Holy Smokes!
Cannabis use is becoming more prevalent among patients with cancer in large part due to the benefits the drug brings, like managing multiple symptoms and patients experiencing minimal treatment-related side effects. As more states legalize or decriminalize cannabis and the stigma on its use decreases, patients appear to have an increased interest in implementing cannabis into their treatment regimen. However, patients and healthcare providers often lack knowledge about cannabis, including its risks and benefits, specific dosing recommendations, and nationwide or state-based legality.

The Cannabis and Cancer Research and Education Clinic (CanCaRE) at HealthPartners Fraunesshuh Cancer Center in St. Louis Park, Minn., looks to bridge this gap. The clinic was developed by Dylan Zylla, MD, MS, an oncologist and medical director of the HealthPartners Cancer Research Center, and Sarah Jax, APRN, CNP, an oncology and hematology advanced practice provider (APP). The initial goals of the clinic were twofold: 1) to provide education for patients with cancer interested in incorporating safe and effective cannabis use into their care plan and 2) to create a robust registry of patients with cancer who are actively using cannabis and leverage this real-world data to inform oncology providers and patients. The CanCaRE clinic offers virtual one-on-one consultations to educate patients about cannabis-related questions and concerns; the clinic also provides updates on completed clinical trials and ongoing research opportunities regarding cannabis use in oncology.

In 2017 the National Academies of Sciences, Engineering, and Medicine concluded that there is substantial evidence that cannabis is a treatment option for chronic pain and chemotherapy-induced nausea and vomiting.

Cannabis in Oncology

At a federal level, cannabis remains classified as a Schedule I drug with no known medical uses. However, the legalization of cannabis, both medically and recreationally, continues to expand at the state level across the United States. Approximately 25 percent of patients with cancer at one comprehensive cancer center in Seattle, Wash., used cannabis within the past year, with nearly two-thirds of patients expressing a moderate to high interest in education about cannabis use during their cancer treatment. Additionally, nearly 40 percent of patients believe that cannabis may have anticancer properties. These patients want information from trusted sources (i.e., their care team) but often report getting information from family, friends, and/or online.
Cannabis Use and Cancer-Related Symptoms
The growing popularity of cannabis use has increased efforts to study its impact on symptom management. Accumulating evidence suggests the cannabis can enhance quality of life through improvement of many cancer-related symptoms. In 2019, we published a comprehensive review article that addresses cannabis’s availability and legality, as well as the safety and efficacy of the drug’s use through review of completed clinical trials and observational studies. In addition, we analyzed the safety and efficacy of cannabis in a state-sponsored cannabis program (the Minnesota Medical Cannabis Program) and found that patients with cancer who used cannabis over a four-month period reported significant improvement in:

- Chemotherapy-induced nausea and vomiting
- Depression
- Disturbed sleep
- Fatigue
- Lack of appetite
- Pain.

In 2017 the National Academies of Sciences, Engineering, and Medicine concluded that there is substantial evidence that cannabis is a treatment option for chronic pain and chemotherapy-induced nausea and vomiting. Of particular interest is the impact cannabis may have on opioid requirements. For patients with cancer-related pain, opioids are often prescribed, but they can lead to troublesome side effects, such as constipation, mental foginess, fatigue, and nausea. Furthermore, the opioid epidemic has made patients fearful of “becoming addicted” to opioids, and thus, patients inquire about alternative analgesic options. In chronic, non-cancer-related pain, cannabis helps patients reduce or eliminate opioid use altogether. Large observational studies in patients with cancer have shown that 36 percent no longer use opioids while using medical cannabis, and nearly 10 percent of patients can reduce overall opioid consumption. Although cannabis may not completely omit the need for opioids in severe cancer-related pain, its ability to limit opioid use could have other beneficial impacts on patients’ quality of life.

Educating Providers about Cannabis
Although patients want information from their cancer provider(s), less than 15 percent of patients actually receive this information from their cancer care teams. Over half of oncologists support the use of medical cannabis, yet most do not feel well-informed to make clinical recommendations. However, oncologists are interested in learning about cannabis. We conducted a statewide survey and discovered that 85 percent of oncology providers want more education about medical cannabis. Despite growing interest, barriers, such as perceived patient cost and inadequate data, limit these discussions with qualified patients. Patients and providers often face certain challenges when considering cannabis. A key goal of the CanCaRE clinic is to provide education and research updates on cannabis to enhance awareness and provide safe, effective, and cost-efficient product recommendations to interested patients.

Cost Considerations
The federal status of cannabis prohibits insurance coverage of medical cannabis unless it is one of the few approved prescriptions by the U.S. Food and Drug Administration (FDA) for synthetic delta-9-tetrahydrocannabinol (e.g., dronabinol, nabilone). However, these FDA-approved agents are infrequently prescribed given their poor tolerability, which may result from omitting the cannabidiol (CBD) that mitigates the unwanted “high” of tetrahydrocannabinol (THC). Similarly, state-based medical cannabis products are not covered by insurance. Therefore, all costs associated with using medical cannabis are out-of-pocket expenses for patients. Oncology providers report that one of the highest barriers to patient use of cannabis was perceived to be costs. Further, approximately 50 percent of patients indicate cost as a barrier to use. On average, patients with chronic, non-cancer-related pain spend about $3,000 in accessing and using cannabis per year. This potentially high expense can be prohibitive for patients already burdened by medical costs related to their cancer treatment. At CanCaRE, we strive to create cost-effective plans through individual dosing regimens for our patients.

Safety Considerations
Another consequence of the federal classification of cannabis is a lack of robust randomized and observational trial data. Cancer care teams can be apprehensive about the safety profile for cannabis, especially regarding its implications on current treatment and potential side effects. Although cannabis is generally perceived as a safe adjunct therapy for standard intravenous chemotherapies, its impact on metabolism of novel targeted agents is less clear. Furthermore, cannabis can have anti-inflammatory and immunomodulatory effects that might impact patients who are receiving immunotherapy. Small, retrospective studies have reported lower response rates and shorter survival in cannabis users who receive immunotherapy. In our CanCaRE clinic, we review this data and generally advise patients to omit or severely limit cannabis use while they are on immunotherapy. Pharmaceutical-grade cannabis extracts may be safer than whole plant/smokeable products as they are tested for potency (i.e., exact amount of THC/CBD/other terpenes) and purity (e.g., toxic chemicals and heavy metals). While lung cancer risk is likely low, there is potential for fungal infection with inhaling raw plant.

State-Specific Laws and Regulations
In Minnesota, medical cannabis is legal through the Minnesota Medical Cannabis Program. Patients who reside in Minnesota and meet at least one of the qualifying conditions are eligible for the registry. For patients with cancer, qualifying conditions include, but are not limited to:

- Cancer associated with severe or chronic pain, nausea or severe vomiting, and/or cachexia or severe wasting
- Terminal illness with a probable life expectancy less than one year and if illness or treatment produces severe or chronic pain, nausea or severe vomiting, and/or cachexia or severe wasting.
These qualifying condition(s) must be confirmed by a healthcare practitioner who is registered with the state to certify patients for the program.

However, medical cannabis and the associated costs for registering with the state program are not covered by health insurance. Annual enrollment in the Minnesota Medical Cannabis Program is $200 (or $50, if patients receive federally funded medical assistance, such as Medicaid or Supplemental Security Income). All cannabis products purchased through the program are out-of-pocket costs for patients.

Once a patient is certified by the state program, he or she can purchase up to a 30-day supply of medical cannabis through one of two state-sponsored dispensaries. At the dispensary, patients consult with a licensed pharmacist to determine the appropriate formulations of cannabis for their specific needs. Current state legislation only allows pharmaceutical-grade extracts. However, this summer, smokeable cannabis plant will be available for eligible adults in the program. Before each subsequent purchase, a self-evaluation is required.

**Anticancer Properties**

At CanCaRE, patients occasionally ask about using cannabis to treat cancer. We recently published a comprehensive review article on cannabis as an antitumor agent through assessment of case reports and clinical data. Additionally, we conducted a nationwide survey to find patients who had an anti-tumor benefit after cannabis use. Although there are intriguing *in vitro* and *in vivo* studies to support this theory, no prospective clinical trials have shown the clear ability of cannabis to treat or control cancer in patients. However, our research center is developing pilot studies that will evaluate the use of high-dose CBD protocols in patients with refractory glioblastoma and other terminal cancers.

**CanCaRE Clinic Referral Process**

All oncology providers at the HealthPartners Frauenshuh Cancer Center are informed of the CanCaRE clinic and encouraged to refer patients who are interested in learning more about cannabis to the clinic. Information about the clinic is printed on small stick cards and fliers, which allows patients to self-refer. One of the cancer center’s lead schedulers is assigned to coordinate all initial and follow-up visits to the CanCaRE clinic. Patients interested in one-on-one education are then scheduled for a video or phone consultation with a CanCaRE APP.

Our current staffing model involves one advanced practice provider (APP), who does all consults and follow-up visits four hours a week. Most CanCaRE patients request a follow-up visit within four to six weeks. Thus far, patient wait times for our consults have averaged less than two weeks. Our cancer center employs 15 oncologists who see about 2,904 new patients each year. This year, we plan to add one additional APP at four hours a week to expand our clinic’s services to our affiliate, HealthPartners Cancer Center at Regions Hospital in St. Paul, Minn., which employs 10 full-time oncologists who see about 1,758 new patients each year.

**Initial CanCaRE Visit and Education**

In addition to addressing patients’ questions, the CanCaRE APP reviews the many common concerns patients have about cannabis use. During the initial 45- to 60-minute consultation, patients are educated on the compounds of medical cannabis (e.g., THC vs. CBD) and how different formulations and doses of these compounds can provide potential relief for different symptoms, such as cancer-related pain, insomnia, and appetite stimulation. The APP also discusses the enrollment process, including information on Minnesota’s two medical

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*Figure 1. Important Questions to Address with Patients when Incorporating Cannabis into the Cancer Treatment Plan*

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cannabis dispensaries, and the costs of cannabis products. Safety of medical cannabis is reviewed, including potential side effects, as well as drug interactions of medical cannabis with patients’ prescribed chemotherapy or immunotherapy regimen.

If a patient meets the criteria for participation in the Minnesota Medical Cannabis Program and wants to enroll, the CanCaRE team works with his or her primary oncologist on how best to get the patient certified by the program. Other costs associated with cannabis certification or product purchasing are discussed at the patient’s consult visit, where we provide detailed pricing lists from each of the state’s cannabis dispensaries.

The CanCaRE APP visits were modeled after our cancer center’s integrated palliative care clinic, and these visits are billed to insurance.

**CanCaRE Registry Data**

A REDCap registry was created to assess patients’ current symptoms, medication use, and cannabis history prior to their initial clinic consult (Figure 2, below). The 16-page CanCaRE Intake Survey is available online at accc-cancer.org/cancare-intake.

Creating the REDCap registry required assistance and input from a multidisciplinary team that includes CanCaRE clinicians, a research intern, staff from our Survey and Evaluation Research Department, and an oncology research coordinator. CanCaRE clinicians use this registry data to tailor patients’ visits to their individualized needs and symptoms and to better inform product recommendations. An intake survey includes questions on patients’ past medical history, including if they have high-risk conditions (e.g., heart disease or schizophrenia). We also obtain a detailed medication history with a focus on antiemetic and anti-anxiety medications, opioids, and other analgesia usage. Finally, patients answer questions about their past and current cannabis use to help determine their ideal product(s) and dosage of cannabis for their treatment.

The registry sends automatic reminders to patients so they complete the intake survey prior to their consult. Following the initial visit, emails are auto-generated for patients and include product and dosing recommendations, as well as their follow-up plans. Finally, a short survey on symptom management and cannabis use is sent via text or email (based on patient preference) every four weeks to capture longitudinal data on product use patterns, efficacy, and safety.

**Metrics and Patient Satisfaction**

CanCaRE welcomed patients in December 2020. As of October 2021, our clinic providers have completed initial consultations with 69 patients and follow-up visits with 12 patients. On average, each appointment takes 40 minutes, with 27 minutes of face-to-face interaction. In April 2021 we implemented the REDCap registry, and approximately 75 percent of our patients completed the intake survey.

CanCaRE patients average in age 62 years old. Ninety-three percent have a solid tumor, with 55 percent having Stage IV cancer (Table 1, right). Of the 80 percent of patients with a current treatment plan, over half have a palliative goal of care. In addition, 61 percent of patients are in their first year of treatment.

In July 2021 we conducted a brief patient satisfaction survey. Twenty patients were contacted six to eight weeks after their initial consult. Ten of the 11 patients who responded felt they had learned and benefited from their appointment and recommended CanCaRE to their family members and friends with cancer.

**Future Directions**

Although the CanCaRE clinic is relatively new, the high level of interest among our patients and clinicians requires strategic planning for future growth. The following are key areas to explore to ensure more patients with cancer can obtain adequate cannabis education:

**CanCaRE Registry Data**

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**Figure 2. CanCaRE REDCap Registry Data from Varying Timepoints**

**Pre-Visit**
- Cancer diagnosis
- Potential confounding diagnoses
- Cancer treatment
- PRO-CTCAE® questionnaires
- Previous cannabis use
- Current medications
- Demographics

**Initial visit**
- Review pre-visit information
- Current cannabis use/products
- New recommendations

**Follow-Up Visit**
- Review/update medical history
- PRO-CTCAE questions from pre-visit survey
- Review/update cannabis
- Review/update medications

PRO-CTCAE® = National Cancer Institute’s Patient Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE®)
Table 1. CanCaRE Metrics and Patient Satisfaction Survey

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<th>Patient Metrics</th>
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<tbody>
<tr>
<td>Average age</td>
<td>62</td>
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<tr>
<td>Current treatment plan</td>
<td>80</td>
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<tr>
<td>First-year treatment</td>
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<tr>
<td>Palliative goal of treatment</td>
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<tr>
<td>Solid tumor</td>
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<tr>
<td>Stage IV</td>
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<tr>
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<tr>
<td>Average total time (min)</td>
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<tr>
<td>Complete pre-visit survey (%</td>
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<tr>
<td>Total follow-ups</td>
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<tr>
<td>Total patients seen</td>
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<table>
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<th>Patient Satisfaction Survey</th>
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<tr>
<td>Learned/benefited (%)</td>
<td>95</td>
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<tr>
<td>Recommend CanCaRE (%)</td>
<td>96</td>
</tr>
<tr>
<td>Response rate (%)</td>
<td>55</td>
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</tbody>
</table>

- Growth and expansion of CanCaRE to serve patients throughout Minnesota
- Analysis of CanCaRE registry data to improve our understanding of the patient experience and better tailor cannabis product recommendations
- Collaboration with other cancer centers across the United States to further enhance education and research opportunities to all patients living with cancer.

Sarah Jax, APRN, CNP, is an oncology/hematology advanced practitioner; Katherine Schmicheen is research intern; and Dylan M. Zylla, MD, MS, is an oncologist and medical director of the HealthPartners Cancer Research Center at HealthPartners Fraenushub Cancer Center in St. Louis Park, Minn.

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Supplemental Material
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References