# Medical Marijuana Is a Fraud

by Ned Rosinsky, MD

June 23—Medical marijuana has now been legalized in 33 states and the District of Columbia, allowing physicians to prescribe marijuana for a variety of ailments, including pain, vomiting, and post-traumatic stress disorder (PTSD). As in the case of the quacks pushing various super-cures from the backs of wagons during the 1800s, the mania for Laetrile as the cure for cancer, or the recent flourishing of stem cell clinics that promise to cure virtually any illness with an infusion of your own stem cells back into you, there have always been unproven treatments hawked by biased so-called healers, and hyped by reports of happy patients who swear by the treatments.

What influences legislators around the country to legalize marijuana for medical use—a substance which is abusable and has been proven in scientific studies to be harmful to memory and other aspects of cognition, certainly more harmful and higher risk than the broad use of stem cells or Laetrile?

**Evaluating the Trials of Medical Marijuana**

The answer involves a definition of what is competent science. In the field of medicine, a proposed treatment of a disorder requires a therapeutic trial, including documentation of effectiveness. In the long-past history of medicine, for many years, the trials were made by individual practitioners on their own patients, usually involving a small number of subjects. The proposed treatment was explained to the patient, so both the patient and practitioner knew what was being used and why it was suspected that it might be helpful. The practitioner would then evaluate the effect of the treatment. This is termed an open trial, because both the patient and the practitioner are aware of what is being given to the patient. This initially certainly sounds like a reasonable approach.

However, there are several significant problems with this kind of study. First, there may be bias on the part of the practitioner or the patient. The practitioner wants the patient to get well, may want a financial benefit, a reputational benefit, or even an ego benefit. The patient may be biased as well, wishing the treatment to

work. There is frequently a placebo effect in which the expectation of improvement frequently results in subjective improvement. The biological and psychological basis for the placebo effect is unclear, but likely involves neurological pathways and possibly hormones that are affected by expectation and a sense of relief that someone is concerned and being helpful.

For example, the size of the placebo effect in studies of antidepressants is well documented, at approximately 30% improvement, so for a given medication to be shown to be effective it must exceed this threshold.

In the case of marijuana, there may be additional bias due to the widespread awareness that success in medical trial use may be used as justification for total legalization, so if the patient or practitioner supports total marijuana legalization, there may be a significant bias towards showing that marijuana is medically effective.

These biases may influence the study in numerous ways. The practitioner may choose patients who are likely to be biased, such as people who are substance abusers, or in the age range of high rate of substance abuse, or in a geographical area of high levels of substance abuse. The practitioner may choose a rating scale that is heavily subjective, such as degree of pain, rather than something more objective such as days lost from work. Most of the purported medical uses of marijuana have been disorders that are quantified subjectively, such as pain, nausea, or anxiety from PTSD.

The issues of bias and placebo effect have been widely recognized since the 1960s as having severely negative effects on the reliability of therapeutic medication trials.

The currently accepted way to avoid these issues is to use a randomized double-blind study, in which the treatment to be tested is compared to a placebo, a "sugar pill," and both the researchers and subjects of the trial are blind as to which subjects are getting the proposed treatment and which the placebo, until all the results are tabulated and analyzed. (Although this population-based approach cannot always be extrapolated to a given individual patient.)

In the early days of the attempts to get marijuana approved for medical use, the main arguments presented to state legislatures were individual testimonials by patients who stated that they felt better or improved in some way by smoking marijuana, or studies that were too small to be definitive, were biased, or were not double-blind. There was an accumulation of such small studies in the 1990s and the first decade after 2000, during which time numerous states approved the use of medical marijuana, largely influenced by these limited studies.

## Meta-Analysis

However, more recently there have been overviews of the accumulated research, termed meta-analyses, which evaluate the total implications of all the studies available. These meta-analyses start out by listing the available studies, and then examining each study in detail to determine reliability. If a study is not randomized double-blind, or if there is bias evident, or if there is a problem with the statistics, then the study is usually eliminated from analysis.

A typical meta-analysis may start out with 100 published studies and end up with 20 that meet standards for reliability. Since the typical studies include fifty to several hundred subjects, the gathering together of 20 such studies usually includes a very large subject population that is usually geographically and socially widely distributed, so it is also more representative of the general population.

With this background, let us review the principal recent meta-analyses of medical marijuana.

## Removing Bias and Error

The most prominent argument used for medical marijuana is pain control; the image of a terminal cancer patient dying in severe pain would naturally move almost anyone to advocate anything that would help.

The European Society for Medical Oncology (ESMO) published in 2019 an overview document titled "Management of Cancer Pain in Adult Patients: ESMO Clinical Practice Guidelines." In the section on Medical Cannabis, a meta-analysis was done using the MEDLINE database from the Internet site *PubMed* reviewing the cancer pain relief from nabixomols, an extract of marijuana containing two potentially therapeutic cannabinoids, D9-tetrahydrocannabinol (THC), and cannabidiol (CBD).

The conclusion, based on randomized, double-blind studies, was that—

> Nabixomols did not demonstrate superiority to placebo in reducing self-reported pain. [and that] Nabixomols [were] not superior to placebo on the primary efficacy endpoint.

A meta-analysis published in *Neuropsychopharmacology* in 2017, "Opioid-Sparing Effect of Cannabi-

noids: A Systematic Review and Meta-Analysis," examined the addition of D9-THC to opioid medication for pain control. The meta-analysis showed some promise in pre-clinical studies, but in controlled double-blind clinical studies,

> Opioid dose changes were rarely reported, and mixed findings were observed for analgesia.... Prospective high-quality-controlled clinical trials are required to determine the opioid-sparing effect of cannabinoids.

In other words, in the real world of pain treatment, no conclusion could be reached indicating any significant benefit.

In a 2015 meta-analysis published by the *Journal of the American Medical Association* (*JAMA*) titled "Cannabinoids for Medical Use: A Systematic Review and Meta-Analysis," the section on pain control assessed 28 individual studies: 13 of those studies evaluated nabixomols, 4 utilized smoked THC, 5 used nabilone, 3 used THC oral spray, 2 used dronabinol, 1 used vaporized cannabis, 1 used ajuvenic acid (a synthetic cannabinoid derivative) capsules, and 1 used oral THC.

The 28 studies were evaluated for bias, and the conclusion was that 17 were at high risk for bias, 9 were at unclear risk, and only 2 were at low risk for bias.

In this meta-analysis, apparently due to the overwhelming number of biased studies, *all* of the studies were used in the analysis. The best pain response was among those smoking THC, which would not be double-blind since the smoker in the THC group would feel the psychological effect of intoxication.

Even with this overwhelmingly biased group of studies, there was no statistical difference in average quality-of-life indicators.

A meta-analysis published in the journal *Pain* in 2018 titled, "Cannabis and Cannabinoids for the Treatment of People with Chronic Noncancer Pain Conditions [CNCP]," contrasted the low rate of effectiveness to the high rate of adverse effects, and concluded:

> It seems unlikely that cannabinoids are highly effective medications for CNCP.

*The Journal of Clinical Psychiatry* "Marijuana Use Is Associated with Worse Outcomes in Symptom Severity and Violent Behavior in Patients with Post Traumatic Stress Disorder."

**In this observational study, initiating marijuana use after treatment was associated with worse PTSD symptoms, more violent behavior, and alcohol use. Marijuana use may actually worsen PTSD symptoms or nullify the benefits of specialized, intensive treatment. Cessation or prevention of use may be an important goal of treatment.**

In contrast to the low-quality and time-limited studies, a large scale, double-blind study was published in *The Lancet* in 2018, titled "Effect of Cannabis in People with Chronic Non-Cancer Pain Prescribed Opioids: Findings From a 4-Year Prospective Study." The study included 1,514 participants in Australia, who were prescribed opioid medications for CNCP.

In this study, marijuana was not provided by the researchers, but the use of marijuana by the participants was evaluated using follow-up questionnaires. The study concluded that the participants with the most pain used the most marijuana, as might be expected given the publicity regarding marijuana helping pain. However, the study also concluded that the marijuana use did not help the pain:

> Cannabis use was common in people with chronic non-cancer pain who had been prescribed opioids, but we found no evidence that cannabis use improved outcomes. People who used cannabis had greater pain and lower self-efficacy in managing pain, and there was no evidence that cannabis use reduced pain severity or interference, or exerted an opioid-sparing effect.

Given this dismal picture of the state of research in the use of marijuana for pain, it is not surprising that the American Cancer Society's 2017 position paper , "Marijuana and Cancer," states,

> The American Cancer Society Cancer Action Network, the Society's advocacy affiliate, has not taken a position on legalization of marijuana for medical purposes because of the need for more scientific research on marijuana's potential benefits and harms.

## The PTSD Argument for Medical Marijuana

The next most common argument for medical marijuana is for post-traumatic stress disorder (PTSD), a condition seen commonly in military combatants, assault victims, and other situations of extreme or chronic

stress. The symptoms include anxiety, depression, and irritability, and may be disabling and long-standing.

The U.S. Department of Veterans Affairs has recommended treatment with antidepressants which are also effective for anxiety, and cognitive-behavioral therapy, both of which are moderately effective.

A meta-analysis in this area titled, "A Review of Medical Marijuana for the Treatment of Post-Traumatic Stress Disorder: Real Symptom Relief or Just High Hopes?" was published in *The Mental Health Clinician* in 2018 and concludes:

> Conflicting data exist for the use of marijuana for PTSD; however, current evidence is limited to anecdotal experiences, case reports, and observational studies, making it difficult to make clinical recommendation.

A large, non-blinded study published in *The Journal of Clinical Psychiatry* in 2015 titled, "Marijuana Use Is Associated with Worse Outcomes in Symptom Severity and Violent Behavior in Patients with Post Traumatic Stress Disorder," studied 2,276 veterans with PTSD and followed their progress with no marijuana prescribed by the researchers. The use of marijuana was documented, and the study concluded:

> In this observational study, initiating marijuana use after treatment was associated with worse PTSD symptoms, more violent behavior, and alcohol use. Marijuana use may actually worsen PTSD symptoms or nullify the benefits of specialized, intensive treatment. Cessation or prevention of use may be an important goal of treatment.

## Treatment for Nausea, Weight Loss, Sleep Disorders

Regarding marijuana and the treatment of nausea, weight loss, sleep disorders, and other conditions, the above-cited *JAMA* meta-analysis concluded:

> There was low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy, weight gain in HIV infection, sleep disorders, and Tourette's Syndrome [a tic disorder].

A meta-analysis of marijuana and treatment of nausea associated with cancer chemotherapy published as a *Cochrane Review* in 2015, titled "Cannabis-Based Medicine for Nausea and Vomiting in People Treated with Chemotherapy for Cancer," concluded:

> There was no evidence of a difference between cannabinoids and prochlorperazine in the proportion of participants reporting no nausea, or no vomiting. However, there were more people withdrawing from the study due to adverse events when they were treated with cannabinoids, such as dizziness, dysphoria (negative emotional feelings), euphoria, and sedation.

Regarding glaucoma, which was an early claim for medical marijuana, a National Academy of Sciences review of the available research published in 2001, "Marijuana and Glaucoma," notes:

> There is no question that marijuana-based medicines can be used to lower IOP [intra-ocular pressure]. But like several other glaucoma medications that have fallen into disuse, their drawbacks outweigh their benefits. This was not the case when the first reports of marijuana's effects were published in the 1970s, a time when relatively few drugs—all of which caused troublesome side effects—were available to treat the condition. Those drugs have been superseded by more effective and less problematic medications. That seems the likely fate of marijuana-based treatments for glaucoma as well.

In summary, the evidence for medical marijuana is generally weak for any significant therapeutic effect, and in the marginal areas in which there is some effect, there are alternative medications already available that are as good or better. Therefore, the only reason for urging the legalization of medical marijuana would be to legitimize marijuana use, as preparation for complete legalization of use. On the other side of the question, the harmful effects of marijuana are well documented regarding memory and other cognitive functions, as well as serving as a gateway drug encouraging the use of even more dangerous substances. The legalization of medical marijuana encourages youth to think it must be harmless, and is used by youth to justify abusing the drug. This harm caused by legalizing medical marijuana is real, palpable, and adversely affects the most vulnerable segments of our population.