

NH Therapeutic Cannabis Medical Oversight Board

SB 477, Chapter 228:2, Laws of 2018, RSA 126-X:12

Annual Report 2019

Membership¹

Jonathan Ballard, MD, Chief Medical Officer, NH DHHS
Virginia Brack, MD, Pediatrics
Heather Brown, Qualifying Patient
Corey Burchman, Alternative Treatment Center (ATC) Clinical Representative (Prime ATC)
David Conway, MD, Obstetrics and Gynecology
Bert Fichman, MD, Palliative Care
Jerry Knirk, MD, Physiatry/Orthopedics
Richard Morse, MD, Neurology
Molly Rossignol, DO, Family/Internal Medicine
Seddon Savage, MD, Addiction
Cornel Stanciu, MD, Psychiatry
Dennis Thapa, MD, Pain Management
Lisa Withrow, APRN, FNP-C, ACHPN, Oncology

Charge

In 2019, the Therapeutic Cannabis Medical Oversight Board (TCMOB; Board) was constituted pursuant to RSA 126-X:12. All members were appointed by the Commissioner of the NH Department of Health and Human Services (DHHS).

The Board's charge, pursuant to RSA 126-X:12, IV, is to "monitor and contribute to the oversight of the clinical, quality, and public health related matters of therapeutic cannabis under this chapter by:

- (a) Reviewing medical and scientific evidence pertaining to currently approved and additional qualifying conditions.
- (b) Reviewing laboratory results of required testing of cannabis cultivated and/or processed by an alternative treatment center and the use of pesticides on products under RSA 126-X:6, III(a)(16).
- (c) Monitoring clinical outcomes.
- (d) Reviewing training protocols for dispensary staff based on models from other states.
- (e) Receiving updates from alternative treatment centers on effectiveness of various strains, types of cannabinoids, and different routes of administration for specific conditions.
- (f) Reviewing best practices for medical providers regarding provider education, certification of patients, and patient access to the program.
- (g) Reviewing any other clinical, quality, and public health related matter relative to use of cannabis under this chapter."

In addition, the Board may make recommendations to the Commissioner of DHHS to add or remove qualifying medical conditions under RSA 126-X:1, IX based on its findings and after receiving input from the public through a public hearing process.

¹ Current members. Gilbert Fanciullo, MD, previously served as the ATC clinical representative.

Lastly, the Board shall make an annual report to the president of the senate, the speaker of the house of representatives, the oversight committee on health and human services established under RSA 126-A:13, the board of medicine, the board of nursing, and the therapeutic use of cannabis advisory council established in RSA 126-X:9.

Meeting Dates

The Board convened six times in 2019, at the offices of DHHS, as follows: March 22, June 5, July 17, September 4, October 9, and November 13.

Meetings were noticed on a webpage maintained by DHHS, <https://www.dhhs.nh.gov/oos/tcp/mob.htm>. Meeting minutes are posted at the same webpage.

Organizational Meeting Summary

Dr. Jonathan Ballard, Chief Medical Officer of DHHS, convened the first meeting on March 22, 2019. Dr. Ballard was elected chairperson for the first six meetings. Representative Jerry Knirk was elected alternate chairperson. DHHS staff presented the history of the Department's Therapeutic Cannabis Program (TCP), and the charge of the TCMOB was reviewed and discussed. Meeting dates were set, relevant legislation from the 2019 legislative session was discussed, and the Board introduced and discussed issues it wished to address in the upcoming year.

Qualifying Medical Conditions

The Board's primary focus in 2019 was on the evaluation of medical conditions proposed by the New Hampshire Legislature to be added as qualifying medical conditions for the therapeutic use of cannabis. In early 2019, the NH House of Representatives, Health and Human Services and Elderly Affairs (HHSEA) Committee retained two bills so that the TCMOB could review medical and scientific literature related to those medical conditions, evaluate whether cannabis use would be appropriate for those conditions, and make a recommendation to the Legislature whether to add or not add any of those conditions to the statutory list of qualifying medical conditions at RSA 126-X:1, IX.

- HB 366 would add opioid addiction, misuse and abuse
- HB 461 would add insomnia, anxiety, and Lyme disease

Early meetings were organizational in terms of developing the criteria for the evaluation of qualifying conditions and what levels of evidence would be used in making recommendations. The Board wished to rely as much as possible on published scientific evidence but would consider anecdotal and clinical evidence, given the relative lack of high quality scientific evidence. Subcommittees were identified for the review of the conditions under consideration in the retained bills described above. At a subsequent meeting those subcommittees reported their initial findings.

The Board recognized the importance of open public hearings when considering qualifying conditions in order to receive public input to help inform decision making. A public hearing on the four conditions was held on September 25 and written comments were accepted during an established written comment period. Administrative rule He-C 403, on the conduct of public hearings held by the TCMOB in order to receive input from the public regarding qualifying medical conditions, has since been approved by the Joint Legislative Committee on Administrative Rules, and adopted by the DHHS Commissioner.

Draft recommendation reports were prepared by a member of each of the subcommittees and were circulated to the Board for review prior to discussion at a subsequent meeting. The Board met on October 9 to discuss the reports and to vote on making recommendations to the NH House HHSEA Committee for their consideration when deciding the disposition of these bills.

The Board voted as follows:

- Recommend adding insomnia as a qualifying condition by a 9-1 vote;
- Recommend not adding anxiety as a qualifying condition by an 8-2 vote;
- Recommend not adding tick-borne illnesses as a qualifying condition by an 8-2 vote; and
- Recommend not adding opioid use disorder as a qualifying condition by a 6-4 vote.

The individual recommendation reports are included as Appendices A through E in this Annual Report. It is important to note that these documents do not reflect a consensus of the Board, but rather reflect the recommendations of the specific authors based on their experience, a literature review, and the public comments received. These are working documents of the Board, and are not intended, written, or edited for journal publication.

Representative Jerry Knirk, who also serves as the Board's legislative liaison, prepared a document for the HHSEA Committee which summarized the deliberations and recommendations of the TCMOB regarding these conditions (Appendix F). At the Board's November 13 meeting, Representative Knirk reported on the actions taken by the HHSEA Committee relative to the Board's recommendations:

- The Committee sustained the Board's recommendations on insomnia, anxiety, and tick-borne illnesses.
- The Committee did not sustain the Board's recommendation regarding opioid use disorder. Instead, the Committee voted to add opioid use disorder as a stand-alone condition, subject to the restrictions of certification only by a provider with specialized addiction training and only for the symptoms of cravings and/or withdrawal. Such restrictions were included in the motion the Board considered, and rejected, when voting on its own recommendation.
- HB 366 and HB 461, both amended by the HHSEA Committee based on the TCMOB recommendations, will next be considered by the full Legislature.

Also at the November 13 meeting, the Board considered the language of SB 175 (another retained bill from the 2019 legislative session), which proposed to remove all qualifying medical conditions from the therapeutic cannabis law and instead allow medical providers broad discretion to certify patients for the therapeutic use of cannabis due to any medical condition a provider believed could potentially be helped by therapeutic cannabis. The Board did not reach consensus on this issue, but the majority of members present voted in favor of a motion supporting the belief that the current knowledge base of the provider community in New Hampshire about therapeutic cannabis is insufficient to justify the proposed change at this time.

Looking Ahead to 2020

Jerry Knirk was elected to serve as Board chairperson for 2020, with Heather Brown serving as the alternate chairperson. The Board looks forward in 2020 to address its other charges. The Board expects that much of its attention over the next year will be to consider issues of provider best practices and clinician education, to continue evaluating qualifying conditions as necessary, driven by bills in the legislature, and to review other qualifying conditions and symptoms already established in statute.

Appendix A

NH Therapeutic Cannabis Medical Oversight Board Qualifying Medical Condition Recommendation Report: Insomnia October 2019

Condition: Insomnia

Recommendation

It is recommended that insomnia be included as a qualifying medical condition, paired with a recommendation that additional studies are needed to both determine the nature of the insomnia and response to treatment and to determine optimal dosing, ratio of CBD:THC or THC or CBD alone, and that perhaps consultation with a sleep disorders center be considered as well, to see if cannabis is appropriate for the type of insomnia for which treatment is being sought. The recommendation would strongly recommend that the sleep medicine providers study cannabis further in the management of sleep disorders, especially insomnia.

Special considerations

1. Pediatric population: unknown effects on the developing brain
2. Pregnant women: unknown effects on the developing fetus
3. Insomnia as a single diagnosis or secondary (associated) one. EX: it may be very useful for pain-mediated insomnia and not useful for depression-mediated insomnia
4. CBD vs. THC vs. whole plant extract containing both. It may be that the CBD alone is adequate and most therapeutic, as in epilepsy treatment.
5. Studies are limited in reaching any conclusions but overall point to beneficial effects more than deleterious effects.
6. At what point can we hope to apply a scientific approach to therapeutic cannabis, or should it be regarded in a different category, somewhere in the alternative medicine area, not subject to the standards of the allopathic medical profession?

Summary from the review of studies available

1. The majority of the studies suggests that the use of THC and THC derivatives, alone or in combination with CBD, may improve self-reported sleep quality, sleep disturbances, and decreased sleep onset latency.
2. Despite the importance of sleep, most of the studies examined sleep as a secondary outcome; there is a lack of placebo-controlled trials examining the use of cannabinoids specifically for treatment of sleep disorders.
3. Many of the available studies used non-standardized, non-validated questionnaires and subjective sleep measures, which leaves something to be desired in terms of the validity of data.
4. Available pharmacological treatments for insomnia and primary sleep disorders include medications such as benzodiazepines and non-benzodiazepine hypnotics. In addition, many other medications are used off label for the treatment of the symptoms. Many of these medications are limited by side effects, adverse effects, and in some cases addiction liability. Cannabinoids have also been associated with some

adverse events such as dizziness, cognitive impairment, increased risk of motor vehicle accidents, psychosis, dependence, depression, and anxiety.

5. Some medications currently used to treat insomnia can affect sleep architecture, but in the study of obstructive sleep apnea patients treated with dronabinol there was no effect seen on sleep architecture, suggesting that cannabinoid preparations (or dosing) may have fewer effects of sleep architecture compared to traditional medications. This does conflict with the results of other studies which demonstrate changes in objective sleep measures following various formulations of cannabis/cannabinoids. Thus, the particular preparation and dosing of cannabinoids may be an important factor, and again more research is needed.

6. Interpretation of the data from the studies is hampered by sample sizes which limits the statistical power of the results; the majority of studies were not looking at sleep as the primary outcome and focused on cannabinoids in the treatment of another primary illness, making it less clear that beneficial effects on sleep are secondary to the successful treatment of the underlying condition and not a direct effect.

7. Future studies are recommended with trial designs to investigate sleep as the primary outcome, have larger sample sizes, validated subjective measures, and objective assessments, to study the effects of cannabinoids in individuals with well-defined sleep disorders. Additionally, the optimal dosing and optimal balance of THC:CBD ratio for the treatment of sleep disorders remains unknown.

Therapeutic Cannabis and Insomnia

Background

1. Insomnia widespread with estimated 10% of adults having chronic insomnia and an additional one-third having occasional or intermittent insomnia on an annual basis.
2. Estimated cost of insomnia and sleep disorders on American economy: billions of dollars directly through health care costs or indirectly through loss of productivity or accidents.
3. Cannabis commonly reported to aid sleep, many report using cannabis to help them relax and achieve sleep.
4. There is thus a great deal of interest in the possible benefits of cannabis on sleep.

Summary of the literature

Numerous studies have investigated the effects of cannabis on sleep. There have been investigations of CBD, THC, THC:CBD, as plant extracts (or consumption of the cannabis plant by smoking or ingestion) and synthetic forms of THC and CBD (dronabinol, naliximols, nabilone). The various studies are difficult to interpret due to different methodologies, sample size, measured endpoints, and presence or lack of a control (untreated or treated with a different medication) group. Nonetheless, after reviewing the data that exists, there can be some conclusions reached, though further study is needed and should be a consideration. Interpretation of the published data must take into account the incomplete and uncertain information provided.

Summary of studies

Eighteen studies investigated effects of THC on sleep using synthetic equivalents of THC, to treat patients with various ailments. Note that sleep was measured as a secondary outcome, not a primary outcome (i.e. the point of the study was not to study sleep). However, the majority of these studies

reported that THC (synthetic) use improved subjective sleep quality. Seven of 18 studies also reported subjective decreases in sleep disturbances and in nightmare frequency.

In addition, in the 1970-80s there were studies looking at the effects of cannabinoids on sleep through the use of objective measurements. One assessed the effects on sleep at two doses of oral THC via EEG in 7 males with varying h/o pre-study cannabis use; showed inconsistent effects on slow wave sleep and REM sleep time. Another study gave drug naïve subjects (n=9) THC and measured the effects on EEG (sleep); they identified increases in stage 2 sleep and decreases in slow wave and REM sleep. A third study gave THC to four subjects just before sleep and showed increased stage 4 sleep and decreased REM in all subjects. Higher doses were associated with more rapid onset of sleep and decreased light sleep (stage 1).

THC for PTSD: findings relating to sleep: PTSD often associated with nightmares and poor sleep quality.

- One study treating with synthetic cannabinoid (nabilone, equivalent to THC) over 7 weeks for PTSD nightmares found improvements on a PTSD scale regarding distressing dreams; the study included subjects with a h/o poor response to standard treatments and showed significant relief in 70% of subjects, with only 22% of placebo-treated subjects showing improvement.
- These results have been replicated in additional studies (2) using other validated measures of sleep quality and other doses; all studies demonstrated significant improvement in sleep quality and frequency of nightmares. As it was not measured, it is unknown if this effect is mediated through suppression of REM sleep; further studies needed.

THC for chronic pain: findings relating to sleep: studies have examined THC effect on pain with sleep as a secondary outcome measure.

- One study looked at chronic pain and THC as adjunctive treatment to opioids and found a subjective decrease of pain interference during sleep as well as subjective decrease in sleep disturbance.
- Study compared oxycodone to nabilone (synthetic THC) and found less analgesia with nabilone and no difference in effect on sleep between the two.
- Study of 27 ALS patients with painful muscle spasms found no subjective change in sleep quality with dronabinol treatment; in contrast, a study of nabilone in diabetic painful neuropathy found dronabinol treatment led to subjective improvements in sleep quality and less sleep disruption by self-reporting.
- Overall, research on THC for chronic pain and sleep is limited and presents mixed results.
 - THC studied against amitriptyline in patients with fibromyalgia and chronic insomnia; both drugs had a favorable effect on sleep, but nabilone was superior.
 - THC vs gabapentin for diabetic neuropathy pain: nabilone group fared better with improvements in sleep, no change for gabapentin-treated group.

THC for obstructive sleep apnea: findings on sleepiness and apnea/hypopnea.

- Several studies reported subjective improvements on sleepiness scales; one study (limited, needs additional study) reported changes in the Apnea/hypopnea index (improvement) with no change in REM sleep or arousal. Overall, studies support benefits of dronabinol on treatment of OSA.

THC for HIV-related disorders: findings relating to sleep.

- One study treated HIV-positive chronic cannabis smokers with dronabinol and measured sleep latency, number of awakenings, and sleep efficiency. Dronabinol improved sleep for the first 8 nights of a 16 night study; no improvement on days 9-16. Unclear if tolerance played a role. Objective measures showed increased NREM sleep and decreased minutes awake. Subjective measures suggested increased quality of sleep and decreased awakenings.

Sleep and Nabiximols (1:1 CBD:THC)

- Nine studies total investigated the effects of Nabiximols as a treatment outcome for sleep. Subjects had MS or chronic pain. All studies were randomized, placebo-controlled, 4-14 weeks, and examined sleep as a secondary outcome. There was a range of doses. No study had objective measures or validated sleep measures, instead using visual analogue scales. 5/9 studies noted improvements in subjective sleep quality at various doses of Nabiximols, and 4/9 reported improvements in sleep disturbance related scores. Generally results reported significant improvements in sleep quality and overall sleep. Some results reported only on subgroups, making them less robust.

Nabiximols for MS and spasticity

- Several studies show that successful treatment of spasticity in MS can lead to improvements in sleep, but studies at times analyzed only subgroups and so results, though promising, are not as readily extrapolatable.

Nabiximols for Chronic Pain

- Five studies looked at nabiximols and chronic pain. Improvements reported in subjective measures of sleep quality and disturbances with administration of nabiximols. One study look for cannabinoids in individuals with rheumatoid arthritis and pain and reported positive treatment results and subjective data. There was good analgesic effects and improvement in subjective sleep quality. Another study looked at peripheral neuropathic pain and again demonstrated self-reported improvement in sleep quality. A larger study (246 patients) with peripheral neuropathic pain randomized to receive either placebo or nabiximols showed a significant improvement in sleep quality based on a 10 point rated sleep scale. Although sleep was a secondary outcome measure and the improvement may have been due to pain control, all studies reported improved overall sleep.

Sleep and Other Cannabis Preparations

- Fourteen studies look that the effects of combinations of cannabinoids treatments including smoked cannabis on sleep quality, sleep disturbances, and sleep onset latency. 6/14 reported favorable outcomes for cannabinoids treatments over placebo with significant improvements within the sleep domains. 2 studies included validated sleep measurement found patient's reported decreased sleep onset latency with the use of cannabinoid treatments. Another study examined patients with neuropathic pain in which they smoked cannabis (1 of 4 different strains with varying THC potencies). The higher THC potency cannabis was associated with less difficulty falling sleep and fewer sleep disturbances as measured on a sleep questionnaire. And another study with healthy volunteers for different treatments

including THC and CBD combinations and THC alone as well as placebo were examined. Measures included EEG performance, sleep onset latency, and subjective assessments of sleepiness and mood. There was no significant effect on sleep seen with the THC alone. The low and medium range dosing THC/CBD combinations showed a decrease in stage III sleep with the higher dose demonstrating increased wakefulness. It was concluded that the activating properties of CBD and the sedative properties of THC could function together to induce sleep while counteracting daytime sleepiness. There were no significant reported changes or effects on sleep in this study.

Conclusions from the review of studies available

1. The majority of the studies suggests that the use of THC and THC derivatives, alone or in combination with CBD, may improve self-reported sleep quality, sleep disturbances, and decreased sleep onset latency.
2. Despite the importance of sleep, most of the studies examined sleep as a secondary outcome; there is a lack of placebo-controlled trials examining the use of cannabinoids specifically for treatment of sleep disorders.
3. Many of the available studies used non-standardized, non-validated questionnaires and subjective sleep measures, which leaves something to be desired in terms of the validity of data.
4. Available pharmacological treatments for insomnia and primary sleep disorders include medications such as benzodiazepines and non-benzodiazepine hypnotics. In addition, many other medications are used off label for the treatment of the symptoms. Many of these medications are limited by side effects, adverse effects, and in some cases addiction liability. Cannabinoids have also been associated with some adverse events such as dizziness, cognitive impairment, increased risk of motor vehicle accidents, psychosis, dependence, depression, and anxiety.
5. Some medications currently used to treat insomnia can affect sleep architecture, but in the study of obstructive sleep apnea patients treated with dronabinol there was no effect seen on sleep architecture, suggesting that cannabinoid preparations (or dosing) may have fewer effects of sleep architecture compared to traditional medications. This does conflict with the results of other studies which demonstrate changes in objective sleep measures following various formulations of cannabis/cannabinoids. Thus the particular preparation and dosing of cannabinoids may be an important factor and again more research is needed.
6. Interpretation of the data from the studies is hampered by sample sizes which limits the statistical power of the results, the majority of studies were not looking at sleep as the primary outcome and focused on cannabinoids in the treatment of another primary illness, making it less clear that beneficial effects on sleep are secondary to the successful treatment of the underlying condition and not a direct effect.
7. Future studies are recommended with trial designs to investigate sleep as the primary outcome, have larger sample sizes, validated subjective measures, and objective assessments, to study the effects of cannabinoids in individuals with well-defined sleep disorders. Additionally, the optimal dosing and optimal balance of THC: CBD ratio for the treatment of sleep disorders remains unknown.

Public Comments

Two comments were received in favor of adding insomnia and anxiety to the list of qualifying conditions; insomnia was not separated out in the comments

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3. Klumpers, LE, Thacker, DL (2019) A Brief Background on Cannabis: From Plant to Medical Indications. *Journal of AOAC International*, Volume 102, #2, 412-420.
4. Opila-Lehman, J, Shannon, S (2016) Effectiveness of Cannabidiol Oil for Pediatric Anxiety and Insomnia as Part of Posttraumatic Stress Disorder: A Case Report. *Perm J* 20 (4): 16-005.
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6. Up-To-Date 2019: Overview of the treatment of insomnia in adults. (Summary and review of the topic of insomnia).
7. Drazdowski, TK, Kliewer, WL, Marcel, M. (2019) college students' using marijuana to sleep relates to frequency, problematic use, and sleep problems. *Journal of American College health*, 1-11.
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Appendix B

NH Therapeutic Cannabis Medical Oversight Board Qualifying Medical Condition Recommendation Report: Anxiety October 2019

Condition: Anxiety

Recommendation

- Do not approve as a qualifying diagnosis
- Do not recommend as a qualifying symptom
- Do not recommend as a stand-alone qualifying diagnosis/condition

Rationale

It would be irresponsible to recommend addressing “anxiety” in isolation, as a symptom rather than as part of a specific diagnosis, which requires careful assessment.

Recommend against chronic use of any THC-containing product (including whole plant) for management of any anxiety spectrum condition, or for use in anyone with any co-morbid anxiety disorder. THC has some evidence for harm in terms of worsening symptomatology particularly in adolescents where suicidality may arise. Acutely and situationally, there may be evidence that low dose THC can improve anxiety while high dose can worsen and induce panic attacks but findings are mixed.

The evidence for CBD-only products (including whole plant) is equivocal. Acute pretreatment (hence not chronic use) in those with the Social Anxiety Disorder type may be effective, although clear conclusions cannot be drawn (limited data). Chronic CBD when combined with THC may worsen anxiety exponentially.

Regarding anxiety as a symptom in those with pain conditions there is emerging evidence of worsening anxiety when whole plant cannabis is concomitantly used with (opioid) pain regimens.

If, however, this condition were to be approved as a qualifying medical condition, would recommend any decisions regarding certifications for any particular anxiety disorder be made by physicians trained in psychiatric disorders who can: make the specific anxiety diagnosis; recognize psychiatric and addictive comorbidities; and are able to provide interventions if suicidality arises. Additionally, extreme diligence is required when cannabinoids are used concomitantly with evidence based pharmacological treatment modalities for management of anxiety due to synergistic sedative effects and drug : herb interactions that can be lethal.

Important concepts to consider

1. Anxiety is not a single condition but an umbrella term, each subset with unique underlying neurobiological basis requiring specifically crafted management. Anxiety (Disorders) per DSM-5:
 - a. Generalized Anxiety Disorder
 - b. Phobias and Specific phobias
 - c. Agoraphobia

- d. Social Anxiety Disorder
 - e. Separation Anxiety Disorder
2. Anxiety disorders are highly prevalent: 33.7% of population is affected by an anxiety disorder during their lifetime (highest of all mental illnesses).
 3. Anxiety disorders are highly comorbid with other psychiatric and addictive disorders: >90% of individuals with an anxiety disorder have another concurrent psychiatric condition. Depressive disorder is most frequent (76.7%), followed by addictive disorders (35.9%) and bipolar (22.3%).
 4. There is evidence for harm (worsening symptoms, increased disease burden, development of suicidality) when whole plant and THC only is used by those with bi- or uni-polar depression
 5. Whole plants contains >500 constituents each found in various proportions with significant pharmacodynamics and pharmacokinetic interactions with other psychopharmacological agents.
 6. American Psychiatric Association: "There is currently no scientific evidence to support the use of cannabis as an effective treatment for any psychiatric illness. Several studies have shown that cannabis use may in fact exacerbate or hasten the onset of psychiatric illnesses. This includes the contribution of cannabis to symptoms of mood disorders, anxiety and psychosis, particularly in young adulthood. Cannabis use is associated with the emergence of mood disorders, particularly symptoms of bipolar disorder, among those with a family history of mood disorder."
 7. In adolescents, regular cannabis use is associated with increased incidence of anxiety disorders as well as increased depression, suicidal ideation, use of other substances, and risky behavior.
 8. Regular cannabis use is associated with an increased risk of developing a cannabis use disorder (9% of episodic users become dependent, and 25-50% of daily users).
 9. Acute THC-only administration is dose dependent – low doses anxiolytic while higher doses induce anxiety. Acute CBD co-administration has mixed findings (Boggs et al 2018).
 10. Animal studies show chronic co-administration of CBD and THC; greater anxiety symptoms than induced by THC alone at high doses (Klein et al 2011).
 11. National Academy of Sciences (2017): Moderate level of evidence supports that whole plant use is associated with: increased incidence of social anxiety disorder in regular users (also increased risk for developing depressive disorders; increased incidence of suicidal ideation and behavior).

Supporting evidence

1. American Psychiatric Association position statement on use of therapeutic cannabis for anxiety disorders.
2. Natural Sciences and Engineering Research Council of Canada (NSERC) and other epidemiological studies.
3. Results of a systematic and comprehensive literature review on the use of CBD only and THC only for treatment / management of anxiety spectrum conditions.
4. National Academy of Science Report.
5. Literature review of studies published since the National Academy of Science Report.

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Summary of findings of comprehensive literature search and analysis of CBD and THC impact on anxiety conditions

“Studies of CBD and THC for Anxiety Disorders”

Two small studies reported mixed findings on the impact of synthetic THC on various anxiety conditions. Another two studies of single dose CBD among people social anxiety disorders reported positive findings. The details of these studies are summarized below.

The anxiolytic properties of a synthetic THC compound, nabilone, were studied using a single dosing paradigm (Glass, Uhlenhuth, Hartel, Schuster, & Fischman, 1981). Here, eight symptomatic individuals diagnosed with either Anxiety Neurosis or Generalized Anxiety Disorder participated in receiving a single dose of 2 mg nabilone, placebo, and then once a week dosing of nabilone of various strengths ranging from 0.5mg to 5 mg over five weeks. Nabilone was not associated with any improvements in anxiety symptoms. Side effects included increase in heart rate and sedation while orthostatic hypotension was noted with higher doses.

A study of daily dosing for a month reported more promising findings. In this double-blinded trial, nabilone 1 mg TID or placebo was administered to 20 participants diagnosed with DSM-1 psychoneurotic anxiety disorders over 28 days followed by a four day washout (Fabre & McLendon, 1981). Anxiety improved in the nabilone group compared the to placebo group as measured by the Hamilton Anxiety Scale. However, Hamilton Anxiety Scale total scores range from 0-56, with scores of 18-24 indicating moderate levels of anxiety. The mean total scores shown for participants in this study were very low: 1.9 on the first treatment day compared to about 1.0 on day 28 in the nabilone group, and 1.7 in the placebo group, this it is unclear how applicable this study would be to patients with clinically significant anxiety disorders. Most participants continued for the duration of the trial despite reports of mild to severe dry mouth among 18 of the participants and drowsiness among three patients.

As for CBD trials, a crossover fMRI scanning study (Crippa et al., 2011) compared a single dose of 400mg oral CBD to placebo in ten treatment-naïve men diagnosed with generalized social anxiety disorder. A significant decrease in anxiety was observed in the CBD pre-treated group on exposure to anxiety-provoking stimulus without appreciable side effects. This was replicated in a subsequent study (Bergamaschi et al.) where 24 treatment-naive patients diagnosed with social anxiety disorder were randomized to receive a single dose of 600mg oral CBD or placebo 90 minutes prior to a simulated public speaking test. The group receiving CBD experienced a significant difference during the speech phase ($p=0.012$) on the anxiety factor of the visual analog mood scale. Additionally, pretreatment with CBD also resulted in less cognitive impairment and less discomfort during both the anticipation and speech phases of the test. Total scores were not reported. No side effects were mentioned. We did not find any prospective trials of repeated or daily dosing of CBD among people with social anxiety or other anxiety disorders in which anxiety disorder symptoms were prospectively assessed. We did not find any studies of defined dose combinations of CBD and THC on people with anxiety disorders.”

Anecdotal Evidence

Public hearing testimony, written testimonies:

Four individuals submitted testimonies.

One from an RN who leads a large network of cannabis nurses. She has “witnessed several patients time and time again benefit from using cannabis oil drops for insomnia and other forms, including the drops for anxiety”. The exact composition of these drops, specific anxiety diagnoses, frequency of use and duration of time was not mentioned.

Second from the president of NH Herbal network and owner of “Mama Kiss Cannabis”. She advocates for use of this “life-changing plant” mainly to manage insomnia but also “symptoms of ADHD and anxiety” based on personal experience (has dealt with a multitude of symptoms related to insomnia, anxiety, pain and autoimmune conditions along others). She notes “legal CBD products” do not alleviate symptoms and it is rather the entire plant that has the effects.

Third from the partner of someone dealing with “severe anxiety as well as other ailments” for who “anti-anxiety medications” have historically led to undesirable adverse effects. Use of cannabis (?whole plant) have “reduced his anxiety without significant negative adverse effects”. The exact composition used, route of administration, specific anxiety diagnosis, frequency of use and duration of time was not mentioned.

Fourth discussed someone’s experience with anxiety symptoms starting at age 13 with past trials of clonazepam and sertraline which led to adverse effects. Ten years since the onset the anxiety has led to manifestation of headaches and insomnia. This individual is not a user but reports his friends have dealt with similar issues and obtaining a cannabis license has led to improved symptoms for them as witnessed over a one week period where he notes “he seems like a completely different person to me, it felt like someone else took over my friend’s body, he was so full of life and happy”. He attached several articles one noting: “low THC/high CBD cannabis was best for reducing perceived symptoms of depression, High THC/high CBD cannabis was best for reducing perceived symptoms of stress, and the use of cannabis to treat depression appears to exacerbate depression over time.”

Appendix C

New Hampshire Therapeutic Cannabis Medical Oversight Board
Qualifying Medical Condition Recommendation Report: Tick-borne Illnesses
October 2019

Condition: Tick-borne Illnesses

Recommendation

Approve as a stand-alone qualifying medical condition

Rationale

1. Currently, no evidence-based studies specific to cannabis use with regard to tick-borne illnesses are available; however, the anti-inflammatory, analgesic, anxiolytic and neuroprotective action of cannabis has been well documented, as has its clinical impact on reducing pain, nausea, anxiety, insomnia and discomfort from dermal rashes.
2. Patients with chronic persistent tick-borne illness infection typically suffer from multiple symptoms including fatigue, impaired cognition (“brain fog”), sleep disorders and pain syndromes. As attested by members of the public via written testimony, as well as noted by some clinicians, many of these symptoms have been reportedly relieved (or significantly reduced) through therapeutic cannabis use.
3. Due to the number of tick-borne illnesses (listed in summary), multitude of potential symptoms (listed in summary) and varying clinical presentation, recommend approval as a stand-alone qualifying medical condition.

Summary

1. Tick-borne illnesses are increasing nationally. Each year, the CDC reports approximately 30,000 cases of Lyme disease, but experts estimate that the true incidence is 10 times higher.
2. Listing of potential tick-borne illnesses in NH (based on types of ticks in the area – per CDC):
 - Lyme disease
 - Babesiosis
 - Ehrlichiosis
 - Bartonella
 - STARI
 - Rocky Mountain Spotted Fever
 - Anaplasmosis
 - Relapsing Fever
 - Powassan Virus disease
 - Heartland Virus
3. Tick-borne illnesses cause multiple symptoms, including:
 - Rash (various rashes dependent upon type of tick-borne illness)
 - Fever, chills

- Diaphoresis
 - Severe headache
 - Insomnia
 - Profound fatigue
 - Muscle and joint pain
 - Anxiety
 - Lymphadenopathy
 - Arthropathies
 - Neuropathic pain
 - Nausea/vomiting/diarrhea
 - Anorexia
 - Seizures
 - Muscular atrophy
 - Numbness in extremities
 - Tremors
4. Tick-borne Illness Rashes. Lyme disease, southern tick-associated rash illness (STARI), Rocky Mountain spotted fever (RMSF), ehrlichiosis, bartonella, and tularemia can result in distinctive rashes:
- Lyme disease: Erythema migrans
 - STARI: red, expanding “bulls’ eye” lesions
 - Rocky Mountain Spotted Fever: small, flat, pink, non-itchy macules on wrists, forearms, ankles and trunk. Can progress to red-to-purple spotted (petechial) rash.
 - Bartonella: unusual streaked rash that resembles stretch marks.
 - Tularemia: skin ulcer appears at the site where the organism entered the body. The ulcer is accompanied by swelling of regional lymph glands, usually in the armpit or groin.
 - Ehrlichiosis: rash ranges from macular to maculopapular to petechial.

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Cannabis Kicks Lyme Disease to the Curb, <http://www.realfarmacy.com/kicks-lyme-disease-to-the-curb/>

Medical Marijuana for Lyme Disease, <https://www.marijuanadoctors.com/conditions/lyme-disease/>

Project CBD, User's Manual: <https://www.projectcbd.org/guidance/cbd-users-manual>

Appendix D

NH Therapeutic Cannabis Medical Oversight Board Qualifying Medical Condition Recommendation Report: Opioid Addiction, Misuse or Abuse October 2019

Condition: Opioid addiction, misuse or abuse

Recommendation

Do NOT recommend adding opioid addiction, misuse or abuse as a qualifying medical condition for the therapeutic use of cannabis.

Note: CBD-only formulations may be effective for symptoms associated with opioid use disorder. However, cannabis products with THC (ie, whole plant cannabis) should be avoided and are not recommended.

Rationale

Cannabidiol (CBD) shows promise in reducing craving for opioids², reducing anxiety associated with withdrawal symptoms, and decreasing cognitive and emotional stress vulnerability. Thus a function for CBD in reducing the risk of relapse. CBD has low reinforcing properties with limited abuse potential and may inhibit drug seeking behavior.¹

Conclusions from both animal and human studies demonstrate that THC is a psychoactive compound with rewarding effects and addictive properties.¹ THC increases the use of illicit opioids, can cause significant anxiety in the individual, and is not recommended by authoritative individuals nor organizations to be associated with treating opioid use disorder.

While cannabis has been used for pain control and has been touted to reduce the use of opioids in pain conditions, thereby ostensibly reducing the risk of developing opioid use disorders, this is not the same as treating opioid use disorder. Currently there are FDA approved medications for opioid use disorder and these show significant reduction in overdose deaths, reduction in HIV and Hepatitis B and C transmission, among other therapeutic outcomes. The addition of cannabis in its whole form is controversial and organizations such as the American Society of Addiction Medicine hold a position against promoting cannabis for medical use, never mind treatment of OUD:

- https://www.asam.org/docs/default-source/public-policy-statements/marijuana-cannabinoids-and-legalization-9-21-20156d6e0f9472bc604ca5b7ff000030b21a.pdf?sfvrsn=e0d26fc2_0
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Patients who have a diagnosis of an opioid use disorder have a higher risk of use disorders of other types as well. There have been suggestions that use of cannabis (ie, smoked, THC) increases the risk of use of other addictive substances including opioids.^{3,4} Additionally, treatment strategies for addiction include those that reduce the risk that the patient be using any psychoactive substances and work on managing the illness with behavioral health changes as well as medications.

Since the above recommendation would be to have restrictions on certifying for therapeutic cannabis, and limiting the product to CBD only, it is recommended to consider using a current product that is available to be prescribed off label. This is Epidiolex.

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Appendix E

NH Therapeutic Cannabis Medical Oversight Board Qualifying Medical Condition Recommendation Report: Opioid Use Disorder October 2019

Condition: Opioid Use Disorder

Recommendation

- **That pure CBD be available** for use in management of opioid withdrawal and as an adjunct to evidence-based interventions for opioid use disorders. (Early studies are promising and to date no harm has been demonstrated with short term use, though it should be noted that long term use has not been studied so effects over time are not known.)
 - Possibilities for making CBD available to patients include:
 - Off label prescription of Epidiolex (pure FDA approved & regulated CBD)
 - Over the counter CBD that has been tested and certified as pure CBD
 - Certification to exclusively certify patients for CBD, not THC containing products.
- **That OUD not be an indication for therapeutic cannabis certification** through the current general therapeutic cannabis certification process.
- That certification
 - **May be provided as an adjunct in the context of evidence-based MAT** by a DATA 2001 waived clinician who is prescribing or authorizing the individual's MAT
 - **May be provided by an ABAM, APA or ACGME certified addiction medicine or addiction psychiatry physician** who follows the patient regularly, with or without other MAT treatment
- That such treatment **must be treated as a clinical trial** because the outcomes of the use of cannabis as a treatment or adjunct for OUD are unknown. To that end
 - The certifying clinician and/or patient must complete and submit a quarterly data sheet (TBD) to DHHS
 - Tracking/analysis of data must be performed
 - Policy may be changed based on clinical trial findings and on evolving scientific literature.

Key contextual information

According to the 2018 Substance Abuse and Mental Health Services Administration National Survey on Drug Use and Health (<https://www.samhsa.gov/data/report/2018-nsduh-annual-national-report>), opioid use disorder (OUD) is the third most common substance use disorder in the United States. Opioid use disorder affects approximately 2.2 million people in the United States, while cannabis use disorder affects 4.4 million and alcohol use disorder affects 14.8 million. However, because mis/overuse of opioids can cause severe respiratory depression, opioid misuse (with or without OUD), is associated with high risk of lethal overdose (47,736 drug overdose deaths in the US in 2017 involved an opioid <https://www.cdc.gov/drugoverdose/epidemic/index.html>) and OUD has become the most common substance use disorder for which people in the U.S. seek treatment. (NSDUH 2018)

Currently three pharmacologic agents are available to treat OUD, along with psychosocial treatment approaches. Strong evidence supports the efficacy of the opioid agonist methadone and the opioid partial agonist buprenorphine in supporting OUD recovery, reducing risk of overdose deaths from OUD,

and improving function. Evidence is accruing in support of the opioid antagonist naltrexone in treatment of OUD as well.

As psychotropic substances that can be associated with misuse, both methadone and buprenorphine require special authorization to use in treatment of opioid addiction; methadone is dispensed only through federally licensed treatment clinics and buprenorphine can be prescribed only by clinicians who receive special education and certification. Naltrexone, which has no demonstrated misuse potential, can be prescribed by any clinicians with prescriptive authority.

Cannabis is a psychotropic agent with demonstrated misuse and addiction potential. Moderate to severe cannabis (addiction) occurs in 9%-30% of users depending on age of onset of use and THC concentrations (active psychotropic cannabinoid) of cannabis used (Budney et al, 2019). Therefore, consideration of cannabis as a potential therapeutic agent in the context OUD must take into consideration potential risks for misuse and potential compounding of addiction and, if authorized for use in this context, care must be appropriately structured to avoid potential harm.

Summary of findings

More studies on cannabis and individual cannabinoids are needed to clarify cannabis and cannabinoid actions on opioid reward, opioid misuse, and opioid use disorder. The current evidence on cannabis and opioid misuse/use disorder is somewhat conflicting; however, taken in aggregate available studies lean towards indicating that cannabis use is associated with greater risk of opioid misuse and poorer functional outcomes. The cannabinoid CBD, and possibly other specific cannabinoids under study, appear to have promise in treatment of OUD. Testimonials from individuals suggest some people with OUD may experience improvement with use of cannabis.

Specific points:

- CBD alone may be helpful in reducing anxiety and craving in early abstinence from opioids in OUD.
- Impact of cannabis on retention in OUD treatment is not clear (one study suggests increased retention, one the opposite).
- Cannabis use appears to be associated with higher risk of development of opioid use disorder in the future.
- Cannabis use during opioid therapy of pain appears to be associated with increased risk of opioid misuse and/or OUD.
- Persons with OUD who also have cannabis use disorder have poorer functional outcomes (homelessness and inpatient hospitalizations) but receive fewer prescriptions for opioids.
- Initially promising epidemiologic findings suggesting that therapeutic cannabis availability reduces opioid overdose deaths on a population wide basis have not held up over time.
- Numerous anecdotal reports suggest that a subset of persons find cannabis helpful in recovery from OUD. This could be through palliation of OUD associated symptoms (sleep disturbance, pain, etc) or through direct effects on limbic reward and addiction mechanisms. Future studies might include analysis of the experiences of advocates who have recovered from OUD through use of cannabis.

Relevant Scientific Evidence

There is considerable scientific literature that addresses potential interactions between cannabis and opioids. Studies generally fall into three issue categories:

1. Impact of cannabis and/or cannabinoids on opioid dose requirements and opioid use in pain treatment
2. Impact of state cannabis laws on opioid use and opioid-related harm
3. Impact of cannabis and/or cannabinoids on opioid misuse and use disorder

It is clear that human endogenous/physiologic opioid and cannabinoid systems are closely inter-related based on observation of both anatomic co-location of opioid and cannabinoid receptors throughout the central and peripheral nervous systems and of the fact that manipulation of cannabinoid and opioid receptors can facilitate or block actions of the other system. It is further clear that these interrelationships are relevant to understanding all three issues above. However, in considering whether opioid use disorder should be an indication for therapeutic cannabis certification, only studies that consider impact of cannabis on opioid misuse and opioid use disorder (OUD) are directly relevant. These are discussed below. Brief note is made, however, of studies addressing the other two issues which are salient to cannabis use in OUD. (Bibliography at the end includes all identified cannabis and opioid citations, many of which are not directly relevant to the OUD issue and therefore not cited here in the narrative here. The bibliography is included in two formats: alphabetical and grouped by issue theme.)

Studies on cannabis and cannabinoid roles with respect to opioid misuse and OUD

Nine studies were identified that specifically address the relationship between cannabis or cannabinoid use and opioid misuse or use disorder.

- One high quality clinical trial found the cannabinoid CBD reduced anxiety and cue-induced craving in early abstinence (up to 7 days) from opioids in the context of OUD. (Hurd et al, 2019)
- One study suggested heavy cannabis use increased retention in treatment of OUD (Socias et al, 2018); however, this study was contrasted by a similar study that found higher dropout rates from OUD treatment in cannabis users. (Franklyn et al, 2017)
- One study examined a large national Veterans data base and found that persons with co-occurring OUD and CUD were at higher risk for homelessness and inpatient psychiatric admissions than persons with OUD or CUD alone, but that the co-occurring group received fewer prescriptions for opioids. (DeAquino et al, 2019)
- Two studies suggested that cannabis use during one period of time is associated with higher risk for development of non-medical use of opioids and/or OUD at a future time. (Butelman et al, 2018; Olfson et al, 2018)
- Three studies examined patients on opioid therapy of pain and found that patients who also used cannabis were at greater risk for misuse of prescribed opioids and/or for development of OUD than those who using opioids alone. Two of these studies evaluated patients with medical cannabis authorization and co-use (Caputi et al, 2018; Nugent et al, 2018), while one evaluated cannabis use noted on urine toxicology screens. (Dibenedetto et al, 2018)

Other studies that may be considered relevant

An epidemiologic study published in 2014 which received much public attention, examined data from 1999-2010 and found that states with therapeutic cannabis availability had lower rates of opioid overdose deaths. However, a replication of the study using the same methodology and extending the study through 2017 showed a reversal of the original findings with overdose deaths higher in states with

therapeutic cannabis. (Shover et al, 2019) If the initial findings had sheld however, this would still not provide relevant support for cannabis as a treatment for OUD, since it could not be assumed that reduction in deaths occurred in persons with OUD, as opposed to persons using opioids for pain treatment or other purposes.

There is conflicting evidence regarding opioid dosing for pain in the presence of co-use of cannabis; however, the evidence in both animals and humans appears to weigh towards suggesting reduced opioid dose requirements to treat pain in the presence of cannabis. (*See list of pain-related articles in bibliography.*) This reflexively suggests to many that if opioid use for pain is reduced in the presence of cannabis, opioid use must also be reduced in in the presence of OUD. However, reductions in opioid dosing for pain likely reflects complementary (synergistic or additive) analgesic mechanisms which can not be reasonably extrapolated to an expectation of reduced opioid consumption in OUD which is mediated entirely different than pain. Indeed, the three studies noted above find higher rates opioid misuse and/or OUD in opioid therapy of pain when cannabis is also used.

Anecdotal Evidence

Public hearing testimony

A public hearing on opioid use disorder as an indication for cannabis was held at which two individuals testified.

One individual related the experience of his brother who had addiction to heroin and who experienced the use of cannabis as instrumental to his recovery from OUD. The reporter noted that use of cannabis alone has not been directly associated with overdose deaths and it is far safer than opioids, so he believed it should be available for use by individuals with OUD in order to reduce harm from opioids.

Another individual reported that she credited cannabis with helping to restore her to a functional life and feelings of normalcy in the presence of long-term, disabling PTSD, chronic pain, anxiety and dysfunctional use of alcohol, cocaine and opioids.

Other testimonials heard in other contexts

Many individuals who appear to be functioning well in recovery from opioid use disorder, have reported—in legislative hearings, on radio call-in shows, to their care providers, and in other contexts—their personal experiences that cannabis has helped them reduce or eliminate misuse of opioids and overcome OUD. Many report their perceptions that it has been life-saving.

While anecdotal evidence should generally be used to inform research, not to determine policy or clinical practice, in this context that includes including rapidly evolving and as yet unclear scientific evidence, it not easily dismissed. I believe it should be accommodated in policy if it is safe to do so.

Information from other states

Arizona, Massachusetts, Hawaii, Maine, Connecticut and New Mexico have reportedly considered OUD as an indication for therapeutic cannabis and have rejected it as qualifying conditions.

New Jersey, New York, Pennsylvania and Illinois recognize OUD as an indication for cannabis with various caveats.

- New York requires that practitioners certifying OUD for cannabis be waived to provide MAT to provide and that practitioners certifying ANY conditions for cannabis use must have taken a state approved therapeutic cannabis course.
https://www.health.ny.gov/regulations/medical_marijuana/
- New Jersey permits cannabis use to ease withdrawal symptoms and as an adjunct MAT treatment program. Patients must be enrolled in an MAT program.
https://www.nj.gov/health/medicalmarijuana/documents/agency_decision_letters/MMP_FAD_conditions_012319.pdf
- Pennsylvania permits cannabis use for opioid use disorder “for which conventional therapeutic interventions are contraindicated or ineffective, or for which adjunctive therapy is indicated in combination with primary therapeutic interventions.”
<https://www.health.pa.gov/topics/programs/Medical%20Marijuana/Pages/Medical%20Marijuana.aspx>
- Illinois permits cannabis as a “substitution” for opioids apparently for any conditions for which an opioid could be legitimately prescribed, presumably pain or OUD. Somewhat incomprehensible to this reader, but here is a link. <http://dph.illinois.gov/topics-services/prevention-wellness/medical-cannabis/opioid-alternative-pilot-program>

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Appendix F

RECOMMENDATIONS OF THE THERAPEUTIC CANNABIS MEDICAL OVERSIGHT BOARD REGARDING HB 366 AND HB 461

Rep. Jerry Knirk, TCMOB member and liaison to the legislature

Oct 12, 2019

The Therapeutic Cannabis Medical Oversight Board (TCMOB) is composed of the medical director of DHHS, a qualifying patient, a clinical representative from an ATC and ten medical providers from various fields, who have the task of advising the therapeutic cannabis program on medical issues, including qualifying conditions. The TCMOB devoted a great deal of time to considering the conditions included in HB 366 and HB 461.

We had preliminary discussions at one meeting and appointed subcommittees to consider each condition. At a subsequent meeting those subcommittees reported their initial findings. We held a public hearing on the four conditions on September 25 and written comments were accepted. Draft reports were prepared by a member of each of the subcommittees and circulated to the board. The board then met on October 9 to finalize recommendations on these four conditions to advise the Health and Human Services and Elderly Affairs Committee of the House of Representatives for their consideration when deciding the disposition of these bills.

The group was very diligent utilizing their personal experience, exhaustive literature reviews, and testimonials from patients to make their recommendations.

Final reports have not been completed at this time. I am summarizing the findings in this document utilizing portions of the draft reports and have obtained permission to circulate the draft reports for the two conditions upon which we had good agreement on the recommendation, agreeing with the report. For the conditions in which the board had conflicting reports or when the decision was not in agreement with the report, I have summarized the reports and the discussion.

INSOMNIA (HB 461)

Recommendation: Include as a qualifying symptom

Vote: 9-1

Summary:

1. The majority of the studies suggests that the use of THC and THC derivatives, alone or in combination with CBD, may improve self-reported sleep quality, sleep disturbances, and decreased sleep onset latency
2. Despite the importance of sleep, most of the studies examined sleep as a secondary outcome; there is a lack of placebo-controlled trials examining the use of cannabinoids specifically for treatment of sleep disorders.

3. Many of the available studies used nonstandardized, non-validated questionnaires and subjective sleep measures, which leaves something to be desired in terms of the validity of data.
4. Available pharmacological treatments for insomnia and primary sleep disorders include medications such as benzodiazepines and non-benzodiazepine hypnotics. In addition, many other medications are used off label for the treatment of the symptoms. Many of these medications are limited by side effects, adverse effects, and in some cases addiction liability. Cannabinoids have also been associated with some adverse events such as dizziness, cognitive impairment, increased risk of motor vehicle accidents, psychosis, dependence, depression, and anxiety.
5. Some medications currently used to treat insomnia can affect sleep architecture, but in the study of obstructive sleep apnea patients treated with dronabinol there was no effect seen on sleep architecture, suggesting that cannabinoid preparations (or dosing) may have fewer effects of sleep architecture compared to traditional medications. This does conflict with the results of other studies which demonstrate changes in objective sleep measures following various formulations of cannabis/cannabinoids. Thus the particular preparation and dosing of cannabinoids may be an important factor and more research is needed.
6. Interpretation of the data from the studies is hampered by sample sizes which limits the statistical power of the results. The majority of studies were not looking at sleep as the primary outcome and focused on cannabinoids in the treatment of another primary illness, making it less clear that beneficial effects on sleep are secondary to the successful treatment of the underlying condition and not a direct effect.
7. Future studies are recommended with trial designs to investigate sleep as the primary outcome, have larger sample sizes, validated subjective measures, and objective assessments and to study the effects of cannabinoids in individuals with well-defined sleep disorders. Additionally, the optimal dosing and optimal balance of THC: CBD ratio for the treatment of sleep disorders remains unknown.

Public comments:

Two comments were received in favor of adding insomnia and anxiety to the list of qualifying conditions; insomnia was not separated out in the comment

Special considerations:

- i. Pediatric population: unknown effects on the developing brain
- ii. Pregnant women: unknown effects on the developing fetus
- iii. Insomnia as a single diagnosis or secondary (associated) one. EX: it may be very useful for pain-mediated insomnia and not useful for depression-mediated insomnia
- iv. CBD vs. THC vs. whole plant extract containing both. It may be that the CBD alone is adequate and most therapeutic, as in epilepsy treatment.
- v. Studies are limited in reaching any conclusions, but overall point to beneficial effects more than deleterious
- vi. At what point can we hope to apply a scientific approach to medical marijuana, or should it be regarded in a different category, somewhere in the alternative medicine area, not subject to the standards of the allopathic medical profession?

Discussion:

Discussion reflected the points made in the report and the above noted vote was taken to include insomnia as a qualifying symptom. Motion was made to make insomnia a free-standing condition and that motion was defeated.

ANXIETY (HB 461)

Recommendation: Do not approve as a qualifying symptom, diagnosis or free-standing diagnosis/condition

Vote: 8-2

Summary:

It would be irresponsible to recommend addressing “anxiety” in isolation, as a symptom rather than as part of a specific diagnosis - which requires careful assessment.

Recommend against chronic use of any THC-containing product (including whole plant) for management of any anxiety spectrum condition, or for use in anyone with any co-morbid anxiety disorder. THC has some evidence for harm in terms of worsening symptomatology particularly in adolescents where suicidality may arise. Acutely and situationally, there may be evidence that low dose THC can improve anxiety while high dose can worsen and induce panic attacks but findings are mixed.

The evidence for CBD-only products (including whole plant) is equivocal. Acute pretreatment (hence not chronic use) in those with the Social Anxiety Disorder type may be effective, although clear conclusions cannot be drawn (limited data). Chronic CBD when combined with THC may worsen anxiety exponentially.

Regarding anxiety as a symptom in those with pain conditions there is emerging evidence of worsening anxiety when whole plant cannabis is concomitantly used with (opioid) pain regimens.

If however anxiety is approved as a qualifying symptom or condition, would recommend any decisions regarding certifications for any particular anxiety disorder to physicians trained in psychiatric disorders who can: make the specific anxiety diagnosis; recognize psychiatric and addictive comorbidities; and are able to provide interventions if suicidality arises. Additionally, extreme diligence is required when cannabinoids are used concomitantly with evidence based pharmacological treatment modalities for management of anxiety due to synergistic sedative effects and drug : herb interactions that can be lethal.

Important concepts to consider:

1. Anxiety is not a single condition but an umbrella term, each subset with unique underlying neurobiological basis requiring specifically-crafted management:
Anxiety (Disorders) per DSM-5:
 - a. Generalized Anxiety Disorder
 - b. Phobias and Specific phobias
 - c. Agoraphobia

- d. Social Anxiety Disorder
 - e. Separation Anxiety Disorder
2. Anxiety disorders are highly prevalent - 33.7% of population is affected by an anxiety disorder during their lifetime (highest of all mental illnesses).
 3. Anxiety are highly comorbid with other psychiatric and addictive disorders - >90% of individuals with an anxiety disorder have another concurrent psychiatric condition. Depressive disorder is most frequent (76.7%), followed by addictive disorders (35.9%) and bipolar (22.3%)
 4. There is evidence for harm (worsening symptoms, increased disease burden, development of suicidality) when whole plant and THC only is used by those with bi- or uni-polar depression
 5. Whole plant contains >500 constituents each found in various proportions with significant pharmacodynamics and pharmacokinetic interactions with other psychopharmacological agents
 6. American Psychiatric Association – “There is currently no scientific evidence to support the use of cannabis as an effective treatment for any psychiatric illness. Several studies have shown that cannabis use may in fact exacerbate or hasten the onset of psychiatric illnesses. This includes the contribution of cannabis to symptoms of mood disorders, anxiety and psychosis, particularly in young adulthood. Cannabis use is associated with the emergence of mood disorders, particularly symptoms of bipolar disorder, among those with a family history of mood disorder.”
 7. In adolescents, regular cannabis use is associated with increased incidence of anxiety disorders as well as increased depression, suicidal ideation, use of other substances and risky behavior.
 8. Regular cannabis use is associated with an increased risk of developing a cannabis use disorder (9% of episodic users become dependent, and 25-50% daily users).
 9. Acute THC-only administration is dose dependent – low doses anxiolytic while higher induce anxiety. Acute CBD co-administration has mixed findings (Boggs et al 2018)
 10. Animal studies show chronic co-administration of CBD and THC; greater anxiety symptoms than induced by THC alone at high doses (Klein et al 2011)
 11. National Academy of Sciences (2017): Moderate level of evidence supports that whole plant use is associated with: increased incidence of social anxiety disorder in regular users (also increased risk for developing depressive disorders; increased incidence of suicidal ideation and behavior)

Public comments:

Comments from four people, discussing personal experience, observed experience in a friend or in patients being treated and one from a person from the retail sector. All supported cannabis for anxiety with anecdotes but no study data.

Discussion:

Discussion reflected the points made in the report, specifically noting the need to diagnose the cause of the anxiety and consider specific treatment, the uncertain of response to cannabis and dose-dependence, and the associated risks. The above noted vote was taken to not include anxiety as a qualifying symptom or condition.

OPIOID USE DISORDER (OUD) (HB 366)

Recommendation: Do not approve as a qualifying condition.

Vote: 4-6 on a vote to approve the following motion [edited here for brevity]:

- That OUD not be an indication for therapeutic cannabis certification through the current general therapeutic cannabis certification process.
- That certification for OUD:
 - May be provided as an adjunct in the context of evidence-based MAT by a DATA 2001 waived clinician who is prescribing or authorizing the individual's MAT
 - May be provided by an ABAM, APA or ACGME certified addiction medicine or addiction psychiatry physician who follows the patient regularly, with or without other MAT treatment
 - Can only be used for treatment of symptoms of cravings and/or withdrawal
- That such treatment for OUD must be treated as a clinical trial because the outcomes of the use of cannabis as a treatment or adjunct for OUD are unknown.

Summary of presented reports:

Two draft reports were submitted, one with recommendation that OUD not be approved as a qualifying condition and the other report proposing a restricted approval.

The report opposing approval noted:

1. Cannabidiol (CBD) shows promise in reducing craving for opioids, reducing anxiety associated with withdrawal symptoms and decreasing cognitive and emotional stress vulnerability. Thus a function for CBD in reducing the risk of relapse. CBD has low reinforcing properties with limited abuse potential and may inhibit drug seeking behavior.
2. Conclusions from both animal and human studies demonstrate that THC is a psychoactive compound with rewarding effects and addictive properties. THC increases the use of illicit opioids, can cause significant anxiety in the individual and is not recommended by authoritative individuals nor organizations to be associated with treating opioid use disorder.
3. While cannabis has been used for pain control and has been touted to reduce the use of opioids in pain conditions, thereby ostensibly reducing the risk of developing opioid use disorders, this is not the same as treating opioid use disorder. Currently there are FDA approved medications for opioid use disorder and these show significant reduction in overdose deaths, reduction in HIV and Hep B and C transmission among other therapeutic outcomes. The addition of cannabis in its whole form is controversial and organizations such as the American Society of Addiction Medicine hold a position against promoting cannabis for medical use never mind treatment of OUD.

4. Patients who have a diagnosis of an opioid use disorder have a higher risk of use disorders of other types as well. There have been suggestions that use of cannabis (ie, smoked, THC) increases the risk of use of other addictive substances including opioids. Additionally, treatment strategies for addiction include those that reduce the risk that the patient be using any psychoactive substances and work on managing the illness with behavioral health changes as well as medications.

5. Since the above recommendation would be to have restrictions on certifying for therapeutic cannabis, and limiting the product to CBD only, it is recommended to consider using a current product that is available, Epidiolex, to be prescribed off label.

The report supporting limited approval recommended:

- That pure CBD be available for use in management of opioid withdrawal and as an adjunct to evidence-based interventions for opioid use disorders. (Early studies are promising and to date no harm has been demonstrated with short term use, though it should be noted that long term use has not been studied so effects over time are not known).
 - Possibilities for making CBD available to patients include:
 - Off label prescription of Epidiolex (pure FDA approved & regulated CBD)
 - Over the counter CBD that has been tested and certified as pure CBD
 - Certification to exclusively certify patients for CBD, not THC containing products.
- That OUD not be an indication for therapeutic cannabis certification through the current general therapeutic cannabis certification process.
- That certification
 - May be provided as an adjunct in the context of evidence-based MAT by a DATA 2001 waived clinician who is prescribing or authorizing the individual's MAT
 - May be provided by an ABAM, APA or ACGME certified addiction medicine or addiction psychiatry physician who follows the patient regularly, with or without other MAT treatment
- That such treatment must be treated as a clinical trial because the outcomes of the use of cannabis as a treatment or adjunct for OUD are unknown. To that end:
 - The certifying clinician and/or patient must complete and submit a quarterly data sheet (TBD) to DHHS
 - Tracking/analysis of data must be performed
 - Policy may be changed based on clinical trial findings and on evolving scientific literature.

Summary of findings of report supporting approval:

More studies on cannabis and individual cannabinoids are needed to clarify cannabis and cannabinoid actions on opioid reward, opioid misuse, and opioid use disorder. The current evidence on cannabis and opioid misuse/use disorder is somewhat conflicting; however, taken in aggregate, available studies lean towards indicating that cannabis use is associated with greater risk of opioid misuse and poorer functional outcomes. The cannabinoid CBD, and possibly other specific cannabinoids under study, appear to have promise in treatment of OUD. Testimonials from individuals suggest some people with OUD may experience improvement with use of cannabis.

Consideration of cannabis as a potential therapeutic agent in the context of OUD must take into consideration potential risks for misuse and potential compounding of addiction and, if authorized for use in this context, care must appropriately structured to avoid potential harm.

Specific points:

- CBD alone may be helpful in reducing anxiety and craving in early abstinence from opioids in OUD
- Impact of cannabis on retention in OUD treatment is not clear (one study suggests increased retention, one the opposite)
- Cannabis use appears to be associated with higher risk of development of opioid use disorder in the future
- Cannabis use during opioid therapy of pain appears to be associated with increased risk of opioid misuse and/or OUD
- Persons with OUD who also have cannabis use disorder have poorer functional outcomes (homelessness and inpatient hospitalizations) but receive fewer prescriptions for opioids.
- Initially promising epidemiological findings suggesting that therapeutic cannabis availability reduces opioid overdose deaths on a population wide basis have not held up over time.
- Numerous anecdotal reports suggest that a subset of persons find cannabis helpful in recovery from OUD. This could be through palliation of OUD associated symptoms (sleep disturbance, pain, etc) or through direct effects on limbic reward and addiction mechanisms. Future studies might include analysis of the experiences of advocates who have recovered from OUD through use of cannabis.

Public comments:

Two people. One noted that cannabis helped his brother in recovery from OUD. The other noted that cannabis helped her personally in recovery from dysfunctional use of alcohol, cocaine and opioids.

Discussion:

Robust discussion ensued but agreement could not be reached. Approval of CBD alone was considered but the current certification process does not provide for CBD-only certification and most CBD (except Epidiolex) contains some THC. Approval restricted to certain providers was discussed and became the motion but was defeated as noted in the vote above. It is important to note that there are three addiction specialists on the board and they each voted against adding OUD as a qualifying condition at this time. The board looks forward to more data and potentially revisiting this condition in the future.

LYME DISEASE (HB 461)

HB 461 requested Lyme Disease as a qualifying condition but the sponsor wished to broaden it to tick-borne illnesses (TBI).

Recommendation: Do not include as a qualifying condition.

Vote: 2-8 on the recommendation to approve TBI as a qualifying diagnosis.

Summary:

The draft report recommended approval as a free-standing condition with the following rationale:

1. Currently, no evidence-based studies specific to cannabis use with regard to Tickborne Diseases are available - however, the anti-inflammatory, analgesic, anxiolytic and neuroprotective action of cannabis has been well documented, as has its clinical impact on reducing pain, nausea, anxiety, insomnia and discomfort from dermal rashes.
2. Patients with chronic persistent Tickborne Disease infection typically suffer from multiple symptoms including fatigue, impaired cognition (“brain fog”), sleep disorders and pain syndromes. As attested by [public providing comment] (written testimony) as well as noted by some clinicians, many of these symptoms have been reportedly relieved (or significantly reduced) through therapeutic cannabis use.
3. Potential TBI in NH
 - ~ Lyme disease
 - ~ Babesiosis
 - ~ Ehrlichiosis
 - ~ Bartonella
 - ~ STARI
 - ~ Rocky Mountain Spotted Fever
 - ~ Anaplasmosis
 - ~ Relapsing Fever
 - ~ Powassan Virus disease
 - ~ Heartland Virus
4. Tickborne diseases cause multiple symptoms- including:
 - ~ Rash (various rashes dependent upon type of TBD)
 - ~ Fever, chills
 - ~ Diaphoresis
 - ~ Severe headache
 - ~ Insomnia
 - ~ Profound fatigue
 - ~ Muscle & joint pain
 - ~ Anxiety
 - ~ Lymphadenopathy
 - ~ Arthropathies
 - ~ Neuropathic pain
 - ~ Nausea/vomiting/diarrhea
 - ~ Anorexia
 - ~ Seizures
 - ~ Muscular atrophy
 - ~ Numbness in extremities
 - ~ Tremors
5. Due to the number of Tickborne Diseases, multitude of potential symptoms and varying clinical presentation, recommend approval as a free-standing qualifying condition.

Though there are no evidence-based studies specifically regarding cannabis with TBI, the report included many references – some studies referencing specific symptom management with

cannabis (though not in the context of TBI), some professional statements, and statements from others regarding their success with regard to using cannabis to reduce symptom burden and two written responses submitted as part of the public hearing.

Discussion:

The board noted the lack of any evidence-based studies and expressed concern about approval based only on anecdotal evidence.

It was pointed out that many of the symptoms of TBI are already included as qualifying symptoms in the therapeutic cannabis statute and could be approved using the current statutory language of RSA 126-X:1-IX.(a) (1) "...one or more injuries or conditions that has resulted in one or more qualifying symptoms under subparagraph (2)."

Concern was expressed about people being certified for early-stage TBI rather than receiving appropriate antibiotic treatment.

After discussion, the vote noted above was taken to not include tick-borne illness as a qualifying condition.