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## Medical Association of the Bahamas Position Paper on Medical Cannabis

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### Key terms

- **Cannabinoid:** a chemical compound that acts on the endocannabinoid system.
- **THC:**  $\Delta^9$ -tetrahydrocannabinol, the main cannabinoid in marijuana, known mostly for its intoxicating effects
- **CBD:** cannabidiol, a cannabinoid found in the cannabis plant, considered to have multiple therapeutic applications. Non-intoxicating. Non addictive.
- **Phytocannabinoids:** naturally occurring cannabinoids found in the cannabis plant. Usually refers to CBD and THC
- **Endocannabinoids:** naturally occurring cannabinoids found in the human body.
- **Pharmaceutical Cannabinoids:** pharmaceutical grade synthetic cannabinoid products
- **Synthetic cannabinoids:** medicinal products containing synthetically produced cannabinoids
- **CBD based products:** products containing CBD that are widely sold as herbal remedies but are not regulated as medicinal products
- **Whole plant cannabis:** buds, leaves and occasionally stems of the cannabis plant that are widely used for its intoxicating effects. Often referred to as marijuana. May have therapeutic applications as well.
- **Receptor:** a molecule found in humans and animals that when activated, initiates some physiological response.
- **Placebo:** an inactive substance or treatment which is designed to have no therapeutic value.

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**Foreword: The Legalization of Marijuana use in the Bahamas  
is a major health Issue.  
(Professor Robin Roberts)**

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Over the past decade, societies at national and global levels, have been pursuing legislation and policies to govern the use of marijuana. The pros and cons of the legislative and regulatory debates are high on the political agenda. The timelines are stamped with urgency; these are high stake issues. There are two powerful underlying forces driving the process. On one front, there is both the lure of profits in the marketplace and the potential for increasing government revenues. Forbes, the foremost US financial magazine, reported in the "The U.S. Cannabis Report 2019 Industry Outlook", that the total legitimate sales of cannabis in states where cannabis is legal are projected to increase at a compound annual growth rate of 14% over the next six years, reaching nearly \$30 billion by 2025. Market research suggest that worldwide legal marijuana revenue will increase to \$103.9 billion by 2024. This would represent an 853% increase in sales from 2018.

On the other front, pharmaceutical derivatives of the cannabis plant have the promise of major breakthroughs in the medical field. Epidiolex, used for treating severe epileptic syndromes has been nothing short of a miracle and was approved in June 2018 by the world's toughest regulator, the Food and Drug Administration. The potential use of the pharmaceutical derivatives of the cannabis plants to treat many common diseases, is growing by leaps and bounds for both prescription drugs as well as over the counter applications. The demand for the use of cannabis derived products is huge.

The momentum for advancing a favorable legislative and regulatory agenda is being refrained primarily by the potential adverse health effects on individuals and the potential burden of its public health implications. It's a case study in the social determinants of disease. A quote from an editorial in The Journal of the American Medical Associations is most fitting, "policy has outpaced science".

It is within this framework that the Medical Association of the Bahamas addresses this complex societal issue. We are the professional physician body with the fiduciary responsibility for the delivery of safe, quality-driven health care. This paper sets out to review the medical issues and implications of legalizing the cannabis plant for pharmaceutical use. We outline the content of this review:

- Global status – Legalizing marijuana for medicinal purposes
- Historical perspective: Stigmatization of marijuana:
- The chemistry of the cannabis plant
- Current status of medical cannabis in The Bahamas
- The MAB's Position Statements.

We have travelled this road before. The current issues on the legalization of marijuana mirrors those that challenged the world with the legalization and commercialization of alcohol. This therapeutic and recreational drug went through periods of prohibition too; but despite the most stringent legislation and policies for alcohol use, the burden of injuries, accidents, premature deaths, and lost productivity, for all generations including the unborn, is incalculable.

The MAB is cautious in its proposal for the medical use of marijuana. The prevailing question from a medical perspective is: Can regulatory approaches to the use of cannabis reduce health and social harms more effectively than prohibition? The economic stakes and potential profits are high, but we must tread carefully and deliberately. The health of our population is at risk in every dimension of marijuana's legality.

## Introduction

To date, there are some 30 countries that allow the use of marijuana for medicinal purposes. Although recreational consumption is still prohibited in most jurisdictions, many countries have adopted policies that have decriminalized cultivation and possession for personal use.

The global destigmatization of marijuana and the economic potential of the cannabis industry have led many Caribbean countries to reconsider their position. In 2018, the CARICOM Regional Commission on Marijuana strongly supported the decriminalization of marijuana by its member states as well as its legalization for medical use (1). Countries such as Jamaica and Belize have already decriminalized possession for personal use, while St Kitts and Nevis, Antigua and Barbuda, St Vincent and the Grenadines, and Trinidad and Tobago have embarked on legislative reform that will take a similar approach.

In 2019, the current Prime Minister, Dr. Hubert Minnis, appointed the Bahamas National Commission on Marijuana to examine the issues surrounding the use of marijuana and to draft a report that is expected to heavily influence local marijuana legislation.

The Medical Association of the Bahamas (MAB) has taken the debate of medical marijuana under review to ensure that the risks, benefits and alternatives are thoughtfully considered. We believe this discussion in particular, should be supported by quality, scientific evidence and not assumptions based on personal, social or religious beliefs. This paper also considers the trends in the region with the understanding of The Bahamas' unique cultural and socioeconomic reality. It does not specifically address the debate on the decriminalization or legalization of marijuana for recreational use although inferences can be made based on the evidence and deductive reasoning.

First and foremost, it is important to understand that although the terms cannabis and marijuana are often used interchangeably, the two are not exactly alike. Cannabis is the scientific name given to a group of plants that include *Cannabis sativa*, *Cannabis indica* and *Cannabis ruderalis*. The colloquial term marijuana is regularly used to describe the buds and leaves of the cannabis plant, usually *Cannabis sativa*, which is high in THC, and is commonly consumed for recreational and religious purposes. The cannabis plant is also the source of CBD and hemp, neither of which are considered to have psychoactive or harmful properties. CBD, when extracted from the cannabis plant, is a non-intoxicating, non-addictive compound that can be incorporated into a variety of medicinal products with clinically proven benefits. Hemp is used to manufacture a range of industrial products such as rope, textiles and clothing, while hemp oil is used as a moisturizing agent in skin, hair and cosmetic products. Hemp, hemp oil and CBD products are currently legal in the United States and most of Europe and are widely available. These benign applications of the cannabis plant are still excluded in current legislation and prohibited from importation and sale. For many, the negative imagery associated with the term marijuana, and cannabis by association, as a dangerous illicit drug, dominates any discussion that examines its potential benefit in medicine.

For this reason the term marijuana will only be used in the remainder of this paper, when discussing historical references or current public perception. The rationale is to provide an objective, dispassionate report on the scientific evidence that examines the medical benefits of the cannabis plant. \*Idaho, South Dakota and Nebraska do not have clear laws regarding CBD and Hemp.

## History of Medical Cannabis

Cannabis has been acknowledged to be of medicinal value for thousands of years. Numerous accounts of its use in ancient Chinese medicine have been cited in the mainstream and scientific literature. Reports of marijuana tea being used for such ailments as malaria and gout date back to 2737 B.C. (2). The Ebers Papyrus, one of the oldest preserved medical texts, dating back to 1,550 B.C., mentions the use of the cannabis plant for inflammation when applied topically (3).

In the mid 1800's, Dr. William B. O'Shaughnessy reported the benefits of the cannabis plant in Cholera, rheumatism and convulsions. O'Shaughnessy's successful use of cannabis was pivotal and led to its widespread adoption in Europe and North America (4). In the early 1900's, Sir William Osler, the father of modern medicine, and a number of other well-known physicians, advocated for the use of cannabis in the treatment of migraines (5). As an unrestricted drug, cannabis was readily available in pharmacies and doctor's offices in liquid form for a variety of ailments.

The popularity of marijuana as a legitimate therapeutic drug declined in the 1920s when the Federal Bureau of Narcotics began to publicize the social ills associated with the growing industry. With the influx of Mexican immigrants who were utilized as farm laborers, came a new practice of smoking marijuana for relaxation and recreational purposes, a habit that was relatively unheard of at the time. Reports soon surfaced that alleged marijuana use in these immigrant communities along the Mexican border, incited violent crimes, sexual inhibition and insanity. Isolated reports amplified by xenophobic undertones began to transform the perception of marijuana as medicine to that of an illicit drug. Harry Anslinger, the first Commissioner of the United States Federal Bureau of Narcotics, was quoted as saying "this marijuana causes white women to seek sexual relations with Negroes, entertainers and any others"(6). Anti-drug campaigners implored the government to bring the trafficking of marijuana under some form of regulation as there was for Opiates and other dangerous drugs. The Marijuana Tax Act of 1937 marked the beginning of marijuana prohibition in the United States, and in 1942, amid political pressures advocating for the ban of all cannabis products, all preparations were removed from the United States Pharmacopoeia and National Formulary (7,8).

It took more than thirty years for medical marijuana to find its way back into the spotlight. This was facilitated by a massive increase in recreational use during the 60s and 70s. In 1964 the main psychoactive component of the cannabis plant, THC, was identified and eventually led to a synthetic oral formulation being approved by the Food and Drug Administration for use in patients suffering from chemotherapy induced nausea and vomiting (CINV) (9). In 2000, Canada became one of the first countries to legalize Cannabis for medical purposes; numerous countries have since followed suit. The "medical marijuana" revolution received mainstream attention in 2013 after it was featured in Dr. Sanjay Gupta's CNN special report "Weed", which reported on children with severe seizure disorders who anecdotally benefitted from CBD (10). The award winning Chief Medical Correspondent for CNN admitted that he had misjudged the medical benefits of the cannabis plant, and personally wrote Attorney General Jeff Sessions asking him to reconsider US marijuana laws to allow much needed research to occur.

## History of Medical Cannabis cont'd

A recent PubMed (medical database) search using the terms “marijuana or cannabis” yielded just over 21,000 citations. Only 4% were randomized clinical trials, which are the foundation for “evidence-based” clinical guidelines and treatment strategies. This underscores the difficulty in making defensible recommendations based on quality scientific data.

Nonetheless, the Medical Association of the Bahamas submits this paper based on the available evidence, which may at times be underwhelming, but compelling enough to formulate an educated, informed position. The Association encourages local, regional and international research in medical cannabis to improve our understanding of its use in health and disease.

## Background

Cannabis is the scientific name given to a genus (group) of plants that are thought to have originated in Asia. Traditionally, three species of the cannabis plant have been recognized; *Cannabis sativa*, *Cannabis idica* and *Cannabis ruderalis*. There are many biologically active compounds in the cannabis plant, collectively called cannabinoids, that are responsible for its physiologic effects. Two of the most extensively studied cannabinoids are THC and CBD, also called *phytocannabinoids*. THC, the psychoactive cannabinoid found predominantly in the flowering tops of the cannabis plant, is exploited in marijuana, and is responsible for the “high” produced during inhalation or ingestion. The physiologic effects of the cannabis plant are produced when cannabinoids act on microscopic structures called receptors that are found throughout the human body. The two main cannabinoid receptors that have been identified are CB1 and CB2. CB1 receptors are distributed widely throughout the brain, central nervous system and gastrointestinal tract. The activation of CB1 receptors produces euphoria, drowsiness, hallucinations and memory impairment but may also modify pain perception, increase appetite and reduce nausea. The CB2 receptor, which is devoid of psychotropic effects and found predominantly in tissues of the immune system, has been shown to have anti-inflammatory properties <sup>(11)</sup>. Other studies suggest that CB2 receptors play a role in antinociception (analgesia) which is of particular interest in neuropathic (nerve) and cancer related pain.

The modern-day movement for cannabis as medicine began with the discovery of endogenous (within the body) compounds that also interact with the CB1 and CB2 receptors. These naturally occurring chemicals, now called *endocannabinoids*, their receptors and the mechanisms by which these endocannabinoids are produced is called the endocannabinoid system (ECS). The two main endocannabinoids; N-arachidonylethanolamide (anandamide) and 2-arachidonylglycerol (2AG) have been found to play a role in maintaining and regulating human health and has become a therapeutic target for a variety of diseases.

Ongoing research on the cannabis plant has identified other compounds (non-cannabinoids) called terpenes and flavonoids. Terpenes are substances that give the cannabis plant its aroma and fragrance but additionally may enhance the physiological effects of cannabinoids; known as “the entourage effect”. Terpenoids have recently become the focus of intense investigation after several studies have shown terpenoids may not only improve the medical benefits of THC by mitigating its toxic side effects but may also have pharmacological properties of its own <sup>(12)</sup>.

Flavonoids are chemicals found in cannabis and other plants that have a variety of functions including contributing to its color, aroma and flavor. Flavonoids have anti-inflammatory effects

and may be useful in the treatment of cardiovascular disease and cancer (13).

## Current status of medical cannabis in The Bahamas

The Dangerous Drugs Act of the Bahamas (DDA 2000) defines Indian hemp as “any plant of the genus *cannabis* whether growing or not from which the resin has not been extracted”. The definition also includes “the resin extracted from any part of such plant; and every compound, manufacture, salt derivative, mixture or preparation of such plant or resin”. The Act further prohibits “any person from cultivating, trading in, importing or bringing into The Bahamas any of these drugs (*Indian hemp, cannabis*) except by a qualified person with special authority of the Minister, for medical or scientific purposes” (14).

The Act bans the cultivation, importation or use of any compound derived from the cannabis plant, which includes CBD and hemp, for medicinal use or otherwise. Ironically, many hemp-based products can be found on the shelves of local pharmacies and convenience stores. The government has been unable to effectively restrict the importation of hemp products because it is widely accessible in the US market. Recent enforcement of the Dangerous Drugs Act to confiscate CBD products but allow importation and sale of hemp products is ambiguous and confusing and must be clarified in future policy statements.

## Position Statements

- 1. The Medical Association recommends the interpretation of "Indian Hemp" in Part 1 (2) of the Dangerous Drugs Act (Chapter 228) be amended to exclude extracts or preparations containing less than 0.3% THC concentration. Notably such an amendment would have implications for not only amending other Parts of the Dangerous Drugs Act (Chapter 228), but the list of preparations in the Psychotropic Schedule 1 of the Dangerous Drugs Act (Application) Order 1994. Further, the schedules for "medicinal drugs" and "patent or propriety preparations" in the Pharmacy Act (Chapter 227) would have to be expanded to include CBD products with less than 0.3% THC, which would be available without a prescription.**

**Rationale:** The term *hemp* (*Indian hemp, Industrial hemp*) is used to describe strains of the cannabis plant with THC concentrations less than 0.3% by dry weight. Hemp is legal in the majority of the United States and most of Europe, and as noted above, and has been cultivated to manufacture many non-medical products such as paper, clothing, and food. Amending the DDA to exclude *Indian hemp or any derivatives, extracts, salts with a THC concentration of less than 0.3% dry weight from the Dangerous Drugs Act*, would allow the importation of cannabis-based derivatives with negligible THC concentrations. If needed, provisions should be made for pharmaceutical cannabinoids (e.g. Nabilone, Dronabinol) whose THC concentrations exceed 0.3%.

- 2. Claims about the health benefits of cannabis are numerous but strong scientific support is lacking in many areas. The Medical Association of the Bahamas believes that there is**

**sufficient evidence to endorse the use of pharmaceutical cannabinoids in the following areas:**

### **Chemotherapy Induced Nausea and Vomiting (CINV)**

Large well conducted clinical trials of cannabis for medical use are lacking, but a review of 23 small randomized controlled trials evaluating the use of cannabis-based medicines in the treatment of (CINV) showed that patients experienced less nausea and vomiting when using cannabis-based therapy compared to placebo <sup>(15)</sup>. Although there is insufficient evidence to support cannabis as first-line treatment for CINV, synthetic pharmaceutical grade THC (Nabilone, Dronabinol) has been approved by the Food and Drug Administration of the United States and is widely used as salvage therapy for patients who have failed conventional medications <sup>(16)</sup>.

### **Chronic Pain**

The data supporting cannabis for chronic pain is inconsistent and often limited by flaws in study design. Multiple studies evaluating its use in neuropathic (nerve) pain have been unable to confirm a significant benefit when compared to placebo <sup>(17,18)</sup>. Other studies show value in patients who have failed conventional therapy <sup>(19)</sup>. A comparative review of the clinical trials evaluating cannabis in chronic pain cited challenges in methodology and study design that prevented strong recommendations for its use. Despite these findings, Canadian and European guidelines support consideration of cannabis-based medication when other therapies have failed

<sup>(20,21)</sup>

### **Multiple Sclerosis**

The largest randomized control trial of cannabis in patients with Multiple Sclerosis (MS) found no significant difference in physician administered tests of spasticity (muscle stiffness and tightness) when cannabis was compared to placebo, but an improvement in patient-reported symptoms when the same comparison was made <sup>(22)</sup>. Two smaller studies looking at the effect of Nabiximols, a pharmaceutical grade oromucosal (mouth) spray, on spasticity in MS, also showed a statistically significant improvement in self-reported spasticity when compared to placebo <sup>(23,24)</sup>. For this reason, the American Academy of Neurology has concluded that some cannabis-based therapies are probably effective at reducing patient reported spasticity associated with MS and MS related pain and hence, may be a useful adjunct to standard therapy.

### **HIV/AIDS**

HIV/AIDS affects more than 5,000 people in the Bahamas and millions globally. Symptoms associated with chronic HIV infection include reduced appetite, weight loss, nausea and vomiting. Cannabis has been proposed as an appetite stimulant for many years and has been studied in patients living with HIV/AIDS who have anorexia (poor appetite) and wasting (weight loss). A study of 143 HIV positive patients who were regular cannabis users, showed that more than 50% of the participants reported improvement in nausea, weight loss, fatigue and other symptoms. Inhalation (smoking) was the preferred route of administration in 71% of users <sup>(25)</sup>. Similar studies in this population have shown an improvement in weight with



Dronabinol (an oral pharmaceutical formulation of THC) when compared to placebo (26,27). Currently there is no evidence to suggest that cannabis consumption adversely affects clinical indicators such as viral load and CD4 counts but it should not replace the more effective therapies such as combination antiretrovirals and megestrol acetate (Megace ®) for the treatment of symptoms (28). Dronabinol has been approved by the United States Food and Drug Administration for the treatment of HIV wasting and could be considered as adjunctive therapy on an individual basis.

**The Medical Association of The Bahamas believes that more research is needed to determine the role of cannabis in the following areas.**

### **Gastrointestinal Disease**

Cannabinoid receptors have been found in the gastrointestinal tract of both animals and humans. Stimulation of CB1 receptors slows down the digestive process and relieves diarrhea. Cannabis has also been shown to improve some of the symptoms associated with Inflammatory Bowel Disease such as abdominal pain, nausea and reduced appetite but may increase the risk of surgery in patients with Crohn's Disease (29). Small clinical trials suggest cannabis may also have a role in the treatment of Irritable Bowel Syndrome but results are not consistent (30,31). Despite these potential therapeutic benefits, Cyclic Vomiting Syndrome (CVS) and Cannabinoid Hyperemesis Syndrome (CHS) are two gastrointestinal disorders associated with chronic cannabis use. Both conditions are associated with severe vomiting and abdominal pain that may require hospitalization. The exact mechanisms of CVS and CHS are unknown but the diagnosis should be considered in anyone with severe nausea and vomiting and a strong history of cannabis abuse (32). Cannabis may also have harmful effects on the liver (liver fibrosis and hepatic encephalopathy) and can diminish the effectiveness of medications used to treat Hepatitis C (33,34). Recently, multiple case reports of cannabis induced pancreatitis (inflammation of the pancreas) have been published that suggest long term cannabis use is a risk factor. Close monitoring will determine if widespread availability will increase the number of cases being reported (35).

### **Cancer**

Scientific experiments on isolated cancer cells show that cannabis may inhibit tumor growth. Researchers have demonstrated that cannabidiol (CBD) can prolong the survival of mice with some types of brain tumors (36). Similar studies in animals with prostate and colon cancer conclude that CBD may have "an encouraging effect on reducing colon cancer growth and decreasing tumor size (37). Case reports and small clinical studies in humans also show a reduction in tumor size and prolonged survival in patients treated with CBD (38,39). Despite these findings, there is still insufficient evidence to prove that cannabis or CBD can safely and effectively treat all types of cancers in humans. Ongoing research is necessary to determine the role of cannabis as an anticancer drug.

### **Glaucoma**

Cannabis is often cited as a therapeutic option for the treatment of glaucoma. While cannabis has been shown to lower the pressure in the eye, the effects are short lived and limited by numerous side effects. There may be a role for cannabis in patients with glaucoma who have failed all currently available therapies and who are unable to have surgery (40,41).

- 3. Although there is little scientific evidence to support the claims of many cannabidiol (CBD) based products, such as CBD and hemp oils, the Medical Association of the Bahamas does not object to their use as these products appear to have limited toxicity and minimal potential for abuse.**

**Rationale:** CBD based products and Hemp oils are readily available in the United States and Canada and claims for their usefulness are numerous. They are marketed as anti-inflammatories, anxiolytics, antidepressants and sleep aids, among other uses. Of noted

importance is the potential use in the treatment of chronic pain, particularly considering the worldwide opioid abuse crisis. CBD products come in the form of sprays, oils, balms and chewables. Side effects such as somnolence (sleepiness), diarrhea and decreased appetite have been reported in some studies but were no more severe than side effects noted with conventional therapy (42,43). The THC concentration in most CBD preparations is negligible and is relatively non-existent in hemp oils. Unfortunately, the CBD industry is unregulated and lacks quality assurance. Rigorous safety studies on these supplements are lacking and in the United States they are not subject to monitoring by the Food and Drug Administration (FDA). A recent study of CBD products found that labelling was often inaccurate, and in many instances CBD content was over labeled and THC content was under labeled. CBD products with understated THC concentrations may produce intoxication or impairment when used in high doses (44). Despite these findings CBD products are generally safe and should not require a special license for importation. As with all medications, caution should be used when administering to children.

**4. The Medical Association of The Bahamas cannot support the use of “whole plant” Cannabis for teas, edibles or any inhalational form for medicinal purposes at this time, as there is insufficient evidence to determine appropriate dosing for symptom control, while minimizing side effects.**

Rationale: The MAB acknowledges the potential benefit of “whole plant” cannabis as a therapeutic option for selected medical illnesses. A carte blanche (unrestricted) endorsement, however, would be irresponsible without a proper regulatory framework for local cultivation and quality control. The concentration of THC in cannabis plants has been increasing over the past few decades and may range from 3% to as high as 20% (45). Eating or smoking THC rich hash oil extracted from the marijuana plant may deliver even higher amounts of THC to the user, leading to considerable side effects. Dabbing, a new trend in cannabis consumption, involves heating a small amount of cannabis extract with THC concentrations that may approach 90% and inhaling the vapors (46). Dabbing can be associated with anxiety, rapid heart rate, psychosis, memory loss and hallucinations (47).

Inhaled (smoked) cannabis in low quantities for medicinal use may not be harmful, but until further research defines accurate dosing for all methods of consumption including edibles, oils and teas, physicians should refrain from making professional recommendations except for compassionate use.

There is a growing concern of cannabis contamination due to poor growing, harvesting and storage practices. The introduction of mold, fungus, bacteria, and harmful pesticides may occur during the cultivation and processing of the cannabis plant. In 1981 an outbreak of *Salmonella enteritis* (intestinal infection) was traced back to contaminated cannabis in 4 states confirming the potential of the plant as a carrier of infection (48). This is particularly important in immunocompromised patients (HIV/AIDS, Cancer) in whom a bacterial or fungal infection could be fatal (49).

Of course, legislation that legalizes cannabis cultivation and possession for personal use would effectively eliminate the need for policies that regulate medical applications. If this occurs, the MAB would advise physicians to take a cautious approach when recommending cannabis until current pharmaceutical standards of safety and efficacy are applied.

**5. The Medical Association of the Bahamas wishes to advise the public that frequent long-term cannabis use is not harmless, particularly when associated with high concentrations of THC. Habitual use and any practice to increase THC content for consumption should therefore be discouraged.**

**Rationale:** The New England Journal of Medicine lists several acute side effects of short-term marijuana use. These include impaired short-term memory, impaired motor coordination, altered judgement, paranoia and psychosis (in high doses).

Long-term effects such as cognitive impairment, altered brain development and addiction are most impactful when onset of use is during adolescence <sup>(50)</sup>. Frequent users of inhaled cannabis should also be aware of the potential for chronic bronchitis and lower respiratory infections such as pneumonia. Co-use with tobacco has been found to increase smoking related lung disease <sup>(51)</sup>.

Habitual cannabis users may require more cannabis to produce the same effect (also known as tolerance). About 8% of people who use cannabis may develop physical dependence during their lifetime. It should be noted that this is considerably lower than with tobacco (24%), alcohol (13%), or cocaine (16%) <sup>(52)</sup>.

A cannabis withdrawal syndrome has been defined and categorized in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-V). It occurs in up to 40% of long-term cannabis smokers and is characterized by symptoms of irritability, anxiety, insomnia, restlessness and depression <sup>(53)</sup>.

There is a growing body of evidence to support the correlation of cannabis and psychosis in predisposed individuals. Cannabis Induced Psychotic Disorder (CIPD) refers to the presence of hallucinations and delusions that occur during or just after cannabis intoxication. The symptoms of CIPD may persist for days or even weeks after cannabis exposure. Clinical studies have confirmed several risk factors for psychotic disorders in cannabis users which include: high potency cannabis, increased frequency of use and younger age at onset of use <sup>(54)</sup>. A retrospective study spanning 20 years reported 41% of patients with CIPD eventually converted to schizophrenia and 47% converted to schizophrenia or bipolar disorder <sup>(55)</sup>. This conversion rate for substance induced psychosis to schizophrenia was higher in cannabis than any other drug examined including amphetamines, cocaine and hallucinogens <sup>(56)</sup>. Local statistics reported by the Public Hospitals Authority show that admissions to the Sandilands Rehabilitation Center for marijuana related illness has more than doubled between 2014 and 2018 <sup>(57)</sup>.

Physicians are advised to warn their patients about the short and long-term effects of habitual cannabis use and the potential for cannabis withdrawal syndrome. A referral for appropriate treatment is recommended when symptoms are present.

6. The Medical Association of The Bahamas supports unrestricted physician access to pharmaceutical cannabinoids that have undergone clinical trials to determine safety, efficacy, dosing and side effects, and have the ability to prescribe these medications at their discretion.

These products include (but are not limited to) the following:

Generic Name	Trade Name	Route of Administration	Active Ingredient	Indication
Nabiximols	Sativex ®	Oromucosal Spray	CBD:THC (1:1)	Multiple Sclerosis
Cannabidiol	Epidiolex	Oral liquid	CBD	LGS / DS*
Nabilone	Cesamet ®	Capsule	Synthetic THC	CINV
Dronabinol	Marinol ®	Tablet	Synthetic THC	CINV HIV wasting syndrome

7. The Medical Association of the Bahamas does not recommend additional regulation for pharmaceutical cannabinoids as the side effect profile does not appear to be any more dangerous than narcotics or other controlled drugs that are currently available.

**Rationale:** Although side effects produced by pharmaceutical cannabinoids have been reported high doses, serious adverse events are rare. Close monitoring of liver function tests is advised with some preparations, but regulation should not exceed what is currently applied to other pharmaceuticals (58,59). Physicians should be aware of the potential drug interactions, particularly in elderly patients and those with chronic diseases of the liver and kidney. THC, for example is degraded by an enzyme in the liver (CYP) that also metabolizes medications such as Coumadin (a blood thinner) and antidepressants. High levels of THC may reduce the degradation of these drugs and lead to toxic levels in the blood (60,61).

**8. The Medical Association of the Bahamas recommends that every precaution be taken to prevent cannabis exposure to children and adolescents. School-based substance abuse prevention programs should be considered. Failure to do so can lead to catastrophic mental and emotional health, and irreversible cognitive performance.**

**Rationale:** There are legitimate concerns that decriminalization of cannabis for personal use will increase accessibility to adolescents. Uruguay, the first country to legalize cannabis found that approximately 17% of adolescents had consumed marijuana in the last year, and that 53% claimed to have easy access to it. The mean age at first marijuana use was 14 years old (62,63,64). It is reasonable to expect that permissive legislation for medical cannabis may also increase unintentional marijuana exposures in pediatric patients as well (65,66).

The developing brain is particularly vulnerable to injury when exposed to psychoactive substances such as THC in the perinatal and adolescent periods. The adverse effects of cannabis can be severe in heavy early adolescent users and include educational failure, persistent mental health issues and progression to other substance use (67). Numerous studies have shown that youth exposure to cannabis negatively impacts high school completion rates and employment status (68,69). Evidence also suggests that early onset chronic cannabis use may precipitate schizophrenia and psychosis in predisposed individuals (70,71).

The government must be proactive in preventing cannabis (and alcohol) use in adolescents and teenagers. School based programs have been found to be effective and should focus particularly on at risk populations (72).

## **Considerations**

### **Cannabis and driving**

The data on cannabis and its impact on motor vehicle accidents is particularly concerning. Cannabis impairs many of the skills required for safe driving such as judgement, processing speed and cognitive function, but this impairment may be less for chronic users than for occasional users (73,74).

Despite these findings, overwhelming evidence confirms that driving under the influence of cannabis (DUIC) negatively impacts road traffic safety. A study conducted by the Insurance Institute for Highway Safety (IIHS) and Highway Loss Data Institute (HLDI) of the United States reported an increase of 6% in motor vehicle accidents in 4 states that have legalized recreational marijuana compared to 4 neighboring states that have not (75).

Additional reports from other countries (Canada, France and Australia) however, confirm an increased risk of traffic accidents when DUIC (76,77,78). The risk is even higher when cannabis is co-consumed with alcohol (79,80,81).

In the Bahamas, motor vehicle accidents (MVA) have been steadily increasing over the past three years. The Royal Bahamas Police Force reported a 28% increase between 2015 and 2017(82). The MAB cautions the government to anticipate the potential impact that DUIC alone and in combination with alcohol, may have on road safety. Any permissive legislation for cannabis possession should be accompanied by those that seek to educate, prevent and penalize users who DUIC.

## **Cannabis edibles**

Food products containing cannabis extract (edibles) have become popular in countries where recreational and medicinal cannabis is legal. While edibles are generally considered to be safe, the delayed high (30-90 minutes) associated with oral cannabis ingestion may lead the user to unintentionally ingest more THC than intended. THC content in edibles may vary substantially and produce transient, psychotic symptoms such as hallucinations, delusions and anxiety, when consumed in high doses (83). Edibles may also be packaged in forms that are appealing to children such as gummies, lollipops and cookies. Healthcare professionals should expect an increase in the number of accidental overdoses, particularly in children, and familiarize themselves with management guidelines (84).

## **Synthetic Cannabis**

Synthetic Cannabis have become a public health crisis in many areas due to its severe life-threatening side effects. Synthetic cannabis products are unregulated and marketed under names such as Spice, K2, Kush, Black Mamba and Joker and sold as natural herbal incense mixtures in smoke shops, novelty stores and on the internet. The chemical structure of these products bears little resemblance to the psychoactive THC, making it difficult to detect in blood and urine, but binds to the same CB1 receptor. Synthetic cannabis can be 2-100 times more potent than THC and can cause heart attacks, seizures, hallucinations and violent behavior. The Center for Disease Control and Prevention (CDC) reports that one state has investigated over 700 synthetic cannabis related illnesses including 11 deaths. The Medical Association of the Bahamas urges the government to have a zero tolerance approach to synthetic cannabis products given its severe toxicity and potential for abuse.

## Conclusion

The time has come for us to re-evaluate our position on cannabis given the scientific evidence which supports its medicinal value in several disease states, and shows its potential in others. We can no longer allow the history of marijuana to eclipse the benefits of cannabis in the future. The Bahamas should contribute to the body of research that will determine how cannabis is used by the medical community.

Whether support for decriminalization and legalization is fueled primarily by economic opportunity, criminal justice reform, or scientific evidence is debatable. A decision to allow cultivation of the cannabis plant for medicinal use must be preceded by a realistic regulatory framework that will demand quality-controls and ensure reproducible levels and maximum concentration limits of the main cannabinoid THC. Most important should be the protection of public health and safety. The economic potential of the cannabis industry should be a secondary consideration and should not jeopardize the physical, mental and social welfare of the country. It is important to mention that the promotion of cannabis as medicine may change the perception of some, particularly the youth, who currently see it as an illegal, addictive drug. The incorporation of cannabis into more acceptable edible forms such as brownies, gummies and hard candies, could attract new users who find smoking offensive. The looming threat of synthetic cannabis must be acknowledged and anticipated. Any subsequent increase in cannabis use by adolescents and young adults as a result of new legislation can have deleterious social effects and compound the challenges we already face in education and unemployment.

The potential threat to road traffic safety when cannabis is used alone or in combination with alcohol should also not be overlooked. The healthcare and insurance sectors are likely to feel the tangible effects of an additional hazard for motorists and pedestrians.

The regulation of cannabis is a complex issue affecting many areas of society. The Medical Association of The Bahamas urges the government to lead the Caribbean community in implementing legislation that promotes public education, health and safety above economic interests. Policies should be dynamic with the ability to respond to our environment and the scientific data as it evolves. A cautious, stepwise approach that seeks to maximize benefit while reducing harm, particularly in those that are most vulnerable, seems prudent.



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### **References**

1. Antoine RMB et al. (2018) Report of the CARICOM Regional Commission on Marijuana
2. Zuardi AW. (2006). History of cannabis as a medicine: A review. *Rev Bras Psiquiatr*; 28: 153-7
3. Aziz, Shadia & Aeron, Abhinav & Kahil, Tarek. (2016). Health Benefits and Possible Risks of Herbal Medicine. 10.1007/978-3-319-25277-3\_6.
4. O'Shaughnessy WB. (1843). On the preparations of the Indian hemp, or gunjah: Cannabis indica their effects on the animal system in health, and their utility in the treatment of tetanus and other convulsive diseases. *Prov Med J Retrospect Med Sci*. 1843 Feb 4; 5(123): 363–369.
5. Baron EP. (2015). Comprehensive Review of Medicinal Marijuana, Cannabinoids, and Therapeutic Implications in Medicine and Headache: What a Long Strange Trip It's Been. *Headache*. Jun;55(6):885-916.
6. <https://timeline.com/harry-anslinger-racist-war-on-drugs-prison-industrial-complex-fb5cbc281189>
7. Musto DF. The marijuana tax act. (1972). *Archives of General Psychiatry*, vol. 26, February pp. 101-108.
8. Bridgeman MB, Abazia DT. (2017). Medicinal Cannabis: History, Pharmacology, And Implications for the Acute Care Setting. *P T*. 2017 Mar; 42(3): 180–188.
9. Nabilone: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2006/018677s0111bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018677s0111bl.pdf)
10. <https://www.youtube.com/watch?v=lkTlzpbShbc>
11. Berdyshev EV. (2000). Cannabinoid receptors and the regulation of immune response. *Chem Phys Lipids*.108:169–190.
12. Russo E. (2011). Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br J Pharmacol*. Aug; 163(7): 1344-1364.
13. Rodríguez-García C, Sánchez-Quesada C, J Gaforio J. (2019). Dietary Flavonoids as Cancer Chemopreventive Agents: An Updated Review of Human Studies. *Antioxidants (Basel)*. May 18;8(5).
14. Dangerous Drugs Act Bahamas (2000).
15. Smith LA, Azariah F, Lavender VTC, et al. (2015). Cannabinoids for nausea and vomiting

in adults with cancer receiving chemotherapy. *Cochrane Database Syst Rev*. Nov 12;(11)

16. Aviram J, Samuelli-Liechtag G. (2017). Efficacy of cannabis-based medicines for pain management. A systematic review and meta-analysis of randomized control trials. *Pain physician*. Sep;20(6):E755-E796
17. Lynch ME, Cesar-Rittenberg P, Hohmann AG. (2014). A double-blind, placebo-controlled, crossover pilot trial with extension using an oral mucosal cannabinoid extract for treatment of chemotherapy-induced neuropathic pain. *J Pain Symptom Manage*. Jan;47(1):166-73.
18. Serpell M1, Ratcliffe S, Hovorka J, Schofield M, Taylor L, Lauder H, Ehler E. (2014). A double-blind, randomized, placebo-controlled, parallel group study of THC/CBD spray in peripheral neuropathic pain treatment. *Eur J Pain*. 2014 Aug;18(7):999-1012.
19. Johnson JR1, Burnell-Nugent M, Lossignol D, Ganae-Motan ED, Potts R, Fallon MT. (2010). Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety, and tolerability of THC:CBD extract and THC extract in patients with intractable cancer-related pain. *J Pain Symptom Manage*. Feb;39(2):167-79.
20. Allan GM, Ramji J, Lindblad AJ. (2018). Simplified guidelines for prescribing medical cannabinoids in primary care. *Can Fam Physician*. Feb;64(2):111-120
21. Häuser W, Finn DP, Kalso E, Krcovski-Skvarc N, Kress HG, Morlion B, Perrot S, Schäfer M, Wells C, Brill S. (2018). European pain federation (EFIC) position paper on appropriate use of cannabis-based medicines and medical cannabis for chronic pain management. *Eur J Pain*. Oct;22(9):1547-1564.
22. Zajicek J, et al. (2003). Cannabinoids for treatment of spasticity and other symptoms related to multiple sclerosis (CAMS study): multicenter randomized placebo-controlled trial. *Lancet*. Nov 8;362(9395):1517-26.
23. Wade DT, et al. (2004). Do cannabis-based medicinal extracts have general or specific effects on symptoms in multiple sclerosis? A double-blind, randomized, placebo-controlled study on 160 patients. *Mult Scler*. Aug;10(4):434-41.
24. Collin C, et al. (2007). Randomized controlled trial of cannabis-based medicine in spasticity caused by multiple sclerosis. *Eur J Neurol*. Mar;14(3):290-6.
25. Woolridge E, Barton S, Samuel J, Osorio J, Dougherty A, Holdcroft A. (2005). Cannabis use in HIV for pain and other medical symptoms. *J Pain Symptom Manage*. Apr;29(4):358-67.
26. Beal J, Olson R, Lefkowitz L, et al. (1997). Long-term efficacy and safety of dronabinol for acquired immunodeficiency syndrome-associated anorexia. *J Pain Symptom Manage*. 14(1):7- 14.
27. Badowski ME, Perez SE. (2016). Clinical utility of dronabinol in the treatment of weight loss associated with HIV and AIDS. *HIV AIDS (Auckl)*. Feb 10;8:37-45.
28. Abrams DI, Hilton JF, Leiser RJ et al. (2003). Short term effects of cannabinoids in patients

with HIV infection: a randomized, placebo-controlled clinical trial. *Ann Intern Med.* 139(4):258-266

29. Naftali T, Bar-Lev Schleider L, Dotan I, Lansky EP, Sklerovsky Benjaminov F, Konikoff FM. Cannabis induces a clinical response in patients with Crohn's disease: a prospective placebo-controlled study. *Clin Gastroenterol Hepatol* 2013; 11:1276–1280
30. Storr M, Devlin S, Kaplan GG, Panaccione R, Andrews CN. Cannabis use provides symptom relief in patients with inflammatory bowel disease but is associated with worse disease prognosis in patients with Crohn's disease. *Inflamm Bowel Dis* 2014; 20:472–480.
31. Klooker TK, Leliefeld KE, van Den Wijngaard RM, Boeckxstaens GE. The cannabinoid receptor agonist delta-9-tetrahydrocannabinol does not affect visceral sensitivity to rectal distension in healthy volunteers and IBS patients. *Neurogastroenterol Motil* 2011; 23:30–
32. Wong BS, Camilleri M, Busciglio I, Carlson P, Szarka LA, Burton D, et al. Pharmacogenetic trial of a cannabinoid agonist shows reduced fasting colonic motility in patients with nonconstipated irritable bowel syndrome. *Gastroenterology* 2011; 141:1638.
33. Sorensen CJ1, DeSanto K2, Borgelt L3, Phillips KT4, Monte AA. Cannabinoid Hyperemesis Syndrome: Diagnosis, pathophysiology and treatment-A systematic review. *J Med Toxicol.* 2017 Mar;13(1):71-87.
34. Hézode C, Zafrani ES, Roudot-Thoraval F, Costentin C, Hessami A, Bouvier-Alias M, et al. Daily cannabis use: a novel risk factor of steatosis severity in patients with chronic hepatitis C. *Gastroenterology* 2008; 134:432–439.
35. Ishida JH, Peters MG, Jin C, Louie K, Tan V, Bacchetti P, et al. Influence of cannabis use on severity of hepatitis C disease. *Clin Gastroenterol Hepatol* 2008; 6:69–75.
36. Barkin JA1, Nemeth Z, Saluja AK, Barkin JS. Cannabis induced acute pancreatitis: A systematic review. *Pancreas.* 2017 Sep;46(8):1035-1038.
37. Singer E., Judkins J., Salomonis N., Matlaf L., Soteropoulos P., Mcallister S., Soroceanu L. Reactive oxygen species-mediated therapeutic response and resistance in glioblastoma. *Cell Death Dis.* 2015;6:e1601–e1611.
38. Honarmand M., Namazi F., Mohammadi A., Nazifi S. Can cannabidiol inhibit angiogenesis in colon cancer? *Comp. Clin. Path.* 2019;28:165–172.
39. Kenyon J., Liu W.A.I., Dalgleiersh A. Report of Objective Clinical Responses of Cancer Patients to Pharmaceutical-grade Synthetic Cannabidiol. *Anticancer Res.* 2018;38:5831–5835.
40. Dall'Stella P.B., Docema M.F.L., Maldaun M.V.C., Feher O., Lancellotti C.L.P., Ware M. Case Report: Clinical Outcome and Image Response of Two Patients With Secondary High-Grade Glioma Treated With Chemoradiation, PCV, and Cannabidiol. *Front. Oncol.* 2019;8:1–7
41. Sun X, Xu CS, Chadha N, Chen A, Liu J. Marijuana for glaucoma: A recipe for disaster.

Yale J Biol Med. 2015 Sep 3;88(3):265-9.

42. Flach AJ. Delta-9-tetrahydrocannabinol (THC) in the treatment of end-stage open angle glaucoma. *Trans Am Ophthalmol Soc.* 2002;100:215-22.
43. VanDolah HJ, Bauer BA, Mauck KF. (2019). Clinicians guide to cannabidiol and hemp oils. *Mayo Clin Proc.* 94(9);1840-1851
44. Devinsky O, Marsh E, Friedman D, Thiele E, Laux L, Sullivan J, Miller I, Flamini R, Wilfong A, Filloux F, Wong M, Tilton N, Bruno P, Bluvstein J, Hedlund J, Kamens R, Maclean J, Nangia S, Singhal NS, Wilson CA, Patel A, Cilio MR. (2016). Cannabidiol in patients with treatment-resistant epilepsy: an open-label intervention trial. *Lancet Neurol.* Mar;15(3):270-8.
45. Bonn-Miller MO, Loflin MJ, Thomas BF, Marcu JP, Hyke T, Vandrey R. (2017). Labeling accuracy of cannabidiol extracts sold online. *JAMA.* Nov 7;318(17) 1708-1709
46. Chandra S, Radwan MM, Majumdar CG, Church JC, Freeman TP, ElSohly MA. (2019). New trends in cannabis potency in USA and Europe during the last decade (2008-2017). *Eur Arch Psychiatry Clin Neurosci.* Feb;269(1):5-15.
47. Al-Zouabi I, Stogner JM, Miller BL, Lane ES. (2018). Butane hash oil and dabbing: insights into use, amateur production techniques, and potential harm mitigation. *Subst Abuse Rehabil.* Nov 2;9:91-101
48. Alzghari SK, Fung V, Rickner SS, Chacko L, Fleming SW. (2017). To dab or not to dab: rising concerns regarding toxicity of cannabis concentrates. *Cureus.* Sep 11;9(9):1676.
49. Taylor DN, Wachsmuth IK, Shangkuan YH, Schmidt EV, Barrett TJ, Schrader JS, Scherach CS, McGee HB, Feldman RA, Brenner DJ. (1982). Salmonellosis associated with marijuana: a multistate outbreak traced by plasmid fingerprinting. *N Engl J Med.* May 27;306(21):1249- 53
50. Dryburgh LM, Bolan NS, Grof CP, Galettis P, Schneider J, Lucas CJ, Martin JH. (2018). Cannabis contaminants: sources, distribution, human toxicity and pharmacological effects. *Br J Clin Pharmacol.* Nov;84(11):2468-2476.
51. Volkow ND, Baler RD, Compton WM, Weiss SRB. (2014). Adverse health effects of marijuana use. *NEJM.* June 5; 370(23) 2219-2227.
52. Joshi M, Joshi A, Bartter T. (2014). Marijuana and lung diseases. *Curr Opin Pulm Med.* Mar;20(2):173-9.
53. Moore T. (2018). Just how dangerous is marijuana? A health risk comparison of alcohol, tobacco and marijuana. Reason Foundation
54. Gorelick DA, Levin KH, Copersino ML, Heishman SJ, Liu F, Boggs DL, Kelly DL. Diagnostic criteria for cannabis withdrawal syndrome. *Drug Alcohol Depend* (2012). 1:141- 147.
55. MacCalluma CA, Russob EB. (2018). Practical considerations in medical cannabis

administration and dosing. *European Journal of Internal Medicine*. 49:12-19

56. Ewing LE, Skinner CM, Quick CM, Kennon-McGill S, McGill MR, Walker LA, ElSohly MA, Gurley BJ, Koturbash I. (2019). Hepatotoxicity of a cannabidiol-rich cannabis extract in the mouse model. *Molecules*. Apr 30;24(9).
57. Alsherbiny MA, Li CG. (2019). Medical cannabis: potential drug interactions. *Medicines (Basel)*. Mar;6(1):3
58. Damkier P, Lassen D, Christensen MMH, Madsen KG, Hellfritsch M, Pottegård A. (2019). Interaction between warfarin and cannabis. *Basic Clin Pharmacol Toxicol*. Jan;124(1):28-31
59. Ley 19.172–Uruguay Poder Legislativo.(2013). [www.parlamento.gub.uy/leyes/ley19172.htm](http://www.parlamento.gub.uy/leyes/ley19172.htm)
60. Junta Nacional de Drogas Presidencia de la Republica Uruguay. Sexta Encuesta Nacional de Hogares sobre consumo de drogas. El consumo de marihuana.2016. [https://medios.presidencia.gub.uy/tav\\_portal/2015/.../NO.../encuesta.pdf](https://medios.presidencia.gub.uy/tav_portal/2015/.../NO.../encuesta.pdf)
61. Villatoro-Velázquez JA, Medina-Mora ME, Fleiz-Bautista C, et al. Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz; Instituto Nacional de Salud Pública; Secretaría de Salud. Encuesta Nacional de Adicciones 2011: Reporte de Drogas. México D.F. INPRFM; 2012.
62. Wang GS, Roosevelt G, Le Lait MC, et al. (2014). Association of unintentional pediatric exposures with decriminalization of marijuana in the United States. *Ann Emerg Med*. 63: 684–689.
63. Wang GS, Roosevelt G, Heard K. (2013). Pediatric marijuana exposures in a medical marijuana state. *JAMA Pediatr*.167(7):630–633.
64. Coffey C, Patton GC. (2016). A review of findings from the Victorian Adolescent Health Cohort Study. *Can J Psychiatry*. Jun; 61(6): 318–327.
65. Lee JY, Brook JS, Finch SJ, Brook DW. (2015). Trajectories of marijuana use from adolescence to adulthood predicting unemployment in the mid 30s. *Am J Addict*. Aug;24(5): 452-9.
66. Beverly HK, Castro Y, Opara J. (2019). Age of First Marijuana Use and Its Impact on Education Attainment and Employment Status. *J Drug Issues*. Apr; 49(2): 228–237.
67. Zammit S, Allebeck P, Andreason S, Lundberg I, Lewis G. (2002). Self-reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. *BMJ*. Nov 23; 325(7374): 1199.
68. Stefanis NC, Delespaul P, Henquet C, Bakoula C, Stefanis CN, Van Os J. (2004). Early adolescent cannabis exposure and positive and negative dimensions of psychosis. *Addiction*. 99:1333–1341
69. Porath-Waller AJ, Beasley E, Beirness DJ. (2010). A meta-analytic review of school-based prevention for cannabis use. *Health Educ Behav*. Oct; 37(5):709-23.

70. Ramaekers JG<sup>1</sup>, Kauert G, Theunissen EL, Toennes SW, Moeller MR. (2009). Neurocognitive performance during acute THC intoxication in heavy and occasional cannabis users. *J Psychopharmacol.* May;23(3):266-77.
71. Ramaekers JG<sup>1</sup>, Theunissen EL, de Brouwer M, Toennes SW, Moeller MR, Kauert G. (2011). Tolerance and cross-tolerance to neurocognitive effects of THC and alcohol in heavy cannabis users. *Psychopharmacology (Berl).* Mar;214(2):391-401.
72. [www.iihs.org](http://www.iihs.org)
73. Laumon B, Gadegbeku B, Martin JL, Biecheler MB. (2005). Cannabis intoxication and fatal road crashes in France: population-based case-control study. *BMJ.* Dec 10;331(7529):1371.
74. Bédard M, Dubois S, Weaver B. (2007). The impact of cannabis on driving. *Can J Public Health.* Jan-Feb;98(1):6-11.
75. Drummer OH, Gerostamoulos J, Batziris H, Chu M, Caplehorn JR, Robertson MD, Swann P. (2003). The incidence of drugs in drivers killed in Australian road traffic crashes. *Forensic Sci Int.* Jul 8;134(2-3):154-62.
76. Ramaekers JG, Robbe HW, O'Hanlon JF. (2000). Marijuana, alcohol and actual driving performance. *Hum Psychopharmacol.* Oct;15(7):551-558.
77. Ramaekers JG, Berghaus G, van Laar M, Drummer OH. (2004). Dose related risk of motor vehicle crashes after cannabis use. *Drug Alcohol Depend.* Feb 7;73(2):109-19.
78. Sewell RA, Poling J, Sofuoglu M. (2009). The effect of cannabis compared with alcohol on driving. *Am J Addict.* May-Jun;18(3):185-93.
79. RBP Statistics (2018). *The Tribune Newspaper*; Jan 18.
80. Wilkinson ST, Radhakrishnan R, D'Souza DC. (2014). Impact of cannabis use on the development of psychotic disorders. *Curr Addict Rep.* Jun 1;1(2):115-128.
81. Wang GS, Roosevelt G, Le Lait MC, Martinez EM, Bucher-Bartelson B, Bronstein AC, Heard K. (2014). Association of unintentional pediatric exposures with decriminalization of marijuana in the United States. 2014. *Ann Emerg Med.* Jun;63(6):684-9.
82. Starzer M.S.K., Nordentoft M., Hjorthøj C. Rates and predictors of conversion to schizophrenia or bipolar disorder following substance-induced psychosis. *Am. J. Psychiatry.* 2017;175:343–350.
83. van Winkel R., Kuepper R. Epidemiological, neurobiological, and genetic clues to the mechanisms linking cannabis use to risk for nonaffective psychosis. *Annu. Rev. Clin. Psychol.* 2014;10:767–791.
84. PHA Statistics Unit 2019