Provider Perspectives on Use of Medical Marijuana in Children With Cancer

Prasanna Ananth, MD, MPH,[a] Clement Ma, PhD,[b,c] Hasan Al-Sayegh, MBChB, MPH,[b] Leah Kroon, MN, RN,[d,e] Victoria Klein, BS,[d] Claire Wharton, BS,[d] Elise Hallez, PNP,[f] Ilana Braun, MD,[c,g] Kelly Michelson, MD, MPH,[f,h] Abby R. Rosenberg, MD, MS,[d,e,i] Wendy London, PhD,[b,c] Joanne Wolfe, MD, MPH[b,c,g]

abstract

BACKGROUND: Although medical marijuana (MM) may have utility in the supportive care of children with serious illness, it remains controversial. We investigated interdisciplinary provider perspectives on legal MM use in children with cancer.

METHODS: We sent a 32-item, cross-sectional survey to 654 pediatric oncology providers in Illinois, Massachusetts, and Washington characterizing MM practices, knowledge, attitudes, and barriers. Forty-eight percent responded; 44% (n = 288) were included in analyses. Providers were stratified by status as legally eligible to certify (ETC) for MM. We used Fisher's exact and Wilcoxon rank tests and univariate and multivariate logistic regression models for group comparisons.

RESULTS: The provider median age was 35 years (range 22–70 years); 33% were ETC (83 physicians; 13 Washington state advance practice providers). Thirty percent of providers received ≥1 request for MM in the previous month. Notably, only 5% of all providers knew state-specific regulations. ETC providers were more likely to know that MM is against federal laws (P < .0001). Whereas most providers (92%) reported willingness to help children with cancer access MM, in adjusted models, ETC providers were less likely to indicate approval of patient MM use by smoking, oral formulations, as cancer-directed therapy, or to manage symptoms (P < .005 for all). Forty-six percent of all providers cited the absence of standards around formulations, potency, or dosing to be the greatest barrier to recommending MM.

CONCLUSIONS: Most pediatric oncology providers are willing to consider MM use in children with cancer and receive frequent inquiries. However, ETC providers endorse less favorable attitudes overall. The absence of standards is an important barrier to recommending MM.

[a]*Section of Pediatric Hematology/Oncology, Department of Pediatrics, Yale School of Medicine, New Haven, Connecticut;* [b]*Department of Pediatric Hematology/Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts;* [c]*Harvard Medical School, Boston, Massachusetts;* [d]*Seattle Children's Cancer and Blood Disorders Center, Seattle, Washington;* [e]*Treuman Katz Center for Pediatric Bioethics, Seattle, Washington;* [f]*Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois;* [g]*Department of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Boston, Massachusetts;* [h]*Center for Bioethics and Medical Humanities, Northwestern University Feinberg School of Medicine, Chicago, Illinois; and* [i]*University of Washington School of Medicine, Seattle, Washington*

Dr Ananth conceptualized and designed the study, oversaw study execution and data collection, reviewed analyses, and drafted and revised the manuscript; Drs Ma, Al-Sayegh, and London planned and conducted the analyses and reviewed and revised the manuscript; Dr Braun provided guidance on the study design and critically reviewed the draft of the manuscript; Drs Michelson and Rosenberg oversaw study execution at their respective sites and reviewed and revised the manuscript; Ms Kroon, Ms Klein, Ms Wharton, and Ms Hallez assisted with study procedures at their respective sites and critically reviewed the draft of the manuscript; Dr Wolfe

WHAT'S KNOWN ON THIS SUBJECT: Existing studies have investigated the impact of widespread marijuana legalization on healthy children. Yet, children with serious illness now have unprecedented access to medical marijuana (MM). This necessitates inquiry into how MM may be perceived by frontline, interdisciplinary providers.

WHAT THIS STUDY ADDS: Most pediatric oncology providers are willing to consider MM use in children with cancer and receive frequent inquiries. However, providers reveal limited knowledge about regulations, and those with legal eligibility to certify endorse less favorable attitudes overall.

To cite: Ananth P, Ma C, Al-Sayegh H, et al. Provider Perspectives on Use of Medical Marijuana in Children With Cancer. *Pediatrics*. 2018;141(1):e20170559

Medical marijuana (MM) has risen to the forefront of controversy throughout the United States.[1–4] MM refers to marijuana use, in plant or extract form, to treat an illness or its symptoms. Twenty-nine states and the District of Columbia have legalized MM for those with serious health conditions, with 8 states legalizing recreational marijuana as well.[5,6] Most jurisdictions consider cancer to be a qualifying condition and include provisions for children with life-threatening illnesses.

Cannabinoids, the chemical components of marijuana, may relieve nausea, anorexia, and neuropathic pain.[7–9] In pediatric cancer care, synthetic cannabinoid, or dronabinol, is routinely prescribed to manage nausea and anorexia.[10] Cannabinoids may also carry an antineoplastic effect, although the evidence is limited to preclinical studies.[11] The American Academy of Pediatrics (AAP) acknowledges MM as a potential supportive measure for children with serious illness.[12,13] Indeed, as children with cancer experience substantial symptom-related suffering,[14] there may be a role for MM in their care.

Nevertheless, MM has not been adopted in pediatrics. First, there is concern for adverse psychiatric and cognitive effects in developing children.[1,15,16] Second, appropriate formulations and dosing are unknown.[17] Third, critics cite concern that MM access may promote illicit use or toxic ingestion.[18,19] Finally, marijuana is a schedule I controlled substance, signifying that there are no currently accepted medical indications and that it carries high potential for abuse; schedule I classification designates procuring, using, or recommending MM as federal offenses.[20]

New state MM policies may influence pediatric oncology practice, particularly for children with intractable symptoms for whom conventional therapies have been exhausted. Previous researchers investigated MM attitudes of adult oncology and palliative care providers.[21–24] Notably, approximately half of adult oncologists espoused favorable attitudes toward MM even when MM was not available legally.[21] Moreover, public opinions are shifting, with >70% of Americans supporting adult MM use if recommended by a medical provider.[20,24–27]

Despite evolving legality and mounting public interest in MM, no studies have explored interdisciplinary provider perspectives on MM use in children with cancer. In this multicenter study, we describe pediatric oncology provider practices, knowledge, attitudes, and barriers regarding legal MM use in children with cancer. We hypothesized a priori that MM knowledge and attitudes might differ depending on whether a pediatric oncology provider is legally permitted to facilitate MM access through a formal certification process. Hence, this study compares the perspectives of providers who are eligible to certify (ETC) versus not eligible to certify (n-ETC) for MM.

METHODS

Study Design and Population

From July 2015 to November 2015, a cross-sectional survey was sent electronically to 654 pediatric oncology providers identified by site-specific principal investigators at 3 National Cancer Institute–designated cancer centers: Dana-Farber/ Boston Children's Cancer and Blood Disorders Center (Boston, MA), Ann & Robert H. Lurie Children's Hospital of Chicago (Chicago, IL), and Seattle Children's Hospital Cancer and Blood Disorders Center (Seattle, WA). Eligible participants included all physicians, nurse practitioners, physician assistants, psychologists, social workers, and registered nurses who longitudinally care for children with cancer in inpatient or outpatient settings. This study was approved by the respective institutional review boards.

Of 654 eligible participants, 313 (48%) responded. We excluded 12 (2%) participants who completed less than half of the survey and 13 (2%) additional participants who did not specify provider type. Ultimately, we included 288 (44%) participants in analyses.

Survey Instrument

We created a 32-item survey for this study to address the following domains: practices, including the frequency with which patients and families requested MM, providers recommended MM, and providers facilitated its procurement; knowledge of state-specific and federal MM regulations, mechanisms of access, cultivation, and possession; MM attitudes, including perceived risk of harm, perceived benefits, and opinions on its utility in symptom control; and barriers to recommending MM. Demographic items were incorporated from an existing instrument, the Survey about Caring for Children with Cancer.[28] Preliminary survey items were revised by a senior research scientist with survey design expertise. Items were also reviewed for face and content validity by national experts in palliative care. The composite survey was piloted with 5 health care providers outside of pediatric oncology who engaged in cognitive debriefing to help refine items.

Four questions pertained to practices. Knowledge was measured with 5 true–false and multiple-choice questions. Responses were coded as correct or incorrect. Attitudes were quantified with 6 questions by using a 5-point (0–4) Likert scale. Likert scales ranged from 1 for "strongly disagree or disapprove" to 4 for "strongly agree or approve," with 0 representing "not sure." Scores were dichotomized into favorable (3–4)

and unfavorable (1–2) attitudes. Two questions addressed barriers to MM recommendation with Likert scale responses as previously stated; a third question on barriers asked respondents to rank potential concerns about MM from greatest to least. Finally, 1 question asked respondents to characterize the appropriate timing of MM use in the course of cancer treatment. Missing responses and responses of "I don't know" or "not sure" were excluded from analyses.

We entered the survey instrument into Research Electronic Data Capture (REDCap), a Health Insurance Portability and Accountability Act–compliant, encrypted, Web-based platform.[29] We invited eligible providers to participate via e-mail, which included a unique survey hyperlink. Two weeks later, eligible participants who had not yet completed the survey received 2 reminders in 2-week intervals. Participants were requested to complete the survey independently, which took ∼10 minutes. Data were automatically entered into a deidentified database in REDCap, optimizing confidentiality. After a 6-week study period, the database was exported for analyses. Providers who completed the survey were entered into a drawing to receive 1 of 8 $25 gift cards for participation.

Study Outcomes

Primary outcomes included knowledge of MM regulations and attitudes about its use in pediatric oncology. Secondary outcomes included practice patterns, barriers to recommending MM, and perspectives on the timing of MM use.

Study Groups

For a segment of analyses, providers were categorized into 2 groups to contrast those who were ETC versus n-ETC for MM. In Massachusetts and Illinois, only physicians are legally ETC. In Washington, physicians, nurse practitioners, and physician assistants are ETC. All other providers are n-ETC in any state. To ensure fidelity in our approach to categorizing providers, we conducted a sensitivity analysis and examined attitudes by provider discipline.

Site Policies

Although MM is legal in states where this study was conducted, the Chicago site officially prohibits pediatric providers from facilitating MM access, which is in accordance with federal law. The Seattle site permits providers to recommend MM under certain circumstances. No formal policy has been established at the Boston site, although some providers have sought state-mandated training to certify for MM.

Statistical Analyses

Survey responses were summarized using descriptive statistics. Provider demographics and MM knowledge were compared among provider types by using the Fisher's exact test for categorical variables and the Wilcoxon rank test for continuous variables. We used univariate logistic regression to characterize whether attitudes differed by provider type. We included significantly associated attitudes in a multivariate logistic regression model, controlling for age, sex, race (white versus any other race), and location of practice. We also constructed a multivariate logistic regression model to analyze differences in practice patterns among provider types, adjusting for state.

To account for multiple comparisons in this study, P values $\leq .005$ were considered statistically significant. Analyses were performed by using SAS 9.4 software (SAS Institute, Inc, Cary, NC).

RESULTS

Demographics

Across the 288 providers, the median age was 35 years (range 22–70 years); 85% (n = 246) were women; 92% (260 of 282) self-identified as white; and 99% (n = 283) were non-Hispanic (Table 1). Forty-nine percent (n = 129) practiced in Massachusetts, 40% (n = 116) practiced in Washington, and 15% (n = 43) practiced in Illinois. Thirty-three percent (n = 96) of providers were ETC, whereas 67% (n = 192) were n-ETC. Of ETC providers (n = 96), 86% (n = 83) were physicians; 14% (n = 13) were nurse practitioners or physician assistants. Of n-ETC providers (n = 192), 89% (n = 170) were nurses, 8% (n = 16) were nurse practitioners or physician assistants, 2% (n = 3) were psychosocial providers, and 2% (n = 3) were other providers. n-ETC providers were significantly younger, mostly women, and more predominantly of white race compared with ETC providers ($P <$ .0001).

Practices

Overall, 30% (85 of 284) of providers reported 1 or more inquiries for MM, including 40% (38 of 95) of ETC providers and 25% (47 of 189) of n-ETC providers (P = .013) (Fig 1). Of those providers receiving MM inquiries, 14% (12 of 83) facilitated access 1 or more times (facilitation occurred in Massachusetts and Washington only). Seventy-nine percent (70 of 85) of all inquiries were for relief of nausea and/or vomiting, 52% (44 of 85) were for anorexia, 26% (22 of 85) were for pain, and 24% (20 of 85) were for depression and/or anxiety. Only 8% (23 of 283) reported sometimes or frequently recommending MM to patients, with no significant differences between ETC and n-ETC providers (unadjusted, P = .8; adjusted by state, P = .79).

TABLE 1 Baseline Characteristics of Pediatric Oncology Providers

	All Providers (N = 288)	Providers Legally ETC for MM (n = 96; 33%)	Providers n-ETC for MM (n = 192; 67%)	P
Demographics				
Age, y, median (range)	35 (22–70); n = 274	41 (30–70); n = 88	32 (22–62); n = 186	<.0001
Women, frequency (%)	246 (85)	61 (64)	185 (96)	<.0001
White race, frequency (%)	260 of 282 (92)	78 of 94 (83)	182 of 188 (97)	<.0001
Hispanic and/or Latino ethnicity, frequency (%)	3 of 286 (1)	2 of 95 (2)	1 of 191 (1)	.26
Practice characteristics, frequency (%)				
Location				
Chicago, Illinois	43 (15)	9 (9)	34 (18)	.18
Boston, Massachusetts	129 (49)	46 (48)	83 (43)	
Seattle, Washington	116 (40)	41 (43)	75 (39)	
Time in practice, y, frequency (%)				
<1	14 of 286 (5)	5 of 95 (5)	9 of 191 (5)	.19
1–5	89 of 286 (31)	26 of 95 (27)	63 of 191 (33)	
6–10	62 of 286 (22)	15 of 95 (16)	47 of 191 (25)	
11–15	52 of 286 (18)	18 of 95 (19)	34 of 191 (18)	
16–20	21 of 286 (7)	10 of 95 (11)	11 of 191 (6)	
>20	48 of 286 (17)	21 of 95 (22)	27 of 191 (14)	

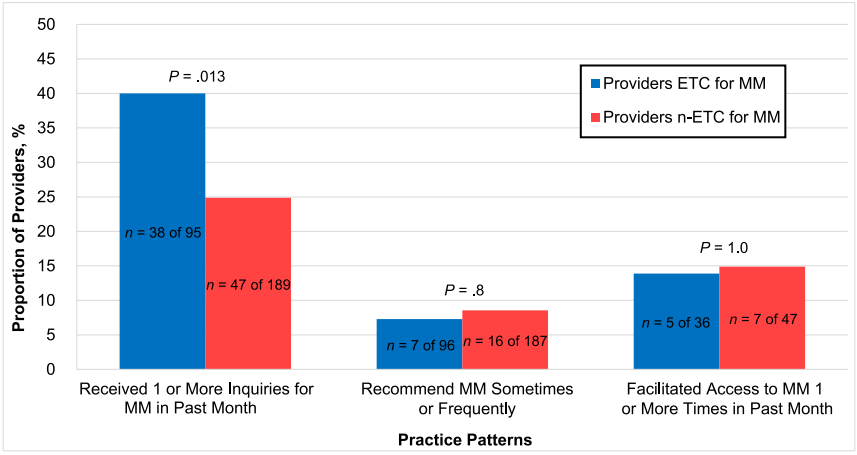

FIGURE 1
Proportions of pediatric oncology providers receiving MM inquiries, making recommendations, and facilitating access, comparing ETC versus n-ETC providers. Of note, only providers who reported receiving inquiries in the previous month were asked whether they facilitated access.

Knowledge

Overall, 86% (245 of 285) of providers knew that their state had legalized MM; 76% (217 of 285) knew that marijuana is considered a controlled substance by the Food and Drug Administration (FDA) (Table 2). Fewer (59%; 165 of 281) knew that MM is against federal laws, and only 5% (14 of 282) accurately identified state-specific regulations concerning MM access, possession, and cultivation. ETC providers were more likely to know that MM is federally prohibited (75%; 70 of 93) compared with n-ETC providers (51%; 95 of 188; P < .0001). Otherwise, we found no significant differences in knowledge by provider type.

Attitudes

Most providers (92%; 240 of 261) were willing to help children with cancer access MM (Table 3). Similarly, most indicated approval of oral MM formulations (89%; 223 of 250) and of using MM to manage symptoms (92%; 236 of 258). Many providers indicated approval of patients smoking MM (57%; 133 of 234) and of using MM as cancer-directed therapy (67%; 158 of 236). A vast majority (93%; 237 of 256) of providers responded favorably to the conduct of clinical trials investigating MM use in children.

In univariate models comparing MM attitudes by provider type, ETC providers were significantly less likely than n-ETC providers to report willingness to help pediatric patients access MM (odds ratio [OR] = 0.26; 95% confidence interval [CI] = 0.1–0.65; P = .0041) (Table 3). ETC providers were also less likely to indicate approval of patient MM use by smoking (OR = 0.33; 95% CI = 0.19–0.59; P = .0002), oral formulations (OR = 0.12; 95% CI = 0.05–0.29; P < .0001), as cancer-directed therapy (OR = 0.04; 95% CI = 0.02–0.08; P < .0001), or to manage symptoms (OR = 0.19; 95% CI = 0.07–0.47; P = .0004). Adjusting for provider age, sex, race, and location of practice, ETC providers continued to have significantly lower odds of indicating approval of patients MM use by smoking (adjusted OR = 0.25; 95% CI = 0.11–0.55; P = .0005), oral formulations (adjusted OR = 0.17; 95% CI = 0.05–0.53; P = .0025), as cancer-directed therapy (adjusted OR = 0.04; 95% CI = 0.01–0.09;

TABLE 2 Knowledge of MM Regulations

	All Providers (N = 288)		Providers Legally ETC for MM (n = 96)		Providers n-ETC for MM (n = 192)		P
	Frequency Correct	% Correct (95% CI)	Frequency Correct	% Correct (95% CI)	Frequency Correct	% Correct (95% CI)	
My state has legalized MM. (Correct answer: True for all states)	245 of 285	86 (81–90)	85 of 95	89 (81–95)	160 of 190	84 (79–89)	.28
Which of the following is false in Illinois? (Only false statement: Illinois state MM laws protect against arrest)	0 of 41	0 (0–9)	0 of 8	0 (0–32)	0 of 33	0 (0–10)	1
Which of the following is false in Massachusetts? (Only false statement: Providers need to write a prescription for MM)	9 of 127	7 (3–13)	7 of 46	15 (6–29)	2 of 81	2 (0–9)	.011
Which of the following is false in Washington? (Only false statement: A registration identification card is required to obtain MM)	5 of 114	4 (1–10)	1 of 41	2 (0–13)	4 of 73	5 (2–13)	.65
Combined response to state-specific questions across all 3 states	14 of 282	5 (3–8)	8 of 95	8 (4–16)	6 of 187	3 (1–7)	.08
Marijuana is considered a controlled substance by the FDA. (Correct answer: True)	217 of 285	76 (71–81)	71 of 95	75 (65–83)	146 of 190	77 (70–83)	.77
MM may be used to treat all the following symptoms, except what? (Correct answer: Constipation)	219 of 286	77 (71–81)	66 of 95	69 (59–79)	153 of 191	80 (74–86)	.054
MM is against federal laws. (Correct answer: True)	165 of 281	59 (53–65)	70 of 93	75 (65–84)	95 of 188	51 (43–58)	<.0001

P < .0001), or to manage symptoms (adjusted OR = 0.16; 95% CI = 0.05–0.52; P = .0026). A sensitivity analysis comparing attitudes by provider discipline yielded comparable results (Supplemental Tables 4 and 5).

Barriers

Many providers (63%; 162 of 259) were not concerned about substance abuse in children who receive MM. Likewise, most providers (80%; 208 of 260) were not concerned about being prosecuted by the federal government for facilitating MM access. These attitudes did not significantly differ by provider type (Table 3). Forty-six percent (n = 136) of providers reported their greatest concern to be the absence of standards around MM formulations, potency, and dosing.

Timing of Use

When asked about circumstances in which providers would consider MM appropriate for children with cancer, most (89%; 255 of 288) responded that MM would be appropriate near the end of life, in treatment of cancer with primarily palliative intent (89%; 255 of 288), or in treatment of progressive or relapsed cancer (76%; 220 of 288) (Fig 2). Fewer providers felt that MM would be appropriate when treating patients with curative intent (52%; 150 of 288) or in the early stages of cancer treatment (35%; 100 of 288). Only 2% (5 of 288) of providers felt that MM was never appropriate. N-ETC providers were more likely to consider MM appropriate in treating cancer from early stages through treatment with primarily palliative intent ($P \leq .004$ for all).

DISCUSSION

Our study is among the first to describe MM perspectives of interdisciplinary providers caring for children with cancer. We found that pediatric oncology providers

TABLE 3 Attitudes and Barriers Regarding MM Use

	All Providers (N = 288), Frequency (%)	Providers Legally ETC for MM (n = 96), Frequency (%)	Providers n-ETC for MM (n = 192), Frequency (%)	Unadjusted OR (95% CI)	Unadjusted P	Adjusted Model N	Adjusted OR[a] (95% CI)	Adjusted P[a]
Willing to help patients access MM	240 of 261 (92)	71 of 84 (85)	169 of 177 (95)	0.26 (0.1–0.65)	.0041	244	0.61 (0.17–2.15)	.44
Approve of patients smoking MM	133 of 234 (57)	29 of 75 (39)	104 of 159 (65)	0.33 (0.19–0.59)	.0002	219	0.25 (0.11–0.55)	.0005
Approve of patients using oral formulations of MM	223 of 250 (89)	56 of 76 (74)	167 of 174 (96)	0.12 (0.05–0.29)	<.0001	236	0.17 (0.05–0.53)	.0025
Approve of using MM as cancer-directed therapy	158 of 236 (67)	19 of 80 (24)	139 of 156 (89)	0.04 (0.02–0.08)	<.0001	222	0.04 (0.01–0.09)	<.0001
Approve of using MM to manage symptoms	236 of 258 (92)	67 of 82 (82)	169 of 176 (96)	0.19 (0.07–0.47)	.0004	244	0.16 (0.05–0.52)	.0026
Favor clinical trials investigating MM use in children	237 of 256 (93)	80 of 85 (94)	157 of 171 (92)	1.43 (0.5–4.1)	.51	—	—	—
Unconcerned about substance abuse among patients who receive MM	162 of 259 (63)	55 of 90 (61)	107 of 169 (63)	0.91 (0.54–1.54)	.73	—	—	—
Unconcerned about prosecution for helping patients access MM	208 of 260 (80)	75 of 91 (82)	133 of 169 (79)	1.27 (0.66–2.44)	.48	—	—	—

—, not included in model.

[a] In multivariate logistic regression, we compared ETC to n-ETC providers (reference group), adjusting for provider age, sex, race, and location of practice.

were commonly willing to consider MM use in children with cancer despite limited knowledge of state and federal regulations. MM inquiries arose frequently, with facilitation occurring at a nonnegligible rate regardless of institutional barriers to MM provision. Interestingly, more favorable attitudes were endorsed by n-ETC providers. N-ETC providers were also significantly more open to MM use in early cancer treatment. ETC providers were increasingly amenable to MM use in advanced stages of cancer or near the end of life. The greatest barrier to recommending MM was reported to be the absence of standards regarding formulations, dosing, and potency.

Several studies over the past decade have ascertained that physicians are apprehensive about adult use of MM.[22,24,26,30–32] This reluctance appears to be driven by the potential for side effects,[33] scant high-quality scientific data,[22,34] unclear dosage guidelines,[17,26] and a lack of regulatory oversight by the FDA, unlike other therapeutic and supportive care drugs.[35] Such concerns are magnified when pediatric clinicians must consider MM use by children and adolescents, particularly because habitual marijuana use is associated with dependence, impaired neurocognitive development, and poor academic achievement in children.[12,15,36,37] Recommending MM may thus be fundamentally problematic for physicians who are accustomed to evidence-based practice, as they cannot be assured by empirical data that benefits outweigh possible harm.[37]

Few prior studies have explored how interdisciplinary providers, including those without legal authority to recommend MM, perceive its use by patients.[24,30,32] Notably, some states enable advance practice providers to certify for MM, and existing literature suggests that the degree to which

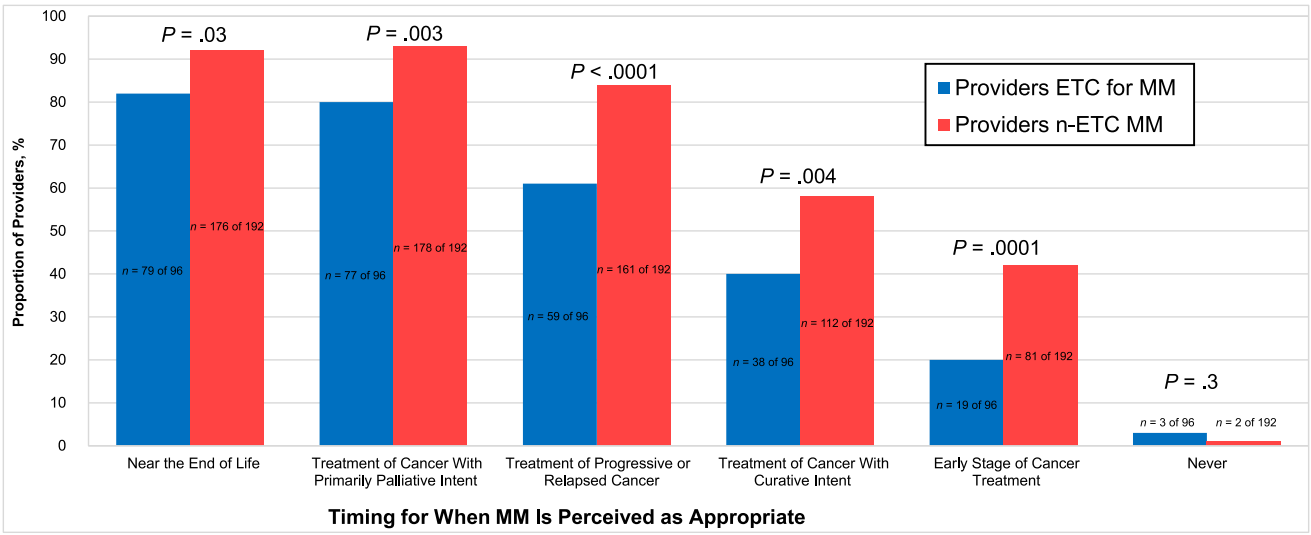

FIGURE 2

Proportions of pediatric oncology providers who would consider MM appropriate at various time points in the course of caring for a child with cancer, comparing ETC versus n-ETC providers.

providers endorse MM may depend more on whether they can legally certify, rather than on particular discipline.[24,30] Consistent with these findings, n-ETC providers in this study reported more permissive attitudes toward MM use in children with cancer. Specifically, n-ETC providers were more likely to convey approval of pediatric patients using MM in smoked or oral formulations, as cancer-directed therapy, or for symptom management, despite scarce evidence to corroborate this use.[35,37] To place these findings in context, n-ETC provider attitudes observed in this study echo those of the general public,[27,38] whereas ETC provider attitudes align more closely with physician-based data.[22,31,33] We surmise that ETC providers, whose licensure and clinical reputation could theoretically be jeopardized by MM recommendation in the face of federal prohibition,[20,39] may be less willing to endorse MM use in children than providers who face fewer legal ramifications.[40] Additionally, responses may have been influenced by institutional policies at study sites that discourage ETC providers from actively recommending or procuring MM for patients.[30]

The paradigm shifts when providers consider patients who are seriously ill. Half of interdisciplinary hospice providers in a previous study reported feeling comfortable recommending MM to adult patients.[24] Similarly, we identified that pediatric providers found MM use for children with advanced cancer or near the end of life to be more permissible than in earlier stages of cancer treatment. This sentiment is reflected in a current AAP position statement, which sanctions the use of MM for "children with life-limiting or seriously debilitating conditions."[12] Although the AAP opposes all other pediatric marijuana use, it recognizes that there may be circumstances in which MM could have benefit. Accordingly, in our study, only 2% of providers stated that MM was never appropriate for a child with cancer. Emerging research indicates that cannabidiol, a nonpsychoactive component of marijuana, can be effective for children with refractory seizures and has a tolerable safety profile.[41] Randomized clinical trials using such MM formulations for supportive care in children with cancer are needed to better understand the therapeutic potential of this agent. It is evident from our study that providers are strongly in support of trials to this end.

A striking aspect of the current study is the frequency with which pediatric oncology providers receive requests for MM. Nearly one-third of all providers fielded inquiries in the previous month alone, including one-quarter of n-ETC providers; 14% of those who received inquiries facilitated access. This frequency of inquiries is comparable to published adult literature.[24,30] Given burgeoning interest in MM, especially in oncology care,[3,35] it is critical that providers who are routinely approached for access to MM possess baseline knowledge on regulations, known benefits, and harm. However, providers in this study were largely unaware of state-specific regulations around MM, and approximately one-quarter did not know that MM is federally illegal. These findings confirm the need for greater education, perhaps through state-based initiatives.[30–32]

One limitation of this study is its cross-sectional design; we are consequently unable to trend attitudes as laws change. In addition, the response rate to this survey (48%) may be

deemed low, albeit comparable to existing provider studies of similar design.[31,42,43] If there were some degree of response bias, respondents might be expected to have more knowledge than nonresponders, and yet, respondents to this survey demonstrated knowledge gaps in several domains. Although this sample is not nationally representative, we reveal confluent attitudes and practices of providers despite differential approaches to legal MM access. In a scenario in which uniform practice guidelines are needed amid variable institutional and state policies, the attitudes of frontline, interdisciplinary providers caring for children with serious illnesses are therefore critically important to report.

CONCLUSIONS

This study identifies that interdisciplinary pediatric oncology providers are overall open to considering MM in children, but ETC providers are more circumspect in its use as a therapeutic or supportive care agent. We reveal high rates of MM inquiries and a need for increased provider education. Future researchers should explore patient and family perspectives on MM, considering substantial interest in and increasing availability of MM. Additionally, this study calls for rigorously designed clinical trials in which researchers investigate the use of MM in children with cancer. Although marijuana policy has, to date, outpaced scientific discovery, the US Drug Enforcement Administration recently agreed to enable broader access to marijuana for investigators conducting medical research.[44] This decree holds promise that a stronger evidence base may soon be available to help providers, patients, and families make informed decisions about using MM in cancer care.

ACKNOWLEDGMENTS

We acknowledge the Pediatric Palliative Care Research Network for its members' contributions to developing the survey instrument. We also thank Madhumitha Sridharan for assistance with REDCap survey implementation.

ABBREVIATIONS

AAP: American Academy of Pediatrics
CI: confidence interval
ETC: eligible to certify for medical marijuana
FDA: Food and Drug Administration
MM: medical marijuana
n-ETC: not eligible to certify for medical marijuana
OR: odds ratio
REDCap: Research Electronic Data Capture

conceptualized and designed the study, assisted with survey design, reviewed analyses, and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

We conducted a sensitivity analysis comparing the results of 2 multivariable models adjusted for provider age, sex, race, and location of practice: (1) comparing attitudes of providers legally ETC for MM with providers n-ETC (reference group), and (2) comparing attitudes of physicians to nonphysicians (reference group). We observed that adjusted ORs and 95% CIs do not substantially differ between models 1 and 2. Results from model 1 are presented in the article (Table 3).

DOI: https://doi.org/10.1542/peds.2017-0559

Accepted for publication Oct 23, 2017

Address correspondence to Prasanna Ananth, MD, MPH, Section of Pediatric Hematology/Oncology, Department of Pediatrics, Yale School of Medicine, 330 Cedar Street, LMP 2082C, New Haven, CT 06520-8064. E-mail: prasanna.ananth@yale.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Dr Ananth was supported by the David A. Abraham Fund at the Dana-Farber Cancer Institute and the Ruth L. Kirschstein National Research Service Award (National Institutes of Health 5-T32-CA-136432-05). Dr Michelson was supported by grants from the Patient-Centered Outcomes Research Institute (grant 1304-6449) and the American Cancer Society. Dr Rosenberg was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health (award KL2TR000421). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. *N Engl J Med*. 2014;370(23):2219–2227
2. Wolk L, Kuehn BM. Colorado tackles medical implications of marijuana. *JAMA*. 2014;311(20):2053–2054
3. Wilkie G, Sakr B, Rizack T. Medical marijuana use in oncology: a review [published online ahead of print March 17, 2016]. *JAMA Oncol*. doi:10.1001/jamaoncol.2016.0155
4. Richter KP, Levy S. Big marijuana–lessons from big tobacco. *N Engl J Med*. 2014;371(5):399–401

5. Lynne-Landsman SD, Livingston MD, Wagenaar AC. Effects of state medical marijuana laws on adolescent marijuana use. *Am J Public Health*. 2013;103(8):1500–1506

6. Furlow B. States and US government spar over medical marijuana. *Lancet Oncol*. 2012;13(5):450

7. de Jong FA, Engels FK, Mathijssen RH, et al. Medicinal cannabis in oncology practice: still a bridge too far? *J Clin Oncol*. 2005;23(13):2886–2891

8. Kogan NM, Mechoulam R. Cannabinoids in health and disease. *Dialogues Clin Neurosci*. 2007;9(4):413–430

9. Sallan SE, Zinberg NE, Frei E III. Antiemetic effect of delta-9-tetrahydrocannabinol in patients receiving cancer chemotherapy. *N Engl J Med*. 1975;293(16):795–797

10. Elder JJ, Knoderer HM. Characterization of dronabinol usage in a pediatric oncology population. *J Pediatr Pharmacol Ther*. 2015;20(6):462–467

11. Velasco G, Hernández-Tiedra S, Dávila D, Lorente M. The use of cannabinoids as anticancer agents. *Prog Neuropsychopharmacol Biol Psychiatry*. 2016;64:259–266

12. Committee on Substance Abuse; Committee on Adolescence. The impact of marijuana policies on youth: clinical, research, and legal update. *Pediatrics*. 2015;135(3):584–587

13. Ammerman S, Ryan S, Adelman WP; Committee on Substance Abuse; Committee on Adolescence. The impact of marijuana policies on youth: clinical, research, and legal update. *Pediatrics*. 2015;135(3). Available at: www.pediatrics.org/cgi/content/full/135/3/e769

14. Wolfe J, Grier HE, Klar N, et al. Symptoms and suffering at the end of life in children with cancer. *N Engl J Med*. 2000;342(5):326–333

15. Levy S. Effects of marijuana policy on children and adolescents. *JAMA Pediatr*. 2013;167(7):600–602

16. Joffe A; American Academy of Pediatrics Committee on Substance Abuse; American Academy of Pediatrics Committee on Adolescence. Legalization of marijuana: potential impact on youth. *Pediatrics*. 2004;113(6):1825–1826

17. Nierengarten MB. Guidelines needed for medical use of marijuana. *Lancet Oncol*. 2007;8(11):965

18. Wall MM, Poh E, Cerdá M, Keyes KM, Galea S, Hasin DS. Adolescent marijuana use from 2002 to 2008: higher in states with medical marijuana laws, cause still unclear. *Ann Epidemiol*. 2011;21(9):714–716

19. Wang GS, Le Lait MC, Deakyne SJ, Bronstein AC, Bajaj L, Roosevelt G. Unintentional pediatric exposures to marijuana in Colorado, 2009–2015. *JAMA Pediatr*. 2016;170(9):e160971

20. Annas GJ. Medical marijuana, physicians, and state law. *N Engl J Med*. 2014;371(11):983–985

21. Doblin RE, Kleiman MA. Marijuana as antiemetic medicine: a survey of oncologists' experiences and attitudes. *J Clin Oncol*. 1991;9(7):1314–1319

22. Charuvastra A, Friedmann PD, Stein MD. Physician attitudes regarding the prescription of medical marijuana. *J Addict Dis*. 2005;24(3):87–93

23. Nussbaum AM, Boyer JA, Kondrad EC. "But my doctor recommended pot": medical marijuana and the patient-physician relationship. *J Gen Intern Med*. 2011;26(11):1364–1367

24. Uritsky TJ, McPherson ML, Pradel F. Assessment of hospice health professionals' knowledge, views, and experience with medical marijuana. *J Palliat Med*. 2011;14(12):1291–1295

25. Khatapoush S, Hallfors D. "Sending the wrong message": did medical marijuana legalization in California change attitudes about and use of marijuana? *J Drug Issues*. 2004;34(4):751–770

26. Adler JN, Colbert JA. Clinical decisions. Medicinal use of marijuana–polling results. *N Engl J Med*. 2013;368(22):e30

27. Pew Research Center. Public support for legalizing medical marijuana: modest rise in percentage favoring general legalization. 2010. Available at: www.people-press.org/2010/04/01/public-support-for-legalizing-medical-marijuana/. Accessed May 2, 2015

28. Rosenberg AR, Dussel V, Kang T, et al. Psychological distress in parents of children with advanced cancer. *JAMA Pediatr*. 2013;167(6):537–543

29. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377–381

30. Carlini BH, Garrett SB, Carter GT. Medicinal cannabis: a survey among health care providers in Washington state. *Am J Hosp Palliat Care*. 2017;34(1):85–91

31. Kondrad E, Reid A. Colorado family physicians' attitudes toward medical marijuana. *J Am Board Fam Med*. 2013;26(1):52–60

32. Brooks E, Gundersen DC, Flynn E, Brooks-Russell A, Bull S. The clinical implications of legalizing marijuana: are physician and non-physician providers prepared? *Addict Behav*. 2017;72:1–7

33. Schwartz RH, Beveridge RA. Marijuana as an antiemetic drug: how useful is it today? Opinions from clinical oncologists. *J Addict Dis*. 1994;13(1):53–65

34. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. *JAMA*. 2015;313(24):2456–2473

35. Ananth P, Reed-Weston A, Wolfe J. Medical marijuana in pediatric oncology: a review of the evidence and implications for practice [published online ahead of print September 19, 2017]. *Pediatr Blood Cancer*. doi:10.1002/pbc.26826

36. Levy S, Weitzman ER. Building a learning marijuana surveillance system. *JAMA Pediatr*. 2016;170(3):193–194

37. Joy JE, Watson SJ Jr, Benson JA Jr, eds. *Marijuana and Medicine: Assessing the Science Base*. Washington, DC: National Academy of Sciences; 1999

38. Palamar JJ. An examination of opinions toward marijuana policies among high school seniors in the

United States. *J Psychoactive Drugs*. 2014;46(5):351–361

39. Chaudhry HJ, Hengerer AS, Snyder GB. Medical board expectations for physicians recommending marijuana. *JAMA*. 2016;316(6):577–578
40. Welsh J. Medical marijuana: a hazy state of affairs for nurses. *Am J Nurs*. 2014;114(8):19–20
41. Devinsky O, Marsh E, Friedman D, et al. Cannabidiol in patients with treatment-resistant epilepsy: an open-label interventional trial. *Lancet Neurol*. 2016;15(3):270–278
42. Braithwaite D, Emery J, De Lusignan S, Sutton S. Using the Internet to conduct surveys of health professionals: a valid alternative? *Fam Pract*. 2003;20(5):545–551
43. Sanderson A, Zurakowski D, Wolfe J. Clinician perspectives regarding the do-not-resuscitate order. *JAMA Pediatr*. 2013;167(10):954–958
44. Drug Enforcement Administration. DEA announces actions related to marijuana and industrial hemp. 2016. Available at: https://www.dea.gov/divisions/hq/2016/hq081116.shtml. Accessed September 9, 2016