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**Report to  
The Vermont Legislature**

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**Review and Analysis of Existing Research on the use of Marijuana  
to Relieve the Symptoms of Post-Traumatic Stress Disorder  
January 15, 2015**

**In Accordance with Act 155 (2014)  
*An Act Relating to Relating to the Regulation of  
Marijuana for Symptom Relief and Dispensaries, Section 6***

**Submitted to:** The General Assembly

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**Review and Analysis of Existing Research on the use of Marijuana  
to Relieve the Symptoms of Post-Traumatic Stress Disorder**

**Act 155, Section 6**

**January 15, 2015**

**Executive Summary**

While there are sporadic anecdotal reports of the use of marijuana for relief of PTSD symptoms, the systematic scientific literature is lacking support for this approach. Marijuana is not an evidence-based treatment for PTSD and in fact has been shown to interfere with otherwise effective, evidence-based cognitive behavioral therapy protocols. Individuals with diagnosed PTSD who request medical marijuana typically have extensive additional lifetime and current substance abuse disorders. Recent reports suggest even non-dependent “recreational” marijuana use among young adults has been shown to adversely and likely permanently affect brain structures which can lead to detrimental later outcomes (e.g. more illicit drug use, early onset memory problems, lowered IQ, less educational attainment, etc.). Furthermore, adult onset of marijuana use among PTSD patients is associated with poorer treatment outcomes in a dose response manner – the higher the dose, the worse the outcomes. Any possible minor short term benefit may be offset by both less effective evidence-based treatment outcomes for PTSD as well as potential long term serious structural and behavioral harm.

# **Review and Analysis of Existing Research on the use of Marijuana to Relieve the Symptoms of Post-Traumatic Stress Disorder**

**Act 155, Section 6**

**January 15, 2015**

## **Introduction**

The act requires the Department of Health, in consultation with the Department of Mental Health, to review and report on the existing research on the treatment of the symptoms of post-traumatic stress disorder, as well as the existing research on the use of marijuana for relief of the symptoms of post-traumatic stress disorder (PTSD)<sup>1</sup>. The Department must report its findings to the General Assembly on or before January 15, 2015.

## **Methodology**

This report was prepared by the division of Alcohol and Drug Abuse Programs of the Vermont Department of Health in conjunction with the Department of Mental Health. We reviewed and summarized a broad array of studies published in peer-reviewed scientific journals. We examined the literatures relevant to the effects of marijuana in general, marijuana specific to symptoms of PTSD, and effective evidence-based treatment for PTSD.

## **Overview of PTSD Cause and Treatment**

As described in the diagnostic criteria, PTSD is typically caused by being either directly or indirectly involved in a traumatic event. Combat soldiers, first responders, and sexual assault victims are at a high risk to develop PTSD. Research that investigates PTSD in the military is most common, primarily because of data availability and the current and recent past US combat involvement (e.g., Iraq, Afghanistan). PTSD among returning soldiers is an obvious and immediate public health concern. Estimates vary widely on the prevalence of PTSD among returning soldiers<sup>2</sup>.

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<sup>1</sup> See Endnote for specification of Diagnostic and Statistical Manual-5<sup>th</sup> Edition (DSM-5) criteria for PTSD. DSM is one of two major nosological systems that categorize, define, and provide limiting criteria for a broad range of mental health and behavioral disorders. It was developed and published by the American Psychiatric Association. It is the standard for both diagnostic and billing purposes.

<sup>2</sup> Sundlin et al. (2010). PTSD after deployment to Iraq: conflicting rates, conflicting claims. *Psychological Medicine*, 40, 367-382.

Depending upon study focus and methodology (e.g., sampling strategies, assessment instrument) rates of PTSD in military personnel who served in Iraq ranged from 1.4% to 31%. In addition, the introduction of DSM-5 in 2013 substantially changed the criteria to qualify for a PTSD diagnosis which has caused controversy.<sup>3</sup> While not directly related to the question at hand, this change in criteria may affect the number of individuals who qualify or who have qualified for a PTSD diagnosis. For example in the Hoge et al. (2014) study, 30% of a group of soldiers who met criteria for PTSD using DSM-IV-TR criteria did not meet diagnostic criteria for DSM-5. Nearly all evidence-based treatments involve a form of cognitive behavioral therapy (CBT).

“Despite some procedural differences across CBT programs, they share two characteristics: (a) helping the patient confront safe trauma reminders either through discussions about the trauma or through approaching trauma-related situations or images; and (b) aiming to disconfirm patients’ dysfunctional, unrealistic perceptions emerging from the traumatic experience.”<sup>4</sup>

CBT subsume a wide variety of approaches (but most appear to be trauma focused). Studies have quite clearly demonstrated both the efficacy and safety of CBT approaches to PTSD. At present there are no stand-alone evidence-based pharmacological treatments for PTSD.

Of the several CBT approaches, exposure therapies have proven to be efficacious and safe.

“Exposure interventions include imaginal exposure, which consists of repeated revisiting of the traumatic memory, as well as in vivo exposure, which involves confronting feared situations that are objectively safe. Treatment programs that include both kinds of

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<sup>3</sup> Hoge et. al., (2014). The prevalence of post-traumatic stress disorder (PTSD) in US combat soldiers: A head-to-head comparison of DSM-5 versus DSM-IV-TR symptom criteria with the PTSD checklist. *The Lancet*, published online August 14, 2014. MacFarlane (2014). PTSD and DSM-5: Unintended consequences of change. *The Lancet*, published online August 14, 2014.

<sup>4</sup> Foa et al. (2013). Challenges and successes in dissemination of evidence-based treatments for post-traumatic stress: Lessons learned from prolonged exposure therapy for PTSD. *Psychological Science in the Public Interest*, 14, 65-111.

exposure...tend to produce better outcomes compared with protocols consisting of only one of the component.”<sup>5</sup>

Furthermore, randomized clinical trials demonstrate that prolonged exposure therapy (PE) appears to be the most effective approach across a wide range of traumas (e.g., rape survivors, male and female veterans, and refugees). PE has been shown to be superior to other forms of treatment for PTSD including treatment that included pharmacotherapy<sup>6,7</sup>.

Thus, evidence-based treatments for PTSD have been clearly identified; however, the diagnostic criteria are so lengthy that not every treatment addresses every symptom. This is likely the moving force behind the anecdotal evidence suggesting that marijuana relieves at least some PTSD symptoms. Few studies have investigated the role of marijuana in PTSD symptom relief. Those that have suggest three important preliminary conclusions:

1. Those who apply for medical cannabis with a diagnosis of PTSD are more likely to have other current or lifetime substance abuse disorders than those who do not have a PTSD diagnosis<sup>8</sup>.
2. Cannabis *may* offer temporary relief for some PTSD symptoms (e.g., sleep disturbance and hyper-vigilance) and simultaneously exacerbate or interfere with treatment of others<sup>9</sup>. However, this relief may be at the expense of an additional substance use disorder which complicates both continued evidence-based treatment and quality of life. Marijuana use assessed after treatment has been associated with lower levels of positive change (i.e., fewer symptom reductions) in a large sample of

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<sup>5</sup> Foa et al. (2013). P. 73

<sup>6</sup> Van Minnen et al. (2010). When do trauma experts choose exposure therapy for PTSD patients? A controlled study of therapist and patient factors. *Behavior Research and Therapy*, 48, 312-320.

<sup>7</sup> NaCaasch et al. (2011). Prolonged exposure therapy for combat- and terror-related posttraumatic stress disorder: A randomized control comparison with treatment as usual. *Journal of Clinical Psychiatry*, 72, 1174-1180.

<sup>8</sup> Bohnert et al. (2014). Positive posttraumatic stress disorder screens among first-time medical cannabis patients: Prevalence and association with other substance use. *Addictive Behaviors*, published online June 2, 2014.

<sup>9</sup> Earleywine & Bolles (2014). Marijuana, expectancies. And post-traumatic stress symptoms: A preliminary investigation. *Journal of Psychoactive Drugs*, 46, 171-177.

military veterans with a PTSD diagnosis<sup>10</sup>. This interference with treatment effectiveness was specific for cannabis users – users of alcohol, opiates, and other drugs did not experience negative treatment effects.

3. Furthermore, recreational marijuana use (nondependent) has been associated with altered brain morphology in young adults that may persist even after cessation of marijuana use<sup>11</sup>.

## Use of Marijuana for PTSD Symptom Relief

First it is important to note three concerns:

1. Marijuana for PTSD symptom relief is not an evidence-based practice.
2. Smoked marijuana can have serious, life altering, possibly irreversible negative cognitive effects and changes in brain structure that often go unacknowledged or minimized by proponents of expanding the range of medical disorders for which marijuana can be used. This is especially true for adolescents and young adults who engage in persistent and long-term use of smoked marijuana<sup>12, 13</sup>.
3. THC levels in marijuana are extremely varied and unregulated. As a result there is no known controlled minimum effective dose of smoked marijuana for any medical disorder.

While there are sporadic anecdotal reports of specific PTSD symptom relief after smoking marijuana there are no systematic studies that can be located to support such relief. In fact, studies have shown that smoking marijuana may be an impediment rather than facilitator of evidence-based treatment for PTSD<sup>14</sup>. This is mainly due to the demonstrated high potential for abuse of the substance among those suffering from PTSD as well as the fact that other current and lifetime substance use disorders are significantly higher in those applying for medical marijuana with a concurrent PTSD diagnosis. A recent study presented at the 2014 Annual Meeting of the American Academy of Addiction Psychiatry examined a representative sample of

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<sup>10</sup> Bonn-Miller et al. (2011). Cannabis use among military veterans after residential treatment for Posttraumatic stress disorder. *Psychology of Addictive Behaviors*, 25, 485-491.

<sup>11</sup> Gilman et al. (2014). Cannabis use is quantitatively associated with nucleus acumbens and amygdala abnormalities in young adult recreational users. *The Journal of Neuroscience*, 34, 5529-5538.

<sup>12</sup> Meier, MH et. al (2012) Persistent Cannabis Users Show Neuropsychological Decline from Childhood to Midlife. *Proceedings of the National Academy of Sciences*. 109(40) e2657-e2664.

<sup>13</sup> Silins et al. (2014). Young adult sequelae of adolescent cannabis use: an integrative analysis. *The Lancet Psychiatry*, 1, 286-293.

<sup>14</sup> Bonn-Miller et al. (2011). *Op. cit.*

veterans admitted to PTSD treatment programs across the United States from 1991 – 2011. After 4 months of treatment, marijuana users had significantly worse outcomes than those who either never used or who stopped marijuana use during or after treatment<sup>15</sup>.

Furthermore, there was a dose response relationship between amount of marijuana smoked and adverse outcomes – the higher the dose, the worse the outcome.

Research on any benefit to smoked marijuana for PTSD is extremely limited<sup>16</sup>. This is primarily a function of the unavailability of the substance for research purposes and the reluctance of federal funding agencies to support medical marijuana protocols. In addition, the supply of government supplied marijuana is restricted since they currently have only one production facility located in Mississippi. One study was conducted in New Mexico shortly after that state became the first<sup>17</sup> to authorize medical marijuana for PTSD<sup>18</sup>. The subjects of this study were the first 80 patients to request an evaluation from a psychiatrist in order to qualify for medical marijuana for PTSD symptoms. Results of this study show dramatic reductions in PTSD symptomatology among patients when using marijuana. Given that patients who qualified for the study were already using marijuana for symptom amelioration and symptoms reported when not using marijuana may have been during withdrawal periods, this study is difficult to interpret definitively. Furthermore, this study of a convenience sample conducted without adequate controls stands alone in the literature in terms of demonstrating large positive effects of marijuana use in PTSD symptom reduction.

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<sup>15</sup> Brauser, D. (2014). Medical Marijuana May Worsen PTSD Symptoms, Increase Violence. <http://www.medscape.com/viewarticle/836588>

<sup>16</sup> An additional source of information on using marijuana for possible PTSD symptom reduction has come from research on animals, in particular mice. These studies suggest that very low doses of the active compound in marijuana (tetrahydrocannabinol; THC) injected into the animal may mitigate a fear response [e.g., Akiriv (2014). Cannabinoids Prevent the Effects of a Footshock Followed by Situational Reminders on Emotional Processing. *Neuropsychopharmacology*, June 5, 2014]. Extrapolating an animal fear response to PTSD in humans is methodologically and practically problematic. Early research from a very small sample of humans (n = 29) indicate that a single low dose of THC was consistent with the finding in the mouse study; however, none of the participants in the research had any PTSD symptoms; and the THC was delivered in capsule form (not smoked) [Rabinak et al. (2013). Cannaboid facilitation of fear extinction memory recall in humans. *Neuropharmacology*, 64, 396-402]. It is important to emphasize that these are analogue studies and neither the animal nor the human model evaluated any actual symptoms of PTSD.

<sup>17</sup> 10 States now allow the use of medical marijuana for a PTSD diagnosis.

<sup>18</sup> Greer et al. (2014). PTSD symptom reports of patients evaluated for the New Mexico medical cannabis program. *Journal of Psychoactive Drugs*, 46, 73-77.



Other studies have shown that cannabis use in PTSD patients can cause significant adverse consequences<sup>19</sup>. The authors' conclusions suggest a placebo-controlled, randomized clinical trial of marijuana for PTSD should be undertaken<sup>20</sup>.

## Conclusions and Recommendations

Marijuana for the treatment of PTSD is not an evidence-based practice and had been shown to potentially interfere with efficacious treatment. Studies have demonstrated that individuals who report using marijuana also have more lifetime and current other substance use disorders. There are virtually no systematic studies on the use of marijuana for PTSD. Furthermore, there is a growing body of research documenting significant adverse behavioral and brain structure and function consequences of even “recreational” marijuana use (especially among adolescents and young adults) as well as poorer PTSD treatment outcomes among those who initiate use as adults. Even if marijuana offered some symptom relief (which has not been clearly delineated) these adverse and likely irreversible consequences of continued marijuana use may outweigh any observed benefit.

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<sup>i</sup> Definition of Post Traumatic Stress Disorder (*Diagnostic and Statistical Manual - 5, American Psychiatric Association, 2013*):

*Criterion A: stressor*

The person was exposed to: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence, as follows: **(one required)**

1. Direct exposure
2. Witnessing, in person
3. Indirectly, by learning that a close relative or close friend was exposed to trauma. If the event involved actual or threatened death, it must have been violent or accidental.

*Criterion B: intrusion symptoms*

The traumatic event is persistently re-experienced in the following way(s): **(one required)**

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<sup>19</sup> Boden et al. (2013). Posttraumatic stress disorder and cannabis use characteristics among military veterans with cannabis dependence. *The American Journal on Addictions*, 22, 277-284.

<sup>20</sup> Such a study was recently approved by the National Institute on Drug Abuse (NIDA) and the Food and Drug Administration (FDA), but the principle investigator did not retain her position at the University of Arizona where the research was to take place. The future of this project is presently uncertain.

1. Recurrent, involuntary, and intrusive memories. Note: Children older than six may express this symptom in repetitive play.
2. Traumatic nightmares. Note: Children may have frightening dreams without content related to the trauma(s).
3. Dissociative reactions (e.g., flashbacks) which may occur on a continuum from brief episodes to complete loss of consciousness. Note: Children may reenact the event in play.
4. Intense or prolonged distress after exposure to traumatic reminders.
5. Marked physiologic reactivity after exposure to trauma-related activity.

*Criterion C: avoidance*

Persistent effortful avoidance of distressing trauma-related stimuli after the event: **(one required)**

1. Trauma-related thoughts or feelings.
2. Trauma-related external reminders (e.g., people, places, conversations, activities, objects, or situations).

*Criterion D: negative alterations in cognitions and mood*

Negative alterations in cognitions and mood that began or worsened after the traumatic event: **(two required)**

1. Inability to recall key features of the traumatic event (usually dissociative amnesia; not due to head injury, alcohol, or drugs).
2. Persistent (and often distorted) negative beliefs and expectations about oneself or the world (e.g., "I am bad," "The world is completely dangerous").
3. Persistent distorted blame of self or others for causing the traumatic event or for resulting consequences.
4. Persistent negative trauma-related emotions (e.g., fear, horror, anger, guilt, or shame).
5. Markedly diminished interest in (pre-traumatic) significant activities.
6. Feeling alienated from others (e.g., detachment or estrangement).
7. Constricted affect: persistent inability to experience positive emotions.

*Criterion E: alterations in arousal and reactivity*

Trauma-related alterations in arousal and reactivity that began or worsened after the traumatic event: **(two required)**

1. Irritable or aggressive behavior
2. Self-destructive or reckless behavior
3. Hypervigilance
4. Exaggerated startle response
5. Problems in concentration
6. Sleep disturbance

*Criterion F: duration*

Persistence of symptoms (in Criteria B, C, D, and E) for more than one month.

*Criterion G: functional significance*

Significant symptom-related distress or functional impairment (e.g., social, occupational).

*Criterion H: exclusion*

Disturbance is not due to medication, substance use, or other illness.

*Specify if:* With dissociative symptoms.

In addition to meeting criteria for diagnosis, an individual experiences high levels of either of the following in reaction to trauma-related stimuli:

1. **Depersonalization:** experience of being an outside observer of or detached from oneself (e.g., feeling as if "this is not happening to me" or one were in a dream).
2. **Derealization:** experience of unreality, distance, or distortion (e.g., "things are not real").

*Specify if:* With delayed expression.