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Abstracts

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Disclosure Statement Scientific Program and Planning Committee

The members of the Scientific Program and Planning Committee have no conflicts of interest to declare.

Top Abstracts: Oral Presentations

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Assessing the Dose, Amount, and Heavy Use Patterns among Adults with HIV Who Use Marijuana

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Objective: Marijuana flower, commonly used to help manage symptoms and conditions, may be obtained either within or outside of the formal medical marijuana system. There is a desire to identify the optimal dose and frequency for different conditions. As part of an ongoing cohort study of marijuana use in persons with HIV, we sought to identify and quantify the average amount of marijuana flower consumed per dose and per day, and to identify the frequency of heavy daily use. **Methods:** Persons with HIV were recruited from community and clinic settings in Florida, self-reported marijuana use was confirmed by urine drug screen. A timeline follow-back was used to inquire about specific doses, patterns, and modes of consumption during the past 30-days, using pictures of marijuana flower to help estimate the amount per dose, and a calendar to identify patterns. We examined the distribution of responses, and present the median amounts due to right skewed distribution of the data. **Results:** The sample included 212 persons with HIV who use marijuana (55% age 50+, 58% male 67% non-hispanic black, 15% Hispanic). Nearly all users obtained marijuana from outside of the formal medical system, and 83% used only marijuana flower in the previous 30 days. Among these users, 52% used daily, with a median quantity of 0.8 grams/day. The most common modes of flower consumption and their median quantity of flower were blunts (48%, 1.0g), joints (42%, 0.5g), and pipes (10%, 0.06g per hit/toke/puff). The proportion who had at least one heavy use day in a month, or heavy use every day of the month was 30% and 6% when heavy use was defined as 3g/day, 43% and 13% for 2g/day, and 59% and 23% for 1g/day. **Conclusion:** The amount of marijuana flower consumed can be hard to estimate. Our results are similar to others in defining the average quantity of a joint or hit/toke. Over half of this sample consumed > 1g flower/day in the previous month. Additional research should compare health outcomes and side effects from these different doses and patterns.

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Health Outcomes among Adults Initiating Medical Marijuana for Chronic Pain: Preliminary Findings from a 12-Month Prospective Study

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Objective: In response to the need of more rigorous data on marijuana use and chronic pain, we conducted a 12-month prospective study to examine the effects of medical marijuana on pain, opioid use, anxiety/depression, and quality of life. **Methods:** Fifty-six adults (age=54.8±11.9, 53.6% male) were recruited from medical marijuana clinics before initiating medical marijuana treatment. Participants completed surveys on various clinical outcomes at baseline (i.e., 2-3 weeks before they started medical marijuana use), 3 months, and 12 months. **Results:** At baseline, the mean of worst and average pain of the group was 8.0±1.6 and 5.9±2.0 respectively, on the scale from 0 to 10, indicating chronic pain. At 3 months (retention rate=93.9%), the proportion of individuals reporting “no more than minor pain in past 24 hours” increased from 12.7% at baseline to 32.6%. The proportion of daily opioid users decreased from 53.6% at baseline to 28.6%. Participants also reported significantly lower levels of worst pain (7.2 vs. 8.0, t=-2.25, p<.05), average pain (5.1 vs 5.9, t=-2.62, p<.05), pain interference (2.8 vs. 3.6, t=-4.12, p<.001), and depression (5.6 vs.8.1, t=-3.64, p<.001), as well as increased hours of sleep (6.1 vs. 5.4, t=4.02, p<.001), sleep quality (1.7 vs. 1.2, t=2.96, p<.01), and quality of life (3.3 vs. 2.8, t=5.01, p<.001), compared to baseline. At 12-months (retention rate=76.0%), 73.7% of the participants were still using medical marijuana. Among these continuous users, 78.6% thought medical marijuana was moderately to extremely effective for their chronic pain; 78.6% were able to reduce or totally quit opioids; 81.4% reported better physical functioning; 78.6% reported better mental health; 85.7% reported better sleep quality; and 85.7% reported better quality of life. On the other hand, 35.7% said they needed a higher dose of medical marijuana now to achieve the same effect; 42.9% reported experiencing some side effects (e.g., blurred vision, dry mouth, paranoia); and 21.4% reported worse cognitive abilities due to medical marijuana use. **Conclusions:** In our sample of primarily middle-aged and older adults with chronic pain, medical marijuana was associated with improved health (e.g., reduced pain, improved sleep) as well as adverse (e.g., side effects, cognitive impairment) outcomes.

Intranasal Delivery of Hemp Derived Extracellular Vesicles (EVs) Reduces Tumor Growth and Enhances Survival in Orthotopic Animal Model of Glioblastoma (GBM)

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Objective: We recently have discovered that hemp derived extracellular vesicles (EVs) are enriched in cannabinoids and present strong anti-glioma properties in vitro. Here, we show more evidence on anti-glioma function of hemp EVs in vitro and their therapeutic efficacy when delivered intranasally in a KR-158 glioma model. **Methods:** EVs were isolated from hemp leaves and flowers using ultracentrifugation and characterized by nanotracking, electron-microscopy and liquid chromatography tandem mass spectrometry (LC-MS/MS) for size distribution, shape and cannabinoid content, respectively. Glioma stem cell proliferation and symmetric division were assessed using the neurosphere assay and a mathematical model. Mice implanted with KR-158-luciferase glioma cells were treated daily with intranasal administration of PBS or hemp EVs (in PBS) for the life time of the animals. Bioluminescent imaging and Kaplan-Meier survival curves were used to assess tumor growth and animal survival. **Results:** Hemp EVs harvested from a cannabidiolic acid rich cultivar presented a median diameter of 128nm with a typical lipid-bilayer structure. LC-MS/MS has shown that cannabidiolic, cannabigerolic, and tetrahydrocannabinolic acids (CBDA, CBGA and THCA) represent 93%, 5%, 2% of the total cannabinoids in the harvested EVs. Treating KR-158 cells with EVs at CBDA concentration equivalent of 0, 0.5, 1, 1.5 μ M in neurosphere culture effectively decreased both percent neurosphere forming frequency (23.42 ± 1.1 , 17.76 ± 0.36 , 12.62 ± 0.71 , 8.18 ± 0.44) and neurosphere size (114.4 ± 2.85 , 119.1 ± 2.62 , 111.4 ± 3.30 , 100.3 ± 2.71) in a dose-dependent manner. 1 μ M hemp EVs significantly reduced fold expansion of glioma cells (46.35 ± 2.07 vs 26.27 ± 0.67) and stem cell symmetrical division rate in glioma stem cells (0.55 ± 0.006 vs 0.45 ± 0.003) compared to the control condition. Intranasal administration of hemp EVs led to accumulation of CBDA and CBGA in brain tumor tissue which resulted in a significant delay in tumor growth and enhanced median survival in KR-158 tumor bearing mice (31 in PBS vs 42 days in hemp EV-treated animals). **Conclusion:** Efficacious delay in the survival of tumor bearing animals treated with intranasal delivery of hemp EVs holds the promise for future clinical application of these EVs in glioma patients.

Medical Marijuana in Florida: The Knowledge, Practices and Attitudes of Providers

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Objectives: To describe the knowledge, practices, and attitudes of Florida Medical Doctors (MDs), Doctors of Osteopathic Medicine (DOs), Physician Assistants (PAs), and Advanced Practice Registered Nurses (APRNs) regarding medical marijuana (MM). **Methods:** We utilized a descriptive Web-based cross-sectional quantitative survey using a sample of Florida providers. The survey questionnaire was adapted from a Washington State MM Healthcare Professional survey instrument to reflect Florida Statutes. A link to this questionnaire was sent to 10,540 providers in Florida through Qualtrics[®]. The distribution was based on stratified random sampling to yield a representative sample number within each group. After evaluating the response rate, a second stratified random sample with 10,540 providers was selected and recruited based on the same distribution. **Results:** A total of 561 providers completed the survey (242 MDs, 39 DOs, 221 APRNs, 59 PAs). Almost two-thirds (63.2%) of respondents were not familiar with Florida Statutes, particularly regarding the conditions that qualify patients for MM. Only one-third (31.7%) has completed continuing education about MM. Furthermore, many providers (86.8%) in Florida reported a lack of access to the MM registry. Provider attitudes included a concern about a lack of evidence-based practice. Only 8.3% (n =40) were qualified providers in the state. Of those who are qualified to provide authorizations, 57.5% (n =23) had provided a MM authorization. Of those who were not qualified to provide an authorization, 23.5% (n=132) had recommended a patient consult with a qualified MM provider. **Conclusions:** This is the first study to report a knowledge deficit of Florida providers regarding MM. Despite legalization of MM in Florida, this research indicates providers have not educated themselves on its use nor are many offering MM authorizations. This finding is significant as it suggests limited access to MM authorizations for patients who qualify and might benefit from MM use. Future research could investigate whether receiving MM training influences provider practices and patient access. Florida policy makers should consider revisions to law making MM more accessible such as adding APRNs as qualified providers.

Cannabis and Cannabinoids for Pain and Anxiety-Related Conditions

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Effectiveness of Medical Marijuana in Older Adults with Chronic Pain

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Objective: Musculoskeletal disorders with associated chronic pain are a common problem in later life. Symptom management in older adults, including chronic pain management can be challenging. Medications, especially opioids, can increase the risk of confusion, constipation, falls and injury. Medical marijuana (MM) is often recommended in the treatment of these conditions. MM use among older adults is rapidly growing more than other age groups. There is a demand for health care providers to understand MM's clinical indications, potential benefits and side effects in older adults. This is an area of study that needs more research since MM has recently become readily available with legislation and the rise of the MM culture within the healthcare arena. **Methods:** Data were collected using RedCap online survey tools for age 60 and older who have an active medical marijuana prescription and chronic pain residing in South Florida. Data were analyzed using descriptive and inferential statistics and management of missing data. **Results:** 77 participants completed the informed consent with 54 completing all of the survey questionnaires. Age ranged from 60~88 years (mean = 74) with most participants identifying as non-Hispanic whites, most are retired and 72% female. The analysis revealed the occurrence of several common side-effects of MM use. The largest side effect reported was an increased appetite (24.1%), followed by change in mood (20.4%), elevated levels in lack of concentration (13%), lethargy (11.1%) and dizziness (9.3%). Only 3 (7.3%) participants reported receiving MM education prior to filling their prescription, with 43% reporting the education was less than 20 minutes. Medical marijuana was considered effective in reduction of overall chronic pain on a visual analog scale ranging from 0 to 100 with a decrease of pain from 71.1 prior to MM use to 35.22 after use. This result was statistically significant [$t(42)=11.68, p<.001$] and indicated a potentially large effect with Cohen's $d=1.82$. **Conclusion:** Medical marijuana should be considered carefully for each patient with frequent monitoring for efficacy and adverse events. There is a critical need to access the current training and advising on patients' ability to safely and effectively use MM.

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Effects of the Non-Psychoactive Cannabinoid Cannabidiol in a Mouse Model of Migraine

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Cannabidiol (CBD), the main non-psychoactive ingredient present in the Cannabis sativa, has therapeutic potential over a wide range of disorders that result from an equally wide range of CBD's pharmacological actions. In particular, CBD has been reported to hold anxiolytic and antidepressant effects, modulates neuronal transmission, and delivers pain relief.

Therefore, CBD may serve as a potential treatment for migraine, a complex condition characterized by the tendency to have headache with sensory disturbances associated with various symptoms including comorbid anxiety and depression. Surprisingly there is limited research on CBD for migraine and there is no scientific evidence to prove that CBD is an effective treatment. The effects of CBD are examined here using a calcitonin-gene related peptide (CGRP)-induced headache model that reliably provides measures of cephalic allodynia, spontaneous pain, altered light sensitivity (photophobia) and conditioned place aversion (CPA) in C57BL/6J mice. As migraine has a strong sex bias toward females, the experiments are conducted in mice of both sexes. We found that cephalic allodynia, as measured by periorbital application of von Frey filaments, induced by peripherally administered CGRP (0.1 mg/kg) was successfully blocked by CBD (30 mg/kg, ip) both in male and female mice. The painful responses manifested as a facial grimace were also attenuated by systemic administration of the same dose of CBD in females. CBD effectively reversed anxiety-like behavior induced by CGRP only in male mice, whereas photophobia and CGRP-induced CPA were unaltered by CBD treatment.

Collectively, these results suggest that CBD may help to relieve migraine-like pain and anxiety associated with headache pain, but may fail in providing protection from other symptoms experienced by migraineurs including photophobia.

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An Exploratory Cross-Sectional Analysis of Cannabidiol Use for Arthritic Joint Pain

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Objective: The purpose of our study was to evaluate evaluating the patient-perceived effect that CBD use has on pain and use of other oral medications in patients with arthritis. We hypothesized that patients who used CBD would report improvements in pain with no difference between groups when compared by type of arthritis. **Methods:** A novel anonymous questionnaire was created to evaluate patients' perceived efficacy of CBD use for arthritis pain. Patients were recruited through online methods including

social media accounts and newsletters (The Arthritis Foundation and Savvy Cooperative). 709 patients initially participated in the survey. Participants were excluded if they didn't have arthritis (N=75), had not tried CBD (N=133), or had incomplete surveys (N=73). Responses to use and pain questions were stratified by subtypes of arthritis. Pearson's chi-squared and Fisher's exact tests were used in the analysis of categorical variables. Pain and pain reduction responses were evaluated with non-parametric Kruskal Wallis Tests. Individual comparisons were evaluated with Mann-Whitney U tests. A two-tailed p-value less than 0.05 was considered statistically significant. **Results:** The influence of CBD was mostly positive in effect on pain intensity (37.9% much better, 45.1% little better), physical function (28.7% much better, 37.4% little better), and sleep quality (37.6% much better and 28.5% little better). Subgroup analysis by diagnosis type (osteoarthritis, rheumatoid, or other autoimmune arthritis) found differences in among groups for physical function (P=0.013), favoring the osteoarthritis group. The cohort reported a 44% reduction in pain after CBD use (2.58-point reduction). The osteoarthritis group had greater percentage reduction (P=0.020) and point reduction (P<0.001) in pain compared to rheumatoid arthritis and other autoimmune arthritis. The majority of respondents reported a reduction or cessation of other medications after CBD use (N=259, 60.5%): reductions in Anti-inflammatories (N=129, 31.1%), Acetaminophen (N=78, 18.2%), Opioids (N=36, 8.6%) and discontinuation of Anti-inflammatories (N=76, 17.8%), Acetaminophen (N=76, 17.8%), and opioids (N=81, 18.9%). **Discussion:** In our convenience sample, participants reported high rates of symptomatic relief. Furthermore, patients using CBD reported reduction and discontinuation of opioids, Tylenol, and anti-inflammatories. The present study suggests that there may be therapeutic benefit to CBD use in patients with arthritis.

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Therapeutic Potential of Cannabidiol and WIN 55, 212-2-Mesylate for Treatment of Anxiety

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Objective: Our objective was to assess reduction or elimination of behaviors following chronic administration of cannabidiol (CBD) using a newly found mouse model (Kv1.3-/- mice) that exhibits anxiety and attention deficit-like behaviors. We hypothesized that CBD isolate (antagonist) and WIN 55, 212-2-mesylate (WIN), an agonist for CB1 and CB2, might be anxiolytic. To test the mouse model, we examined dose-responsiveness, sex-dependency, route of delivery, and also metabolically phenotyped mice using a comprehensive lab animal monitoring system. **Methods:** Two-month-old Kv1.3-/- or wildtype mice were phenotyped for anxiety behaviors using the elevated plus maze (EPM), the light-dark box (LDB), and the marble burying test. Mice were dosed daily, 30 minutes prior to performing a behavioral test. Mice of both sexes were separated into cohorts in which they were designed to receive an intraperitoneal injection of either drug (WIN = 1 mg/kg; CBD = 5 mg/kg) or vehicle solution at equivalent

volume. Acute cohorts received daily dosage for 5 days and chronic cohorts received 20 doses over a 30 day interval. **Results:** Without drug treatment, both genotypes exhibited anxiety-like behaviors in the LDB and EPM, preferring dark side or closed arms of the apparatuses, respectively. With acute WIN treatment, Kv1.3-/- mice showed lessened anxiety in the LDB. Following chronic WIN treatment, they showed no change in LDB behavior. Acute and chronic WIN treatment in Kv1.3-/- mice mitigated anxiety in the EPM, but showed no effect on anxiety for wildtype mice if acutely administered and heightened anxiety following chronic treatment. For cohorts treated acutely with CBD, Kv1.3-/- mice showed enhanced anxiety behaviors in the LDB. Mice of both genotypes showed enhanced anxiety behaviors in the EPM following acute CBD treatment. **Conclusion:** In conclusion, our data showed that CBD may act as an anxiogenic drug in both wildtype and Kv1.3-/- mice. WIN acted as an anxiolytic drug for mice with trait anxiety (Kv1.3-/-), which was ineffective in these mice long-term, and ineffective acutely in wildtype mice exposed to state anxiety. We have collected and are analyzing chronic effects of WIN and CBD on body weight, energy expenditure, fuel utilization, and locomotor activity.

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Management of SCI Induced Chronic Pain in Rats Using Cannabidiol and β -Caryophyllene

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Objective: Medical marijuana is often used to relieve pain, but there is a paucity of preclinical studies which evaluate the effects of cannabis components in chronic pain models. Spinal cord injuries (SCI) frequently result in chronic pain which may be significantly attenuated using marijuana and its medicinal extracts. The goal of this study was to evaluate the effects of two cannabis components, Cannabidiol (CBD) and β -caryophyllene (BCP), and their potentially synergistic pain-relieving combination. **Methods:** Using male and female Sprague-Dawley rats, spinal cord injuries were induced using a clip compression model at mid-thoracic levels. To assess neuropathic pain symptoms, we evaluated the development of tactile allodynia, cold allodynia, and heat hyperalgesia. First, we conducted dose-response analyses for both drugs using a battery of behavioral tests including the Von Frey test, the acetone evaporation test, and the Hargreaves test. Rats were tested at baseline and every 30 minutes for 2 hours post-injection. If some analgesic effects remained, they were again tested at 5- and 24-hours post-drug administration. CBD was tested at 0.1-5 mg/kg (ip) and BCP was orally administered (oral gavage) at 10-50 mg/kg. We then assessed for potential synergism using isobolographic analysis based on ratios of the single drug A50 values. **Results:** Both CBD and BCP administered individually reduced cold and tactile hypersensitivity in both male and female rats. The combination of CBD and BCP produced synergistic effects for cold allodynia in both male and female rats. Additive effects were observed in male rats for tactile allodynia. The effects of both compounds and the combination appeared less potent in females compared to males, suggesting that sex differences will need to be considered when

developing cannabinoid pain-reducing strategies. We observed no overt side effects from combining CBD and BCP. **Conclusion:** These findings support the further development of cannabis extracts as potentially safe and effective therapeutics in the management of chronic SCI pain.

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Cannabis-Derived Terpenes as Novel Neuropathic Pain Therapeutics: Preclinical Mouse Studies and Possible Cannabinoid Receptor Involvement

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Objective: Anecdotal reports suggest cannabis may be an effective analgesic. Cannabis contains a multitude of compounds (i.e., terpenes) that have not been well studied and may hold therapeutic promise as pain therapeutics. We examined the ability of a subset of terpenes found in cannabis: γ -terpinene, α -terpineol, β -caryophyllene to reverse mechanical allodynia (i.e., light touch sensitivity) in mice experiencing paclitaxel chemotherapy-induced peripheral neuropathy (CIPN) and in the chronic constriction injury of the sciatic nerve (CCI) neuropathic pain model. To examine cannabinoid receptor involvement within both neuropathic pain models we also tested each terpene in mice lacking either functional cannabinoid type 1 receptors (CB1R (-/-)) or cannabinoid type 2 receptors (CB2R (-/-)). **Methods:** Male and female wildtype, CB1R (-/-), CB2R (-/-) mice on a C57BL/6J background were used in all experiments. CIPN was induced with one cycle of paclitaxel, consisting of a total of four intraperitoneal injections of paclitaxel (8 mg/kg per injection), and injections are given every other day. Separate cohorts underwent CCI surgery utilizing chromic gut suture to ligate the sciatic nerve. Mechanical allodynia was assessed via von Frey filaments. After the presence of mechanical allodynia was confirmed, mice were injected intraperitoneally (i.p.) with vehicle, α -terpineol (5.6-178 mg/kg) β -caryophyllene (56-320 mg/kg) or γ -terpinene (56-320 mg/kg) and tested. **Results:** Each terpene dose-relatedly reversed mechanical allodynia in both models. Higher doses of each terpene were required to achieve maximal reversal in the CIPN model. The rank order potency of the terpenes was α -terpineol > β -caryophyllene > γ -terpinene. Compared to wildtype mice, both CB1R (-/-), CB2R (-/-) mice treated with α -terpineol displayed a significant rightward shift in potency to reverse mechanical allodynia in both models. β -caryophyllene-induced reversal of mechanical allodynia underwent a significant rightward shift in potency in CB2R (-/-) mice in both models. Both CB1R (-/-) and CB2R (-/-) mice treated with γ -terpinene displayed a significant rightward shift in potency to reverse CIPN mechanical allodynia. This contrasts with the CCI model as only CB1R (-/-) mice displayed a rightward shift. **Conclusions:** These findings suggest these terpenes may have differential cannabinoid receptor activity. Cannabis-based terpenes may yield novel analgesics.

Education, Practices, and Safety

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An Analysis of Adverse Events Reported for Cannabis-Derived and Synthetic Cannabis-Related Drug Products Using the FDA Adverse Event Reporting System (FAERS)

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Background: There are been no studies that have comprehensively reviewed safety profiles, including reported adverse drug events (ADEs), for cannabis-derived and synthetic products approved in the United States (U.S.) and internationally. **Objective:** To examine ADE reports for cannabis-derived (i.e., Epidiolex), synthetic cannabis-related (i.e., Marinol, Syndros, Cesamet, and Sativex), and unspecified cannabidiol (CBD) drug products, and to describe ADE reports by characteristics, reactions, and outcomes reported. **Methods:** Data from the FDA Adverse Event Reporting System were analyzed from 1985 to Q3/2019. Brand and generic product names as well as common names (e.g., "CBD") were used to extract reports. Characteristics of the ADE were described by the cannabinoid product's role in the event, reporter type, and country. Reactions were described by Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms. **Results:** After de-duplication, there were 3,445 unique ADE reports, of which 1,892 were for Marinol or Syndros, 655 for Epidiolex, 374 for Cesamet, 183 for Sativex, and 341 for unspecified CBD. The cannabinoid product's role in the ADE was as concomitant or interacting (62.6%) more frequently than as a primary or secondary suspect drug (37.4%) with the exception of Epidiolex (primary or secondary suspect drug 96.6%). ADEs were most often reported by physicians (33.1%), other health professionals (27.9%), and consumers (28.2%). Reports originated most often in the U.S. for a majority of the ADEs, followed by Canada (11.1%) and Germany (6.5%). The most frequently reported reactions were seizure (6.0%), death (3.6%), decreased appetite (2.6%), and vomiting (2.2%). The most frequent reaction for Marinol or Syndros was death (4.9%); seizure (26.0%) for Epidiolex; therapeutic product effect incomplete (7.5%) for Cesamet; multiple sclerosis relapse (7.1%) for Sativex; and off-label use (3.8%) for unspecified CBD. Hospitalizations (40.9%) were the most frequent outcome, followed by other serious medical events (38.5%) and death (16.8%). **Conclusion:** Frequently reported reactions with cannabis-derived and synthetic cannabis-related products were related to the indications for which they are approved. However, death was the second most frequent reaction overall and which accounted for one in six reported outcomes. Presence of these ADEs warrants further safety evaluation.

Clinical Decision Making by Medical Marijuana Physicians in Florida: A Qualitative Assessment

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Medical marijuana (MMJ) was legalized in November 2016 with the passing of Amendment 2 in the state of Florida. Since the legalization, many studies have been conducted to understand the direct effect MMJ has on specific medical conditions. Unlike most allopathic drugs, MMJ does not target single ailments or specific conditions and does not follow precise recommending guidelines. There is scarce knowledge on how patient characteristics, including medical conditions, affect a physician's direct recommendations and registry limits.

To obtain insight on the effect patient characteristics have on the clinical decision-making process, we conducted ten qualitative interviews of MMJ physicians who are certified to order MMJ for patients in Florida. Interview topics ranged from typical daily practice to specific recommendations for patient histories. Each interview was transcribed and thematically analyzed. Five major patient characteristics that influence a physician's recommendation emerged from the interviews: patient medical history, co-medications, lifestyle, marijuana experience level and counter-indications. Each category was analyzed further to understand how the characteristic influenced the practice of recommending and ordering product.

Physicians emphasized the equivalent importance of reviewing a patient's medical history, lifestyle, and past marijuana experiences while also expressing the need to look holistically at the individual patient. Instead of the characteristics determining what the physician recommends for the patient and orders through the registry, the characteristics dictate the education given to the patient so that the patient may lead and determine their own individual care.

Educating Minorities about Marijuana for Medical Use and the Consequences of Unlawful Use of Marijuana

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Objectives: Florida A&M University (FAMU) established the Medical Marijuana Education and Research Initiative (MMERI) to educate minorities about marijuana for medical use and the impact of the unlawful use of marijuana, pursuant to Sec. 381.986 F. S. This presentation provides an overview of how MMERI, has educated and engaged individuals throughout the State of Florida, using on-site classes, print and broadcast media, over myriad communications channels, including the MMERI website (mmeri.famu.edu), podcasts and videocasts. After the onset of the COVID-19 global pandemic, MMERI moved to online technologies, including an E-Newsletter and Conversations on Cannabis, a virtual forum broadcast over Zoom, to expand its education, communication

and community engagement reach throughout Florida. In addition to the number of events, minorities and Floridians served, and percentage ethnically, the facilitator will reveal numerical findings and qualitative insight derived from pre/post assessments, as well as satisfaction surveys. **Methods:** This overview consists of descriptive statistics with comparative analyses using both quantitative and qualitative data to organize, summarize and report on selected education and outreach activities. The effectiveness of the education and outreach activities were measured by participant feedback on the pre/post assessment for the Basic Medical Marijuana Education course, as well as satisfaction surveys. **Result:** The number and types of activities and events and participants served, reveal MMERI's compliance with its legislative mandate to educate minorities. However, the invaluable data extracted from assessment and surveys, provided critical insight showing participants not only moved from one level of competency to a higher one in the cognitive domain: but in the affective domain as well. The responses illustrated participants viewed medical marijuana more favorable when compared to unlawful usage of marijuana, after viewing MMERI's presentations. The demographics revealing the ethnicity of Floridians served in descending order as: 55% Whites, 24% Hispanics; 16% Blacks; 3% Asians; and 2% Mixed/Others, exemplifies MMERI's commitment to diversity. **Conclusion:** FAMU's MMERI educated minorities about marijuana for medical use and the impact of the unlawful use of marijuana, pursuant to Sec. 381.986 F.S.

Priorities for Medical Marijuana Research from the Perspective of Physicians, Dispensary Owners/Staff, and Patients: A Survey Study

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Objective: More patients are turning to medical marijuana as an alternative treatment yet there are apparent knowledge gaps on risk-benefit of medical marijuana for a variety of indications. This study aimed to determine the priorities for medical marijuana research from the perspective of multiple stakeholders including patients, clinicians, and industry representatives. **Methods:** An anonymous survey was administered to attendees of the 2019 American Medical Marijuana Physicians Association annual meeting in Orlando, Florida. Respondents completed the survey on paper or cellphone via Qualtrics. The survey included questions on demographics and ranking of medical marijuana research topic area priorities. **Results:** 46 participants (56.5% female, mean age = 51.6±14.1) responded to the survey. A majority were medical marijuana qualified physicians in Florida (56.5%), 30.5% other physician or clinician, and 21.7% medical marijuana patients (some participants selected more than one group that they belonged to). On a scale from "1-not important" to "5-extremely important", the top five priority topics for medical marijuana research rated by this group included: chronic pain (3.7±0.7), dosing and/or medical marijuana product choice (3.7±0.5), research on the human

endocannabinoid system (3.6 ± 0.5), different THC/CBD ratios (3.5 ± 0.7), and research in middle aged/older adults (3.4 ± 0.6). **Conclusions:** Findings from this survey indicate that medical marijuana stakeholders perceived a broad range in research topics as priorities. Future research is needed to advance the knowledge in these areas and provide guidance to patients, physicians and the medical marijuana industry.

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Drug Interactions with Cannabinoids

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Cannabis (*Cannabis sativa* L; marijuana) has been widely used for both recreational, ceremonial, and medical purposes. The increasing popularity of cannabis use recreationally, and increasingly as medical cannabis in the majority of US States, there is growing concern of potential drug-drug interactions (DDIs) with conventional medications. We have previously demonstrated potent in vitro inhibition of cannabinoids on carboxylesterase 1 (CES1), the major esterase present in the liver. Methylphenidate ([MPH], Ritalin®, others), a known CES1 substrate, is indicated for treatment of attention-deficit/hyperactivity disorder (ADHD) in both pediatric and adult patients. In this study, the inhibition mechanism and potency of the major cannabinoids $\Delta 9$ -tetrahydrocannabinol (THC) and cannabidiol (CBD) were assessed utilizing an in vitro system of human liver S9. THC and CBD inhibited the hydrolysis of MPH reversibly with mixed competitive-noncompetitive and mostly competitive characteristics, respectively.

Excessive nonspecific binding (>95%) of both cannabinoids to the protein and tube wall was noticed in the incubation mixture. After correcting for the fractions bound, the estimated unbound inhibition constants (K_i) for THC and CBD were 0.031 and 0.091 μ M.

A static mechanistic model integrated with the estimated parameters predicted a mild pharmacokinetic interaction between MPH and THC from smoking a cannabis cigarette and a strong interaction between MPH and CBD from recommended doses of CBD solution (Epidiolex®). A clinical study of DDIs sponsored by the Consortium for Medical Marijuana Clinical Outcomes Research is presently underway to verify these predictions.

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Developing Methods for the Rapid Identification of Heavy Metals and Microplastics in CBD Oil

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This project aims to establish rapid and reliable analytical techniques to determine heavy metal and microplastic impurities in CBD oil. Cannabis has shown great promise for the treatment of many medical conditions. Resulting from this, the therapeutic application of cannabis and its constituent phytocannabinoids (i.e. THC and CBD), continues to garner significant clinical and public attention. There are, however, substantial uncertainties surrounding the nature and content of contaminants in cannabis plants. An in-depth understanding of plant contaminants and toxin effects on the stability of plant compounds and the effect on human health is necessary. Cannabis presents a complex system, there are many challenges associated with understanding the contaminants present and much uncertainty exists regarding the quality, safety, and legal status of the CBD oils. In this work, our aims were to: 1) develop a methodology to rapidly quantify the heavy metal contaminants in commercially available samples of CBD oil via Wavelength Dispersive X-ray Fluorescence (WDXRF); and 2) identify microplastic polymer contaminants in CBD oil using coupled Thermal Gravimetric Analysis – Differential Scanning Calorimetry (TGA–DSC). Our goal is to develop reliable, rapid, efficient, inexpensive analytical methodologies for the determination of key contaminants within the cannabis plant and to accelerate research in this promising industry to ensure consumer/patient safety.

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Therapeutic Properties of Cannabigerol (CBG)

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Objective: Cannabigerol (CBG), is the precursor molecule to most cannabinoids including delta 9-tetrahydrocannabinol (THC) and cannabidiol (CBD). Non-psychoactive cannabinoids, such as CBD and CBG, show promise for attenuating substance seeking behavior along with anti-inflammatory, analgesic, and anti-epileptic activity. CBG, in particular, displays potency at distinct non-cannabinoid receptors: alpha-2 adrenoceptors, PPAR α/γ , and serotonin 5-HT $1A$ receptor. We propose CBG as a novel therapeutic in the cannabinoid class of drugs with potential for pain, inflammation, and psychiatric disorders (substance abuse, ADHD, etc.). **Methods:** To study the potential effects of CBG, we performed an array of biochemical, molecular, and radiotelemetric studies to better characterize its molecular mechanism and potential hazards. Mouse models were used to assess analgesic applications of CBG and radiotelemetry sensors were used to monitor blood pressure. Receptor binding characteristics have been investigated for CBG, CBD, and THC. **Results:** Data suggest that CBG acutely lowers

blood pressure in conscious, freely-moving mice as measured by radiotelemetry. Moreover, it shows a non-significant trend for acute pain reduction in mice, and further study is needed. CBG displays a fundamentally different pharmacological profile from CBD and THC. **Conclusion:** Novel compounds of the Cannabis sativa plant show promise as new pharmacotherapeutics; however, most still do not yet have thorough characterization of therapeutic uses and adverse effects. CBG provides new opportunities and hazards as its popularity increases among cannabinoid supplement users. Our findings suggest that CBG has unique pharmacological potential for pain and blood pressure regulation, presumably due to its affinity for alpha-2 adrenoceptors. Translational and clinical research must be prioritized to reduce harm from pharmacological interactions and investigate CBG's ability to modulate diseases as a therapeutic.

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Which is Better: Vaping or Smoking Flower? A Perspective from Certifying Physicians in Florida

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Objective: To compare medical marijuana (MMJ) qualified physicians' opinions regarding the effectiveness, dosing ability, product consistency, side effects, safety, and affordability of vaping vs. smoking as administration modes. **Methods:** We conducted a state-wide anonymous MMJ physician survey developed by the Consortium for Medical Marijuana Clinical Outcomes Research. The survey was distributed among 1600 certified MMJ physicians in Florida via mail and e-mail between June and October 2020 and included questions on opinions related to MMJ practices. This abstract presents a descriptive analysis of the responses to the question: "For each of the following characteristics, indicate whether you think Smoking (flower) or vaping is better, or if there is no difference". Chi-Square tests were used to compare the proportion of physicians that endorsed "smoking is better" vs "vaping is better" on each characteristic. **Results:** A total of 116 MMJ physicians (7.3% response rate) from 29 Florida counties responded to the survey. The mean (SD) age was 57 (12) years old, and 70% were males. The majority of physicians thought there is no difference between vaping and smoking flower for safety over time (54%), overall side effects (63%), coughing and breathing side effects (45%), and affordability for patients (48%), but believed vaping to be better for product consistency over time (44%), ability to find consistent doses (57%), and ensuring optimal doses (41%), while smoking was perceived to be better for overall therapeutic effects (49%). The Chi-Square tests showed no differences between smoking and vaping for safety over time, overall side effects, and coughing and breathing side effects. However, more physicians thought smoking was better for overall therapeutic effects (49% vs. 14%, p-value<0.0001) and affordability (35% vs. 17%, p-value=0.0109), while vaping was better for product consistency over time (44% vs.

18%, p-value=0.0011), ability to find a consistent dose (57% vs. 13%, p-value<0.0001), and ability to ensure optimal dose (41% vs. 20%, p-value=0.0098). **Conclusion:** The majority of surveyed MMJ physicians believed there is no difference between smoking and vaping for cannabis-associated side-effects, that vaping is better for ensuring optimal dose and dose and product consistency, while smoking is better for overall therapeutic effects.

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Improving Communication between Medical Providers and Patients about Medical Cannabis by Strengthening Cannabis Knowledge among both Groups

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Objective: Primary care physicians are now increasingly likely to need to address cannabis use with their patients as its use is becoming more common. It is imperative to have good communication for shared decision making between medical providers and their patients. My goal was to see if strengthening cannabis knowledge results in an improvement in communication between medical providers and patients. **Methods:** Presentations were given to small groups of patients and medical staff on a variety of cannabis topics. Everyone received general information about the process of obtaining a medical marijuana certification in Florida, products available and where to find additional resources but patients' education also focused more in depth on how to choose products to help them with their conditions. Surveys were offered to all participants and were scored on a 1-5 likert scale. Additionally, an educational display and website (<https://physicianscannabiscompendium.com>) were created to reach out to a wider audience as social distancing limited in person interactions. **Results:** A total of 281 surveys were completed. Medical staff completed 43 and patients/caregivers completed 238. All groups reported an improvement in knowledge about the topics that were reviewed. Patients who qualified for a recommendation on the same day rated the greatest improvement in communication ability followed by those who qualified later. Caregivers and medical staff rated their communication ability about cannabis lowest; however, caregivers felt most comfortable talking with a primary care doctor about it. Medical staff were the least comfortable talking with their own doctor about cannabis. Providers, pharmacists, nurses and medical assistants overall felt more comfortable than front desk staff, pharmacy techs and housekeeping staff in talking with patients about cannabis. **Conclusion:** Overall, there was a perceived improvement in knowledge about cannabis and ability to communicate about it. There was a slightly smaller improvement in comfort talking about cannabis between the groups reported by participants to be due to stigma and legal concerns. More work is still needed to bridge the gap between providers and patients to improve communication for shared decision making.

Prescribing Measures Associated with Medical Marijuana Physician Authorization Status in Florida

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Objective: The Medical Use of Marijuana Act became effective in Florida in 2017, which permitted the purchase and use of medical marijuana as treatment or adjuvant therapy for a series of qualifying conditions. Physicians that complete a required course are eligible to become authorized to order medical marijuana for patients. The purpose of this study was to describe physicians who are authorized to order medical marijuana by specialty, and then compare physician Medicare prescription measures by authorization status. **Methods:** The publicly available registry of cannabis-authorized physicians was downloaded from the Florida Department of Health's Office of Medical Marijuana Use (OMMU). Physician records were linked to the Centers for Medicare and Medicaid Services' (CMS) Medicare Part D Prescriber Public Use File for the year 2017 by the physician's National Provider Identifier (NPI). The CMS data were used to identify physician specialty as well as the following prescription measures for average total claims in 2017 to Medicare: opioids, long-acting opioids, and name brand medications. Remaining unlinked physicians from the CMS data were classified as not authorized to order medical marijuana. Proportion of physician specialties meeting each prescription measure were calculated by authorization specialty. **Results:** There were a total of 2,274 physicians authorized and 68,932 physicians not authorized to order medical marijuana who had filed at least one Medicare claim in the state of Florida in 2017 (3.19% authorized). The specialties with the highest average opioid claims were Interventional Pain Management (authorized: 3283.53+/-374.03 vs. unauthorized: 2460.77+/-199.02), followed by pain management (authorized: 1748.47+/-286.16 vs. unauthorized: 1728.64+/-185.61), and anesthesiology (authorized: 1470.79+/-364.30 vs. unauthorized: 721.34+/-82.70), and these also represented the specialties with highest average long-acting opioid claims. Authorized physicians specializing in rheumatology (884.33+/-243.92), internal medicine (820.45+/-52.22), and cardiology (600.59+/-139.77) had the highest brand name prescribing, while the following unauthorized physicians had the highest brand name prescribing: endocrinology (1435.96+/-59.19), geriatric medicine (1205.66+/-265.26), and pulmonary disease (832.94+/-63.98). **Conclusion:** Physicians authorized to prescribe medical marijuana prescribed, on average, more opioids to Medicare patients than their non-authorized specialist counterparts in Florida, while prescribing fewer brand name medications as compared with non-authorized specialist counterparts.

Cannabis Use Patterns and Behavior

Pilot Study on CBD and Quality of Life in Retired Elite Athletes

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Background: Cannabis Clinicians Colorado conducted a Pilot Study on CBD and Quality of Life in Retired Elite Athletes. The study looked at a variety of CBD routes of administration monitored by four data points in a small cohort. As pilot studies investigate feasibility rather than efficacy, this presentation summarizes the data and offers potential areas for further study. **Methods:** A placebo-controlled study of cannabidiol (CBD) as a supplement to current therapies in retired elite level athletes with medical issues resulting from their competitive years. 24 subjects received a 60-day supply of either an escalating measured-dose daily CBD supplement or a placebo, in one of six possible routes of administration: capsule, sublingual tincture, sublingual tablet, sublingual nano-emulsified oil, or nasal spray. Subjects underwent twice-monthly monitoring by WAVi QEEG scan, Roberto cognition testing, clinical observation, and e-diary Quality of Life assessment surveys during the study. **Conclusions:** The data is promising enough to warrant further study. This was an un-funded study using donated product and a "throwing spaghetti at the wall" approach to routes of administration. Cannabis therapies are well known to fall outside of the conventional medical model of a single chemical compound having a marked effect at a measured dose, so a wide rate of variation was expected. Subjects reporting no results no matter what the dosage, or conversely, reporting adverse psychoactive effects with CBD alone, fit within the investigator's clinical experience. Interestingly, many subjects who reported feeling nothing still showed changes on the WAVi QEEG that placebo subjects did not. Of subjects who reported feeling better, the 50 mg per day dose showed the best results with fewest side effects. Taking more did not result in additional improvements. This may be an area for further study. A surprising find was Quality of Life improvements were significantly more pronounced with capsules than other product types. A review of the data tools used offered useful information and subjects offered suggestions on how to improve them.

Growth of the Medical Marijuana Program in Florida from February 2018 to January 2021

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Background/Objective: Medical cannabis (MC) has been accessible to Floridians for the treatment of certain debilitating medical conditions since summer 2017. This study describes trends in participation and product utilization within the Florida MC program. **Methods:** In this descriptive study, we accessed the Florida Department of Health Office of Medical Marijuana Use (OMMU) weekly reports detailed MC utilization from February 2018 until January 2021. MC was defined as types of different MC products available in Florida, namely Medical Marijuana (MMJ), low-THC MC, and MMJ for smoking. Weekly numbers of patients with licensure to use MC, MC-authorizing physicians, and dispensed amounts of MC products were extracted. We plotted trends, ratio of patients per MC-authorized physician, dispensed MC per patient, and dispensed MC per physician. **Results:** Between 2018-2021 (1,071 days), the amount of MC patients increased from 51,050 to 465,426 (9.1-fold increase), and the number of MC-authorized physicians increased from 1,035 to 2,733 (2.6-fold increase). The patients per physician ratio increased from 49 to 170 patients per physician (3.5-fold increase). During the same period, the amount of dispensed MMJ (in THC) per week increased from 13,776 g to 148,266 g (10.8-fold increase), and dispensed low-THC MC (in CBD) per week increased from 960 g to 3,402 g (3.5-fold increase). Dispensed MC for smoking increased from 266,921 g in July 2019 to 1,470,532 g by January 2021 (5.5-fold increase). The amount of dispensed MMJ in grams of THC per patient remained steady throughout the study period, whereas the ratio of dispensed low-THC MC in grams of CBD per patient decreased to less than half (-61%). Dispensing of THC (in grams) per licensing physician had increased 4.1 times in early 2021, when compared to February 2018. **Conclusion:** Both the number of patients and amount of MC have grown steadily from 2018 to 2021 in Florida. Increases in utilization were most pronounced for MMJ, though the total amount dispensed per patient remained relatively constant, while the use of low-THC per patient decreased. MC physicians in early 2021 manage more MC patients and their licensure results in more MC dispensing, as compared to early 2018.

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

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Objective: Marijuana (MJ) use (for both medical and recreational purposes) is increasing among patients following medical marijuana legalization, and it is critical for health professionals to have a better understanding of the relationship between marijuana

use and mental health disorders, including substance use disorders (SUDs). Despite the potential of medical MJ to assist with these 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, if the passage of medical marijuana laws (MML) is associated with changes in substance use or mental health diagnoses or treatment related health costs remains unclear. The purpose of this study was to examine the association between state MML and substance use and other mental health disorder diagnoses and associated health care costs. **Methods:** Using MarketScan Health Claims data, we examined treatment costs associated with 8 different mental health and substance use disorder diagnoses in 2012 and 2018 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). **Results:** In 2012, 19 states had passed MML. Preliminary independent T-test analyses indicated that in 2012, states that passed MML have higher rates of OUD, CUD, AUD, PTSD, DD, and PD ($p < .001$) than those that did not yet pass MML. Similarly, healthcare costs were significantly higher across all disorders examined in states with MML compared to those without MML. A similar pattern of results was observed for the data collected in 2018, by which 34 states passed MML. **Conclusion:** Preliminary findings suggest that states with MML have had higher proportions of individuals with disorders related to opioid, cannabis, and alcohol use; and trauma, depression, and psychosis. Similarly, healthcare costs were significantly higher across the disorders examined in states with MML compared to those without MML. More research is needed to examine trends across states and over time to get a better understanding of the influence of MML on the prevalence and costs of these disorders.

Feasibility of Real-Time Monitoring of Posttraumatic Stress Disorder Symptoms, Sleep Quality among Patients on Medical Marijuana

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Posttraumatic stress disorder (PTSD) is a debilitating disorder that occurs following a life-threatening trauma. PTSD is associated with sleep disturbances, nightmares, and poor mental health quality of life. Medical marijuana (MMJ) is often used to improve sleep and other PTSD-related symptoms, but at this point, we lack evidence on its effectiveness as a therapy for PTSD. **Objective:** This presentation will demonstrate the feasibility of engaging persons with PTSD in a follow-up study and assessing in real-time using smartphones, and present the main outcomes of the study. **Methods:** Fifteen persons who met PTSD criteria and seeking to start MMJ for their symptoms were recruited from medical cannabis clinics in North-Central Florida. Participants were assessed at three-time points: baseline – before starting MMJ, and 30- and 70-days after MMJ initiation using PTSD checklist for DSM-5

(PCL-5), Pittsburgh Sleep Quality Index (PSQI), Positive and Negative Affect Schedule (PANAS), and PROMIS Global Health. Ecological Momentary Assessment (EMA) was conducted using smartphones longitudinally four-times a day for one week at baseline, dose-adjustment, and stable-dose phases respectively. **Results:** We have screened 61 individuals, of which 24 (39%) were eligible; 17/24 (71%) consented to participate in the study. One participant withdrew after consent; 16/17 (94%) completed the Baseline Assessment. One participant was lost to follow-up after the baseline survey; 15/17 (88%) completed the Baseline survey and EMA. All 15 (100%) completed all study assessments (Dose-Adjustment EMA, 30-day survey, Stable-Dose EMA, and 70-day survey). Participants' mean age was 44 years (SD 11.9), 80% were white, and 60% were female. Majority (73%) used other drugs in their lifetime. Results demonstrated significant improvements at 30- and 70-day follow-up in PTSD score [F(2,24)=13.25], PSQI score [F(2,25)=16.54], Sleep quality [F(2,27)=22.57], Sleep duration [F(2,27)=8.33], nightmares [F(2,26)=13.87], negative affect [F(2,26)=9.82], and mental health [F(2,27)=8.44]. All outcomes were statistically significant at $p < 0.05$. **Conclusion:** This pilot demonstrated the feasibility of engaging persons with PTSD on MMJ in a study involving daily EMA assessments and surveys at follow-up. This pilot also demonstrated improvements in sleep and well-being, and decreases in PTSD symptoms and nightmares following MMJ, with effects lasting at least 70 days after initiation.

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Review of Medical Marijuana Use in HIV/AIDS

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Objective: The use of medical marijuana for treating many medical conditions has become widespread in the USA and around the world, even though the legal status of marijuana use varies across the United States. The recreational and medicinal use of cannabis may be increasing among individuals with HIV due to growing reports of its potential to treat and manage symptoms of HIV/AIDS, such as pain. However, the medical benefits of marijuana use in HIV, as well as its harmful effects, continue to be ardently debated. This review identified and evaluated recent studies assessing the association between marijuana use and HIV outcomes. **Methods:** Our database search included Web of Science, Embase, PubMed, and the Cochrane library using the following inclusion criteria: English language, USA-based study dated between May 2016 – December 2020, health outcomes relating to marijuana use in HIV, studies focused on cannabis use. We excluded preclinical studies and any abstract-only articles. Studies were categorized based on design and scored based on quality and risk of bias using the ROBINS-I tool for observational studies. **Results:** Twenty-eight studies out of 1722 search hits met inclusion criteria, and 22 were observational studies with cohort or cross-sectional designs. Studies examined outcomes on adherence (7 out of 22), viral suppression (10 out of 22), and pain (5 out of 22). The 11 studies that

focused on adherence and viral suppression showed no significant positive effect, but only 1 study determined a positive effect on pain. Also, 3 out of 11 studies examining adherence were rated low quality while none were rated moderate or high quality. Some studies revealed a high prevalence use of marijuana among people living with HIV/AIDS (from 31% to 56%), especially in adolescents and young adults. **Conclusion:** There is not enough evidence to support marijuana use in improving adherence and viral suppression as an effective treatment option for HIV/AIDS. However, there is limited evidence to support that marijuana is an effective treatment for alleviating pain among HIV/AIDS patients. This review suggests the need for high-quality research measurements in the assessment of marijuana use in HIV.

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Community-Level Factors Associated with Medical Marijuana Prescriber Authorizations in Florida

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Objective: Florida expanded access to medical marijuana in 2017, where change in state law permitted the purchase and use of medical marijuana as treatment or adjuvant therapy for a series of qualifying conditions. Medical marijuana is required to be purchased through a licensed medical marijuana treatment center (MMTC) dispensary under certified order from an authorized physician. The purpose of this study was to map MMTC and authorized physician location concentration by geographic area, and compare concentration of medical marijuana service availability by community characteristics. **Methods:** MMTC and authorized physician lists were downloaded from Florida Department of Health's Office of Medical Marijuana Use (OMMU) public database. Location data (zip code and county) were used to map MMTC and physician concentrations using Tableau software. MMTC and physician counts were adjusted per 100,000 residents per county. Medical marijuana orders were then mapped per county adjusted for 100,000 population. **Results:** A total of 2,274 authorized medical marijuana physicians and 239 MMTCs had valid location data for 2017. Walton County had the most concentrated number of medical marijuana orders (2941 per 100,000 residents), followed by a zip code within Pinellas County [Tampa area] (1379 orders/100,000 residents), and a zip code within Collier County [Naples area] (133 orders/100,000 residents). Three zip codes within Broward County [Fort Lauderdale area] each had the highest concentration of MMTCs (562MMTCs/100k residents; 351MMTCs/100k residents; 226MMTCs/100k residents). **Conclusion:** Medical marijuana authorized physicians and MMTCs are concentrated in distinct regions throughout Florida. Orders for medical marijuana in Florida were more concentrated in northern and central Florida regions, while MMTCs were more concentrated in southern urban regions.

Patient Perception on the Efficacy and Regulations of Medical Marijuana

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Objective: The objective of this research study was to assess the efficacy of the use of cannabis and its derivatives for medicinal purposes. This survey-structured study aimed to examine two primary aspects. The first aspect of this study sought to investigate patient perspectives on utilizing medical marijuana versus FDA-approved medications for their diagnosed medical condition. The second aspect sought to evaluate patient perception on the public policies that regulate medical marijuana. **Methods:** A preliminary literary review was conducted to assess the current uses of cannabis for medicinal purposes. The knowledge gained from this literature was then used to create a Qualtrics questionnaire containing ten questions on cannabis use for mental health conditions, chronic pain, digestive issues, and a slew of various debilitating disorders. The questionnaire was administered to 30 participants who hold a medical marijuana card in the state of Massachusetts. The participants were screened, and informed consent was provided to them explaining the overview of the study and reassuring their anonymity. Following the completion of the questionnaire, the information was reviewed, and the data was extrapolated to analyze the efficacy of cannabis product use for individuals with diagnosed medical conditions. **Results:** The results indicate that medical marijuana patients prefer cannabis products and its derivatives over FDA-regulated pharmaceuticals. Secondly, the results also show that those with a medical marijuana card believe policies should be implemented in more states to make cannabis accessible to those battling various medical conditions. Although the laws and regulations of cannabis differ from state to state, the use of medical marijuana has been shown to be an effective method of treatment for an array of both emotional and physical conditions. **Conclusion:** Despite limitations such as long-term effects on patients and the wide variety of health conditions of the participants, cannabis used for medicinal reasons has been shown to be an effective method of treatment. Furthermore, participants believe that more states should adopt similar policies to Massachusetts that make medical marijuana accessible to patients with emotional and/or physical conditions that cause a decrease in their functionality and quality of life.

Cannabis as a Novel Therapeutic

Role of CBD Exosomes in Triple Negative Breast Cancer

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Breast Cancer predominantly affects women in the United States, and around 10-14 % of all breast cancers are triple negative type (TNBC), which are having limited effective therapeutic options readily available. Anti-cancer potential of cannabidiol (CBD) is well demonstrated in various cancers but poor solubility and increased metabolism by CYP enzymes limit the bioavailability of CBD. So, we hypothesize that therapeutic usage of human umbilical cord stem cell derived exosomes (hUCMSCs-EX) will serve as an ideal delivery platform not only for increasing the bioavailability and anticancer effects of CBD but also for overcoming resistance of docetaxel (DTX) and Doxorubicin (DOX) in MDA-MB-231 (i.e., CB1, CB2, and CD44 receptors expressing) cells. Synthetic CBD (Purisys™, GA; GMP grade) showed cytotoxic effects in both 2D and 3D cultures of MDA-MB-231, MDA-MB-468 and Doxorubicin (DOX) resistant MDA-MB-231 cells. RNA sequencing revealed alterations of various genes, among which GADD45A, GADD45G, Integrin alpha 5, integrin beta 5 were identified to be affected by CBD treatment in MDA-MB-231 cells. Flow cytometry of cell cycle analysis revealed that CBD induces G1 phase cell cycle arrest in MDA-MB-231 and MDA-MB-468 cells. CBD was found to be a potent sensitizer and increased the sensitization of Docetaxel (DTX) and DOX to MDA-MB-231 (by 8.2 and 2.5-fold respectively) and MDA-MB-468 (by 4.6 and 3-fold respectively) cells. Moreover, CBD (2.5 μM) pre-treatment significantly improved the sensitivity of DOX in DOX resistant MDA-MB-231 cells response by 4-fold higher when compared to DOX alone. We also developed stable formulation of CBD loaded exosomes (CBD-EX) by using sonoporation technique. CBD-EX significantly decreased the proliferation of TNBC cells. In addition, CBD-EX (2.5 μM; i.p. twice a week) in combination with DOX (2 mg/kg i.v. twice a week) significantly decreased the tumor burden in MDA-MB-231 xenografts in comparison to CBD and DOX combination alone. This suggests the role of CBD-EX in improving the sensitivity of DOX. In summary, our results demonstrate that CBD shows not only anticancer activity against MDA-MB-231, MDA-MB-468 and DOX-resistant MDA-MB-231 cells but also acts as a potent chemosensitizer for conventional chemotherapeutics.

THC Slows Progressive Weight Loss in a Rodent Model of Anorexia Nervosa

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Objective: Consistent with its complex and poorly understood etiology, the course of anorexia nervosa (AN) is highly variable, effective pharmacotherapies are limited, and relapse is common. Thus, a critical need exists for new drug therapies that target symptoms of AN. In this regard, our group is interested in the endocannabinoid system, based on its involvement in regulating food intake, energy expenditure, and reward processing, all of which are dysregulated in AN. Additionally, clinical studies report impaired cannabinoid signaling in AN patients, and daily treatment with Δ^9 -tetrahydrocannabinol (THC) has been shown to attenuate weight loss in the pre-clinical rodent model of activity-based anorexia (ABA). An important limitation of existing studies showing THC's ability to attenuate ABA-induced weight loss is that THC treatment is started in healthy animals that have not developed symptoms of ABA. With respect to developing new pharmacotherapies, a better approach would be to initiate cannabinoid treatment after, rather than before, animals have developed ABA. Here, we tested the hypothesis that treatment with THC would rescue the ABA phenotype and restore normal endocannabinoid function in female rats that had experienced significant weight loss in the ABA paradigm. **Methods:** Female rats were exposed to the ABA paradigm, which combines restricted feeding (90 min access to food/day) with unlimited access to running wheels (RWs). Following 15% weight loss, rats received once-daily intraperitoneal injections of THC (1 mg/kg) or vehicle for 7 days. Throughout the experiment, food intake, RW activity, and body weight were monitored daily. **Results:** Our analysis of the first cohort of rats ($n = 8$) revealed similar daily food intake in the THC- and vehicle-treated groups (~4.4g/day). However, THC-treated rats displayed about a 50% decrease in RW activity, relative to vehicle-treated rats (treatment average = 7257 \pm 1437 vs. 14051 \pm 508 revolutions/day, $p < 0.05$), and this resulted in a reduction in the rate of weight loss over the treatment period in THC- versus vehicle-treated rats. **Conclusion:** These preliminary findings suggest that daily THC treatment helps to rescue the ABA phenotype in underweight, symptomatic female rats primarily through a reduction in energy expenditure. (Funded by the Consortium for Medical Marijuana Clinical Outcomes Research)

Acute Effects of Cannabis on Cognition in Aging

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Cannabis is the most widely used illicit drug in the United States, with individuals over the age of 65 becoming the fastest growing demographic of cannabis users. Cannabis can have multiple benefits such as serving as a pain management tool, appetite

stimulant and sleep aid that make it appealing for individuals coping with age related health conditions.

As the number of older adults in the US expected to reach 90 million by 2050, however, it is imperative to understand the potential cognitive impacts of cannabis use in this population. Across species, aged individuals exhibit deficits in cognitive functions supported by the prefrontal cortex (PFC) and the hippocampus. These same cognitive functions are impaired by acute administration of cannabis or delta-9-tetrahydrocannabinol (THC) in young subjects; however, effects in aged subjects have been less well evaluated. The primary goal of the current study was to use a rat model to determine whether the cognitive effects of acute exposure to cannabis smoke differ between young and aged subjects. Male and female young adult (6 mo.) and aged (24 mo.) Fischer 344xBrown Norway F1 hybrid rats were tested on both a PFC-dependent delayed response working memory task and a hippocampal-dependent trial-unique non-match to location (TUNL) task in touchscreen operant chambers. The delayed response task required rats to remember the location of a visual stimulus over variable delay periods ranging from 0-24 s. The TUNL task required rats to remember the location of a visual stimulus with varying degrees of discriminability from other, distractor stimuli in the absence of delays. A semi-randomized, within-subjects experimental design was used such that each rat was exposed to smoke from burning, 0, 3, and 5 cannabis cigarettes immediately prior to test sessions in each task. In the delayed response task, acute exposure to cannabis smoke impaired accuracy in young rats but enhanced accuracy in aged rats. In contrast, in the TUNL task, cannabis smoke had no effects on performance in either age group.

Considered together, this pattern of results suggests that in aged rats, which exhibit impaired cognitive performance relative to young, cannabis smoke can enhance PFC-dependent cognition, but has no effect on hippocampus-dependent cognition.

The Effect of Cannabis Compound Tetrahydrocannabinol on Fibrotic Pathways; Implications Beyond Fibrosis

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Objective: Cannabis use by patients with inflammatory bowel disease (IBD) has become increasingly popular. Cannabis improves symptoms but may increase the need for surgery in patients with Crohn's disease (CD). Previously, our group has shown tetrahydrocannabinol (THC), a primary constituent of cannabis, inhibits profibrotic gene expression in human intestinal myofibroblasts (hIMF). Here we studied the mechanism of the major fibrotic signaling pathway involving the TGF-1/Smad family of proteins. **Methods:** hIMFs were stimulated with 5ng/ml transforming growth factor beta 1 (TGF) and pretreated with vehicle or 0.5-2 μ M THC for 24h. Cellular protein and mRNA were isolated, quantified, and analyzed by Western blot and qPCR and expressed as fold vehicle control. For analysis of phosphorylated proteins, the intensity of the phosphorylated protein was normalized by the intensity of the corresponding total protein and expressed as a ratio.

Results: As expected, stimulation with TGF increased gene expression of SMAD7 (fold increase; 4.69 ± 0.15 ; $p < 0.0001$). THC did not change SMAD7 mRNA levels suggesting that THC was not acting through the canonical SMAD2/3 pathway. This was confirmed at the protein level where TGF increased the ratio of phosphorylated SMAD2/3 protein (P-SMAD2/3) to total SMAD2/3 protein (3.06 ± 0.09 -fold; $p = 0.02$). Pretreatment with $1 \mu\text{M}$ THC did not prevent the increased P-SMAD2/3 levels, and THC treatment alone had insignificant effect on P-SMAD2/3 to total SMAD2/3 ratio (0.8 ± 0.02 -fold). To address a second pathway, TGF stimulation increased phosphorylated RAC-alpha serine/threonine-protein kinase (AKT) protein. Phosphorylated (P-AKT) to total AKT protein was increased 2.01 ± 0.45 -fold ($p = 0.15$), however 24hr pretreatment with $1 \mu\text{M}$ THC reduced P-AKT/AKT levels 0.78 ± 0.31 -fold ($p = 0.15$). THC alone also reduced the P-AKT/AKT to 0.87 ± 0.27 -fold. **Conclusion:** THC did not alter SMAD7 mRNA or P-SMAD2/3 protein levels suggesting the canonical pathway is not responsible for its anti-fibrotic action. THC may mediate this effect through a SMAD-independent AKT pathway. In hIME, an important cell type in CD, THC has potentially beneficial effects on fibrosis. It should be noted however, that aberrant AKT signaling is the underlying defect found in several pathologies (cancer, diabetes, cardiovascular disease) and AKT phosphorylates over 100 different substrates, therefore the potential impact of THC in patients could be substantial and not immediately apparent.

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Oral Administration of CBD Improves Histopathological and Cognitive Outcomes Following Traumatic Brain Injury

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Objective: Traumatic brain injury (TBI) is a leading cause of death and disability with 69 million individuals sustaining TBI each year. Long-term complications, such as cognitive impairment, headache, sleep disturbances, and neurological comorbidities are primary complaints. Currently, there is a severe lack of treatment options to lessen the negative impact injury-induced disorders have on quality of life. Cannabidiol (CBD) is a nonpsychoactive, plant-derived compound that has beneficial outcomes in several nervous system disorders due to its anti-inflammatory and anti-apoptotic properties. Thus, we sought to evaluate a clinically-relevant oral administration of CBD to investigate its potential to reverse TBI-induced pathology in a preclinical model of TBI. **Methods:** Adult rats were exposed to a moderate fluid-percussion pulse over the right parietal cortex. CBD was orally administered (5 mg/kg) in 1 ml of peanut oil 1 hour post-surgery followed by 1x/day for 6 subsequent days via oral gavage. Outcome measures included spatial memory acquisition/retention and short-term memory via the Morris water maze. We also investigated whether CBD was cytoprotective through volumetric analyses of cortical contusion and quantifying cortical atrophy. Immunohistochemistry was utilized to assess microglia reactivity in various brain

structures. **Results:** After TBI, cognitive assessment revealed no CBD effect on spatial memory acquisition/retention, however short-term working memory skills trended towards uninjured levels. Histological assessment revealed reduced cortical atrophy and decreased contusion volume in animals treated with CBD. Furthermore, in the hippocampus and cortical penumbra, preliminary analyses showed CBD administration significantly decreased activated microglia phenotypes and reduced overall microglia numbers, two hallmark indicators of TBI-induced neuroinflammation. **Conclusion:** CBD has been shown to mediate neuroprotection and inflammatory pathways. We anticipated oral administration would mitigate some of the behavioral deficits and loss of cytoarchitecture after TBI. While positive trends were present, there was a lack of strong significance. However, because of preliminary analyses showing reduction in microglial reactivity and overall numbers, we propose that a higher oral dose may be more efficacious in reversing neuropathological sequelae. While the therapeutic potential of CBD after brain injury has yet to be fully elucidated, its neuroprotective, anti-apoptotic, and anti-inflammatory properties make it a promising

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Pharmacokinetics of Different Cannabidiol Oil Formulations in Sprague Dawley Rats

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Objectives: With the changing legal status of cannabis and an increase in availability and use of products derived from the plant, it is important to explore assertions related to these products. Cannabidiol (CBD) is the major cannabinoid found in hemp-type cannabis and the number of CBD products on the market, and the claims made regarding these products, continues to grow with little supporting research. A phenomenon known as the “entourage effect” is commonly referred to in the CBD industry and asserts that products formulated from whole-plant extracts will have better bioavailability and overall effect than those formulated from CBD isolate as they contain terpenes and flavonoids and additional cannabinoids. The goal of this study was to determine if there was a significant difference in the pharmacokinetics of CBD, in male and female rats, when delivered as isolate, broad-spectrum (whole plant extract with Δ -9-tetrahydrocannabinol (Δ -9-THC) extracted out), or full-spectrum (whole plant extract with $< 0.3\%$ Δ -9-THC) product. **Methods:** Male and female Sprague Dawley rats were dosed orally with high (150 mg/kg) and low (50 mg/kg) dose CBD in three different oil formulations. Blood samples were drawn at different time points up to 48 hours and analyzed using liquid chromatography tandem mass spectrometry. **Results:** The results of this study found that there was a statistically significant difference between the bioavailability of the full spectrum product and the broad and isolate product. This may indicate that the processes of isolation of CBD and/or removal of Δ -9-THC may cause changes to the product that affect its bioavailability. Another major finding from this study was that there is a shift in the time to maximum concentration of about 8 hours

between low and high doses indicating a nonlinear pharmacokinetic process. To determine if this process is occurring during the absorption or elimination phase, in vitro permeability experiments will be performed. **Conclusions:** This research will inform further study into which compounds may increase the bioavailability of CBD. Additionally, in silico modeling using this data will be performed to translate this data to across species.

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Cannabis, Female Orgasm, and Female Orgasmic Disorder: Comprehensive Literature Review

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Objective: This presentation will highlight a comprehensive literature review at the intersection of cannabis and female orgasm over the last century. Study participants reporting positive cannabis effects on female orgasm are numerous. Within these reports, one can also find occasional anecdotal mention from subjects who believe that cannabis helped in alleviating female orgasmic disorders as defined by the Diagnostic and Statistical Manual for Mental Disorders, 5th Edition. **Methods:** Comprehensive Literature Review. **Results:** Themes in the literature on cannabis and its effect on female orgasm include enhanced and more frequent orgasms and decreased sexual dysfunction. A few researchers found cannabis to be sexually inhibiting in women and one researcher found cannabis could be used to either enhance or inhibit sexual functioning depending on its intention for use. Recent research found women who use cannabis more frequently and used cannabis before sex were more than twice as likely to report satisfactory orgasms. No research was found to evaluate cannabis' effect on women who have female orgasmic disorder. **Conclusion:** Female orgasmic disorder as defined by the Diagnostic and Statistical Manual for Mental Disorders, 5th Edition, uses a broad definition and includes women who have never had an orgasm with women who have had orgasms and uses the specifiers of lifelong, acquired, situational or generalized to define the subtype of the disorder. This broad definition overshadows the fact that Directed Masturbation is the only empirically validated treatment for female orgasmic disorder and is specific to the specifier of "lifelong." Acquired and situational orgasmic disorders are common yet research describes a less optimistic prognosis with treatments such as Sensate Focus and Directed-Cognitive Behavioral Approaches considered to be 'probably efficacious' but not empirically validated. Situational orgasmic disorders were found to affect the largest percentage of women with female orgasmic disorder. Research showing the

percentage of women suffering from female orgasmic disorder has not changed in 50 years. The lack of validated treatments for female orgasmic disorder and the research on cannabis and female orgasm makes a convincing case to evaluate if cannabis could be a treatment for female orgasmic disorder.

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Can Cannabis be a Treatment for Female Orgasmic Disorder?

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Objective: This study will evaluate if cannabis could be a treatment for female orgasmic disorder. The Diagnostic and Statistical Manual for Mental Disorders, 5th Edition (DSM-5) defines female orgasmic disorder (FOD) as reduced intensity, delay, infrequency, and/or absence of orgasm. Women with FOD may never have had an orgasm (lifelong), may have experienced orgasms at one time but no longer (acquired), or may have orgasms in certain situations but not in others (situational). **Background:** Female orgasmic disorder (FOD) affects up to 41% of women worldwide, and the percentage of women suffering from FOD has not changed in 50 years. Causes of the problem may include: lack of communication, lack of sex education, high religiosity, focus on penile-vaginal intercourse, and women focusing on men's pleasure rather than their own. Anecdotal contributions suggest that cannabis enhances the quality of women's orgasm or helps women orgasm who have had orgasmic difficulties. Yet, no formal studies have evaluated cannabis as a treatment for FOD. Although FOD is not a listed condition for use in the 36 U.S. states with medical marijuana programs, cannabis is being used for that purpose. Recent reports identified a sex therapist in California, and a medical office in Massachusetts have publicly acknowledged using cannabis as a treatment for FOD and other sexual disorders. Women are also reporting secondary sexual benefits to their sexuality while being treated with cannabis for other medical problems. **The 'Why':** Female orgasmic disorder is associated with anxiety, depression, poor self esteem, adverse effects on quality of life, shame, faking orgasms and relational and interpersonal distress. Little progress has been reported on this problem despite that more than a third of women nationwide in need of assistance. **Methods:** I will be using a mixed-method approach, including an online survey and follow-up interviews to evaluate women who have female orgasmic disorder and use cannabis to answer the question if women who are receiving cannabis benefit in the treatment for female orgasmic disorder. Project in progress.

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