

# Preventing Oversight on Medical Cannabis Legislation in Malaysia: Analysis of Risks, Benefits and Regulation Requirements

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## Abstract

The United Nations Office on Drug and Crime (UNODC) ranked cannabis as the most widely used substance worldwide in 2021. It has been predicted that the use will dramatically increase in the next five years due to an increasing number of countries starting to legalise it for medical purposes. In 1983, Malaysia declared the substance use problem as a national emergency. Since then, the government has taken many steps to establish a 'country without illicit drugs'. To analyse risks, benefits and regulations of medical cannabis, a narrative review synthesising the findings of literature retrieved from computerised database search was conducted. Increasing evidence shows that legalising cannabis leads to an increased number of people starting to abuse this substance and become dependent on it, including the country that became the first to legalise cannabis. Although there are claims and studies reported that medical cannabis is needed to treat certain diseases, the decision to legalise cannabis in Malaysia needs to carefully weigh the risks and benefits.

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After all, there are other FDA-approved medicines clinically proven to be safe and effective alternatives that are currently available to treat such diseases. The control of cannabis licensing and selling needs to be taken into serious consideration before deciding on the regulatory status of cannabis. Therefore, the best way to prevent the spike of cannabis abuse in Malaysia is by prohibiting possession, planting, harvesting and processing cannabis, even for personal use. The lack of high-quality clinical trials regarding the benefits and harms of cannabis for medical purposes should also be a major consideration before the decision to legalise cannabis is made.

**Keywords:** Benefits, Legislation, Medical Cannabis, Regulations, Risks

## Introduction

Medical cannabis has been controversially coined since day one of its introduction. Many countries have legislatively amended cannabis from controlled to lesser regulated or unregulated substance groups. This is reflected in the United Nations Office on Drug and Crime (UNODC) report 2021, when cannabis was ranked as the most widely used substance worldwide. The prominent urge for the legalisation in several countries is mainly due to industrial and economic pressure and, to a certain extent, for medical reasons. In Malaysia, there is an overwhelming demand for the legalisation of medical cannabis specifically from the medical cannabis advocacy groups. Diverse stakeholders such as researchers, economists and politicians have also been lobbying the government with their expert opinions, market value projections and even political power. The advantages, especially from this country's medical and economic perspectives, are plausibly underscored. Numerous talks and seminars were conducted to invite interests from industrial players and grassroots community. They will, in due course, be the end-users of the developed substance. When tossing the information directly to the civil society, the incongruent basic understanding, such as the plant origin, cultivation control, compound involved for medical purposes, clinical use and related legislative issues, is far more worrying. Although a few Asian countries have followed suit with the decriminalisation and legalisation move, the Malaysian government is still maintaining its status quo to allow a more comprehensive evaluation of the implication of risks and benefits for the community of interest.

A narrative review was performed involving the literature retrieved from computerised database search on cannabis plant species, varieties

and relevant compounds, its recreational effects especially in the long run, evidence and recommendations on its medical use, the legalisation requirements as well as the implication of risks and benefits on the population. The search was conducted via PubMed, Cochrane Library, Google Scholar, official reports and websites from the United Nations Office, World Health Organisation, National Institute of Drug Abuse, Ministry of Health Malaysia and the National Anti-drug Agency with keywords 'Cannabis', 'Medical Cannabis', 'Marijuana', 'Medical Marijuana', 'Benefits', 'Risk', 'Legalisation' and 'Regulation'. Summary of evidence retrieved in English language was synthesised and reviewed by five experts from the Substance Use Disorder Research Group (SUDRG), Kulliyah of Pharmacy, International Islamic University Malaysia (IIUM).

## Understanding the Cannabis sp. Plant and Its Effects

Cannabis is a herbaceous plant consisting of at least three main species, namely *Cannabis sativa* L., *Cannabis indica* and *Cannabis ruderalis*. *Cannabis sativa* is the most widely found and grown species worldwide. This plant contains at least 540 types of alkaloids and >100 phytocannabinoids with the main ones being delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).<sup>1</sup> THC is the main alkaloid of cannabis that exerts the psychoactive effects or affecting the mind of its users.<sup>2</sup> CBD, on the other hand, is a non-psychotomimetic compound with some evidence on its medical and health benefits.<sup>3</sup> CBD constitutes 40% of the plant's active substances.<sup>4</sup> The active constituent of cannabis resides in dried leaves, resin, seeds, stems, flowers and oil of the plant, and these make the whole plant usable and consumable.<sup>5</sup> The oil, originated from the dry exudates of the leaves, is better known as hashish.<sup>6</sup> The term cannabis or

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- 1 M.R. Amin and D.W. Ali, 'Pharmacology of Medical Cannabis' (2019) *Adv Exp Med Biol* 1162, 151-165.
  - 2 F. Zulfiqar and others, 'Cannabisol, a novel D9-THC dimer possessing a unique methylene bridge, isolated from *Cannabis sativa*' (2012) 53 *Tetrahedron Letters* 3560-3562.
  - 3 D.L. Boggs and others, 'Clinical and Preclinical Evidence for Functional Interactions of Cannabidiol and  $\Delta^9$ -Tetrahydrocannabinol' (2018) 43(1) *Neuropsychopharmacology* 142-154.
  - 4 A.R.M. Scheir and others, 'Cannabidiol: a *Cannabis sativa* constituent, as an anxiolytic drug' (2012) 34(1) *Official Journal of the Brazilian Psychiatric Association* S104-S117.
  - 5 W. Hall and L. Degenhardt, 'Medical marijuana initiatives: are they justified? How successful are they likely be?' (2003) 17(10) *CNS Drugs* 689-697.
  - 6 D.E. Greydanus and others, 'Marijuana: current concept' (2013) (42) *Frontiers in Public Health* 1, 1-17.

marijuana refers to cannabis plants with high THC content while hemp refers to cannabis plants with low THC content (<0.3%) and high CBD content that has low risk of abuse.<sup>7</sup>

The primary effects of THC from cannabis are mediated through partial agonism of central and peripheral cannabinoid receptors of the endogenous cannabinoid system; cannabinoid 1 receptor (CB<sub>1</sub>R) and cannabinoid 2 receptor (CB<sub>2</sub>R).<sup>8</sup> Its predominant action at the CB<sub>1</sub>R receptor is believed to produce its psychoactive effects such as euphoria (high), anxiety, paranoia, perceptual alteration and cognitive deficits; whereas its action at the CB<sub>2</sub>R is primarily responsible for some immunological and anti-inflammatory cascades.<sup>9</sup> Since THC is excreted via hepatic and renal mechanisms, a more exaggerated and prolonged side effects are expected in individuals with hepatic or renal impairment.<sup>10</sup>

In contrast to THC, evidence showed that CBD exerts its pharmacological effects in vivo through facilitatory interaction with serotonin 1A (5-HT<sub>1A</sub>).<sup>11</sup> It was also found to have some activities at delta and  $\mu$  opioid receptors.<sup>12</sup> Hence, many pre-clinical and clinical studies conducted to evaluate its potential on health and medical benefits.

Globally, cannabis is among the psychoactive substances with high consumption after tobacco and alcohol. In 2019, about 200.4 million or around 4% of the world's population aged 15-64 years were cannabis

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- 7 R.E. Aluko, 'Hemp seed (*Cannabis sativa* L.) proteins: composition, structure, enzymatic modification, and functional or bioactive properties' in S. Nadathur, J.P.D. Wanasundra and L. Scanlin (eds), *Sustainable protein sources* (Academic Press, 2017).
  - 8 G.A. Cabral and others, 'CB2 receptors in the brain: role in central immune function' (2008) 153(2) *British Journal of Pharmacology* 240–251.
  - 9 R.G. Pertwee, 'The diverse CB1 and CB2 receptor pharmacology of three plant cannabinoids: delta9-tetrahydrocannabinol, cannabidiol and delta9-tetrahydrocannabivarin' (2008) 153(2) *British Journal of Pharmacology* 199–215.
  - 10 S. Medina and M. Khawand-Azoulai, 'Palliative Care and Symptom Management in Breast and Gynecological Cancers in Adrian Cristian (ed), *Breast Cancer and Gynecologic Cancer Rehabilitation* (Elsevier, 2021).
  - 11 F.V. Gomes and others, 'Cannabidiol injected into the bed nucleus of the stria terminalis reduces the expression of contextual fear conditioning via 5-HT1A receptors' (2012) 26(1) *Journal of Psychopharmacology* 104–113; I.E.M. Magen and others, 'Cannabidiol ameliorates cognitive and motor impairments in bile-duct ligated mice via 5-HT1A receptor activation' (2010) 159(4) *British Journal of Pharmacology* 950–957; C.A. Stern and others, 'On disruption of fear memory by reconsolidation blockade: evidence from cannabidiol treatment' (2012) 37(9) *Neuropsychopharmacology* 2132–2142.
  - 12 Pertwee (n 9).

users.<sup>13</sup> In Malaysia, statistics on drug use from 2018 to 2020 showed that cannabis use was only recorded between 3% to 5%. However, tobacco and cannabis are believed to be the starting substances of a person's involvement with other illicit drugs.<sup>14</sup>

### **Recreational Cannabis**

The use of cannabis with tobacco or nicotine is a very common case.<sup>15</sup> Cannabis is mixed with tobacco when smoking due to the perfect complement by targeting the similar neuronal receptor system in the brain that leads to intense 'high' state<sup>16</sup> as these two substances can be consumed through the same route. Initially, the combination of these substances is used to assist in burning or to titrate the effect of cannabis. Eventually, this led the cannabis users to nicotine exposure and dependence.<sup>17</sup> The THC constituent in cannabis eases the anxiety-generating properties of nicotine.<sup>18</sup> Moreover, smoking tobacco cancels out the sedative effects of cannabis.

Addiction and dependence on cannabis can occur even if some claim that cannabis does not cause addiction. In the United States of America (US) for example, addiction and dependence on marijuana increased from 30.2% in 1992 to 35.6% in 2002. Addiction and dependence on cannabis can occur within a year in users who start smoking marijuana. Being the leading substance used by the population worldwide, cannabis use and abuse are predicted to increase even more in five years.<sup>19</sup> Cannabis

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13 United Nations Office on Drugs and Crime, *World Drug Report 2021* (United Nations publication, Sales No. E.21.XI.8).

14 Agensi Antidadah Kebangsaan, Kementerian Dalam Negeri, *Buku Maklumat Dadah* (Putrajaya, 2020).

15 K.W. Clements and others, 'The demand for marijuana, tobacco and alcohol: inter-commodity interactions with uncertainty' (2009) 39(1) *Empirical Economics* 203-239; D.E. Ramo and J.J. Prochaska, 'Prevalence and co-use of marijuana among youth adult cigarette smokers: an anonymous online national survey' (2012) 7(5) *Addiction Science & Clinical Practice*.

16 M.L. Rubinstein and others 'Frequent marijuana use is associated with greater nicotine addiction in adolescent smokers' (2014) 141 *Drug and Alcohol Dependence* 159-162; J.S. Zeiger and others, 'Subjective effects for alcohol, tobacco, and marijuana association with cross-drug outcomes' (2012) 123 *Drug and Alcohol Dependence* S53-S58.

17 Rubinstein and others (n 16).

18 G.L. Ream and others, 'Smoking tobacco along with marijuana increases symptoms of cannabis dependence' (2008) 95(3) *Drug and Alcohol Dependence* 199-208.

19 World Drug Report, *Booklet 2: Global overview of drug demand and drug supply* (Vienna, Austria, UNODC Research, 2021).

is strongly believed to serve as gateway to other 'harder' substances such as amphetamines, cocaine and heroin. The percentage of cannabis harm rate is 20% compared to 23% for amphetamines. The harmful effects on other people are higher than that on users of both cannabis and amphetamines.<sup>20</sup> Cannabis consumption can increase the risk of road accidents due to movement control disorders, cause psychological disorders and increase the risk of developing psychosis and depression. Because cannabis can also interfere with brain function associated with learning and memory processes, taking cannabis can lead to the risk of job loss and dropouts in learning, especially for adolescents.<sup>21</sup>

Various studies were conducted to assess the long-term effects of cannabis use on health. Respiratory system problems such as chronic cough, increased production of phlegm, pneumonia, chest pain, decreased lung function and lung infections were reported among cannabis users. In addition, the use of high amounts of cannabis and smoke resulting from the habit of smoking cannabis could be the cause of cancer.<sup>22</sup> Although some studies claimed that THC and CBD might lower the risk of cancer, their evidence was still relatively weak.<sup>23</sup>

According to the National Institute of Drug Abuse (NIDA) report, smoking cannabis is more dangerous than smoking cigarettes because the inhaled tar remains in the lungs in higher quantities.<sup>24</sup> This is closely related to the methods and tools used to smoke the cannabis. The consumption of one cannabis pipe is equivalent to the consumption of 2.5 to 5 cigarettes for high amount of cannabis use.<sup>25</sup> About 50% of the THC in a joint (rolled cannabis for smoking) enters the brain within minutes.<sup>26</sup>

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20 D.J. Nutt and others, 'Drug harms in the UK: a multicriteria decision analysis' (2010) 376(9752) *Lancet* 1558-1565.

21 V. Antičević and others, 'The personality traits and social characteristics of Croatian heroin addicts and cannabis users' (2011) 35(3) *Collegium antropologicum* 701-707; J.L. Bottorf and others, 'Relief-oriented use of marijuana by teens' (2009) 4(1) *Substances Abuse Treatment, Prevention, and Policy*; J. McLaren and R. Mattick 'Towards a national cannabis strategy' (2003) 6(1) *Of Substance: The National Magazine on Alcohol, Tobacco, and Other Drugs* 15; J. Pereira and T. Wiegand, 'Marijuana' (2014) 3 *Encyclopedia of Toxicology* 157-159. Elsevier Inc.

22 J. McLaren and R. Mattick, 'Towards a national cannabis strategy' (2013) 4(1) *Of Substance: The National Magazine on Alcohol, Tobacco and Other Drugs* 15.

23 Greydanus and others (n 6).

24 McLaren and Mattick (n 22); M.L. Howden and M.T. Naughton, 'Pulmonary effects of marijuana inhalation' (2011) 5(1) *Expert Review of Respiratory Medicine* 87-92.

25 Greydanus and others (n 6).

26 J. Pereira and T. Weigand, 'Marijuana' (2014) *Encyclopedia of Toxicology*, 2nd Ed. Elsevier Inc.

Cannabis consumption can also cause harmful effects to the heart, especially for the elderly and those with a history of heart disease.<sup>27</sup> Such harmful effects include heart attack, stroke, rapid heartbeat and heart failure.<sup>28</sup> Heart rate was found to increase within two minutes after smoking cannabis even at low concentrations.<sup>29</sup> This is also supported by other studies that found smoking cannabis could instantly increase heart rate by 20% to 100% and this effect lasted for three hours.<sup>30</sup> Users also experienced a 4.8% increased risk of having a heart attack within the first hour of smoking cannabis. The abnormality to the heart was almost identical to that observed in cocaine users.<sup>31</sup>

### **Medical Cannabis**

History shows that cannabis has been used for millennia to reduce pain and other somatic and psychological symptoms. Cannabis-based products for medical use contain cannabinoids derived from the cannabis plant, including THC, CBD, or a combination of THC and CBD. Synthetic cannabinoids for medical use typically mimic the effects of specific cannabinoids such as THC.<sup>32</sup> Cannabis in its natural form or pharmaceutically produced drugs (e.g., dronabinol) have been studied over the recent years and reported to have potential efficacy in reducing pain, muscle spasticity, fibromyalgia, chemotherapy-induced nausea and vomiting, intractable childhood epilepsy (e.g., Lennox-Gastaut syndrome), Chron's disease, ulcerative colitis, dementia, Alzheimer's, anxiety, post-traumatic stress disorder (PTSD), multiple sclerosis (MS), glaucoma, as well as to help improve the appetite of patients with acquired immunodeficiency syndrome (AIDS).

A THC/CBD combination product (e.g., nabiximols or Sativex®), is a prescription-based botanical drug developed from a 1:1 combination of

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27 McLaren and Mattick (n 22).

28 Greydanus and others (n 6).

29 A. Liguori and others, 'Separate and combined side effects of marijuana and alcohol on mood, equilibrium and simulated driving' (2002) 163(3) *Psychopharmacology* 399-405.

30 Z. Latif and N. Garg, 'The impact of marijuana on the cardiovascular system: a review of the most common cardiovascular events associated with the marijuana use' (2020) 9(6) *Journal of Clinical Medicine* 1925.

31 Greydanus and others (n 6).

32 T.P. Freeman and others, 'Changes in delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) concentrations in cannabis over time: systematic review and meta-analysis' (2021) 116(5) *Addiction* 1000.

two selected cannabis strains. One strain, tetranabinex yields a high THC content and the other, nabidiolex yields a high CBD content. The flowers are dried, extracted and utilised to formulate nabiximols. Nabiximols mainly consists of THC and CBD (70%w/w) and other phytocannabinoids derived from the plant material.<sup>33</sup> The 1:1 combination of THC:CBD appears to allow for higher doses of THC without increasing the risk of adverse effects as CBD acts to antagonise some of the psychoactive and sedative effects of THC without interfering with intended THC effects such as muscle relaxation and reduction of spasticity.<sup>34</sup>

Recently, many Malaysians were shocked by the news involving a local singer-composer who allegedly grew marijuana for the treatment of his mental disorder.<sup>35</sup> However, the use of cannabis or its psychoactive substance as a drug has been questioned in terms of its effectiveness and safety for such purposes. On the other hand, epidemiological study evidence confirms that marijuana use may increase the risk of psychotic disorders or psychosis.<sup>36</sup> In fact, the psychotropic effects of THC resemble the symptoms of psychotic disorders, including paranoia, sensory changes, euphoria and hallucinations.<sup>37</sup>

Psychosis is a mental disorder that impairs the ability to distinguish reality from fiction. This includes delusions, hallucinations and disorganised speech and behaviour.<sup>38</sup> High dose of cannabis can lead to hallucination manifested as sensing things that are not actually present.<sup>39</sup> There is also risk of developing schizophrenia in heavy cannabis users. In addition, for those who already suffer from this illness, the disease will worsen. It is proven that the rate of hospitalisation is increased

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33 E. Russo and G.W. Guy, 'A tale of two cannabinoids: the therapeutic rationale for combining tetrahydrocannabinol and cannabidiol' (2006) 66(2) *Medical Hypotheses* 234–246.

34 D.L. Boggs and others, 'Clinical and Preclinical Evidence for Functional Interactions of Cannabidiol and  $\Delta^9$ -Tetrahydrocannabinol' (2018) 43(1) *Neuropsychopharmacology* 142–154.

35 See <<https://www.nst.com.my/news/crime-courts/2022/03/783271/singer-composer-suspected-cultivating-ganja-plants-remanded-seven>> accessed 12 April 2022.

36 S. H. Gage and others, 'Association between cannabis and psychosis: epidemiologic evidence' (2016) 79(7) *Biological psychiatry* 549–556.

37 D.C. D'Souza and others, 'The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: implications for psychosis' (2004) 29(8) *Neuropsychopharmacology* 1558–1572 <doi: 10.1038/sj.npp.1300496>.

38 McLaren and Mattick (n 22).

39 Greydanus and others (n 6); Barrett and others, 'Hallucinations following acute cannabis dosing; a case report and comparison to other hallucinogenic drugs' (2018) 3(1) *Cannabis and Cannabinoid Research* 85–93.



in schizophrenic patients who took cannabis.<sup>40</sup> Repeated exposure to cannabis sensitised the mesolimbic pathway in the brain, which makes it vulnerable to people with underlying psychosis.<sup>41</sup> Cannabis will damage the endocannabinoid system due to the disturbance that it may cause. The risk of getting schizophrenia is raised by two times due to cannabis interference with the endocannabinoid system.<sup>42</sup> Psychosis effects are far stronger to those who took cannabis at the early stage (before 16 years old) because the brain is still developing and will be more exposed to alterations caused by cannabis and its constituents. Increased risk of depression, anxiety and paranoia has been observed in cannabis users at this age.<sup>43</sup>

Some studies suggested that CBD might attenuate the schizophrenia-like symptoms in people who use cannabis.<sup>44</sup> However, research does not support recommending medical cannabis (THC or CBD) to treat patients with schizophrenia. Further research should examine THC and CBD in schizophrenia with and without comorbid cannabis use disorder (CUD) and may consider the role of CBD in mitigating symptom exacerbation from THC.<sup>45</sup>

The current body of evidence regarding cannabinoid therapeutics in psychiatry is still scant and it is considered premature to recommend cannabinoid-based interventions. Indeed, few studies revealed tentative support for CBD for reducing social anxiety and mixed evidence for adjunctive use in schizophrenia. Weak evidence from case studies suggested that medical cannabis might be useful to improve sleep and PTSD. The results from preliminary research involving THC showed that there was no benefit for depression or for CBD in mania. Only one study suggested some potential benefits for an oral cannabinoid/terpene combination for attention deficit hyperactivity disorder (ADHD).<sup>46</sup>

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40 Greydanus and others (n 6).

41 A.J. Porath-Waller and others, 'A meta-analytic review of school based prevention for cannabis use' (2010) 37(5) *Health Education & Behavior* 709-723.

42 Greydanus and others (n 6).

43 A.J. Porath-Waller and others (n 41); Liguori and others (n 29); W. Hall and Degenhardt, 'Cannabis use and the risk of developing psychotic disorder' (2008) 7(2) *World Psychiatry* 68-71.

44 C. Morgan and H. Curran, 'Effects of cannabidiol on schizophrenia-like symptoms in people who use cannabis' (2008) 192(4) *British Journal of Psychiatry* 306-307.

45 S. Ahmed and others, 'The Impact of THC and CBD in Schizophrenia: A Systematic Review' (2021) 23(12) *Front Psychiatry* 1225.

46 J. Sarris and others, 'Medicinal cannabis for psychiatric disorders: a clinically-focused systematic review' (2020) 20(1) *BMC Psychiatry* 24 <doi: 10.1186/s12888-019-2409-8>.

In the case of dementia, there is no evidence that cannabinoids are effective in the treatment of behavioural disorders or other symptoms of dementia<sup>47</sup> and there is no relevant evidence-based clinical guidelines regarding the use of medical cannabis for treating dementia.<sup>48</sup> Whereas for multiple sclerosis (MS) patients, nabiximols was reported as safe and effective for patients with MS whose spasticity could not be treated with the first-line oral drugs. However, there is no scientific evidence that smoking marijuana can be beneficial to patients with MS.<sup>49</sup>

Cannabis-based drugs have been found to be useful for treating refractory chemotherapy-induced nausea and vomiting. However, current study methods and chemotherapy regimens as well as newer anti-emetic drugs may change this conclusion.<sup>50</sup>

The same goes for studies that investigate the effectiveness of cannabis to reduce pain associated with cancer. A systematic review included five studies which showed pain reduction, two showed no change while six could not provide certainty. Authors concluded that the potential benefits of treating chronic neuropathic pain with cannabis-based medicines (herbal cannabis, plant-derived or synthetic THC, THC/CBD oromucosal spray) may be outweighed by their potential harmful effects.<sup>51</sup>

Cannabis has also been used for fibromyalgia, a clinically well-defined chronic condition of unknown aetiology characterised by chronic widespread pain that often co-exists with sleep problems and fatigue. Treatment focuses on reducing the main symptoms and disabilities, as well as improving quality of life. However, there are no convincing and high-quality studies that nabilone, a synthetic drug derived from

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47 S. Krishnan and others, 'Cannabinoids for the treatment of dementia' (2009) 2 *Cochrane Database of Systematic Reviews* Art. No.: CD007204. <DOI: 10.1002/14651858.CD007204.pub2>.

48 K. Pephrah and S. McCormack, *Medical Cannabis for the Treatment of Dementia: A Review of Clinical Effectiveness and Guidelines* (Ottawa, Canadian Agency for Drugs and Technologies in Health, 2019).

49 Y.D. Fragoso and others, 'Cannabis and multiple sclerosis' (2020) 20(8) *Expert Review of Neurotherapeutics* 849-854 <doi: 10.1080/14737175.2020.1776610>.

50 L.A. Smith and others, 'Cannabinoids for nausea and vomiting in adults with cancer receiving chemotherapy' (2015) 11 *Cochrane Database of Systematic Reviews* <DOI: 10.1002/14651858.CD009464.pub2> .

51 M. Mücke and others, 'Cannabis-based medicines for chronic neuropathic pain in adults' (2018) 3 *Cochrane database of systematic reviews* <DOI: 10.1002/14651858.CD012182.pub2>.

cannabis, plays a role in treating people with fibromyalgia. Furthermore, tolerability to nabilone was found to be low in these patients.<sup>52</sup>

As for the treatment of rheumatoid arthritis-related pain, one small, low-quality study assessing oromucosal cannabis versus placebo found a small difference in favour of cannabis in the oral rating score of 'pain at the moment' after a five-week period of treatment. However, patients who received cannabis were more likely to experience the incidence of side effects, such as dizziness (26%), dry mouth (13%) and light headedness (10%). In conclusion, cannabis has more pronounced side effects and its potential harms outweigh any benefits that patients get.<sup>53</sup>

Cannabis has also been studied for Lennox-Gastaut syndrome (LGS), an age-specific epilepsy syndrome characterised by multiple seizure types, including drop seizures. LGS has a characteristic electroencephalogram, an onset before age 8 years old and an association with drug resistance. A recent systematic review included two studies involving CBD in children and adolescents which did not show overall cessation or reduction of seizures. On the other hand, 72 more people per 1000 experienced adverse effects with add-on cannabidiol that led to their discontinuation from the study.<sup>54</sup>

There are still no clear results of studies on the effectiveness and safety of cannabis and cannabis oil in adults with active Crohn's disease or ulcerative colitis (UC). Also, there is no evidence for the use of cannabis or CBD to maintain UC in remission.<sup>55</sup>

Medical cannabis in patients with glaucoma was investigated in 14 eligible publications, including one systematic review without meta-analysis and one book section. Of all studies, one investigated the effect of medical cannabis on intraocular pressure, and this study indicated no change in the outcome.<sup>56</sup>

Finally, the evidence for the efficacy and safety of cannabis and CBD for AIDS patients is also being disputed. The studies were short-term

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52 B. Walitt and others, 'Cannabinoids for fibromyalgia' (2016) 7 *Cochrane Database of Systematic Reviews* <DOI: 10.1002/14651858.CD011694.pub2>.

53 B.L. Richards and others, 'Neuromodulators for pain management in rheumatoid arthritis' (2012) 1 *Cochrane Database of Systematic Reviews* <DOI: 10.1002/14651858.CD008921.pub2>.

54 F. Brigo and others, 'Anti-seizure medications for Lennox-Gastaut syndrome' (2021) 4 *Cochrane Database of Systematic Reviews* <DOI: 10.1002/14651858.CD003277.pub4>.

55 T.S. Kafil and others, 'Cannabis for the treatment of ulcerative colitis' (2018) 11 *Cochrane Database of Systematic Reviews* <DOI: 10.1002/14651858.CD012954.pub2>.

56 S.A. Millar and others, 'A systematic review of cannabidiol dosing in clinical populations' (2019) 85(9) *British Journal of Clinical Pharmacology* 1888–900.

and involved a small number of patients. Long-term data showing on-going effects on AIDS-related morbidity and death and safety to patients taking effective antiretroviral therapy are still needed.<sup>57</sup>

In summary, most of the studies on the safety and efficacy of marijuana reported results that were inconclusive or mixed. Only studies involving the use of cannabis in the treatment of chronic non-cancer pain, cancer, epilepsy and MS reported better effects. However, there are several studies in the treatment of cancer, chronic non-cancer pain, Crohn's disease, glaucoma and MS have found that the patients either felt worse or did not experience any significant differences. Furthermore, among the reviews of high-quality studies, the use of cannabis reported to have a better effect was only for the treatment of chronic non-cancer pain and epilepsy.

## **Legislation**

Legislative provisions in the form of possession, distribution, cultivation and use of cannabis for recreational and medical purposes are currently different from country to country. Most countries still prohibit the use of cannabis for recreational purposes and it is still subject to the laws governing the substance. However, some countries have adopted a policy of decriminalisation whereby the possession of this substance is no longer a crime. Among the countries that have allowed the use of cannabis for recreational purposes include Canada, the US, and the Netherlands. Some countries such as Canada and Uruguay also allow the sale of cannabis commercially and in the Netherlands, the sale of cannabis is allowed in licensed stores.

In the US, Colorado had become the first state to legalise cannabis in December 2012 for recreational sales, followed by Washington. Initially, about 20 states including Columbia had legalised cannabis for medical purposes.<sup>58</sup> Immediately, following legalisation in Colorado, 136 retail stores obtained license to sell cannabis throughout Colorado. The public can buy up to one ounce of taxable cannabis for either recreational or medical purposes if they present a medical marijuana registry card or better known as the 'red card'.<sup>59</sup>

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57 E.E. Lutge and others, 'The medical use of cannabis for reducing morbidity and mortality in patients with HIV/AIDS' (2013) 4 *Cochrane Database of Systematic Reviews* <DOI: 10.1002/14651858>.

58 R.G. Morris and others, 'The effect of medical marijuana laws on crime: evidence from state panel data, 1990-2006' (2014) 9(3) *PloS One* e92816.

59 R. Benmaamar, 'Colorado: a first in the USA for legal sale of marijuana' (2014) 15(2) *The Lancet oncology* E55.

To date, a total of 44 countries have allowed cannabis use for medical purposes including Thailand, the only country in Southeast Asia that has allowed cannabis oil to be used. Users are allowed to possess cannabis oil containing THC in an amount not exceeding 0.2% for medical purposes and must have a recognised prescription or certificate. Cannabis was listed as a controlled drug under the Thai Narcotics Act. The license for the production and sale of cannabis products is still strictly regulated by the Thai government. The current laws and regulations for those who are caught smoking or possessing cannabis is still a long time of incarceration. Recently, the Thai government has officially removed cannabis and hemp from the Category V list of Narcotics Act.<sup>60</sup> As a result, all parts of cannabis plants including flowers and seeds are allowed for use of medical and research purposes. Cannabis for recreational use is still not allowed in Thailand, but cultivation of cannabis plants is permissible for personal use only and it must be in small amounts and registration with the authorities is required. The Thai government established a multilevel system around manufacturing, prescribing, monitoring and evaluation, to ensure appropriate implementation of the changed legislation and to mitigate against potential adverse outcomes. Although composition of cannabis in products legalised for medical purposes has been standardised, THC content is still varied between batches, which signifies strict quality control for manufacturing is highly warranted. Due to the limited availability of the authorised products and prescribers, people continue to obtain cannabis-based products from folk healers and black markets.<sup>61</sup>

In the US, cannabis is classified as a Schedule 1 substance under the Controlled Substances Act and remains illegal at the federal level. Medical cannabis is currently legal in 37 states of the US and as of mid2021, it is estimated that there were 5.4 million state-legal patients of medical cannabis.<sup>62</sup> Although medical cannabis is legal at state level, the US Department of Justice reserves the right to enforce the laws enacted by the Congress when pursuing prosecutions related to marijuana offences. At the state level, dispensaries of cannabis are allowed but

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60 See <<https://thediplomat.com/2022/02/thailand-drops-cannabis-from-its-list-of-controlled-narcotics/>>.

61 N. Zinboonyahgoon and others, 'Medicinal cannabis in Thailand: 1-year experience after legalization' (2021) 162 *Pain* S105-S109.

62 See <<https://www.mpp.org/issues/medical-marijuana/state-by-state-medical-marijuana-laws/medical-marijuana-patient-numbers/>> accessed 12 April 2022.

some states put restrictions on the dosage form and doses of products that are allowed to be dispensed. For instance, Minnesota only allows liquid extract products, while New York allows ingested doses with not more than 10mg of THC and not a smoked product.<sup>63</sup>

In Malaysia, strict laws are still imposed on all cannabis-related offences including mandatory death sentence if an individual has more than 200g of cannabis as stipulated under the Dangerous Drugs Act 1952.<sup>64</sup> The use of cannabis for recreational and medical purposes has yet to be allowed in Malaysia despite efforts to allow the use of cannabis for medical purposes have been discussed in the cabinet since 2018.<sup>65</sup>

The legalisation of substances with a high risk of abuse or addiction for medical purposes requires comprehensive data to weigh the benefits and risks to patients and the public. Malaysia needs to examine and learn from the experience of countries that have approved the cultivation of cannabis plants for their own use and medical purposes. For example, in Australia, the legalisation of medical cannabis began in November 2016. Views from the public, scientific data and explanations from experts have been considered towards allowing cannabis-based products to be prescribed for a range of diseases by registered medical practitioners specifically trained to treat patients using medical cannabis products. Australia has published clinical guidelines allowing more than 30,000 indications for over 100 types of cannabis products for medical purposes primarily for chronic diseases.<sup>66</sup> Transparency at every level in producing, distributing and using cannabis products to treat patients is essential to avoid a greater risk of abuse and harm among the public. Malaysia should scrutinise the risks at all levels to prevent the issues of smuggling and abuse from worsening in the country.

The US National Institute of Drug Abuse (NIDA) stated that it is relatively safer to use medical cannabis with accurate composition of chemicals extracted from the plant compared to the whole cannabis

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63 See <<https://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx>> accessed 15 April 2022.

64 See <<https://www.pharmacy.gov.my/v2/en/documents/dangerous-drugs-act-1952-and-regulations.html>> accessed 12 April 2022.

65 See <<https://www.straittimes.com/asia/se-asia/malaysia-in-talks-to-become-first-in-asia-to-allow-medical-pot>> accessed 12 April 2022.

66 N. Lintzeris and others, 'Medical cannabis use in the Australian community following introduction of legal access: the 2018–2019 Online Cross-Sectional Cannabis as Medicine Survey (CAMS-18)' (2020) 17(1) *Harm Reduction Journal* 37 <<https://doi.org/10.1186/s12954-020-00377-0>>.

plant itself.<sup>67</sup> Nevertheless, there was insufficient evidence regarding the significant effectiveness of specific disease treatment as well as the long-term adverse outcomes among patients receiving medical cannabis such as stroke, psychosis and any mental disorders. For example, a meta-analysis highlighted that marijuana use among adolescents increased the risk of depression and suicide attempts by 1.37 and 3.46 times more than those who did not use marijuana respectively,<sup>68</sup> and caused early onset of psychosis.<sup>69</sup> Severe mental disorders can cause serious problems to individuals receiving medical cannabis for chronic diseases which could harm the public.

When an addictive substance is made into prescription medicines, the risk of abuse should be carefully evaluated. The opioid epidemic in the US stemmed from addiction developed in patients from taking oxycodone (OxyContin®) has led to a lawsuit filed against Purdue Pharma that initially claimed safety without much warning of the medication addictive effects.<sup>70</sup> It was well reported that the three most abused and misused prescription medicines included opioids, central nervous system depressants and stimulants.<sup>71</sup> The fact that cannabis can act as a stimulant drug, a tranquilizer and hallucinogen may certainly pose the risk of abuse and psychiatric problems.<sup>72</sup> The prescription medicines designed with clinically efficacious sedative, analgesic, anxiolytic, anaesthetic or stimulant properties has also led to the emergence for their abuse.<sup>73</sup> In

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67 See <<https://nida.nih.gov/publications/research-reports/marijuana/marijuana-safe-effective-medicine>> accessed on 14 April 2022.

68 G. Gobbi and others, 'Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood: A Systematic Review and Meta-analysis' (2019) 76(4) *JAMA Psychiatry* 426-434 <doi:10.1001/jamapsychiatry.2018.4500>.

69 S. J. Van der Steur and others, 'Factors moderating the association between cannabis use and psychosis risk: a systematic review' (2020) 10(2) *Brain sciences* 97.

70 P.C. Webster, 'Oxycodone class action lawsuit filed' (2012) 184(7) *Canadian Medical Association Journal* E345-E346 <<https://doi.org/10.1503/cmaj.109-4158>>.

71 National Institute of Drug Abuse (NIDA) (2022) <<https://nida.nih.gov/publications/research-reports/misuse-prescription-drugs/overview>> accessed on 14 April 2022.

72 E.F. Domino, 'Neuropsychopharmacologic studies of marijuana: Some synthetic and natural THC derivatives in animals and man' (1971) 191(1) *Marijuana: Chemistry, Pharmacology, and Patterns of Social Use* 166-191; A.D. Hathaway and J. Sharpley 'The cannabis experience: An analysis of flow' in D. Jacquette (ed), *Cannabis: What were we just talking about?* (Wiley-Blackwell, 2010) <<https://doi.org/10.1002/9781444324440.ch3>>.

73 S. H. Hernandez and L.S. Nelson, 'Prescription drug abuse: insight into the epidemic' (2010) 88(3) *Clinical pharmacology and therapeutics* 307-317 <<https://doi.org/10.1038/clpt.2010.154>>.

the US, the 2018 National Survey on Drug Use and Health has reported that prescription pain reliever misuse was the second most common form of illicit drug use.<sup>74</sup> Lessons should be learned from the opioid epidemic that happened in the US that led to nearly 500,000 people dying from an overdose involving any opioid, including prescription and illicit opioids between 1999–2019.<sup>75</sup>

The prevalence of prescription medicine abuse was highly dependent on ease of access. Regulation and legalisation of medical cannabis can be carefully studied in comparison to prescription opioids. For example, despite being regulated in Schedule II, the US population consumed opioid pain medications for 80% of the global opioid supply between 2001–2010, with an overall increase of 149% between 1997–2007 and a steady rise of emergency department visits for prescription-controlled drugs including opioids.<sup>76</sup>

In Malaysia, pain medications such as tramadol, morphine and oxycodone were the most common opioids used at the public hospital outpatient settings.<sup>77</sup> However, there was a lack of documentation regarding data addressing prevalence of adverse events, abuse or misuse of prescribed opioids. In Canada, it was reported that 58% of drug-related deaths in Ontario were attributed to opioids with approximately one-third of deaths involving oxycodone.<sup>78</sup> Data transparency and high-quality research in the local context must be available to ensure that medical cannabis does not add to the existing problems of substance abuse, misuse or addiction. For example, the US Department of Health and Human Services outlines the activities to prevent prescription medicine abuse and misuse within the following eight domains: 1) surveillance, 2) drug abuse prevention, 3) patient and public education, 4) provider education, 5) clinical practice tools, 6) regulatory and oversight activities,

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74 Substance Abuse and Mental Health Services Administration, 'Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health' (2020) <<https://www.samhsa.gov/data/>>.

75 Centre for Disease Control and Prevention (CDC), 'Wide-ranging online data for epidemiologic research (WONDER)' (2020) <<http://wonder.cdc.gov>>.

76 L. Manchikanti and others, 'Therapeutic use, abuse, and nonmedical use of opioids: a ten-year perspective' (2010) 13(5) *Pain physician* 401–435.

77 C.S. Zin and others, 'Trends and patterns of analgesic prescribing in Malaysian public hospitals from 2010 to 2016: tramadol predominately used' (2018) 11 *Journal of Pain Research* 1959–1966 <<https://doi.org/10.2147/JPR.S164774>>.

78 P. Madadi and others, 'Characteristics of Opioid-Users Whose Death Was Related to Opioid-Toxicity: A Population-Based Study in Ontario, Canada' (2013) 8(4) *PLoS ONE* e60600 <<https://doi.org/10.1371/journal.pone.0060600>>.



7) drug abuse treatment, and 8) overdose prevention initiatives.<sup>79</sup> The multifaceted approaches must be inclusive, properly documented and evaluated continuously considering the changes in various aspects occurring in the community over the years. By passing medical cannabis laws, some studies reported that there was an increase in the number of individuals who use, abuse and become dependent on cannabis.<sup>80</sup> This number is much lower in the state that did not authorise cannabis as a legal substance.<sup>81</sup>

The laws in regulating medical cannabis should also be tightened in relation to prescriptions, sales, purchases, usages and so on. In terms of enforcement of illicit substance abuse, the National Anti-Drug Agency in Malaysia has reported a decrease in the arrests of cannabis use cases over a 5-year period compared to the total of all cases of illicit drugs of 8.7% (2016), 3.9% (2017), 4.3% (2018), 2.7% (2019) and 2.1% (2020).<sup>82</sup> The decrease in the arrest rate however does not necessarily mean that its use among civilians is reduced. Rather, the arrest rate is affected by various factors such as the COVID-19 pandemic, number of operations, enforcement, the accuracy of urine tests and so on. Additional risk assessments and planning in law enforcement are needed to ensure that cannabis abuse does not increase when medical cannabis is legalised in Malaysia.

In comparison to cigarettes and other tobacco products that have been legalised despite proven to increase the economic burden due to various diseases and deaths, generally cannabis was seen as less harmful and posed medicinal benefits because data from high-quality studies were

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79 Centre for Disease Control and Prevention (CDC), 'Addressing Prescription Drug Abuse in the United States Current Activities and Future Opportunities' (2013) Behavioral Health Coordinating Committee Prescription Drug Abuse Subcommittee, US Department of Health and Human Services.

80 R.L. Pacula, 'Examining the impact of marijuana legalization on marijuana consumption: insights from the economic literatures' (2010) *RAND Drug Policy Research Center* 1-24; S. Harper and others, 'Do medical marijuana laws increase marijuana use? Replication study and extension' (2012) 22(3) *Medical Marijuana Laws and Marijuana Use* 207-212; J. Scheurmeyer and others, 'Temporal trends in marijuana attitudes, availability and use in Colorado compared to non-medical marijuana states: 2003-2011' (2014) 140 *Drug and Alcohol Dependence* 145-155.

81 Substance Abuse and Mental Health Data Archive, *National survey on drug use and health* (Rockville, Maryland, 2014).

82 Agensi Anti-Dadah Kebangsaan (AADK), 'Statistic Trend of Number of Drug Addicts Detected According to Type of Drugs, 2016 – 2020' (2021) <<https://www.adk.gov.my/en/statistic-trend-of-number-of-drug-addicts-detected-according-to-type-of-drugs-2016-2020/>> accessed 14 April 2022.

still insufficient. Data on the harms related to cigarettes and other tobacco products have been well reported worldwide over several decades. In Malaysia, cigarettes have also been declared as prohibited or *haram* by the National Fatwa Council in March 1995 and are regulated in accordance with the Control of Tobacco Product Regulations (CTPR) 2004 under the Food Act 1983. On the other hand, cannabis as a prohibited drug is regulated under Section 2 of the Dangerous Drugs Act 1952 and is still not legalised for personal or medical use.<sup>83</sup>

## Conclusion

Since CBD and THC compounds originated from the same species of *Cannabis sativa*, there is a fine line between medical and recreational use of cannabis. Legalisation of cannabis might expose unnecessary risks of addiction and psychiatric disorders in the population. This is especially true if large-scale cultivation is allowed in this country, even with the implementation of strict rules and regulations. Most of the studies on the safety and efficacy of cannabis reported either weak or inconclusive results. Reviews of high-quality studies reported the use of cannabis is to have a better effect only for the treatment of chronic non-cancer pain and specific type of epilepsy. From the legislation perspective, comprehensive regulations and guidelines at every step of cultivation, production, handling and usage should be established before the legalisation to avoid any deviation. Not only that, enforcement of the laws must be at par with other countries such as Australia or Canada and capable of controlling the appropriate use of cannabis in the community, strictly for medical purposes. At this juncture, the motion to legalise the medical use of cannabis is not urgent and, at the same time, must not be oversighted.

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83 Ministry of Health Malaysia (MOH), 'Soalan lazim: Kanabis (Cannabis)' (2020). Program Perkhidmatan Farmasi <<https://www.pharmacy.gov.my/v2/ms/entri/soalan-lazim-kanabis-cannabis.html>> accessed 14 April 2022.

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