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Meeting Report

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Proceedings of the 2022 Cannabis Clinical Outcomes Research Conference

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Abstract
The Consortium for Medical Marijuana Clinical Outcomes Research, a multi-university collaboration established by the state of Florida in the USA, hosted its second annual Cannabis Clinical Outcomes Research Conference (CCORC) in May 2022. CCORC was held as a hybrid conference, with a scientific program consisting of in-person and virtual sessions. CCORC fostered and disseminated current research on clinical outcomes of medical marijuana while stimulating collaboration and engagement between the scientific community, policymakers, industry representatives, clinicians, and other interested stakeholders. Three themes emerged from conference sessions and speakers: (1) disentangling research findings comparing use and outcomes of medical and nonmedical cannabis, (2) addressing barriers and promoting facilitators for clinical cannabis research, and (3) resolving uncertainties around cannabis dosing. The third annual CCORC is planned for the summer of 2023 in Florida, USA.

Introduction

Currently, some form of cannabis is legal in all but three states in the USA [1]. Florida approved cannabis, referred to as medical marijuana in the state legislation, for persons with qualifying conditions in 2016, and there are over 700,000 registrants in this state's medical marijuana program as of 2022. Given the limited data on the safety and effectiveness of medical marijuana, the Florida State legislature established the Consortium for Medical Marijuana Clinical Outcomes Research to conduct, disseminate, and support scientific research on clinical outcomes. These Consortium goals are achieved through the development of research infrastructure and support, evidence synthesis and dissemination, a grants program, a research data repository, and a community outreach program [2]. The Cannabis Clinical Outcomes Research Conference (CCORC) aligns with the Consortium's mission to increase research engagement, promote collaboration, and disseminate findings.

Conference Format

CCORC 2022 was held in a hybrid format (for more information, see www.ccorc.mmjoutcomes.org) on May 19th and 20th in Lake Nona-Orlando, FL, USA. The 2nd

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annual CCORC expanded upon the research agenda presented from the 1st CCORC in 2021 [3], to fulfill three main objectives: (1) disseminating research investigating medical cannabis use, efficacy, safety, and other relevant outcomes, (2) providing a venue for clinical and research educational opportunities related to medical cannabis, (3) fostering research collaboration and stakeholder engagement among Consortium member institutions and beyond.

The 2022 CCORC program included three keynote presentations, six oral presentations from top-scoring abstract submissions, panel discussions, two methods workshops, and a poster session featuring twenty-six research abstracts selected following peer review. Keynote presentations were recorded and are available on the conference website, as are digital versions of posters.

These presentations will be available online to registrants until December 2022. Accepted abstracts are included in this issue of *Medical Cannabis and Cannabinoids*. CCORC 2022 had over 120 registrants, including 30 students and 25 virtual attendees. Registrants included researchers, students, clinicians, government officials, and industry from Florida and around the globe. Registrants were able to earn Continuing Medical Education (CME) or Continuing Pharmacy Education (CPE) credits for attending components of the scientific program. Three main themes on clinical cannabis research conduct and interpretation emerged throughout the conference: (1) disentangling research findings comparing medical and nonmedical cannabis use, (2) addressing barriers and promoting facilitators for clinical cannabis research conduct, and (3) resolving uncertainties around cannabis dosing.

Disentangling Research Findings Comparing Medical and Nonmedical Cannabis Use and Outcomes

Given the rapidly changing laws regarding medical cannabis use, it is a research priority to understand the characteristics of medical versus nonmedical cannabis users, the clinical outcomes associated with each considering the various indications and reasons for use, and the implications and generalizability of research findings examining one or the other. Dr. Kent Hutchison (University of Colorado-Boulder), a keynote speaker at the conference, emphasized that research questions for cannabis regardless of medical or nonmedical use should be reframed to focus on the risk-benefit rather than solely on the harm. He noted that we are still in the early stages of understanding medical cannabis use and its safety and effectiveness. Dr. Staci Gruber (Harvard Medical School), another keynote speaker, further discussed the differences in use patterns and observed clinical outcomes between medical and nonmedical cannabis users. Nuanced motives for use are associated with differences in exposure to cannabis and cannabinoids and, ultimately, differences in clinical outcomes. One example of this distinction was illustrated by Dr. Karina Villalba's (University of Central Florida) oral presentation describing young adult cannabis users in Florida, where she emphasized that "we are at the starting point of understanding what a typical [medical] cannabis user looks like." Access to medical cannabis may also play a role in defining medical and nonmedical users within Florida. Dr. Amie Goodin (University of Florida) presented that up to one-fourth of Florida counties have no certified cannabis-authorizing clinicians and half have no cannabis dispensaries, resulting in pronounced disparities in access across the state. Speakers agreed that inferences from early cannabis research that focused on nonmedical use and safety outcomes may have limited value for the assessment of medical marijuana risk-benefit for the various clinical indications. Importantly, even if evidence for certain indications such as pain is growing, such findings may have limited generalizability to patients with other indications, resulting in a vast research agenda to create such evidence.

Barriers and Facilitators for Conducting Clinical Cannabis Research

Dr. Samer Narouze (Ohio State University), a keynote speaker, emphasized the paucity of translational research and various shortcomings with available evidence including a lack of consistency in the definition of clinical outcomes, sample size constraints, and difficulties with blinding and other methodological issues imposing potential bias, resulting in inconsistencies in the findings of meta-analyses attempting to summarize evidence to guide clinical recommendations for cannabis use. Throughout the conference, researchers and clinicians discussed barriers to conducting clinical cannabis research. These barriers included measurement and data collection issues, regulatory and institutional challenges such as navigating institutional review board regulations, and the investigational new drug approval process for clinical trials. During a panel discussion organized and moderated by Dr. Robert Cook (University of Florida), Sheila Austin (a regulatory compliance official at the Uni-

versity of Florida), Dr. Paul Borsa (a sports medicine researcher at the University of Florida), and Dr. Anthony Ferrari (the chief scientific officer of Sunmed) shared details regarding their efforts to conduct clinical cannabis research. The panel discussed their specific experience in preparing to conduct a clinical trial to examine the effect of cannabidiol (CBD) on recovery after injury in a population of adults, and the regulatory requirements to be met prior to study implementation were significant. The CBD formulation was deemed to require designation as an investigational new drug for the context of this research purpose. The team shared their experience with jointly navigating the investigational new drug process in conjunction with coordinating challenging regulatory requirements with the local IRB and other agencies. This team successfully developed and implemented the trial, and their experience provided a unique opportunity to illustrate how collaboration between these individuals and organizations at the initial phases of study protocol development helped overcome some of the existing barriers and facilitated the research process for this trial.

The conference also highlighted activities, tools, and infrastructure offered by the Consortium to help facilitate conducting cannabis clinical research. One such tool, the Connect and Advance Research for Medical Marijuana Analysis (CARMMA) database, fosters collaboration among connecting researchers, clinicians, and industry representatives. The Consortium also maintains protocols for clinical research that can be shared with researchers. These protocols allow for improved data collection and measurement standardization in cannabis research and represent valuable resources for new researchers. Despite these efforts, there was consensus that the single most critical facilitator of cannabis research would be removal of the regulatory barriers inherent in the classification of cannabis as a Schedule I controlled substance in the USA.

Resolving Uncertainties around Cannabis Dosing

A final theme that emerged throughout conference presentations and discussion was the lack of standardization and absence of guidelines for cannabis dosing for most clinical conditions and patient populations. There is significant variability among doses employed within clinical trials for cannabis and cannabinoid products, even in trials examining the same condition. Noteworthy, trials commonly use lower doses than reflected in medical marijuana certifications and products with lower THC-CBD ratios than typically available to consumers in dispensaries. Medical marijuana dispensaries in Florida provide information on cannabis product types (e.g., routes of administration, THC/CBD concentrations), but limited guidance on dosing. Dosing recommendations for specific product types and dosing for individual patients typically fall on the clinician, but currently, there is little evidence to guide dosing recommendations. Clinicians, therefore, rely on experience from other clinicians or experiences from their patients to determine dosing regimens for each patient [4]. Clinicians and researchers would both benefit from dosing standardization to identify effective initiating doses for different indications [5]. One consensus document suggests a global cannabis unit of 5 mg THC to standardize doses for all products based on experimental data comparing delivery of THC via different routes of cannabis or cannabis-derived product administration without consideration for delivery of other physiologically active compounds contained within cannabis [6]. The National Institute of Drug Abuse (NIDA) also recommends 5 mg of THC as a standard measurement unit for research purposes [7]. Both of these recommendations isolate THC regardless of the cannabis product and do not account for CBD or other physiologically active compounds in their "standard unit". Despite this limitation, if adopted, this type of standardized unit could be used for clinical dosing and research and may ultimately improve clinical communications that could promote safety. These consensus documents for a standard cannabis dosing unit have not yet been widely implemented for clinical applications, however, and CCORC presenters and attendees agreed that further examination of the clinical utility of a standardized dosing unit is warranted.

Conclusion

CCORC 2022 encouraged collaboration and thoughtful discussion among researchers, clinicians, and industry representatives. Several resources to promote and facilitate cannabis clinical outcomes research were identified and shared with attendees during the event. Enhanced evidence on cannabis effectiveness and safety, considering specific indications as well as dose and route, remains the highest priority for the medical marijuana research agenda. The conference also provided a vehicle for disseminating the latest research on cannabis and cannabinoid therapeutic potential and safety concerns in treating several medical and psychiatric conditions. The third annual CCORC is planned for summer 2023 in Florida, USA.

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Conflict of Interest Statement

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Author Contributions

Concept and design; administrative, technical, or material support; and supervision: Goodin and Winterstein. Acquisition, analysis, or interpretation of data and critical revision of the manuscript for important intellectual content: all authors. Drafting of the manuscript: Smolinski, Goodin, and Sajdeya. Obtained funding: Cook and Winterstein.

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