gulf Coast University

Vice-Chair of the Consortium Board

Dr. Martha Rosenthal is a Professor of Neuroscience & Physiology at Florida Gulf Coast University, where she teaches courses in cannabis, drugs and society, neuroscience, human physiology, and human sexuality. Dr. Rosenthal received her bachelor's degree in biology from the University of Virginia, her master's degree in neuropharmacology from Brown University, and her Ph.D. in neuroscience from UCLA. She began her career teaching in the College of Pharmacy at the University of Florida, and then moved to Fort Myers to be one of the founding faculty members of FGCU.

Dr. Rosenthal is the Director of the Cannabis Research, Education, and Workforce initiative (CREW) at FGCU, and runs the cannabis professional certificate program. She is the author of a number of textbooks, including Drugs: Mind, Body, and Society. Dr. Rosenthal has been honored to receive the Teacher of the Year award at both the University of Florida and at FGCU and to have presented a TED talk about sex and gender.

JACQUELINE SAGEN, PHD

Professor of Neurological Surgery, University of Miami

Dr. Jacqueline Sagen is a Professor of Neurological Surgery at the Miami Project to Cure Paralysis, University of Miami Miller School of Medicine. She received her B.A. in Neuroscience from Northwestern University, Ph.D. in Pharmacology from the University of Illinois College of Medicine in 1984 and an M.B.A. in Entrepreneurship from University of Illinois at Chicago in 1994. She completed a postdoctoral fellowship in 1986 and joined the faculty at University of Illinois College of Medicine in the Department of Anatomy and Cell Biology as Assistant/Associate Professor through 1995. From 1995-1998 she was Associate Director, Pharmacology and Behavioral Research, CytoTherapeutics, Inc and Adjunct Associate Professor of Cellular Technology, Brown University, prior to her current position at University of Miami.

Research in Dr. Sagen's laboratory over the past 35 years has been focused on exploring novel therapeutic strategies for chronic pain management that have the potential to provide sustained relief on a long-term or permanent basis. As chronic pain syndromes are often resistant to traditional pain interventions and/or limited by untoward side effects and possible analgesic dependence, the long term goal of work in her lab is to identify and develop more potent interventive approaches to improve the quality of life of these patients. A primary initiative in her lab is the generation of gene therapies and cell transplantation that can provide a continually renewable source of pain-reducing substances. The identification of superior alternatives to opioids, such as cannabinoids, is a current focus of her research. She has published over 150 articles and book chapters and holds 6 patents in the field of novel pain therapies. She serves on numerous scientific review panels for NIH, DoD, VA, CIRM, and private foundations, and is faculty representative on the FDP.

CHARLES A. WEATHERFORD, PHD

Vice President for Research, Florida A&M University

Charles Weatherford is the Vice President for Research at Florida A&M University (FAMU). Dr. Weatherford is also the Director of the FAMU Industrial Hemp Pilot Project, Principal Investigator on the FAMU Medical Marijuana Education and Research Initiative, Director of the FAMU Center for Plasma Science and Technology, as well as a Professor in the FAMU Department of Physics.

He received his Ph.D. in Atomic and Molecular Physics from Louisiana State University in 1974. Dr. Weatherford is a Fellow of the American Physical Society and a Fellow of the National Society of Back Physicists. Dr. Weatherford has a Patent Disclosure 2018: "Field-Assisted Muon-Catalyzed Fusion", 224 journal publications, 5 book articles, and 2 books. He was PI or Co-PI on $60.5 million in Research Grants and Contracts. His research interests include Materials and Energy for National Security, Correlation in Many-Body Quantum Chemistry, Laser-Matter Interactions, High-Energy Density Science, Field-Assisted Muon-Catalyzed Fusion, and Computational Science.

CORE FACULTY AND STAFF OF THE CONSORTIUM FOR MEDICAL MARIJUANA CLINICAL OUTCOMES RESEARCH

ALMUT G. WINTERSTEIN, RPH, PHD, FISPE

Distinguished Professor & Chair, Pharmaceutical Outcomes & Policy; Dr. Robert and Barbara Crisafi Chair in Medication Safety; College of Pharmacy, Director, Center for Drug Evaluation and Safety, University of Florida

Consortium Director

Almut Winterstein, RPh, PhD, FISPE received her pharmacy degree from Friedrich Wilhelm University in Bonn, Germany and her PhD in Pharmacoepidemiology from the Charité Humboldt University in Berlin, Germany.

Since joining the UF College of Pharmacy in 2000, Dr. Winterstein has served as principal investigator on more than 25 extramurally funded grants and contracts and published more than 400 manuscripts and conference abstracts. Her research interests have centered on the post-marketing evaluation of drugs in pediatrics and perinatal care, infectious disease and psychiatry and the evaluation and improvement of quality surrounding medication use using real-world data. As an internationally recognized expert in drug safety, she has chaired the Food and Drug Administration's Drug Safety and Risk Management Advisory Committee from 2012-2018. Recognizing her contributions in pharmacoepidemiology, Dr. Winterstein was inducted as a fellow of the International Society of Pharmacoepidemiology in 2013 and served as president of the society from 2020-2021.

Before she became department chair in 2016, Dr. Winterstein served as graduate program director in her department, which included responsibility for a M.S. program for the FDA. She has chaired more than two dozen PhD committees and was awarded the University of Florida Mentoring.

ROBERT L. COOK, MD, MPH

Professor, Epidemiology, Medicine

Consortium Associate Director

Director, Southern HIV & Alcohol Research Consortium (SHARC) College of Public Health & Health Professions, University of Florida

Robert L. Cook, MD, MPH is a Professor of Epidemiology at the University of Florida, with a joint appointment in the Division of General Internal Medicine.

Over the past 20 years, Dr. Cook's research has focused on strategies to improve health outcomes related to HIV and sexually transmitted diseases. He is the Director of the Southern HIV Alcohol Research Consortium (SHARC), which supports collaborative research and training related to alcohol and HIV infection across the state of Florida.

Dr. Cook's research is translational, ranging from basic science to implementation science, and he is currently the PI or MPI of 4 major NIH grants with over $10 million in total research support. Most recently, Dr. Cook has begun to study the effects of marijuana on HIV-related health and cognition, the systemic connections between the gut microbiome and neuro-inflammation, the use of clinical information systems to improve quality of clinical pain management, and the use of real-time monitoring to measure alcohol consumption.

Mentoring is also an important aspect of Dr. Cook's academic career. He has served as PhD dissertation chair for 8 students, PhD committee member for over 30 students, and mentor for numerous additional trainees, post-docs and junior faculty.

AMIE J. GOODIN, PHD, MPP

Assistant Professor, Pharmaceutical Outcomes & Policy; College of Pharmacy, University of Florida

Lead for Consortium Evidence Core

Amie J. Goodin, PhD, MPP is an Assistant Professor within the Department of Pharmaceutical Outcomes and Policy (POP) at the University of Florida. Dr. Goodin received her Master of Public Policy degree from the University of Kentucky (UK) and completed her Doctor of Philosophy degree at UK's Martin School of Public Policy, with specialization in pharmaceutical outcomes and an additional Certificate in Informatics. She completed a Postdoctoral Fellowship at University of Florida POP, specializing in pharmacoepidemiology methods while continuing her work in Health Services Research.

Dr. Goodin previously worked at the Institute for Pharmaceutical Outcomes and Policy as well as the Center for the Advancement of Pharmacy Practice, both of which were housed in the UK College of Pharmacy. Currently, Dr. Goodin's research projects incorporate mixed-method approaches to assess the impact of policy changes related to treatment access and utilization for Substance Use Disorders, particularly among persons enrolled in Medicaid and pregnant women.

JOSHUA D. BROWN, PHARMD, PHD, MS

Assistant Professor, Pharmaceutical Outcomes & Policy; College of Pharmacy, University of Florida

Lead for Memory

Joshua D. Brown, PharmD, PhD, MS joined the University of Florida in 2016. Dr. Brown has training in clinical pharmacy and pharmacoepidemiology having received PharmD and MS degrees from the University of Arkansas for Medical Sciences and a PhD from the University of Kentucky. During his graduate training, Dr. Brown focused on research related to medication safety and effectiveness in high-risk populations, especially older adult and geriatric patient groups. He has also conducted research on medical devices, drug-drug interactions, and healthcare policy. As a graduate student, Dr. Brown was recognized as the Pfizer-Humana Research Fellow and received two Young Investigator Awards from the International Society for Thrombosis and Hemostasis.

Dr. Brown's research program continues to evaluate the effectiveness and safety of medications used in real-world populations. He conducts research focusing on drug-drug interactions with hormonal contraceptives and anticoagulants and evaluates medication safety in older adult populations. His research has been funded by the U.S. Food and Drug Administration, the Bill & Melinda Gates Foundation, and the UF Institute on Aging. Dr. Brown has been recognized as a Claude D. Pepper Scholar in aging research, was invited to the National Academy of Medicine's Emerging Leaders Symposium, and was awarded an early career recognition by the Academy of Managed Care Pharmacy.

YAN WANG, PHD

Assistant Professor, Epidemiology; College of Public Health & Health Professions, University of Florida

Consortium Lead for Clinical Core

Yan Wang, PhD is an Assistant Professor of Epidemiology at the University of Florida. Dr. Wang has training and expertise in both psychology and epidemiology. She received her MS and PhD in Child and Family Studies from Syracuse University in 2013. She joined the Department of Epidemiology as a postdoctoral research associate in 2014, working on NIH funded projects on risk behaviors among rural-to-urban migrants in China.

Her research focuses on leveraging advanced methodology and new technology (e.g., wearable sensor) to improve health behavior monitoring and intervention. One of her current research projects focuses on improving alcohol use monitoring using a wearable alcohol biosensor and ecological momentary assessment. She is also working on a UF funded pilot project to investigate the real-time and long-term health effects of medical marijuana among patients with chronic pain. Dr. Wang has also worked on a number of NIH funded projects including those on mental health and risk behaviors among rural-to-urban migrants in China, alcohol use and marijuana use among persons living with HIV/AIDS in Florida, and advanced quantum modeling on sexual risk behaviors.

One of her research papers, "Stress and Alcohol Use in Rural Chinese Residents: A Moderated Mediation Model Examining the Roles of Resilience and Negative Emotions" published in the journal Drug and Alcohol Dependence has been recognized by the Matilda White Riley Early Stage Investigator Honor Program, sponsored by the National Institutes of Health Office of Behavioral and Social Sciences Research (NIH/OBSSR).

JEEVAN JYOT, PHD, PMP

College of Pharmacy, University of Florida

Consortium Program Coordinator

Dr. Jyot received her PhD in Microbiology and Molecular Biology from the Institute of Microbial Technology (India) and completed her postdoctoral fellowship and was an Assistant Scientist at Division of Infectious Diseases and Global Medicine, Department of Medicine, University of Florida. In addition she has Project Management Professional credentials.

Dr. Jyot has previously served as Research Program Coordinator at Division of Research Program Development (DRPD) at Office of Research at University of Florida. Currently, Dr. Jyot is part of the Department of Pharmaceutical Outcomes and Policy (POP) at the University of Florida and serves the Medical Marijuana Clinical Outcomes Research Consortium.

ANNA SHAVERS, MPA

College of Public Health & Health Professions, University of Florida

Consortium Communications Specialist

Anna Shavers, MPA is the Communications Specialist of the Consortium for Medical Marijuana Clinical Outcomes Research.

Anna received her Master of Public Administration with a focus in Public Health Administration at Troy University. Her background includes various roles in marketing, communications, and health outreach initiatives. Before joining the Consortium for Medical Marijuana Clinical Outcomes Research, Anna served with the Peace Corps as a Community HIV/AIDS Outreach Coordinator in South Africa.

LIST OF REVIEWERS OF THE 2021 RESEARCH GRANTS PROGRAM

*reviewers who reviewed more than one proposal

Caroline Arout	Columbia University Irving Medical Center	Assistant Professor
Richard Balkin	University of Mississippi	Professor
Mark Beasley	University of Alabama	Professor
Tammy Chung*	Rutgers University	Professor
Kathlene Curtis	Oklahoma State University	Professor
Natacha De Genna	University of Pittsburgh	Assistant Professor
Emily Dworkin	University of Washington	Assistant Professor
Susan Ferguson	University of Washington	Associate Professor
Sylvia Fitting	University of North Carolina	Assistant Professor
Staci Gruber	Harvard Medical School	Associate Professor
Richard Hansen	Auburn University	Professor
Coleen Hegg	Michigan State University	Associate Professor
Thomas Heinbockel	Howard University	Professor
Claire Hulsebosch	University of Texas Health Sciences Center	Professor
Martin Kaczocha*	Stony Brook University	Assistant Professor
Barbara Kaplan	Mississippi State University	Associate Professor
Kevin King	University of Washington	Professor
Steven Kinsey	University of Connecticut	Associate Professor
Stephen Lenz	University of Mississippi	Associate Professor
Charles Leonard	University of Pennsylvania	Assistant Professor
Kabirullah Lutfy	Western University of Health Sciences	Professor
Rhoderick Machekano	Elizabeth Glaser Pediatric AIDS Foundation	Senior Director
Stephen Mahler	University of California Irvine	Assistant Professor
Michael Mason*	University of Tennessee	Professor
Ryan McLaughlin	Washington State University	Associate Professor
Aimee McRae-Clark*	Medical University of South Carolina	Professor
LaTrice Montgomery	University of Cincinnati College of Medicine	Research Assoc. Professor
Tim Moran	Johns Hopkins University	Professor
Meera Nair	University of California Riverside	Associate Professor
Dinesh Pashankar	Yale University School of Medicine	Professor
Godfrey Pearlson	Yale University	Professor
Matthew Pearson	University of New Mexico	Research Assoc. Professor
Kristina Phillips	Center for Integrated Health Care Research (CIHR)	Research Investigator
Ana Pocivavsek	University of Southern Carolina	Assistant Professor
JayChandra Ramapuram	Auburn University	Professor
Kumar Ravi	Alabama Life Research Institute	Professor
Xuan-Zheng Shi	University of Texas Medical Branch (UTMB)	Professor
Deepika Slawek	Albert Einstein College of Medicine	Assistant Professor
Andrew Steelman	University of Illinois, Urbana-Champagne	Associate Professor
Prem Subramaniam	Columbia University	Assoc. Research Scientist
Ryan Vandrey	Johns Hopkins University School of Medicine	Professor
Dionna Whitney Williams	Johns Hopkins University School of Medicine	Assistant Professor
Kelly Young-Wolff	Kaiser Permanente & UC, San Francisco	Research Scientist
Anjie Zhen	University of California Los Angeles	Assistant Professor

Consortium for Medical Marijuana
Clinical Outcomes Research

www.mmjoutcomes.org