VERMONT ACADEMIC DETAILING PROGRAM

Cannabinoids

The University of Vermont
LARNER COLLEGE OF MEDICINE
OFFICE OF PRIMARY CARE

This page is intended to be blank to facilitate double-sided photocopying.

VERMONT ACADEMIC DETAILING PROGRAM

THE VERMONT ACADEMIC DETAILING PROGRAM delivers education sessions to healthcare professionals throughout Vermont. The Program is offered by the University of Vermont's Larner College of Medicine Office of Primary Care with funding from public and private sources, including the State of Vermont. We receive no funding from the pharmaceutical industry. Our goal is to promote high quality, evidence-based, patient-centered, and cost-effective treatment decisions by healthcare professionals.

Program Contact Information

Laurie McLean, Vermont Academic Detailing Program Coordinator
The Vermont Academic Detailing Program
UVM Larner College of Medicine Office of Primary Care, UHC Campus, Arnold 5
1 South Prospect Street, Burlington, Vermont 05401
Phone: (802) 656-2179; Email: opc@uvm.edu; Web: www.vtad.org

Academic Detailers

Amanda G. Kennedy, PharmD, BCPS
Email: amanda.kennedy@uvmhealth.org

Richard G. Pinckney, MD, MPH
Email: richard.pinckney@uvmhealth.org

Charles D. MacLean, MD
Email: charles.maclean@uvmhealth.org

Gary Starecheski, RPh
Email: gary.starecheski@uvmhealth.org

Note: The academic detailers have no conflicts of interest to declare.

Continuing Education Credit

In support of improving patient care, The Robert Larner College of Medicine at The University of Vermont is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

AMA:
The University of Vermont designates this live activity for a maximum of 1 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ANCC:
This program has been reviewed and is acceptable for up to 1 Nursing Contact Hours.

Vermont Board of Pharmacy:
Pharmacists may claim this live activity as 1 AMA PRA Category 1 Credit for Vermont licenses.

VERMONT ACADEMIC DETAILING PROGRAM

Topic: Cannabinoids

This session highlights the practical aspects of managing patients prescribed or using cannabinoids in primary care, with a focus on the available evidence-base. This session includes information about prescription, medical marijuana, and over-the-counter cannabinoid products (e.g. CBD) and discusses the risks and benefits of various options. The session also includes resources for patient education.

Objectives

1. To review the evidence-base for cannabinoid products, including prescription, medical marijuana, and over-the-counter options (e.g. CBD)
2. To provide patient education resources for patients interested in learning more about cannabinoids

Notes

- **The content of this activity is on the topic of Pharmacotherapeutics.** This topic includes drug specific information, safe prescribing practices, new evidence-based updates for medications, and patient-related medication resources.
- Pharmacists should be aware that this credit will not be automatically reported to the NABP CPE Monitor.

Accreditation Council for Continuing Medical Education (ACCME)

- The academic detailers of the Vermont Academic Detailing Program have no conflicts or commercial interests. This includes not having conflicts or commercial interests in the cannabinoid industry.
- The content of this session is not intended to support or refute the use of cannabinoids, but rather to ensure balance by presenting the available evidence from peer-reviewed sources, where available. The content does not recommend dosing or management strategies of Schedule I controlled substances.
- The Vermont Academic Detailing Program follows the CME Clinical Content Validation policy: http://www.accme.org/accreditation-rules/policies/cme-clinical-content-validation

Cannabis Overview

Cannabis is a plant that contains chemically active compounds, including cannabinoids, terpenoids, flavonoids, and alkaloids.

Cannabinoids

- Over 140 cannabinoids identified (e.g. THC, CBD, CBN)
- Most potent is trans-Δ-9-tetrahydrocannabinol (D9-THC)
- Most abundant are THC and cannabidiol (CBD)

Terpenoids or Terpenes

- Hundreds identified
- Not unique to cannabis; aromatic compounds (essential oils) commonly produced by plants and fruit
- Responsible for aroma and flavor
- Examples: myrcene, limonene
- Likely have their own therapeutic effects

Chemovars

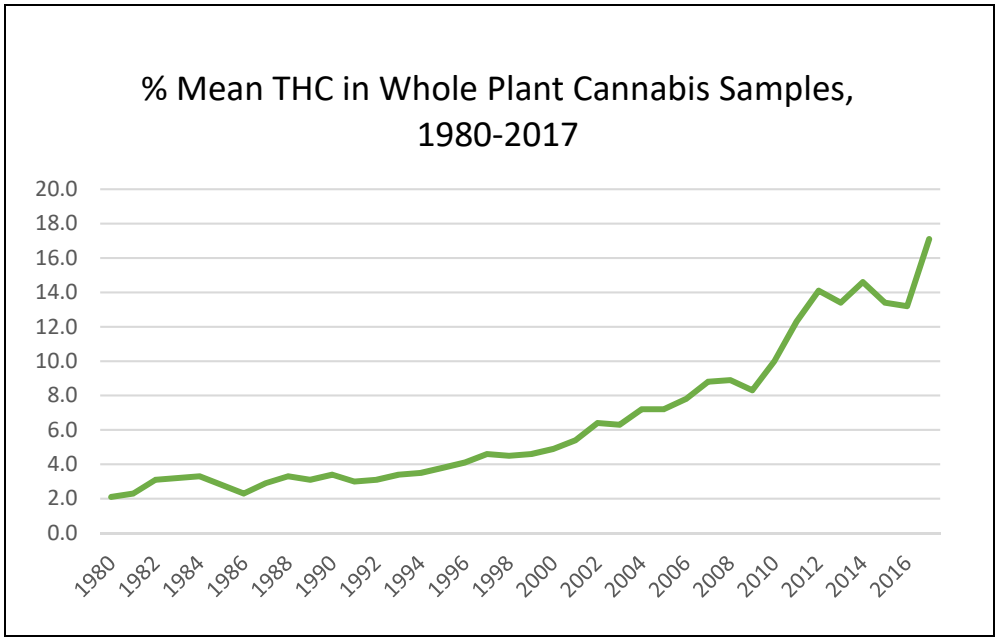
- Various species (*C. sativa*, *C. indica*, hybrids) and chemovars ("strains") within species are grown to intensify individual compounds
- Plants with low THC are used to manufacture fibers: fish nets, strings, ropes, textiles, paper
- **Cannabis is considered hemp when no part of the plant contains more than 0.3% THC (dry weight). Marijuana is any plant with more than 0.3% THC.**
- Literature suggests species distinction is irrelevant due to "ubiquitous interbreeding and hybridization" and suggests it is more important to characterize based on biochemical and pharmacological properties, also known as "chemovars," or chemical varieties

"Entourage effect"

- Refers to the synergy of cannabinoids, terpenoids (and possibly other compounds) in the cannabis plant that may explain perceived benefits in effectiveness or reduced side effects of whole plant cannabis versus synthetic or isolated THC/CBD
- Often used as an argument for supporting whole plant cannabis

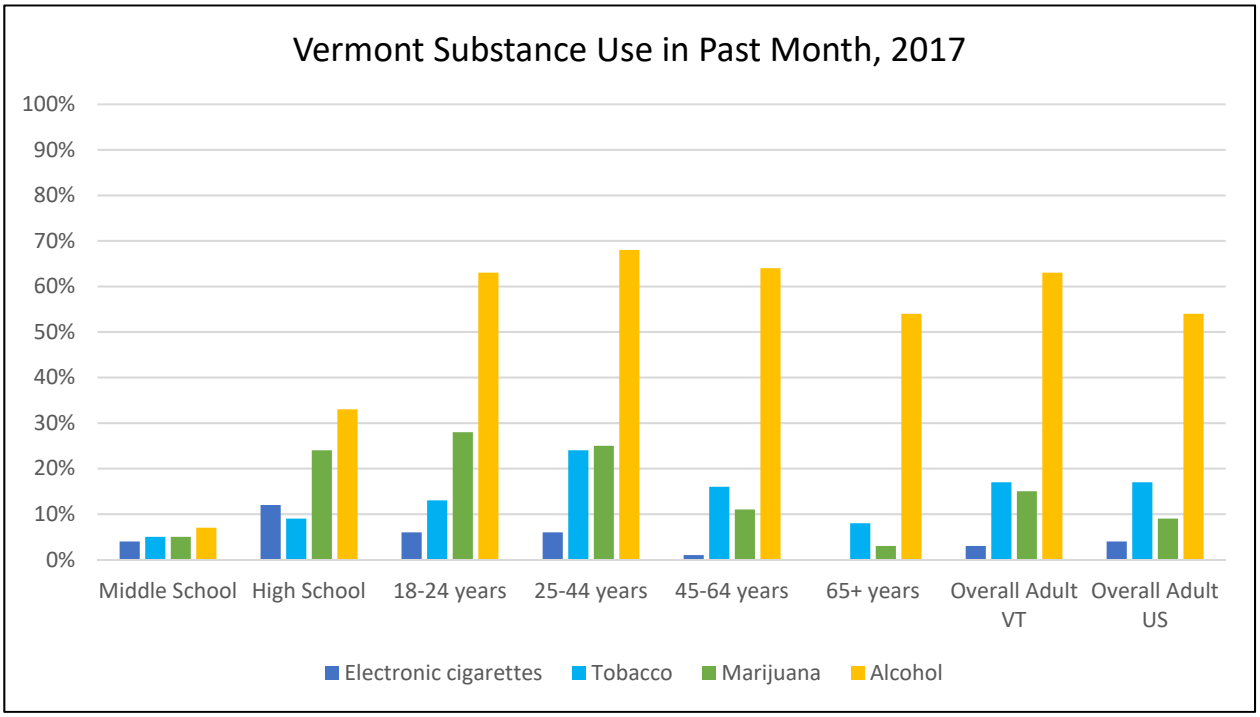
- Bonini SA, et al. Cannabis sativa: A comprehensive ethnopharmacological review of a medicinal plant with a long history. J Ethnopharmacol. 2018;227:300-315. PMID: 30205181
- Gallily R, et al. The Anti-Inflammatory Properties of Terpenoids from Cannabis. Cannabis Cannabinoid Res. 2018;26;3:282-290. PMID: 30596146
- Hanuš LO, et al. Phytocannabinoids: a unified critical inventory. Nat Prod Rep. 2016;33:1357-1392. PMID: 27722705
- H.R.2-115th Congress (2017-2018). Agriculture Improvement Act of 2018. Subtitle G—Hemp Production, SEC. 297A. Definitions. https://www.congress.gov/115/bills/hr2/BILLS-115hr2enr.pdf
- McPartland JM. Cannabis Systematics at the Levels of Family, Genus, and Species. Cannabis Cannabinoid Res. 2018;3:203-212. PMID: 30426073
- Russo EB. The Case for the Entourage Effect and Conventional Breeding of Clinical Cannabis: No "Strain," No Gain. Front Plant Sci. 2019 Jan 9;9:1969. PMID: 30687364

Cannabis-related Statistics



Mean THC concentrations have steadily increased from 2.1% in 1980 to 17.1% in 2017.

Source of samples: Confiscated samples from the Drug Enforcement Administration (DEA) in agreement with the National Institute on Drug Abuse (NIDA), analyzed by the University of Mississippi
1980-1992: N=19,278 samples; PMID: 10641915
1993-2007: N=43,877 samples; PMID: 20487147
2008-2017: N=18,108 samples; PMID: 30671616



Data from: Behavioral Risk Factor Surveillance System (BRFSS) (adult telephone survey) and the Youth Risk Behavior Survey (YRBS) (conducted in schools). http://www.healthvermont.gov/stats/surveys Accessed June 2019. Steigerwald S, et al. Smoking, Vaping, and Use of Edibles and Other Forms of Marijuana Among U.S. Adults. Ann Intern Med. 2018;169:890-892. PMID: 30167665.
Prescription Misuse: 8% of VT adults said they had ever misused a prescription drug. 1% said they did so in the last 30 days. During their lifetime, 10% of high school students reported having ever misused prescription pain medicine or stimulants.

Cannabinoid Comparison Chart - *Cannabis*

Generic Name	DEA Schedule	Notes	Typical Cost
Whole Plant *Cannabis*			
Medical Marijuana	I	Use authorized under: 8 V.S.A. Chapter 86, Therapeutic Use of Cannabis. The Vermont Marijuana Registry is regulated by the Department of Public Safety Possible whole plant dosing range (**GRAMS**): • Average daily dose of dried herbal cannabis used by patients with chronic pain was 2.5 grams per day (12.5% THC)[1] • "Use of high doses of THC-predominant cannabis above 5 grams per day is probably unjustified"[2] Possible THC dosing range (**MILLIGRAMS**):[2] • 1.25 mg to 15 mg THC-equivalent divided BID-TID • Start low and slowly titrate • If once-daily dosing, consider administration at bedtime to limit adverse effects • Doses exceeding 20–30 mg/day may increase adverse events or induce tolerance without improving efficacy "The amount of marijuana allowed to be collectively possessed by a registered patient and the patient's registered caregiver, is no more than two mature marijuana plants, seven immature plants, and two ounces of usable marijuana. Usable marijuana includes marijuana infused products."[3]	$325 per ounce[4] (28 grams; % THC varies)
Recreational or "Adult Use" Marijuana	I	H.511 (legalizes possession and limited cultivation for adults 21+; took effect 7/1/18) one ounce or less of marijuana and two mature and four immature marijuana plants for a person who is 21 years of age or older 1 joint contains about 0.66 grams (SD 0.45) of marijuana[6]	$300-345 per ounce[5] (28 grams; % THC varies)

[1]Ware MA, et al. Cannabis for the Management of Pain: Assessment of Safety Study (COMPASS). J Pain. 2015 Dec;16(12):1233-1242. PMID: 26385201

[2]MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. Eur J Intern Med. 2018 Mar;49:12-19. PMID: 29307505

[3]Department of Public Safety. Vermont Crime Information Center https://vcic.vermont.gov/marijuana-registry/faq. Accessed June 20, 2019.

[4]https://www.burlingtonfreepress.com/story/news/local/vermont/2019/04/03/day-life-vermont-biggest-weed-business-medical-marijuana-dispensary/3055011002/

[5]Vermont data based on self-reported pricing. priceofweed.com Accessed June 2019.

[6]Mariani JJ, et al. Quantification and comparison of marijuana smoking practices: blunts, joints, and pipes. Drug Alcohol Depend. 2011 Jan 15;113(2-3):249-51. PMID: 20863627

Cannabinoid Comparison Chart - THC

Generic Name	US Trade Name	DEA Schedule	Notes	Typical Monthly Cost
Delta-9-tetrahydrocannabinol (THC)-based products and analogs				
Dronabinol (synthetic THC)	Marinol	III	FDA-approved indications • anorexia associated with weight loss in patients with AIDS • nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. Oral capsule: 2.5 MG, 5 MG, 10 MG Dosing range: 2.5mg-20mg per day (divided)	$110 (generic)
Dronabinol (synthetic THC)	Syndros	II*	FDA-approved indications • anorexia associated with weight loss in patients with AIDS • nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. Available as a 5mg/ml oral solution with calibrated oral syringe Dosing range: 2.1mg – 8.4mg twice daily (note that nausea/vomiting dosing in mg/m^2)	$1000+
Nabilone (synthetic THC analog; chemically similar to THC)	Cesamet	II	FDA-approved indications • chemotherapy-induced nausea and vomiting in patients with inadequate response to conventional antiemetic treatments Available in 1mg capsules Dosing range: 1mg-6mg per day (divided)	$2000+

*Oral solutions of dronabinol are Schedule II. Fed Regist. 2017 Nov 22;82(224):55504-6. PMID: 29232070

Cannabinoid Comparison Chart - CBD

Generic Name	US Trade Name	DEA Schedule	Notes	Typical Monthly Cost
Cannabidiol (CBD)-based products				
Cannabidiol	Epidiolex	V*	FDA approved indications: • Treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2+ years Available as a 100mg/ml oral solution Dosing: 2.5 mg/kg twice daily, max 10mg/kg twice daily	$2000+ (Specialty Pharmacy)
Cannabidiol (Cannabis-derived)	N/A	I	Extracted from plants with more than 0.3% THC. CBD products may also contain THC. Allowable for purchase in Vermont in dispensaries with a Vermont Marijuana Registry card (as of July 2019). Dosing considerations: • No established dosing guidelines or maximum doses • Possible starting doses of with 2.5–20 mg per day of oral preparations divided twice or three times daily	$100-150 (varies widely)
Cannabidiol (Hemp-derived)	N/A	I	Extracted from plants with 0.3% THC or less (dry weight). CBD products may also contain THC. Allowable for purchase in VT stores. FDA does not allow CBD products to be sold as dietary supplements.	$40-60 (varies widely)
Combination products				
nabiximols	Sativex	N/A	2.7 mg of THC and 2.5 mg CBD plus terpenoids per spray	Not available in USA

*DEA order places FDA-approved drugs that contain CBD derived from cannabis and no more than 0.1 percent tetrahydrocannabinols in Schedule V. Federal Register Volume 83, No. 189, September 28, 2018. https://www.govinfo.gov/content/pkg/FR-2018-09-28/pdf/FR-2018-09-28.pdf

- FDA Regulation of Cannabis and Cannabis-Derived Products: Questions and Answers. https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers#farmbill. Accessed July 2019.
- MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. Eur J Intern Med. 2018 Mar;49:12-19. PMID: 29307505
- Clinical Resource, Comparison of Cannabinoids. Pharmacist's Letter/Prescriber's Letter. September 2018.
- Prices from GoodRx.com (May 2019), https://www.niceguysdelivery.com/menu (May 2019), vitaminshoppe.com (May 2019).

This page is intended to be blank to facilitate double-sided photocopying.

Whole Plant Cannabis and Delta-9-tetrahydrocannabinol (THC)

General Overview

Characteristic	Smoking/vaping	Oral
Onset (minutes)	5-10	60-180
Duration (hours)	2-4	6-8
How long to avoid driving? (hours)	2-8	6-8

- MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. Eur J Intern Med. 2018 Mar;49:12-19. PMID: 29307505 and Barnett G, et al. Behavioral pharmacokinetics of marijuana. Psychopharmacology (Berl). 1985;85:51-6. PMID: 2984710

Adverse Effects

FDA Alert (October 2019)	warns "consumers to stop using vaping products containing THC amid more than 1,000 reports of lung injuries—including some resulting in deaths—following the use of vaping products." https://www.fda.gov/consumers/consumer-updates/vaping-illness-update-fda-warns-public-stop-using-tetrahydrocannabinol-thc-containing-vaping
Central Nervous System	euphoria, confusion, dizziness, numbness, nightmares, visual disturbances, headache, feeling intoxicated, drowsiness, anxiety, cognitive impairment, emotional changes, mental slowness, impaired reaction time, dysphoria
Cardiovascular	tachycardia, orthostatic hypotension, hypertension, palpitations, paroxysmal atrial fibrillation, peripheral vasodilation
Respiratory	cough and symptoms of chronic bronchitis when smoked
Other	dry mouth, nausea, syncope, hyperemesis

Selected Drug Interactions

CNS Depressants (e.g. benzodiazepines, alcohol, opioids, muscle relaxants)	potentiated CNS depressant effects
Anticholinergics	delirium and tachycardia with tricyclic antidepressants and anticholinergics
Antidepressants	increased serum lithium levels, possibility of manic episodes with selective serotonin-reuptake inhibitors (SSRI's)
Alpha-agonists (e.g. clonidine, guanfacine)	tachycardia and cardiovascular events
Sildenafil	risk of myocardial infarction with sildenafil
Systemic corticosteroids	increased risk of immunosuppression

Data for adverse effects and drug interactions from: Parmar JR, et al. Medical marijuana patient counseling points for health care professionals based on trends in the medical uses, efficacy, and adverse effects of cannabis-based pharmaceutical drugs. Res Social Adm Pharm. 2016 Jul-Aug;12:638-54. PMID: 26443472 and Micromedex (June 2019)

Cannabidiol (CBD)

- Psychoactive, generally non-intoxicating (some intoxicating properties relative to placebo)
- CBD may reduce adverse effects of THC, but this may be dose dependent
  - Low doses enhance intoxicating effects of THC, particularly in infrequent cannabis users
  - High doses decrease intoxicating effects of THC

- Bhattacharyya S, et al. Opposite effects of delta-9-tetrahydrocannabinol and cannabidiol on human brain function and psychopathology. Neuropsychopharmacology. 2010;35:764-74. PMID: 19924114
- Curran HV, et al. Keep off the grass? Cannabis, cognition and addiction. Nat Rev Neurosci. 2016;17:293-306. PMID: 27052382
- Englund A, et al. Cannabidiol inhibits THC-elicited paranoid symptoms and hippocampal-dependent memory impairment. J Psychopharmacol. 2013;27:19-27. PMID: 23042808
- Morgan CJ, et al. Cannabidiol attenuates the appetitive effects of Delta 9-tetrahydrocannabinol in humans smoking their chosen cannabis. Neuropsychopharmacology. 2010;35:1879-85. PMID: 20428110
- Solowij N1, et al. A randomised controlled trial of vaporised Δ9-tetrahydrocannabinol and cannabidiol alone and in combination in frequent and infrequent cannabis users: acute intoxication effects. Eur Arch Psychiatry Clin Neurosci. 2019;269:17-35. PMID: 30661105

Adverse Effects of CBD

Central Nervous System	somnolence, fatigue, malaise, insomnia
Gastrointestinal	decreased appetite, diarrhea
Hepatic	transaminase elevations

Selected Drug Interactions

CNS Depressants, including alcohol	Increase risk of sedation and somnolence
Benzodiazepines	Increase in benzodiazepine effects (Epidiolex produces a 3-fold increase in plasma concentrations)
Narrow therapeutic index medications, including seizure medications	May increase or decrease levels of Epidiolex or the interacting drug, requiring dose adjustment. Check specific drug interactions using the package insert, Natural Medicines Database, or other drug interaction resource.
Valproate	Increase liver transaminases and thrombocytopenia. This combination requires monitoring.

Data for adverse effects and drug interactions from: Epidiolex package insert:
https://www.epidiolex.com/sites/default/files/EPIDIOLEX_Full_Prescribing_Information.pdf

Note: Drug interactions and adverse effects likely vary by dose and formulation (e.g. topical). Doses used for seizures are likely much higher than for other indications.

Shopping for CBD: Buyers Beware!

Hemp Oil

- Hulled hemp seed, hemp seed protein powder, and hemp seed oil come from the seeds of the *Cannabis* plant
- Hemp seeds do not naturally contain THC or CBD
- Hulled hemp seed, hemp seed protein powder, and hemp seed oil are generally recognized as safe (GRAS) by the FDA.
- Marketing of products with names such as “Hemp oil”, and “Hemp seed oil” likely do not contain CBD.

CBD

- CBD products are not approved or regulated by the FDA. They are *not* dietary supplements or over-the-counter medications.
- **Of 84 CBD products tested, only 31% were accurately labeled (43% were under-labeled, 26% were over-labeled). THC was detected (up to 6.43 mg/mL) in 18 (21%) of the 84 samples tested.**

- Bonn-Miller MO, et al. Labeling Accuracy of Cannabidiol Extracts Sold Online. JAMA. 2017;318:1708-1709. PMID: 29114823
- FDA. What You Need to Know (And What We’re Working to Find Out) About Products Containing Cannabis or Cannabis-derived Compounds, Including CBD. https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis Accessed July 2019.
- FDA Regulation of Cannabis and Cannabis-Derived Products: Questions and Answers. https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers Accessed July 2019.

This page is intended to be blank to facilitate double-sided photocopying.

Impaired Driving

19,906 impaired VT adult drivers per month, due to cannabis

- US Census = 510,434 VT adults
  - 15% have used cannabis in past month = 76,565 VT adults
    - 26% report driving within 3 hours of use = 19,906 VT adults

Data from Behavioral Risk Factor Surveillance System (BRFSS) (adult telephone survey) http://www.healthvermont.gov/sites/default/files/documents/pdf/HSVR_BRFSS_2017.pdf (page 47). Data accessed June 2019. https://www.census.gov/quickfacts/VT. Data accessed October 2019.

THC impairs driving	• Evidence supports that THC impairs driving. **Greatest risks are within 5 hours of use.**
THC probably increases motor vehicle accidents, but not as much as alcohol	• Estimates suggest THC is associated with motor vehicle accidents (up to double the risk of sober drivers), however data are mixed
CBD does not mitigate impairment	• CBD does not mitigate the driving impairment associated with THC
No standard roadside evaluations	• Law enforcement officers are trained to detect impaired driving using a variety of roadside tests. There is currently no national standard for quantitative testing.

Educate patients about the risks of cannabis use and driving

Evidence Table of Driving Impairment

THC impairs driving

Available trials are generally small randomized, within-subject designs in young recreational cannabis users. THC doses vary. Studies show THC impairs driving through inappropriate line crossings, running traffic lights, subjective drowsiness, and impairment in complex tasks associated with a high-crash risk, among other tasks. Blood levels do not correlate with level of impairment.

- Bolbecker AR, et al. Disturbances of postural sway components in cannabis users. Drug Alcohol Depend. 2018;190:54-61. PMID: 29983392
- Bondallaz P, et al. Cannabis and its effects on driving skills. Forensic Sci Int. 2016 Nov;268:92-102. PMID: 27701009
- Chow RM, et al. Driving Under the Influence of Cannabis: A Framework for Future Policy. Anesth Analg. 2019;128:1300-1308. PMID: 31094805
- Hartley S, et al. Effect of Smoked Cannabis on Vigilance and Accident Risk Using Simulated Driving in Occasional and Chronic Users and the Pharmacokinetic-Pharmacodynamic Relationship. Clin Chem. 2019;65(5):684-693. PMID: 30872375
- Micallef J, et al. Cannabis smoking impairs driving performance on the simulator and real driving: a randomized, double-blind, placebo-controlled, crossover trial. Fundam Clin Pharmacol. 2018;32(5):558-570. PMID: 29752828
- Ogourtsova T, et al. Cannabis use and driving-related performance in young recreational users: a within-subject randomized clinical trial. CMAJ Open. 2018;6(4):E453-E462. PMID: 30323055
- Tank A, et al. On the impact of cannabis consumption on traffic safety: a driving simulator study with habitual cannabis consumers. Int J Legal Med. 2019 Jan 30. PMID: 30701315

CBD does not mitigate impairment associated with THC

Randomized, double-blind, within-subjects crossover design, of healthy volunteers (n = 14) with a history of light cannabis use participating in simulated driving after 125 mg THC-dominant (11% THC; < 1% CBD), THC/CBD equivalent (11% THC, 11% CBD), or placebo (< 1% THC/CBD) cannabis. Both active cannabis types demonstrated impaired driving (increased lane weaving and decreased cognitive performance) Subjective drug effects (e.g., "stoned") and confidence in driving ability did not vary with CBD content.

- Arkell TR, et al. Cannabidiol (CBD) content in vaporized cannabis does not prevent tetrahydrocannabinol (THC)-induced impairment of driving and cognition. Psychopharmacology (Berl). 2019 May 1. PMID: 31044290

THC and Motor Vehicle Accidents

Meta-analyses and secondary analyses suggest anywhere from a nonsignificant increase to a doubling of risk of THC-associated motor vehicle accidents.

- Harper S, Palayew A. The annual cannabis holiday and fatal traffic crashes. Inj Prev. 2019 Jan 29. PMID: 30696698
- Lane TJ, et al. Traffic fatalities within US states that have legalized recreational cannabis sales and their neighbours. Addiction. 2019 Feb 4. PMID: 30719794
- Rogeberg O, et al. The effects of cannabis intoxication on motor vehicle collision revisited and revised. Addiction. 2016;111(8):1348-59. PMID: 26878835

THC vs. Alcohol

Direct comparison data are unavailable. “The average risk increase associated with cannabis intoxication and recent use based on a random-effects meta-analysis is 1.35 (1.12–1.61), implying an upper bound OR associated with high THC driving of approximately 2. These risks are one to two orders of magnitude lower than the estimated risks of high Blood Alcohol Concentration levels.” (Rogeberg) The relative risk of being killed in a single-vehicle crash for drivers with BACs of 0.05–0.079 is at least seven times that of drivers at 0.00 BAC (no alcohol).

- Fell JC, Voas RB. The effectiveness of a 0.05 blood alcohol concentration (BAC) limit for driving in the United States. Addiction. 2014 Jun;109(6):869-74. PMID: 24898061
- Rogeberg O1, et al. Response: Cannabis intoxication, recent use and road traffic crash risks. Addiction. 2016;111:1495-8. PMID: 27324455

Recreational Cannabis Use

Think about the demographics of your clinic…

Age	Self-reported cannabis use in past month
Middle School	5%
High School	24%
18-24 years	28%
25-44 years	25%
45-64 years	11%
65+ years	3%
Overall Adult VT	15%
Overall Adult US	9%

2017 Data from: Behavioral Risk Factor Surveillance System (BRFSS) (adult telephone survey) and the Youth Risk Behavior Survey (YRBS) (conducted in schools). http://www.healthvermont.gov/stats/surveys Accessed June 2019. Steigerwald S, et al. Smoking, Vaping, and Use of Edibles and Other Forms of Marijuana Among U.S. Adults. Ann Intern Med. 2018;169:890-892. PMID: 30167665.

Factors associated with cannabis use

- Age 10-35 years
- Mood, anxiety, or psychotic disorders
- Alcohol use
- Tobacco use
- Misuse other substances
- Poor functioning at work or school
- Poorly controlled chronic pain

Symptoms associated with cannabis use

- Depression and anxiety
- Psychosis
- Recurrent respiratory tract infections
- Chronic cough
- Sleep disturbances
- Poor school or work performance
- Relationship difficulties
- Nausea and vomiting

Turner SD, et al. Approach to cannabis use disorder in primary care: focus on youth and other high-risk users. Can Fam Physician. 2014 Sep;60(9):801-8, e423-32. PMID: 25217674

Pre-screen <u>all</u> patients for cannabis use by asking,
"Have you smoked marijuana, or used cannabis in any form, in the past year?"

Cannabis Use Disorder

Fast Facts!

- Of patients who have used cannabis in the last year, but who do not currently have cannabis use disorder, **25%** will develop cannabis use disorder and **5%** will develop dependence in the next 3 years. Blanco C, et al. Cannabis Use and Risk of Psychiatric Disorders: Prospective Evidence From a US National Longitudinal Study. JAMA Psychiatry. 2016:388-95. PMID: 26886046

- After alcohol, marijuana has the highest rate of dependence or abuse among all drugs, due to the prevalence of use. Budney AJ, et al. Marijuana dependence and its treatment. Addict Sci Clin Pract. 2007;4:4-16. PMID: 18292704

Screen patients who answer positively to using cannabis in the past year by asking about quantity and frequency of use

Risk factors for cannabis use disorder

- Daily or almost daily use
- Patient reports relief of anxiety as primary reason for using cannabis
- Repeated unsuccessful attempts to reduce or stop use
- Medical, social, legal, or financial harms from cannabis use
- Expressions of concern from family or friends

Practice Tip: Consider using the Drug Abuse Screening Test, Short Form (DAST-10) to assist in making the diagnosis: https://www.bu.edu/bniart/files/2012/04/DAST-10_Institute.pdf

Currently there are no approved pharmacotherapies for cannabis use disorder. Little-to-no evidence of benefit for SSRIs, other antidepressants, bupropion, buspirone and atomoxetine, or gabapentin. Behavioral health interventions (e.g. CBT) reduce frequency of use and severity of dependence in the short term.

- Gates PJ, Sabioni P, Copeland J, Le Foll B, Gowing L. Psychosocial interventions for cannabis use disorder. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD005336. PMID: 27149547
- Nielsen S, et al. Pharmacotherapies for cannabis dependence. Cochrane Database Syst Rev. 2019 Jan 28;1:CD008940. PMID: 30687936

DSM-V Diagnostic Criteria for Cannabis Use Disorder

A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Cannabis is often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.
3. A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.
4. Craving, or a strong desire or urge to use cannabis.
5. Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.
7. Important social, occupational, or recreational activities are given up or reduced because of cannabis use.
8. Recurrent cannabis use in situations in which it is physically hazardous.
9. Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.
10. Tolerance, as defined by either a need for markedly increased amounts of cannabis to achieve intoxication or desired effect, or markedly diminished effect with continued use of the same amount of cannabis.
11. Withdrawal, developing within approximately 1 week after cessation: irritability, anger or aggression, anxiety, depressed mood, restlessness, sleep difficulty, and decreased appetite or weight loss. At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache.

For complete cannabis and substance use criteria, see American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), American Psychiatric Association, Arlington 2013.

This page is intended to be blank to facilitate double-sided photocopying.

Considerations for Marijuana Registry Health Care Professional Verification Forms

Vermont Requirements

Do you have a treating relationship with this patient (for at least 3 months)?	☑

Have you completed a full history and physical exam of the patient?	☑

Have you diagnosed the patient with a "debilitating medical condition"?* • Acquired immune deficiency syndrome or human immunodeficiency virus • Cancer • Crohn's disease • Glaucoma • Multiple Sclerosis • Parkinson's disease • Post-traumatic stress disorder (only allowed if the patient is undergoing behavioral therapy) • Chronic, debilitating condition that produces one or more of the following intractable symptoms: cachexia or wasting syndrome; chronic pain; severe nausea; or seizures	☑

*Note: Eligible conditions are based on state rules, not effectiveness data from randomized trials

Additional Notes for Vermont patients and providers:

- Healthcare professionals include MD, DO, NP, PA, APRN
- Registration cards must be renewed annually
- Understand that the signed medical verification form is not considered a prescription, but is designed to confirm the patient has a debilitating medical condition
- Dispensaries may not dispense more than two ounces (56.7 grams) of usable marijuana to a registered patient during a 30-day period
- A registered patient may only select one dispensary and may only obtain marijuana by appointment (5 currently operating dispensaries in VT)
    - Champlain Valley Dispensary (Burlington and South Burlington)
    - Grassroots Vermont (Brandon)
    - PhytoCare Vermont (Bennington)
    - Southern Vermont Wellness (Brattleboro and Middlebury)
    - Vermont Patients Alliance (Montpelier)
- For complete rules, see Vermont Statute Title 18, Chapter 86. https://legislature.vermont.gov/statutes/fullchapter/18/086

Other Considerations

Is the patient at low risk for substance use disorders? Negative for the following: • Alcohol: Alcohol Use Disorders Identification Test (AUDIT-C) • Opioids: SOAPP-R (Screener and Opioid Assessment for Patients with Pain, Revised) • Stimulants or other substances: Drug Abuse Screening Test, Short Form (DAST-10) • Tobacco use • Personal or family history of substance abuse • Urine screen for controlled substances • Unexpected prescription in VPMS • Age less than 30 years • History of incarceration	☑

Is the patient at low risk for cannabis use disorder? Negative for the following: • Persistent desire or unsuccessful efforts to cut down or control cannabis use • Problems with relationships, work, school, or home due to cannabis use • Giving up activities due to cannabis use • Using cannabis in hazardous situations (e.g. driving) • Drug Abuse Screening Test, Short Form (DAST-10)	☑

Is cannabis unlikely to worsen any of the patient's current diagnoses? (cannabis may worsen ADHD, depression, cognitive impairment)	☑

Is cannabis unlikely to risk a patient's employment or financial assistance? (law enforcement, commercial drivers' licenses, federal employees, daycare workers, military, Section 8 housing, etc.)	☑

Sign a Marijuana Registry Health Care Professional Verification Form only if the benefits outweigh the risks

- For cannabis and substance use criteria, see American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), American Psychiatric Association, Arlington 2013.
- Turner SD, et al. Approach to cannabis use disorder in primary care: focus on youth and other high-risk users. Can Fam Physician. 2014 Sep;60(9):801-8, e423-32. PMID: 25217674

Clinical Evidence

Myth	There is no research on cannabinoids.
Fact	It is true that cannabinoids are classified as DEA Schedule I, which makes research difficult. However, trials of oral THC related to chemotherapy-induced nausea and vomiting have been ongoing for at least 40 years (with mixed results). • Sallan SE, et al. Antiemetic effect of delta-9-tetrahydrocannabinol in patients receiving cancer chemotherapy. N Engl J Med. 1975;293:795-7. PMID: 1099449 • Colls BM. Cannabis and cancer chemotherapy. Lancet. 1980;1:1187-8. PMID: 6104004
Caution	Available randomized trials have generally small sample sizes with moderate-to-high risk of bias. Primary outcomes are generally negative, with some secondary outcomes positive. Oddly, many trials with negative primary outcomes still report titles and abstracts that sound positive.

Effectiveness for Selected Primary Care Indications

Condition	THC	CBD
Anxiety	Conflicting results. May worsen anxiety	Data limited to public speaking
Crohn's Disease	High risk of bias; limited data	Not effective; limited data
Fibromyalgia	Not effective; data limited to nabilone	Not studied
Glaucoma	High risk of bias; limited data	Not studied
Insomnia	Not studied for primary insomnia	High risk of bias; limited data
Pain (Chronic, Neuropathic)	Mixed data with sativex, nabilone, inhaled cannabis, dronabinol	Not studied
Pain (Chronic, non-neuropathic)	High risk of bias; limited data	Not studied
Parkinson's Disease	High risk of bias; limited data	Psychotic symptom improvement in patients with psychosis in Parkinson's. May worsen resting tremor.
Seizure Disorder	Not studied	Possibly or likely effective (Epidiolex) for Lennox-Gastaut syndrome or Dravet syndrome

Note: The Vermont Academic Detailing Program conducted an independent review of the literature and at times, our conclusions are more conservative than those reported by other sources. For example, the National Academies of Sciences, Engineering, and Medicine concluded in their 2017 report that there is conclusive or substantial evidence that cannabis or cannabinoids are effective for the treatment of chronic pain in adults. Our review suggests that this evidence applies to neuropathic pain, but not other types of chronic pain.

Reference: National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: Current state of evidence and recommendations for research. Washington, DC: The National Academies Press.

Evidence Table for Effectiveness

Condition	References
Anxiety	• Bergamaschi MM, et al. Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients. Neuropsychopharmacology 2011;36:1219-26. PMID: 21307846 • Linares IM, et al. Cannabidiol presents an inverted U-shaped dose-response curve in a simulated public speaking test. Braz J Psychiatry. 2019;41:9-14. PMID: 30328956 • Twomey CD. Association of cannabis use with the development of elevated anxiety symptoms in the general population: a meta-analysis. J Epidemiol Community Health. 2017;71:811-816. PMID: 28053188 • Zuardi AW, et al. Effects of ipsapirone and cannabidiol on human experimental anxiety. J Psychopharmacol 1993;7(1 Suppl):82-8. PMID: 22290374
Crohn's Disease	• Kafil TS, et al. Cannabis for the treatment of Crohn's disease. Cochrane Database Syst Rev. 2018;11:CD012853. PMID: 30407616 • Naftali T et al. Low-Dose Cannabidiol Is Safe but Not Effective in the Treatment for Crohn's Disease, a Randomized Controlled Trial. Dig Dis Sci. 2017;62:1615-1620. PMID: 28349233
Fibromyalgia	• Walitt B, et al. Cannabinoids for fibromyalgia. Cochrane Database Syst Rev. 2016;7:CD011694. PMID: 27428009
Glaucoma	• Merritt JC, et al. Effect of marihuana on intraocular and blood pressure in glaucoma. Ophthalmol 1980;87:222-8 PMID: 7053160 • Panahi Y, et al. The arguments for and against cannabinoids application in glaucomatous retinopathy. Biomed Pharmacother. 2017;86:620-627. PMID: 28027538
Insomnia	• Babson KA, et al. Cannabis, Cannabinoids, and Sleep: a Review of the Literature. Curr Psychiatry Rep. 2017;19:23. PMID: 28349316 • Carlini EA, Cunha JM. Hypnotic and antiepileptic effects of cannabidiol. J Clin Pharmacol 1981;21(8-9 Suppl):417S-27S. PMID: 7028792
Parkinson's Disease	• Consroe P, et al. Open label evaluation of cannabidiol in dystonic movement disorders. Int J Neurosci 1986;30:277-82. PMID: 3793381 • Lotan I, et al. Cannabis (medical marijuana) treatment for motor and non-motor symptoms of Parkinson disease: an open-label observational study. Clin Neuropharmacol. 2014;37:41-4. PMID: 24614667 • Zuardi AW, et al. Cannabidiol for the treatment of psychosis in Parkinson's disease. J Psychopharmacol 2009;23:979-83. PMID: 18801821
Pain (Chronic, Neuropathic)	• Andreae MH, et al. Inhaled cannabis for chronic neuropathic pain: A meta-analysis of individual patient data. J Pain. 2015;16:1221-1232. PMID: 26362106 • Mücke M, et al. Cannabis-based medicines for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2018 Mar 7;3:CD012182. PMID: 29513392 • Nugent SM, et al. The Effects of Cannabis Among Adults With Chronic Pain and an Overview of General Harms: A Systematic Review. Ann Intern Med. 2017;167:319-331. PMID: 28806817 • Ware MA, et al. Smoked cannabis for chronic neuropathic pain: a randomized controlled trial. CMAJ. 2010;182:E694-701. PMID: 20805210 • Wilsey B, et al. Low-dose vaporized cannabis significantly improves neuropathic pain. J Pain. 2013;14:136-148. PMID: 23237736
Pain (Chronic, Non-Neuropathic)	• Whiting PF, et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. JAMA. 2015;313:2456-73. PMID: 26103030
Seizure Disorder	• Devinsky O, et al. Effect of Cannabidiol on Drop Seizures in the Lennox-Gastaut Syndrome. N Engl J Med. 2018;378(20):1888-1897. PMID: 29768152 • Thiele EA, et al. Cannabidiol in patients with seizures associated with Lennox-Gastaut syndrome (GWPCARE4): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2018;391:1085-1096. PMID: 29395273

Cannabinoids

VERMONT ACADEMIC DETAILING PROGRAM

VS.

What is a cannabinoid/medical cannabis?

Cannabis is a plant. The buds or flowers of this plant contain chemicals called "cannabinoids."

The most common cannabinoids are:

- **THC** (delta-9-tetrahydrocannabinol), and
- **CBD** (cannabidiol)

Medical marijuana contains varying amounts of THC and CBD. In Vermont, access to medical marijuana from a licensed dispensary requires that a health care provider sign a Health Care Professional Verification Form.

PRESCRIPTION CANNABINOIDS

THC and CBD are approved by the FDA for a small number of medical conditions and are available as prescriptions from a pharmacy.

WHOLE PLANT CANNABIS

Whole plant cannabis is for medical or recreational use and can be inhaled (smoked or vaporized), ingested (e.g. edible), or used on the skin (topical).

CBD

CBD does not make people feel "high" and is made from whole plant cannabis or from hemp. CBD may be purchased in a dispensary or in stores.

HEMP OIL

Products made from hemp seeds and hemp oil likely do not contain THC or CBD.

CBD is always pure and natural

MYTH!

CBD you buy without a prescription is not tested by the FDA. One study tested 84 CBD products and the label matched what was in the bottle only 31% of the time. THC was detected in about 20% of the products tested.

Cannabis is becoming stronger

FACT!

Studies have found that from 1980 to 2017, the amount of THC in cannabis plants has increased from 2% to 17%.

Cannabis does not cause addiction

MYTH!

About 1 in 10 people who use cannabis develop Cannabis Use Disorder. This number is higher for those who start using cannabis as a teenager.

CBD does not cause any side effects

MYTH!

Although advertised as "non-psychoactive", CBD can still cause drowsiness, dizziness and mood changes.

Updated: July 2019

What side effects can cannabis use lead to?

Cannabis
Memory problems
Anxiety
Changes in mood
Drowsiness
Uncontrolled vomiting

Smoke Inhalation
Lung disease
Chronic cough

How do I know if my cannabis use might be a problem?

- You use cannabis daily/almost daily
- Your primary reason for using cannabis is relief of anxiety
- You have tried to stop using cannabis and have been unable to
- Your family or friends are concerned about your cannabis use

What conditions is cannabis effective for?

Epidiolex® (prescription CBD) is beneficial for certain types of seizures in children

CBD and/or THC may be effective for anxiety, multiple sclerosis, rheumatoid arthritis, and neuropathic pain, but the research so far is very limited

Although there are many stories of cannabis helping, we need more information to know how to balance the risks and benefits

If I am thinking of using cannabis, how can I use it safely?

LET ALL of your health care providers know that you are using cannabis

DO NOT drive within 8 hours or consume alcohol after using cannabis

AVOID cannabis if:
- you are pregnant or breastfeeding
- you have a psychiatric or mood disorder
- if cannabis will impact your job or government assistance

For more information: https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis

- Adapted from: Rx Files Cannabis: Questions about cannabis and the answers that may surprise you. 2018. https://www.rxfiles.ca
- Allan GM, et al. Simplified guideline for prescribing medical cannabinoids in primary care. CFP. 2018;64(2):111-120.
- Bonn-Miller MO, et al. Labeling Accuracy of Cannabidiol Extracts Sold Online. JAMA. 2017;318:1708-1709.
- Budney AJ, et al. Marijuana dependence and its treatment. Addict Sci Clin Pract. 2007;4(1):4-16.
- MacCallum CA, et al. Practical considerations in medical cannabis administration and dosing. Eur J Intern Med. 2018;49:12-19.
- Turner SD, et al. Approach to cannabis use disorder in primary care: focus in youth and other high-risk users. Can Fam Physician. 2014;60(9):801-808.
- Volkov ND, et al. Adverse health effects of marijuana use. NEJM. 2014;370(23):2219-2227

Updated: July 2019

IMPORTANT REMINDER

You must claim your CMIE credits within 30 days of attending this session!

Please **www.highmarksce.com/uvmmed** to claim your CMIE credit.

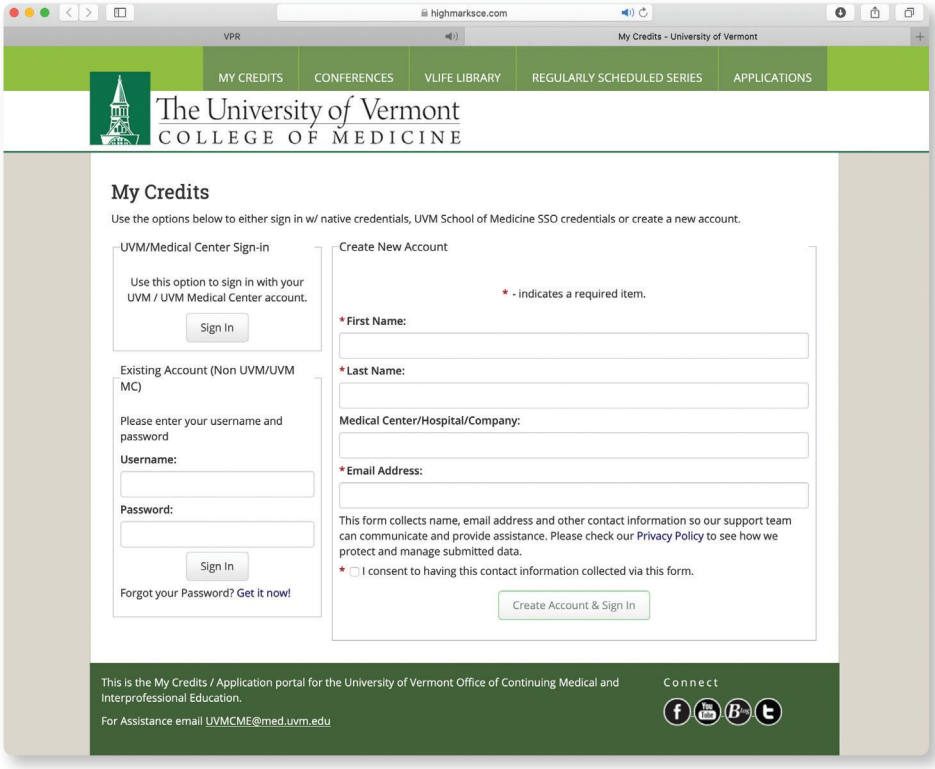
Continuing education credits are offered through the Office of Continuing Medical and Interprofessional Education (CMIE) at the University of Vermont (UVM) Robert Larner M.D. College of Medicine

Credits are only awarded online

The UVM Office of Primary Care is unable to claim credits for you

CMIE credits must be claimed within
30 days of attending a session

Tip: UVMMC Providers should generally claim credit through their UVMMC account



TWO WAYS TO CLAIM YOUR CREDITS:

Log into: **www.highmarksce.com/uvmmed**. Use the Claim Credit drop down box to find "Vermont Academic Detailing." Click "List sessions by activity." Find the session you attended and click "Add Credits" Follow the prompts to finish claiming credit.

Scan the QR code provided by the Academic Detailer

NEED HELP WITH THE CMIE SYSTEM?

Phone (802) 656-2292
Email UVMCME@med.uvm.edu
Online www.med.uvm.edu/cme/my-credits

The University of Vermont
LARNER COLLEGE OF MEDICINE
OFFICE OF PRIMARY CARE

This page is intended to be blank to facilitate double-sided photocopying.

The Vermont Academic Detailing Program: Attendance and Program Evaluation

Requested for program evaluation, reports and funding requirements; information will be reported in aggregate.

Name: _____ Date: _____

What role best describes you?

	Provider / Pharmacist
	Physician (MD and DO)
	Naturopathic physician (ND)
	Nurse Practitioner
	Physician Assistant
	Pharmacist
	Other prescriber (Specify):
To claim CMIE credit, please visit: https://www.highmarksce.com/uvmmed	

	Resident / Student
	Medicine
	Nursing
	Pharmacy
	Other

	Staff / Other
	Non-prescribing nurse
	Medical Assistant
	Office Manager
	Other

If you would like a certificate of completion for today's session, please include your mailing address on the back of this form. This is not CMIE.

My job title is: _____

My email address is: _____

Please rate the following for today's session:

1=STRONGLY DISAGREE TO 5= STRONGLY AGREE ☹ 😐 ☺

1.	Program met stated objectives	1	2	3	4	5
2.	Program provided unbiased, evidence-based content, where available	1	2	3	4	5
3.	Program topic was appropriate for your needs	1	2	3	4	5
4.	Program had practical clinical value	1	2	3	4	5
5.	Program speakers were prepared	1	2	3	4	5
6.	Program format was appropriate	1	2	3	4	5
7.	Overall impression of the program was favorable	1	2	3	4	5
8.	Time for discussion was appropriate	1	2	3	4	5
9.A	Do you feel the information presented will impact your prescribing?		Yes	No	N/A	
9.B	Do you feel the info. presented will impact your practice/patient care?		Yes	No	N/A	
10.	Would you be willing to attend a similar session in the future?		Yes	No		
11.	Was this program free of commercial bias?		Yes	No		
12.	What is your gender? _____					
13.	What is your birth year? _____					
14.	Are you Hispanic or Latino? _____					
15.	What is your race? (please circle) White Black or African American American Indian/Alaskan Native Asian Native Hawaiian/Pacific Islander More Than One Race Prefer Not to Answer					
16.	What future topics would you like addressed? _____					
17.	Other comments or feedback? _____					