

Resource Document on Marijuana as Medicine

Approved by the Joint Reference Committee, October 2013

The findings, opinions, and conclusions of this report do not necessarily represent the views of the officers, trustees, or all members of the American Psychiatric Association. Views expressed are those of the authors." -- *APA Operations Manual*.

Tauheed Zaman, M.D.
Richard N. Rosenthal, M.D.
John A. Renner, Jr., M.D.
Herbert D. Kleber, M.D.
Robert Milin, M.D.

Abstract

The medical use of marijuana has received considerable attention as several states have voted to remove civil and criminal penalties for patients with qualifying conditions. Yet, on a national level, marijuana remains a schedule I substance under the Controlled Substances Act (CSA), the most restrictive schedule enforced by the Drug Enforcement Administration (DEA) (1). The Food and Drug Administration (FDA), responsible for approving treatments after appropriate and rigorous study, additionally does not support the use of marijuana for medical purposes. This juxtaposition of practice and policy has prompted many professional medical organizations to issue official positions on the topic. This statement reflects the position of the American Psychiatric Association (APA) on the use of marijuana for psychiatric indications. It does not cover the use of synthetic cannabis-derived medications such as Dronabinol (Marinol), which has been studied and approved by the FDA for specific indications.

Medical Indications for Marijuana as Medicine

Much of the evidence supporting marijuana use for non-psychiatric medical diagnoses remains anecdotal. The indications with the most evidence include: severe nausea and vomiting associated with cancer chemotherapy (2), cachexia associated with Acquired Immune Deficiency Syndrome (AIDS) (3), spasticity secondary to neurological diseases such as muscular sclerosis (4), management of neuropathic pain (5), and rheumatoid arthritis (6). Several medical organizations have issued statements regarding indications for marijuana as medicine based on scientific evidence.

Contribution of Marijuana to Psychiatric Illness

There is currently no scientific evidence to support the use of marijuana 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, as evidenced by both international trials and meta-analyses (7-9). This includes the contribution of marijuana to symptoms of mood disorders, anxiety and psychosis, particularly in young adulthood^{10, 11}. Cannabis use is associated with the emergence of mood disorders,

particularly symptoms of bipolar disorder, among those with a family history of mood disorder (12). Among those with major depressive disorder, co-morbid cannabis use is associated with increased rates of both suicidal ideation and attempts, raising grave safety concerns (13). Among those with a predisposition to psychotic disorders, cannabis may hasten the emergence of both positive and negative psychotic symptoms (14). The use of higher potency cannabis, for longer periods of time and with more frequency, is also associated with increased risk of psychosis (15).

Several studies have demonstrated the link between marijuana use and mood, anxiety and psychotic disorders among adolescents. Cannabis use is associated with increased depression, suicidal ideation, use of other substances and risky behavior among adolescents¹⁶. Regular adolescent cannabis use is also associated with increased incidence of anxiety disorders (17). Cannabis use significantly increases the risk of psychotic disorders among young adults (18). Additionally, younger age of cannabis use is associated with an earlier onset of psychosis among those at risk (19). Adolescents with a history of cannabis use tend to have higher severity of illness, lower psychosocial functioning, less insight, and longer courses of untreated psychosis compared to those without a history of cannabis use²⁰. These findings are of particular concern as symptoms often persist into adulthood, and therefore cannabis use may increase the risk of lifelong symptoms and disability due to mental illness.

Serious Adverse Effects of Marijuana Use

Cognitive and Functional

Marijuana use is associated with serious cognitive problems such as short-term memory deficits, poor concentration, attention, and information processing (21). These impairments might be caused by neurotoxic effects of cannabis on the developing brain, the effects of which can lead to long-term cognitive problems well into adulthood (22, 23). Adolescents with daily cannabis use show deficits in learning up to six weeks after stopping marijuana use (24). This may contribute to significantly decreased academic achievement, including increased rates of school dropout, failure to enter higher education or attain higher degrees (25). Among both adolescents and adults, cannabis significantly impairs driving, particularly as the drug affects automatic driving functions in a highly dose-dependent fashion (26). Cannabis use, particularly in combination with alcohol, greatly increases the risk of motor vehicle crashes due to effects on cognition and coordination (27). Addiction and burden of psychiatric illness:

Cannabis use is associated with an increased risk of developing a cannabis use disorder. Studies indicate that 9% of users become dependent on cannabis, and this number increases to 25-50% among daily users and to 1 in 6 among adolescents (28). Adolescents remain at particular risk for cannabis use disorder, and can experience significant withdrawal symptoms including appetite changes, restlessness, irritability, depression, twitches and shakes, perspiration, and thoughts/cravings of cannabis (29). Marijuana use is also associated with poorer outcomes among those with mental illness. Among individuals with schizophrenia, cannabis use is associated with poorer long-term clinical outcomes (30). Individuals with psychotic illness may be more sensitive to both the psychosis-inducing and mood-altering effects of cannabis (31). This may explain why even among those taking medications for psychotic disorders, cannabis use is associated with an increased risk of relapse into psychotic symptoms (32).

Legalization of medical marijuana may reduce the perceived risks of use, the perception of societal disapproval, or the barriers to access, and potentially increase the incidence of the adverse events noted above.

Summary

Given the gravity of concerns regarding marijuana as medicine, professionals in both neurology and psychiatry have emphasized the importance of prospective studies to understand the mechanisms by which cannabis functions, and its impact on mental health and behavior before instituting changes in practice and policy (33, 34).

Organizations with Position Statements on Marijuana as Medicine as of April 2013

- American Academy of Child and Adolescent Psychiatry (AACAP)
- American Academy of Pediatrics (AAP)
- American Medical Association (AMA)
- American Society of Addiction Medicine (ASAM)
- American Cancer Society
- National Multiple Sclerosis Society

References

1. Food and Drug Administration. "FDA Statement: Inter-agency advisory regarding claims that smoked marijuana is medicine." Revised April 2006.
2. Duran M, Perez E, Abanades S, Vidal X, Saura C, Majem M, Arriola E, Rabanal M, Pastor A, Farre M, Rams N, Laporte JR, Capella D. Preliminary efficacy and safety of an oromucosal standardized cannabis extract in chemotherapy-induced nausea and vomiting. *Br J Clin Pharmacol* 2010 Nov;70(5): 656-63.
3. Haney M, Gunderson EW, Rabkin J, Hart CL, Vosburg SK, Comer SD, Fotlin RW. Dronabinol and marijuana in HIV-positive marijuana smokers: Caloric intake, mood, and sleep. *J Acquir Immune Defic Syndr*. 2007 Aug 15;45(5): 545-54.
4. Lakhani SE, Rowland M. Whole plant cannabis extracts in the treatment of spasticity in multiple sclerosis: a systematic review. *BMC Neurol* 2009 Dec 4;9:59.
5. Martin-Sanchez E, Furukawa TA, Taylor J, Martin JL. Systematic review and meta-analysis of cannabis treatment for chronic pain. *Pain Med* 2009 Nov;10(8): 1353-68
6. Richards BL, Whittle SL, Buchbinder R. Neuromodulators for pain management in rheumatoid arthritis. *Cochrane Database Syst Rev*. 2012 Jan 18;1.
7. Semple DM, McIntosh AM, Lawrie SM. Cannabis as a risk factor for psychosis: a systematic review. *J Psychopharmacol*. 2005 Mar; 19(2):187-94.
8. Moore TH, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet*. 2007 Jul 28;370(9584):319-28.
9. Large M, Sharama S, Comptom MT, Slade T, Nielssen O. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. *Arch Gen Psychiatry*. 2011 Jun;68(6): 555-61.
10. van Laar M, van Dorsselaer S, Monshouwer K, de Graaf R. Does cannabis use predict the first incidence of mood and anxiety disorders in the adult population? *Addiction*. 2007 Aug;102(8): 1251-60
11. Degenhardt L, Coffey C, Romaniuk H, Swift W, Carlin JB, Hall WD, Patton GC. The persistence of the association between adolescent cannabis use and common mental disorders into young adulthood. *Addiction*. 2013 Jan;108(1):124-33..
12. Duffy A, Horrocks L, Milin R, Doucette S, Persson G, Grof P. Adolescent substance use disorder during the early stages of bipolar disorder: a prospective high-risk study. *J Affect Disord*. 2012 Dec 15;142(1-3):57-64.
13. Lynskey M, Glowinski A, Todorov A, Buchholz K, Madden P, Nelson E, Statham D, Martin N, Heath A, Phil D. Major depressive disorder, suicidal ideation, and suicide attempt in twins discordant for cannabis dependence and early-onset cannabis use. *Arch Gen Psychiatry*. 2004 Oct;61(10): 1026-32.

14. Kahn RS, Linszen DH, van Os J, Wiersma D, Bruggeman R, Cahn W, de Haan L, Krabbendam L, Myin-Germeys O. Evidence that familial liability for psychosis is expressed as differential sensitivity to cannabis: An analysis of patient-sibling and sibling-control pairs. *Arch Gen Psychiatry*. 2011 Feb; 68(2): 138-147.
15. Di Forti M, Morgan C, Dazzan P, Pariante C, Mondelli V, Reis Marques T, Handley R, Luzzi S, Russo M, Paparelli A, Butt A, Stilo SA, Wiffen B, Powell J, Murray RM. High potency cannabis and the risk of psychosis. *Br J Psychiatry*. 2009 Dec;195(6):488-491.
16. Office of National Drug Control Policy, Executive Office of the President. Teen marijuana use worsens depression: An analysis of recent data shows "self-medicating" could actually make things worse. 2008.
17. Degenhardt L, Coffey C, Romaniuk K, Swift W, Carlin JB, Hall WD, Patton GH. The persistence of the association between adolescent cannabis use and common mental disorders into young adulthood. *Addiction*. 2013 Jan;108(1):124-33.
18. McGrath J, Welham J, Scott J, Varghese D, Degenhardt L, Hayatbakhsh MR, Alati R, Williams GM, Bor W, Najman JM. Association between cannabis use and psychosis-related outcomes using sibling pair analysis in a cohort of young adults. *Arch Gen Psychiatry*. 2010 67(5):440-447.
19. Dragt S, Nieman DH, Becker HE, van de Fliert R, Dingemans PM, de Hann L, van Amelsvoort TA, Linszen DH. Age of onset of cannabis use is associated with age of onset of high-risk symptoms for psychosis. *Canadian J of Psychiatry*. 2010 Mar;55(3):165-171.
20. Schimmelmann BG, Conus P, Cotton S, Kupferschmid S, McGorry PD, Lambert M. Prevalence and impact of cannabis use disorders in adolescents with early onset first episode psychosis. *Eur Psychiatry*. 2012 Aug;27(6):463-9.
21. Kleber, H.D., DuPont, R.L. Physicians and Medical Marijuana: Commentary. *Am J Psychiatry*. 2012 June;169(6): 564-568.
22. Meier MH, Caspi A, Ambler A, Harrington H, Houts R, Keefe RS, McDonald K, Ward A, Poulton R, Moffitt TE. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Nat Acad Sci USA*. 2012 Oct 2;109(40):E2657-64.
23. Pope HG Jr, Gruber AJ, Hudson JI, Cohane G, Huestis MA, Yurgelun-Todd D. Early-onset cannabis use and cognitive deficits: what is the nature of the association? *Drug Alcohol Depend*. 2003 Apr 1;69(3):303-10.
24. Sheinsburg AD, Brown SA, Tapert SF. The influence of marijuana use on neurocognitive functioning in adolescents. *Curr Drug Abuse Rev*. 2008 Jan;1(1):99-111.
25. Fergusson DM, Horwood LJ, Beautrais AL. Cannabis and educational achievement. *Addiction*. 2003 Dec;98(12):1681-92.
26. Sewell RA, Poling J, Sofuoglu M. The effect of cannabis compared with alcohol on driving. *Am J Addict*. 2009 May-Jun;18(3):185-93.
27. Ramaekers JG, Berghaus G, van Laar M, Drummer OH. Dose related risk of motor vehicle crashes after cannabis use. *Drug Alcohol Depend*. 2004 Feb 7;73(2):109-19.
28. National Institute on Drug Abuse. "Drug Facts: Marijuana." Revised December 2012. <http://www.drugabuse.gov/publications/drugfacts/marijuana>
29. Milin R, Walker S, Duffy A. Assessment and treatment of comorbid psychotic disorders and bipolar disorder. *Clinical Manual of Adolescent Substance Abuse Treatment*. Washington, DC: American Psychiatric Publishing Inc, 2011.
30. Foti DJ, Kotov R, Guey LT, Bromet EJ. Cannabis use and the course of schizophrenia: 10-year follow-up after first hospitalization. *Am J Psychiatry*. 2010 Aug;167(8): 987-993.
31. Henquet C, van Os J, Kuepper R, Delespaul P, Smits M, à Campo J, Myin-Germeys I. Psychosis reactivity to cannabis use in daily life: an experience sampling study. *Br J Psychiatry*. 2010 Jun; 196(6): 447-453.
32. Levy E, Pawliuk N, Joober R, Abadi S, Malla A. Medication-adherent first-episode psychosis patients also relapse: Why? *Canadian J Psychiatry*. 2012 Feb;57(2): 78-84.
33. Croxford JL. Therapeutic potential of cannabinoids in CNS disease. *CNS Drugs*. 2003; 17(3): 179-202.
34. Hall W, Lynskey M. The challenges in developing a rational cannabis policy. *Curr Opin Psychiatry*. 2009 May;22(3):258-62.