

Proceedings of the 2024 Cannabis Clinical Outcomes Research Conference

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Introduction

The federal government of the USA is in the process of reclassifying cannabis from a schedule I controlled substance to a schedule III controlled substance [1]. Most individual states had implemented medical cannabis programs prior to this reclassification, with Florida implementing a medical cannabis program in 2016 via expanding their earlier compassionate use program [2]. As of the summer of 2024, there are over 880,000 Florida registrants, making Florida one of the largest state medical cannabis programs in the USA by total enrollment [3].

Despite significant participation in the medical cannabis program, where approximately one in twenty persons in Florida are enrolled, there is limited evidence on safety and effectiveness of medical cannabis for several

of the health conditions that render a person eligible for medical cannabis programs. To address the evidence gaps, Florida state legislature established the Consortium for Medical Marijuana Clinical Outcomes Research and charged the Consortium to conduct, disseminate, and support scientific research on clinical outcomes related to cannabis use. These charges are addressed by Consortium leadership, with significant contributions from member institutions and researchers, by developing research infrastructure and collaboration, evidence syntheses and dissemination of research findings, a grants program, a research data repository, and a community outreach program [3]. The Cannabis Clinical Outcomes Research Conference (CCORC) aligns with the Consortium's mission to increase stakeholder engagement with research, promote collaboration in research between scientific and clinical communities, and to disseminate research findings.

Meeting Report

The CCORC was held in a hybrid format on May 30th and 31st in Lake Nona, Orlando, FL, USA. The fourth annual CCORC expanded upon the research agenda

presented at the third and second CCORC in 2023 and 2022, respectively [4, 5], to fulfill three main objectives agreed upon by the scientific program committee: (1) To disseminate findings from research investigating medical cannabis and cannabinoid use, efficacy, and safety, (2) to provide a venue for clinical and research educational opportunities related to medical cannabis, (3) to foster research collaboration and stakeholder engagement between Consortium member institutions and the broader scientific, clinical, and public health communities. The CCORC meeting had over 100 registrants, where attendees included researchers, students, clinicians, government officials, and industry representatives from Consortium member institutions and around the globe. Clinician attendees were able to earn up to 3.5 h of continuing medical education or continuing pharmacy education (CPE) credits for attending or participating in components of the scientific program.

Scientific Program

The full scientific program is available from www.ccorc.mmjoutcomes.org. The 2024 CCORC program included 3 keynote presentations, 12 oral presentations from top-scoring abstract submissions, 2 symposia, and 2 poster sessions featuring 34 research abstracts that were selected by the scientific program committee following peer review. Keynote presentations were recorded and are archived on the conference website for those that registered for the meeting. Digital versions of posters are hosted on the conference website and all poster abstracts as well as oral presentation abstracts are included in the abstract supplement in this issue of *Medical Cannabis and Cannabinoids*.

Abstracts selected for oral presentations covered a broad range of methodological applications toward understanding the effects of cannabis and cannabinoids. The individual studies covered wide-ranging topics from mapping the pharmacological interactions between cannabis constituents and oxycodone in rats, the use of marijuana products in young adults with inflammatory bowel diseases, and the impact of medical marijuana use on certain breast cancer outcomes. The main themes on clinical cannabis research conduct and interpretation that emerged from keynote and oral presentations included (1) examining the effects of cannabis when used in persons who have mental health conditions, particularly post-traumatic stress disorder (PTSD), (2) translation of basic science research findings into clinically actionable evidence, and (3) identifying and quantifying problematic cannabis use, whether in the general population or where specific safety

risks are present. Examples of research presented at CCORC that are in alignment with these themes are described in the three sections below.

Effects of Cannabis when Used with Mental Health Conditions

One keynote speaker, Dr. Matthew Hill of the University of Calgary, presented research that set the stage in this area of evaluating cannabis as a potential therapeutic in mental health conditions. Dr. Hill's presentation explored the state of the science about potential therapeutic applications of cannabis and cannabinoids for symptoms that occur specifically in PTSD and symptoms thereof, including sleep. His team's work on endogenous endocannabinoid signaling as well as evaluation of therapeutic use of cannabis in PTSD has spanned preclinical and clinical research, with most recent evidence indicating that there could be a role for cannabis or cannabis-containing products in the treatment of PTSD [6, 7]; however, high-quality, definitive, research indicating clinical risk-benefit remains elusive [8, 9].

Other research presented at CCORC related to evaluation of risk benefit of cannabis use where mental health conditions or symptoms were assessed in the context of safety. For example, a presentation showcasing findings from the ongoing Herbal Heart Study indicated that young adults with subclinical cardiovascular risks reported symptoms of depression and anxiety, among other mental health concerns, more frequently when using cannabis, than similar peers that did not report using cannabis. Another presenter shared findings from a study that investigated contextual learning ability in people that used cannabis and also had PTSD, where it was reported that "heavy" cannabis use was associated with lower contextual learning as indicated via the Mnemonic Similarity Task.

Translation of Basic Science Research Findings into Clinically Actionable Evidence

Another theme consistently addressed in research presented at the 2024 CCORC was the translation of basic science research findings into clinically actionable evidence. A keynote speaker presenting several studies that exemplified this theme was Dr. Ryan Vandrey of Johns Hopkins University. Dr. Vandrey's presentation showcased recent work that quantified discrepancies in cannabinoid doses as compared with dose and product content information printed on cannabis product labels [10] and then built upon several examples from his team's work that demonstrates the significant variation in cannabis pharmacokinetic profiles based on THC or CBD concentration as well as route of administration, all of which have significant implications for

how a cannabis or cannabinoid would be dosed in clinical trials (and in practice) [11, 12]. These data indicate that we still need to answer important clinical questions about the effects of use of CBD in addition to THC when cannabis is trialed for therapeutic purposes.

Other research presented in alignment with this theme showcased findings from a study that examined pharmacokinetic interactions between oxycodone and CBD in the brain as well as in blood plasma, where it was reported that CBD co-administration with oxycodone was observed to potentiate oxycodone analgesia but not necessarily the rewarding effects. Another study highlighting translational science with important clinical applications examined the state of the science on exosome delivery of cannabinoids for use in treatments providing symptom relief for cancer patients.

Identifying and Quantifying Problematic Cannabis Use

A third emergent theme focused on identifying and quantifying problematic cannabis use, whether that be in the context of cannabis use disorder (CUD) or when cannabis use, in itself, could be problematic as in certain populations experiencing elevated risks. A keynote presentation by Dr. Margaret Haney of Columbia University highlighted selected findings from her work that has developed and expanded the evidence base on CUD, including what is known regarding withdrawal from cannabis as well as treatment for CUD. Some of Dr. Haney's most recent research includes randomized clinical trials evaluating the effectiveness of pharmacological treatments for CUD [13], as well as investigation of potential pharmacological treatments for specific cannabis withdrawal symptoms [14, 15].

Other research presented in this theme included an investigation of other substances present in toxicology reports of decedents from poisonings, where other substances noted in cannabis users included kratom, opioids, and alcohol. Research presented with implications for this theme involved identifying cannabis use during pregnancy, where differences were noted in cannabis use self-report status by sociodemographic characteristics, which could inform communication tailoring for risk screening in clinical practice.

Opportunities in Cannabis Clinical Outcomes Research

In addition to presentations of primary research findings, CCORC 2024 offered attendees information through symposia about opportunities in cannabis research, including unique data availability for Consortium members.

One such data source available to members is derived from the *Medical Marijuana and Me* (also known as "M3") study, which consists of participant self-reported measures of cannabis use behaviors and experiences, including medical and sociodemographic information, from a cross-sectional cohort of current cannabis users as well as a prospectively enrolled cohort of new cannabis users that were longitudinally followed over a 9-month period. Attendees were provided with an overview of the latest findings on select health conditions from the longitudinal cohort from M3 [16]. In addition to M3 data, the opening of the application process for data sharing for elements from the Medical Marijuana Clinical Outcomes Research Repository (MEMORY) was launched for Consortium members at CCORC 2024. MEMORY is a unique data bank developed by the Consortium that represents detailed information derived from Florida's medical marijuana use registry, including data such as certification and dispensations in the medical marijuana use program, as linked with other data sources such as birth and death certificates as well as Medicaid administrative billing claims [17]. The MEMORY data represent over 1 million unique individuals that have been certified for medical marijuana use in Florida. These data allow for longitudinal assessment of health outcomes as well as opportunities for investigating real-world use patterns and safety outcomes associated with medical marijuana in a large, diverse population.

An overarching point of discussion that echoed throughout presentations and symposia conducted at CCORC was uncertainty regarding the future of cannabis clinical outcomes research in the face of upcoming changes in the US regulatory environment. The recent decision to classify cannabis as a schedule III controlled substance in the US may have wide-ranging implications for cannabis clinical outcomes research as researchers may potentially benefit from more favorable regulatory conditions that could serve to incentivize high-quality research. As regulatory frameworks continue to develop for cannabis and cannabinoids, it is important that clinical risk benefit is rigorously evaluated before cannabis is trialed as a therapeutic for new conditions or symptoms in which risk benefit is not already established. CCORC will continue to operate as a venue to facilitate and disseminate research that evaluates effectiveness and safety of cannabis use.

Conclusion

The fourth annual CCORC encouraged collaboration in research and facilitated thoughtful discussion of research findings among key research and clinician

stakeholders in both Consortium-affiliated communities and beyond. Resources to further promote and facilitate cannabis clinical outcomes research were shared with attendees during the event, which included a novel data repository of medical cannabis program registrant dispensing data, as well as a prospectively enrolled cohort of new and current medical cannabis users who were comprehensively surveyed on use behaviors and clinical characteristics. Experts presenting keynote addresses emphasized the importance of filling evidence gaps on cannabis use measurement, as well as effectiveness and safety in mental health applications, such as PTSD and CUD. The conference also provided a vehicle for disseminating the latest research on cannabis therapeutic potential as well as safety concerns in several conditions where cannabinoids are trialed. The fifth annual CCORC will be held in summer 2025 in Florida, USA, and the conference Website will post updates regarding program developments.

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Conflict of Interest Statement

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Author Contributions

Concept and design, administrative, technical, or material support, and supervision: A.J.G. and A.G.W. Acquisition, analysis, or interpretation of data and critical revision of the manuscript for important intellectual content: A.J.G., J.J., M.M.H., R.L.C., Y.W., and A.G.W. Drafting of the manuscript: A.J.G. Obtained funding: R.L.C. and A.G.W.

Data Availability Statement

Data were not collected to inform this meeting report. All accepted abstracts that were presented at this meeting are included in the abstract supplement.

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