2019

A Systematic Review of Medical Students' and Professionals' Attitudes and Knowledge regarding Medical Cannabis as a Proxy for Forecasting Trends in the Medical Community's Acceptance of Therapeutic Hallucinogens

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A Thesis Presented

By

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To the Keck Science Department

Of Claremont McKenna, Pitzer, and Scripps Colleges

In partial fulfillment of

The degree of Bachelor of Arts

Senior Thesis in Human Biology

December 9th, 2019

Contents:

Abstract ..... p. 3
Introduction ..... p. 5
Methods ..... p. 11
Results ..... p. 22
Discussion ..... p. 33
Conclusion ..... p. 42
References ..... p. 43

Abstract

Background: In recent years, the renewed global interest in both hallucinogens' and cannabis' therapeutic properties has resulted in shifting attitudes and legislative policies worldwide. The aim of this systematic review is to explore the existing literature on medical professionals' and students' attitudes and knowledge regarding medicinal cannabis (MC) to assess any relevant and significant trends which may forecast analogous trends in the nascent clinical acceptance of hallucinogens.

Methods: Using Google Scholar and PubMed, a literature search was performed to identify studies pertaining to healthcare professionals' and medical students' knowledge and attitudes regarding MC. This systematic search yielded 43 studies published between 1971 and 2019; inclusion criteria included the following: 1) the studies were complete and not simply abstracts or systematic reviews; 2) they provided relevant data regarding respondents' knowledge and attitudes regarding MC; 3) they were published in English and originated in a country with a healthcare system and legislative policies comparable to that of the USA; and 4) they contained medical professional (or student) respondents only; or, if the respondents included mixed groups, the study segregated and sorted data based on one's status as a medical professional or non-medical professional. Studies were then coded according to the following five guiding research questions: 1) Do respondents believe that cannabis should be legalized for medicinal purposes, and have these opinions changed significantly over time?; 2) Are respondents confident in their level of knowledge regarding cannabis' health effects and clinical applications?; 3) Are respondents adequately convinced of cannabis' therapeutic potential? What are respondents' main concerns regarding the

incorporation of cannabis into the medical system?; 4) What current gaps in knowledge exist, and how can the medical community become better informed about the therapeutic uses of cannabis?; and 5) Are there significant differences between the knowledge and opinions of healthcare students' versus healthcare professionals' with respect to any of the aforementioned research questions?

Results: At a multi-national level (from 1990 to present), both medical students' and professionals' support for the legalization of MC has significantly increased ($r(19) = .44$, $p = .045$). Moreover, medical professionals favor the legalization of MC at a significantly higher rate than students (52% vs. 42%, respectively; χ^2 (1, $N = 9019$) = 50.72 $p < .001$). Furthermore, an assessment of both respondents' desire for more educational material on MC and respondents' concerns regarding MC's potential to cause dependence and addiction showed a ceiling effect, with respondents consistently reporting high levels of desire for more educational material and a high level of concern regarding MC's addictive potential, but with no significant changes over time ($r(13) = -.10$, $p = .713$ & $r(11) = -.13$, $p = .673$, respectively).

Discussion: This systematic review yielded several statistically-significant trends pertaining to healthcare professionals' and medical students' knowledge and attitudes about MC. As MC use and legalization continues to proliferate internationally, further studies are needed to elucidate complex sociocultural barriers to the acceptance of MC, which are likely to be closely correlated with barriers to the clinical acceptance of therapeutic hallucinogens. Limitations, cross-cultural mechanisms, clinical implications, and recommendations for future research are discussed.

Introduction:

Hallucinogens are a broad class of pharmacological compounds which reliably and temporarily induce profound sensory distortions and shifts in cognition. The three main families of hallucinogenic drugs are: serotonergic (i.e. "classical") psychedelics, such as psilocybin (the main psychoactive compound in hallucinogenic mushrooms), LSD, MDMA, and DMT (the active ingredient in the shamanic, Amazonian brew *ayahuasca*); dissociative anesthetics, e.g. ketamine, PCP, and dextromethorphan (DXM); and deliriants, which are principally found in members of the *Solanaceae* (nightshade) family of plants. Additionally, some researchers consider cannabis and its derivatives medicinal hallucinogens, and ethnographic anthropological research has also demonstrated that the ingestion of certain animals and their associated products (i.e. venom, glandular secretions, etc.) have been used by various indigenous cultures as a form of ritualistic hallucinogen use (Groark, 1996).

The western medical community started appropriating hallucinogens as a powerful psychiatric tool in the early 20th century, as advances in chemistry allowed for the extraction and chemical isolation of these compounds from their organic sources. Initially, western clinicians were bewildered by the profound psychoactive effects of hallucinogens, and consequently labeled them "psychotomimetics"– substances which can reliably replicate psychosis and other abnormal psychological states (Mangini, 1998). Continued research also revealed that these compounds produced "a lowering of inhibitions in patients undergoing psychoanalysis," leading to "particularly vivid and intense awareness of personality problems" (Rochester & Kirchner, 1999; Mangini, 1998). Clinicians soon realized that hallucinogens could have widespread psychiatric applications in the treatment of various

personality, mood, and behavioral disorders. Throughout the mid 20th century, psychiatrists adapted hallucinogen-based therapies to treat a variety of conditions, including: addiction, (treatment-resistant) depression, anxiety associated with terminal illness, and post-traumatic stress disorder (PTSD) (Byock, 2018). Despite researchers' extensive findings supporting the general safety and efficacy of hallucinogen-assisted psychotherapies, international legislation swiftly imposed a sweeping prohibition on all hallucinogen possession, use, and research in 1971 after reports surfaced of widespread unethical research practices amongst a large subset of clinicians. Moreover, the international geopolitical and social atmosphere at the time reflected a strong schism between conservative values and progressive ideals, and many right-leaning politicians worried that the proliferation of hallucinogens would further disrupt the global geopolitical order. Consequently, biomedical research into hallucinogens stalled for the remainder of the 20th century, and only recently have investigators begun petitioning governments for permits to resume studies.

In several cases in various countries, exemptions have been made for the use of psychedelics as part of religious practices. In 1993, the Unites States passed official legislation stating that drug laws may be trumped by the right to freely practice religion, in accordance with the Religious Freedom Restoration Act (Elsey, 2017). Nevertheless, legal interpretation over what constitutes "religious practices" continues to limit citizens' access to hallucinogens (Labate & Feeney, 2012). As of May 2019, the city of Denver, Colorado became the first American municipality to decriminalize adult recreational use of psilocybin (Foody, 2019). However, as some governments move toward deregulation and renewed

scientific research, others continue to enact strongly oppositional legislation, highlighting the current ignorance, confusion, and misinformation still enshrouding hallucinogens. To combat the growing "research chemical" phenomenon, whereby clandestine chemists synthesize novel chemical analogs of regulated hallucinogens to evade legal prosecution, the UK parliament passed the Psychoactive Substances Act in 2016, designed to stop the proliferation of these novel compounds (Elsey, 2017). Most notably, the bill levies a strict prohibition on all hallucinogenic-derivatives and sidesteps the need to demonstrate any potential for harm, which further hampers researchers' ability to reopen investigations into the therapeutic potential of hallucinogens.

The United States Drug Enforcement Administration (DEA) currently sorts drugs, substances, and certain chemicals used to make drugs into five distinct categories—i.e. schedules—depending upon the drug's acceptable medical use and the drug's abuse or dependency potential (Drug Enforcement Administration [DEA], n.d.). Although investigations into Schedule 1 (the most restrictive classification, asserting that the substance has no accepted medical use) hallucinogens (primarily the serotonergic, psychedelic class) remain severely limited in the US, researchers have made use of somewhat atypical hallucinogens that fall into less stringent schedules. Ketamine—a dissociative hallucinogen—is currently listed under the Schedule III category due to its principal use as a general anesthetic at high doses. Researchers who recognized its latent psychiatric benefits began conducting off-label trials in patients suffering from severe treatment-resistant depression (TRD). As a result, the FDA recently has approved limited clinical trials of ketamine for TRD, and the Russian government has also extensively

supported the use of ketamine to treat various addiction-related disorders (Winkelman & Roberts, 2007). FDA-approved studies of ketamine have now reached Phase IV– meaning multicenter, randomized, double-blind investigations involving thousands of participants are now underway (Winkelman & Roberts, 2007).

The history of cannabis in medicine is highly analogous to that of classical hallucinogens. Archaeological inquiry has revealed that cannabis use has been prevalent in human society for at least five millennia, and it was even widely used as a medical therapy in the United States in the 19th and early 20th centuries; in fact, it was first included in the *United States Pharmacopoeia* in 1850 (Bridgeman & Abazia, 2017). The first federal restrictions on cannabis occurred in 1937, with the passage of the Marihuana Tax Act, which heavily regulated its sale and usage. Subsequently, cannabis was dropped from the *United States Pharmacopoeia* in 1942, and legal penalties for its possession increased in 1951 and 1956 with the enactment of the Boggs and Narcotic Control Acts, respectively. Finally, the Controlled Substances Act of 1970 relegated cannabis to schedule I status at the federal level, imposing limitations on research by restricting the procurement of cannabis for academic purposes (Bridgeman & Abazia, 2017). Moreover, cannabis remains illegal under international law, as outlined in the United Nations' Single Convention on Narcotic Drugs (1961), which places cannabis and its derivative products in Class IV – the most restrictive category, analogous to the DEA's Schedule I designation.

Notwithstanding, 33 U.S. states and several dozen nations across the globe have passed laws permitting the renewed medicinal use of cannabis in recent years and decades (Hanson & Garcia, 2019; Bifulco & Pisanti, 2015). Therefore, an assessment of the ongoing

trends surrounding the reintegration of cannabis into accepted medical practice provides insight into how the medical community may reinvestigate formerly prohibited and stigmatized therapies– including hallucinogens. Fortunately, dozens of studies regarding clinicians', patients', medical students', and public health professionals' attitudes and knowledge regarding medicinal cannabis (MC) have been published in recent decades. Several of these studies predate the first legislative bill legalizing medicinal cannabis in California (in 1996), and many studies were conducted between 1996 and 2019– when 32 other states and several countries—including Canada, Australia, and Israel—legalized cannabis for therapeutic purposes (Bridgeman & Abazia, 2017; Hanson & Garcia, 2019; Fischer, Kuganeson, & Room, 2014; Thomsen, 2016; Kloosterman, Blum, Leichman, & Barak, 2015). Data from these studies can be analyzed along several categorical and temporal parameters to elucidate specific trends regarding the medical community's overall attitudes and opinions regarding the clinical reintroduction of MC, which helps reveal ways in which the medical community can improve its acceptance of novel hallucinogenic therapies in the future. When assessing the content of these studies, some central, guiding research questions included the following:

1. Do healthcare students and professionals believe that cannabis should be legalized for medicinal purposes? Have these opinions changed significantly over time?
2. Are healthcare students and professionals confident in their level of knowledge regarding cannabis' health effects and clinical applications?
3. Are healthcare students and professionals adequately convinced of cannabis' therapeutic utility? What are healthcare professionals' main concerns regarding the incorporation of cannabis into the medical system?
4. What current gaps in knowledge exist, and how can the medical community become better informed about the therapeutic uses of cannabis?

5. Are there significant differences between the knowledge and opinions of healthcare students' versus healthcare professionals' with respect to any of the aforementioned research questions?

Initially, several hypotheses were developed in accordance with the guiding research questions. Question 1 assessed respondents' support for the legalization of MC. It was expected that support for the legalization of MC would increase over time due to ongoing sociocultural and legislative trends favoring legalization, which may serve to reduce stigma and increase the normalization of cannabis within the medical community. Question 5 assessed differences between medical students and medical professionals regarding their knowledge and opinions of MC– a consideration which applies to all the guiding research questions. It was expected that students would demonstrate greater support for the legalization of MC than medical professionals, given the premise that many medical professionals may have been educated during an era in which cannabis was largely demonized within society and the medical community, and the established research finding that (at least within the United States) younger individuals are adopting more permissive views towards marijuana (Schmidt, Jacobs, & Spetz, 2016). With respect to research question 2, which assesed respondents' self-reported confidence regarding their knowledge of MC, it was hypothesized that confidence levels would rise as the number of years following MC legalization in the country of a study's publication increased, due to respondents' from those countries having an increased likelihood of being exposed to cannabis in clinical settings. Moreover, it was expected that professionals (as opposed to students) would express greater confidence in their knowledge of MC, given their more extensive medical training and clinical experience. Question 3 investigated respondents'

belief in cannabis' medical utility. It was hypothesized that respondents' from more recently published studies would espouse greater faith in cannabis' medical utility due to the ongoing proliferation of cannabis within diverse clinical settings. Additionally, it was predicted that students would express greater faith in cannabis' medical utility under the premise that students (being younger, on average, than professionals) would be more likely to have been raised in a sociopolitical climate more accepting of cannabis' medical applications. Finally, with respect to research question 4, which assessed current gaps in knowledge and ways to improve knowledge of MC within the medical community, it was expected that respondents from more recent studies would express an increased desire for further education, given the heightened acceptance of cannabis as a legitimate medical therapy in recent years. In light of the parallel legislative hurdles and cultural stigmatization surrounding both cannabis and hallucinogens, this systematic review will provide an important framework for better understanding how the medical community can work to overcome sociocultural obstacles which impede the acceptance of potentially groundbreaking therapies.

Methods:

Using both Google Scholar and PubMed, a literature search was performed to identify studies pertaining to healthcare students' and professionals' knowledge and attitudes regarding therapeutic and non-therapeutic uses of cannabis. Studies which solicited the opinions of M.D.'s, R.N.'s P.A.'s, Pharm.D.'s, and medical and pharmacy students were all included in the search. Most inquiries utilized relevant keywords, such as:

"attitudes on medical marijuana" and "physicians' perspectives on cannabis," etc. Additionally, when viewing a study on PubMed and Google Scholar, both databases provide the researcher with extensive lists of related studies– helping to augment the simple keyword search protocol.

The literature search only included English-language papers, and generally focused on studies originating in the United States. However, the search eventually expanded to include international studies from countries with generally similar healthcare systems and legislative policies towards (medicinal) cannabis– including Ireland, Canada, Israel, Serbia, and Australia. While some of these nations slightly differ from the United States in terms of their national healthcare systems and legislative policies toward cannabis, it was determined that the value gained from including global perspectives on this issue was at a sufficiently low cost to the validity of the comparisons drawn. Studies met criteria for inclusion if they satisfied all of the following requirements: 1) they were complete studies and not simply abstracts or systematic reviews; 2) they provided relevant data regarding one or more of the aforementioned guiding research questions; 3) they were published in English and originated in a country with a healthcare system and legislative policies (towards [medicinal] cannabis) comparable to that of the United States; and 4) they contained medical professional (or student) respondents only; or, if the respondents included mixed groups with non-medical professionals, the study segregated and sorted data based on one's status as a medical professional or non-medical professional. Studies were excluded from further analysis if they failed to meet any one of these four specified

requirements. Overall, 43 studies were identified as meeting all the necessary criteria for inclusion.

Data from studies which met all four inclusion criteria were subsequently incorporated into a master spreadsheet, which included the following: last name of the first author listed on the study; year and country of publication; total number of participants included in the study; the type(s) of participants featured in the study (i.e. oncologists, RN's, etc., and the number of each type of participant if several were included in the same study); mean age of the study cohort; percent breakdown of participants by gender; percentage of participants who reported a Caucasian ethnicity; and mean number of years in practice for the study cohort. While sorting through papers to extract data pertaining to the four aforementioned guiding research questions, it became apparent that while most papers addressed similar topics, they often phrased their questions in slightly different ways. For example, Chan, Knoepke, Cole, McKinnon, and Matlock (2016) asked respondents to either agree or disagree with the following statement: "physicians should recommend marijuana as medical therapy," whereas other researchers, such as Ananth et al. (2018) asked respondents to state whether or not they—as physicians—would be willing to prescribe marijuana to a patient. Though these questions may not be exactly analogous, they both address the question of whether or not physicians should be allowed to authorize MC. Therefore, it was determined that both questions could be analyzed under the same category: in this instance, both were filed under research question 1: "Do healthcare professionals believe that cannabis should be legalized for medicinal purposes?" Similar judgment calls were made in numerous other instances when the phraseology of certain

studies did not directly align with the phraseology used in the spreadsheet. Throughout the collection process, data pertaining to the five guiding research questions were further subdivided into seven specific research questions; a full layout of the phraseological sorting process—in accordance with the seven derived research questions tabulated in the master spreadsheet—is provided below:

Analysis and sorting by research question phraseology:

- Research question 1: Do you believe that physicians deserve the legal right to prescribe cannabis to patients? (i.e. Do you believe that cannabis should be legalized for therapeutic purposes?)

  Qualified survey questions included the following phrases:
  - “Doctors should be able to legally prescribe marijuana as medical therapy” (Charuvastra, Friedmann, & Stein, 2008 and Philpot, Ebbert, & Hurt, 2019).
  - "Doctors should recommend medical marijuana (MMJ; as medical therapy)?" (Chan et al., 2017 and Kondrad & Reid, 2013).
  - "Marijuana should be made available by prescription” (Doblin & Kleiman, 1991; Schwartz, Voth, & Sheridan, 1997; Uritsky, McPherson, & Pradel, 2011; and Karanges, Suraev, Elias, Manocha, & McGregor, 2018).
  - "Cannabis should be legalized/available for medicinal purposes” (Norberg et al., 2012; Mathern, Beninsig, & Nehlig, 2014; Sideris et al., 2018; Bega, Simuni, Okun, Chen & Schmidt, 2016; and Crowley, Collins, Delargy, Laird & Van Hout, 2017).
  - "Clinicians should be able to authorize MC without fear of legal action" (Carlini, Garrett & Carter, 2015).
  - "MMJ should be legalized in all states" (Moeller & Woods, 2015).
  - "Specialist physicians should have authority to prescribe CTP” (Ziemianski et al., 2015 and Balneaves, Alraja, Ziemianski, McCuaig & Ware, 2018).
  - "The use of CTP should be legalized/approved in Serbia” (Kusturica, Tomas, Sabo, Tomic & Horvat, 2019 and Stojanovic et al., 2017).
  - "MD's should play a role in MMJ authorization” (Ebert et al., 2015).
  - "MJ should be legalized provided it is under medical supervision” (Burke & Marx, 1971).
  - “There should be some form of legalized marijuana use" (Lieff et al., 1973).

- "Are you willing to help patients access MMJ?" (Ananth et al., 2018).

- Research question 2: Do you feel confident in your level of knowledge regarding the health effects of cannabis?

  Qualified survey questions included the following phrases:
  - "Do you feel confident in your ability to prescribe marijuana, or would you require more knowledge before prescribing?" (Doblin & Kleiman, 1991).
  - "Self-reported knowledge of cannabis" (reported on a 1-5 Likert scale; responses of 3, 4, or 5 [acceptable, strong, and very strong knowledge, respectively] were approved and consolidated for analyses reporting "confidence in knowledge of medicinal cannabis") (Norberg et al., 2012).
  - "Self-reported knowledge of MMJ efficacy" (1-5 Likert scale; responses of 4 or 5 [strong and very strong knowledge, respectively] were approved and consolidated for analyses reporting "confidence in knowledge of medicinal cannabis") (Ricco, Danner, Pereira & Philbrick, 2017).
  - "How much knowledge do you have about medical marijuana?" (6 categories: very little knowledge, some knowledge, moderate knowledge, substantial knowledge, high level of knowledge, and professional level of knowledge; "substantial knowledge," "high level of knowledge," and "professional level of knowledge" were approved and consolidated for analyses reporting "confidence in knowledge of medicinal cannabis") (Szyliowicz & Hilsenrath, 2019).
  - "Do you feel adequately prepared to answer patients' questions about MMJ?" (Philpot et al., 2019).
  - "Do you consider yourself well-informed about the endocannabinoid system?" (Sideris et al., 2018).
  - "Do you consider yourself knowledgeable about MMJ therapy?" (Michalec, Rapp & Whittle, 2015 and Mitchell, Gould, LeBlanc & Manuel, 2016).
  - "Confidence in discussing risks and benefits of medical cannabis" (4 categories: very confident; somewhat confident; somewhat not confident, not at all confident; "very confident" and "somewhat confident" responses were approved and consolidated for analyses reporting "confidence in knowledge of medicinal cannabis") (Zylla, Steele, Eklund, Mettner & Arneson, 2018).
  - "I have good knowledge around the (side) effects of medicinal cannabis" (Karanges et al., 2018 and Kusturica et al., 2019).
  - "I know how to talk to providers about the risks and benefits of MMJ use" ("confident" and "somewhat confident" responses were approved and

consolidated for analyses reporting “confidence in knowledge of medicinal cannabis”) (Caligiuri, Ulrich & Welter, 2018).

- “Do you feel sufficiently knowledgeable to make recommendations regarding MMJ?" (Braun et al., 2018).
- “Self-reported competency in MMJ pharmacology” (1-7 Likert scale; responses of 5-7 [good, very good, and excellent, respectively] were approved and consolidated for analyses reporting “confidence in knowledge of medicinal cannabis”) (Hwang, Arneson & St. Peter, 2016).
- "Do you feel confident regarding your current knowledge of [cannabinoids]? (responses of “confident” and “somewhat confident” were approved and consolidated for analyses reporting “confidence in knowledge of medicinal cannabis”) (Fitzcharles et al., 2014 and Ablin, Elkayam & Fitzcharles, 2016).
- “Knowledge of pharmacology and indications" (responses indicating a “medium-high” or “high” level of knowledge were approved and consolidated for analyses reporting “confidence in knowledge of medicinal cannabis”) (Ebert et al., 2015)
- "How would you rate your knowledge on the systemic effects of cannabis?” (Crosby, 2018).
- “Rate your knowledge on factual information regarding marijuana" (responses indicating “moderate” and “high” levels of knowledge were approved and consolidated for analyses reporting “confidence in knowledge of medicinal cannabis”) (Burke & Marx, 1971).

- Research question 3: Do you believe that cannabis has any therapeutic utility?

  Qualified survey questions included the following phrases:

  - “If marijuana were legally available, I would recommend the use of marijuana to a patient” (filed under the survey subscale “belief that marijuana has medical benefits”) (Chan et al., 2017).
  - “Marijuana helps patients who suffer from chronic, debilitating medical conditions” (Ebert et al., 2015; Carlini et al., 2015; and Kondrad & Reid, 2013).
  - “Do you believe that MMJ can help prevent nausea and vomiting (in patients receiving chemotherapy or radiation)?” (Luba, Earleywine, Farmer & Slavin, 2018; Braun et al., 2018; and Doblin & Kleiman, 1991).
  - “Do you approve of using MMJ to help manage patients’ symptoms?” (Ananth et al., 2018).
  - “Do you think MMJ has medical benefits/efficacy?” (Uritsky et al., 2011; Mitchell et al., 2016; and Szyliowicz & Hilsenrath, 2019).

- "Do you believe legalization [of cannabis] would be medically efficacious?" (Cogswell & Harris, 2015).
- "Do you believe that MC is a legitimate medical therapy?" (Philpot et al., 2019).
- "Do you recognize MMJ as an oncological therapy?" (Moeller & Woods, 2015).
- "Do you have a patient who you agree would benefit from medical cannabis?" (Karanges et al., 2018).
- "To what extent do you think medical marijuana is a useful adjunct to standard treatments for pain?" (Braun et al., 2018).
- "Are you certain about MMJ's therapeutic value?" (Ziemianski et al., 2015 and Balneaves et al., 2018).
- "Cannabis has a role in palliative care" (Crowley et al., 2017).
- "Assess your concern regarding the limited evidence of therapeutic benefits from MMJ" (1-7 Likert scale [1 = least concern, 7 = most concern]; responses of 1-3 were approved and consolidated for analyses reporting "confidence in cannabis' medical efficacy") (Hwang et al., 2016).
- "Do you believe [medical] marijuana/CBD has efficacy in treating (childhood) epilepsy?" (Jacobs, Montebello, Monds & Lintzeris, 2018; Ablin et al., 2016; and Mathern et al., 2015).
- "Do you believe that marijuana has an acceptable role in medicine?" (Martins-Welch, Nouryan, Kline & Modayil, 2017).
- "I am familiar with the possible therapeutic effects of cannabis" (Kusturica et al., 2019).
- "Do you agree that cannabis and its derivatives could potentially have therapeutic effects?" (Stojanovic et al., 2017).

- Research question 4: Do you believe that marijuana should be legalized for recreational use?

  Qualified survey questions included the following phrases:
  - "(Do you believe that) marijuana should be legalized for recreational use?" (Berlekamp, Rao, Patton & Berner, 2019; Schwartz et al., 1997; Moeller & Woods, 2015; Chan et al., 2017; and Kondrad & Reid, 2013).
  - "What legal action should be taken for the possession of marijuana: 1) No legal action; 2) Citation with a fixed fine; 3) Misdemeanor; 4) Felony? (Linn, Yager & Leake, 1989).
  - "Marijuana should be regulated in the same way as alcohol" (Lieff et al., 1973).
  - "Should cannabis be made recreational?" (Bega et al., 2017).

- "Are you in favor of legalizing cannabis for non-medical purposes?" (Ebert et al., 2015).
- "Free access should be granted for the use of marijuana" (Burke & Marx, 1971).
- "All marijuana should be legalized" (Uritsky et al., 2011).

- Research question 5: Do you desire additional education regarding MMJ and/or do believe that education on (medical) cannabis should be made readily available to medical professionals?

  Qualified survey questions included the following phrases:
  - "(More) training about medical marijuana should be incorporated into medical/pharmacy school curriculum" (Caligiuri et al., 2018; Moeller & Woods, 2015; Bega et al., 2017; and Chan et al., 2017).
  - "Continuing medical education (CME) about medical marijuana should be made available to (primary care) physicians" (Carlini et al., 2017; Ebert et al., 2015; and Kondrad & Reid, 2013).
  - "People in my position should receive education about cannabis" (1-5 Likert; responses of "somewhat agree" and "fully agree" were approved and consolidated for analyses reporting "yes" for the stated research question) (Norberg et al., 2012).
  - "Do you feel that more education about marijuana is needed?" (Szyliowicz & Hilsenrath, 2019).
  - "Are you interested in learning more about MC?" (Zylla et al., 2018 and Philpot et al., 2019).
  - "It would be helpful to have additional education about MMJ" (Michalec et al., 2015).
  - "How strong is the need for education on CTP?" (responses reporting a "strong" or "very strong" need were approved and consolidated for analyses reporting "yes" for the stated research question) (Ziemianski et al., 2015 and Balneaves et al., 2018).
  - "Dispensing cannabis in the pharmacy requires additional education" (Stojanovic et al., 2017).

6. Research question 6: [For U.S.-based papers only] Do you believe that the United States should amend cannabis' federal status as a schedule 1 controlled substance (the most restrictive classification, asserting that the substance has no accepted medical use)?

   Qualified survey questions included the following phrases:
   - "Do you favor the Drug Enforcement Agency (DEA) reclassifying marijuana so that it is no longer a schedule 1 drug?" (Bega et al., 2017; Chan et al., 2017; and Kondrad & Reid, 2013).

- "Do you support the rescheduling of marijuana to permit its use in medicine?" (Schwartz et al., 1997 and Doblin & Kleiman, 1991).
- "Cannabis should be rescheduled so that it is no longer a schedule 1 drug with no medical benefits" (Carlini et al., 2017).
- "Do you favor change in (federal) marijuana control?" (Burke & Marx, 1971).

7. Research question 7: Are you concerned about cannabis' dependence/addiction potential?

   Qualified survey questions included the following phrases:
   - "(Do you believe that) marijuana can be addictive (yes/no)?" (Kusturica et al., 2019; Uritsky et al., 2011; Carlini et al., 2017; Chan et al., 2017; and Kondrad & Reid, 2013).
   - "Are you concerned about substance abuse among patients who receive MMJ?" (Ananth et al., 2018).
   - "Are you concerned with MMJ's potential for abuse/misuse/diversion?" (Michalec et al., 2015).
   - "Do you believe / are you concerned that addiction and dependence are potential side effects of MC?" (Stojanovic et al., 2017; Martins-Welch et al., 2017; and Karanges et al., 2018).
   - "On the scale of 1-7 (1 = no concern, 7 = most concern), how concerned are you about the psychoactive effect and potential addiction from cannabis use?" (responses of 5-7 were approved and consolidated for analyses reporting "concern about MMJ's addictive potential") (Hwang et al., 2016).
   - "The risk of addiction/physiological dependence would reduce my willingness to prescribe MMJ (1-5 Likert scale [1 = would not reduce my prescribing, 5 = would greatly reduce my prescribing]; responses of 4 and 5 were approved and consolidated for analyses reporting "concern about MMJ's addictive potential") (Jacobs et al., 2018).

<u>Statistical Analysis:</u>

IBM SPSS version 25 (IBM Corp., Armonk, NY: IBM Corp.) was used to run all statistical analyses. Tests performed included Pearson's *r* bivariate correlations and 2x2 Chi-square (χ^2) tests. Pearson's *r* was used to determine the significance of correlations between two continuous variables (e.g. percentages and years of publication) and chi-square tests were

used to assess relationships between two categorical variables (e.g. proportion of respondents reporting yes vs. no and respondent subgroups [i.e. students vs. medical professionals]); for both tests, p-values below .05 constituted statistical significance.

In this systematic review, chi-square tests were used to assess the presence or absence of statistically-significant differences between the two main survey cohorts—medical students and medical professionals—with respect to their knowledge and opinions concerning: MC legalization (research question 1, Fig. 4); self-reported confidence regarding one's knowledge of MC (research question 2, Fig. 7); belief in MC's medical utility (research question 3, Fig. 9); support for recreational legalization of cannabis (research question 4, Fig. 12); and support for the U.S. government's federal rescheduling of cannabis (research question 6, Fig. 14). For these analyses, the total number of individual respondents from all the relevant studies who reported either "yes" or "no" to each research question were pooled into groups (i.e. all medical professional respondents reporting yes; all student respondents reporting no, etc.), then, a chi-square analysis determined if there were significant differences in the relative frequencies between each category.

Additionally, Pearson's *r* bivariate correlations were used to assess any relevant differences in entire studies' responses to the research questions over time (i.e. by the year of the study's publication). In this systematic review, Pearson's *r* was used to assess significant temporal trends regarding respondents': support for the legalization of MC (both medical professionals and students together, and just medical professionals alone; research question 1, Figs. 1 & 2); support for the recreational legalization of cannabis (research question 4, Fig. 11); desire for more educational material regarding MC (research question

5, Fig. 13); and concern about MC's potential to cause addiction and dependence (research question 7, Fig. 15).

Furthermore, some temporal analyses (all using Pearson's *r* bivariate correlations) assessed respondents' opinions regarding MC with respect to the number of years preceding or following MC legalization in the state or country of the study's publication. For these analyses, the year of MC legalization was identified for each state or country and labeled as "year 0"; then, the year of MC legalization was subtracted from the year of the study's publication to yield the number of years distancing the study from the year of MC legalization. For example, Australia legalized MC in 2016, and Norberg, et al. (Australia) published their study in 2012; therefore, Norberg, et al. (2012) received a score of -4 (years) with respect to years preceding or following MC legalization (2012-2016 = -4). This type of analysis was used to assess temporal trends regarding respondents': support for the legalization of MC (research question 1, Fig. 3) and self-reported confidence regarding one's knowledge of MC (research question 2, Fig. 6).

Finally, some temporal analyses featured a preponderance of studies conducted in a truncated time period, with only a few outlying studies published many years apart from the central cohort; in these instances, the outliers were excluded from analysis. For example, figure 1 assessed respondents' attitudes towards MC legalization over time, and featured 15 (out of 21) studies published in 2015 or later. Therefore, the two studies conducted in the 1970's were excluded from this analysis due to their extreme deviation from the overall mean year of publication.

Results:

An analysis of question 1 (Do you believe that physicians deserve the legal right to prescribe cannabis to patients? [i.e. Do you believe that cannabis should be legalized for therapeutic purposes?]) found that both medical students' and professionals' support for the legalization of MC has significantly increased over time ($r(19) = .44$, $p = .045$; 1990 to present; Fig. 1).

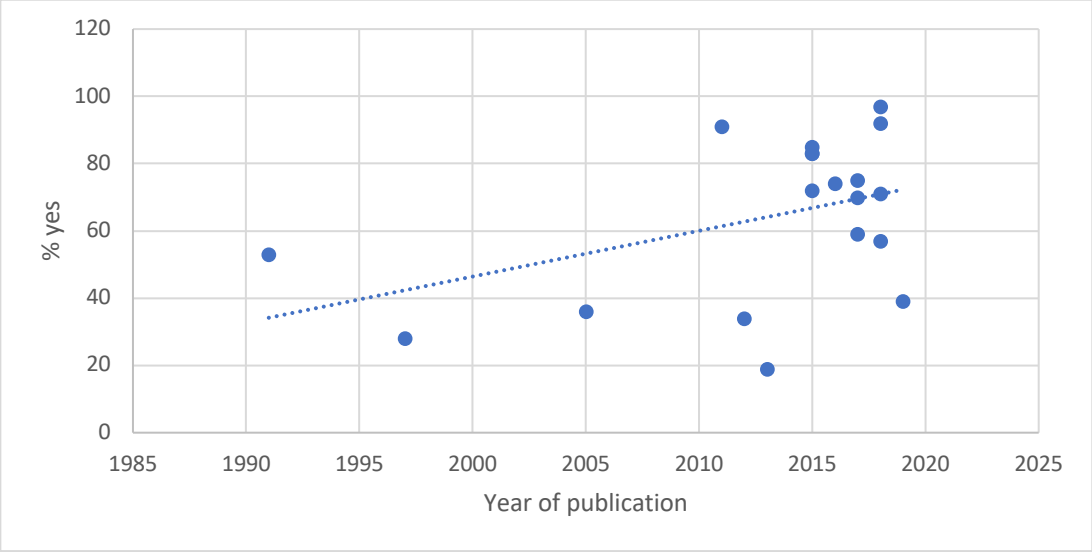

Figure 1. The percentage of respondents' agreeing with question 1 (Do you believe that physicians deserve the legal right to prescribe cannabis to patients? [i.e. Do you believe that cannabis should be legalized for therapeutic purposes?]) with respect to the year of the study's publication (2 pre-1990 outliers removed; 21 studies total; $r(19) = .44$, $p = .045$).

Additionally, an analysis of only medical professionals (i.e. following the removal of the 4 student-only studies) yielded a similar trend regarding increased support for the legalization of MC with respect to time, but the correlation did not meet statistical significance ($r(15) = .42$, $p = .093$; Fig. 2).

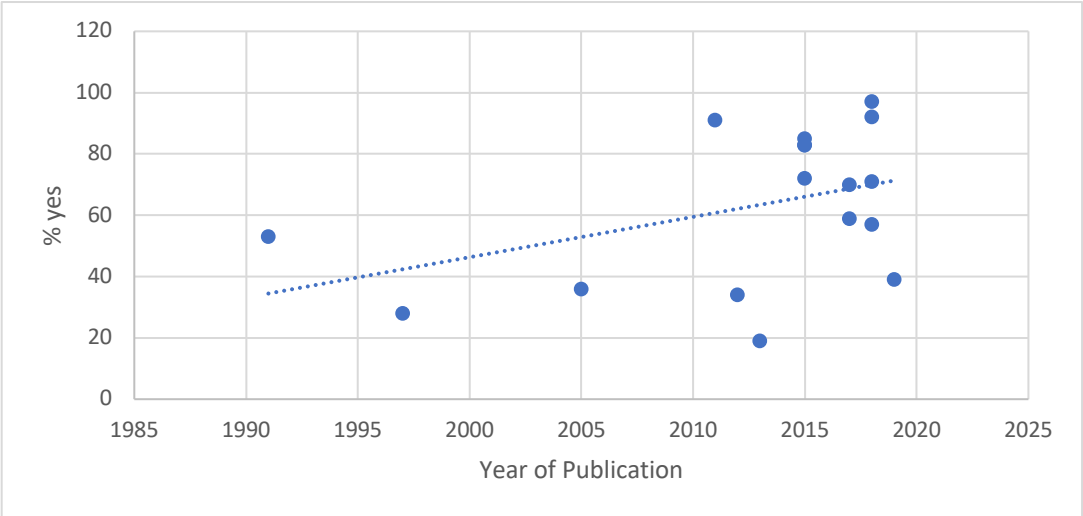

Figure 2. The percentage of professional respondents' agreeing with question 1 (Do you believe that physicians deserve the legal right to prescribe cannabis to patients? [i.e. Do you believe that cannabis should be legalized for therapeutic purposes?]), with respect to the year of the study's publication (post-1990 studies only; 17 studies total; $r(15) = .42$, $p = .093$).

In assessing whether the amount of years following or preceding the legalization of MC in the state or country of a study's publication affected respondents' support for the legalization of MC, no significant correlation was observed ($r(9) = .25$, $p = .453$; Fig. 3).

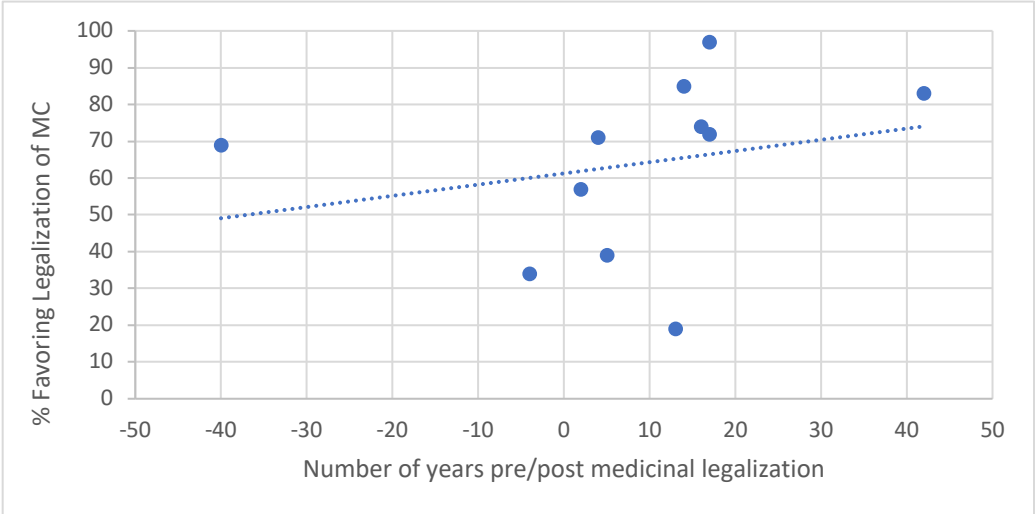

Figure 3. The percentage of respondents' (both professionals and students) agreeing with question 1 (Do you believe that physicians deserve the legal right to prescribe cannabis to patients? [i.e. Do you believe that cannabis should be legalized for therapeutic purposes?]) compared to the amount of years separating the year of publication from the year MC was legalized in the state of country of the study's publication (11 studies; $r(9) = .25$, $p = .453$).

Comparing students' attitudes towards the legalization of MC against those of medical professionals revealed a significant difference between the two cohorts, with medical professionals favoring legalization at a significantly higher rate than students (52% vs. 42%, respectively; χ^2 (1, N = 9019) = 50.72 p < .001; Fig. 4).

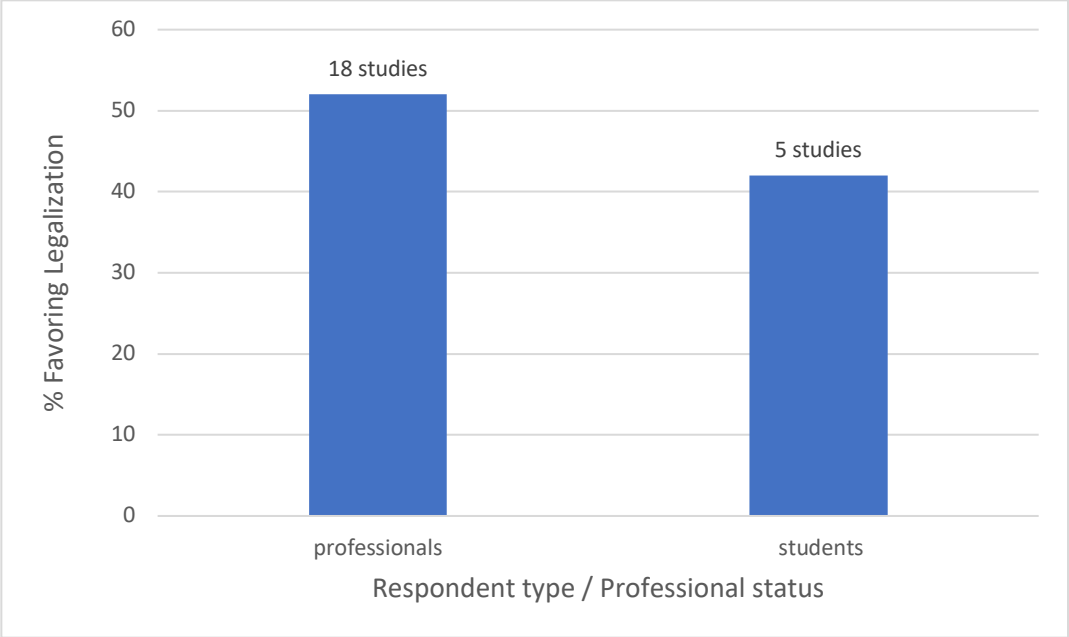

Figure 4. The percentage of respondents agreeing with research question 1 (Do you believe that physicians deserve the legal right to prescribe cannabis to patients? [i.e. Do you believe that cannabis should be legalized for therapeutic purposes?]) – based on respondent status as either a healthcare professional (N = 7108) or as a medical or pharmacy student (N = 1911) (χ^2 (1, N = 9019) = 50.72, p < .001).

Finally, figure 5 shows that support for the legalization of MC varies by the country of the study's publication; Canada demonstrated the greatest support for the legalization of MC (89%, N = 608, 2 studies) and the United States demonstrated the least support for the legalization of MC (42%, N = 5853, 13 studies).

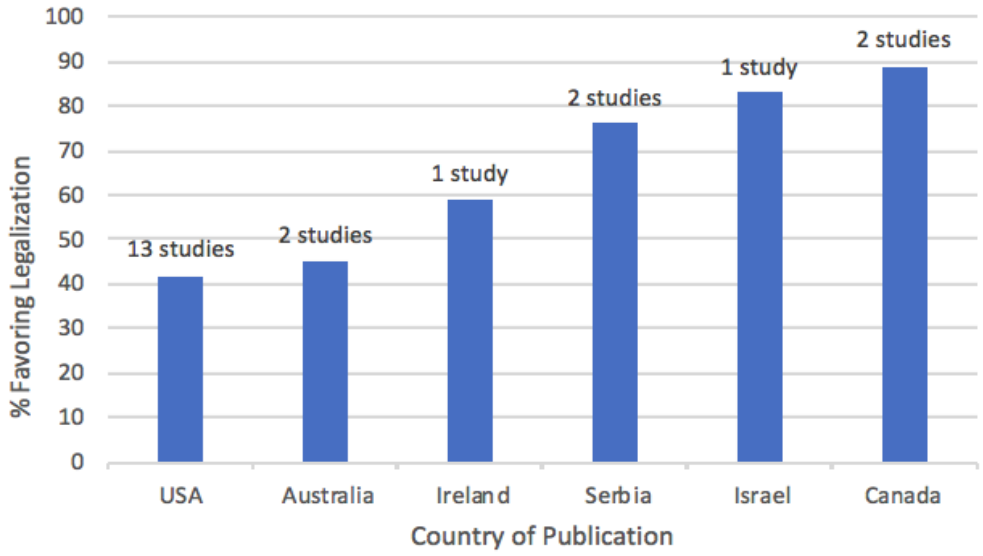

Figure 5. The percentage of respondents agreeing with research question 1 (Do you believe that physicians deserve the legal right to prescribe cannabis to patients? [i.e. Do you believe that cannabis should be legalized for therapeutic purposes?]) – based on country of the study's publication (USA [*N* = 5853]; Australia [*N* = 1304]; Ireland [*N* = 565]; Canada [*N* = 608]; Serbia [*N* = 396]; and Israel [*N* = 71]).

Research question 2 evaluated respondents' self-reported level of confidence regarding their knowledge of cannabis and its health effects. In assessing whether the amount of years following or preceding the legalization of MC in the state or country of a study's publication affected respondents' self-reported level of confidence, no statistically-significant relationship was observed ($r(13) = .32$, $p = .246$; Fig. 6).

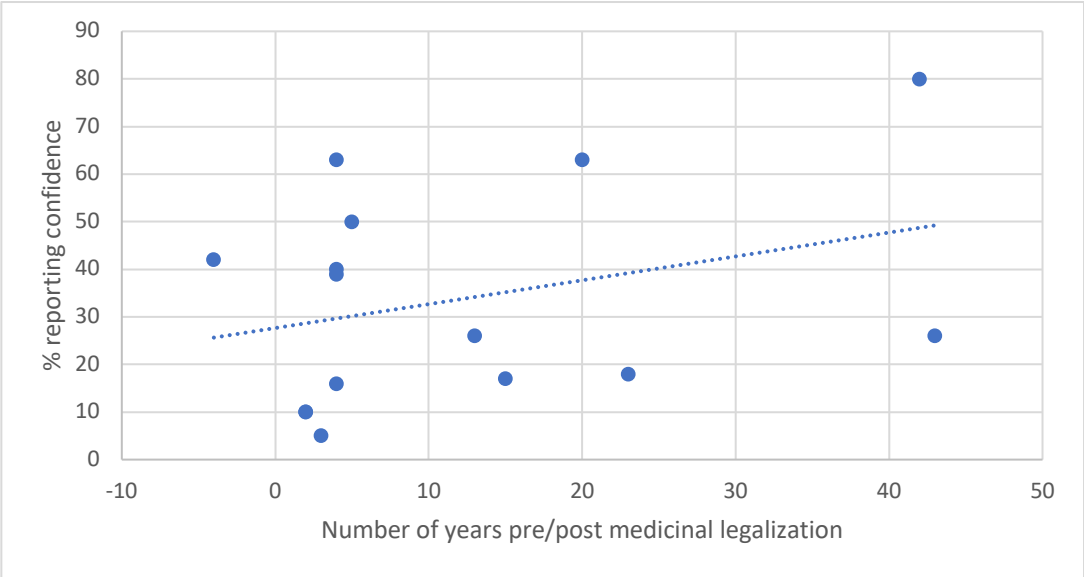

Figure 6. Survey respondents' self-reported level of knowledge about MC (% claiming an adequate level of knowledge, or better) compared to the amount of years separating the year of publication from the year MC was legalized in the state of country of the study's publication (15 studies; $r(13) = .32$, $p = .246$)

Analysis of respondents' self-reported confidence (regarding knowledge of MC) by respondent type (medical professionals vs. students) reveals significant differences between the two cohorts (χ^2 (1, N = 6711) = 293.88, $p < .001$; Fig. 7); overall, students reported the greatest confidence in their self-reported knowledge of MC, with medical professionals (on average) reporting significantly lower rates of confidence regarding their knowledge of MC (57% vs. 33%, respectively).

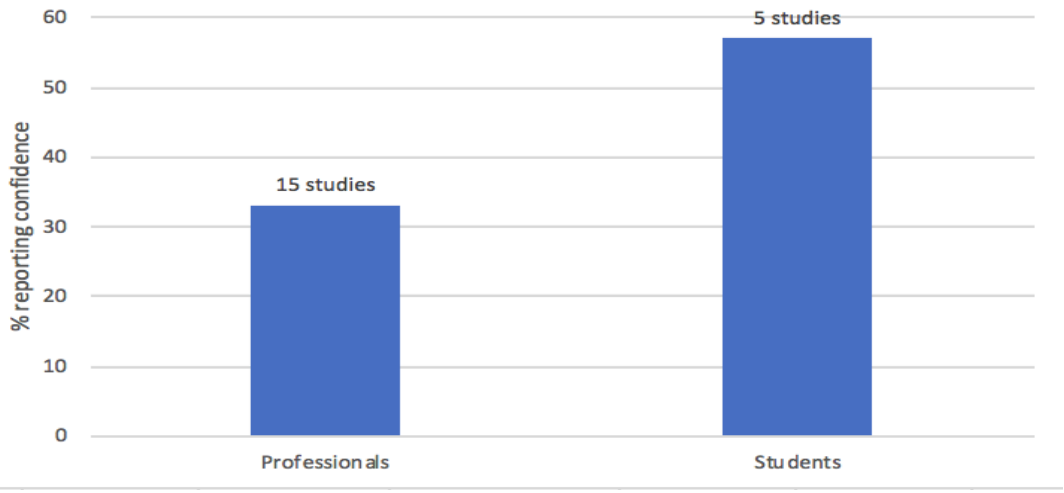

Figure 7. Respondents' self-reported confidence in their knowledge of MC (% claiming an adequate level of knowledge, or better) by respondent type: medical professionals (N = 5035) vs. students (N = 1676) (χ^2 (1, N = 6711) = 293.88, p < .001).

Finally, figure 8 shows that respondents' self-reported confidence in their knowledge of MC varies by the country of the study's publication; Israeli respondents reported the highest rates of self-reported confidence in their knowledge of MC (67%, N = 94; 2 studies), while Canadian respondents reported the lowest rates of self-reported confidence in their knowledge of MC (18%, N = 876; 2 studies).

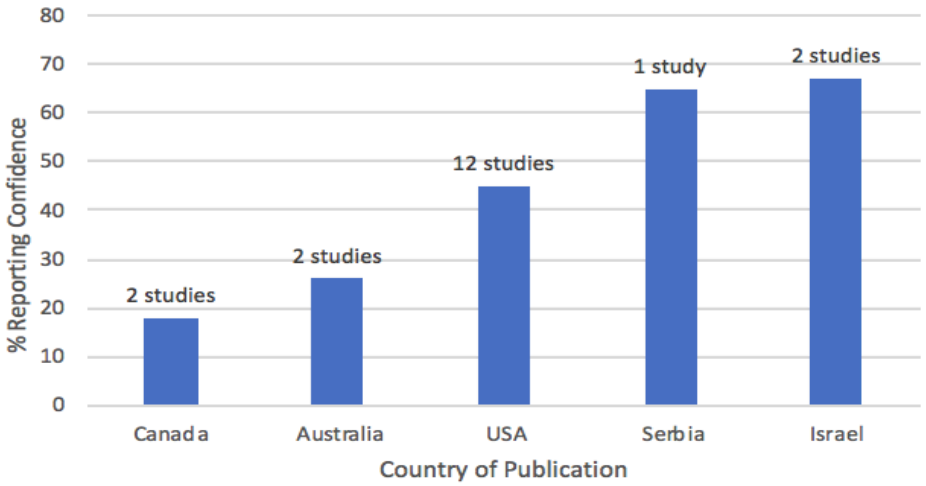

Figure 8. Respondents' self-reported confidence in knowledge regarding MC (% claiming an adequate level of knowledge, or better) by country of the study's publication: Australia (N = 1300); USA (N = 4125); Canada (N = 876); Serbia (N = 316); and Israel (N = 94).

Research question 3 assessed respondents' belief in cannabis' medical utility. A comparison of medical students' versus medical professionals' belief in cannabis' medical utility yielded a significant difference, with students reporting greater faith in cannabis' medical utility than medical professionals (77% vs 65%, respectively; χ^2 (1, N = 8647)= 59.64, p < .001; Fig. 9).

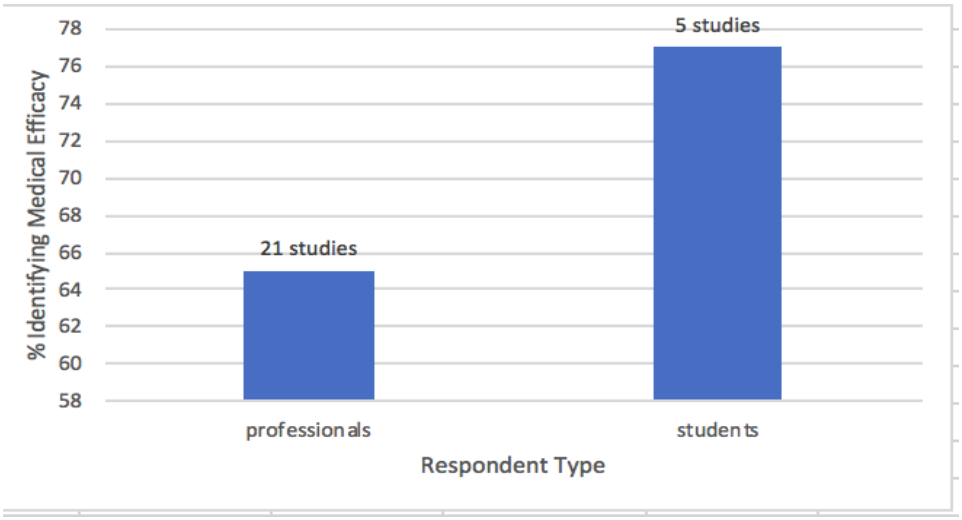

Figure 9. Percentage of respondents' espousing belief in cannabis' medical efficacy by respondent type: medical professionals (N = 7529) and students (N = 1118) (χ^2 (1, N = 8647) = 59.64, p < .001).

Additionally, figure 10 shows that respondents' belief in cannabis' medical utility varies by the country of the study's publication; Serbian respondents reported the highest rates of belief in cannabis' medical utility (84%, N = 396; 2 studies) while Australian respondents reported the lowest rates of belief in cannabis' medical utility (49%, N = 726; 2 studies).

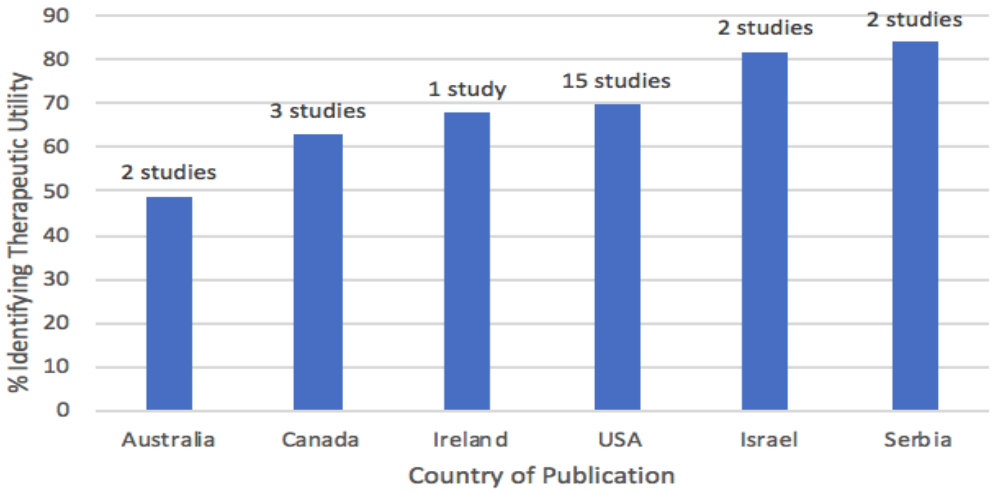

Figure 10. Percentage of respondents' espousing belief in cannabis' medical utility by country of the study's publication: USA (*N* = 5260); Canada (*N* = 1353); Australia (*N* = 726); Ireland (*N* = 565); Israel (*N* = 95); and Serbia (*N* = 396).

Research question 4 evaluated respondents' belief that cannabis should be legalized for recreational (i.e. non-medical) purposes. In assessing whether medical students' and professionals' attitudes towards the legalization of recreational cannabis has changed over time, no statistically-significant relationship was observed ($r(9) = .11$, $p = .746$; Fig. 11).

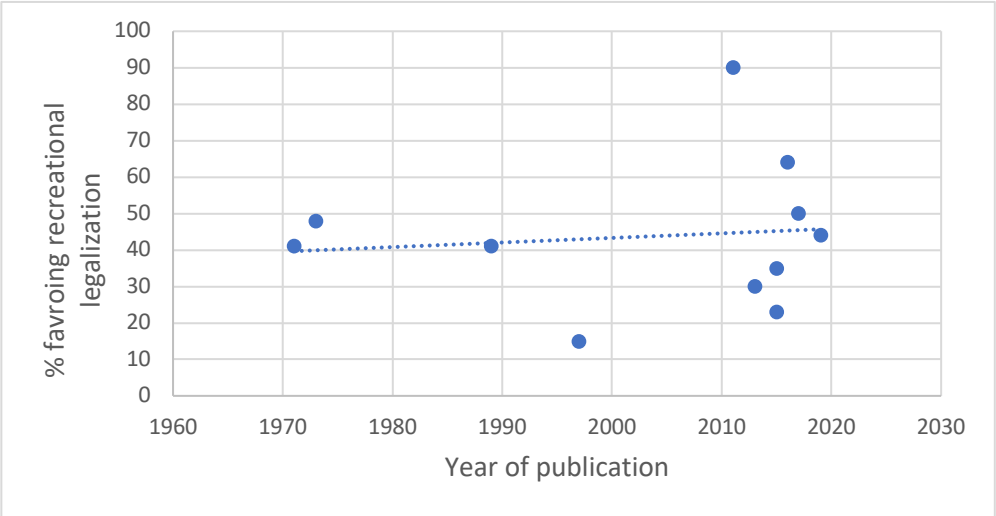

Figure 11. Percentage of survey respondents' espousing support for the legalization of cannabis for recreational (non-medical) purposes by year of publication (11 studies; $r(9) = .11$, $p = .746$).

A comparison of medical students' versus medical professionals' attitudes regarding the recreational legalization of cannabis yielded a statistically-significant difference, with students demonstrating greater support for recreational legalization than medical professionals (43% vs. 30%, respectively; χ^2 (1, N = 4136) = 78.88, p < .001; Fig. 12).

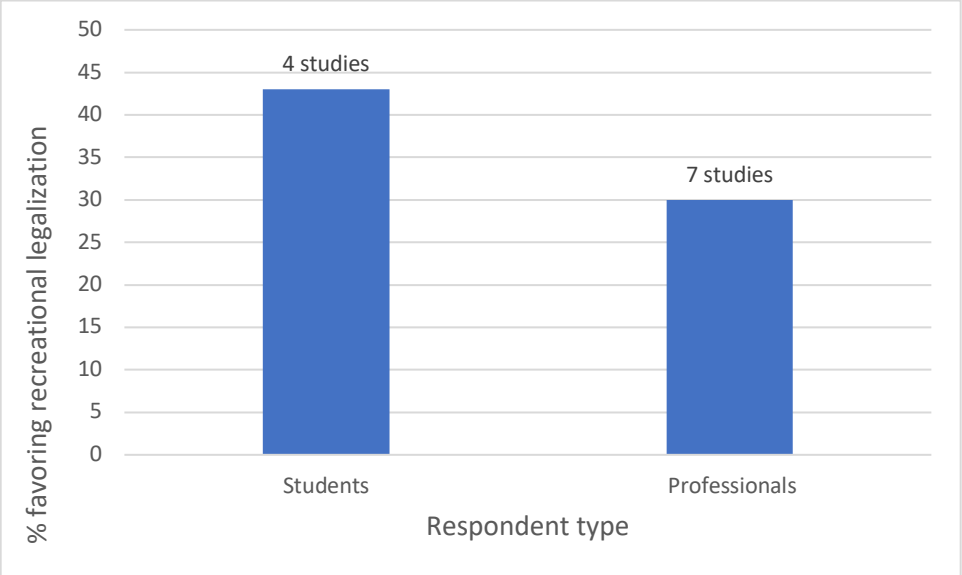

Figure 12. Percentage of respondents' espousing support for legalization of recreational cannabis use by respondent type: students (N = 1834) vs. medical professionals (i.e. MD's, Pharm.D.'s, DO's, PA's, RN's; N = 2302) (χ^2 (1, N = 4136) = 78.88, p < .001).

Research question 5 assessed whether respondents desired more education about MC, and if they believed that information about MC should be incorporated into medical school curricula. An assessment of respondents' personal or general desire for more knowledge regarding MC with respect to the year of the study's publication yielded no significant differences over time (r(13) = -.10, p = .713; Fig. 13).

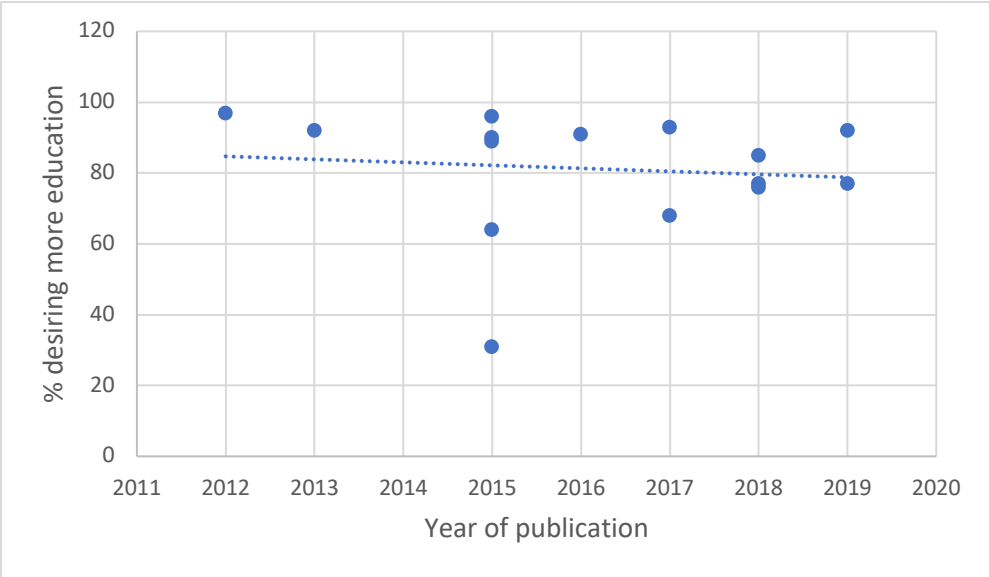

Figure 13. Percentage of survey respondents reporting a personal or general desire for more education on MC by year of publication (15 studies, $r(13) = -.10$, $p = .713$).

Research question 6 assessed U.S.-based respondents' opinions regarding the federal rescheduling of cannabis. A comparison of medical students versus professionals yielded significant differences regarding each group's level of support for the federal rescheduling of cannabis, with students supporting more lenient federal regulations at a higher rate than professionals (60% vs. 46%, respectively; χ^2 (1, N = 4249) = 70.76, $p < .001$; Fig. 14).

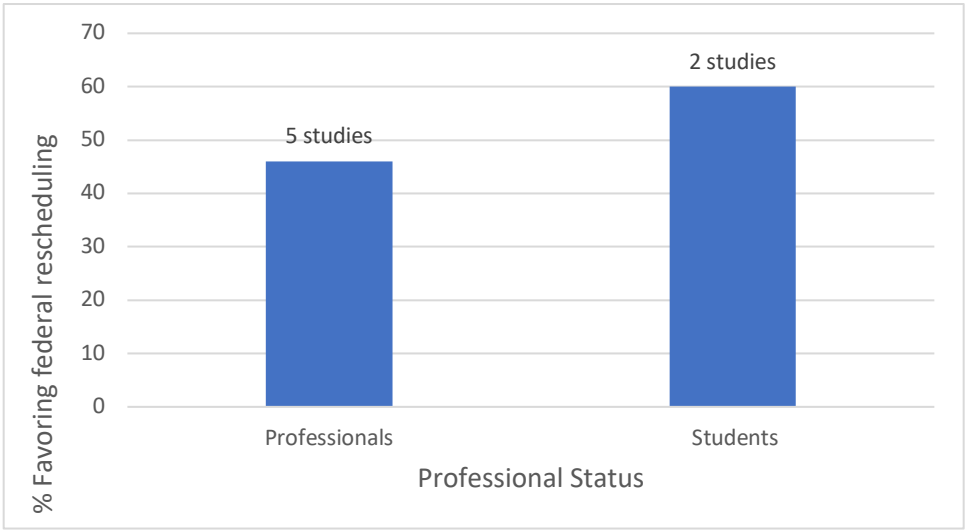

Figure 14. Percentage of respondents (U.S. only) espousing support for the federal rescheduling of cannabis by respondent type/professional status: medical professionals (i.e. MD's, Pharm.D.'s, DO's, PA's, RN's; *N* = 3045) vs. students (N = 1204) (χ^2 (1, *N* = 4249)= 70.76, *p* < .001).

Finally, research question 7 asked respondents if they were concerned about MC's potential to cause addiction or dependence in patients. In assessing whether respondents' levels of concern regarding MC's potential to cause addiction or dependence has changed over time, no statistically-significant relationship was observed (*r*(11) = -.13, *p* = .673; Fig. 15).

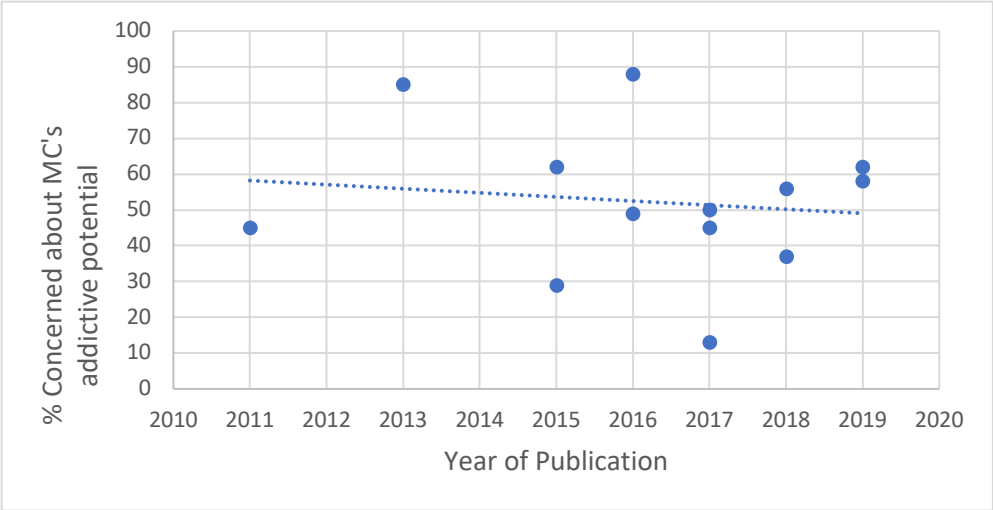

Figure 15. The percentage of survey respondents who are concerned about MMJ's addiction/dependence potential by year of publication (13 studies; *r*(11) = -.13, *p* = .673).

Discussion:

This systematic review assessed contemporary and relevant trends pertaining to medical professionals' and students' opinions and knowledge regarding medicinal cannabis (MC). The analyses conducted in this review sought to address the following five specific, guiding research questions:

1. Do healthcare students and professionals believe that cannabis should be legalized for medicinal purposes? Have these opinions changed significantly over time?
2. Are healthcare students and professionals confident in their level of knowledge regarding cannabis' health effects and clinical applications?
3. Are healthcare students and professionals adequately convinced of cannabis' therapeutic utility? What are healthcare professionals' main concerns regarding the incorporation of cannabis into the medical system?
4. What current gaps in knowledge exist, and how can the medical community become better informed about the therapeutic uses of cannabis?
5. Are there significant differences between the knowledge and opinions of healthcare students' versus healthcare professionals' with respect to any of the aforementioned research questions?

With respect to research question 1, it was hypothesized that support for the legalization of MC would increase over time. For research question 5 (whose significance applies to all other questions), it was expected that students would demonstrate greater support for the legalization of MC than medical professionals. Regarding research question 2, it was hypothesized that confidence levels would rise as the number of years following MC legalization in the country of a study's publication increased; moreover, it was expected that professionals (as opposed to students) would express greater confidence in their knowledge of MC. For question 3, it was hypothesized that respondents' from more

recently published studies would espouse greater faith in cannabis' medical utility; additionally, it was predicted that students would express greater faith in cannabis' medical utility. Finally, with respect to research question 4, it was expected that respondents from more recent studies would express an increased desire for further education.

Altogether, this systematic review identified several significant trends pertaining to medical students' and professionals' knowledge and attitudes regarding MC. Most notably, it was found that both medical students' and professionals' support for the legalization of MC has significantly increased over the last three decades, and that medical professionals are more likely to endorse the legalization of MC than students (52% vs. 42%, respectively). Furthermore, an assessment of both respondents' desire for more educational material on MC and respondents' concerns regarding MC's potential to cause dependence and addiction showed a ceiling effect, with respondents consistently reporting high levels of desire for more educational material and a high level of concern regarding MC's addictive potential, but with no significant changes over time. Lastly, support for the legalization of MC, respondents' self-reported confidence regarding their knowledge of MC, and respondents' belief in cannabis' medical utility all showed considerable differences across countries.

Question 1 assessed respondents' support for the legalization of MC. It was expected that support for the legalization of MC would increase over time due to ongoing sociocultural and legislative trends favoring legalization, which may serve to reduce stigma and increase the normalization of cannabis within the medical community. Results from this systematic review supported the hypothesis, as respondents' level of support for the

legalization of MC was shown to significantly increase from 1990 to the present day (see Fig. 1). Also, it was expected that students would demonstrate greater support for the legalization of MC than medical professionals, given the premise that many medical professionals may have been educated during an era in which cannabis was largely demonized within society and the medical community, and the established research finding that (at least within the United States) younger individuals are adopting more permissive views towards marijuana (Schmidt et al., 2016). However, results from this systematic review actually indicated the reverse, with medical professions demonstrating greater support for the legalization of MC than students (see Fig. 2). This finding can perhaps be explained by entertaining the premise that students may want to espouse more orthodox viewpoints during their educational years, so as not to appear overly progressive and radical, which could possibly jeopardize their clinical accreditation. Furthermore, it was hypothesized that respondents' support for the legalization of MC would be highest in countries that took early legislative steps to legalize MC, due to the established research finding that the passage of medical marijuana laws tends to correlate with more lenient views towards cannabis– especially among younger people (Schmidt et al., 2016); this expectation was largely confirmed, as Canadian respondents demonstrated the greatest support for the legalization of MC (89%), while U.S. respondents demonstrated the least support for the legalization of MC (42%). Canada legalized MC nationwide in 2001, while many states within the U.S. still fully prohibit the medical prescription of cannabis.

Question 2 assessed respondents' self-reported confidence regarding their knowledge of MC. It was hypothesized that confidence levels would rise as the number of

years following MC legalization in the country of a study's publication increased, due to respondents' from those countries having an increased likelihood of being exposed to cannabis in clinical settings; however, no statistically-significant relationship was observed (see Fig. 4). Moreover, it was expected that professionals (as opposed to students) would express greater confidence in their knowledge of MC, given their more extensive medical training and clinical experience; however, the opposite result was observed with 57% of students reporting an adequate (or better) knowledge of MC and just 33% of medical professionals reporting an adequate (or better) knowledge of MC (see Fig. 5). This finding could be the result of students—and younger respondents in general—having more lenient attitudes towards cannabis, thereby resulting in a greater perceived sense of knowledge about MC– or, it could be a manifestation of the Dunning-Kruger effect, a cognitive bias in which individuals with an inferior understanding of a concept tend to overestimate their own perceived level of knowledge (Kruger & Dunning, 1999). Furthermore, it was hypothesized that respondents from countries with a longstanding legal acceptance of MC would demonstrate greater levels of confidence regarding their knowledge of MC under the premise that respondents' from those countries would have an increased likelihood of being exposed to cannabis in clinical settings. The data largely supported this hypothesis, as Israeli respondents (where MC has been legal since 1973) reported the greatest levels of confidence (67%, see Fig. 6), while Canadian respondents (where MC has been legal since 2001) reported the lowest levels of confidence (18%).

Question 3 investigated respondents' belief in cannabis' medical utility. It was hypothesized that students would express greater faith in cannabis' medical utility under

the premise that students (being younger, on average, than professionals) would be more likely to have been raised in a sociopolitical climate more accepting of cannabis' medical applications. This hypothesis was supported by the data, with 77% of students expressing belief in cannabis' medical utility as opposed to 65% of medical professionals (see Fig. 7). Similarly, it was anticipated that respondents' from countries with a longstanding legal acceptance of MC would espouse greater faith in cannabis' medical utility; however, the data did not support this hypothesis, as Serbian respondents reported the greatest belief in cannabis' medical utility (84%, see Fig. 8) despite the fact that MC remains illegal in Serbia, while Australian respondents reported the lowest levels of belief in cannabis' medical utility (49%), despite the fact that Australia federally legalized MC in 2016. The Serbian respondents' exceptionally high faith in cannabis' medical utility, despite its nationwide illegality, once again suggests a Dunning-Kruger effect, as these physicians are unlikely to have significant clinical experience with MC.

Research question 4 assessed respondents' support for the recreational legalization of cannabis. It was expected that support for recreational legalization would increase over time due to ongoing sociopolitical trends favoring the decriminalization and legalization of recreational cannabis; however, no significant trends were observed over time (see Fig. 9). Rather, the data indicates that approximately one in two respondents (i.e. 50%) favor the legalization of recreational cannabis, regardless of the year of the study's publication. Likewise, it was expected that students would express greater support for recreational cannabis, under the premise that younger respondents tend to hold more permissive views toward cannabis regulation (Schmidt et al., 2016). The results supported this hypothesis, as

43% of students reported support for recreational legalization, as opposed to only 30% of medical professionals (see Fig. 10).

Question 5 assessed respondents' desire for more educational material regarding MC, including supplemental educational programs for professionals, and the incorporation of cannabis-related material into the existing medical school curriculum. It was expected that respondents from more recent studies would express an increased desire for further education, given the heightened acceptance of cannabis as a legitimate medical therapy in recent years. However, no significant change in respondents' desire for more education was observed over time, and the data actually indicated an apparent ceiling effect, with around 80% of respondents desiring more educational material– regardless of the year of the study's publication (see Fig. 11).

Research question 6 assessed U.S.-based respondents' opinions regarding the federal rescheduling of cannabis. Once again, it was expected that students would express greater support for the federal rescheduling of cannabis, under the principle that younger respondents tend to espouse more permissive views towards cannabis regulation (Schmidt et al., 2016). The data supported this hypothesis, as 60% of students indicated support for more lenient federal restrictions of cannabis use, as opposed to only 46% of medical professionals (see Fig. 12).

Lastly, research question 7 asked respondents if they were concerned about MC's potential to cause addiction or dependence in patients. It was expected that older studies would reflect greater levels of concern, given the established research finding that the perceived harmfulness of marijuana has decreased significantly since 1991 (Keyes et al.,

2016). However, no significant change over time was observed, and the results indicated a potential ceiling effect, with approximately one in two respondents (i.e. 50%) expressing concern for MC's addiction and dependence potential, regardless of the year of the study's publication (see Fig. 13).

It is important to note that this systematic review was impacted by several identifiable limitations. Firstly, there was a general dearth of accessible studies reporting medical professionals' and students' knowledge and attitudes regarding MC; however, the 43 studies included in this systematic review provided sufficient data to yield substantive and meaningful results. Notwithstanding, there was significant variability between the individual studies, including: incongruency in the survey methods and individual phraseologies used in data collection; differences in cannabis regulatory policy in the states and countries in which the surveys were conducted; and differences in the proportions of the types of respondents who answered the surveys (i.e. MD's, pharmacists, RN's, etc.). For instance, many studies included cohorts of medical professionals who specialized in a variety of subfields (e.g. neurology, pharmacy, oncology, rheumatology, etc.); therefore, the analyses presented in this systematic review are generalized findings that combine the responses of all medical professional subtypes. This necessary methodological procedure led to the overall generalization of the medical professional cohort, consequently nullifying any potential differences or distinctions within the overarching "medical professional" group. In addition, far more studies assessed the opinions of medical professionals (32 studies) as opposed to those of medical students (9 studies), which limits the strength of the comparisons made between the two cohorts. Also, while the 43 studies provided

enough data to conduct a meaningful systematic review, most did not provide the necessary metrics required to perform an even more comprehensive meta-analysis. Going forward, more studies should begin to yield the requisite effect sizes required to perform meta-analyses as the surveys used in these studies begin to include more data pertaining to mediation analyses and pre/post comparisons.

Furthermore, it was not possible to accurately assess countrywide (U.S., specifically) differences in respondents' knowledge and attitudes regarding MC due to: an insufficient number of representative studies from all U.S. states; highly variable sample sizes between studies conducted in different states; and the highly disparate legislative policies regarding (medicinal) cannabis in U.S. states. In addition, a major preponderance of studies collected for this systematic review were published after 2010 (37 out of 43), which limits the statistical power of long-term temporal analyses, resulting in a reduced range of years in which comparisons can be made to assess changes in knowledge and attitudes over time.

Crucially, this systematic review has important implications for both the continued adoption of MC within the global medical community and for the possible implementation of therapeutic hallucinogens into generally accepted medical practice. Firstly, the results from this review indicate that clinicians' acceptance of MC—a controversial, formerly stigmatized alternative therapy—has significantly increased in recent decades, which suggests that a similar trend may arise with respect to hallucinogens, given their analogous status as a culturally stigmatized alternative therapy. Moreover, results from this review clearly show that medical professionals' strong desire for more educational material on MC has not significantly changed over the last several decades. Hence, it would strongly

behoove the medical community to begin acknowledging this widespread and longstanding desire for more education, as it can only serve to benefit both medical professionals and patients to have a clinical staff that is well-versed and confident regarding their knowledge of alternative therapies. Providing clinicians with comprehensive and scientifically-sound educational material regarding the effects of alternative therapies will be a major step in assuaging the ongoing stigma and misinformation currently surrounding both MC and hallucinogens within the medical community. However, it must not be overlooked that at the present moment, very little educational material is even available regarding cannabis and hallucinogens due to the preponderance of highly restrictive legislative policies which limits their status as subjects of scientific inquiry. Lastly, results from this review found that medical students are significantly more likely to report high levels of confidence regarding their knowledge of MC compared to medical professionals, indicating a tendency for younger respondents to possibly overestimate their knowledge of alternative therapies. This tendency has critical importance regarding the hypothetical clinical implementation of hallucinogens, given the potential for young, zealous physicians to overestimate their knowledge of hallucinogens' clinical effects– the very scenario which largely led to a multi-national moratorium on hallucinogen research in the mid-20th Century. Therefore, establishing an objective set of scientifically-sound research and educational protocols regarding the management of MC and hallucinogens will be imperative for mitigating any potential barriers which might arise between more orthodox, senior clinicians and younger, more progressive clinicians as alternative therapies continue to augment the standard medical canon.

Conclusion:

This systematic review provided a multi-variate analysis of the existing literature on medical professionals' and students' attitudes and knowledge regarding medicinal cannabis (MC) to assess any relevant and significant trends which might also be useful in forecasting analogous trends in the nascent clinical acceptance of hallucinogens. It was found that both medical students' and professionals' support for the legalization of MC has significantly increased over the last several decades. Additionally, respondents' desire for more educational material on MC and respondents' concerns regarding MC's potential to cause dependence and addiction showed a ceiling effect, with respondents consistently reporting a high level of desire for more educational material and a high level of concern regarding MC's addictive potential, but with no significant changes over time. These findings indicate that clinicians from around the world are increasingly accepting of alternative and formerly stigmatized therapies, but there is also a strong and longstanding desire for more knowledge and educational material regarding these novel therapies. Hence, results from this systematic review should encourage the medical community to more seriously consider honest and comprehensive investigations into these (formerly) socio-politically stigmatized therapies to allow for their safe and effective potential integration into generally accepted medical practice.

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