

The Problem of Cannabis Use: the Role of the Ministry of Health

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Consensus

BACKGROUND

A group of researchers and clinicians from several specialties – gathered by the Coordination of National Institutes of Health and High-Specialty Hospitals (Coordinación de Institutos Nacionales de Salud y Hospitales de Alta Especialidad) – has jointly analyzed the main addiction problems confronting the country in order to identify fields for the inter-institutional cooperation and make proposals of public policy. This group previously published a document on the abuse of alcohol and now it is dealing with the cannabis use. The working group identified the consumption of this substance as the second priority of the problem of drugs use in our country.

INTRODUCTION

Cannabis has been the subject of an important international debate. Some people who propose its legalization consider that this measure would decrease traffickers' earnings. There is a consensus that its use should not be grounds for imprisonment. Some groups promote its medicinal use, others recognize some potential health benefits but do not document the risks of smoked cannabis, thus they think that the alternative shall be the use of medication containing the active substance (THC), which health benefits are above of the damages caused.

These arguments that reach our youths do not indicate that cannabis is a safe drug. When compared with other drugs it has a lower toxicity level and it is associated with less social

consequences, although it is present in these consequences; for example, it is used when driving. There is evidence that the greater the level use, the greater the possibility that other drugs are used.¹ Intoxication affects short-term memory, attention, common sense as well as other cognitive functions, and also coordination and balance; it can raise one's heart rate. In the long term, in chronic users, there is evidence of more lasting cognitive deficits, reversible after continuous abstinence. It also has been associated with an increased risk for cancer, depression and psychosis. Its utero exposure has long-term consequences. For instance, evidence exists that during adolescence there is a worse performance on tasks that require visual memory, analysis and integration on persons who were exposed during gestation.²

Therefore, this is a problem that we must solve with evidence-based information and with measures allowing us to support the healthy development of our children and youths.

Neurobiological Mechanisms of Cannabis

Cannabis sativa is a plant that puts up delta-9-tetrahydrocannabinol (THC), which is its active component.³ In cannabis sativa this component is present at 5% and at higher concentrations in hashish: 10%-20%; with modifications in its cultivation a 19%-30% concentration has been achieved. THC reaches the brain in a few minutes. Typically, the user experiences the subjective effects within 30 minutes after having smoked. It is also administered orally and topically. THC is eliminated after a long period of time, from one to four weeks. The more experienced smokers eliminate it

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more quickly. Biodegradation mechanisms are mainly hepatic, including the P-450 enzyme complex. Finally, metabolites are eliminated as feces and urine.

Cannabis has effects on any subject who uses it. This happens because THC activates a couple of receptors located in the Central Nervous System (CNS) and in different other parts of the body. These are the cannabinoid receptors (CB) 1 and 2. CB1 receptor has a privileged expression in the CNS; while the CB2 in the immune system.

Endocannabinoids. In 1992, Mechoulam et al. described an isolated lipid molecule from the brain of the pig that has similar cannabis properties; called anandamide.³ Two years later, another lipid was described, called oleamide.⁴ This one is also combined with the cannabis receptors (CB1 and CB2) and when it is systemically administered it causes several effects that are similar to those induced by THC.

Cannabinoid Receptor Type 1 (CB1). This receptor is widely distributed in the brain, including hypothalamus, amygdala, hippocampus, cerebral cortex, brainstem and other structures in which it is located in the terminals of glutamatergic, cholinergic, noradrenergic and GABAergic neurons. The main function of CB1 is to reduce the possibility of releasing such neurotransmitters.⁵

Endocannabinoids and the Reward/Motivation System. This system is located in the brain and is primarily made up of two structures: the nucleus accumbens (NAc) and the ventral tegmental area (VTA).^{3,6} The VTA activates the NAc at the same time that it deactivates the amygdala – the nucleus involved in the generation of the subjective feeling of fear – and the prefrontal cortex, cortical area widely studied and recognized as a crucial component for the decision-making. Then, the mechanisms that generate the subjective feeling of pleasure actively disregard fear and reasoning. The mechanism by which the VTA activates and deactivates said structures is dopamine release. Dopamine receptors D1 are exciters, while D2 are inhibitors. Hence, NAc neurons mainly express D1 and the ones from the amygdala and prefrontal cortex-D2. Axon terminals that reach the VTA and the NAc express CB1. Therefore, their activation facilitates the highest activation of neurons from both structures; and this leads the subject to experience the subjective feeling of pleasure. It bears mention that there could be a genetic predisposition for developing cannabis dependence.⁷ Its manifestation depends on the confluence of development factors and on the context, a matter dealt with in the following subsection.

An additional observation illustrates one of the reasons by which adolescents are more vulnerable to the effects of not only cannabis, but of any substance of abuse. As mentioned above, on adolescents the prefrontal cortex involved in the decision-making is immature. Such cortex matures until approximately 30 years of age.⁸ Thus, adolescents make decisions practically without considering the consequences of its use.

Psychosocial Risk Factors. Scientific evidence shows that not all individuals are under the same risk to start and de-

velop dependence. Dependence is based on a combination of factors that increase vulnerability and a lack of factors regarding the individual's protection (for example, supervision of parents, high self-esteem, etc.). The factors that increase vulnerability may be: biological factors if related to the sensitivity to the drug effects; genetic factors indicating a predisposition from those persons who develop drug dependence if coming across with the substances; and environmental factors that can include drug exposure and the experience of vicissitudes during childhood, especially with victims of violence.⁹

Vulnerability is defined as the probability that a person has to develop certain condition, which is in turn determined by the magnitude of emotional, cognitive, social and intra- and interpersonal risk factors. Such factors are defined as the conditions that precede the problem and increase the possibility that the latter occurs. Thus, for example, suffering from an emotional disturbance during early childhood, and reaching adolescence without treating it, is a risk factor for substance abuse since the probability that this happens is increased as an attempt of the individual to face his/her emotional problem.

There are risk factors that are common for all drugs and specific for cannabis. This drug is one of the most popular illegal drugs worldwide and it can be the "front door" for the use of other substances. A very important risk factor is having a relationship with users of substances.^{10,11}

Other recognized factors are social isolation, low social competence, low assertiveness, deficient interpersonal conflict resolution, lack of pro-social attitudes and low capacity to cope with adverse situations.

Within family context, there is a significant correlation between the use of drugs in youths and the consumption of substances & the antisocial behavior of family members, besides a family attitude tolerant of consumption and/or a family atmosphere of conflict or violence and mistreatment, including sexual abuse. Regarding school matters, there are factors such as poor school performance, absenteeism, school expulsion or dropout, lack of interest for studying or for school activities.

Low risk perception for consumption and high accessibility of the substance are other risk factors. Also, positive attitudes and expectations regarding consumption and low behavioral control regarding situations that favor the use of substances, low self-esteem, despair and other more or less serious depressive symptoms are commonly associated factors.¹²⁻¹⁷

The highest risk age to start cannabis use – as well as the highest risk age for its effects – is adolescence and diminishes or stops with life changes like the beginning of work activities in full-time jobs or marriage.¹⁸⁻²²

The attention-deficit disorder coexists with the use of substances, between 34% and 63%. Parenting styles have suggested that when there is an appropriate intimacy, au-

tonomy and care and protection behaviors there is a lower substance use. Likewise, there is a lower use with authoritarian styles and a greater parental supervision.²³ The media and the social norms in favor of substance use play an influential role, too.

Studies conducted in Mexican Youth Integration Centers (*Centros de Integración Juvenil*) found the following predictive factors of illicit drug abuse: exposure to school stressors, depressive disorders, connections with consumers, poor impulse control and low risk perception. As predictive dependency factors the accessibility and exposure are added to family stressors.²⁴⁻²⁶

Epidemiological Background. The National Addictions Survey reports that cannabis is one of the preferred substances of the population. Actually, since a measurement conducted in 1988, cannabis has been within the top places preference among the population. For the 2008 measurement,²⁷ its use increased from 3.5 to 4.2%. Its cumulative incidence reaches 4.2%. Survey data indicate that adolescents between 12 and 17 years old are more likely to use drugs when they have the opportunity than those who have reached the legal age of adulthood. Furthermore, they are 69 times more likely to use cannabis when given free, than their schoolmates who have not been exposed.

Cannabis use begins more often during adolescence. Drugs consumption typically starts at an early age. Data indicate that half of the users (55.7%) starts before the age of majority. Therefore, they also face important risks that make necessary to consider mechanisms to protect them from potential health damage during this period of their lives.

On the other hand, the most recent survey conducted on high school students of the Federal District²⁸ states that the use of cannabis "once in a lifetime" records a prevalence of 11.4%, an increase of 2.6 percentage points with regard to 2006. Such increase is slightly greater for men, whose use ranged from 11.2% in 2006 to 14.0% in 2009, while for women was from 6.4% to 8.8%, respectively.

Characteristics of Cannabis Users in Specialty Treatment Centers. As for drug users requesting treatments in Youth Integration Centers, during the first half of 2010 the use of cannabis "once in a lifetime" was reported by 8,509 cases (72.4% out of the total). Those who declared that have been used it within the 30 days before their treatment admission (4,416 cases) have some distinguishing features, compared to those who did not consume it during this period of time.

Among the significant differences between cannabis active users and the rest of the served population, a younger age when starting treatment stands out (21.3 vs. 24.6 years); a higher proportion of men (7.9 men to every woman against 3.4 men to every woman) as well as a younger age to start tobacco use (14 vs. 14.8 years), alcohol (14.3 vs. 14.9 years) and illicit drugs (15.2 vs. 17.2 years). Likewise, cannabis users during the last month, stated to have used a larger number of illicit drugs once in a lifetime (2.9 vs. 2.1), with a

higher use of medical use depressants (primarily benzodiazepines), hallucinogens, stimulants and crack.

In the last month, cannabis users also reported a high proportion of combined use of substances (two or more substances in a single day, including the use of alcohol); with a difference of over 17 points regarding the rest of the compared population (65.2% vs. 48.0%); as well as a greater frequency of abuse in illicit drugs use (57.7% of current cannabis users took drugs everyday or every third day, against 37.1% with this frequency of use in the rest of the population).²⁹

Psychosocial Consequences of Cannabis Use. Cannabis repercussions on the individual's and society's health leads to the need for establishing effective policies that reduce consequences such as violence, illnesses or suffering of users and their relatives, since they ignore the effects of this substance on their children's life, which causes stress and negative feelings that may affect their physical and mental health.

Considering that the effects of youths' use, besides running the risk to have an addiction, includes consequences such as distortion of perception, affection of memory, of common sense and of learning skills as well as difficulties to think and solve problems, the effects in society are derived from these consequences.

Foreign research clearly proves that cannabis has the potential to cause problems in everyday life or worsen the existing problems of a person, besides affecting his/her status and social life. Several studies associate cannabis smoking employers with greater absence, lateness, accidents, employees' compensation claims and workload. In general, cannabis-smoking students score lower and are less likely to graduate from secondary school than their non-smoking schoolmates are.

In Utero and Unweaned Baby Damage due to Maternal Cannabis Use. When a woman uses cannabis during pregnancy or breastfeeding, there is a possibility to harm the baby's brain.

Within this context, lab experience with animals is higher than with human beings.

The central nervous system (CNS) exposure to cannabis originated the "teratogenic brain and neural development damage" concept. This occurs because the THC crosses the blood-brain barrier and is eliminated by breast milk when the endocannabinoid system already exists, which harms the CNS's development. Such aggression causes disorders on the neurogenesis, the differentiation among neurons, the synaptogenesis, the myelinization and the glia migration, among others. Although this damage does not cause malformation of the CNS, it does generate functional abnormalities usually not detected on newborns.

The drug effects do not cause a phenotypic alteration on the CNS such as seizure crisis or psychomotor retardation but the damage is expressed as hyperactivity, impulsivity, attention and memory disorders, anxiety and depression that are associated with child or adolescence delinquency, but not with adulthood.

Other associated problems are: deficit in weight and height as well as sleep patterns disturbances. When the use surpasses 12 months before pregnancy the risk to develop rhabdomyosarcoma, neuroblastoma, urogenital malformation and microcephaly increases from two to five times.

These effects may be modulated by certain factors such as the mother's drug exposure time, the dose and the way of contact, as well as their association with other "licit" and "illicit" substances.³⁰⁻³³

Psychiatric Comorbidity. Some studies correlate cannabis use and its potential association with psychopathology in certain patients, explained from two perspectives: 1. The self-medication hypothesis (in which the subject tries to improve his/her psychiatric symptoms with cannabis) and 2. The theory that postulates that the substance is the cause or predisposing factor of psychosis. In the latter case, three situations may occur: a) patients with a predisposing genetic load, which in the presence of the substance would appear phenotypically as a psychosis; b) patients with no predisposing genetic load, in whom substances per se could induce psychosis and c) vulnerable persons who were repeatedly subjected to the use of the substance may develop a psychosis by a phenomenon of progressive awareness. Any of the above possibilities include factors such as: young adults, males, unemployment, low educational level, history of schizoid, paranoid or Schizotypal personality, conduct disorders and conflictive family dynamics.

On the other hand, with regard to self-medication, it is estimated that in schizophrenia patients the risk to have a substance use disorder throughout their life is 4.6 times higher than general population, with a probability of five times higher for Cannabis.

In addition, the relation among cannabis use, psychosis and depression has been reported; cannabis use may cause precipitate severe psychotic patterns and increase the risk of chronic schizophrenia in vulnerable persons, exacerbating, in general, the symptoms. Although some studies show that cannabis use during adolescence increases the risk to suffer schizophrenia, it is difficult to establish a direct causality of cannabis with schizophrenia (Table 1).

Something that provides sufficient support is the presence of the Amotivational Syndrome (characterized by apathy, adynamia, anergy, reluctance, putting off decision-making and impending tasks to a later time, that is, procrastination; as well as the lack of disease awareness and thus not requesting medical care) suffered by the subjects, secondary to their chronic use and in susceptible population, which significantly impacts on the different stages of the individual and his/her family's life.³³⁻⁴¹

Cannabis and Medical Indications

The analysis and evaluation of the cannabis's potential medical uses have a scientific basis since –as mentioned previ-

Table 1. Cannabis Use and Mental Health.

Author	Association
McKay y Tennant (2000) Hall y Degenhardt (2000)	Precipita el inicio o recaída de la esquizofrenia en sujetos predisponentes y exacerba los síntomas.
Andreasson (1987) Zammit (2002)	Incrementa 6 veces el riesgo de esquizofrenia en grandes consumidores adolescentes.
Bovasso (2001)	Los síntomas depresivos son 4 veces más frecuentes en consumidores de cannabis.
Rey (2002)	Asociación entre el uso de cannabis y depresión.
Van Os (2002)	Fuerte asociación entre cannabis y psicosis.
Arsenault (2002)	Los sujetos con consumo de cannabis a los 15 años muestran una probabilidad 4 veces superior de presentar un trastorno esquizofreniforme a los 26 años. No hay asociación con trastornos depresivos.

ously – in the body exist cannabinoid receptors (CB1 and CB2) on which the different cannabis components act. Participation and dysregulation of such receptors have identified in several illnesses, consequently, their modulation has potential therapeutic benefits.

Cannabis contains over 60 phytocannabinoids where THC is the most abundant. From the rest of cannabinoids the most studied are cannabidiol (CBN), a product of the THC oxidation that contains 10% of the effect; cannabidiol (CBD) not having any psychoactive effect but it does have anti-inflammatory, analgesic, anti-psychotic, anti-ischemic, anxiolytic and anti-epileptic effects; and cannabigerol (CBG) with potential therapeutic effects in psychosis, epilepsy, anxiety, sleep disturbances, neurodegeneration, ischemia, emesis, food intake, type 1 diabetes, osteogenesis and cancer. In spite of the long list of potential benefits, their assessment has been difficult since many are two-phase effects: with severely, major activity at lower doses; and minor activity with a dose increase and chronic use.

Studying smoked or eaten cannabis therapeutic effect is neither possible nor correct for the following three reasons: 1. Depending on the plant, the cannabinoids concentration is different with a THC ranging from 1 to 30%, although in average is approximately 10%. 2. The way of smoking is quite variable, regarding both the depth of inhalation and its frequency and 3. Cannabis smoke contains many tobacco carcinogens and, because of its way of smoking, the lungs retain three times more tar and five times more carbon monoxide. Therefore, to medically assessing the activity of cannabinoids it would be necessary that the pharmaceutical industry produce some forms with fixed doses, regularly low and avoiding toxic effects. The following medications are approved in some countries, in certain cases with restrictions: Marinol (2.5 mg dronabinol tablets), Sativex (2.7 mg

Table 2. Estado del uso médico de cannabinoides en presentación farmacéutica.

Indication	Effect	Status de aprobación
Náusea y vómito secundario a quimioterapia	No agrega beneficio a lo convencional	Sí, en algunos países como cuarta línea de tratamiento
Anorexia secundaria a SIDA		Yes
Anorexia secundaria a cáncer	No es superior al acetato de megestrol	No
Anorexia nervosa	No parece tener actividad	No
Esclerosis múltiple	Mejora espasticidad y dolor neuropático	Yes
Esclerosis lateral amiotrófica	Mejora apetito y sueño pero no calambres y fasciculaciones	No
Lesión espinal	Mejoría en dolor y espasticidad	No
Epilepsia	Puede disparar o suprimir convulsiones. En la mayoría sin efecto	No
Dolor secundario a cáncer	Equivalente a codeína con más efectos secundarios	Sí, junto con analgésicos y algunas restricciones
Dolor neuropático		Sí, con analgésicos en algunos países en cuarta línea
Hiperactividad vesical	Mejora la urgencia e incontinencia	Yes
Glaucoma	No es superior a tratamientos convencionales	No
Artritis reumatoide, enfermedad de Parkinson, enfermedad de Crohn, psoriasis y urticaria	Possible beneficio	Requiere más investigación

THC oral spray + 2.5 mg CBD per spraying) and Cesamet (1 mg nabilone tablets).

The medical use status of pharmaceutical cannabinoid forms in other countries is shown in Table 2.

As can be seen, medical indications of cannabinoids are minimal and none is irreplaceable by other medications. While different doses utilized were not presented, in general they are low (a 2.5 mg Marinol tablet equals one inhalation of smoked cannabis). For example, the dose in anorexia apart from AIDS is two tablets a day.

Use of these medications must be carefully monitored and not be given to children under the age of 18 or persons with previous history of hypersensitivity, psychiatric problems (particularly schizophrenia), liver, kidney and cardiopulmonary diseases, pregnancy, breastfeeding and men with fertilization plans. Likewise, the combination with other medications must be monitored, since their effect may be modified. Their combination with alcohol may increase the sedative effect of the latter. It bears mention that one inhalation of smoked cannabis may produce blood levels of THC, which effect in driving coordination may be similar to 0.05% of alcohol (2-3 drinks).

In summary, physiological and medical effects of cannabinoids may be multiple since there are distributed receptors throughout the body. For many years, this aspect has aroused interest among the scientific community regarding its research. Although limited, some medical indications have been established for the use of cannabinoids

by the existing pharmaceutical forms. There are prescribing guidelines allowing to use these medications with reasonable safety; a situation that cannot be extrapolated to the medical use of smoked cannabis, since the approved dose may be easily exceed and the smoke contains many toxic substances.⁴²

Health Damage Associated with Cannabis Use. Extended use can lead to addiction. When people get into this point the drug interferes in many aspects of their lives, but they cannot quit even if they want to. The risk is higher for those who start the use during adolescence when the brain has not matured fully. Persons who develop dependence on this substance may have an abstinence syndrome similar to the one experienced when a tobacco smoker quits. They also may experience irritability, difficulty sleeping, an uncontrollable desire and anxiety for using the drug, and they can become more aggressive during this period.

Health damages associated with cannabis use have not been accurately assumed in the belief that its consumption is lower than nicotine's and that the number of users is lower. It is likely that there is a belief that health damages are lower than those caused by the use of tobacco products. In addition, it is likely that the use has more risks associated with consumption habits. For instance, cannabis smokers –as mentioned above– make deeper inhalations and keep smoke longer in their lungs. The way users prepare cannabis in the rolling paper result in more herb than the content in a tobacco cigarette. They never use filters, which imply a

Table 3. Pulmonary and extrapulmonary damages associated with cannabis use.

Pulmonary	Extrapulmonary
Respiratory Symptoms	Oral Complications
Chronic bronchitis	Cancer
Lung Function and airway resistance	Automobile Accidents
Lung Cancer	Cardiovascular Diseases
Bronchial Hyperreactivity	Erectile Dysfunction
Bullous Emphysema	
Pneumothorax	

higher inhalation compared to tobacco. These factors cause a higher concentration of potentially toxic substances than tobacco's concentration.

Health damage associated with cannabis use could be divided into pulmonary and extrapulmonary damage (Table 3).

Respiratory System Damage

Respiratory Symptoms. Cannabis smokers have more respiratory symptoms than nonsmokers do. Aldington⁴³ compared in a study cannabis-only smokers versus cannabis-combined-with-tobacco smokers, tobacco-only smokers and nonsmokers. It was observed that cannabis smokers presented more wheezing, cough, chest tightness and chronic bronchitis symptoms than nonsmokers. The frequency of these symptoms is comparable to that of tobacco-only smokers. However, when subjects smoke both nicotine and cannabis cigarettes, they present more symptoms than either of these two, separately (Table 4).

Decline in Lung Function. In cannabis smokers exists a dose-response relationship and a decline of the FEV1 and FVC ratio. Furthermore, an increase of the airway resistance and of the total lung volumes was detected; changes that overall suggest that smoking cannabis can be a risk to develop COPD (Chronic Obstructive Pulmonary Disease). In the same study,⁴³ researchers determined the presence of emphysema within a small cannabis smokers group. Other researchers have observed this data.⁴⁴

Lung Cancer. Smoking is the number one cause of lung cancer. Since it is difficult to find cannabis-only smokers who have never smoked tobacco, there are scarce studies stating an association between cannabis use and lung cancer. Nevertheless, there are elements in cannabis content and in the form of its use that make possible the association. For example, cannabis contains twice the amount of polycyclic aromatic hydrocarbons with carcinogenic potential favoring – together with the smoke remaining longer in lungs – the stay of carcinogenic products in the lungs. New Zealand is a country where users do not regularly combine cannabis and tobacco. A case-control study⁴⁵ was conducted in that country, resulting a clear distinction between cannabis-only

Table 4. Respiratory Symptoms

	Only cannabis	Cannabis + tobacco	Only tobacco	Non-smokers
Wheezing	26.7%	34.1%	30.4%	11.1%
Cough	29.3%	28.6%	40.2%	4.9%
Chest tightness	49.3%	53.9%	40.0%	34.6%
Chronic bronchitis	18.7%	30.8%	13.0%	2.5%

(Modified Aldington, 2008).

smokers and tobacco-only smokers. The control group included individuals who have neither smoked cannabis nor tobacco as well as individuals who mixed both. It was found that the relative risk of developing lung cancer is 5.7 times higher in cannabis-only smokers.

Bronchial Hyperreactivity and Allergic Hypersensitivity. A group of researchers in Spain⁴⁶ proved that an important percentage of cannabis users have cannabis positive IgE and bronchial challenge tests. Coincidentally, this group showed more respiratory symptoms: bullous emphysema, pneumothorax and pulmonary fibrosis. There are some reports of these entities associated with cannabis use. Although the cases are documented, more evidence is required to categorically determine this relationship.

Cannabis users have more respiratory symptoms than nonsmokers. Some symptoms –such as chest tightness– increase with both tobacco and cannabis use. Table 4 shows the symptoms of these four populations.⁴⁵

Non-pulmonary Complications

Oral Complications. They have been associated with several complications ranging from altered mental states –when combining some local anaesthetics⁴⁷ to xerostomia, leukoedema and an increased likelihood of oral candidiasis.⁴⁸

Head and Neck Cancer. A case-control study⁴⁹ of 173 patients diagnosed with head and neck squamous carcinoma and 176 cancer-free subjects, found that cannabis smokers have a high risk for developing this type of neoplasm. It is worth underscoring that these findings persisted after adjusting by smoking, gender, age, race, education and other confounders. Such researchers found a positive cause-dose ratio effect. Thus, for smokers who used more and for a longer time, the risk was higher.

Automobile Accidents

A review found that the most important non-pulmonary complications are automobile accidents related to acute cannabis use. As previously mentioned, this affects time and distance perception. Two puffs of a cannabis cigarette may cause an effect on the nervous system similar to the effect caused by non-permitted serum levels of alcohol.⁵⁰

Cardiovascular Diseases

In addition, heart attack and hypertensive crises cases associated with cannabis use have been described.⁵⁰ However, further evidence is required.

Erectile Dysfunction

A recent study has aimed at the potential cannabis effects on men's sexual health. Its data suggests the existence of an effect⁵¹ but further research is required in this regard.

Cannabis use goes beyond the social landscape associated to the illicit drug use and the effects on mental health. In fact, a series of evidences point out that the effect beyond those described can be a multisystem effect. The reasons why this damage has not involved a clear explanation are connected to the hidden use and banning. This aspect is very important because, while ignoring health damage, it will be more difficult to organize prevention campaigns using health arguments and not only with addiction arguments that per se, would be sufficient.

Considerations Regarding the Treatment

The real challenge for dealing with addictions is to constantly and consistently maintain non-use over time. Within this section, the craving for use the drug acquires a paramount value in psychopharmacological management, being important to have an ongoing and permanent follow-up. Objectives for the keeping non-use stage are: a) To promote and maintain sobriety, b) In case of failure, to carry out harm reduction through moderate intake, c) To generate alternatives to solve critical situations, d) To correct precipitating and associated factors, e) Deal with complications, f) Apply relapse preventive strategies.

As general principles, management of addictions should be based on the following aspects:⁵²

1. There is no single treatment for everyone.
2. Treatment should be immediately provided.
3. An effective treatment provides for the multiple necessities of the subject, not only his/her drug use.
4. Individualized treatment and health care plan are to be assessed on an ongoing basis and modified accordingly, in order to guarantee that the plan covers the person's changing needs.
5. For an effective treatment, it is crucial to adhere to it for an appropriate time.
6. Advices (either individualized or in group) as well as other forms of behavior therapy, are central to the effectiveness of an addiction treatment.
7. For many patients medications constitute an important part of treatment, especially if combined with advice and other behavior therapies.
8. Those addicts or individuals with drug abuse, who si-

multaneously present a mental illness, should undergo a comprehensive treatment for both disorders.

9. Medical detoxification is only the first step for addiction treatment since, by itself, contributes very little to modifying the habit of use in the long term.
10. Treatment should not be voluntary for being effective.
11. The possibility of drug use during treatment must be controlled on an ongoing basis.
12. Treatment programs should include detection of diseases such as AIDS, hepatitis B and C, tuberculosis and other infectious diseases as well as advice patients to change their behaviors, in order to avoid their or other persons' infection.
13. A drug recovery program may be a very long process and usually requires multiple treatment periods.

Another central issue is the psychotherapeutic approach in which it is necessary to clarify and support the diagnosis, set the short- and long-term objectives, as well as establishing the terms of the therapeutic contract. During the initial phase, participation of patient's family members is necessary. In this first phase, the objective is to achieve the patient's conviction to remain in abstinence.

Subsequently, some of the factors that led him/her to the consumption of substances shall be tackled. Thus, the patient must learn to handle anxiety as well as to integrate gradual abandonment of defense psychological mechanisms such as negation and projection, also strengthening self-care awareness. It is possible that sexual, family or other type of problems become evident which should be addressed. Likewise, it is also essential to be assisted by Support Groups like Alcoholics Anonymous and Narcotics Anonymous, in order to control and restructure the patient and reintegrate him/her into the different areas of their life. With the foregoing intervention, many patients finish their treatment or remain in abstinence, carry on with the identification and resolution of intrapsychic conflicts as well as make a permanent moral inventory of their daily actions they repair everyday, hence the conflict areas diminish and the patient readapts to society.

It is important to mention that, following the said guidelines, the outlook shall be more favorable. Nonetheless, the natural evolution of the illness provides for relapse, thus therapeutic guidelines should spread such relapse patterns out so that each pattern shortens until total remission.

Psychosocial interventions shall include the next objectives: a) establishment and maintenance of the therapeutic alliance; b) monitoring of the patient's medical condition; c) treatment of the states of intoxication and abstinence; d) development and provision of compliance of an individualized therapeutic program; e) prevention of relapses; f) individual and family health education; g) reduction of comorbidity and of consumption consequences and h) integration of the interventions made along with the coordination of professionals from other disciplines, non-governmental organizations.

Table 5. Referencias normativas en el campo de la cannabis

Punitivo	Derecho a la salud y obligaciones del Estado Mexicano	Administrativa
En México no está penado el uso de drogas (ciertas cantidades) sino el tráfico, la producción (esto es, la manufactura, fabricación, elaboración, preparación o acondicionamiento de algún narcótico), el transporte, el tráfico, el suministro gratuito, la prescripción y el comercio (esto es, vender, comprar, adquirir o enajenar algún narcótico). También se imponen penas a quienes aporten recursos o colaboren financieramente en los delitos anteriores, a quienes siembren o permitan que se siembre en terrenos de su posesión alguna planta cuyo alcaloide esté prohibido y realicen actos de publicidad o propaganda para favorecer el consumo de narcóticos.	Constitución Mexicana, artículo 4. La Convención Única de 1961, su Protocolo y el Convenio sobre Sustancias Psicotrópicas. La Convención de Viena de 1988. Ley General de Salud, regula: 1. Promoción de la salud (artículo 73). 2. La atención médica (en sus funciones preventiva, curativa y rehabilitadora a que se refiere el artículo 33). 3. Las personas que usen habitualmente estupefacientes o sustancias psicotrópicas (artículo 74). 4. Al programa contra la farmacodependencia que evalúa el Consejo Nacional contra las Adicciones.	NORMA Oficial Mexicana NOM-028-SSA2-1999, Para la prevención, tratamiento y control de las adicciones. 2.1 NOM-001-SSA1-1993, Que instituye el procedimiento por el cual se revisará, actualizará y editarán la Farmacopea de los Estados Unidos Mexicanos. 2.2 NOM-025-SSA2-1994, Para la prestación de servicios de salud en unidades de atención integral hospitalaria médico-psiquiátrica. 2.3 NOM-010-SSA2-1993, Para la prevención y control de la infección por virus de la inmunodeficiencia humana. 2.4 NOM-009-SSA2-1993, Para el fomento de la salud del escolar. 2.5 NOM-017-SSA2-1994, Para la vigilancia epidemiológica. 2.6 NOM-168-SSA1-1998, Del expediente clínico. Reglamento de Control Sanitario de Actividades, Establecimientos, Productos y Servicios destinado a los actos de control sanitario de la fabricación de estupefacientes y sustancias psicotrópicas, prescripción médica, expendio, importación y exportación de unos y otras.
Código Penal Federal Título VII capítulo I: "Delitos contra la salud". Capítulo VI: substancias psicotrópicas. Ley General de Salud, Capítulo 5: "Estupefacientes".		

Considerations on the Analysis of Cannabis Legalization. The analysis to assess the drug legalization process is complex, since it includes medical and economic aspects as well as multiple social situations both national and international. About cannabis legalization, medical and socio-economic arguments have been put forward, the latter in connection with the drug trafficking reduction and its relevant consequences. The arguments defending the legalization, based on its medicinal properties, are obsolete, since today we know that all medicinal properties are covered by different cannabinoids-free medications. Certain countries approve some cannabinoids' medical indications based on the use of oral compounds produced by the pharmaceutical industry –as previously mentioned– and not by smoked cannabis, since the smoke contains many toxic compounds. On the other hand, the THC concentration required to obtain a pharmacological effect is minimum and its concentration varies widely from one plant to another. The conventional "recreational" use that most of its users give cannabis far exceeds the blood levels compatible with a medical indication; reaching different levels of toxicity.

As for the argument of possible benefits for its use control, international evidence indicates that this is not likely to happen. Studies have been conducted in the USA focused on high school students (equivalent to the Mexican third high school grade) on the amount of use according to the risk perception that cannabis may cause. Between 1975 and 2008 the use increases as the risk perception diminishes and vice versa.⁵³ This implies that if cannabis were legalized in

Mexico, the youth would receive a clear message asserting that cannabis is not so harmful.

The so mentioned argument of other countries experience –mainly Holland– must be analyzed carefully and in no way be considered as an example to follow. In Holland, it was legalized in 1976 and the use, which had been already diminished the previous year, remained stable during seven years. Between 1984 and 1996, the use was increased from 15 to 44%, while the allowed amount was reduced from 30 to 5 grams. Initially, the use was limited to "coffee shops" in Amsterdam that in 1980 were nine in all. They became 71 in 1985 and in 1997 there were between 1,200 and 1,500 throughout Holland.⁵⁴ As for the number of users, in 2001 37% of the population aged over 12 years in Amsterdam had tried cannabis and 11% in populations of less than 500 houses.⁵⁵ With these data it cannot be considered that Holland is a good example to follow, particularly if we take into account that in Mexico, at a similar age, the use is much lower. On the other hand, a big difference between Holland and Mexico is that our country represents a pathway to the country with the highest drug consumption worldwide. Therefore, a legalization process in Mexico is not possible without a close relationship with the USA.

Synthesis of the Legal Framework in Addiction Matters in Mexico. The legal framework on addictions in our country is wide and responds to different dimensions: a) Punitive. It refers to the standards that regulate and penalize traffic, production and distribution of several illicit substances; b) Right to Good Health and Obligations of the Mexican Government.

It refers to the government's obligation to guarantee every citizen, suffering from any addiction, access to health care, and to the government's obligations assumed internationally; c) Administrative. All types of regulations on the handling of licit substances that may cause addictions and on the regulation of institutions that provide treatment. Thus, the legal framework includes the Political Constitution of the United Mexican States, the international treaties ratified by our country, federal laws, state laws, and Mexican official regulations, decrees, covenants and standards.

Table 5 sums up part of the legislation.

Cannabis is not an innocuous drug-it has negative health consequences and there are no elements to justify its legalization for medical purposes. The measure could have more negative than positive consequences regarding health and quality of life of children, adolescents and youths due to their growth stage and neuronal susceptibility, which varies among individuals. Legalization would facilitate access to the drug, conveying a minor risk message to the population; which in turn has been associated to a higher use.

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