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Cannabis use among patients with cutaneous lymphoma: A cross-sectional survey

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ABSTRACT

Objectives: To evaluate patterns of cannabis use in patients with cutaneous lymphoma (CL), as well as the association between cannabis use and itch specifically.
Design: Cross-sectional survey created in partnership with the Cutaneous Lymphoma Foundation (CLF).
Setting: The online survey was distributed electronically via email to the CLF listserv and links posted to social media over a 2-week period.
Main outcome measures: Respondents were classified as current cannabis users, prior users, and never users. A visual analog scale (VAS) was used to assess itching severity, improvement of itch, and interest in learning about cannabis.
Results: A total of 119 patient responses (61% female, mean age 59 y) were included in analysis. The majority had mycosis fungoides or Sézary syndrome (74%; 88/119) and early stage (IA-IIA) disease (56%; 48/86). Mean VAS itch score was 3.2 + 2.8 for the cohort. Over half (55%; 60/110) reported ever having used cannabis, with 22% (24/110) endorsing current cannabis use. Common methods of cannabis use were smoking (54%) and vaporizing (46%). 25% (6/24) of current users reported using cannabis specifically to treat itch; these respondents noted that cannabis resulted in moderate improvement of itching (mean 6.6/10). There was strong interest in learning more about cannabis and cancer, and most desired this information from their CL doctor/nurse.
Conclusions: Cannabis use is common among patients with CL, and patients report improvement of itching as a result of using cannabis. Further studies are needed to elucidate the risks and benefits of cannabis use in this patient population.

1. Introduction

Primary cutaneous lymphomas are a group of non-Hodgkin lymphomas that present in the skin and are classified as cutaneous T-cell lymphomas (CTCLs) or cutaneous B-cell lymphomas (CBCLs). Pruritus affects a significant proportion of patients with cutaneous lymphoma and can be a distressing symptom for patients. Pruritus is particularly common among those with CTCL, with up to 65% of patients reporting this symptom.[1] The degree of pruritus for patients with CTCL has been shown to correlate with advanced stage and worse survival.[2] Pruritus associated with cutaneous lymphoma is often not fully responsive to standard treatments, such as oral antihistamines and topical corticosteroids.[3]

In 2019, an estimated 48.2 million (17.5%) of Americans aged 12 or older reported using cannabis during the past year.[4] Approximately 10% of adult cannabis users in the United States report use of cannabis specifically for medical purposes.[5] Cannabis is currently approved for medical use in 36 states as well as for recreational use in 14 states.[6] Despite an increase in the availability of cannabis, much of the data available to patients regarding the risks and benefits of use originates

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from non-scientific sources: medical cannabis users report their knowledge regarding cannabis is primarily obtained from personal experiences and from the internet, including social media websites.[7]

Cannabis has been explored for many indications, particularly in the realm of palliative care, where pain and symptom control are a priority.[8] A focus of medical cannabis use has been within the field of oncology, due to its potential use as an antiemetic and for refractory cancer pain.[9–11] A study of adult cancer patients found that the most common indication for medical cannabis was pain (76%).[12] Another study of patients at a cancer center in Washington state found that 24% of patients had used cannabis in the last year, primarily for physical and neuropsychiatric symptoms.[13]

Interest in the impact of cannabis for dermatologic conditions has also increased due to the purported immunosuppressive, anti-inflammatory and anti-pruritic properties of cannabis.[14] Preclinical studies conducted by Oláh et al. suggest that cannabidiol (CBD) and other non-psychotropic phytocannabinoids have lipostatic, anti-proliferative, and anti-inflammatory effects on human sebocytes.[15,16] A recent open-label trial by Maida et al. demonstrated rapid wound closure of previously non-healing venous leg ulcers in patients treated with topical cannabis-based medicines.[17] There is also preliminary evidence that cannabis and its derivatives may play a role in the treatment of itch. The application of topical creams containing endocannabinoid lipids has shown relief of the pruritus associated with asteatotic eczema and uremic pruritus.[18,19]

We examined patterns of cannabis use and perceptions towards cannabis in a national sample of patients with cutaneous lymphoma. We hypothesized that there is a subset of patients with cutaneous lymphoma using cannabis specifically to treat itch. We also examined the association of disease stage and progression on cannabis use.

2. Materials and methods

A cross-sectional, anonymous survey of cutaneous lymphoma patients was conducted over a 2-week period in July 2019. We partnered with the Cutaneous Lymphoma Foundation (CLF), a non-profit patient advocacy organization, for distribution of this national survey. The 46-item questionnaire was distributed electronically via email and links posted to a social media patient affinity group. At the time of distribution, the CLF Facebook group had approximately 1900 members, while the email listserv had approximately 1200 members. Patient-reported survey responses were collected and managed using REDCap electronic data capture tools hosted at the University of Washington.[20,21] This study was reviewed and determined to be exempt from institutional review board review by the University of Washington Human Subjects Division (STUDY00005313).

Independent measures addressed demographics, cutaneous lymphoma type and stage, current treatments (including antipruritic medications), and itching severity. Survey content regarding cannabis use was adapted from previous studies by Pergam et al., Naing et al., and the PatientsLikeMe medical marijuana survey.[13,22,23] Questions were included to assess current and past cannabis use, frequency and methods of use (smoking, vaping, edibles, liquids, tinctures, topicals), reasons for use (selections included depression/to improve mood, fatigue, pain, anxiety, itch, improve appetite, nausea/stomach upset, “it helps treat my cancer”, “it helps me deal with stress”, "it helps me cope with my illness”, “I use cannabis (marijuana) recreationally/for enjoyment”), and impact of legalization on use (“Does or would legalization of cannabis (marijuana) make you more likely to use cannabis?”). Respondents were characterized as self-reported current users, prior users, and never users. Visual analog scale (VAS) was utilized for items assessing itching severity, interest in learning about cannabis (“Are you interested in learning more about cannabis (marijuana) use and cancer?), impact of legalization (”Does or would legalization of cannabis (marijuana) make you more likely to use cannabis?”), and improvement of symptoms (“To what degree has cannabis (marijuana) helped to improve your symptom(s)?” and “To what degree has cannabis (marijuana) helped to improve your itching?”). VAS scores for degree of improvement of symptoms were defined as minimal (0–3.3), moderate (3.4–6.6), or major (6.7–10).

Linear regression was used to model the relationship between number of current treatments and VAS itch score. Demographic variables that are categorical were compared between cannabis user groups using the chi-squared test (or Fisher’s test when appropriate) or t-test. P values less than 0.05 were considered statistically significant. All statistical analyses were performed using R software (version 4.1.0; R Foundation for Statistical Computing).

3. Results

A total of 128 survey responses were received; 9 incomplete responses were excluded, leaving 119 respondents for final analysis. Demographics of the cohort are summarized in Table 1. The majority of patients had mycosis fungoides (MF) or Sézary syndrome (SS) (74%; 88/119), followed by CD30 + lymphoproliferative disorders (primary cutaneous anaplastic large cell lymphoma or lymphomatoid papulosis; 31%; 26/119). Among patients with MF/SS who reported their stage (N = 86), 56% had early-stage disease (stages IA, IB, or IIA) while 22% had advanced-stage disease (stages IIB through IVB). The most frequently reported antipruritic treatments currently used by our cohort were emollients (45%), topical corticosteroids (36%), oral antihistamines/antipruritics (15%), and gabapentin (13%) (Table 2). The mean VAS itch score in our cohort overall was 3.15 (± 2.83) on a 0–10 scale. The VAS itch score increased by 0.35 points for every additional treatment method used (including skin-directed and systemic treatments) ($p = 0.021$).

Overall, 55% (60/110) of those surveyed in our cohort reported ever having used cannabis. Specifically, 24/110 respondents (22%) reported currently using cannabis, with nearly half of these patients (n = 10) starting cannabis use after their cutaneous lymphoma diagnosis. Of the 24 patients currently using cannabis, only 38% had told their cutaneous lymphoma physician/team about their cannabis use. The majority (79%; 19/24) of active users used cannabis at least once a week and 67% (16/24) used cannabis at least daily; 33% (8/24) used cannabis multiple times a day. The most common methods of cannabis use reported were smoking (54%), vaporizing (46%), edibles (33%), and topical creams/ointments (29%). Although most (63%; 15/24) active users obtained cannabis from a medical or recreational dispensary, 38% (9/24) acquired their cannabis from a source outside of a dispensary (i.e., growing cannabis, obtaining from friend/dealer).

Active users reported using cannabis most frequently for anxiety and to help deal with stress, followed by pain and depression/to improve mood. A quarter (6/24) of active users reported using cannabis specifically to treat itch. In addition, 13% (3/24) reported using cannabis because they believed it helped treat their lymphoma. Regardless of reasons for use, cannabis use was associated with self-reported improvement of symptoms overall (mean 6.2/10). Among patients using cannabis for itch, cannabis use was associated with moderate improvement of itching (mean 6.6/10).

There were no significant differences in cannabis use (ever users vs. never users) by age or employment status. In addition, no significant difference was found between current vs. prior cannabis use by stage of cutaneous lymphoma, average VAS itch score, or worsening disease status (Table 3). A significantly higher proportion of patients identifying as non-white did not feel comfortable discussing cannabis use with their cutaneous lymphoma doctor (0.707 vs. 0.402, $p = 0.001$).

Among all respondents, there was a strong interest in learning more about cannabis in the context of cancer (mean 7.5/10), with the most cited reason being that cannabis “is considered a natural treatment”. Although 68% (75/110) preferred to go to a cutaneous lymphoma doctor/nurse for this information, only 0.8% (1/119) had received information about cannabis from their cancer team (Fig. 1). Patients

Table 1
Demographics of respondents.

	Value[a]
Gender	
Female	65 (61)
Male	39 (37)
Prefer not to say	2 (2)
Age, years (range 23–83 years)	59 + 15.6
Race/ethnicity	
Asian	3 (3)
American Indian or Alaska Native	0
Black or African American	4 (4)
Hispanic or Latino	7 (7)
Native Hawaiian or Other Pacific Islander	0
White	87 (85)
Multiple races	1 (1)
Education	
High school or less	10 (9.5)
Some college	19 (18)
Associate's or Bachelor's degree	49 (47)
Graduate or professional degree	27 (26)
Employment	
Disabled	6 (5)
Employed	50 (42)
Student	2 (1.7)
Retired	46 (39)
Unemployed	4 (3.4)
Health insurance/coverage status	
Commercial insurance	60 (50)
Medicare	46 (39)
Medicaid	2 (1.7)
Veterans Affairs or Tricare	4 (3.4)
Charity care	0
Other	13 (11)
No insurance or coverage	5 (4.2)
Time since diagnosis	
< 1 year	20 (18)
1–5 year	42 (37)
> 5 years	52 (46)
6–10 years	24
11–20	14
> 20	14
Status of lymphoma[b]	
Newly diagnosed	12 (10)
Getting worse	12 (10)
Stable or improving	96 (81)
Type of cutaneous lymphoma†	
CBCL	8 (6.7)
Mycosis Fungoides/Sézary Syndrome	88 (74)
pcALCL or LyP	31 (26)
Other	2 (1.7)
Unsure	2 (1.7)
Stage (MF/SS only)	
Early (IA-IIA)	48 (56)
Advanced (IIB-IVB)	19 (22)
Unsure/don't know	19 (22)
Itch score (VAS)	
Overall	3.15 ± 2.83
Early (IA-IIA)	2.61 ± 2.55
Advanced (IIB-IVB)	4.51 ± 2.95

Abbreviations: CBCL, cutaneous B-cell lymphoma; pcALCL, primary cutaneous anaplastic large cell lymphoma; LyP, lymphomatoid papulosis; MF, mycosis fungoides; SS, Sézary syndrome; VAS, visual analog scale.

[a] Values are no. (%) or mean + standard deviation; respondents with missing values were excluded from the corresponding summary: gender (n = 13), age (n = 22), race/ethnicity (n = 17), education (n = 14), time since diagnosis (n = 5), stage (n = 2).

[b] Multiple selections were possible, so percentages exceed 100%.

reported the most frequent sources of information about cannabis use were websites/blogs (22%), social media (20%), and friends/family members (19%). Over one-third reported that they had not received any information. Patients did report that legalization of cannabis does/would make them somewhat more likely to use cannabis (mean 6.0/10-point scale).

Table 2
Itch treatments among patients with cutaneous lymphoma.

	Number (%)[a]
Emollients (moisturizers)	53 (45)
Topical corticosteroids	43 (36)
Topical anesthetics (lidocaine, pramoxine)	8 (7)
Topical antihistamines (Benadryl)	9 (8)
Oral antihistamines/antipruritics (Benadryl, hydroxyzine)	18 (15)
Aprepitant	0
Gabapentin	15 (13)
Mirtazapine	1 (0.8)
Other[b]	6 (5)

[a] Multiple selections were possible, so percentages exceed 100%.

[b] Includes cannabis and naltrexone.

Table 3
Cannabis use and demographics (current vs. prior vs. never users).

	Cannabis use[a]			
	Current users (N = 24)	Prior users (N = 36)	Never users (N = 50)	P-value[b]
Disease Stage				1.00
Early (IA-IIA)	7 (47)	14 (52)		
Advanced (IIB-IVB)	8 (53)	13 (48)		
Itching severity VAS	1.4 (0.7–3.1)	3.2 (0–5.4)		0.22
Current status of disease				1.00
Worsening	2 (9)	3 (8)	5 (10)	
Improving, stable, observation, or in remission	21 (91)	33 (92)	45 (90)	

Abbreviations: VAS, visual analog scale.

[a] Values are no. (%) or median (inter-quartile range).

[b] Comparison of cannabis current/prior/never user groups using chi-squared test or t-test.

4. Discussion

We found that cannabis use is more common among patients with cutaneous lymphoma than the general population, with 55% reporting lifetime cannabis use and 22% reporting current use. Specifically the proportion of active users in our cohort is double that of the general United States population, where an estimated 31.6 million people aged 12 or older (11%) report using cannabis in the past month.[4] Notably this difference becomes even greater in comparison to rates among older adults (> 50 years), with recent studies estimating past-year cannabis use between 4.2% and 8.9%.[24,25] These studies of older adults provide a more suitable comparison for our findings given the mean age of 59 years in our cohort. Although there is a lack of existing literature about rates of cannabis use in dermatology, the prevalence of cannabis use in our cohort is similar to the prevalence reported for cancer patients. A 2018 study of patients attending cancer centers in Canada found that 43% reported any lifetime cannabis use, with 18% of patients reporting use within the last 6 months.[26] In addition, the Pergam et al. study of cancer patients in Washington state found that 66% had ever used cannabis and 21% used cannabis in the last month.[13] Interestingly, we found that nearly half of current cannabis users in our study started using cannabis after their cutaneous lymphoma diagnosis. This suggests that the high rates of cannabis use in these patients may be at least partially associated with seeking treatment options for symptoms related to their disease.

Respondents in our study reported using a variety of cannabis products, with smoking and vaporizing being the most common methods of use. Among active users, nearly 30% reported using topical cannabis products (creams, ointments, etc.). The rate of topical application is important to note given the increase in both availability and demand of topical cannabis products for medical uses, including pain,

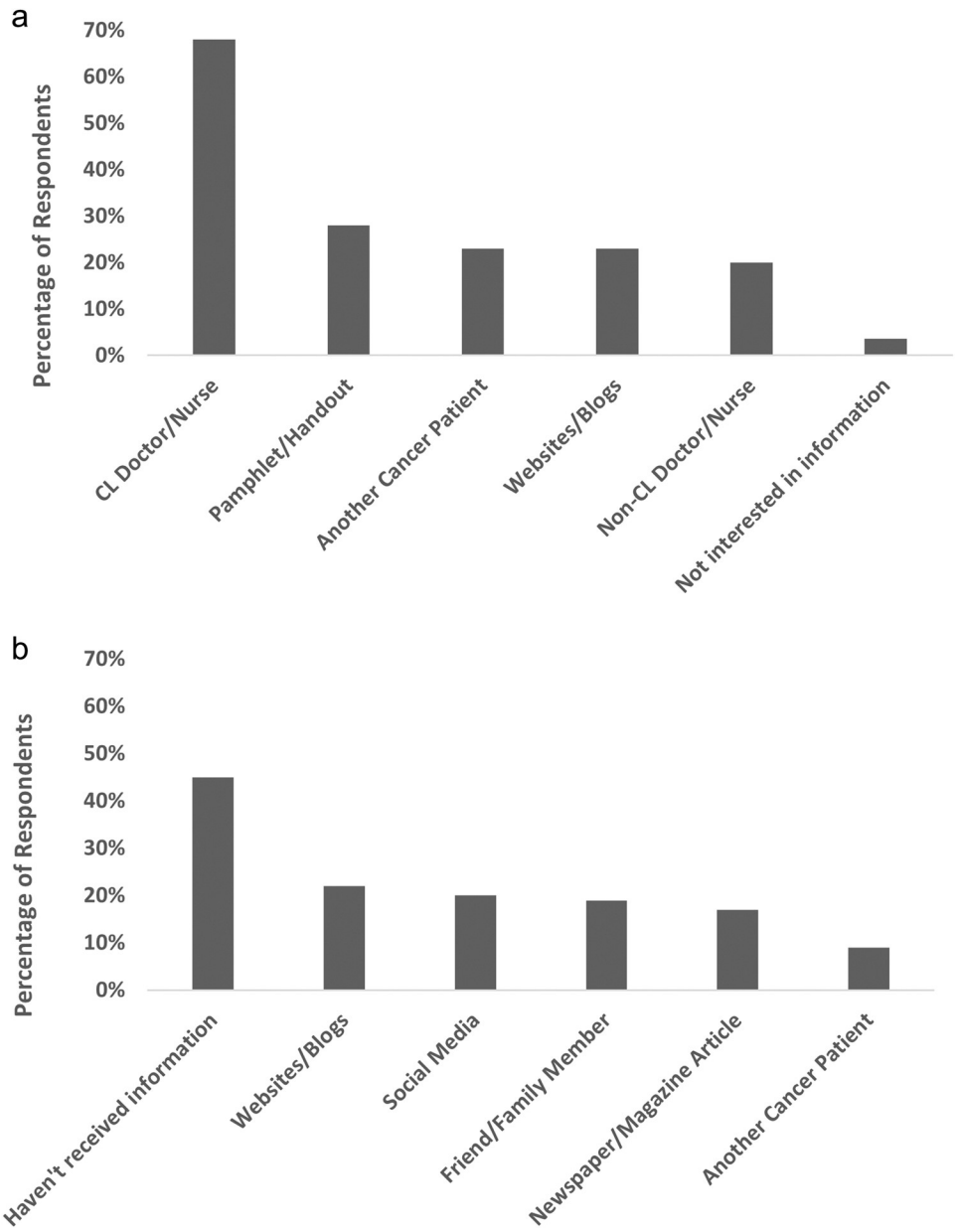

Fig. 1. a. Cutaneous lymphoma patients' desired sources of information about cannabis use and cancer. The responses were not mutually exclusive. Abbreviations: CL, cutaneous lymphoma. **b.** Cutaneous lymphoma patients' current sources of information about cannabis use and cancer. The responses were not mutually exclusive.

pruritus, and general skincare.[27–29] We did not assess if respondents' cannabis products contained tetrahydrocannabinol (THC), cannabidiol (CBD), or a combination of both. Preclinical and early clinical data that cannabinoids, particularly topical CBD, may be useful for relief of inflammatory symptoms and pruritus,[30,31] and distinction between the types of cannabinoids used and response will be important to examine in future studies.

We also found that most (63%) active users in our cohort obtained cannabis from a medical or recreational dispensary. Although we did not specifically inquire about cannabis laws for each respondent's state of residence, it is possible that patients living in states without legalized medical cannabis would be more likely to obtain it illegally in inhaled forms (i.e., smoking or vaporizing). Alternatively, patients from states with access to medical and/or recreational dispensaries may have higher consumption of non-inhaled products such as edibles, as suggested by previous studies.[32,33] Further investigations are needed to clarify patterns of cannabis sources as well as potential differences between the variety of cannabis products available to patients. Active cannabis users in our cohort reported use for a wide variety of reasons, most frequently for depression and/or anxiety (63%) and pain (46%). These indications for use are comparable to a 2017 national online survey which found that the most common medical reasons for marijuana use were anxiety (49%), insomnia (47%), chronic pain (42%), and depression (39%).[34] In a recent U.S. study analyzing state registry data on medical cannabis qualifying conditions, chronic pain was the most common condition reported by patients at 67.5%.[35] Several trials have found preliminary evidence that cannabis improves chronic and neuropathic pain.[36,37] Furthermore, a 2017 report from the National Academies of Sciences, Engineering, and Medicine suggests cannabis can be beneficial for cancer patients, noting there is "conclusive or substantial evidence" that cannabis is effective for the treatment of chronic pain in adults.[38] It is also important to note the concerns regarding the safety of cannabis use in immunosuppressed populations, such as the potential for fungal contamination of cannabis products.[39,40] It is clear that more research is

needed to further investigate the efficacy and possible risks of cannabis use in this patient population.

Notably 25% of our active users reported using cannabis specifically to treat itching, with those respondents also reporting noticeable improvement of their itch that they attributed to their cannabis use. Among those using cannabis for itch, vaporizing and topical creams/ointments were the most common methods of use. These findings are supported by clinical studies that have shown a reduction in pruritus by cannabis in several dermatologic diseases, including atopic dermatitis, psoriasis, and prurigo nodularis.[41,42] Additionally, in a preliminary study of patients with uremic pruritus on maintenance hemodialysis, topical application of a cream containing structured physiological lipids with endocannabinoids completely eliminated pruritus in 38% of patients after 3 weeks.[18] In our cohort, however, we did not find a statistically significant difference between the average VAS itch score of cannabis users vs. non-users.

The frequency of cannabis use in this study reinforces the findings from our prior study investigating integrative medicine (IM) use in patients with CTCL, which demonstrated that a majority (59%) of patients were using at least one form of IM for their disease.[43] This aligns with the known association of advanced-stage disease with greater itching severity,[1] as patients with later disease stage often require more complex treatment regimens and may have symptoms that are less responsive to conventional treatments. The chronic, intractable pruritus of cutaneous lymphoma causes significant distress to patients with an adverse effect on health-related quality of life.[44] It is likely that conventional therapies are not sufficiently controlling itch in this population, and patients are looking for effective alternatives such as cannabis.

It is important to note that the mean itch score of 3.15 in our study is slightly lower compared to a larger cohort of CTCL patients with a mean of 4.2.[1] This could suggest that our data may under-represent itching severity and therefore the number of treatment methods used in the larger cutaneous lymphoma population.

Patients with cutaneous lymphoma in our cohort reported that legalization of cannabis does or would make them more likely to use cannabis. Respondents also had a high level of interest in learning more about cannabis use and cancer, with nearly 70% desiring this information from their cutaneous lymphoma provider, though most who did receive information received it from sources like websites/blogs and social media. This is important, as there is increasing availability of internet-based information on cannabis. In a recent study analyzing internet sources on medical cannabis, content varied widely across sites; cannabis was frequently mentioned for treatment of health conditions without empirical support for these claims.[45] A 2019 survey also found that websites of dispensaries in Canada, the United States, and Europe contained numerous unsubstantiated claims regarding dermatologic uses of medical cannabis.[46] Furthermore, many healthcare providers report considerable gaps in cannabis knowledge and consider this to be a barrier to educating and supporting patients on medical cannabis use.[47,48] Notably cannabis coaches or cannabis literate doctors were not included as an option on our survey, although this may be a source of information for some patients in medical cannabis legal states.[49,50] Although many patients in our cohort desired information about cannabis use from their healthcare providers, only a small fraction actually received this. True patient centered care will require efforts to promote physician education and open communication between patient and physicians regarding cannabis use.

Patients in our cohort who identified as non-white reported feeling less comfortable discussing cannabis with their cutaneous lymphoma doctor than those who identified as white. This finding is likely related to the complex history of federal drug policy and its impact on marginalized communities; one such example is the War on Drugs, during which disproportionately high numbers of African-American people were incarcerated.[51] People of color are also more highly scrutinized for using cannabis than white people.[52,53] A study by Mortensen et al. found that when criminal or "stoner" stereotypes were used by the media they were more likely to feature people of color.[54] This discomfort around discussing cannabis use with their physician reported by non-white respondents in our cohort is especially notable as literature supports that patients have increased comfort in discussing their healthcare problems and have higher patient experience ratings when there is racial/ethnic concordance between patients and their physicians.[55,56] This is problematic as there is a significant lack of diversity of physicians caring for these patients; dermatology, for example, is one of the least diverse of all medical specialties.[57]

We did not find a significant correlation between cannabis use and age or employment status. This differs from prior literature that cannabis use is more common among young adults and unemployed individuals,[4,58,59] although these trends may change with the increasing cost of cannabis in the current market. Although we hypothesized that patients with advanced stage and/or worsening disease would be more likely to use cannabis, we found no such differences in our cohort. Our data suggest that use patterns may not differ based on numerous demographic factors, but the lack of such differences could also be attributable to response bias and the relatively small sample size in our study.

There are several limitations to this preliminary study. The small sample size may limit the generalizability of our findings. Our data may be subject to selection bias, with patients who have a strong interest in cannabis being more likely to participate in the survey. Although respondents may have initially been hesitant to disclose their cannabis use due to its status as an illicit drug, this was likely not a concern after consenting to participate in the study given the anonymous, online survey format. In addition, this survey was distributed electronically via social media and email listservs of a cutaneous lymphoma specific organization, and therefore a response rate could not be determined. It is also important to note that our survey study is cross-sectional in nature, and we cannot identify a temporal relationship between variables; additional studies are needed to further investigate potential associations of cannabis use with itch and other patient demographics. Although the mean age of our cohort (59 years) is similar to the average age of cutaneous lymphoma patients,[60] the majority (61%) of our respondents identified as female as opposed to the previously documented male predominance of CTCL patients.[61] Our sample also contained a low number of non-white respondents; as incidence rates of CTCL are higher among those who identify as African-Americans than those who identify as white, our data may not be entirely generalizable.[62] Additionally, our cohort had an over-representation of patients with MF/SS and a lower proportion of those with CBCL as compared to the reported relative frequencies in the greater cutaneous lymphoma population.[63]

In summary, we found that cannabis use is more common among patients with cutaneous lymphoma when compared to the general United States population. Patients with cutaneous lymphoma are interested about using cannabis as an adjunct treatment and are eager to engage with their medical care team regarding its use. Although those who have used cannabis to treat symptoms of their disease reported improvement, additional studies are needed to further evaluate the risks and benefits of cannabis use in this patient population. We hope that the findings of this preliminary study may guide future projects or generate hypotheses to further investigate the patterns of cannabis use among patients with cutaneous lymphoma.

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CRediT authorship contribution statement

Heather M. Mahurin: Writing – original draft, Writing – review & editing. **Olivia R. Ware:** Conceptualization, Writing – review & editing. **Tyler D. Coolman:** Conceptualization, Writing – review & editing.

Philip A. Stevenson: Data curation, Formal analysis. **Steven A. Pergam:** Conceptualization, Writing – review & editing. **Michi M. Shinohara:** Conceptualization, Investigation, Supervision, Writing – review & editing.

Declarations of interest

Steven A. Pergam reports support from Global Life Technologies, Inc (research grant to institution); serves on the Vaccines and Related Biological Products Advisory Committee (FDA), International Council Member (ICHS), and ACIP, Zoster Vaccine Committee (CDC); and participation in clinical trials with Chimerix and Merck.

Michi M. Shinohara reports honoraria from Medscape Live (Cutaneous Malignancies Forum November 2020); participation on the Medical Advisory Council for the Cutaneous Lymphoma Foundation; and serves on the Board of Directors for the Women's Dermatologic Society, Society of Dermatology Hospitalists, and United States Cutaneous Lymphoma Consortium.

The authors have no other potential conflicts of interest to disclose.

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