Senate Judiciary Subcommittee on Crime and Terrorism

"Researching the Potential Medical Benefits and Risks of Marijuana"

July 13, 2016

Questions for the Record from Senator Richard Blumenthal for Dr. Susan Weiss, director, Division of Extramural Research, National Institute on Drug Abuse (NIDA), National Institutes of Health (NIH)

Question #1: How should lawmakers think about future research?

I was a strong supporter of provisions in the 2012 Food and Drug Administration Safety and Innovation Act that sought to address the harms caused by synthetic marijuana. And just a few weeks ago we had another hearing on the synthetic drug crisis because scheduling law is still struggling to keep up with the new and dangerous compounds that are emerging and wreaking havoc on families and communities.

But on the heels of some promising research, the Surgeon General, Vivek Murthy, has come out and said that marijuana potentially has medical benefits, and that we need to do more research.

Dr. Weiss, in your testimony you indicated that current evidence does not support the conclusion that certain components of marijuana, such as the CBD cannabinoid, have the potential for abuse. You also noted evidence suggesting potential therapeutic benefits from several components of marijuana. But primarily, it seems that you underscored the need for further research.

What steps should lawmakers take to make sure we are adequately researching the potential benefits and risks of medical marijuana? How can we, as lawmakers, along with the NIDA, balance the need to break barriers to research with the need to keep certain dangerous compounds from leading to abuse and fatalities?

Response: As discussed in our testimony, NIDA has been working closely with the Office of National Drug Control Policy (ONDCP), the Drug Enforcement Administration (DEA), and the Food and Drug Administration (FDA) to identify ways of facilitating more research on

marijuana and its constituent cannabinoids while maintaining compliance with the international treaties and the Controlled Substances Act (CSA). There are a number of factors that have contributed to the slow pace of research on marijuana and its constituent compounds.

- The Schedule I registration process and required protocol review: NIDA has heard from some researchers that this process creates administrative burdens that can act as disincentives to conducting research. To help ease this burden NIDA and the DEA have been communicating directly, with the specific aim of reducing the time to it takes for researchers to get their Schedule I registration. Schedule I status of cannabidiol (CBD): Currently, evidence suggests that CBD does not have abuse liability. FDA has indicated that a human abuse liability study will be necessary to make a final determination on the abuse liability of CBD, which would be factored into the scheduling recommendation. NIH and FDA are in the process of finalizing the details regarding the methodology and budget needed to conduct this study.
- Single source of marijuana for research purposes: As noted in our testimony, there is currently only one DEA-registered source of marijuana for research in the country. However, in August 2016 DEA announced a new policy that is designed to increase the number of entities registered under the Controlled Substances Act (CSA) to grow (manufacture) marijuana to supply legitimate researchers in the U.S.
- Clarifying the path from use of NIDA-supplied marijuana to market: As discussed in our testimony, pharmaceutical companies would need to transition from using NIDA-supplied marijuana products to other sources before FDA approval and marketing. Additional studies would likely be needed, per FDA requirements, for post-approval changes in product manufacturing, to demonstrate equivalency between the marijuana used in the clinical trials and the drug product that will be marketed. Further, the efforts by DEA to make marijuana available from additional sources, discussed above, could help to address this issue.
- Limited funding: While the percentage of grant proposals for cannabinoid research submitted to NIH that receive funding is equivalent to other categories of research, funding availability does impact the pace of research.

Question #2: What potential role is there for medical marijuana in combatting the opioid crisis?

I'm sure you're aware of the many conversations that we've had in this body on the horrible opioid crisis that is plaguing many states, including my home state of Connecticut. In 2012, Connecticut saw 86 heroin overdose deaths, and one overdose of heroin and fentanyl. In 2015, Connecticut saw 415 heroin deaths, and 107 fentanyl deaths. Today we have been debating the Comprehensive Addiction and Recovery Act, which I believe is an important step forward in addressing this public health emergency even though I believe it has significant flaws. As you well know, we need all of the information and help we can get to combat the scourge of opioid abuse.

In your testimony, you mentioned that there is some evidence that cannabinoids may help treat substance use disorders like opioid addiction. There is also evidence indicating that states with medical marijuana programs are linked to decreases in opioid abuse and mortality.

a. Bearing in mind that further research is needed, what potential role could cannabinoids play in helping treat opioid abuse?

Response: One of the pillars of the Secretary's Opioid Initiative is to improve opioid prescribing practices to reduce the use of opioid pain relievers and prevent and reduce prescription opioid misuse[1]. NIH is actively involved in this initiative and development of non-opioid treatments for pain is a high priority research area. There are numerous studies that have suggested a potential role for cannabinoids in mediating and potentially treating pain. For example:

- Activating cannabinoid receptors in pain processing regions, from peripheral nerves, to the spinal cord and the pain-perception systems of the brain has been shown to suppress pain[2].
- Drugs that selectively activate the CB_2 cannabinoid receptor show promise in relieving pain without unwanted psychotropic side effects[3].
- A recent meta-analysis identified moderate-quality evidence to support the use of cannabinoids for chronic pain[4], and a recent review by the American Academy of Neurology[5] concluded that there is strong evidence for the efficacy of oral cannabis

extract for spasticity and pain associated with multiple sclerosis (MS) and moderate evidence for the efficacy of THC and nabiximols for pain associated with MS[6,7].

- Cannabidiol (CBD), a component of marijuana that all available evidence suggests is non-psychotropic, also shows therapeutic potential for pain[8].
- In one study of vaporized cannabis, significant improvement in pain was present at low doses that had minimal psychoactive effects[9].
- Initial studies have suggested that cannabinoids may enhance the pain relieving properties of opioids, reducing the dose of opioids needed for pain relief, which could reduce adverse outcomes including overdoses [10,11]

Note that the majority of these studies refer to the cannabinoid components of marijuana and not to smoked marijuana. The marijuana plant itself is not considered an ideal medication candidate because:

- It is an unpurified plant containing numerous chemicals that have not been fully characterized.
- The variability of active components makes it difficult to reproduce a consistent dose.
- It is often consumed by smoking, potentially contributing to adverse effects on lung health.
- Its cognitive- and motor-impairing effects may limit its utility.

Pain is a condition for which a large proportion of patients in medical marijuana states seek treatment[12,13] and, as noted in your question, medical marijuana laws have been associated with changes in opioid prescribing and outcomes. Two recent studies found an improvement in adverse opioid outcomes associated with the legalization of marijuana for medicinal use. The first found that the implementation of medical marijuana laws was associated with a slowing of the increase in opioid overdose deaths, an effect that strengthened in each year following the implementation of legislation [15]. The second showed that access to medical marijuana dispensaries is associated with a reduction in opioid prescribing, self-report of nonmedical prescription opioid use, treatment admissions for prescription opioid use disorders, and in prescription opioid overdose deaths[16]. Though these studies are not definitive, and marijuana use can be associated with its own harms[17]; one recent study found that increased availability of medical marijuana dispensaries was associated with increased risk for cannabis use disorders[18]. However, these studies raise the possibility that marijuana-derived products may have a role as

alternative or adjunct treatments for pain with potential utility for reducing the use of opioids needed to control pain. More research is needed to investigate this possibility.

Cannabinoids are also being studied for their potential to treat substance use disorders, including opioid use disorder. While the evidence base is less robust than that supporting the efficacy of cannabinoids for pain treatment, preclinical studies have suggested that CBD reduces the rewarding properties of opioids, reduces relapse-like behaviors, and has the potential to mitigate symptoms of opioid withdrawal[19]. Pilot data in human subjects show a reduction in heroin craving after treatment with cannabidiol[20]. More research is needed to determine if these preliminary findings can translate into meaningful clinical outcomes.

b. What steps do you believe need to be taken in order to fully realize the benefits of cannabinoid research in combatting the opioid crisis?

Response: More research is needed to follow up on these findings to determine if they will translate to therapeutic benefits for human health. Preclinical and early clinical findings frequently fail to translate to safe and effective therapeutics[21], so the true potential of cannabinoids for the treatment of pain and opioid use disorders cannot be determined without large-scale, randomized controlled trials (RCTs) . As noted in our testimony, nabiximols (trade name Sativex), which contains THC and CBD in equal proportions, has been approved throughout most of Europe and in a number of other countries for the treatment of spasticity and pain associated with MS, however, it has not been approved in the United States, and results from two Phase 3 clinical trials for severe refractory cancer pain were not encouraging[22]. In this case, as in others, it is possible that this medication may be effective for other types of pain or for less severe pain, however, more clinical trials are needed to test these possibilities and potentially develop therapeutics that can pass the rigorous standards required for FDA drug approval.

In addition to our research portfolio on the roles of the cannabinoid and opioid systems in pain, NIDA has funded numerous studies that will provide data relating to medical marijuana and opioids, specifically:

- Effects of access to medical marijuana on substance use, including nonmedical use of prescription opioids (DA031816-05, DA039293-01A1, DA037341-02, DA032693-04)

- Mental and physical functioning of a cohort of pain patients seeking medical marijuana treatment (DA033397-03)
- The impact of medical marijuana policies on health outcomes (DA034067-03)

Question #3: What role might medical marijuana play in treating post-traumatic stress?

As ranking member on the Senate Committee on Veterans Affairs, I am keenly aware of the mental toll that war has taken on our service members, especially through posttraumatic stress. Due to its devastating effects, especially on people who have so bravely served our country, I believe we need to look at every possible method of treatment. In your testimony, you mentioned that there is some evidence that cannabinoids may help treat posttraumatic stress.

a. Can you talk more about what research has suggested about the potential for cannabinoids to help treat PTSD, especially combat-related PTSD?

Response: Both preclinical and human laboratory studies have suggested that cannabinoids may have therapeutic potential for the treatment of PTSD. However, it should be noted that the marijuana plant contains over 100 cannabinoids and, as noted above, at different doses cannabinoids can have opposite effects. Careful research is needed to determine whether any of the components of marijuana have therapeutic potential for the treatment of PTSD.

Studies have shown that PTSD is associated with several changes in the body's endogenous cannabinoid – or endocannabinoid – system including:

- increased cannabinoid receptor 1 (CB_1) receptor availability in the brain [23];
- changes in concentrations of naturally occurring or endogenous cannabinoids[24,25];
- genetic variations in an enzyme that degrades endogenous cannabinoids (FAAH)[26]; and

CB_1 receptors are present in areas of the brain involved in the processing of anxiety and fear, and can affect how threats are perceived. Studies in animal models support the critical role of CB_1 receptors, and the broader endocannabinoid system, in appropriately matching level of anxiety to the danger posed by a perceived threats[27,28] and for appropriate extinction of aversive memories[29,30]; functions that are disrupted in patients with PTSD. Preclinical research has shown that:

- THC reduces anxiety in some animal models of PTSD; importantly, efficacy was dependent on dose with low doses reducing anxiety and high doses increasing anxiety[31,32].

- [7]WIN 55,212-2, a cannabinoid that activates CB_1 receptors[33,34] and cannabidiol (CBD)[35] also show dose-dependent efficacy for enhancing fear extinction – the process where a cue that once elicited fear (such as loud noises eliciting fear associated with combat) gradually stops being associated with fear.

As noted in our testimony, one study found that THC administration may help facilitate fear extinction in healthy subjects which could have implications for treating patients with PTSD[36]. Several human studies have examined cannabinoids for the treatment of PTSD. Most of these studies have been small, non-randomized, lacking sufficient control groups and power, and they have produced mixed results, of the positive findings:

- A study using Nabilone, a synthetic cannabinoid similar in structure to THC, to treat insomnia, nightmares, and pain in patients presenting with serious mental illness successfully reduced many PTSD symptoms including pain[37].
- Human studies utilizing oral Dronabinol, a synthetic cannabinoid identical to THC, to aid fear extinction showed some improvement in reactivity to fear related cues; however, fear extinction was not improved[38].

These and other findings suggest that the endocannabinoid system plays a role in the brain functions that are impaired in patients with PTSD and that this system is a potential therapeutic target for these patients. There is growing evidence that people, including veterans, are using marijuana to cope with PTSD symptoms, with usage tending to increase as the severity of PTSD symptom increases[39(p),40–43] ; however, studies have shown mixed results on the efficacy of marijuana for reducing PTSD symptoms and an increasing number of veterans with PTSD are being diagnosed with cannabis use disorder[44]. Also, note that these studies refer to the cannabinoid components of marijuana and not to smoked marijuana. The marijuana plant itself is not considered an ideal medication candidate because:

- It is an unpurified plant containing numerous chemicals that have not been fully characterized.
- The variability of active components makes it difficult to reproduce a consistent dose.
- It is often consumed by smoking, potentially contributing to adverse effects on lung health.
- Its cognitive- and motor-impairing effects may limit its utility.

Further research is needed to determine which cannabinoids, at what doses, may be safe and effective for the treatment of PTSD.

b. What steps do you believe need to be taken in order to fully realize the benefits of cannabinoid research in helping our veterans recover from invisible wounds of war?

Response: As discussed above, additional research is needed to determine which cannabinoids, at what doses, may be safe and effective for the treatment of PTSD. Preclinical and early clinical findings frequently fail to translate to safe and effective therapeutics, so the true potential of cannabinoids for the treatment of PTSD cannot be determined without large-scale, randomized controlled trials (RCTs). In addition, comparative effectiveness studies will be needed to determine how marijuana and/or cannabinoids compare to conventional behavioral and pharmacotherapies currently used to treat PTSD (e.g. prazosin, selective serotonin reuptake inhibitors, second-generation antipsychotics)[36].

References

1. United States Department of Health and Human Services. HHS takes strong steps to address opioid-drug related overdose, death and dependence. May 2015. https://www.hhs.gov/about/news/2015/03/26/hhs-takes-strong-steps-to-address-opioid-drug-related-overdose-death-and-dependence.html

2. Guindon J, Hohmann AG. The endocannabinoid system and pain. *CNS Neurol Disord Drug Targets*. 2009;8(6):403-421.

3. Deng L, Guindon J, Cornett BL, Makriyannis A, Mackie K, Hohmann AG. Chronic cannabinoid receptor 2 activation reverses paclitaxel neuropathy without tolerance or cannabinoid receptor 1-dependent withdrawal. *Biol Psychiatry*. 2015;77(5):475-487. doi:10.1016/j.biopsych.2014.04.009.

4. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. *JAMA*. 2015;313(24):2456. doi:10.1001/jama.2015.6358.

5. Koppel BS, Brust JCM, Fife T, et al. Systematic review: efficacy and safety of medical marijuana in selected neurologic disorders: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2014;82(17):1556-1563. doi:10.1212/WNL.0000000000000363.

6. Tsang CC, Giudice MG. Nabilone for the Management of Pain. *Pharmacother J Hum Pharmacol Drug Ther*. 2016;36(3):273-286. doi:10.1002/phar.1709.

7. Zettl UK, Rommer P, Hipp P, Patejdl R. Evidence for the efficacy and effectiveness of THC-CBD oromucosal spray in symptom management of patients with spasticity due to multiple sclerosis. *Ther Adv Neurol Disord*. 2016;9(1):9-30. doi:10.1177/1756285615612659.

8. Ward SJ, McAllister SD, Kawamura R, Murase R, Neelakantan H, Walker EA. Cannabidiol inhibits paclitaxel-induced neuropathic pain through 5-HT(1A) receptors without diminishing nervous system function or chemotherapy efficacy. *Br J Pharmacol*. 2014;171(3):636-645. doi:10.1111/bph.12439.

9. Wilsey B, Marcotte T, Deutsch R, Gouaux B, Sakai S, Donaghe H. Low-dose vaporized cannabis significantly improves neuropathic pain. *J Pain Off J Am Pain Soc*. 2013;14(2):136-148. doi:10.1016/j.jpain.2012.10.009.

10. Abrams DI, Couey P, Shade SB, Kelly ME, Benowitz NL. Cannabinoid-opioid interaction in chronic pain. *Clin Pharmacol Ther*. 2011;90(6):844-851. doi:10.1038/clpt.2011.188.

11. Lynch ME, Clark AJ. Cannabis reduces opioid dose in the treatment of chronic non-cancer pain. *J Pain Symptom Manage*. 2003;25(6):496-498.

12. Reinarman C, Nunberg H, Lanthier F, Heddleston T. Who are medical marijuana patients? Population characteristics from nine California assessment clinics. *J Psychoactive Drugs*. 2011;43(2):128-135. doi:10.1080/02791072.2011.587700.

13. Kondrad E, Reid A. Colorado Family Physicians' Attitudes Toward Medical Marijuana. *J Am Board Fam Med*. 2013;26(1):52-60. doi:10.3122/jabfm.2013.01.120089.

14. Bradford AC, Bradford WD. Medical Marijuana Laws Reduce Prescription Medication Use In Medicare Part D. *Health Aff (Millwood)*. 2016;35(7):1230-1236. doi:10.1377/hlthaff.2015.1661.

15. Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010. *JAMA Intern Med*. 2014;174(10):1668. doi:10.1001/jamainternmed.2014.4005.

16. Powell D, Pacula RL, Jacobson M. Do Medical Marijuana Laws Reduce Addictions and Deaths Related to Pain Killers? November 2015. http://www.rand.org/content/dam/rand/pubs/working_papers/WR1100/WR1130/RAND_WR1130.pdf.

17. Volkow ND, Baler RD, Compton WM, Weiss SRB. Adverse health effects of marijuana use. *N Engl J Med*. 2014;370(23):2219-2227. doi:10.1056/NEJMra1402309.

18. Mair C, Freisthler B, Ponicki W, Gaidus A. The impacts of marijuana dispensary density and neighborhood ecology on marijuana abuse and dependence. *Drug Alcohol Depend*. 2015;154:111-116. doi: 10.1016/j.drugalcdep.2015.06.019.

19. Prud'homme M, Cata R, Jutras-Aswad D. Cannabidiol as an Intervention for Addictive Behaviors: A Systematic Review of the Evidence. *Subst Abuse Res Treat*. 2015;9:33-38. doi:10.4137/SART.S25081.

20. Hurd YL, Yoon M, Manini AF, et al. Early Phase in the Development of Cannabidiol as a Treatment for Addiction: Opioid Relapse Takes Initial Center Stage. *Neurotherapeutics*. 2015;12(4):807-815. doi:10.1007/s13311-015-0373-7.

21. Talevi A, Bellera CL, Di Ianni M, Gantner M, Bruno-Blanch LE, Castro EA. CNS drug development - lost in translation? *Mini Rev Med Chem*. 2012;12(10):959-970.

22. GW Pharmaceuticals. GW Pharmaceuticals and Otsuka Announce Results from Two Remaining Sativex Phase 3 Cancer Pain Trials. October 2015. http://www.gwpharm.com/GWPOtsukaResults271015.aspx.

23. Neumeister A, Normandin MD, Pietrzak RH, et al. Elevated brain cannabinoid CB1 receptor availability in post-traumatic stress disorder: a positron emission tomography study. *Mol Psychiatry*. 2013;18(9):1034-1040. doi:10.1038/mp.2013.61.

24. Hauer D, Schelling G, Gola H, et al. Plasma concentrations of endocannabinoids and related primary fatty acid amides in patients with post-traumatic stress disorder. *PloS One*. 2013;8(5):e62741. doi:10.1371/journal.pone.0062741.

25. Hill MN, Bierer LM, Makotkine I, et al. Reductions in circulating endocannabinoid levels in individuals with post-traumatic stress disorder following exposure to the World Trade Center attacks. *Psychoneuroendocrinology*. 2013;38(12):2952-2961. doi:10.1016/j.psyneuen.2013.08.004.

26. Pardini M, Krueger F, Koenigs M, et al. Fatty-acid amide hydrolase polymorphisms and post-traumatic stress disorder after penetrating brain injury. *Transl Psychiatry*. 2012;2:e75. doi:10.1038/tp.2012.1.

27. Haller J, Varga B, Ledent C, Freund TF. CB1 cannabinoid receptors mediate anxiolytic effects: convergent genetic and pharmacological evidence with CB1-specific agents. *Behav Pharmacol*. 2004;15(4):299-304.

28. Patel S, Hillard CJ. Pharmacological evaluation of cannabinoid receptor ligands in a mouse model of anxiety: further evidence for an anxiolytic role for endogenous cannabinoid signaling. *J Pharmacol Exp Ther*. 2006;318(1):304-311. doi:10.1124/jpet.106.101287.

29. Marsicano G, Wotjak CT, Azad SC, et al. The endogenous cannabinoid system controls extinction of aversive memories. *Nature*. 2002;418(6897):530-534. doi:10.1038/nature00839.

30. Jenniches I, Ternes S, Albayram O, et al. Anxiety, Stress, and Fear Response in Mice With Reduced Endocannabinoid Levels. *Biol Psychiatry*. 2016;79(10):858-868. doi:10.1016/j.biopsych.2015.03.033.

31. Ruehle S, Remmers F, Romo-Parra H, et al. Cannabinoid CB1 receptor in dorsal telencephalic glutamatergic neurons: distinctive sufficiency for hippocampus-dependent and amygdala-dependent synaptic and behavioral functions. *J Neurosci Off J Soc Neurosci*. 2013;33(25):10264-10277. doi:10.1523/JNEUROSCI.4171-12.2013.

32. Rubino T, Guidali C, Vigano D, et al. CB1 receptor stimulation in specific brain areas differently modulate anxiety-related behaviour. *Neuropharmacology*. 2008;54(1):151-160. doi:10.1016/j.neuropharm.2007.06.024.

33. Pamplona FA, Bitencourt RM, Takahashi RN. Short- and long-term effects of cannabinoids on the extinction of contextual fear memory in rats. *Neurobiol Learn Mem*. 2008;90(1):290-293. doi:10.1016/j.nlm.2008.04.003.

34. Pamplona FA, Prediger RDS, Pandolfo P, Takahashi RN. The cannabinoid receptor agonist WIN 55,212-2 facilitates the extinction of contextual fear memory and spatial memory in rats. *Psychopharmacology (Berl)*. 2006;188(4):641-649. doi:10.1007/s00213-006-0514-0.

35. Lin H-C, Mao S-C, Su C-L, Gean P-W. The role of prefrontal cortex CB1 receptors in the modulation of fear memory. *Cereb Cortex N Y N 1991*. 2009;19(1):165-175. doi:10.1093/cercor/bhn075.

36. Betthauser K, Pilz J, Vollmer LE. Use and effects of cannabinoids in military veterans with posttraumatic stress disorder. *Am J Health-Syst Pharm AJHP Off J Am Soc Health-Syst Pharm*. 2015;72(15):1279-1284. doi:10.2146/ajhp140523.

37. Cameron C, Watson D, Robinson J. Use of a synthetic cannabinoid in a correctional population for posttraumatic stress disorder-related insomnia and nightmares, chronic pain, harm reduction, and other indications: a retrospective evaluation. *J Clin Psychopharmacol*. 2014;34(5):559-564. doi:10.1097/JCP.0000000000000180.

38. Klumpers F, Denys D, Kenemans JL, Grillon C, van der Aart J, Baas JMP. Testing the effects of Δ9-THC and D-cycloserine on extinction of conditioned fear in humans. *J Psychopharmacol Oxf Engl*. 2012;26(4):471-478. doi:10.1177/0269881111431624.

39. Bonn-Miller MO, Vujanovic AA, Boden MT, Gross JJ. Posttraumatic stress, difficulties in emotion regulation, and coping-oriented marijuana use. *Cogn Behav Ther*. 2011;40(1):34-44. doi:10.1080/16506073.2010.525253.

40. Bonn-Miller MO, Vujanovic AA, Feldner MT, Bernstein A, Zvolensky MJ. Posttraumatic stress symptom severity predicts marijuana use coping motives among traumatic event-exposed marijuana users. *J Trauma Stress*. 2007;20(4):577-586. doi:10.1002/jts.20243.

41. Bonn-Miller MO, Babson KA, Vandrey R. Using cannabis to help you sleep: heightened frequency of medical cannabis use among those with PTSD. *Drug Alcohol Depend*. 2014;136:162-165. doi:10.1016/j.drugalcdep.2013.12.008.

42. Potter CM, Vujanovic AA, Marshall-Berenz EC, Bernstein A, Bonn-Miller MO. Posttraumatic stress and marijuana use coping motives: the mediating role of distress tolerance. *J Anxiety Disord*. 2011;25(3):437-443. doi:10.1016/j.janxdis.2010.11.007.

43. Bonn-Miller MO, Vujanovic AA, Drescher KD. Cannabis use among military veterans after residential treatment for posttraumatic stress disorder. *Psychol Addict Behav J Soc Psychol Addict Behav*. 2011;25(3):485-491. doi:10.1037/a0021945.

44. Bonn-Miller MO, Rousseau GS. Marijuana Use and PTSD Among Veterans. *VA Health Care PTSD Natl Cent PTSD*. http://www.ptsd.va.gov/professional/co-occurring/marijuana_use_ptsd_veterans.asp.