

CLINICAL PRACTICE GUIDELINES FOR MANAGEMENT OF CANNABIS DEPENDENCE

Dr. Shiv Gautam¹, Dr. I.D. Gupta², Dr. Aftab Khan³

INTRODUCTION

The cannabis plant has been used by humans in China, India and the Middle East for approximately 8,000 years for its fiber and as a medicinal agent. Cannabis was introduced to Europeans in the 9th Century via Napoleon's troops returning from Egypt and to Britain for medical use by a surgeon who has served in India. There was some recreational use in Persian bohemian demimonde in the late 19th Century.

Recreational cannabis use was introduced in the United States in the 1930 from Mexico and spread via Jazz Musician to cities in the Northeastern United States. International Drug Control Treaties banned its use in United States in 1938 and in most other countries in 1961. It was used in Bohemian circles in the United States in the 1940 and 1950 before gradually disseminated to wider US Youth Population in late 1960s and through the 1970s and 1980s. Its use was disseminated via movies, media and popular culture to many other developed countries in 1970s and 1980s.

EPIDEMIOLOGY

Drug abuse monitoring system (DAMS) collected data from treatment center from 23 States, 2 Union territories and Delhi (year 2002). Total sample of users is 16942. According to study the mean average age is 35.3, sample for study was equally distributed in rural (51.7%) and urban area (48.3%).

For both rural and urban areas, most common substance is alcohol (43.9%), heroin (11.1%), cannabis (11.1%), opium (8.61%), propoxyphene (2.6%) and others (18.5%). Others includes tobacco and non-narcotic analgesics.

Surveys in three northern Indian states in 1989 and 1991 (Indian Council of Medical Research, 1993) found a lifetime prevalence rate of 3 percent and a prevalence of current use of 1 percent, with no evidence of any increase between 1989 and 1991. In Varanasi a study of 4326 college students revealed that overall cannabis use among them was 4.5 per cent (Reddy et al. 1993).

In southern India, a lifetime prevalence of use of 7 percent has been reported, with 2.5 percent current users.

Machado (1994) conducted a household survey in a rural area of India, an urban slum area and in city found the following prevalence of ever use of cannabis 3.2 percent, 3.2 percent in the rural area and 2.7 percent in the city.

CANNABIS - Derived from female plant - *Cannabis sativa*. Primary psychoactive component D-9-tetrahydrocannabinol [D-9-THC]. (D-9-THC is present in all parts of plant but flowering tops and resins contain the highest concentration).

1-Professor & Head, 2-Astt. Professor, 3-Resident Doctor
Psychiatric Centre, SMS Medical College, Jaipur

CANNABIS PREPARATION AND METHOD OF USE

PREPARATION	PREPARED FORM	METHODS OF USE
Marijuana (0.5-5% THC)	Dried flowering tops and leaves of plant	May be mixed with tobacco and smoked as a 'Joint' or smoked in a pipe with or without tobacco.
Hashish (2-8% THC)	Dried cannabis resin	<ul style="list-style-type: none">• Smoked with or without tobacco• May be cooked in food and eaten
Hashish Oil (15-20% THC)	Extracting THC from Hashish or Marijuana in oil	<ul style="list-style-type: none">• Few drops may be applied to cigarette, pipe or joint.• Oil can be heated and vapors inhaled
Bhang	Leaves and stems of plant	By oral route

Etiology and Pathophysiology

Cannabis use disorders

Dependence develops as a result of repeated use of drug, and frequency of use is one of most important prediction of developing dependence (Kandel et al 2000).

There are 2 types of G-protein coupled cannabinoid receptors:

TYPE	LOCATION
CB1 receptor	Lipid membranes of Neurons in the central nervous system with high densities in the hippocampus, cerebellum and striatum.
CB2 receptor	Lipid membranes of various type of cells in immune system.

D-9-THC is partial agonist that activating both CB1 and CB2 receptor (Hall and Solowij 1998).

The cannabinoid system plays a modulatory role in regulating many different functions including mood, motor control, perception, appetite, sleep, memory, cognition, reproductive function and immune response (Ameri 1999).

Like most other dependence producing drugs, cannabis produces its reinforcing effect by activating the mesolimbic dopaminergic 'reward' pathway which consist of dopaminergic neuron in ventral tegmental area (VTA), that projects to the nucleus accumbens, increasing dopamine levels in the shell of nucleus accumbens (Dianna et al. 1998).

Discontinuation of cannabis use increases corticotrophins releasing factor (CRF) in the central amygdala and decreases dopaminergic transmissions in the limbic system, resulting in withdrawal symptoms (Rodrigues et al. 1997).

Cannabis Induced Disorder: The mechanism causing the Euphoria Experienced during cannabis intoxication is activation of mesolimbic dopaminergic reward pathway (Diana et al. 1998a, Gardener 1999).

Genetic Factors

A study of female twins reported that genetic factors accounted for 60-80% of the variance in liability for cannabis dependence (Kendler and Prescott 1998). Tsuang et al. (1999) found in study of male twins that genetic factors contributed significantly to progression from first exposure or opportunity to use can cannabis to initial use of cannabis , from initial use to use more than five times and from use more than five times to regular use.

True et al (1999) reported in another study of male twins that genetic factors were responsible for 44% and common environmental factors for only 21% of the variance in risk of developing cannabis dependence.

Another possible etiology for cannabis dependence is that some individuals may be 'self-medicating' themselves for underlying psychiatric symptoms. Some patients with depression, anxiety or negative symptoms of Schizophrenia report that marijuana use alleviates their symptoms (Peralta et al 1992, Dixon et al 1991, Warner et al 1994).

Correlates of Cannabis Use

- Age** : First use of cannabis typically begins in the teens and heaviest rates of use occur in early 20s.
- Gender** : Higher among men than women
- Income** : A positive relationship has been found between income in adolescence and early adult life and cannabis use with those earning more money more likely to report cannabis use.
- Socioeconomic Status** : The relationship between cannabis use and socio-economic status (SES) is weak.

Cultural Factors: Cannabis is more common in North and Central India. Traditionally cannabis is consumed in Pockets of UP, Varanasi, Allahabad and on the banks of Ganges, where has been a social acceptance for use of cannabis on occasions of Indian Festivals like holi and Mahashivratri. In Rajasthan cannabis is more prevalent in Central Rajasthan (Shekhawati Belt) and Palimarwar where Bagichi Culture (A Small oasis created in 1-2 bighas of land with a well) is prevalent. People are gathered there in evening and involved in recreational activities and abuse intoxicants commonly cannabis.

DIAGNOSTIC AND CRITERION

ICD-10 CRITERIA	DSM-IV-TR CRITERIA
F.12 - Mental and behavioral disorder due to use of cannabinoid.	304.30 Cannabis dependence With physiological dependence without physiological dependence.
Following character code used to specify the clinical conditions	Early full remission
Fix. 0 Acute intoxication due to use of cannabinoid	Early partial remission
A. The general criteria for acute intoxication must be met	Sustained full remission.
<p>B. There must be dysfunctional behavior or perceptual abnormalities including at least one of following;</p> <ol style="list-style-type: none"> 1. Euphoria and disinhibition 2. Anxiety or agitation 3. Suspiciousness or paranoid ideations 4. Temporal slowing. 5. Impaired judgment 6. Impaired attention 7. Impaired reaction time 8. Visual, auditory and tactile illusions 9. Hallucination with preserved orientation 10. Depersonalization 11. Derealization 12. Interference with personal functioning 	<p>Sustained total remission. In a controlled environment. Cannabis-Induced Disorders</p> <p>292.89 Cannabis intoxication with perceptual disturbance</p> <p>292.81 Cannabis intoxication delirium</p> <p>292.11 Cannabis - induced anxiety disorder</p> <ul style="list-style-type: none"> - With onset during intoxication - With generalized anxiety - With panic attacks - With obsessive compulsive symptoms - With phobic symptoms
C. At least one of following sign must be present	292.9 Cannabis - related disorder - Not otherwise specified.
<ol style="list-style-type: none"> 1. Increased appetite 2. Dry mouth 3. Conjunctival injection 4. Tachycardia 	
F _{1x} .1 Harmful use	
F _{1x} .2 Dependence syndrome	

ICD-10 CRITERIA	DSM-IV-TR CRITERIA
<p>F_{1x}.3 Withdrawal state due to cannabis- This is ill-defined syndrome for which definitive diagnostic criteria cannot be established at present time. It occurs following cessation of prolonged high dose of cannabis. It has been reported variously as lasting from several hours to up to 7 days. Symptoms and signs include anxiety, irritability, tremor of outstretched hands, sweating and muscle aches.</p>	<p>292.89 Cannabis Intoxication</p> <p>A. Recent use of cannabis</p> <p>B. Clinically significant maladaptive behavior or psychological changes i.e. 3 impaired motor coordination, Euphoria, anxiety, sensation of slowed time, impaired judgment, social withdrawing that developed during or shortly after cannabis use.</p> <p>C. Two (or more) of following signs, developing within 2 hours of cannabis use</p>
<p>F_{1x}.4 Withdrawal state with delirium</p>	<p>1. Conjunctival injection</p>
<p>F_{1x}.5 Psychotic disorder</p>	<p>2. Increased appetite</p> <p>3. Dry mouth</p> <p>4. Tachycardia</p> <p>D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.</p>

ASSESSMENT:

CANNABIS - RELATED DISORDER

(A) Cannabis Use Disorder -

Cannabis Dependence: Obtain a good history indicating that cannabis use is impairing the patient's ability to function either physiologically or psychologically (Patient's performance at work, ability to carry out social and family obligations and physical health)

Cannabis Abuse: Criteria focus on adverse consequences of cannabis use that could potentially result from just a single use such as failure to fulfill obligation at work, school or home, participation in potentially dangerous activities having cannabis related legal problems or social or interpersonal difficulties.

People with cannabis dependence have been using cannabis more regularly and for a longer duration (one or more years) and acute problems associated with abuse have turned into chronic problems associated with dependence.

(B) Cannabis Induced Disorder

Cannabis Intoxication - Assessment made according to ICD-10 and DSM-IV TR criteria.

Cannabis Intoxication Delirium - It is a rare complication even if recent cannabis use has been reported a full diagnostic work up should be performed to rule out a concomitant treatable neurological condition (Halikas 1974, Johns 2001).

Cannabis - induced Psychotic Disorder: Two type of psychotic disorder: One featuring delusions, the other Hallucination. A careful history is required to establish whether patient has a preexisting psychotic disorder or whether symptoms arose *de novo* after cannabis consumptions.

In a review of studies of patients with cannabis - induced psychotic disorder, it was found that most of studies had not excluded individuals with a pre-existing Axis I disorder, which would render the individual vulnerable to psychotic symptoms even in the absence of cannabis use. At present, it seems possible that majority of cannabis - induced psychotic or anxiety disorders represent exacerbations of pre-existing DSM-IV AXIS I psychiatric disorder in individuals who become intoxicated with the drug (Gruber and Pope 1994).

Cannabis - induced Anxiety disorder:

Specifiers: With generalized anxiety, with panic attacks, with obsessive - compulsive symptoms and with phobic symptoms.

People who experience anxiety after using cannabis are typically inexperienced users who react to novel experience of perceptual distortions and intensified sensation with anxiety and even panic reactions rather than employment (Thomas, 1996, Johns 2001).

Co-morbidity

Studies reported that individual with cannabis use disorder have high rate of other substance abuse disorder (Miller et al. 1990) as well as other types of axis/ disorders (Regier et al. 1990; Troisi et al. 1998).

Conversely studies of several psychiatric population (Brandy et al. 1991; Alterman et al., 1982, Johns 2001) with a number of different Axis I diagnosis. The course of Axis I illness is often adversely affected by Cannabis use, cannabis may exacerbate psychotic symptoms in patient with schizophrenia (Andreasson et al. 1989), precipitate hypomanic or manic episodes in bipolar patients (Gruber et al., 1994), trigger panic reactions in patient with panic disorder (Szuster et al., 1988).

Cannabis use also co morbid with conduct disorder in children and adolescents and with antisocial personality disorder in adults (Weller et al, 1985; Henry et al., 1993).

Despite these finding, Cannabis use has not been shown to induce any psychiatric disorder *de novo* in non predisposed individual (Hall et al 200 , John et al. 2001).

COURSE:

About third of adolescents who try cannabis will use it regularly for some period of time, whereas only about 10% will go on to develop long term dependence lasting into adulthood (Hall and Solowij 1998). Even among these persistent user, the majority will stop use by age 30 years so less than 2% of adults will exhibit cannabis dependence during their twenties and probably less than 1% of adults will continue use into their thirties. Small minority of patients continue to suffer from cannabis dependence follow a chronic or relapsing course similar to those who suffer from dependence on other substance. (Miller et al. 1989; Hall and Solowij 1998, Jhonston et al. 2001, Hser et al. 2001, Kandel and Chen 2000).

'Amotivational syndrome' associated with chronic cannabis use, characterized by subjective reports of lack of direction, motivation and ambition (Mellinger et al. 1976, Meesty et al. 1995, Kuptfer et al. 1973). This 'amotivational syndrome' appears to result from the effect of continuous intoxication and resolve when cannabis is discontinued (John 2000).

Cannabis-Induced Disorders:

Cannabis induced psychotic and anxiety disorders as well as cannabis intoxication delirium rarely persist beyond the period of acute intoxication with the drug.

If symptoms persist for more than 24 to 49 hours after acute cannabis intoxication suggest another Axis 1 disorder, rather than cannabis itself is responsible for symptoms.

Review of Literature regarding Management

- Four controlled studies of treatment of cannabis-dependent individual. In three of the studies, the subjects were seeking treatment specifically for cannabis dependence, whereas fourth study involves schizophrenic patients undergoing treatment for marijuana dependence (Stephens et al 1994; Budhey et al 2000; Sigmon et al 2000; Stephens et al 2000).
- The first study found no difference in the out come between cognitive – behavioral relapse prevention group and support group overall, 16% of subjects had decreased use and 15% were abstinent when assessed 12 month after treatment (Stephens et al. 1994)
- In second study compared a motivational enhancement group, a motivational enhancement plus cognitive behavioral therapy group combined with a voucher based incentive programme that rewarded, bi-weekly urine screen that were negative. The group with voucher-based incentive program achieved a higher rate of abstinence during the study period and at the end of study than either of the other two treatment groups (Budhey et al 2000).
- In third study similar success using monetary reward for negative urine was also reported in a small trial of schizophrenic patients undergoing treatment for marijuana dependence (Sigmon et al 2000).
- Last study compared brief motivational therapy with a cognitive-behavioral relapse prevention support group and a control group consisting of subjects put on a waiting 45%. No difference was found between two active treatment groups, subjects in both treatment groups were using significantly less marijuana and reported significantly fewer symptoms of dependence and fewer. Marijuana related problems than subjects in the control group (Stephens et al 2000).

PRACTICE GUIDELINES

These practice guidelines, developed to define the critical and desired elements of substance abuse services, are largely derived from the research literature and recommend interventions with proven efficacy. The guidelines are designed to educate practitioners in best practice models thereby reducing clinical variation across the country and improving outcomes. **Treatment should be individualized, clinically-driven and outcomes-driven, assessment-based and allow for a continuum of care with a broad range of services of demonstrated value.**

DIAGNOSIS OF Marijuana Dependence

To diagnose Marijuana dependence following quick and reliable test (CAGE) can be administered similar to those commonly used to diagnose alcohol dependence (American Psychiatric Press, 1999).

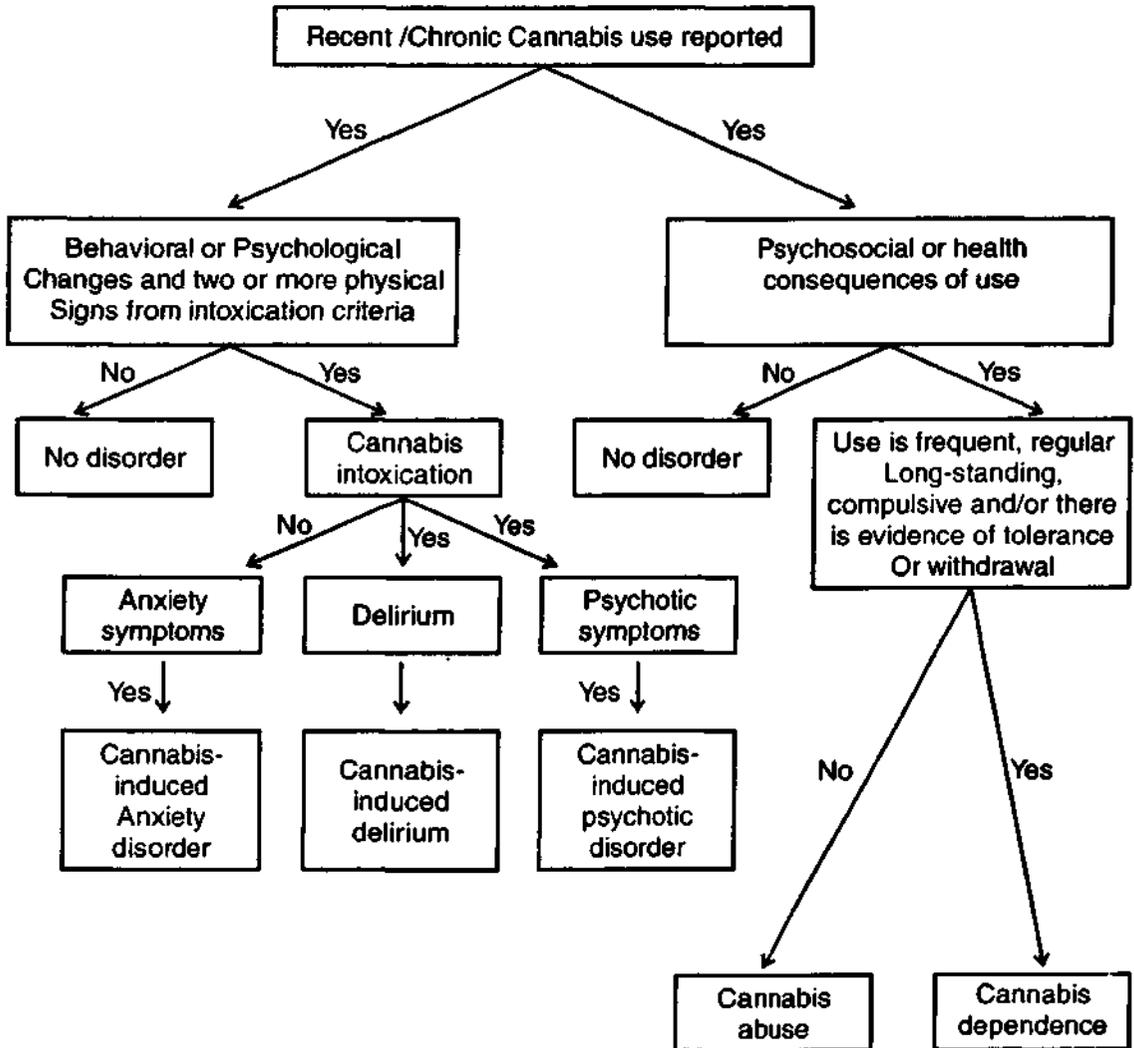
1. **C** - Have you felt the need to **C**ut down on your marijuana use?
2. **A** - Are you easily **A**ngered when questioned about your use?
3. **G** - Do you feel **G**uilt about your marijuana use?
4. **E** - Do you smoke first thing in the morning (**E**ye opener)

An accurate history must be taken and all dependencies must be recognized.

Drug Testing: Urine testing generally identifies cannabinoid metabolite. Because these substances are fat soluble, they persist in bodily fluids for extended periods and are excreted slowly.

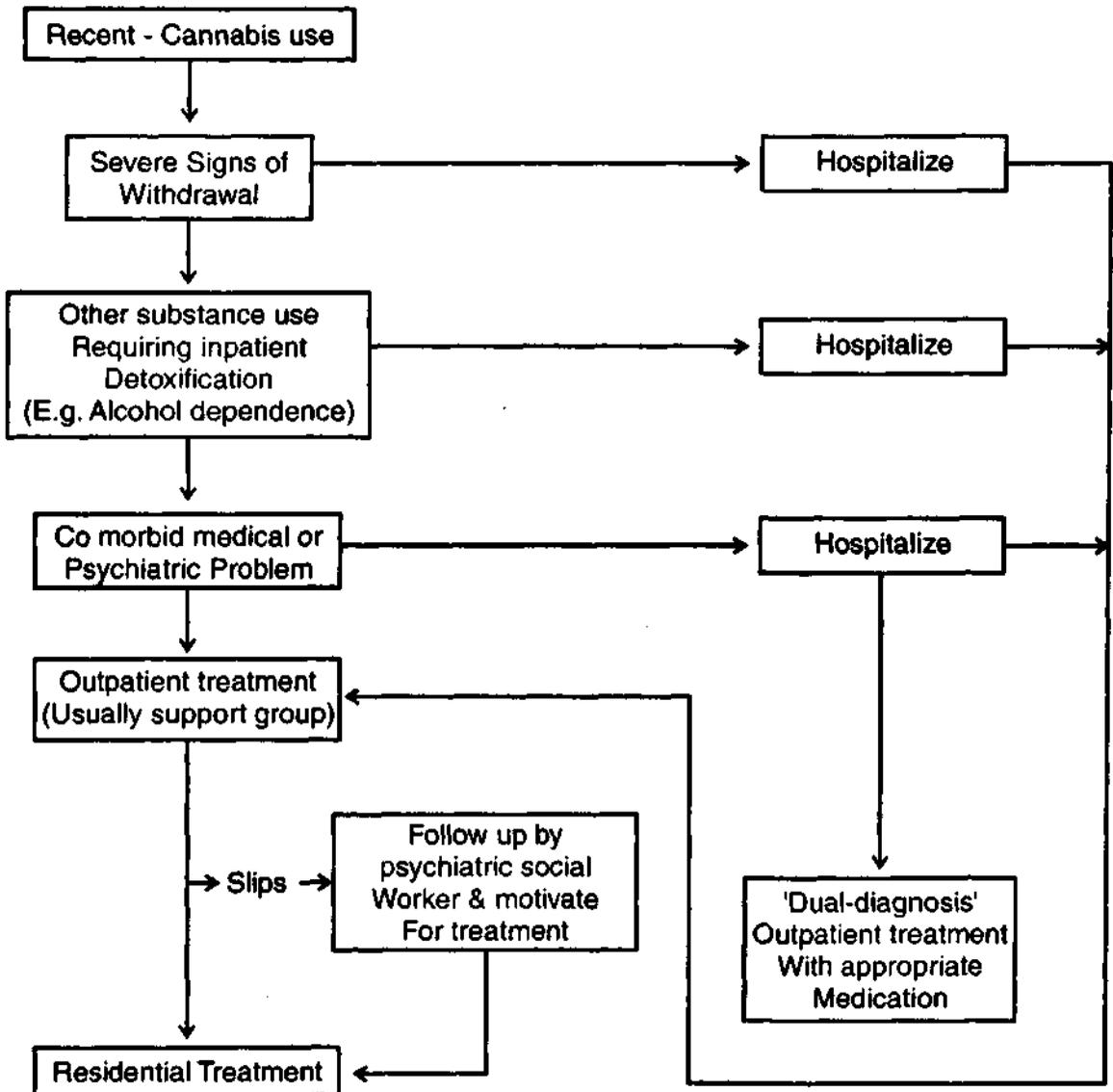
When to treat?

In patients presenting with chronic cannabis use in absence of Psychosocial or health consequences should be treated symptomatically and in some situations need not require any treatment at all as it may be culturally acceptable. However in cases presenting with Behavioral or Psychological changes treatment should be initiated. (See Diagnostic Decision tree & Treatment Algorithm)



DIAGNOSTIC DECISION TREE FOR CANNABIS USE DISORDER

Treatment - Decision Algorithm for Cannabis use disorder



As with all other drugs of abuse, the ultimate goal in treatment of cannabis dependence is abstinence. The process of treatment begins with detoxification followed by maintenance. Chronic users usually experience a withdrawal syndrome during detoxification.

- Since detoxification is not life threatening, detoxification generally does not require hospitalization unless it is complicated by detoxification from other drugs or by co morbid. Axis I disorders that do require hospitalization for safe treatment.
- To help a patient tolerate the 7 to 10 day withdrawal. Period, practitioners should provide psychological support (e.g. reassurance that the symptoms will resolve in a little over a week).
- The foundation of maintenance treatment, as with other types of substance use disorders, is regular attendance at groups that provide education and support.
- The most important feature of cannabis abuse or dependence is that it is often co morbid with other Axis I disorder. Toxicology screening for other drugs of abuse is imperative because the most common co morbid Axis I disorders are other type of substance abusè.
- Psychological reason for cannabis use should be investigated (use for relaxation or improving mood may be indicative of efforts to sell and medicate, underlying anxiety or mood disorders).
- Thus treatment programme for cannabis dependence should include a dual-diagnosis component.

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