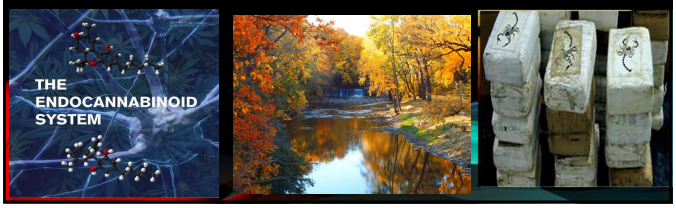
HOT THERAPEUTIC TOPICS FOR THE DENTAL TEAM: FROM WEED TO WEIGHT LOSS

Karen A. Baker, M.S., B.S. R.Ph, Associate Professor
Oral Pathology, Radiology and Medicine
University of Iowa College of Dentistry



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MAJOR TOPICS WE WILL COVER THIS MORNING

- Common SUD Drugs and Underlying Mental Health Dx.
- Clinical Pharmacology of Cannabis & Physiologic Effects
- Identifying Cannabis Use Disorder in Your Patients
- Dental Treatment Considerations for Cannabis Users
- Other SUD and Dental Management
- New Hypertension Guidelines-How High is TOO High?
- Dental Treatment Concerns for New Weight Loss Drugs
  -Semaglutide (Ozempic,Wegovy) & Tirzepatide (Mounjaro)

FDA CDC ADA American Dental Association

2

Disclosure Statement

No relevant financial relationship(s) or nonfinancial relationship(s)

- I have no relevant financial or nonfinancial relationships in the products or services described, reviewed, evaluated or compared in this presentation.

3

THIS MATERIAL QUALIFIES FOR IOWA OPIOID LICENSURE HOURS

- Understanding the Disease of Substance Use Disorder
- Common SUD Drugs and Underlying Mental Health Disorders
- Clinical Pharmacology of Cannabis & Physiologic Effects
- Identifying Cannabis Use Disorder in Your Patients
- Dental Treatment Considerations for Cannabis Users
- Dental Implications for Non-Opioid SUDs and MOUDs if available
  - Alcohol – three maintenance drugs available in the U.S.
  - BZDPs – buprenorphine for short term management
  - CNS stimulants, Hallucinogens, Inhalants, Ketamine

FDA Nobel Biocare CDC ADA American Dental Association

4

5

NIDAMED

Words Matter
Terms to Use and Avoid When Talking About Addiction

This handout offers background information and tips for providers to keep in mind while using person-first language, as well as terms to avoid to reduce stigma and negative bias when discussing addiction. Although some language that may be considered stigmatizing is commonly used within social communities of people who struggle with substance use disorders (SUDs), clinicians can show leadership in how language can destigmatize the disease of addiction.

Stigma and addiction

What is stigma?
Stigma can be defined as a label with an associated stereotype that elicits a negative response. Typical stigma related to addiction patients: they are dangerous, unpredictable, incapable of managing treatment, at fault for their condition, etc.

Where does it come from?
For people with an SUD, stigma may stem from antiquated and inaccurate beliefs that addiction is a moral failing, instead of what we know it to be—a chronic, treatable disease from which patients can recover and continue to lead healthy lives.

How does it affect people with SUD?
- Stigmatizing attitudes can reduce willingness of individuals with SUD to seek treatment.[1,2]
- Because clinicians are typically the first points of contact for a person with an SUD, health professionals should "take all steps necessary to reduce the potential for stigma and negative bias."[3] Take the first step by learning the terms to avoid and use on the next page.
- Use person-first language and let individuals choose how they are described.[4]

What is person-first language?
Person-first language maintains the integrity of individuals as whole human beings—by removing language that equates a person to their condition or has negative connotations.[5] For example, "person with a substance use disorder" has a neutral tone and distinguishes the person from his or her diagnosis.[4]

6

Terms to avoid, terms to use, and why

Consider using these recommended terms to reduce stigma and negative bias when talking about addiction.

Instead of...	Use...	Because...
Addict **User** **Substance or drug abuser** **Junkie** **Alcoholic** **Drunk** **Substance dependence** **Former addict** **Reformed addict**	• Person with opioid use disorder (OUD)/SUD or person with opioid addiction • Patient • Person in recovery or long-term recovery **For heavy alcohol use:** • Unhealthy, harmful, or hazardous alcohol use • Person with alcohol use disorder	• Person-first language. • The change shows that a person "has" a problem, rather than "is" the problem.[2] • The terms to avoid elicit negative associations, punitive attitudes, and individual blame.[2]
Addicted baby	• Baby born to mother who used drugs while pregnant • Baby with signs of withdrawal from prenatal drug exposure • Baby with neonatal opioid withdrawal/ neonatal abstinence syndrome • Newborn exposed to substances	• Babies cannot be born with addiction because addiction is a behavioral disorder—they are simply born manifesting a withdrawal syndrome. • Using person-first language can reduce stigma.
Habit	• Substance use disorder • Drug addiction	• Inaccurately implies that a person is choosing to use substances or can choose to stop.[6] • "Habit" may undermine the seriousness of the disease.

7

Terms to avoid, terms to use, and why

Consider using these recommended terms to reduce stigma and negative bias when talking about addiction.

Instead of...	Use...	Because...
Abuse	**For illicit drugs:** • Use **For prescription medications:** • Misuse, used other than prescribed	• The term "abuse" was found to have a high association with negative judgments and punishment.[4] • Legitimate use of prescription medications is limited to their use as prescribed by the person to whom they are prescribed. Consumption outside these parameters is misuse. • Consider the motivation and intent of misuse (e.g., level, reasons) to determine whether the specific instance suggests SUD.
Opioid substitution Replacement therapy	• Opioid agonist therapy • Medication treatment for OUD • Pharmacotherapy	• It is a misconception that medications merely "substitute" one drug or "one addiction" for another.[4]
Clean	**For toxicology screen results:** • Testing negative **For non-toxicology purposes:** • Being in remission or recovery • Abstinent from drugs • Not drinking or taking drugs • Not currently or actively using drugs	• Use clinically accurate, non-stigmatizing terminology the same way it would be used for other medical conditions.[4] • Set an example with your own language when treating patients who might use stigmatizing slang. • Use of such terms may evoke negative and punitive implicit cognitions.[7]
Dirty	**For toxicology screen results:** • Testing positive **For non-toxicology purposes:** • Person who uses drugs	• Use clinically accurate, non-stigmatizing terminology the same way it would be used for other medical conditions.[4] • May decrease patients' sense of hope and self-efficacy for change.[2]

8

Confusing Nomenclature: Equating Addiction & Abuse

Addiction risk factors:
- Genetics
- Trauma
- Early life use

DSM-5 "New" DSM-5 *Substance Use Disorder Criteria* lumps markedly different conditions into one - mild, moderate, and severe. This all-encompassing language is leading to a loss of understanding of addiction.

Appropriate Use	Misuse	Abuse	ADDICTION
Use without consequence	Use in a manner that may lead to significant consequences across all life areas	Life consequences: Self-moderating successful use. More significant problem in an early stage	Moderation not effective. Condition leads to death without intervention.

Our current evaluation and treatment system lacks the ability to reliably differentiate abuse from addiction in the early stages of the condition

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9

CATEGORIES OF SUD SYMPTOMS

Symptoms of substance use disorders in the DSM-5 fall into four categories: 1) impaired control; 2) social problems; 3) risky use, and 4) physical dependence.

Impaired Control	Social Problems	Risky Use	Physical Dependence
Using more of a substance or more often than intended Wanting to cut down or stop using but not being able to	Neglecting responsibilities and relationships Giving up activities they used to care about because of their substance use Inability to complete tasks at home, school or work	Using in risky settings Continued use despite known problems	Needing more of the substance to get the same effect (tolerance) Having withdrawal symptoms when a substance isn't used

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10

SUD IS A CHRONIC DISEASE WITH VARYING SEVERITY

Three Levels of Severity

The DSM-5 includes guidelines for clinicians to determine how severe a substance use disorder is depending on the number of symptoms. Two or three symptoms indicate a mild substance use disorder; four or five symptoms indicate a moderate substance use disorder, and six or more symptoms indicate a severe substance use disorder. A severe SUD is also known as having an addiction.

Doctors determine the severity level of the substance use disorder to help develop the best treatment plan. The higher the severity, the more intensive the level of treatment needed.

Most patients are likely to need ongoing treatment and recovery support using a chronic care model for several years. A doctor should monitor progress and adjust the plan as needed.

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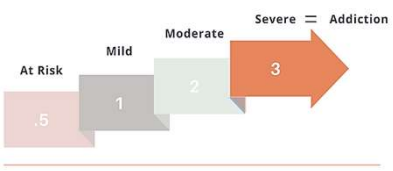
11

Like other illnesses, addiction gets worse over time. Similar to stages of cancer, there are levels of severity to describe a substance use disorder.

Levels of Severity of Substance Use Disorders



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12

Types of Substances

Alcohol	Marijuana	Opioids	Nicotine
Beer Wine Spirits	Marijuana THC	Heroin Fentanyl Prescription Pain Killers	Nicotine, cigarettes or vapes
Stimulants	**Sedatives**	**Synthetics**	**Hallucinogens**
Cocaine Methamphetamine	Benzodiazepines GHB	Synthetic Cannabinoids (K2/Spice) Synthetic Cathinones (Bath Salts) Ketamine GHB	MDMA, Ecstasy/Molly LSD PCP (Phencyclidine) Peyote (mescaline) psilocybin

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13

IS SUD PREVALENT PRIMARILY IN YOUNG PEOPLE?

14

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., Editor

Substance-Use Disorders in Later Life

Susan W. Lehmann, M.D., and Michael Fingerhood, M.D.

SUBSTANCE-USE DISORDERS HAVE BEEN DECLARED A NATIONAL PUBLIC health emergency.[1] Although the rates of substance use are generally lower among older adults than among younger people, this review focuses on older adults.[2] Physiological changes in hepatic metabolism that occur with aging affect the pharmacokinetics of both alcohol and other substances, leading to increased susceptibility to harmful effects. Older adults are more likely than younger people to have multiple chronic health conditions and to be using prescription medications that can interact with alcohol and other substances, putting them at increased risk for adverse consequences. To complicate matters, detecting substance-use disorders can be especially challenging in the presence of multiple coexisting medical conditions. Usual social indicators of impaired function, such as difficulty at work, driving errors, or legal charges, may be irrelevant for a person who is retired, is no longer driving, or is consuming substances at home rather than in public. Yet unrecognized substance-use disorders can cause substantial harm to older adults in the form of an increased risk of falls, confusion, cognitive impairment, and medical morbidity, which can contribute to hospitalizations and health care costs, as well as loss of independence.

Large-scale epidemiologic studies conducted over the past 25 years have provided important information about rates of substance use, but longitudinal prospective studies, which would provide data on changing patterns of use, are lacking. In addition, definitions of older age vary among studies, ranging from 45 years of age or older to 65 years of age or older, making it difficult to distinguish differences between middle-aged and older adults. This article addresses the current trends and research related to the prevalence, detection, and management of alcohol-use disorder, prescription-medication misuse, and use of illicit substances among older adults.

From the Johns Hopkins University School of Medicine, Baltimore. Address reprint requests to Dr. Lehmann at the Johns Hopkins University School of Medicine, 600 N. Wolfe St., Meyer 4-181, Baltimore, MD 21287, or at slehman@jhmi.edu.

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Table 2. Signs of Possible Problematic Substance Use in Older Adults.

Psychiatric symptoms: sleep disturbances, frequent mood swings, persistent irritability, anxiety, depression
Physical symptoms: nausea, vomiting, poor coordination, tremors
Physical signs: unexplained injuries, falls, or bruises; malnutrition; evidence of self-neglect, such as poor hygiene
Cognitive changes: confusion and disorientation, memory impairment, daytime drowsiness, impaired reaction time
Social and behavioral changes: withdrawal from usual social activities, family discord, premature requests for refills of prescription medications

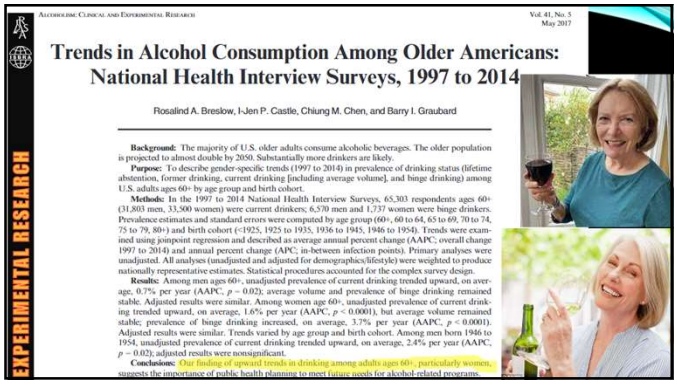
15

Table 1. Use of DSM-5 Criteria for the Diagnosis of Substance-Use Disorder in Older Adults.*

DSM-5 Criterion	Application of Criterion for Older Adult
Substance taken in greater amount than intended	Older adult may be impaired using the same amount taken when younger
There is persistent desire or unsuccessful effort to cut down or control use	Older adult may not realize use is problematic, especially with long-term use
There is excessive time spent to obtain, use, or recover from the substance	Same
There is craving for the substance	Same
Repeated use leads to inability to perform role in the workplace or at school or home	Role impairment is less pertinent; older adult may be retired and may be living alone
Use continues despite negative consequences in social and interpersonal situations	Same
Valued social or work-related roles are stopped because of use	Effect of substance use on social roles is less obvious if older adult is no longer working
Repeated substance use occurs in potentially dangerous situations	Same; older adult may be at increased risk for impaired driving
Substance use not deterred by medical or psychiatric complication	Same; medical consequences can be serious, including confusion, falls with injury, and psychiatric symptoms
Tolerance develops: increasing amount is needed to obtain effects	Symptomatic impairment may occur without an obvious need for increasing the amount
Withdrawal syndrome occurs or patient takes substance to prevent withdrawal	Withdrawal syndrome can occur with more subtle symptoms such as confusion

* DSM-5 denotes *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition.

16



ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH
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EXPERIMENTAL RESEARCH

Trends in Alcohol Consumption Among Older Americans: National Health Interview Surveys, 1997 to 2014

Rosalind A. Breslow, I-Jen P. Castle, Chiung M. Chen, and Barry I. Graubard

Background: The majority of U.S. older adults consume alcoholic beverages. The older population is projected to almost double by 2050. Substantially more drinkers are likely.

Purpose: To describe gender-specific trends (1997 to 2014) in prevalence of drinking status (lifetime abstention, former drinking, current drinking [including average volume], and binge drinking) among U.S. adults ages 60+ by age group and birth cohort.

Methods: In the 1997 to 2014 National Health Interview Surveys, 65,303 respondents ages 60+ (31,803 men, 33,500 women) were current drinkers; 6,570 men and 1,737 women were binge drinkers. Prevalence estimates and standard errors were computed by age group (60+, 60 to 64, 65 to 69, 70 to 74, 75 to 79, 80+) and birth cohort (<1925, 1925 to 1935, 1936 to 1945, 1946 to 1954). Trends were examined using joinpoint regression and described as average annual percent change (AAPC); overall change 1997 to 2014) and annual percent change (APC; in-between infection points). Primary analyses were unadjusted. All analyses (unadjusted and adjusted for demographics/lifestyle) were weighted to produce nationally representative estimates. Statistical procedures accounted for the complex survey design.

Results: Among men ages 60+, unadjusted prevalence of current drinking trended upward, on average, 0.7% per year (AAPC, $p \sim 0.02$); average volume and prevalence of binge drinking remained stable. Adjusted results were similar. Among women age 60+, unadjusted prevalence of current drinking trended upward, on average, 1.6% per year (AAPC, $p < 0.0001$), but average volume remained stable; prevalence of binge drinking increased, on average, 3.7% per year (AAPC, $p < 0.0001$). Adjusted results were similar. Trends varied by age group and birth cohort. Among men born 1946 to 1954, unadjusted prevalence of current drinking trended upward, on average, 2.4% per year (AAPC, $p \sim 0.02$); adjusted results were nonsignificant.

Conclusions: Our finding of upward trends in drinking among adults ages 60+, particularly women, suggests the importance of public health planning to meet future needs for alcohol-related programs.

17

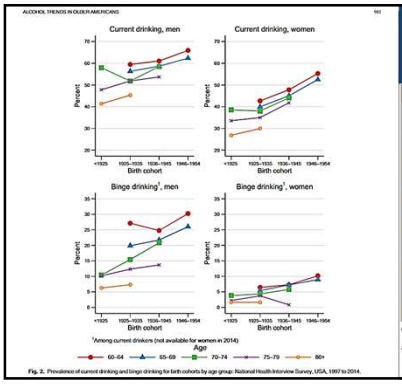


Fig. 2. Prevalence of current drinking and binge drinking for birth cohorts by age group: National Health Interview Survey, USA, 1997 to 2014.

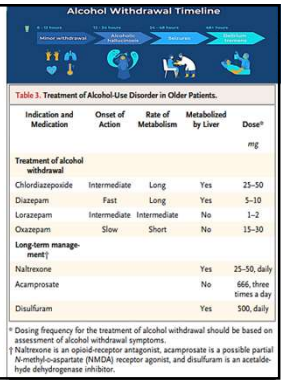


Table 3. Treatment of Alcohol-Use Disorder in Older Patients.

Indication and Medication	Onset of Action	Rate of Metabolism	Metabolized by Liver	Dose*
				mg
Treatment of alcohol withdrawal				
Chlordiazepoxide	Intermediate	Long	Yes	25–50
Diazepam	Fast	Long	Yes	5–10
Lorazepam	Intermediate	Intermediate	No	1–2
Oxazepam	Slow	Short	No	15–30
Long-term management†				
Naltrexone			Yes	25–50, daily
Acamprosate			No	666, three times a day
Disulfuram			Yes	500, daily

* Dosing frequency for the treatment of alcohol withdrawal should be based on assessment of alcohol withdrawal symptoms.
† Naltrexone is an opioid-receptor antagonist, acamprosate is a possible partial *N*-methyl-D-aspartate (NMDA) receptor agonist, and disulfuram is an acetaldehyde dehydrogenase inhibitor.

18

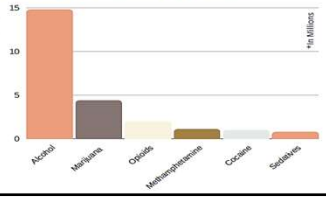
Prevalence in the U.S.

In the United States, over 20 million people suffer from addiction – that's one in seven people.[2] Nearly 50 percent of people in the U.S. know someone who has suffered or is currently suffering from a substance use disorder.[3] And 23 million Americans are in recovery, proving that a person can be treated and recover from this illness.[4]

Alcohol use disorder is the most prevalent addiction in the U.S., followed by marijuana and opioid use disorder. The types of substance use disorder broken down from 2018 data shows:[2]

- 14.8 million people aged 12 or older had an alcohol use disorder;
- 4.4 million people aged 12 or older had a marijuana use disorder;
- 2 million people had an opioid use disorder;
- 1.1 million people had a methamphetamine use disorder;
- 997,000 people had a cocaine use disorder; and
- 751,000 people had a sedative use disorder.

Figure 1
Prevalence of Substance Use Disorders



19

Addiction Facts and Figures

People in the U.S. suffer from addiction

1 in 7

are expected to develop a substance use disorder at some point in their lives.

of people in the U.S. know someone who has suffered or is currently suffering from a substance use disorder

23 MILLION

Americans are in recovery, proving that a person can be treated and recover from this illness.

<18

90% of Americans with a substance use disorder began using substances before the age of 18.

Research suggests genetic factors account for about half of a person's likelihood of developing a SUD.

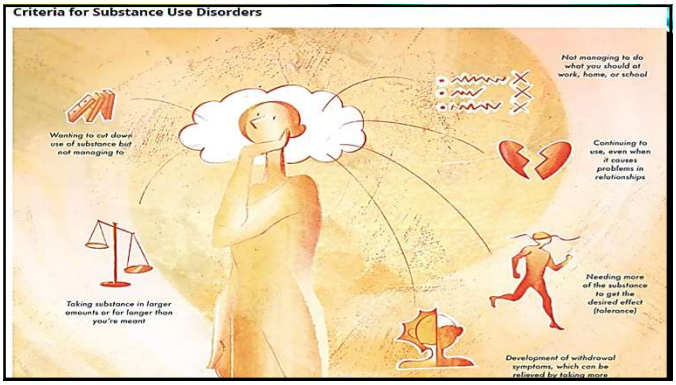
Only about 10 percent of people with a substance use disorder receive any type of specialty treatment.

The DSM-5 has helped change how we think about addictions by not overly focusing on withdrawal.

The DSM-5 has eleven criteria for substance use disorders based on decades of research.

20

Criteria for Substance Use Disorders



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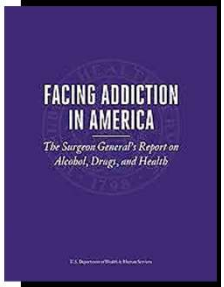
CHAPTER 2.
THE NEUROBIOLOGY OF SUBSTANCE USE, MISUSE, AND ADDICTION



Chapter 2 Preview

A substantial body of research has accumulated over several decades and transformed our understanding of substance use and its effects on the brain. This knowledge has opened the door to new ways of thinking about prevention and treatment of substance use disorders.

This chapter describes the neurobiological framework underlying substance use and why some people transition from using or misusing alcohol or drugs to a substance use disorder—including its most severe form, addiction. The chapter explains how these substances produce changes in brain structure and function that promote and sustain addiction and contribute to relapse. The chapter also addresses similarities and differences in how the various classes of addictive substances affect the brain and behavior and provides a brief overview of key factors that influence risk for substance use disorders.

22

KEY FINDINGS*

- Well-supported scientific evidence shows that addiction to alcohol or drugs is a chronic brain disease that has potential for recurrence and recovery.
- Well-supported evidence suggests that the addiction process involves a three-stage cycle: binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation. This cycle becomes more severe as a person continues substance use and as it produces dramatic changes in brain function that reduce a person's ability to control his or her substance use.
- Well-supported scientific evidence shows that disruptions in three areas of the brain are particularly important in the onset, development, and maintenance of substance use disorders: the basal ganglia, the extended amygdala, and the prefrontal cortex. These disruptions: (1) enable substance-associated cues to trigger substance seeking (i.e., they increase incentive salience); (2) reduce sensitivity of brain systems involved in the experience of pleasure or reward, and heighten activation of brain stress systems; and (3) reduce functioning of brain executive control systems, which are involved in the ability to make decisions and regulate one's actions, emotions, and impulses.
- Supported scientific evidence shows that these changes in the brain persist long after substance use stops. It is not yet known how much these changes may be reversed or how long that process may take.
- Well-supported scientific evidence shows that adolescence is a critical "at-risk period" for substance use and addiction. All addictive drugs, including alcohol and marijuana, have especially harmful effects on the adolescent brain, which is still undergoing significant development.

* Well-supported: when evidence is derived from multiple rigorous human and nonhuman studies; Supported: when evidence is derived from rigorous but fewer human and nonhuman studies.

23

A Basic Primer on the Human Brain

To understand how addictive substances affect the brain, it is important to first understand the basic biology of healthy brain function. The brain is an amazingly complex organ that is constantly at work. Within the brain, a mix of chemical and electrical processes controls the body's most basic functions, like breathing and digestion. These processes also control how people react to the multitudes of sounds, smells, and other sensory stimuli around them, and they organize and direct individuals' highest thinking and emotive powers so that they can interact with other people, carry out daily activities, and make complex decisions.

The brain is made of an estimated 86 billion nerve cells—called neurons—as well as other cell types. Each neuron has a cell body, an axon, and dendrites (Figure 2.1). The cell body and its nucleus control the neuron's activities. The axon extends out from the cell body and transmits messages to other neurons. Dendrites branch out from the cell body and receive messages from the axons of other neurons.

Neurons communicate with one another through chemical messengers called neurotransmitters. The neurotransmitters cross a tiny gap, or synapse, between neurons and attach to receptors on the receiving neuron. Some neurotransmitters are inhibitory—they make it less likely that the receiving neuron will carry out some action. Others are excitatory, meaning that they stimulate neuronal function, priming it to send signals to other neurons.

Neurons are organized in clusters that perform specific functions (described as networks or circuits). For example, some networks are involved with thinking, learning, emotions, and memory. Other networks communicate with muscles, stimulating them into action. Still others receive and interpret stimuli from the sensory organs, such as the eyes and ears, or the skin. The addiction cycle disrupts the normal functions of some of these neuronal networks.

Figure 2.1: A Neuron and its Parts

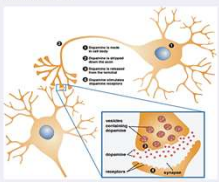
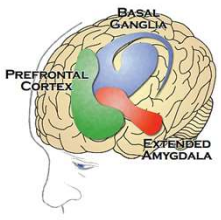


Figure 2.2: Areas of the Human Brain that Are Especially Important in Addiction



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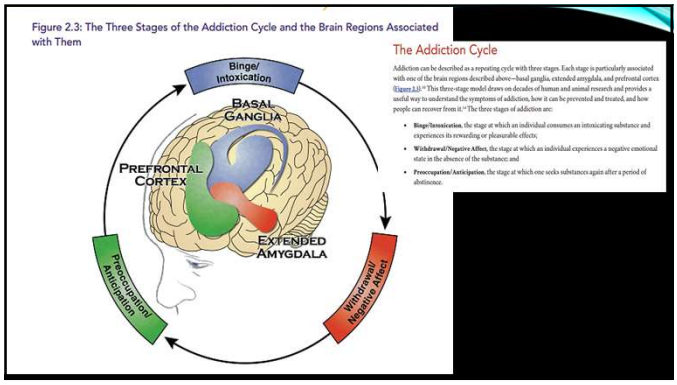

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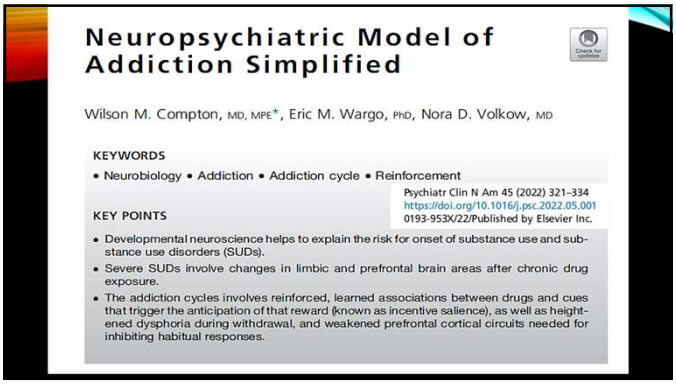

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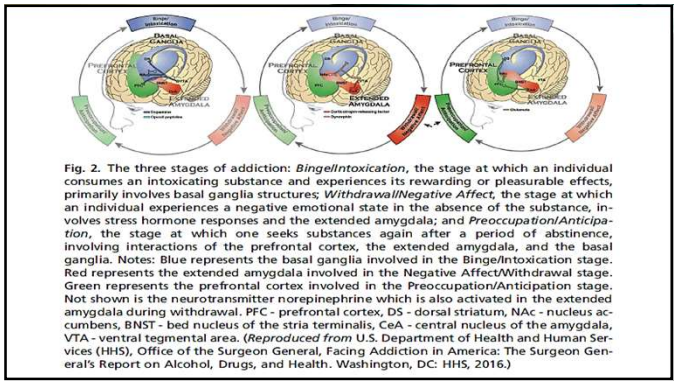

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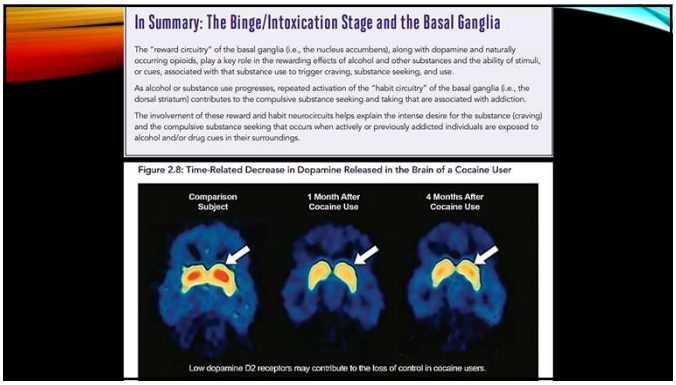

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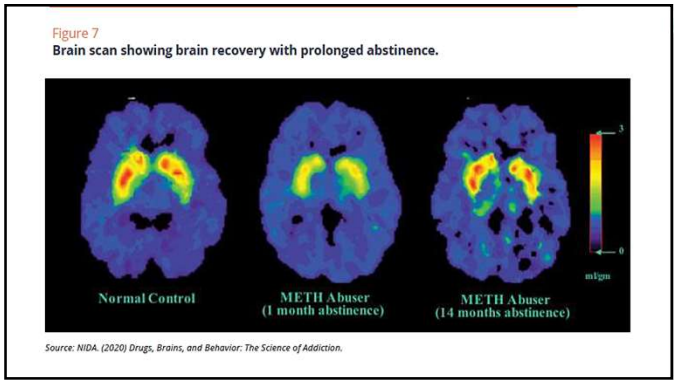

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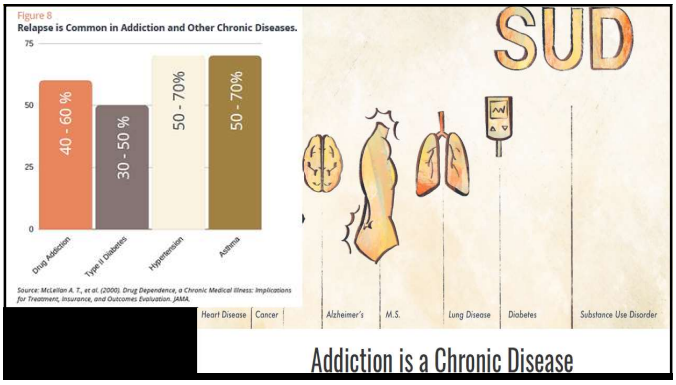


30

Box 1
Reinforcement (dopamine signaling) mechanisms for major drug classes

OPIOIDS

Opioids, including morphine heroin, fentanyl, and prescription analgesics such as oxycodone, increase dopamine signaling in the basal ganglia indirectly through their actions at specific opioid receptors, especially the mu opioid receptor. Preclinical research shows that the activation of mu-opioid receptors on gamma aminobutyric acid (GABA) cells in the VTA disinhibits dopamine neurons increasing their activity and enhancing dopamine release in the NAC.[49]

ALCOHOL

Alcohol's reinforcing effects have been associated with processes involving multiple molecular targets, including the enhancement of opioid signaling through mu-opioid receptors. Alcohol also enhances GABAergic neurotransmission via its direct effects on GABA-A receptors which are believed to contribute to reward and to its anxiolytic effects.[4]

31

Box 1
Reinforcement (dopamine signaling) mechanisms for major drug classes

STIMULANTS (COCAINE AND AMPHETAMINE-LIKE SUBSTANCES)

The reinforcing effects of stimulants are mediated by their direct effects on dopamine neurons. Cocaine enhances dopamine levels primarily by inhibiting the dopamine transporter, thus reducing the reuptake of dopamine from the synapse. Amphetamine-like substances, however, both inhibit the transporter and directly increase vesicular dopamine release.[47] In either case, the net effect is to increase dopamine in the NAC. The effects of this class of drugs are also mediated by increases in the activation of the other monoamine systems, serotonin and norepinephrine.[47] The bias toward a particular monoamine system depends on the specific stimulant. For example, cathinones (bath salts) have a greater effect on serotonin than does amphetamine, which is biased toward dopamine and norepinephrine systems.[50]

32

Box 1
Reinforcement (dopamine signaling) mechanisms for major drug classes

BENZODIAZEPINES

Benzodiazepines are allosteric modulators of GABA-A receptors, meaning that their binding shifts the way the receptor responds to its standard ligands. Although both GABA and dopamine neurons in the VTA express these receptors, benzodiazepines bind to those containing the alpha-1 subunit, which is only found on GABA neurons in the VTA and is lacking in VTA-dopamine neurons.[51–53] The resulting inhibition of VTA-GABA neurons enhances dopamine release. In human studies, benzodiazepines enhance the subjective effects of opioids, including "high" and "liking," indicating that these drugs' rewarding properties may be synergistic, accounting for their common couse.[54] Combining the 2 classes of drugs has also been implicated in increasing the risk for overdose, due to their shared effect of inhibiting respiration.[54–56]

33

Box 1
Reinforcement (dopamine signaling) mechanisms for major drug classes

NICOTINE

The reinforcing effects of nicotine are mediated by multiple receptors in the VTA and NAC,[4] and its actions at nicotinic acetylcholine receptors (nAChR) alpha-4 beta-2 subtype seem to be integral to these effects.[57] In addition to increasing dopamine discharge rate, nicotine changes the pattern of discharge to favor a phasic or bursting mode.[58] Dopamine bursting promotes the formation of associations between stimuli and rewards, and this may be the basis for reinforcement-enhancing effects of nicotine in combination with other substances.[25,59] Analyzing data from 2 cohort studies, Kandel and Kandel found that cocaine dependence was highest in users who had first smoked cigarettes and that concurrent smoking around the time of cocaine initiation was associated with more persistent cocaine use and addiction—consistent with the priming effect they found in an animal model. Conversely, cocaine does not seem to prime the nicotine response.[22] Nicotine's linkages to later addiction to other classes of drugs such as opioids are not fully established.

34

Box 1
Reinforcement (dopamine signaling) mechanisms for major drug classes

CANNABINOIDS

Cannabinoids activate type 1 cannabinoid receptors (CB1) in the VTA, but the mechanism by which this activation facilitates dopamine release is not well understood. Cannabis receptor pharmacology research is providing clues. For example, in light of the sometimes contradictory reinforcing and aversive effects of cannabis, Spiller and colleagues document the importance of the balance of both CB1 and CB2 receptor activation in cannabis effects.[60] Their work suggests that reinforcing and aversive effects may be mediated by differential CB1 and CB2 receptor expression.

35

Table 3.1: Risk Factors for Adolescent and Young Adult Substance Use

Risk Factors	Definition	Adolescent Substance Use	Young Adult Substance Use
Individual/Peer			
Early initiation of substance use[46,47]	Engaging in alcohol or drug use at a young age.	✔	✔
Early and persistent problem behavior[47,49]	Emotional distress, aggressiveness, and "difficult" temperaments in adolescents.	✔	
Rebelliousness[48,50]	High tolerance for deviance and rebellious activities.	✔	✔
Favorable attitudes toward substance use[51,52]	Positive feelings towards alcohol or drug use, low perception of risk.	✔	✔
Peer substance use[53-55]	Friends and peers who engage in alcohol or drug use.	✔	✔
Genetic predictors[56]	Genetic susceptibility to alcohol or drug use.	✔	✔
Family			
Family management problems (monitoring, rewards, etc.)[57-60]	Poor management practices, including parents' failure to set clear expectations for children's behavior, failure to supervise and monitor children, and excessively severe, harsh, or inconsistent punishment.	✔	✔
Family conflict[61-63]	Conflict between parents or between parents and children, including abuse or neglect.	✔	✔
Favorable parental attitudes[64,65]	Parental attitudes that are favorable to drug use and parental approval of drinking and drug use.	✔	✔
Family history of substance misuse[66,67]	Persistent, progressive, and generalized substance use, misuse, and use disorders by family members.	✔	✔

36

Risk Factors	Definition	Adolescent Substance Use	Young Adult Substance Use
School			
Academic failure beginning in late elementary school[64,69]	Poor grades in school.	✔	✔
Lack of commitment to school[70,71]	When a young person no longer considers the role of the student as meaningful and rewarding, or lacks investment or commitment to school.	✔	✔
Community			
Low cost of alcohol[50,72]	Low alcohol sales tax, happy hour specials, and other price discounting.	✔	✔
High availability of substances[73,74]	High number of alcohol outlets in a defined geographical area or per a sector of the population.	✔	✔
Community laws and norms favorable to substance use[75,76]	Community reinforcement of norms suggesting alcohol and drug use is acceptable for youth, including low tax rates on alcohol or tobacco or community beer tasting events.	✔	✔
Media portrayal of alcohol use[77-79]	Exposure to actors using alcohol in movies or television.	✔	
Low neighborhood attachment[80,81]	Low level of bonding to the neighborhood.	✔	
Community disorganization[82,83]	Living in neighborhoods with high population density, lack of natural surveillance of public places, physical deterioration, and high rates of adult crime.	✔	
Low socioeconomic status[84,85]	A parent's low socioeconomic status, as measured through a combination of education, income, and occupation.	✔	
Transitions and mobility[85,86]	Communities with high rates of mobility within or between communities.	✔	

37

Table 3.2: Protective Factors for Adolescent and Young Adult Substance Use

Protective Factors	Definition	Adolescent Substance Use	Young Adult Substance Use
Individual			
Social, emotional, behavioral, cognitive, and moral competence[87,88]	Interpersonal skills that help youth integrate feelings, thinking, and actions to achieve specific social and interpersonal goals.	✔	✔
Self-efficacy[89,90]	An individual's belief that they can modify, control, or abstain from substance use.	✔	✔
Spirituality[91,92]	Belief in a higher being, or involvement in spiritual practices or religious activities.	✔	✔
Resiliency[88]	An individual's capacity for adapting to change and stressful events in healthy and flexible ways.	✔	✔
Family, School, and Community			
Opportunities for positive social involvement[93,94]	Developmentally appropriate opportunities to be meaningfully involved with the family, school, or community.	✔	✔
Recognition for positive behavior[93]	Parents, teachers, peers and community members providing recognition for effort and accomplishments to motivate individuals to engage in positive behaviors in the future.	✔	✔
Bonding[95-97]	Attachment and commitment to, and positive communication with, family, schools, and communities.	✔	✔
Marriage or committed relationship[98]	Married or living with a partner in a committed relationship who does not misuse alcohol or drugs.		✔
Healthy beliefs and standards for behavior[97,99]	Family, school, and community norms that communicate clear and consistent expectations about not misusing alcohol and drugs.	✔	✔

38

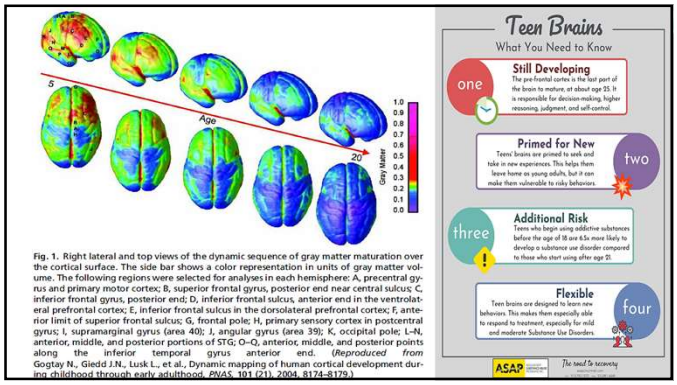
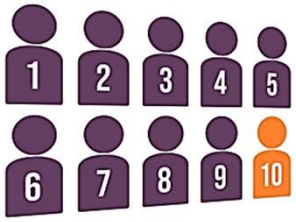


Fig. 1. Right lateral and top views of the dynamic sequence of gray matter maturation over the cortical surface. The side bar shows a color representation in units of gray matter volume. The following regions were selected for analyses in each hemisphere: A, precentral gyrus and primary motor cortex; B, superior frontal gyrus, posterior end near central sulcus; C, inferior frontal gyrus, posterior end; D, inferior frontal sulcus, anterior end in the ventrolateral prefrontal cortex; E, inferior frontal sulcus in the dorsolateral prefrontal cortex; F, anterior limit of superior frontal sulcus; G, frontal pole; H, primary sensory cortex in postcentral gyrus; I, supramarginal gyrus (area 40); J, angular gyrus (area 39); K, occipital pole; L–N, anterior, middle, and posterior portions of STG; O–Q, anterior, middle, and posterior points along the inferior temporal gyrus anterior end. (*Reproduced from* Gogtay N., Giedd J.N., Lusk L., et al., Dynamic mapping of human cortical development during childhood through early adulthood. *PNAS*, **101** (21), 2004, 8174–8179.)

39

Substance Use Disorders are Pediatric-Onset Diseases

- 9 out of 10 adults (90%) with substance use disorders initiated their use before age 18
- The earlier and heavier the use, the more likely a person will develop later problems
- All substance use puts adolescents at increased risk for a variety of adverse health outcomes



National Center on Addiction and Substance Abuse at Columbia University. (2011). Adolescent Substance Use: America's #1 Public Health Problem. New York, NY: Author.

www.OneChoicePrevention.org 4

40

Signs, Symptoms & Early Intervention

Because substance use disorder is a progressive disease, intervening in the early stages greatly improves outcomes. Families should take warning signs seriously.[10] Concerned significant others may report these signs and symptoms:

- Their loved one starts behaving differently for no apparent reason — such as acting withdrawn, frequently tired or depressed, or hostile
- Disinterest in activities that were previously enjoyable
- Loss of money, missing valuables, and borrowing
- Change in daily routine
- Loss of interest in overall health, hygiene, preventative and dental care
- Changes in mood
- Change in weight or appearance
- Change in sexual behavior
- Change in weight, eating or sleeping habits
- A decline in performance at work or school
- Change in peer group
- Secrecy regarding phone
- A tendency to disappear for hours at a time
- Deteriorating relationships
- Inability to be present when in conversation

26 Addiction Policy Forum

41

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Drug use among youth: National survey data support a common liability of all drug use

Robert L. DuPont[a,*], Beth Han[b], Corinne L. Shea[a], Bertha K. Madras[c,d]

[a] Institute for Behavior and Health, Inc., 6191 Executive Blvd, Rockville, MD 20852, USA
[b] Substance Abuse and Mental Health Services Administration, 5600 Fishers Lane, Rockville, MD 20852, USA
[c] McLean Hospital, 115 Mill Street, Belmont, MA 02478, USA
[d] Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA

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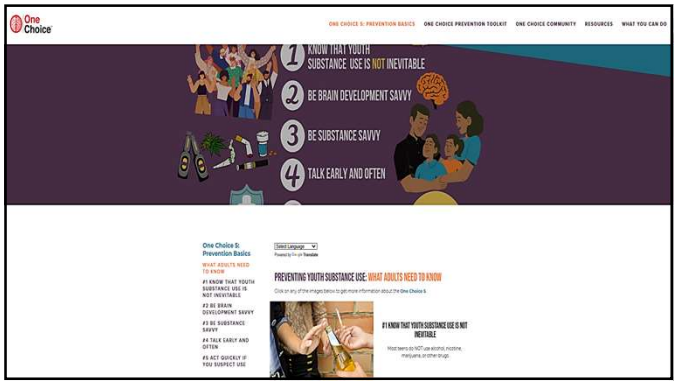
ABSTRACT

The prevalence of substance use disorders in adults is higher if substance use is initiated during adolescence, underscoring the importance of youth substance use prevention. We examined whether the use of one substance by adolescents is associated with increased risk for using any other substance, regardless of use sequences. In 2017 we examined data from 17,000 youth aged 12–17 who participated in the 2014 National Survey on Drug Use and Health, a sample of nationally representative data on substance use among the U.S. civilian, non-institutionalized population aged 12 or older. Descriptive analyses and multivariable logistic regression models were applied. After controlling for age, sex, and race/ethnicity, compared with youth without past-month marijuana use, youth with past-month marijuana use were 8.9 times more likely to report past-month cigarette use, 5.6, 7.9 and 15.8 times more likely to report past-month alcohol use, binge use, or heavy use (respectively), and 9.9 times more likely to report past-month use of other illicit drugs. The prevalence of past-month use of cigarettes, marijuana, and other illicit drugs was significantly higher among past-month alcohol users compared with youth without past-month alcohol use, and increased as intensity of alcohol use rose. Among past-month cigarette smokers, the prevalence of marijuana, other illicit drugs, and alcohol use were each significantly higher than youth without past-month cigarette use. Youth marijuana use, cigarette smoking, or alcohol consumption is associated with other substance use. This finding has importance for youth prevention, supporting a message no use by youth of any substance.

42



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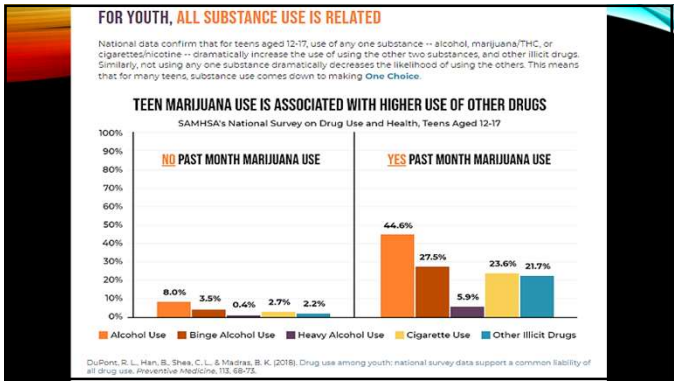

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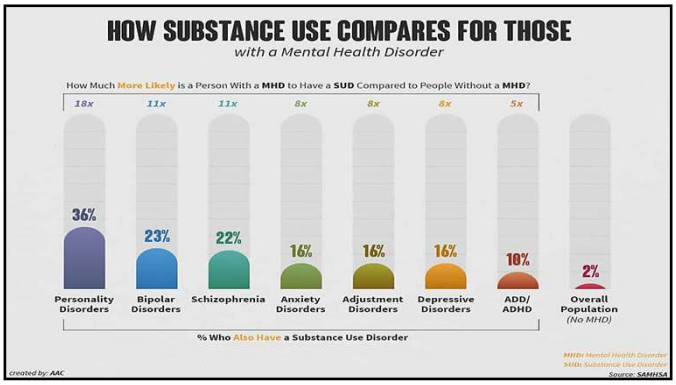

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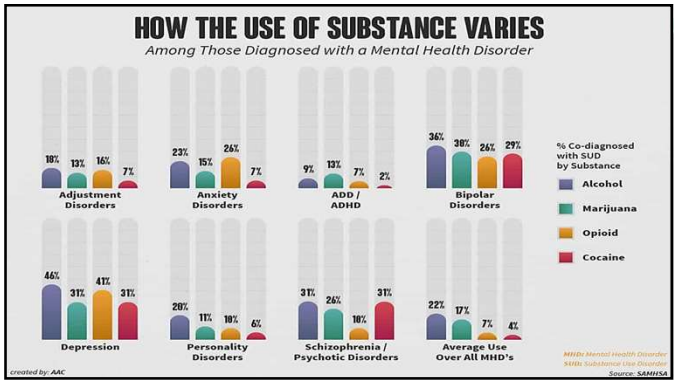

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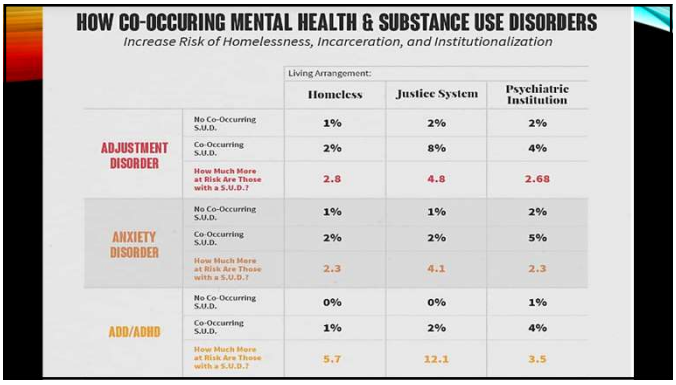

		Living Arrangement: Homeless	Justice System	Psychiatric Institution
ADJUSTMENT DISORDER	No Co-Occurring S.U.D.	1%	2%	2%
	Co-Occurring S.U.D.	2%	8%	4%
	How Much More at Risk Are Those with a S.U.D.?	2.8	4.8	2.68
ANXIETY DISORDER	No Co-Occurring S.U.D.	1%	1%	2%
	Co-Occurring S.U.D.	2%	2%	5%
	How Much More at Risk Are Those with a S.U.D.?	2.3	4.1	2.3
ADD/ADHD	No Co-Occurring S.U.D.	0%	0%	1%
	Co-Occurring S.U.D.	1%	2%	4%
	How Much More at Risk Are Those with a S.U.D.?	5.7	12.1	3.5

48

HOW CO-OCCURING MENTAL HEALTH & SUBSTANCE USE DISORDER

Increase Risk of Homelessness, Incarceration, and Institutionalization

		Living Arrangement: Homeless	Justice System	Psychiatric Institution
BIPOLAR DISORDER	No Co-Occurring S.U.D.	2%	1%	5%
	Co-Occurring S.U.D.	3%	4%	7%
	How Much More at Risk Are Those with a S.U.D.?	1.8	2.7	1.5
DEPRESSION	No Co-Occurring S.U.D.	2%	1%	4%
	Co-Occurring S.U.D.	3%	2%	6%
	How Much More at Risk Are Those with a S.U.D.?	1.9	2.9	1.6

49

HOW CO-OCCURING MENTAL HEALTH & SUBSTANCE USE DISORDERS

Increase Risk of Homelessness, Incarceration, and Institutionalization

		Living Arrangement: Homeless	Justice System	Psychiatric Institution
PERSONALITY DISORDER	No Co-Occurring S.U.D.	0%	2%	4%
	Co-Occurring S.U.D.	2%	23%	7%
	How Much More at Risk Are Those with a S.U.D.?	5.3	9.5	1.8
PSYCHOTIC DISORDER	No Co-Occurring S.U.D.	2%	2%	10%
	Co-Occurring S.U.D.	3%	4%	12%
	How Much More at Risk Are Those with a S.U.D.?	1.5	2.1	1.1

S.U.D. = Substance Use Disorder

50

BJPsych The British Journal of Psychiatry (2020) 216, 69–78. doi: 10.1192/bjp.2019.166

Review

The prevalence of personality disorders in the community: a global systematic review and meta-analysis

Catherine Winsper, Ayten Bilgin, Andrew Thompson, Steven Marwaha, Andrew M. Chanen, Swaran P. Singh, Ariel Wang and Vivek Furtado

Background
Personality disorders are now internationally recognised as a mental health priority. Nevertheless, there are no systematic reviews examining the global prevalence of personality disorders.

Aims
To calculate the worldwide prevalence of personality disorders and examine whether rates vary between high-income countries and low- and middle-income countries (LMICs).

Method
We systematically searched PsychINFO, MEDLINE, EMBASE and PubMed from January 1980 to May 2018 to identify articles reporting personality disorder prevalence rates in community populations (PROSPERO registration number: CRD42017065094).

Results
A total of 46 studies (from 21 different countries spanning 6 continents) satisfied inclusion criteria. The worldwide pooled prevalence of *any* personality disorder was 7.8% (95% CI 6.1–9.5). Rates were greater in high-income countries (9.6%, 95% CI 7.9–11.3%) compared with LMICs (6.3%, 95% CI 2.6–6.1%). In univariate meta-regressions, significant heterogeneity was partly attributable to study design (two-stage *v.* one-stage assessment), country income (high-income countries *v.* LMICs) and interview administration (clinician *v.* trained graduate). In multiple meta-regression analysis, study design remained a significant predictor of heterogeneity. Global rates of cluster A, B and C personality disorders were 3.8% (95% CI 3.2, 4.4%), 2.8% (1.6, 3.7%) and 5.0% (4.2, 5.9%).

Conclusions
Personality disorders are prevalent globally. Nevertheless, pooled prevalence rates should be interpreted with caution due to high levels of heterogeneity. More large-scale studies with standardised methodologies are now needed to increase our understanding of population needs and regional variations.

Declaration of interest
None reported.

Keywords
Personality disorder; prevalence; systematic review; meta-analysis; LMIC.

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51

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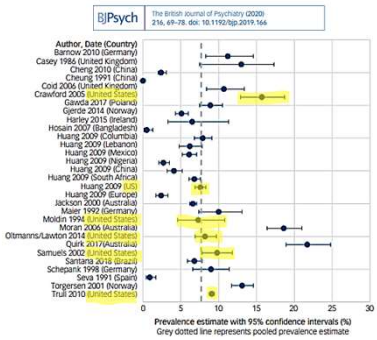

Fig. 2 The pooled prevalence of 'any' personality disorder in community populations.

52

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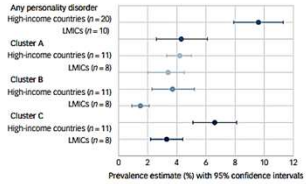

Fig. 3 Personality disorder pooled prevalence according to country income status.
LMIC, low- and middle-income country.

53

The Three Personality Disorder Clusters

Cluster A
The Odd, Eccentric Cluster
Includes:
- Paranoid Personality Disorder
- Schizoid Personality Disorder
- Schizotypal Personality Disorder

Cluster B
The Dramatic, Unpredictable Cluster
Includes:
- Antisocial Personality Disorder
- Borderline Personality Disorder
- Histrionic Personality Disorder
- Narcissistic Personality Disorder

Cluster C
The Anxious, Fearful Cluster
Includes:
- Avoidant Personality Disorder
- Dependent Personality Disorder
- Obsessive-compulsive Personality Disorder

54

PD MOST LIKELY TO HAVE CO-OCCURRING SUD

- Antisocial – more likely male & impulsive, irresponsible and maybe criminal behavior
- Borderline-more women & fear of abandonment, unstable, intense relationships, anger issues, self-harm
- Avoidant-chronic feelings of inadequacy, highly sensitive to being negatively judged by others, pleaser
- Paranoid-more men & believe others are trying to demean, harm or threaten them. Severely limited social lives, stubborn, hostile

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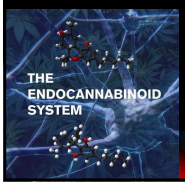
WHAT'S NEXT FOR RECREATIONAL CANNABIS: IMPLICATIONS FOR DENTISTRY

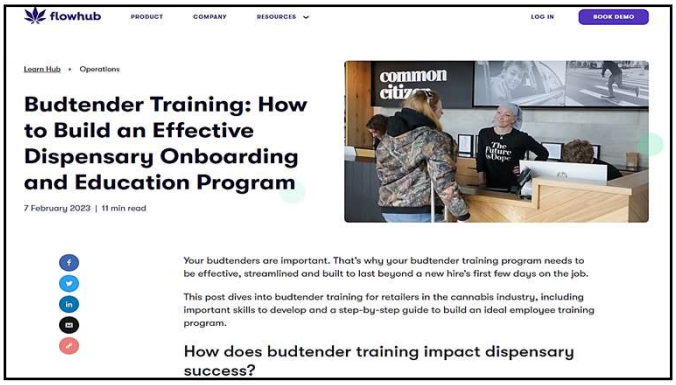


Karen A. Baker, M.S., B.S. R.Ph, Associate Professor
Oral Pathology, Radiology and Medicine
University of Iowa College of Dentistry

56

ANNUAL CANNABIS DAY IS APRIL 20TH

57



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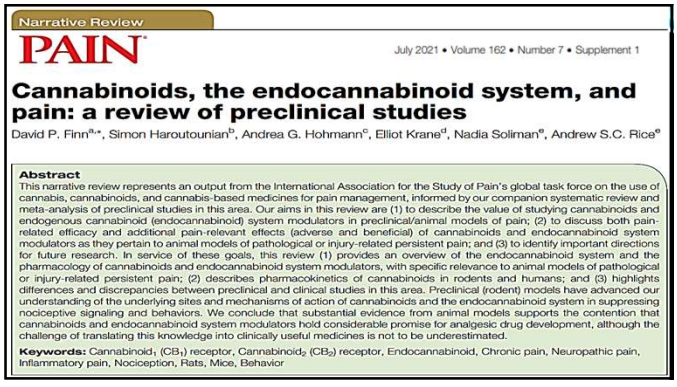
Narrative Review
PAIN
July 2021 • Volume 162 • Number 7 • Supplement 1

Cannabinoids, the endocannabinoid system, and pain: a review of preclinical studies

David P. Finn[a,*], Simon Haroutounian[b], Andrea G. Hohmann[c], Elliot Krane[d], Nadia Soliman[e], Andrew S.C. Rice[e]

Abstract
This narrative review represents an output from the International Association for the Study of Pain's global task force on the use of cannabis, cannabinoids, and cannabis-based medicines for pain management, informed by our companion systematic review and meta-analysis of preclinical studies in this area. Our aims in this review are (1) to describe the value of studying cannabinoids and endogenous cannabinoid (endocannabinoid) system modulators in preclinical/animal models of pain; (2) to discuss both pain-related efficacy and additional pain-relevant effects (adverse and beneficial) of cannabinoids and endocannabinoid system modulators as they pertain to animal models of pathological or injury-related persistent pain; and (3) to identify important directions for future research. In service of these goals, this review (1) provides an overview of the endocannabinoid system and the pharmacology of cannabinoids and endocannabinoid system modulators, with specific relevance to animal models of pathological or injury-related persistent pain; (2) describes pharmacokinetics of cannabinoids in rodents and humans; and (3) highlights differences and discrepancies between preclinical and clinical studies in this area. Preclinical (rodent) models have advanced our understanding of the underlying sites and mechanisms of action of cannabinoids and the endocannabinoid system in suppressing nociceptive signaling and behaviors. We conclude that substantial evidence from animal models supports the contention that cannabinoids and endocannabinoid system modulators hold considerable promise for analgesic drug development, although the challenge of translating this knowledge into clinically useful medicines is not to be underestimated.

Keywords: Cannabinoid$_1$ (CB_1) receptor, Cannabinoid$_2$ (CB_2) receptor, Endocannabinoid, Chronic pain, Neuropathic pain, Inflammatory pain, Nociception, Rats, Mice, Behavior

59

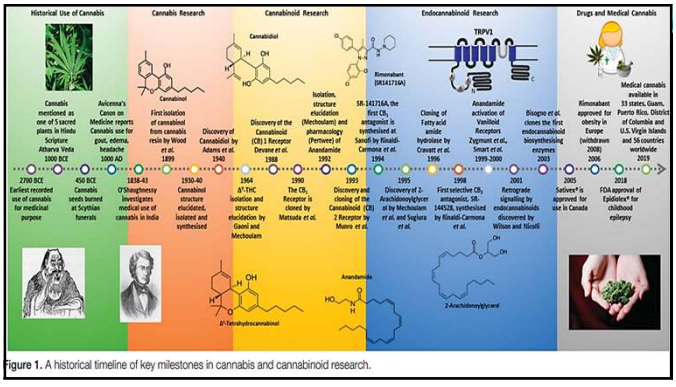

Figure 1. A historical timeline of key milestones in cannabis and cannabinoid research.

60

Terminology and Definitions (Adapted from Soliman et al., 2019, after modification from Hauser et al., 2018).

Term	Definition	Examples/typical products
(Herbal) cannabis	The whole plant or parts or material from the plant (eg, flowers, buds, resin, leaves)	*Cannabis sativa*, hashish
Medical or medicinal cannabis	The term "medical/medicinal cannabis" (or "medical/medicinal marijuana") is used for cannabis plants, plant material, or full plant extracts used for medical purposes.	Bedrocan, Bedrobinol, tilray 10THC/10CBD
Cannabis-based (or cannabis-derived) medicines	Medicinal cannabis extracts or products with regulatory approval for marketing as a therapeutic with defined and standardized THC and/or CBD content.	Nabiximols (Sativex), dronabinol (Marinol), Epidiolex
Cannabinoids	Cannabinoids are biologically active constituents of cannabis, or synthetic compounds, usually having affinity for and activity at cannabinoid receptors.	THC, CBD, CP55,940, WIN55,212-2, HU210, nabilone
Phytocannabinoid	A cannabinoid found in cannabis plants or purified/ extracted from plant material	THC, CBD
Endocannabinoid	An endogenous ligand found in the body of humans and other animals and which has affinity for, and activity at, cannabinoid receptors	Anandamide, 2-AG
Modulators that decrease endocannabinoid system activity	Directly block cannabinoid receptors or reduce signalling indirectly via impeding action of endogenous ligand through actions at a distinct site	Cannabinoid receptor antagonists (rimonabant [SR141716A], AM251, SR144528, AM630), negative allosteric modulators (PSNCBAM-1), DAGL inhibitors (RHC80267)
Modulators that increase or enhance endocannabinoid system activity	In addition to individual phytocannabinoids, cannabis-derived or cannabis-based medicines, and cannabis extracts, other pharmacological approaches under development for manipulation of the endocannabinoid system include selective synthetic cannabinoid receptor agonists, inhibitors of the catabolism (eg, fatty acid amide hydrolase [FAAH] inhibitors), transport (eg, fatty acid–binding protein [FABP] inhibitors) or reuptake of endocannabinoids, or positive allosteric modulators of cannabinoid receptor signalling.	FAAH inhibitors (PF-04457845, URB597, URB937), anandamide transport inhibitors (AM404, VDM11), MGL inhibitors (URB602, -JZL184, MJN110), positive allosteric modulators of the CB_1 receptor (ZCZ011, GAT211)

CBD, cannabidiol; CB_1, cannabinoid type 1; DAGL, diacylglycerol lipase; FABP, fatty acid–binding protein; THC, Δ^9-tetrahydrocannabinol; 2-AG, 2-arachidonoyl glycerol; MGL, monoacylglycerol lipase.

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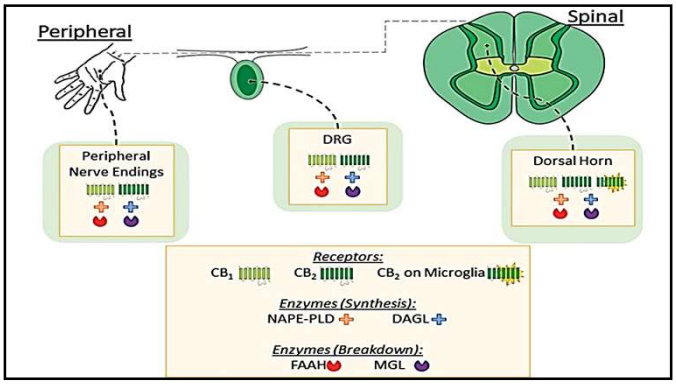

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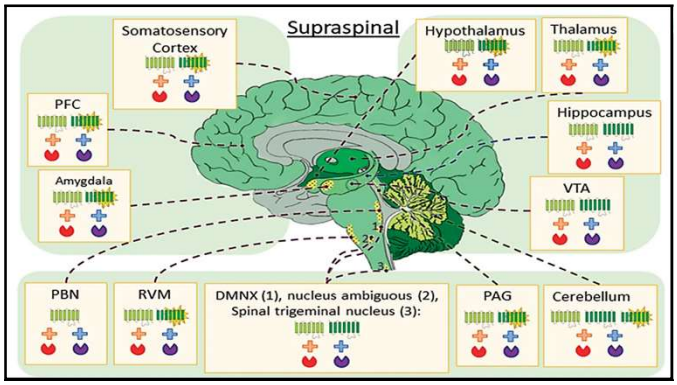

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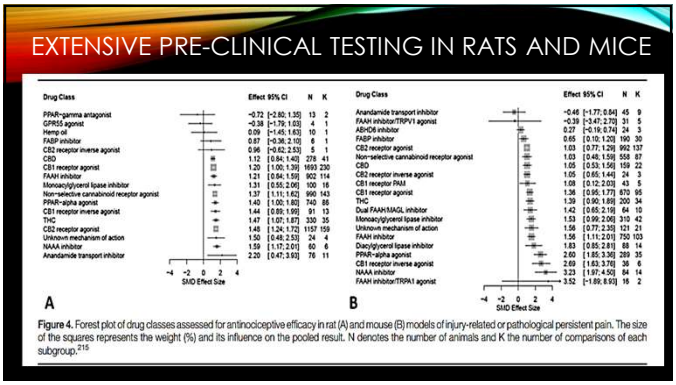

Figure 4. Forest plot of drug classes assessed for antinociceptive efficacy in rat (A) and mouse (B) models of injury-related or pathological persistent pain. The size of the squares represents the weight (%) and its influence on the pooled result. N denotes the number of animals and K the number of comparisons of each subgroup.[215]

64

MEANWHILE..WHAT ARE ALL THE HUMANS USING?

- Two major cannabinoids are:
  - ▲9-tetrahydrocannabinol (THC)
  - Cannabidiol (CBD)
- Recreational cannabis has high THC:CBD ratio for psychoactivity
- Medical cannabis has more CBD to reduce the "high" but still benefit
- Eating the female plant does NOT make you high because the THC/CBD isn't in active form until decarboxylated
- Dramatic rise in THC content since 2005 has produced dire consequences

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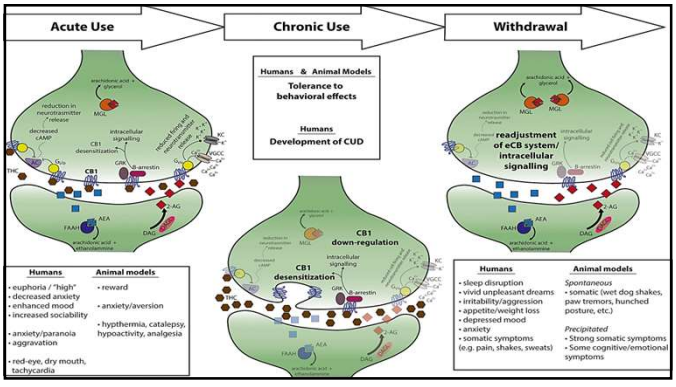

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REVIEW ARTICLE

Legalized Cannabis in Colorado Emergency Departments: A Cautionary Review of Negative Health and Safety Effects

Brad A. Roberts, MD University of New Mexico, Department of Emergency Medicine, Albuquerque, New Mexico
Partner, Southern Colorado Emergency Medicine Associates, Pueblo, Colorado

Section Editor: Mark I. Langdorf, MD, MHPE
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DOI: 10.5811/westjem.2019.4.39935

Cannabis legalization has led to significant health consequences, particularly to patients in emergency departments and hospitals in Colorado. The most concerning include psychosis, suicide, and other substance abuse. Deleterious effects on the brain include decrements in complex decision-making, which may not be reversible with abstinence. Increases in fatal motor vehicle collisions, adverse effects on cardiovascular and pulmonary systems, inadvertent pediatric exposures, cannabis contaminants exposing users to infectious agents, heavy metals, and pesticides, and hash-oil burn injuries in preparation of drug concentrates have been documented. Cannabis dispensary workers ("budtenders") without medical training are giving medical advice that may be harmful to patients. Cannabis research may offer novel treatment of seizures, spasticity from multiple sclerosis, nausea and vomiting from chemotherapy, chronic pain, improvements in cardiovascular outcomes, and sleep disorders. Progress has been slow due to absent standards for chemical composition of cannabis products and limitations on research imposed by federal classification of cannabis as illegal. Given these factors and the Colorado experience, other states should carefully evaluate whether and how to decriminalize or legalize non-medical cannabis use. [West J Emerg Med. 2019;20(4)557–572.]

67

REPORTED CARDIOVASCULAR EVENTS ARE ALARMING

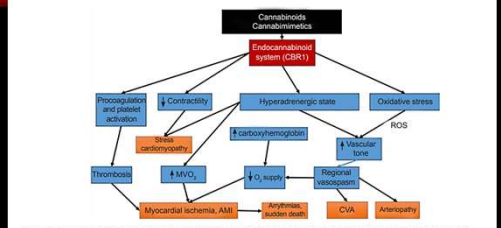

Figure 7. Flow diagram demonstrating pathophysiologic pathways to common major adverse cardiovascular events reported in users of cannabis and related chemicals.[6] *AMI*, acute myocardial infarction; *CBR1*, cannabinoid receptor 1; *CVA*, cerebrovascular accident; MVO_2 myocardial oxygen consumption (demand); O_2, oxygen; *ROS*, reactive oxygen species.

68

YET THESE SITES SAY THIS IS A "DEBUNKED MYTH"

69

CANNABIS SATIVA FLOWERS OR BUDS CONTAIN THC

- Delta-9 Tetrahydrocannabinol produces psychoactive effects
- Cannabidiol is not supposed to contain any psychoactives

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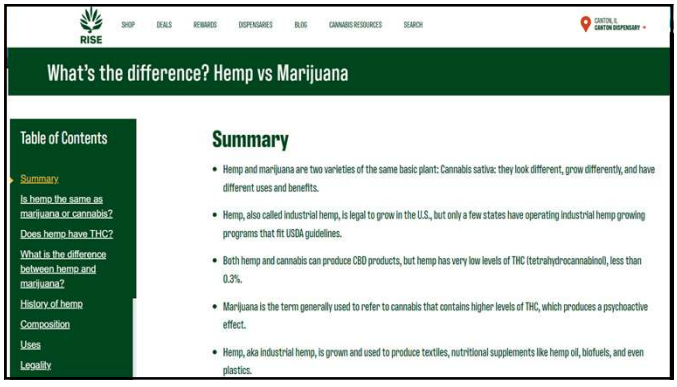

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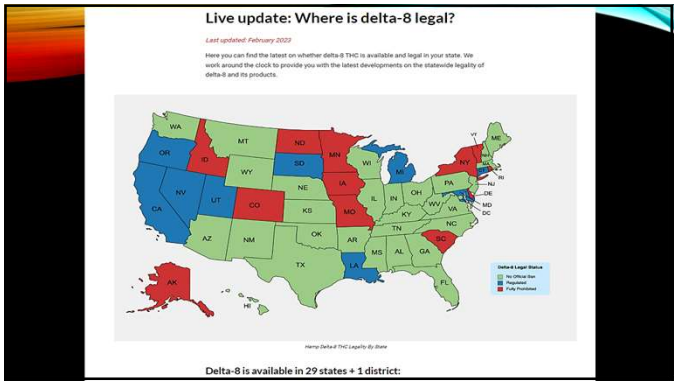
1. Delta-8 THC products have not been evaluated or approved by the FDA for safe use and may be marketed in ways that put the public health at risk.

The FDA is aware of the growing concerns surrounding delta-8 THC products currently being sold online and in stores. These products have not been evaluated or approved by the FDA for safe use in any context. Some concerns include variability in product formulations and product labeling, other cannabinoid and terpene content, and variable delta-8 THC concentrations. Additionally, some of these products may be labeled simply as "hemp products," which may mislead consumers who associate "hemp" with "non-psychoactive." Furthermore, the FDA is concerned by the proliferation of products that contain delta-8 THC and are marketed for therapeutic or medical uses, although they have not been approved by the FDA. Selling unapproved products with unsubstantiated therapeutic claims is not only a violation of federal law, but also can put consumers at risk, as these products have not been proven to be safe or effective. This deceptive marketing of unproven treatments raises significant public health concerns because patients and other consumers may use them instead of approved therapies to treat serious and even fatal diseases.

72



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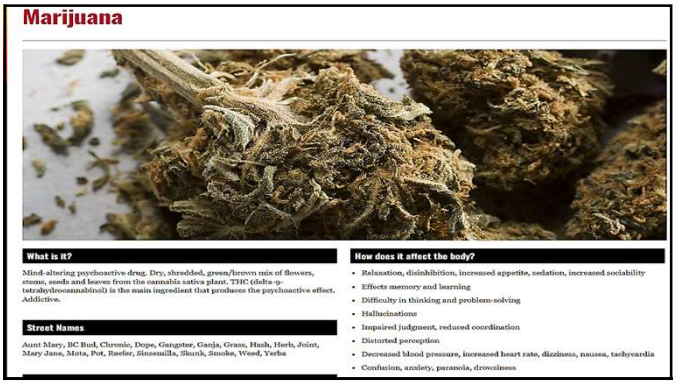

74

CANNABIS PRODUCTS CONTAIN THC & MAYBE CBD

- Different types of cannabis edibles
- Edibles come in many forms:
- Gummies and chews
- Brownies, cookies, and other baked goods
- Chocolates and caramels
- Ice cream
- Mints and breath strips
- Lozenges and lollipops
- Sodas and other drinks
- Novelty items like beef jerky, potato chips, and more

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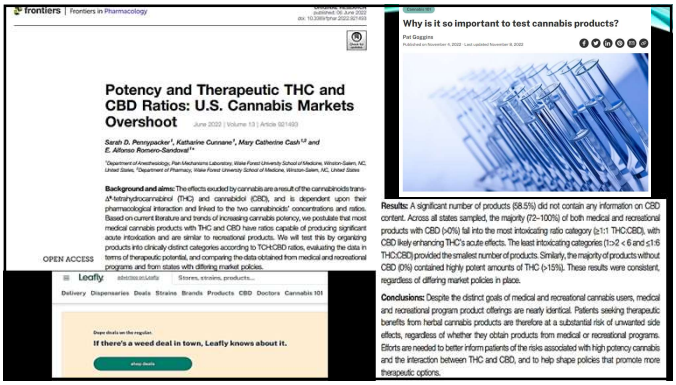

76

WHAT TYPE OF CANNABIS EDIBLES GET YOU HIGHEST?

- Hard candy and pastille edibles, like lollipops, gum, mints, and lozenges, as well as beverages, have some of the quickest onset times because they are absorbed primarily through the oral mucous membranes rather than the gastrointestinal tract
- Chewy and sweet edibles like gummies, caramels, and chocolates have a median onset time because they do have to be digested but that process is fairly quick due to composition.
- Baked goods tend to have the most delayed onset largely due to their density and the energy required to digest and metabolize.
- In general, combining edibles with alcohol produces effects ranging from unpleasant to DANGEROUS. AVOID THIS COMBO.

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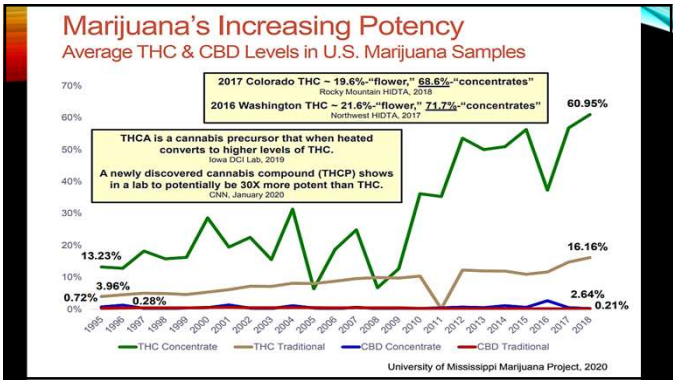

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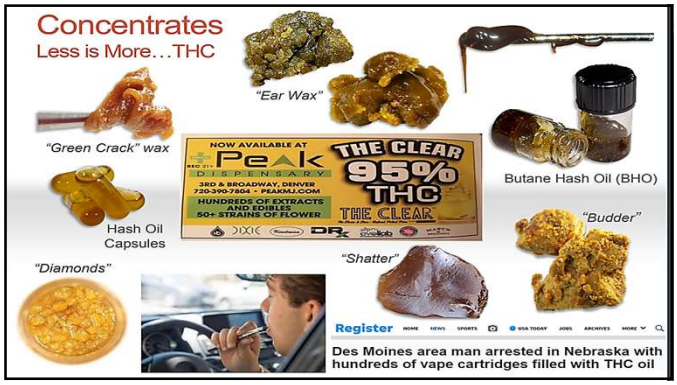

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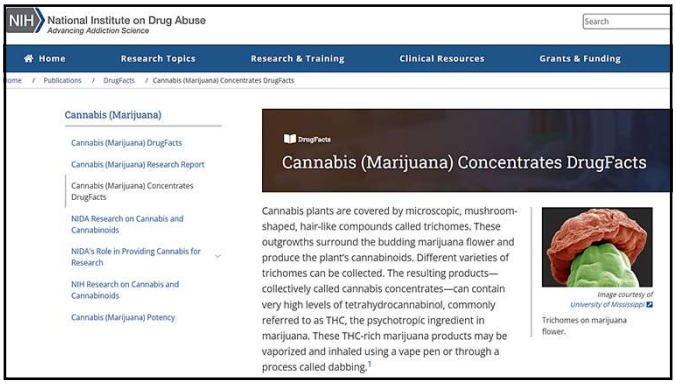

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How are concentrates made?

Marijuana concentrates can be made in a commercial environment with modern equipment or prepared in a home setting.[2] They are produced in various ways, including:

- dry processing
- dry ice processing
- water-based processing
- combining pressure with heat
- using nonflammable carbon dioxide solvents
- using flammable solvents, including butane (lighter fluid), propane, ether or alcohol[1]

Using flammable solvents is popular because the products have high THC levels,[1] users report longer-lasting effects,[1] and it is a relatively inexpensive and efficient production method.[2] Butane is a commonly used solvent, producing the potent marijuana concentrate *butane hash oil* (BHO).[2]

81

What does the final product look like?

The products resulting from these methods may be:

- a gooey liquid wax
- a soft solid with a texture like lip balm
- a hard, amber-colored solid

Image courtesy of pixabay.com. CC0

Hash oil and waxes can be consumed using vape pens. Solids can also be placed on a heated platform usually made of titanium, quartz, or ceramic, where they are vaporized by high heat and inhaled through a dabbing tool, often called a rig.[2]

82

What's the difference between concentrates, extracts, and dabs?

The terms used to describe these products vary. Concentrates is a broad term referring to all products that have been extracted from the plant. Although extracts and concentrates are often used interchangeably, some people define extracts as products manufactured using solvents, but not those pulled from the plant with non-solvent methods. Dabs may refer to products made exclusively from butane hash oil; however, the term is sometimes used colloquially for concentrates extracted in other ways. There are also post-production methods that lead to further variations in products and terms.[3]

83

What are the health effects of concentrates?

There are adverse effects associated with marijuana use in any form,[3] though additional research is needed to understand how the use of concentrate may differ from smoking dried marijuana buds. Marijuana concentrates have very high levels of THC. Solvent-based products tend to be especially potent, with THC levels documented at an average of about 54-69% and reported to exceed 80%, while non-solvent based extraction methods produce average THC levels between 39-60%.[4] In comparison, the THC content in marijuana plant material, which is often used in marijuana cigarettes, is lower—with samples seized by the U.S. Drug Enforcement Agency averaging just over 15%.[5] Not only do concentrates have high levels of THC, but dabbers inhale the entire amount all at once—in a single breath.[2] As a result, concentrates can deliver extremely large amounts of THC to the body quickly. The risks of physical dependence and addiction increase with exposure to high concentrations of THC, and higher doses of THC are more likely to produce anxiety, agitation, paranoia, and psychosis.[6] Additional research is needed to understand how the use of concentrate affects these risks.

84

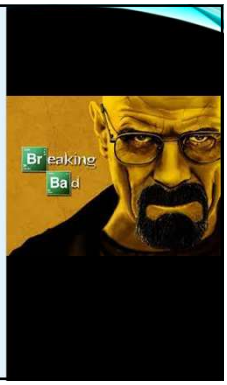
DABBING IS DANGEROUS DUE TO POTENCY, POTENTIAL CONTAMINANTS, AND SOLVENTS

In addition, contaminants in concentrate products may be cause for concern. One study noted that 80% of tested concentrate samples were contaminated in some form, not only with pesticides (which is also a concern for dried bud), but also with residual solvents that were not fully purged in the manufacturing process. Users of BHO, for example, likely inhale some butane and other impurities along with the vaporized THC.[2] It is important to note that direct inhalation of concentrated butane among recreational inhalant users carries multiple risks, including reported deaths.[7] However, it is unclear what negative health outcomes result from the inhalation of residual butane, other solvents, or leftover contaminants during the dabbing process.

85

Points to Remember

- Cannabis plants are covered by microscopic, mushroom-shaped, hair-like compounds called trichomes which surround the budding marijuana flower and produce the plant's cannabinoids.
- Trichomes can be collected and made into concentrates, including extracts and dabs.
- Concentrates can contain very high levels of THC, the psychotropic ingredient in marijuana.
- Concentrates can be vaporized and inhaled using a vape pen or by dabbing.
- Concentrates can be made in commercial settings or in a home through several methods, including dry ice- and water-based processing and the use of solvents.
- Using flammable solvents, such as butane, propane, ether or alcohol, is popular because it produces high THC levels, longer-lasting effects, and it's relatively inexpensive.
- Using butane as a solvent produces the potent marijuana concentrate butane hash oil (BHO).
- Exposure to high levels of THC increases the risks of physical dependence and addiction. Higher doses of THC are more likely to produce anxiety, agitation, paranoia, and psychosis.
- Contamination with pesticides and residual solvents that weren't fully removed during production is a concern. People who use BHO likely inhale some butane and other impurities along with the vaporized THC.



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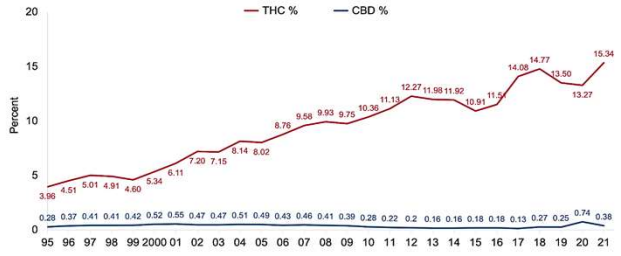
Percentage of THC and CBD in Cannabis Samples Seized by the DEA, 1995-2021



SOURCE: U Miss, Potency Monitoring Project

87

I Am One and I Make One Choice for Health

A Data-Informed, Youth-Driven, Prevention Message

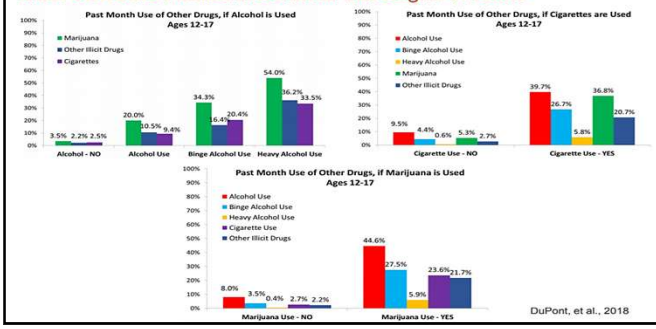
Institute for Behavior and Health, Inc.

www.OneChoicePrevention.org

88

Precursors to Substance Use Disorders (SUDs)

Most SUDs are Rooted in Behavior that Begins in Teens

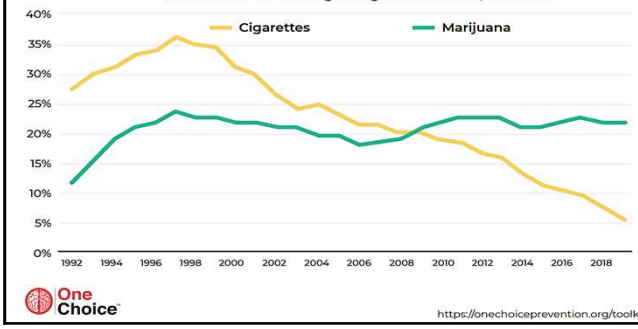


DuPont, et al., 2018

89

TEENS MORE LIKELY TO USE MARIJUANA THAN CIGARETTES

Past month use among 12th grade students, 1992-2019



One Choice

https://onechoiceprevention.org/toolkit

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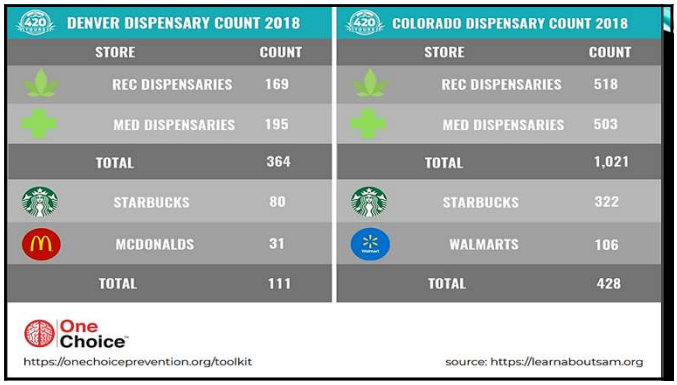

DENVER DISPENSARY COUNT 2018	
STORE	COUNT
REC DISPENSARIES	169
MED DISPENSARIES	195
TOTAL	364
STARBUCKS	80
MCDONALDS	31
TOTAL	111

COLORADO DISPENSARY COUNT 2018	
STORE	COUNT
REC DISPENSARIES	518
MED DISPENSARIES	503
TOTAL	1,021
STARBUCKS	322
WALMARTS	106
TOTAL	428

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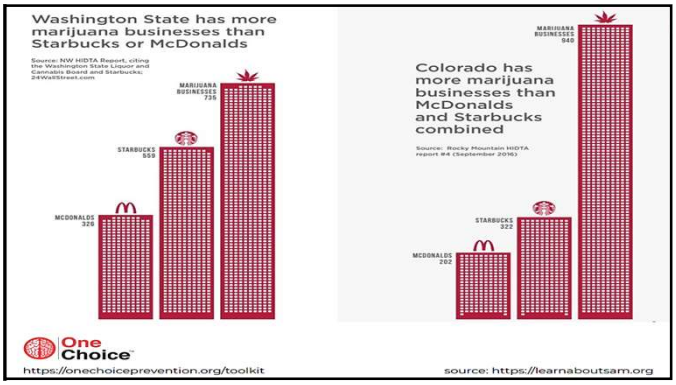

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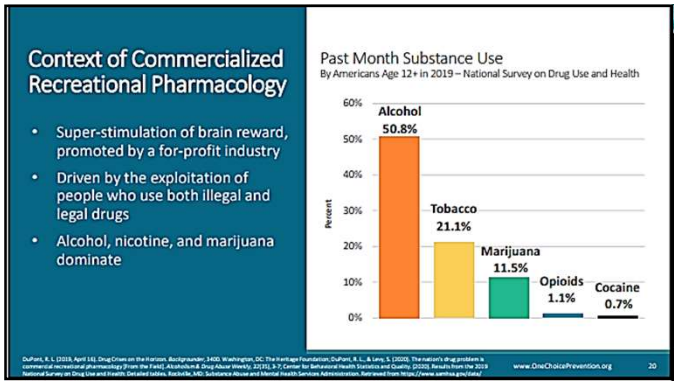

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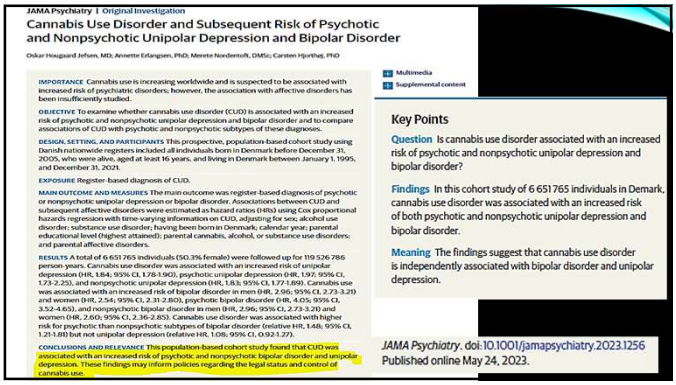

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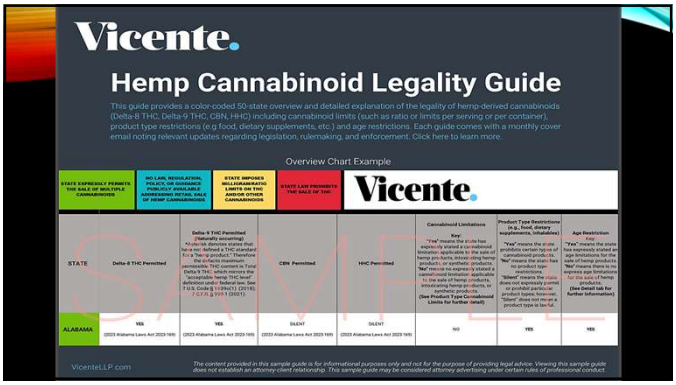

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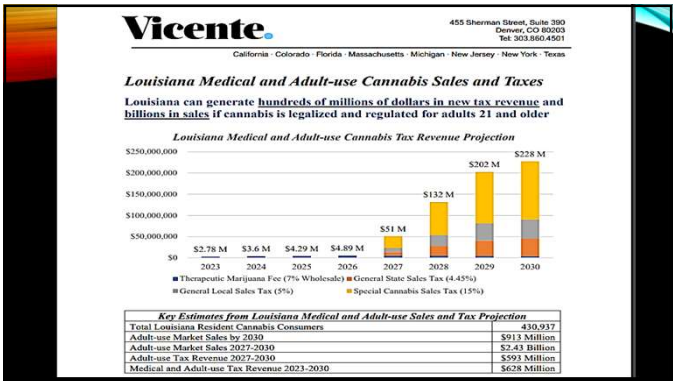

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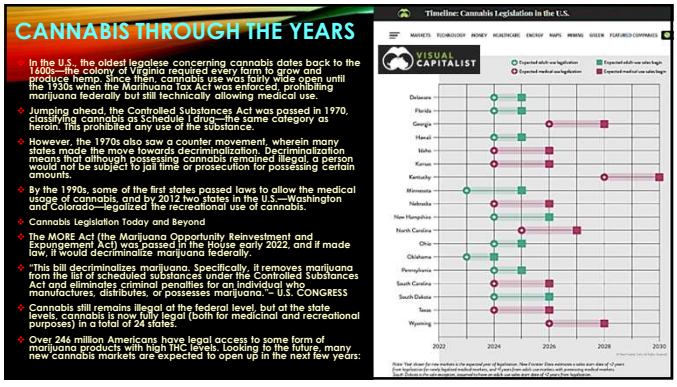

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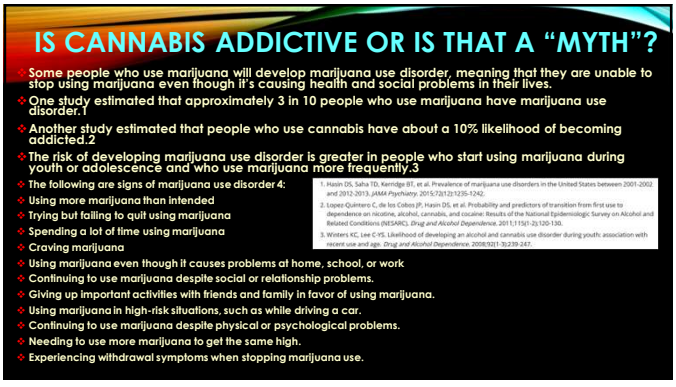

102

Table 3. DSM-5 Diagnostic Criteria for Cannabis Use Disorder and Cannabis Withdrawal Syndrome*

Cannabis Use Disorder†	Cannabis Withdrawal Syndrome
A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by ≥2 of the following within a 12-mo period:	Cessation of cannabis use that has been heavy and prolonged
Cannabis is often taken in larger amounts or over a longer period than was intended.	≥3 of the following signs and symptoms develop within approximately 1 wk after cannabis cessation:
There is a persistent desire or unsuccessful efforts are made to cut down or control cannabis use.	Irritability, anger, or aggression
A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.	Nervousness or anxiety
Recurrent cannabis use results in a failure to fulfill major role obligations at work, school, or home.	Sleep difficulty (e.g., insomnia, disturbing dreams)
Cannabis use continues despite persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.	Decreased appetite or weight loss
Important social, occupational, or recreational activities are given up or reduced because of cannabis use.	Restlessness
Cannabis use recurs in situations in which it is physically hazardous.	Depressed mood
Cannabis use continues despite knowledge of a persistent or recurrent physical or psychological problem likely to have been caused or exacerbated by use.	≥1 of the following physical symptoms, causing substantial discomfort:
Craving or a strong desire or urge to use cannabis	Abdominal pain
Tolerance	Shakiness/tremors
Withdrawal	Sweating
	Fever
	Chills
	Headache
	Distress or impairment
	No other explanation for symptoms
	Symptoms generally resolve in 7–14 d but may persist for weeks

DSM-5 = *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*.
* Adapted from reference 11.
† Characterized as mild if 2 or 3 criteria are met, moderate if 4 or 5 criteria are met, and severe if >6 criteria are met.

103

Cannabis

The Cannabis Use Disorder Identification Test – Revised (CUDIT-R)

Have you used any cannabis over the past six months? YES / NO

If YES, please answer the following questions about your cannabis use. Circle the response that is most correct for you in relation to your cannabis use over the past six months:

1.	How often do you use cannabis?	Never 0	Monthly or less 1	2–4 times a month 2	2–3 times a week 3	4 or more times a week 4
2.	How many hours were you "stoned" on a typical day when you had been using cannabis?	Less than 1 0	1 or 2 1	3 or 4 2	5 or 6 3	7 or more 4
3.	How often during the past 6 months did you find that you were not able to stop using cannabis once you had started?	Never 0	Less than monthly 1	Monthly 2	Weekly 3	Daily or almost daily 4
4.	How often during the past 6 months did you fail to do what was normally expected from you because of using cannabis?	Never 0	Less than monthly 1	Monthly 2	Weekly 3	Daily or almost daily 4
5.	How often in the past 6 months have you devoted a great deal of your time to getting, using, or recovering from cannabis?	Never 0	Less than monthly 1	Monthly 2	Weekly 3	Daily or almost daily 4
6.	How often in the past 6 months have you had a problem with your memory or concentration after using cannabis?	Never 0	Less than monthly 1	Monthly 2	Weekly 3	Daily or almost daily 4
7.	How often do you use cannabis in situations that could be physically hazardous, such as driving, operating machinery, or caring for children:	Never 0	Less than monthly 1	Monthly 2	Weekly 3	Daily or almost daily 4
8.	Have you ever thought about cutting down, or stopping, your use of cannabis?	Never 0		Yes, but not in the past 6 months 2		Yes, during the past 6 months 4

Scores of 8 or more indicate hazardous cannabis use.
Scores of 12 or more indicate a possible cannabis use disorder, for which further intervention may be required.

104

nature genetics

Article https://doi.org/10.1038/s41588-023-01563-z

Multi-ancestry genome-wide association study of cannabis use disorder yields insight into disease biology and public health implications

Received: 26 June 2023
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Published online: 20 November 2023
Check for updates

A list of authors and their affiliations appears at the end of the paper

As recreational use of cannabis is being decriminalized in many places and medical use widely sanctioned, there are growing concerns about increases in cannabis use disorder (CanUD), which is associated with numerous medical comorbidities. Here we performed a genome-wide association study of CanUD in the Million Veteran Program (MVP), followed by meta-analysis in 1,054,365 individuals (n_{case} = 64,314) from four broad ancestries designated by the reference panel used for assignment (European n = 886,025, African n = 123,208, admixed American n = 38,289 and East Asian n = 6,843). Population-specific methods were applied to calculate single nucleotide polymorphism-based heritability within each ancestry. Statistically significant single nucleotide polymorphism-based heritability for CanUD was observed in all but the smallest population (East Asian). We discovered genome-wide significant loci unique to each ancestry: 22 in European, 2 each in African and East Asian, and 1 in admixed American ancestries. A genetically informed causal relationship analysis indicated a possible effect of genetic liability for CanUD on lung cancer risk, suggesting potential unanticipated future medical and psychiatric public health consequences that require further study to disentangle from other known risk factors such as cigarette smoking.

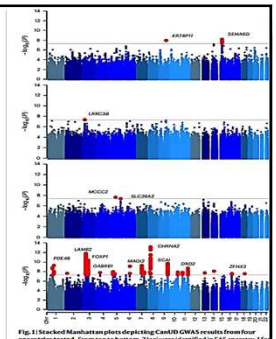

Fig. 1 | Stacked Manhattan plots depicting CanUD GWAS results from four ancestries tested. From top to bottom, 2 loci were identified in EAS ancestry, 1 for AMR, 2 for AFR, and 22 for EUR (red dots). Nearby genes are shown for orientation. *P* values were calculated with bidirectional Wald's test. The field standard GWS threshold of $P < 5 \times 10^{-8}$ (horizontal red line) was used to determine significant associations. Other colors indicate different chromosomes. Chr, chromosome.

105

Article https://doi.org/10.1038/s41588-023-01563-z

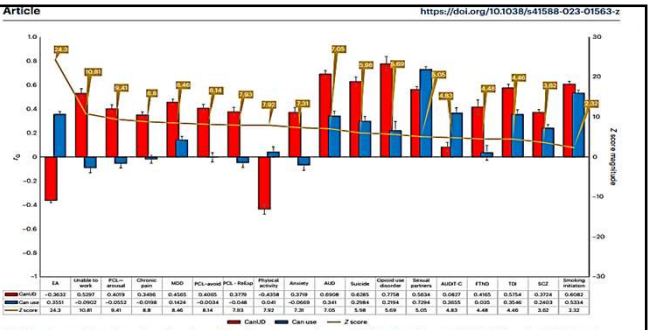

Fig. 2 | Genetic correlations. Comparison of genetic correlations between CanUD and cannabis use[39]. Left axis depicts the range of r_G between 1 and −1. Red bars and blue bars depict the r_G point estimate per trait for CanUD and cannabis use, respectively. Black error bars represent the standard error. Right axis displays the absolute magnitude of the *Z* statistic for the difference in r_G between CanUD and cannabis use (gold line). SNP-based heritability for each comparison trait is included in the table. EA, educational attainment; ReExp, re-experience; AUDIT-C, Alcohol Use Disorders Identification Test-Consumption; TDI, Townsend deprivation index.

106

PERCEPTION IS CANNABIS IS HARMLESS AND SAFER THAN ALCOHOL

JAMA Network Open.

Original Investigation | Substance Use and Addiction

Nondisordered Cannabis Use Among US Adolescents

Ryan S. Sultan, MD; Alexander W. Zhang, BA; Mark Olfson, MD, MPH; Mahrie H. Reviere, MPH; Frances R. Levin, MD

May 3, 2023

Abstract

IMPORTANCE Cannabis use is increasingly viewed by adolescents as not harmful. Youths with cannabis use disorder (CUD) are recognized by clinicians as being at risk for adverse outcomes, yet little is known about the associations between subclinical cannabis use (ie, nondisordered cannabis use [NDCU]) and adverse psychosocial events.

OBJECTIVE To describe the prevalence and demographics of NDCU and to compare associations of cannabis use with adverse psychosocial events among adolescents with no cannabis use, NDCU, and CUD.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study used a nationally representative sample derived from the 2015 to 2019 National Survey on Drug Use and Health. Participants were adolescents aged 10 to 17 years, separated into 3 distinct groups: nonuse (no recent cannabis use), NDCU (recent cannabis use below diagnostic threshold), and CUD. Analysis was conducted from January to May 2022.

EXPOSURES CUD, NDCU, or cannabis nonuse. NDCU was defined as endorsing recent cannabis use but not meeting the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) (DSM-5) CUD criteria. CUD was defined using DSM-5 criteria.

Key Points

Question Is nondisordered cannabis use (NDCU) among US adolescents associated with adverse psychosocial events?

Findings In this cross-sectional study of 68,203 adolescents, NDCU was approximately 4 times more common than cannabis use disorder (CUD). NDCU and CUD were both significantly associated with adverse psychosocial events in a stepwise gradient manner.

Meaning These findings suggest that adolescents with NDCU or CUD had increased odds of adverse psychosocial events.

+ Supplemental content

Table 2. Associations of Degrees of Adolescent Cannabis Use With Adolescent Psychosocial Events*

Adverse adolescent psychosocial event	Nondisordered cannabis use (n = 6971)* OR (95% CI)	P value	Cannabis use disorder (n = 1675)* OR (95% CI)	P value
Mental health				
≥1 MDE in the past year	2.40 (2.15-2.67)	<.001	3.48 (2.95-4.11)	<.001
Recent suicidal ideation	2.63 (2.39-2.90)	<.001	4.01 (3.42-4.70)	<.001
Cognition				
Recent slower thoughts	2.28 (2.05-2.53)	<.001	3.35 (2.87-3.92)	<.001
Recent difficulty concentrating	2.35 (2.13-2.59)	<.001	3.35 (2.89-3.89)	<.001
Academic performance				
≥1 d of school skipped in the past month	2.36 (2.08-2.69)	<.001	4.40 (3.72-5.20)	<.001
≤C+ GPA in the past semester	1.94 (1.75-2.15)	<.001	3.56 (3.12-4.06)	<.001
Delinquency				
≥1 arrests for breaking the law in the past year	5.60 (4.34-7.21)	<.001	17.72 (14.03-22.38)	<.001
≥1 serious fights in the past year	1.67 (1.49-1.88)	<.001	3.38 (2.92-3.93)	<.001
≥1 attacks with intent to harm in the past year	1.92 (1.61-2.28)	<.001	4.72 (3.92-5.69)	<.001

107

Policy Ahead of the Science

Medical Cannabis Laws Versus Scientific Evidence

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Gregory Malik Burnett, MD, MBA, MPH[a,b]
David A. Gorelick, MD, PhD, DLFAPA, FASAM[c], Kevin P. Hill, MD, MHS[d,e,*]

KEYWORDS

- Medical cannabis • Drug policy • Cannabinoids • Cannabidiol • Research
- Evidence-based medicine

KEY POINTS

- Three-quarters (37) of US states, the District of Columbia, and 3 territories have legalized medical cannabis.
- Forty-two different conditions in various jurisdictions qualify patients to receive medical cannabis.
- The number of qualifying conditions per jurisdiction varies from 5 to 29.
- Fifty percent of qualifying conditions have no or insufficient evidence of benefit from medical cannabis.
- Nine percent of qualifying conditions have limited evidence of harm from medical cannabis.

Table 1
Cannabis-based products with US Food and Drug Administration approval

Name (Brand Name)	Route of Administration	CSA Schedule	Approved Indications
Synthetic cannabinoids			
Dronabinol (Marinol, Syndros)	Synthetic THC	Oral	III	Severe nausea/vomiting Cachexia/weight loss
Nabilone (Cesamet)	Synthetic THC analogue	Oral	II	Severe nausea/vomiting
Phytocannabinoids				
Cannabidiol (Epidiolex)	Cannabidiol extract	Sublingual	Not scheduled	Seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, tuberous sclerosis complex in patients >1 y of age
Nabiximols (Sativex)	1:1 THC/CBD extract	Oral	NDA pending	Muscle spasms/multiple sclerosis, neuropathic cancer pain

108

Table 4
Prevalence and strength of evidence for qualifying medical conditions

Year Law Enacted	Medical Condition	# Of Jurisdictions with Approval	% of Jurisdictions with Approval	Evidence Grade Phytocannabinoids	Evidence Grade Synthetic Cannabinoids
1996	Multiple sclerosis/muscle spasms	39	95	2	1
1996	HIV/AIDS	36	88	0.5	0
1996	Cancer	36	88	0	0
1996	Epilepsy/seizures	35	85	0	0
1996	Intractable/chronic pain	33	80	2	0
1996	Glaucoma	33	80	−0.5	0
1996	Cachexia/wasting syndrome	29	71	0	0
2004	Crohn disease/IBD	27	66	1	0
1996	Severe nausea/vomiting	24	59	2	0
2008	ALS	23	56	0	0
2007	Parkinson disease	17	41	0.5	0
1999	Alzheimer disease	16	39	1	0.5
1999	Hepatitis C	15	37	0	0
2004	Terminal illness	15	37	0	0
2013	Neurologic malformation/trauma	14	34	0.5	0
2013	Tourette syndrome	9	22	0.5	1
1996	Arthritis (severe)	9	22	0	0
2010	Muscular dystrophy	7	17	0	0
2012	Fibromyalgia	6	15	1	1
2004	Peripheral neuropathy	6	15	0	0
2007	Huntington disease	6	15	0	0.5
2012	Sickle cell anemia	6	15	0	0
2011	Migraine	5	12	1	0

Legend

Score	Interpretation
−2	Conclusive or substantial evidence of harm
−1	Moderate evidence of harm
−0.5	Limited evidence of harm
0	No or insufficient evidence to support or refute benefit or harm
0.5	Limited evidence of benefit
1	Moderate evidence of benefit
2	Conclusive or substantial evidence of benefit

109

WHAT ABOUT MORE RECENT PSYCH CONDITIONS?

Table 5
Prevalence and strength of evidence of qualifying psychiatric conditions

Year Law Enacted	Psychiatric Condition	# Of Jurisdictions Listing	% of Jurisdictions Listing	Evidence Grade Cannabinoids	Evidence Grade Synthetic Cannabinoids
2011	PTSD	31	76	−0.5	0.5
2016	Autism spectrum disorder	15	37	0.5	0
2018	Opioid use disorder	7	17	0	0.5
2015	Anxiety	5	12	1	1
2015	Depression	2	5	0	−0.5
2019	Obsessive compulsive disorder	1	2	0	0
2021	Panic disorder	1	2	0	0

Legend

Score	Interpretation
−2	Conclusive or substantial evidence of harm
−1	Moderate evidence of harm
−0.5	Limited evidence of harm
0	No or insufficient evidence to support or refute benefit or harm
0.5	Limited evidence of benefit
1	Moderate evidence of benefit
2	Conclusive or substantial evidence of benefit

110

Box 1
Medical cannabis qualifying conditions by strength of evidence

Conclusive or substantial evidence of benefit
Cachexia/wasting syndrome, epilepsy/seizures, multiple sclerosis/muscle spasms, severe nausea/vomiting, intractable/chronic pain

Moderate evidence of benefit
Alzheimer disease, anxiety, Crohn disease/inflammatory bowel disease, fibromyalgia, migraine, obstructive sleep apnea, posttraumatic stress disorder (synthetic), Tourette syndrome

Limited evidence of benefit
Autism spectrum disorder, human immunodeficiency virus/acquired immunodeficiency syndrome, neurologic malformation/trauma, opioid use disorder, Parkinson disease

No or insufficient evidence to support or refute benefit or harm
Amyotrophic lateral sclerosis, arthritis, cancer, cachexia/wasting syndrome, cirrhosis, cystic fibrosis, dysmenorrhea, Ehlers-Danlos syndrome, fibrous dysplasia, hepatitis C, Huntington disease, interstitial cystitis, macular degeneration, muscular dystrophy, obsessive compulsive disorder, panic disorder, peripheral neuropathy, polycystic kidney disease, sickle cell anemia, Sjögren syndrome, systemic lupus erythematosus, terminal illness

Limited evidence of harm
Depression, glaucoma, chronic pancreatitis, posttraumatic stress disorder (phyto)

Moderate evidence of harm
None

Substantial evidence of harm
None

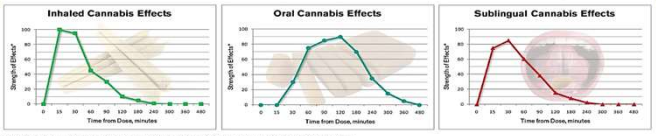
111

CANNABIS CONSUMPTION METHODS

strength, onset, and duration of effects over time

How Cannabis is consumed directly impacts the strength of effects, how long it takes effects to become noticeable (onset), and how long the effects will last (duration).

These charts show estimated strength, onset, and duration of effects across 3 common cannabis consumption methods:



*Strength of effects is rated subjectively based on research review (see below), 100 = peak strength of inhaled cannabis effects

Inhalation
Smoking, Vaporizing
- Fast Onset
- Strong Effects Peak
- Rapid Decline in Effects Strength
- Short Duration of Experience

Oral Consumption
Edibles, Beverages
- Delayed Onset
- Drawn-out Effects Peak
- Gradual Decline in Effects Strength
- Long Duration of Experience

Sublingual Absorption
Melting Edibles Under Tongue, Tinctures
- Mid-range Onset
- Drawn-out Effects Peak
- Gradual Decline in Effects Strength
- Mid-range Duration of Experience

112

INDIVIDUAL EXPERIENCES DIFFER WIDELY SO START LOW AND GO SLOW WITH GUMMIES!

Edibles dosing chart Leafly

THC per dose	Dose category	What to expect	Edible recommendation
1 – 2.5 mg	Microdose	Most users don't experience intoxication at this dose, but may feel that their pain, anxiety, and nausea have abated without affecting their cognition.	Mints
3 – 5 mg	Low	This dose helps with pain, nausea, inflammation, and may help with sleep. New users will likely feel a degree of intoxication, including feeling less coordinated and more silly. A 5mg dose is when a "high" begins to set in for many new and/or inconsistent consumers.	Infused seltzer, some gummies, honey sticks
10 – 15 mg	Moderate	This is an ideal dose for more experienced users looking to have fun, sleep, or manage pain. New users may feel overwhelmed.	Gummies, single-dose baked goods, savory snacks, some beverages
20 – 30 mg	High	This dose is only recommended for experienced edible consumers: expect strong euphoria and impaired coordination and/or perception. May be beneficial for chronic illness, insomnia, or severe pain.	Infused chocolate bars, THC-infused condiments
50 – 100 mg	Acute	An effective dose for experienced users seeking relief from intense physical pain, PMS, MS, cancer treatment, and other conditions. Not recommended for those dealing with mental health issues. May cause nausea or disrupt the sensations of inconsistent consumers.	Infused baked goods
100 – 500 mg	Macrodose	A useful dose for patients with GI absorption issues and other severe medical conditions like cancer. This is an intensely intoxicating dose, and many users risk experiencing adverse effects. Consume with caution and intention.	Infused elixirs and tonics

113

Risks and Benefits of Cannabis and Cannabinoids in Psychiatry

Kevin P. Hill, M.D., M.H.S., Mark S. Gold, M.D., Charles B. Nemeroff, M.D., Ph.D., William McDonald, M.D., Adrienne Grzenda, M.D., Ph.D., Alik S. Widge, M.D., Ph.D., Carolyn Rodriguez, M.D., Ph.D., Nina V. Kraguljac, M.D., John H. Krystal, M.D., Linda L. Carpenter, M.D.

Objective: The United States is in the midst of rapidly changing laws regarding cannabis. The increasing availability of cannabis for recreational and medical use requires that mental health clinicians be knowledgeable about evidence to be considered when counseling both patients and colleagues. In this review, the authors outline the evidence from randomized double-blind placebo-controlled trials for therapeutic use of cannabinoids for specific medical conditions and the potential side effects associated with acute and chronic cannabis use.

Methods: Searches of PubMed and PsycInfo were conducted for articles published through July 2021 reporting on "cannabis" or "cannabinoids" or "medicinal cannabis." Additional articles were identified from the reference lists of published reviews. Articles that did not contain the terms "clinical trial" or "therapy" in the title or abstract were not reviewed. A total of 4,431 articles were screened, and 841 articles that met criteria for inclusion were reviewed by two or more authors.

Results: There are currently no psychiatric indications approved by the U.S. Food and Drug Administration (FDA) for cannabinoids, and there is limited evidence supporting the therapeutic use of cannabinoids for treatment of psychiatric disorders. To date, evidence supporting cannabinoid prescription beyond the FDA indications is strongest for the management of pain and spasticity.

Conclusions: As cannabinoids become more available, the need for an evidence base adequately evaluating their safety and efficacy is increasingly important. There is considerable evidence that cannabinoids have a potential for harm in vulnerable populations such as adolescents and those with psychotic disorders. The current evidence base is insufficient to support the prescription of cannabinoids for the treatment of psychiatric disorders.

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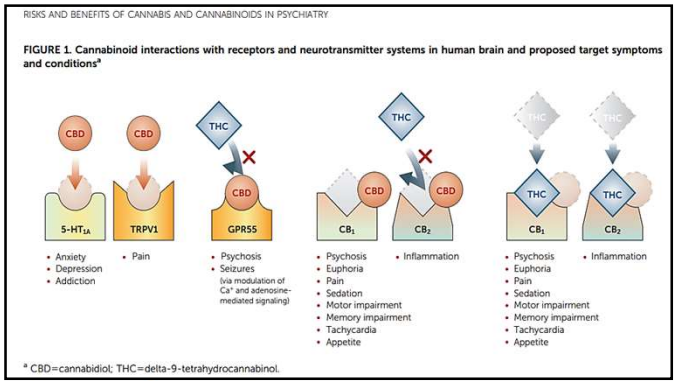
114



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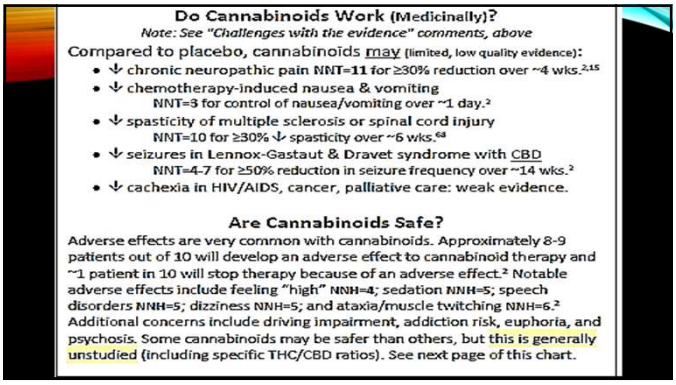

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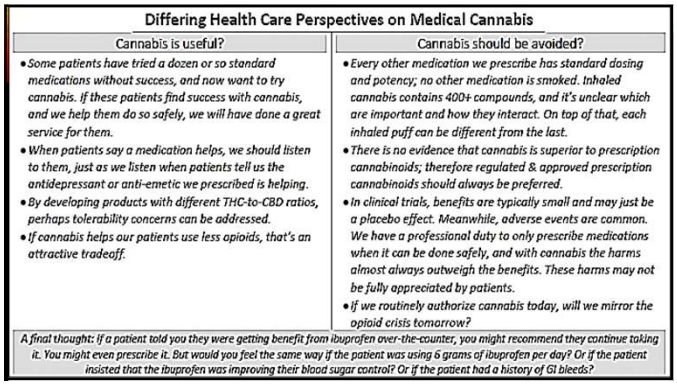

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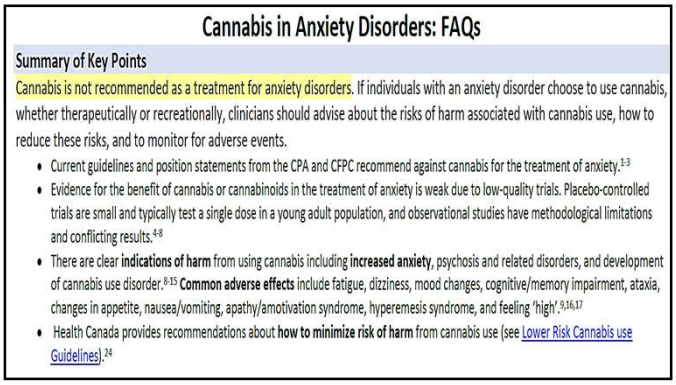

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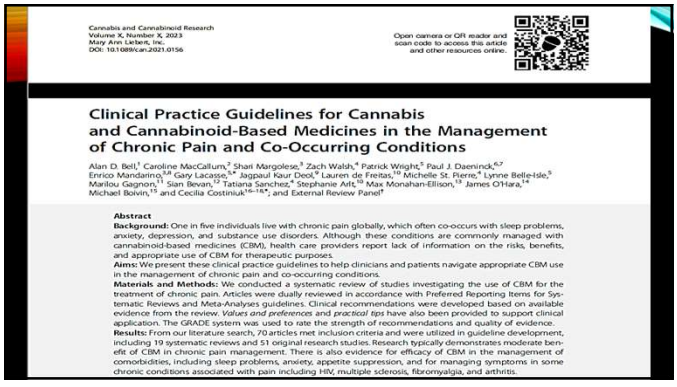

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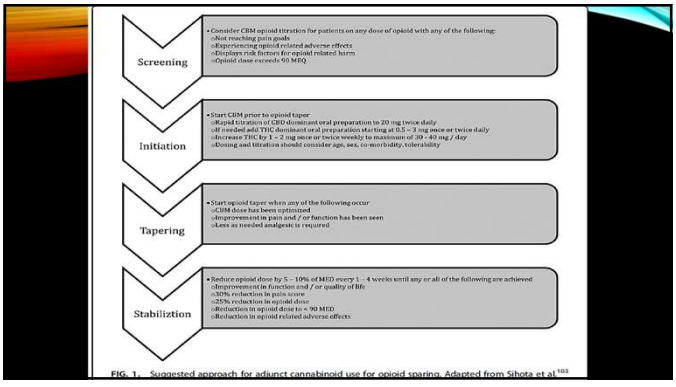

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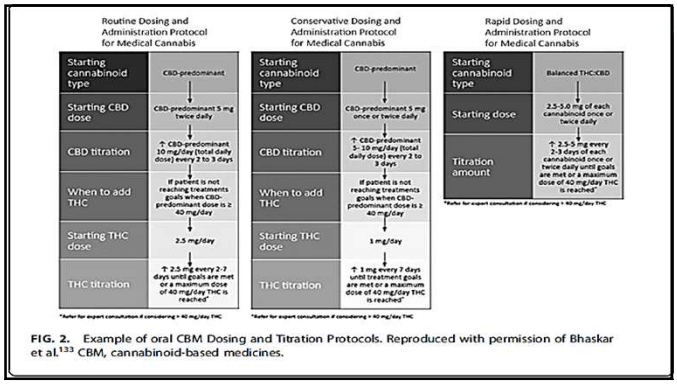
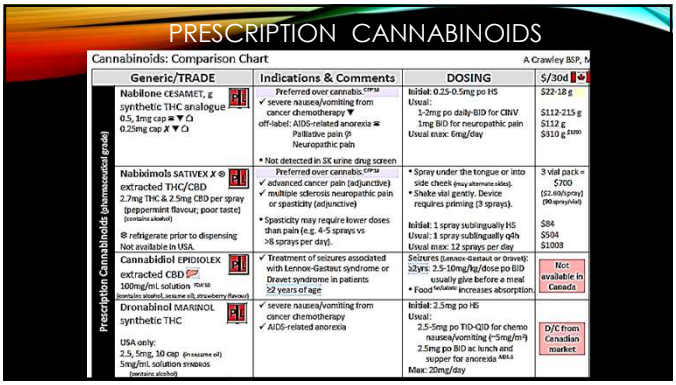


FIG. 2. Example of oral CBM Dosing and Titration Protocols. Reproduced with permission of Bhaskar et al.[133] CBM, cannabinoid-based medicines.

121



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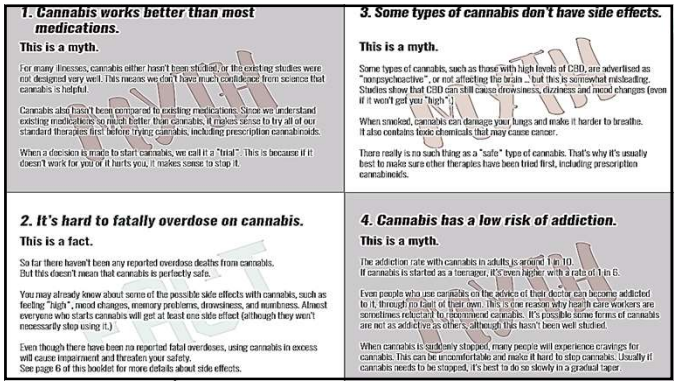

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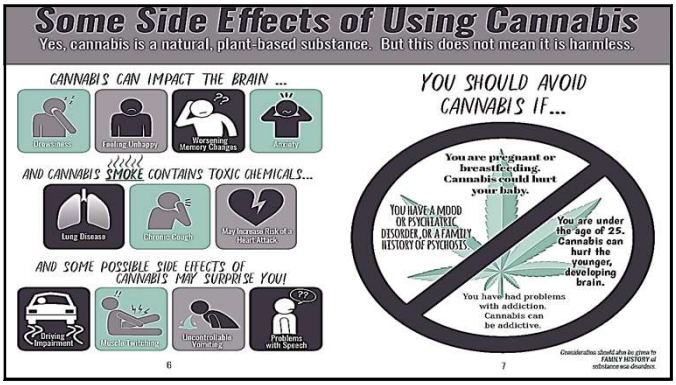

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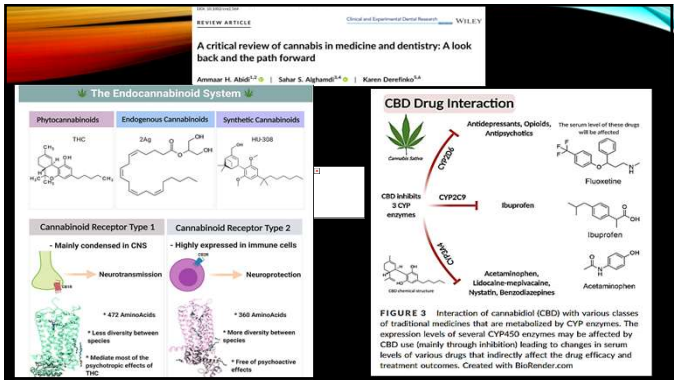

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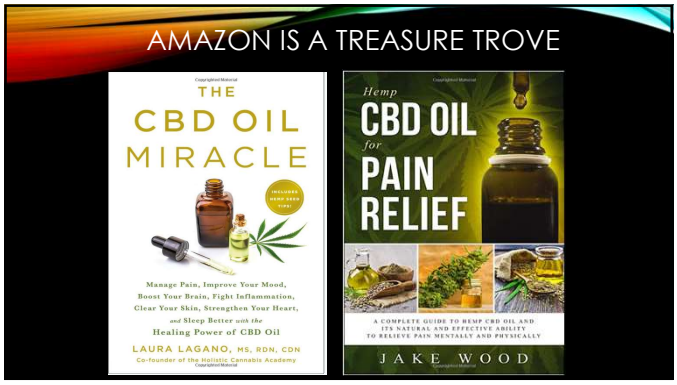

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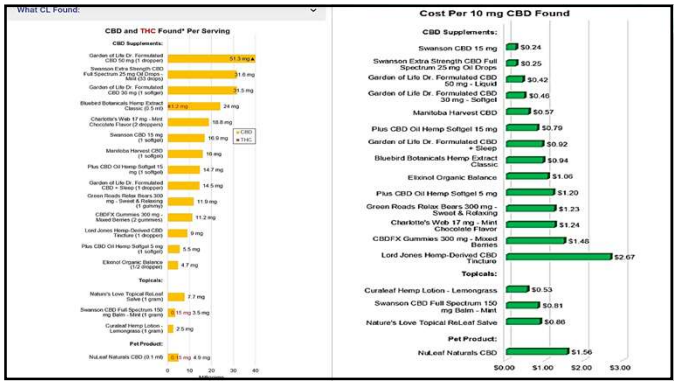
128



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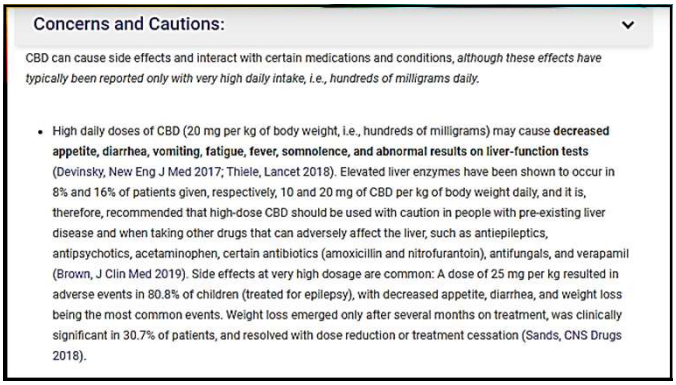

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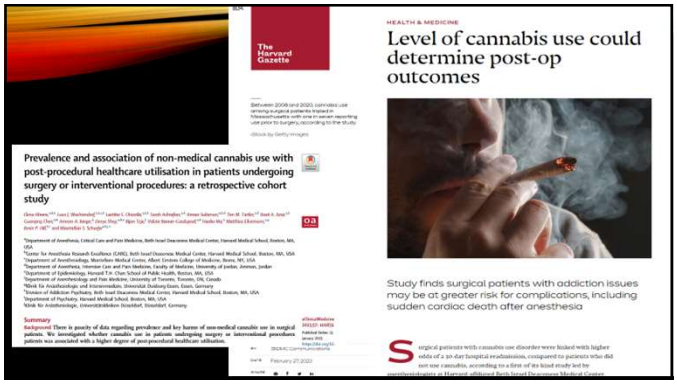

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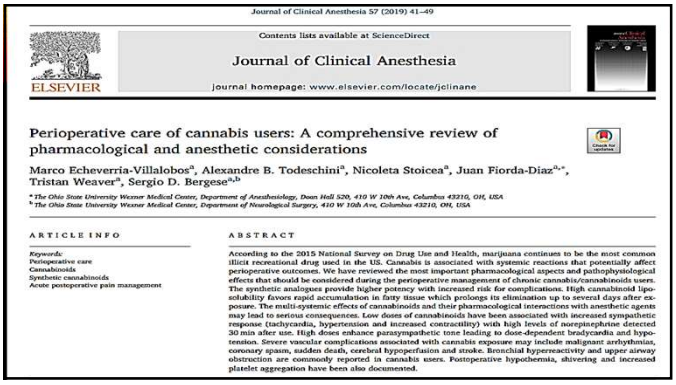

132

Table A
Main physiologic effects of cannabinoids.

System	CB-R	Physiologic effects	
Cardiovascular	CB1-R	Newly users, naïve, SCB	a) Dose-dependent; initial β-adrenergic effect + parasympathetic inhibition: ↑ HR, ↑ LV contractility, ↑ CO, ↑ SBP, VPCs, AFib, malignant arrhythmias (VTach, VFib, Brugada pattern) b) After 30 min of exposure: Norepinephrine levels peak and stay elevated up to 120 min after cessation
		Chronic and/or heavy-users (THC ≥ 10 mg)	a) Strong parasympathetic response + baroreflexes deregulation: ↓ HR, postural hypotension (not compensated by sympathetic stimulation); cardiac arrest b) Coronary spasm in patients with coronary disease → MI c) MI in young individuals due to an increase in MVO_2, high levels of COHb, and coronary thrombosis
	VR	Heavy users (THC ≥ 10 mg)	Mesenteric vasodilation through release of CGRP
Cerebrovascular	CB1-R	Naïve users or Low-dose THC	Vasodilation and ↑CBF
		Chronic use, heavy "spice" or K2 consumption	Cerebral vasospasm → ischemic stroke (posterior cerebral circulation affected in half of the cases)
Respiratory	CB1-R	Chronic or heavy user	a) ↑ bronchial tone → bronchial hyperreactivity b) Pharyngeal and uvular edema → upper airway obstruction c) Diffuse alveolar hemorrhage and necrotizing bronchiolitis → pulmonary edema d) Pulmonary embolism (more common with SCB)
Temperature	CB1-R	Chronic use, heavy smoking, SCB	Altered central thermoregulation → intraoperative hypothermia → severe postoperative shivering
Coagulation	CB1-R?	Chronic or heavy user	a) Increased clotting time b) Decreased platelet count c) Increased risk of bleeding in patients taking warfarin

CB-R: cannabinoid receptor; CB1-R: cannabinoid receptor type 1; HR: heart rate; LV: left ventricle; CO: cardiac output; SBP: systolic blood pressure; VPCs: ventricular premature contractions; AFib: atrial fibrillation; VTach: ventricular tachycardia; VFib: ventricular fibrillation; THC: tetrahydrocannabinol; MI: myocardial infarction; MVO_2: myocardial oxygen consumption; COHb: carboxyhemoglobin; CGRP: calcitonin gene-related peptide; VR: vanilloid receptor; CBF: cerebral blood flow; SCB: synthetic cannabinoids.

133

Table B
Preoperative considerations in cannabis users.

Variable	Comments
Level of exposure	- New users vs chronic/heavy users - Recreational vs medical use - Frequency of dosage or smoking - Time elapsed since last exposure
Chronic users	- Use of "spice" or K2 (if recreational use) - Past medical history of hyperemesis episodes, hyperreactive airway, and severe shivering with previous surgery
Scheduled surgery	Elective surgeries should be avoided for at least 72 h from last exposure

What is Spice/ K2, Synthetic Marijuana?

K2 and Spice are just two of the many trade names or brands for synthetic designer drugs that are intended to mimic THC, the main psychoactive ingredient of marijuana. These designer synthetic drugs are from the synthetic cannabinoid class of drugs that are often marketed and sold under the guise of "herbal incense" or "potpourri."

These products are being abused for their psychoactive properties and are packaged without information as to their health and safety risks.

134

DENTAL MED HISTORY MUST INCLUDE ACCURATE INFORMATION ON CANNABIS USE

New Users	Chronic Users
• Tachycardia and systolic hypertension (within 2 hours from consumption) • Malignant arrhythmias (AFib, VFib, VTach, Brugada pattern) • Coronary spasm if previous CAD • Airway hyperreactivity or UAO (uvulitis)	• Bradycardia → Tachycardia • Postural / Orthostatic hypotension • Sinus arrest • Hyperreactive airway • Intraoperative hypothermia → PO "shivering" • Coronary vasospasm / myocardial infarction

Fig. 2. Major perioperative physiologic findings in cannabinoid users.

135

HIGH TIMES

Half of Dentists Say Patients Arrive to Checkups Stoned, Survey Finds

Most would agree that a visit to the dentist is a less than ideal outing. And what do cannabis consumers often turn to before tackling something less than ideal? Grab the stash, light up, get a little toasty and press on, of course.

Cannabis: Oral Health Effects

Key Points

- Cannabis smoking is associated with periodontal complications, xerostomia, and leukoplakia as well as increased risk of mouth and neck cancers.
- Historically, cannabis has been smoked as marijuana, but is increasingly available in other forms, including edible and topically applied products.
- Cannabis use has increased in recent years, along with state legalization, although it remains federally banned.

Dental Care Implications

Signs and symptoms of an active (intoxicated) cannabis user include:[15, 37]

- Euphoria
- Hyperactivity
- Tachycardia
- Paranoia
- Delusions
- Hallucinations

136

SCIENTIFIC REPORT

Local Anesthetic Efficacy in Marijuana Users and Nonusers: A Pilot Study

Michael C. Moran, DDS, MSD;* Lisa J. Heaton, PhD;† Brian G. Leroux, PhD;‡ and Natasha M. Flake, DDS, PhD, MSD*

*Department of Endodontics, University of Washington School of Dentistry, ‡Department of Oral Health Sciences, University of Washington School of Dentistry

Objective: Despite the common clinical impression that patients with a history of drug use are challenging to anesthetize with local anesthesia, literature on this clinical phenomenon is sparse. The objective of this pilot study was to assess if differences in local anesthetic efficacy for dental treatment exist between marijuana users and nonusers.
Methods: Subjects were healthy adult males and females who qualified as either chronic marijuana users or nonusers. All subjects had an asymptomatic, vital maxillary lateral incisor that responded to an electric pulp test (EPT). A standard maxillary infiltration injection technique was employed using 1.7 mL 2% lidocaine with 1:100,000 epinephrine over the test tooth, and the tooth was tested with an EPT at 3-minute intervals.
Results: A total of 88% of nonusers (15/17) and 61% of users (11/18) were successfully anesthetized, defined as anesthesia onset within 10 minutes and lasting at least 15 minutes. The difference in the proportion of anesthetized subjects was not statistically significant ($P = .073$). For subjects with successful anesthesia, there was no significant difference between nonusers and users in the onset or duration of anesthesia.
Conclusion: No significant differences in local anesthetic efficacy with respect to local anesthetic success, onset, or duration of action were found between chronic marijuana users and nonusers. However, larger studies are likely needed to provide more definitive evidence.

137

AAOMS PUBLISHED THIS PAPER ON CANNABIS IN 2023

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Clinical Paper

Implications of Cannabis Use for Patients Undergoing Office-based Anesthesia and Oral and Maxillofacial Surgery

Introduction

Cannabis, widely known as marijuana, comes from the Cannabis sativa plant. It is the most used "drug" worldwide, with more than 180 million reported users across the globe in 2018.[1] In the U.S., cannabis remains a federally classified Schedule I substance. However, multiple states have legalized its use for medicinal and recreational purposes, leading to an increase in its popularity – particularly among the younger population with 36 percent of 12th graders and 43 percent of college students reported having used it in the past year.[2]

anesthesia or a combination of both. Invariably, encounters with cannabis users will occur. Therefore, OMSs need to be prepared and understand how to best manage these patients. This paper will discuss the pertinent physiologic and pharmacologic effects of cannabis, its potential interactions with common medications used in the office setting and potential challenges that OMSs may face in managing patients who use cannabis.

Different Forms of Cannabis for Intake

Marijuana is commonly used and abused. Patients may be

138

Table 1

Sedation Medications Needed for Cannabis Users Versus Non-users

Sedation	Non-Cannabis Users 255 patients	Cannabis Users 25 patients	Difference in Dose	% Increase in Dose Needed
Fentanyl (mcg)	109.91	125.93	25 mcg	14%
Midazolam (mg)	7.61	9.15	3 mg	19.5%
Propofol (mg)	13.83	44.81	30 mg	220.5%

Adapted from Reference 20

Table 2

Cannabis Products: Frequency and Techniques of Use

Frequency	Technique	Marijuana Product
Monthly (infrequent use)	Smoking	Flower
Weekly	Vaporize or Dab	Concentrate
Daily	Vape Pen	K2/Spice
Multiple times a day	Edibles	Medical Marijuana and THC Dose

Reference 4

139

Table 3

Signs and Symptoms of Concern on History and Physical

Medical History	Cannabis User	Comorbidity
Questions & Answers	Cough, Sputum, Wheeze	Asthma, Bronchitis, COPD
	Chest Pain & Palpitations	CAD
	Dysrhythmias → A-fib, PSVT, Atrial Flutter, PVCs, 2nd degree AV block, and VT	CAD
Use of Other Recreational Drugs		
	Hyperemesis with Chronic Marijuana Use	

Reference 4

Table 4

Signs and Symptoms Seen in New, Naïve and Chronic Users

New User	Tachycardia within 2 hours MH use
Naïve User	↑ SBP within 2 hours MH use
	Dysrhythmias: AFib, Aflutter, PVCs, PSVT, AV Block, VT
	Dyspnea, Sputum and Wheeze
Chronic User	Bradycardia or Tachycardia
	Orthostatic Hypotension
	Dysrhythmias
	Hyperactive Airway
	Dyspnea, Sputum and Wheeze

References 4, 13, 15

140

Table 5

Withdrawal in Heavy Users of Marijuana

Typical Products of Heavy Users	High potency flower, marijuana concentrates, synthetic K2/Spice, multiple times per day
Onset	Day 1
Peak Symptoms	Day 4 (range of 1 to 8 days)
Resolution of Symptoms	Greater than 16 days

References 1, 8, 21, 22

Table 6

Marijuana Withdrawal in General

Signs and Symptoms	Frequency
Sleep Difficulty	14% Most reported symptom
Irritability	14%
Anxiety	13%
Headache	12%
Depressed Mood	11%
Physical Descriptions	
Irritability, Anger, Aggression	
Anxiety, Nervousness	
Insomnia, Restless, Depressed Mood	
Abdominal Cramps	
Tremors	
Sweating, Fever, Chills	
Headaches	

References 1, 8, 21, 22

141

AAOMS RECOMMENDATIONS FOR TREATMENT

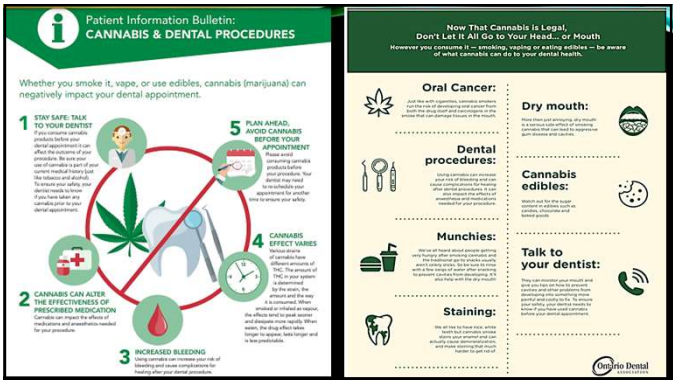
- THC should NOT be used for anti-anxiety premedication
- Elective surgery should be canceled for patients who are acutely intoxicated from marijuana.
- Ideally, no cannabis should be used 72 hours prior to oral surgery.
- Medicinal marijuana should be continued for oral surgery patients
- CUD patients are prone to "rocky" or "combative" anesthetics so a deep level of sedation maintained with a pump is better than intermittent bolus administration of sedation agents.
- PONV prophylaxis should be increased while maintaining a deeper level of anesthesia for induction and maintenance.
- Higher doses of BZDPs, opioids, and hypnotics will be required.

142

BOTTOM LINE FOR DENTAL TREATMENT

- Obtain accurate history on recent and chronic cannabis use
- Determine level of intoxication for informed consent legalities
- Anticipate the following changes in heavy chronic users:
  - Increased risk of perisurgical bleeding
  - Increased heart rate which could limit vasoconstrictor dosing
  - INCREASED post procedural pain has been seen in heavy users
  - Patient may be tolerant to CNS depressants or have idiosyncratic responses to psychoactive drugs due to heavy THC use
  - Safest treatment planning approach is no cannabis for 24 hours
    - Many patients self-medicate for anxiety and/or pain so this approach may not be realistic!

143



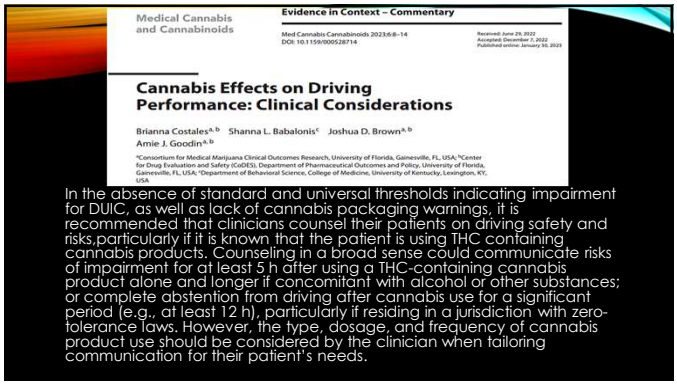
144

145

DID YOUR PATIENT DRIVE THEMSELVES TO YOUR OFFICE?

- Driving under the influence of cannabis has been identified as a public health concern as medical and recreational cannabis availability increases in some countries and rapidly in the United States.
- A recent randomized clinical trial found similar levels of acute driving impairment with THC-dominant cannabis and with a combination of THC-CBD equivalent cannabis using on-road driving tests that provided real-world conditions; however, CBD-dominant cannabis did not produce significant cognitive or psychomotor impairment compared with placebo in this trial.
- Media coverage of this study conveyed the findings as CBD-dominant cannabis not causing driving impairment while THC-dominant cannabis does, with the latter lasting up to 4 h post-dose.
- It is recommended that clinicians counsel about the risks of driving impairment when patients disclose use of cannabis products containing THC.

146



In the absence of standard and universal thresholds indicating impairment for DUIC, as well as lack of cannabis packaging warnings, it is recommended that clinicians counsel their patients on driving safety and risks,particularly if it is known that the patient is using THC containing cannabis products. Counseling in a broad sense could communicate risks of impairment for at least 5 h after using a THC-containing cannabis product alone and longer if concomitant with alcohol or other substances; or complete abstention from driving after cannabis use for a significant period (e.g., at least 12 h), particularly if residing in a jurisdiction with zero-tolerance laws. However, the type, dosage, and frequency of cannabis product use should be considered by the clinician when tailoring communication for their patient's needs.

147

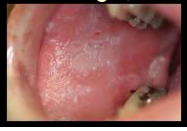
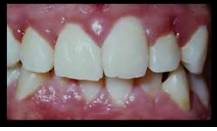
WHAT DO THE CANADIANS DO ABOUT DRIVING?

(Am J Public Health. 2017;107:e1–e12. doi:10.2105/AJPH.2017.303818)

148

BOTTOM LINE ON DENTAL IMPLICATIONS FOR CHRONIC DAILY CANNABIS USERS

- Xerostomia and increased snacking results in increased caries.
- Smoking cannabis can produce cannabis stomatitis which is characterized by hyperkeratosis and leukoplakia.
- Tobacco & cannabis smoking concomitantly may pose an increased risk of developing oral and neck cancer.
- Chronic cannabis use results in immunosuppression which can predispose to oral fungal,viral and bacterial infections.

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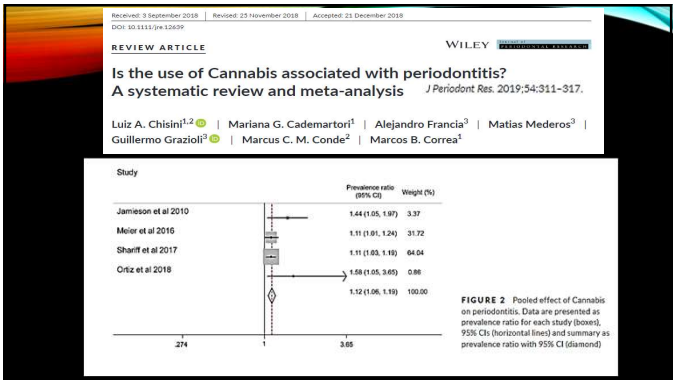
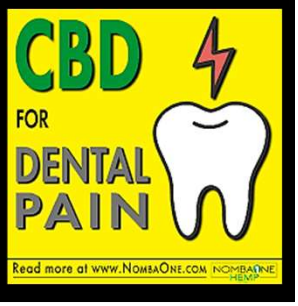


150

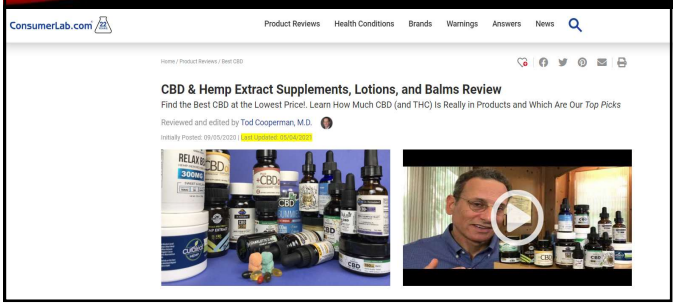
HOW EFFECTIVE IS CBD FOR ACUTE OR CHRONIC PAIN?

Applying CBD **directly to the affected tooth and gums** will work more effectively to relieve your toothache than taking it another way.



151

CONSUMERLAB IS A GREAT RESOURCE FOR ACCURATE SUPPLEMENT INFORMATION

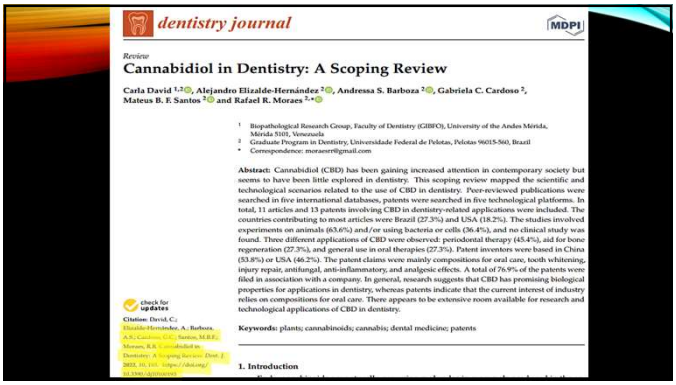


152

IS CBD EFFECTIVE IN THE TREATMENT OF PAIN?

A review of several experimental pain studies (using heat or pressure) on healthy people found that cannabis (marijuana) and cannabinoids may not reduce the intensity of pain, but may **make pain feel less unpleasant and more tolerable**. Although none of the studies tested CBD exclusively, the products containing CBD (in addition to THC), such as cannabis extracts, were shown to be more effective than those containing exclusively THC or THC analogues (De Vita, JAMA Psych 2018). A subsequent clinical trial found that CBD *alone* did not reduce pain threshold, tolerance or severity compared to placebo, and suggested that a reduction in pain "unpleasantness" may largely be due to the placebo effect – the *expectation* that CBD will reduce pain. In the study, participants who were given 50 mg of CBD orally as a liquid (99.46% CBD in coconut oil with no detectable THC) but were told they were taking a placebo, 30 minutes before a pain-inducing heating element was applied to the forearm, reported a similar reduction in "unpleasantness" as those who were given a placebo (coconut oil) but told they were given CBD (De Vita, Exp Clin Psychopharmacol 2021).

153



dentistry journal MDPI

Review

Cannabidiol in Dentistry: A Scoping Review

Carla David [1,2], Alejandro Elizalde-Hernández [2], Andressa S. Barboza [2], Gabriela C. Cardoso [2], Mateus B. F. Santos [2] and Rafael R. Moraes [2,*]

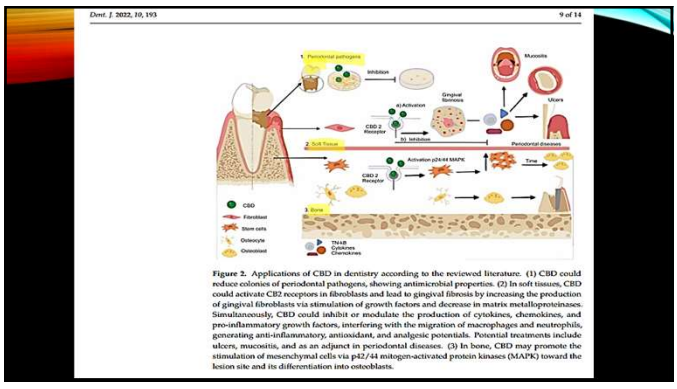
[1] Biopathological Research Group, Faculty of Dentistry (GIBFO), University of the Andes Mérida, Mérida 5101, Venezuela
[2] Graduate Program in Dentistry, Universidade Federal de Pelotas, Pelotas 96015-560, Brazil
* Correspondence: moraesrr@gmail.com

Abstract: Cannabidiol (CBD) has been gaining increased attention in contemporary society but seems to have been little explored in dentistry. This scoping review mapped the scientific and technological scenarios related to the use of CBD in dentistry. Peer-reviewed publications were searched in five international databases, patents were searched in five technological platforms. In total, 11 articles and 13 patents involving CBD in dentistry-related applications were included. The countries contributing to most articles were Brazil (27.3%) and USA (18.2%). The studies involved experiments on animals (63.6%) and/or using bacteria or cells (36.4%), and no clinical study was found. Three different applications of CBD were observed: periodontal therapy (45.4%), aid for bone regeneration (27.3%), and general use in oral therapies (27.3%). Patent inventors were based in China (53.8%) or USA (46.2%). The patent claims were mainly compositions for oral care, tooth whitening, injury repair, antifungal, anti-inflammatory, and analgesic effects. A total of 76.9% of the patents were filed in association with a company. In general, research suggests that CBD has promising biological properties for applications in dentistry, whereas patents indicate that the current interest of industry relies on compositions for oral care. There appears to be extensive room available for research and technological applications of CBD in dentistry.

Keywords: plants; cannabinoids; cannabis; dental medicine; patents

1. Introduction

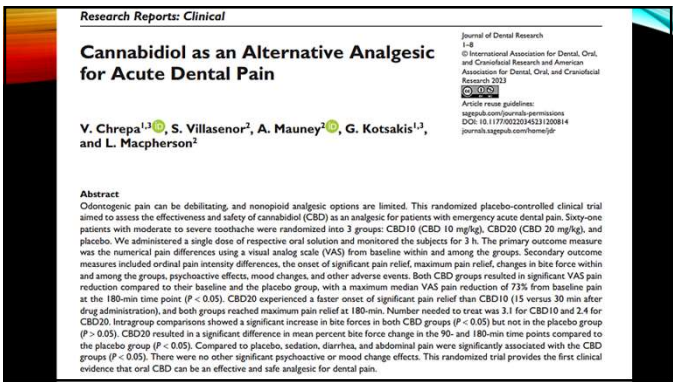
154



Dent. J. 2022, *10*, 193 9 of 14

Figure 2. Applications of CBD in dentistry according to the reviewed literature. (1) CBD could reduce colonies of periodontal pathogens, showing antimicrobial properties. (2) In soft tissues, CBD could activate CB2 receptors in fibroblasts and lead to gingival fibrosis by increasing the production of gingival fibroblasts via stimulation of growth factors and decrease in matrix metalloproteinases. Simultaneously, CBD could inhibit or modulate the production of cytokines, chemokines, and pro-inflammatory growth factors, interfering with the migration of macrophages and neutrophils, generating anti-inflammatory, antioxidant, and analgesic potentials. Potential treatments include ulcers, mucositis, and as an adjunct in periodontal diseases. (3) In bone, CBD may promote the stimulation of mesenchymal cells via p42/44 mitogen-activated protein kinases (MAPK) toward the lesion site and its differentiation into osteoblasts.

155



Research Reports: Clinical

Cannabidiol as an Alternative Analgesic for Acute Dental Pain

Journal of Dental Research 1–8
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DOI: 10.1177/00220345231200814
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V. Chrepa[1,3], S. Villasenor[2], A. Mauney[2], G. Kotsakis[1,3], and L. Macpherson[2]

Abstract

Odontogenic pain can be debilitating, and nonopioid analgesic options are limited. This randomized placebo-controlled clinical trial aimed to assess the effectiveness and safety of cannabidiol (CBD) as an analgesic for patients with emergency acute dental pain. Sixty-one patients with moderate to severe toothache were randomized into 3 groups: CBD10 (CBD 10 mg/kg), CBD20 (CBD 20 mg/kg), and placebo. We administered a single dose of respective oral solution and monitored the subjects for 3 h. The primary outcome measure was the numerical pain differences using a visual analog scale (VAS) from baseline within and among the groups. Secondary outcome measures included ordinal pain intensity differences, the onset of significant pain relief, maximum pain relief, changes in bite force within and among the groups, psychoactive effects, mood changes, and other adverse events. Both CBD groups resulted in significant VAS pain reduction compared to their baseline and the placebo group, with a maximum median VAS pain reduction of 73% from baseline pain at the 180-min time point ($P < 0.05$). CBD20 experienced a faster onset of significant pain relief than CBD10 (15 versus 30 min after drug administration), and both groups reached maximum pain relief at 180-min. Number needed to treat was 3.1 for CBD10 and 2.4 for CBD20. Intragroup comparisons showed a significant increase in bite forces in both CBD groups ($P < 0.05$) but not in the placebo group ($P > 0.05$). CBD20 resulted in a significant difference in mean percent bite force change in the 90- and 180-min time points compared to the placebo group ($P < 0.05$). Compared to placebo, sedation, diarrhea, and abdominal pain were significantly associated with the CBD groups ($P < 0.05$). There were no other significant psychoactive or mood change effects. This randomized trial provides the first clinical evidence that oral CBD can be an effective and safe analgesic for dental pain.

156

61 PATIENTS WITH MODERATE TO SEVERE TOOTHACHE

Table 1. Inclusion/Exclusion Criteria.

Inclusion Criteria	Exclusion Criteria
Healthy adults 18–75 y old, ASA class I or II	ASA class III or IV, patients with hepatic impairment, pregnant[a] or lactating women
Permanent tooth with moderate to severe odontogenic pain (i.e., ≥30 on a 100-mm VAS)	Patients on drugs metabolized by enzymes that also metabolize CBD (e.g., clobazam, diazepam, topiramate, warfarin)[b]
Clinical pulpal diagnosis of irreversible pulpitis or pulpal necrosis and periapical diagnosis of symptomatic apical periodontitis	Self-reported prior experience inhaling cannabis (either via smoking or vaporization)
Test negative for recent cannabis use and/or other drugs of abuse including alcohol (urine tests collected at screening visit)[c]	Use of opioids in the month prior to screening/treatment visit and/or NSAIDS or acetaminophen 6 h prior to treatment
Participant able to understand the forms (English or Spanish) and provide informed written consent	Unwilling to participate

ASA, American Society of Anesthesiologists; CBD, cannabidiol; NSAID, nonsteroidal anti-inflammatory drug; VAS, visual analog scale.
[a]Pregnancy test will be performed at the screening visit.
[b]Epidiolex is metabolized by CYP3A4 and CYP2C19 and has the potential to inhibit CYP2C8, CYP2C9, and CYP2C19 at clinically relevant concentrations; therefore, we chose to avoid potential drug interactions.
[c]Cannabis trials often present with high placebo effect. Cannabis-naive subjects are thus proposed to minimize this effect as well the possibility of tachyphylaxis.

157

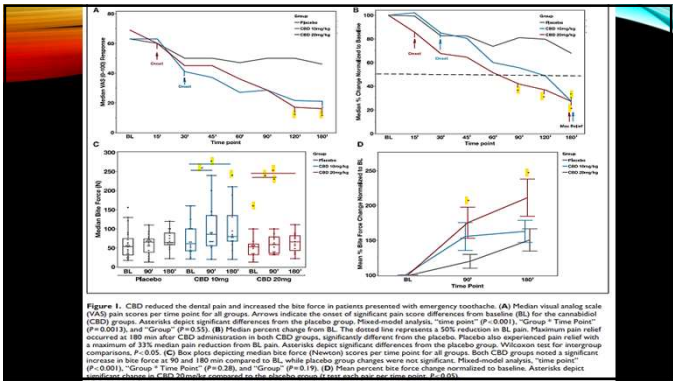


Figure 1. CBD reduced the dental pain and increased the bite force in patients presented with emergency toothache. **(A)** Median visual analog scale (VAS) pain scores per time point for all groups. Arrows indicate the onset of significant pain score differences from baseline (BL) for the cannabidiol (CBD) groups. Asterisks depict significant differences from the placebo group. Mixed-model analysis, "time point" ($P < 0.001$), "Group * Time Point" ($P = 0.0013$), and "Group" ($P = 0.55$). **(B)** Median percent change from BL. The dotted line represents a 50% reduction in BL pain. Maximum pain relief occurred at 180 min after CBD administration in both CBD groups, significantly different from the placebo. Placebo also experienced pain relief with a maximum of 33% median pain reduction from BL pain. Asterisks depict significant differences from the placebo group. Wilcoxon test for intergroup comparisons, $P < 0.05$. **(C)** Box plots depicting median bite force (Newton) scores per time point for all groups. Both CBD groups noted a significant increase in bite force at 90 and 180 min compared to BL, while placebo group changes were not significant. Mixed-model analysis, "time point" ($P < 0.001$), "Group * Time Point" ($P = 0.28$), and "Group" ($P = 0.19$). **(D)** Mean percent bite force change normalized to baseline. Asterisks depict significant change in CBD 20 mg/kg compared to the placebo group (t test each pair per time point, $P < 0.05$).

158

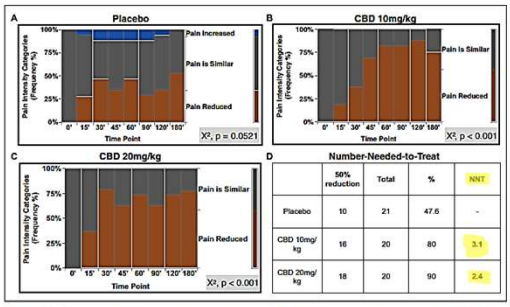


Figure 2. The frequency of "Pain Reduced" category significantly increased with time in both CBD groups. Pain intensity assessment for **(A)** placebo, **(B)** CBD 10 mg/kg, and **(C)** CBD 20 mg/kg. Pain categories compared to baseline (BL) pain: "pain increased," "pain similar," and "pain reduced," χ^2 tests, $P < 0.05$. **(D)** Number needed to treat (NNT) for a 50% reduction in BL pain for the experimental groups. CBD, cannabidiol.

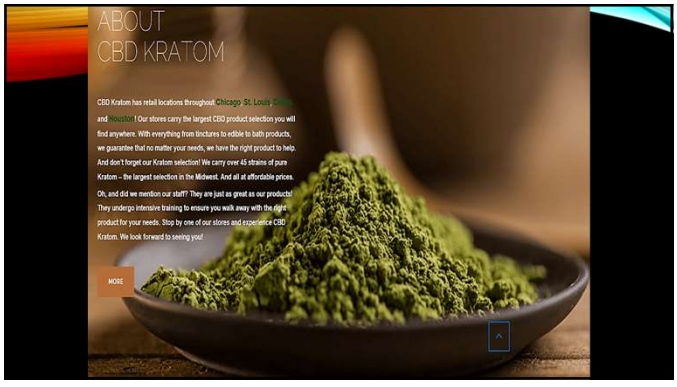
159

Table 3. Adverse Events Reported within the 3-h Observation Period and after the Observation Period at the 7-d Follow-up Visit.

Side Effects	CBD10, n (%)	CBD20, n (%)	Placebo, n (%)	χ^2, P Value	CBD10, n (%)	CBD20, n (%)	Placebo, n (%)	χ^2, P Value
n	21	20	23		18	18	22	
Time Point	3 h				3 h < t < 7 d			
CNS disorders								
Somnolence	3 (14.2)	3 (15)	1 (4.3)	>0.05	1 (5)	0	1 (4.5)	>0.05
Convulsion (seizure)	0	0	0	>0.05	0	0	0	>0.05
Ataxia (impaired coordination)	0	0	0	>0.05	0	0	0	>0.05
Pyrexia (fever)	0	0	0	>0.05	0	0	0	>0.05
Sedation	6 (28.5)	3 (15)	0	0.01	1 (5)	0	0	>0.05
Abnormal behavior	0	0	0	>0.05	0	0	1 (4.5)	>0.05
Headache	2 (9.5)	1	0	>0.05	0	0	0	>0.05
Psychomotor hyperactivity	0	0	0	>0.05	0	0	0	>0.05
Gastrointestinal disorders								
Decreased appetite	2 (9.5)	1 (5)	0	>0.05	0	0	0	>0.05
Nausea	1 (4.7)	0	0	>0.05	1 (5)	0	0	>0.05
Diarrhea	1 (4.7)	4 (20)	0	0.03	2 (11)	3 (16.6)	0	>0.05
Vomiting	0	1 (5)	0	>0.05	0	2 (11)	0	>0.05
Abdominal pain	1 (4.7)	4 (20)	0	0.03	0	4 (22.2)	0	0.006
Respiratory disorders								
Nasopharyngitis	1 (4.7)	0	0	>0.05	0	0	0	>0.05
Pneumonia	0	0	0	>0.05	0	0	0	>0.05
Infectious disorders								
Viral infection	0	0	0	>0.05	0	0	0	>0.05
Pharyngitis streptococcal	0	0	0	>0.05	0	0	0	>0.05
Gastroenteritis viral	0	0	0	>0.05	0	0	0	>0.05
Rash	0	0	0	>0.05	0	0	0	>0.05
Fatigue	3 (14.2)	4 (20)	1 (4.3)	>0.05	1 (5)	2 (11)	0	>0.05
Other								
Dry mouth	1 (4.7)	0	1	>0.05	0	0	0	>0.05
Anxiety	0	0	0	>0.05	0	0	0	>0.05
Paresthesia (tingling)	1 (4.7)	0	1 (4.3)	>0.05	0	0	1 (4.5)	>0.05
Hot flushes	1 (4.7)	0	0	>0.05	0	0	1 (4.5)	>0.05
Angina (chest tightness)	1 (4.7)	0	0	>0.05	0	0	0	>0.05
Double vision	0	0	1 (4.3)	>0.05	0	0	1 (4.5)	>0.05

χ^2 tests, $P < 0.05$.
CNS, central nervous system.

160



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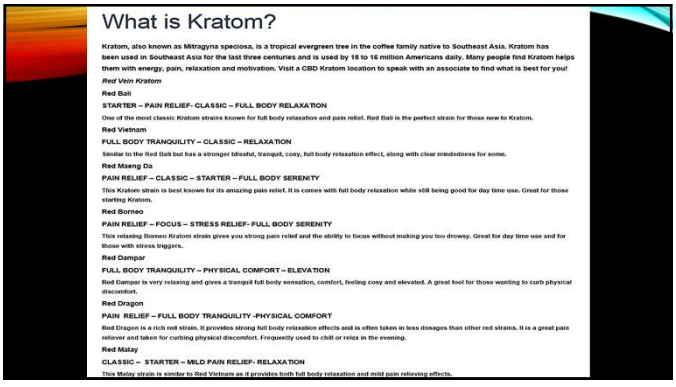
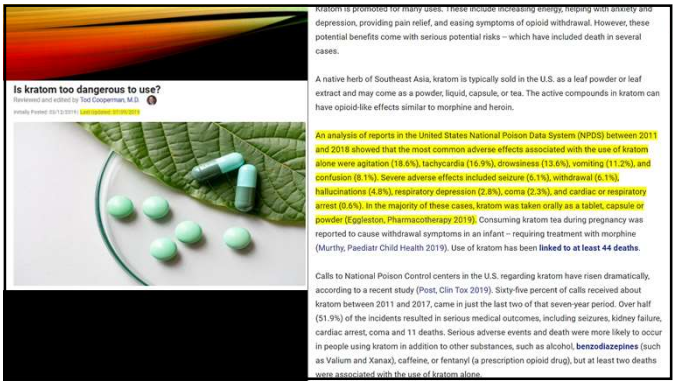


162

How does kratom affect the brain?

Kratom can cause effects similar to both opioids and stimulants. Two compounds in kratom leaves, *mitragynine* and *7-a-hydroxymitragynine*, interact with opioid receptors in the brain, producing sedation, pleasure, and decreased pain, especially when users consume large amounts of the plant. Mitragynine also interacts with other receptor systems in the brain to produce stimulant effects. When kratom is taken in small amounts, users report increased energy, sociability, and alertness instead of sedation. However, kratom can also cause uncomfortable and sometimes dangerous side effects.

163



164

165

CONCLUSIONS ABOUT RECREATIONAL CANNABIS

- Recreational cannabis will likely spread to most or all states
- Cannabis potency was 3-4% THC in the 70s and an average of 19% today
- High potency cannabis products contain up to 90% THC with no data
- Recent cannabis use compromises informed consent and increases pulse
- Signs & sx include red conjunctiva, slowed responses, slurred speech
- Increased tolerance to CNS depressants is seen with daily cannabis use
- Post-procedural cannabis use may LOWER pain threshold & increases the risk of bleeding and hyperemesis complications.
- CUD can be treated with N-acetyl-cysteine, gabapentin or systemic CBD.
- REGULAR USE DURING TEEN YEARS INCREASES INCIDENCE OF SCHIZOPHRENIA!
- Cannabis is a gateway drug and it IS addictive.

166

USEFUL RESOURCES FOR DENTAL PRACTICE

- www.consumerlab.com - $45 a year practical review of products
- www.samsha.gov – accurate information on SUD
- www.amersa.org - health professional resources for SUD
- www.drugfree.org – patient information resources
- www.dea.gov – status and scope of illicit drug problem in the U.S.
- www.drugabuse.gov –access to local treatment resources
- www.nida.nih.gov – comprehensive site for drug abuse info
- www.streetdrugs.org – names and appearances of illicit drugs

167

WHAT'S NEXT FOR RECREATIONAL CANNABIS: IMPLICATIONS FOR DENTISTRY

168

169

MECHANISTIC CLASSIFICATIONS OF DRUGS OF ABUSE

TABLE 32–1
The mechanistic classification of drugs of abuse.[a]

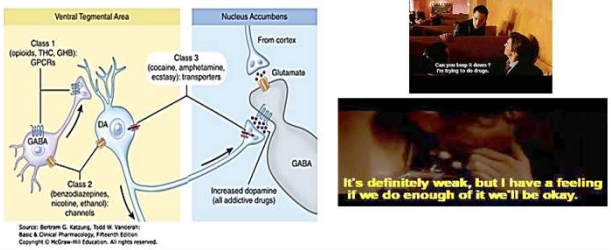
Name	Main Molecular Target	Pharmacology	Effect on Dopamine (DA) Neurons	R[2]
Drugs That Activate G Protein-Coupled Receptors				
Opioids	μ-OR ($G_{i/o}$)	Agonist	Disinhibition	4
Cannabinoids	CB_1R ($G_{i/o}$)	Agonist	Disinhibition	2
γ-Hydroxybutyric acid (GHB)	$GABA_BR$ ($G_{i/o}$)	Weak agonist	Disinhibition	?
LSD, mescaline, psilocybin	$5\text{-}HT_{2A}R$ (G_q)	Partial agonist	—	1
Drugs That Bind to Ionotropic Receptors and Ion Channels				
Nicotine	nAChR ($\alpha4\beta2$)	Agonist	Excitation	4
Alcohol	$GABA_AR$, 5-HT$_3$R, nAChR, NMDAR, Kir3 channels		Excitation, disinhibition (?)	3
Benzodiazepines	$GABA_AR$	Positive modulator	Disinhibition	3
Phencyclidine, ketamine	NMDAR	Antagonist	—	1
Drugs That Bind to Transporters of Biogenic Amines				
Cocaine	DAT, SERT, NET	Inhibitor	Blocks DA uptake	5
Amphetamine	DAT, NET, SERT, VMAT	Reverses transport	Blocks DA uptake, synaptic depletion	5
Ecstasy	SERT > DAT, NET	Reverses transport	Blocks DA uptake, synaptic depletion	7

5-HT$_2$R, serotonin receptor; CB_1R, cannabinoid-1 receptor; DAT, dopamine transporter; GABA, γ-aminobutyric acid; Kir3 channels, G protein–coupled inwardly rectifying potassium channels; LSD, lysergic acid diethylamide; μ-OR, μ-opioid receptor; nAChR, nicotinic acetylcholine receptor; NET, norepinephrine transporter; NMDAR, *N*-methyl-D-aspartate receptor; R, receptor; SERT, serotonin transporter; VMAT, vesicular monoamine transporter; ? indicates data not available.

170

NEUROPHARMACOLOGIC CLASSIFICATION OF ADDICTIVE DRUGS

Neuropharmacologic classification of addictive drugs by primary target (see text and Table 32–1). DA, dopamine; GABA, γ-aminobutyric acid; GHB, γ-hydroxybutyric acid; GPCRs, G protein–coupled receptors; THC, Δ^9-tetrahydrocannabinol.



Source: Bertram G. Katzung, Todd W. Vanderah: Basic & Clinical Pharmacology, Fifteenth Edition
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171

ARE THERE LESS ADDICTIVE DRUGS OF ABUSE?

- These drugs don't target dopamine as specifically
- They alter perception without causing strong sensations of reward and euphoria associated with dopamine receptor activation
- These agents primarily target cortical and thalmic tracts
  - Example drugs
    - LSD
    - Cocaine
    - Ketamine
    - Ecstasy
    - Psilocybin

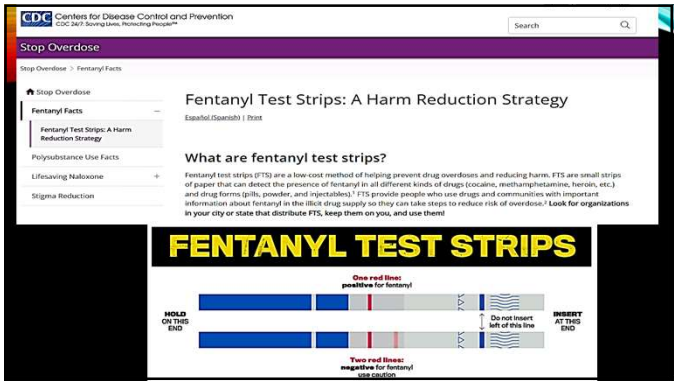
172

REVIEW OF MAIN CATEGORIES FOR DRUGS OF ABUSE

- Opioids
- Cannabinoids
- GHB
- LSD, Mescaline, Psilocybin
- Nicotine
- BZDP
- Alcohol
- Inhalants
- Cocaine
- Amphetamines
- Ecstasy/MDMA

173

174



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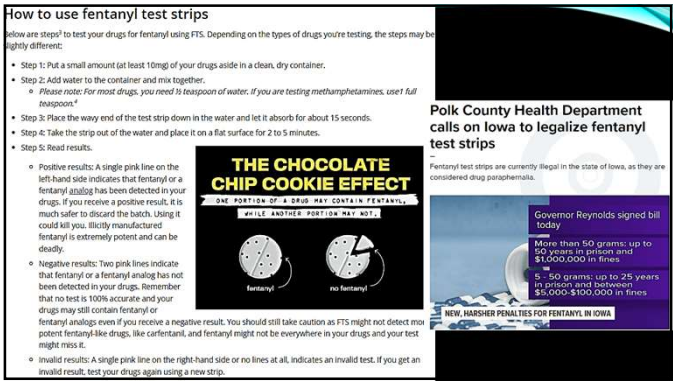

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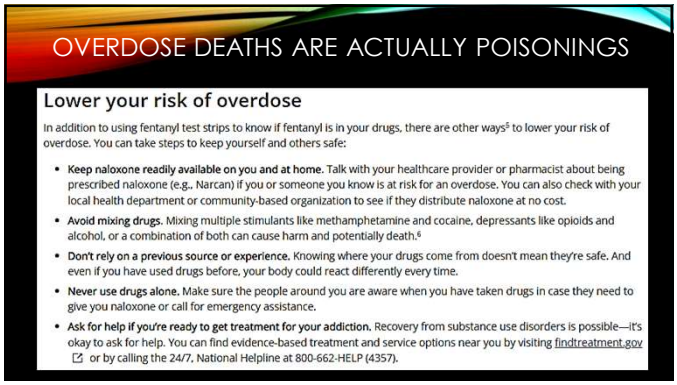

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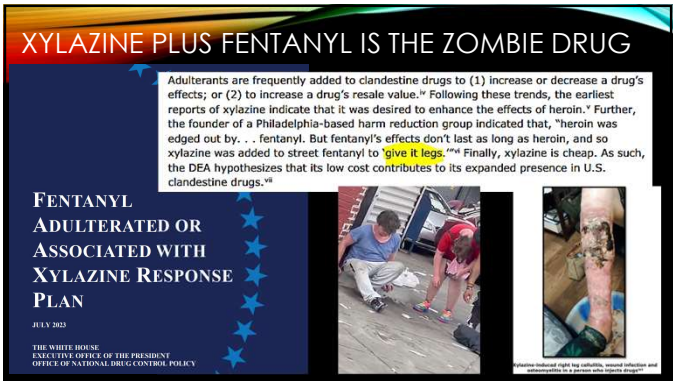

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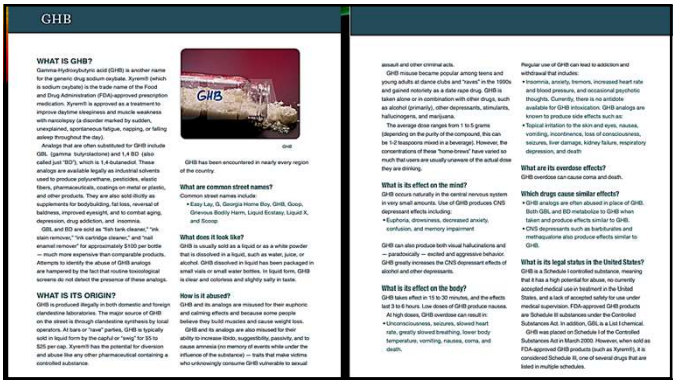

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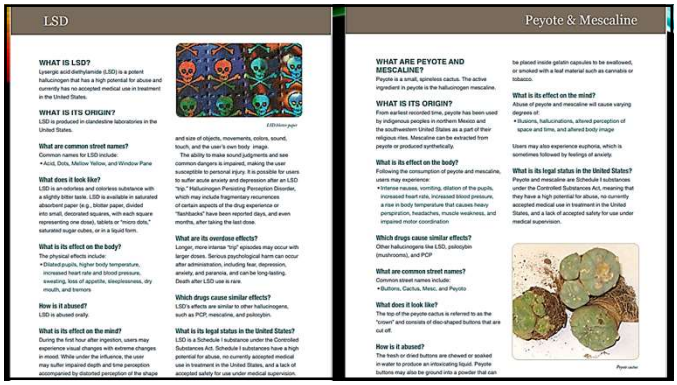

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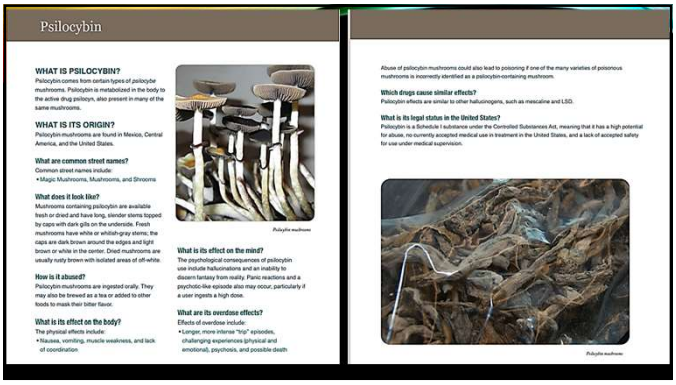

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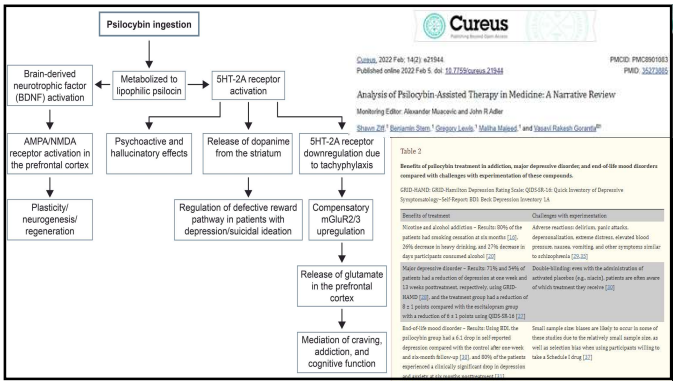

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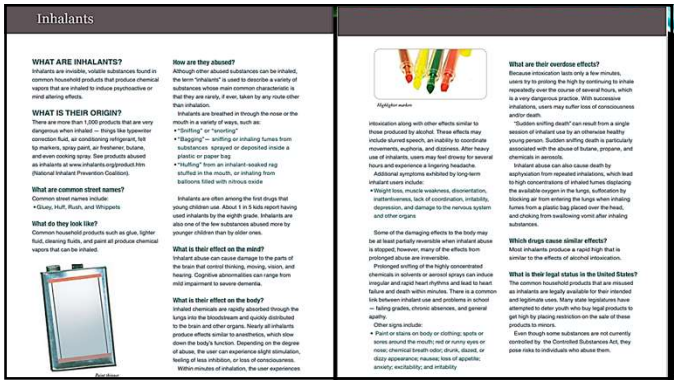

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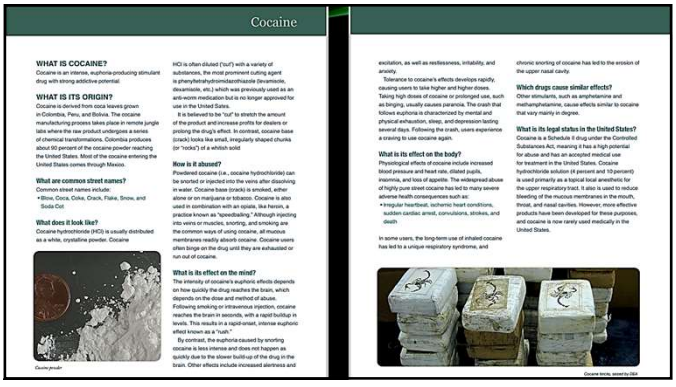

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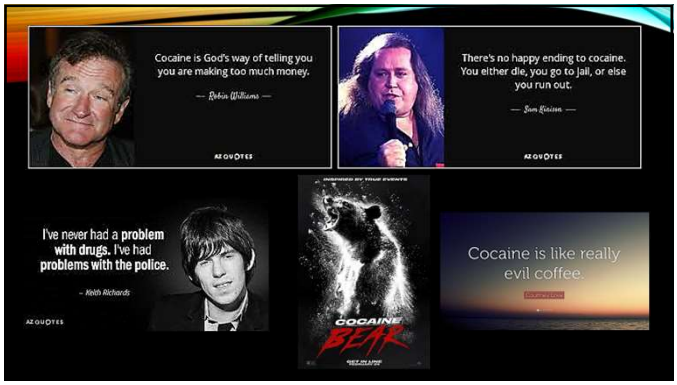

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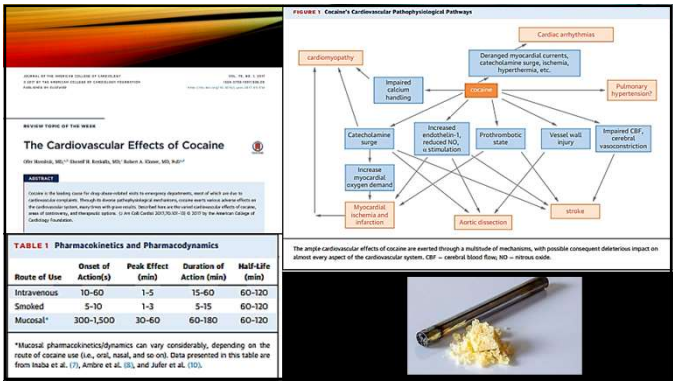

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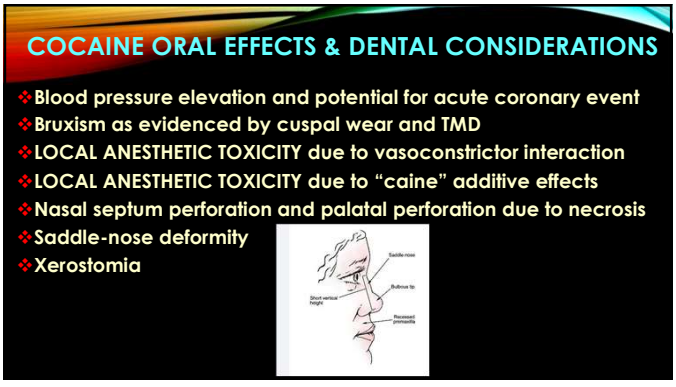


192

Amphetamines

WHAT ARE AMPHETAMINES?
Amphetamines are stimulants that speed up the body's system. Some are legally prescribed and used to treat attention-deficit hyperactivity disorder (ADHD).

WHAT IS THEIR ORIGIN?
Amphetamines were first marketed in the 1930s as Benzedrine in an over-the-counter inhaler to treat nasal congestion.
By 1937 amphetamines were available by prescription in tablet form and were used in the treatment of the sleeping disorder narcolepsy and ADHD.
Over the years, the use and abuse of clandestinely produced amphetamines have spread. Today, clandestine laboratory production of amphetamines has mushroomed, and the abuse of the drug has increased dramatically.

What are common street names?
Common street names include:
- Bennies, Black Beauties, Crank, Ice, Speed, and Uppers

What do they look like?
Amphetamines can look like pills or powder. Common prescription amphetamines include amphetamine and dextroamphetamine (Adderall®), dextroamphetamine (Dexedrine®), lisdexamphetamine (Vyvanse™) and methamphetamine (Desoxyn®).

How are they abused?
Amphetamines are generally taken orally or injected. However, the addition of "ice," the slang name of crystallized methamphetamine hydrochloride, has promoted smoking as another mode of administration. Just as "crack" is smokable cocaine, "ice" is smokable methamphetamine.

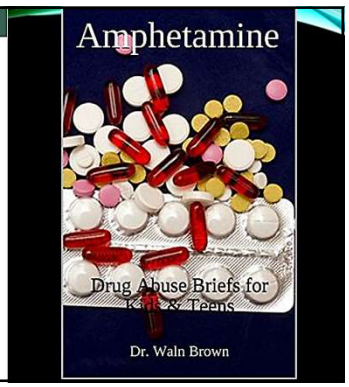
What is their effect on the mind?
The effects of amphetamines are similar to cocaine, but their onset is slower and their duration is longer. In contrast to cocaine, which is quickly removed from the brain and is almost completely metabolized, methamphetamine remains in the central nervous system longer, and a larger percentage of the drug remains uncharged in the body, producing prolonged stimulant effects.
Chronic abuse produces a psychosis that resembles schizophrenia and is characterized by paranoia, picking at the skin, preoccupation with one's own thoughts, and auditory and visual hallucinations. Violent and erratic behavior is frequently seen among chronic users of amphetamines.

What is their effect on the body?
Physical effects of amphetamine use include:
- Increased blood pressure and pulse rates, insomnia, loss of appetite, and physical exhaustion

What are their overdose effects?
Overdose effects include:
- Agitation, increased body temperature, hallucinations, convulsions, and possible death

Which drugs cause similar effects?
Drugs that cause similar effects include:
- Diamethyltryptamine, phendimetrazine, cocaine, crack, and khat

What is their legal status in the United States?
Many amphetamines are Schedule II stimulants, which means that they have a high potential for abuse and a currently acceptable medical use (in FDA-approved products). Pharmaceutical products are available only through a prescription that cannot be refilled.



193

Methamphetamine

WHAT IS METHAMPHETAMINE?
Methamphetamine (meth) is a stimulant. The FDA-approved brand-name medication is Desoxyn®.

WHAT IS ITS ORIGIN?
Mexican drug trafficking organizations have become the primary manufacturers and distributors of methamphetamine throughout the United States, including in Hawaii. Domestic clandestine laboratory operators also produce and distribute meth but on an exponentially smaller scale. The methods used depend on the availability of precursor chemicals.
Currently, this domestic clandestinely produced meth is mainly made with diverted products that contain pseudoephedrine. Mexican methamphetamine is made with different precursor chemicals. The Combat Methamphetamine Epidemic Act of 2005 requires retailers of non-prescription products containing pseudoephedrine, ephedrine, or phenylpropanolamine to place these products behind the counter or in a locked cabinet.
Consumers must show identification and sign a logbook for each purchase.

What are common street names?
Common street names include:
- Ballu, Bikers Coffee, Black Beauties, Chalk, Chicken Feed, Crank, Crystal, Glass, Go-Fast, Hiroppn, Ice, Meth, Methlies Quick, Poor Man's Cocaine, Shabu, Shards, Speed, Stove Top, Tina, Trash, Tweak, Uppers, Ventana, Vidrio, Yaba, and Yellow Bam

What does it look like?
Regular meth is a pill or powder. Crystal meth resembles glass fragments or shiny blue-white "rocks" of various sizes.


Methamphetamine in blackest form

How is it abused?
Meth is swallowed, snorted, injected, or smoked. To intensify the effects, users may take higher doses of the drug, take it more frequently, or change their method of intake.

What is its effect on the mind?
Meth is a highly addictive drug with potent central nervous system (CNS) stimulant properties.
Those who smoke or inject it report a brief, intense sensation, or rush. Oral ingestion or snorting produces a long-lasting high instead of a rush, which reportedly can continue for as long as half a day. Both the rush and the high are believed to result from the release of very high levels of the neurotransmitter dopamine into areas of the brain that regulate feelings of pleasure. Long-term meth use results in many damaging effects, including addiction.
Chronic meth users can exhibit violent behavior, anxiety, confusion, insomnia, and psychotic features including paranoia, aggression, visual and auditory hallucinations, mood disturbances, and delusions — such as the sensation of insects creeping on or under the skin.
Such paranoia can result in homicidal or suicidal thoughts. Researchers have reported that as much as 50 percent of the dopamine-producing cells in the brain can be damaged after prolonged exposure to relatively low levels of meth. Some studies suggested that the use of methamphetamine may also result in serotonergic neurotoxicity.

What is its effect on the body?
Taking even small amounts of meth can result in:
- Increased wakefulness, increased physical activity, decreased appetite, rapid breathing and heart rate, irregular heartbeat,, increased blood pressure, and hyperthermia (overheating)

High doses can elevate body temperature to dangerous, sometimes lethal, levels, and cause convulsions and even cardiovascular collapse and death. Meth use may also cause extreme anorexia, memory loss, and severe dental problems.

What are its overdose effects?
High doses may result in death from stroke, heart attack, or multiple-organ problems caused by overheating.

Which drugs cause similar effects?
Cocaine and potent stimulant pharmaceuticals, such as amphetamines and methylphenidate, produce similar effects.

What is its legal status in the United States?
Methamphetamine is a Schedule II stimulant under the Controlled Substances Act, which means that it has a high potential for abuse and a currently acceptable medical use (in FDA-approved products). It is available only through a prescription that cannot be refilled. Today there is only one legal meth product, Desoxyn®. It is currently marketed in 5, 10, and 15-milligram tablets (immediate release and extended-release formulations) and has very limited use in the treatment of obesity and ADHD.


Methamphetamine in blackest form

194

Ecstasy/MDMA

WHAT IS ECSTASY/MDMA?
3,4-methylenedioxymethamphetamine (MDMA) acts as both a stimulant and hallucinogen, producing an energizing effect, distortions in time and perception, and enhanced enjoyment of tactile experiences.
Adolescents and young adults use it to reduce inhibitions and to promote:
- Euphoria, feelings of closeness, empathy, and sexuality

Although MDMA is known among users as ecstasy, researchers have determined that many tablets sold as ecstasy may not contain any MDMA, or may contain MDMA in combination to other harmful drugs, such as:
- Methamphetamine, ketamine, cocaine, cathinones, and caffeine

In addition, other drugs similar to MDMA, such as 3,4-methylenedioxyamphetamine (MDA) or para-methoxyamphetamine (PMA), are often sold as ecstasy, which can lead to overdose and death when the user takes additional doses to obtain the desired effect.

WHAT IS ITS ORIGIN?
MDMA is a synthetically produced drug. Western Europe is the primary source for MDMA seized in the United States. Some MDMA coming in from Canada is also seized, but with significantly fewer incidents than from Europe.

What are common street names?
Common street names include:
- Adam, Beans, Clarity, Disco Biscuit, E, Ecstasy, Eve, Go, Hug Drug, Lover's Speed, MDMA, Peace, STP, X, and XTC

What does it look like?
MDMA is mainly distributed and sold in tablet form often with logos, creating brand names for users to seek out. The colorful pills are often hidden among colorful candies. MDMA is also distributed in capsules, powder, and liquid forms.

How is it abused?
MDMA use mainly involves swallowing tablets (50-150 mg), which are sometimes crushed and snorted, occasionally smoked, but rarely injected. MDMA is also available as a powder.
Users may take MDMA by "stacking" (taking three or more tablets at once) or by "piggy-backing" (taking a series of tablets over a short period of time) tablets. One trend among young adults is referred to as "randy flipping," which is the co-abuse of MDMA and LSD.
MDMA is considered a "party drug" or "club drug" As with many other drugs of abuse, MDMA is rarely used alone. It is common for users to mix MDMA with other substances, such as alcohol and marijuana.

What is its effect on the mind?
MDMA mainly affects brain cells that use the chemical serotonin to communicate with each other. Serotonin helps to regulate mood, aggression, libido, sleep, and sensitivity to pain. Clinical studies suggest that MDMA may increase the risk of long-term, perhaps permanent, problems with memory and learning.
MDMA causes changes in perception, including euphoria and increased sensitivity to touch, energy, sensual and sexual arousal, need to be touched, and need for stimulation.
Some unwanted psychological effects include:


MDMA/Ecstasy pills

- Confusion, anxiety, depression, paranoia, sleep problems, and drug craving

The onset of these effects usually occur within 30 to 45 minutes of after administration and usually last 4 to 6 hours, but they may last weeks.

What is its effect on the body?
Users of MDMA experience many of the same effects and face many of the same risks as users of other stimulants such as cocaine and amphetamines. These include increased motor activity, alertness, heart rate, and blood pressure. Some unwanted physical effects include:
- Muscle tension, tremors, involuntary teeth clenching, muscle cramps, nausea, faintness, chills, sweating, and blurred vision

Severe dehydration can result from the combination of the drug's effects and the crowded and hot conditions in which the drug is often taken.
Studies suggest chronic use of MDMA can produce damage to the serotonin system.

What are its overdose effects?
In high doses, MDMA can interfere with the body's ability to regulate temperature. On occasions, this can lead to a sharp increase in body temperature (hyperthermia), resulting in liver, kidney, or cardiovascular system failure, swelling of the brain, and even death. Furthermore, repeated use of MDMA over a short period of time may lead to potentially harmful concentrations of MDMA within the body due to the complex metabolism of MDMA.

Which drugs cause similar effects?
MDMA produces both amphetamine-like stimulation and mild mescaline-like hallucinations.

What is its legal status in the United States?
MDMA is a Schedule I drug under the Controlled Substances Act, meaning it has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision.

195

Rohypnol ®

WHAT IS ROHYPNOL?
Rohypnol® is a trade name for flunitrazepam, a CNS depressant that belongs to a class of drugs known as benzodiazepines. Flunitrazepam is also marketed as generic preparations and other trade name products outside of the United States.
Like other benzodiazepines, Rohypnol® produces sedative-hypnotic, anti-anxiety, and muscle relaxant effects. This drug has never been approved for medical use in the United States by the Food and Drug Administration. Outside the United States, Rohypnol® is commonly prescribed to treat insomnia. Rohypnol® is also referred to as a "date rape" drug.

WHAT IS ITS ORIGIN?
Rohypnol® is smuggled into the United States from other countries, such as Mexico.

What are common street names?
Common street names include:
- Circles, Forget Pill, Forget-Me-Pill, La Rocha, Lunch Money Drug, Mexican Valium, Pingus, R2, Reynolds, Roach, Roach 2, Roaches, Roaches, Roopies, Rebutal, Rochas Dos, Rohypnol, Roofies, Rophies, Ropias, Ropies, Row-Drug, Ruffies, and Wolfies

What does it look like?
Prior to 1997, Rohypnol® was manufactured as a white tablet (0.5-2 milligrams per tablet), and when mixed in drinks, was colorless, tasteless, and odorless. In 1997, the manufacturer responded to concerns about the drug's role in sexual assaults by reformulating the drug.
Rohypnol® is now manufactured as an oblong olive green tablet with a speckled blue core that when dissolved in light-colored drinks will dye the liquid blue. However, generic versions of the drug may not contain the blue dye.

How is it abused?
The tablet can be swallowed whole, crushed and snorted, or dissolved in liquid. Adolescents may abuse Rohypnol® to produce a euphoric effect often described as a "high." While high, they experience reduced inhibitions and impaired judgment.
Rohypnol is also used in combination with alcohol to produce an exaggerated intoxication.
In addition, abuse of Rohypnol® may be associated with multiple-substance abuse. For example, cocaine users may use benzodiazepines such as Rohypnol® to relieve the side effects (e.g., irritability and agitation) associated with cocaine binges.
Rohypnol is also misused by physically and psychologically incapacitate victims targeted for sexual assault. The drug is usually placed in the alcoholic drink of an unsuspecting victim to

incapacitate them and prevent resistance to sexual assault. The drug leaves the victim unaware of what has happened to them.

What is its effect on the mind?
Like other benzodiazepines, Rohypnol® slows down the functioning of the CNS producing:
- Drowsiness (sedation), sleep (pharmacological hypnosis), decreased anxiety, and amnesia (no memory of events while under the influence of the substance)

Rohypnol® can also cause:
- Increased or decreased reaction time, impaired mental functioning and judgment, confusion, aggression, and excitability

What is its effect on the body?
Rohypnol® causes muscle relaxation. Adverse physical effects include:
- Slurred speech, loss of motor coordination, weakness, headache, and respiratory depression

Rohypnol® also can produce physical dependence when taken regularly over a period of time.

What are its overdose effects?
High doses of Rohypnol®, particularly when combined with CNS-depressant drugs such as alcohol and heroin, can cause severe sedation, unconsciousness, slow heart rate, and suppression of respiration that may be sufficient to result in death.

Which drugs cause similar effects?
Drugs that cause similar effects include GHB (gamma hydroxybutyrate) and other benzodiazepines such as alprazolam (e.g., Xanax®), clonazepam (e.g., Klonopin®), and diazepam (e.g., Valium®).

What is its legal status in the United States?
Rohypnol® is a Schedule IV substance under the Controlled Substances Act. Rohypnol® is not approved for manufacture, sale, use, or importation to the United States. However, it is legally manufactured and marketed in other countries. Penalties for possession, trafficking, and distribution involving one gram or more are the same as those of a Schedule I drug.


Blister pack of Rohypnol® tablets

196

Ketamine

WHAT IS KETAMINE?
Ketamine is a dissociative anesthetic that has some hallucinogenic effects. Ketamine distorts the perception of sight and sound and makes the user feel disconnected and not in control. It is referred to as a "dissociative anesthetic hallucinogen" because it makes patients feel detached from their pain and environment.
Ketamine can induce a state of sedation (feeling calm and relaxed), immobility, relief from pain, and amnesia (no memory of events while under the influence of the drug) and is abused for the dissociative sensations and hallucinogenic effects. Ketamine has also been used to facilitate sexual assault.
Ketamine is an approved medical product as an injectable, short-acting anesthetic for use in humans and animals and as esketamine (Spravato®; the active form of the drug) as a nasal spray for treatment resistant depression.

WHAT IS ITS ORIGIN?
Ketamine is produced commercially in a number of countries, including the United States. Most of the ketamine illegally distributed in the United States is diverted or stolen from legitimate sources, particularly veterinary clinics, or smuggled into the United States from Mexico.
Distribution of ketamine typically occurs among friends and acquaintances, most often at nightclubs, parties, music festivals, and concerts; street sales of ketamine are rare.

How is it abused?
Ketamine, along with the other "club drugs," has become popular among teens and young adults at dance clubs, musical festivals, and concerts.
Ketamine is manufactured commercially as a powder

Vials containing liquid Ketamine

or liquid. Powdered ketamine is also formed from pharmaceutical ketamine by evaporating the liquid using hot plates, warming trays, or microwave ovens, a process that results in the formation of crystals, which are then ground into powder.

What are common street names?
Common street names include:
- Cat Tranquilizer, Cat Valium, Jet K, K9 Kat, Purple, Special K, Special La Coke, Super Acid, Super K, and Vitamin K

What does it look like?
Ketamine comes in a clear liquid and a white or off-white powder. Powdered ketamine (100 milligrams to 200 milligrams) typically is packaged in small glass vials, small plastic bags, and capsules as well as paper, glassine, or aluminum foil folds.
Powdered ketamine is cut into lines known as bumps and snorted, or it is smoked, typically in marijuana or tobacco cigarettes. Liquid ketamine is injected or mixed into drinks. Ketamine is found by itself or often in combination with MDMA, amphetamine, methamphetamine, or cocaine.

What is its effect on the mind?
Ketamine produces hallucinations. It distorts perceptions of sight and sound and makes the user feel disconnected and not in control. A "Special K" trip is touted as better than that of LSD or PCP because its hallucinatory effects are relatively short in duration, lasting approximately 30 to 60 minutes as opposed to several hours.
Slang for experiences related to Ketamine or effects of ketamine include:
- "K-land" (refers to a mellow & colorful experience)
- "K-hole" (refers to the out-of-body, near death experience)
- "Baby food" (users sink in to blissful, infantile inertia)
- "God" (users are convinced that they have met their maker)

The onset of effects is rapid and often occurs within a few minutes of taking the drug, though taking it orally results in a slightly slower onset of effects. Ketamine may cause unwanted side effects such as: agitation, depression, cognitive difficulties, unconsciousness, and amnesia.
Hallucinogen Persisting Perception Disorder (HPPD) has been reported several weeks after ketamine use and may include experiencing prolonged visual disturbances

What is its effect on the body?
A couple of minutes after taking the drug, the user may experience an increase in heart rate and blood pressure that gradually decreases over the next 10 to 20 minutes. Ketamine can make users unresponsive to stimuli. When in this state, users experience:
- Involuntarily rapid eye movement, dilated pupils, salivation, tear secretions, and stiffening of the muscles, possible nausea


Ketamine in various forms

What are its overdose effects?
An overdose can cause unconsciousness and dangerously slowed breathing.

Which drugs cause similar effects?
Other hallucinogenic drugs such as LSD, PCP, and mescaline can cause hallucinations. There are also several drugs such as GHB, Rohypnol®, and other depressants that are misused for their amnesiac or sedative properties to facilitate sexual assault.

What is its legal status in the United States?
Since the 1970s, ketamine has been marketed in the United States as an injectable, short-acting anesthetic for use in humans and animals. In 1999, ketamine, including its salts, isomers and salts of isomers, became a Schedule III non-narcotic substance under the Controlled Substances Act. It currently has accepted medical uses for short-term sedation and anesthesia. In addition, in 2019, FDA approved the S(+) enantiomer of ketamine (esketamine) nasal spray version (Spravato®) for treatment-resistant depression that is only available at a certified doctor's office or clinic. Ketamine has the potential for abuse, which may lead to moderate or low physical dependence or high psychological dependence.

197

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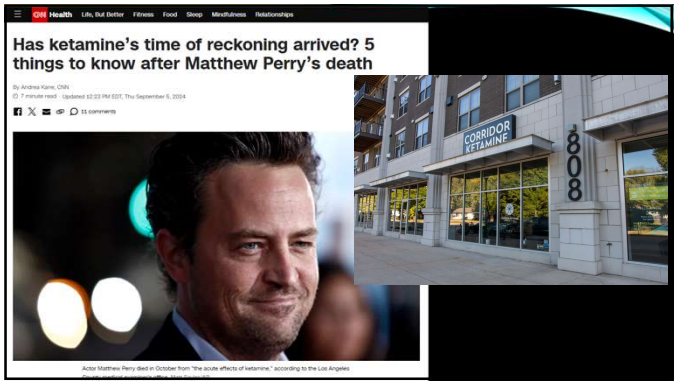

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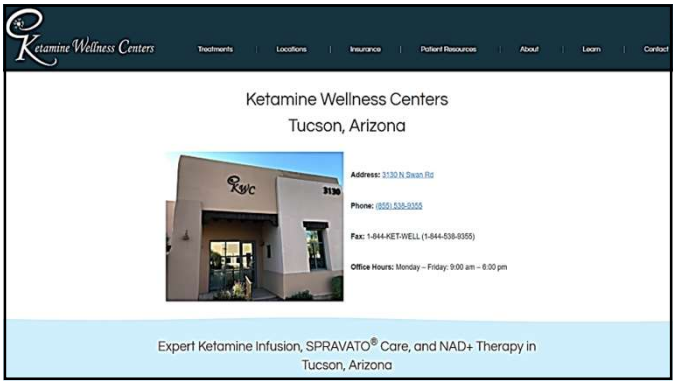

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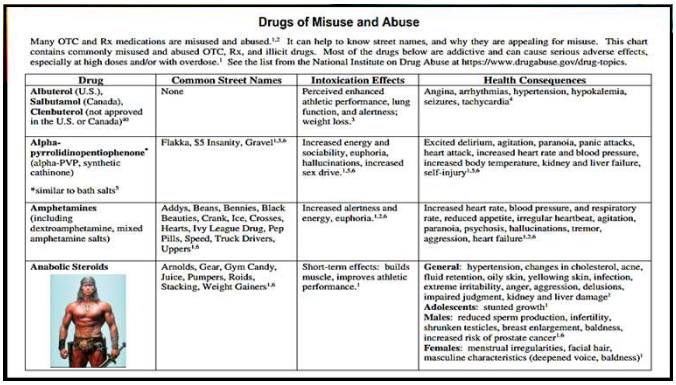

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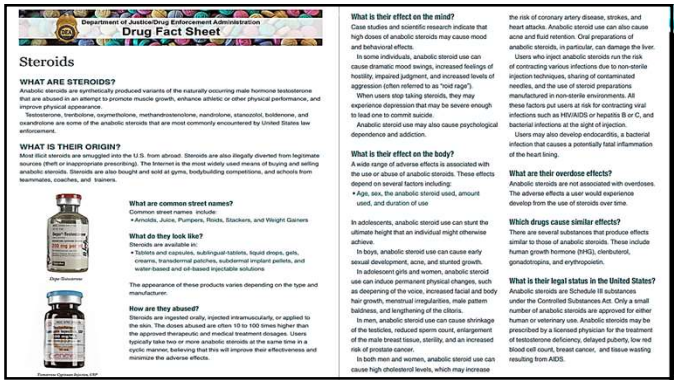

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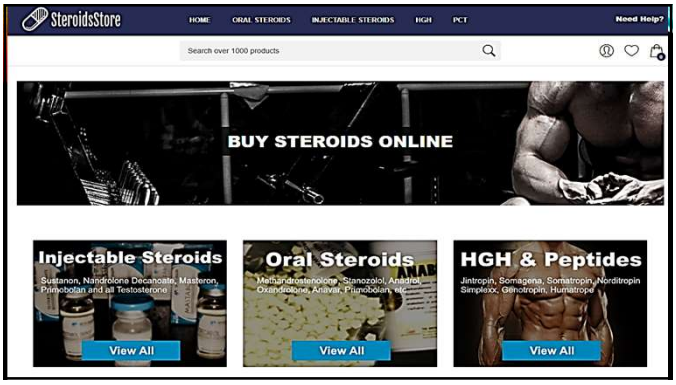

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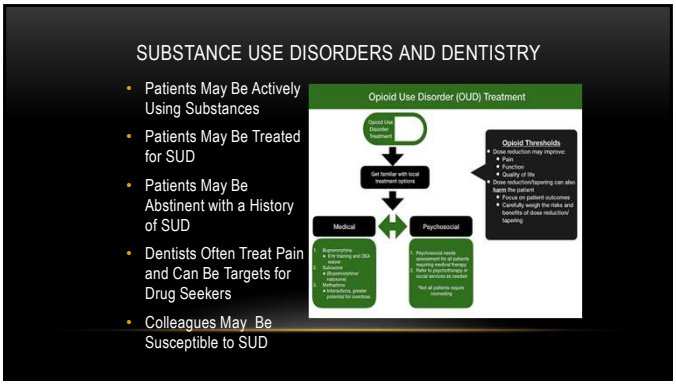

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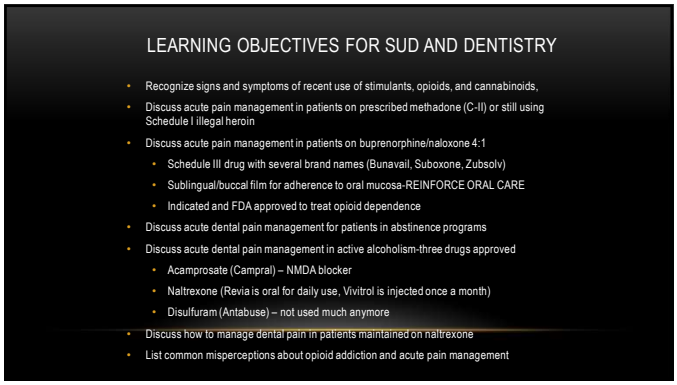

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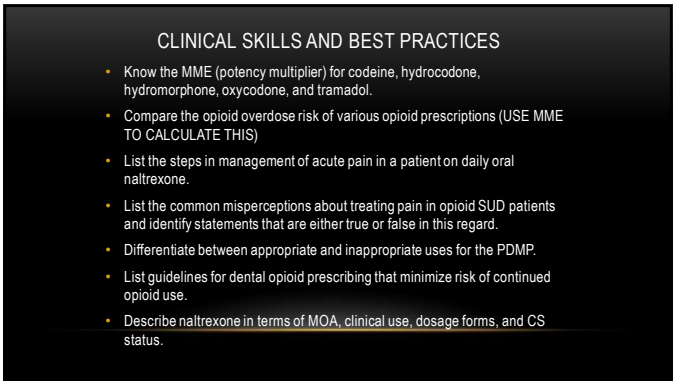

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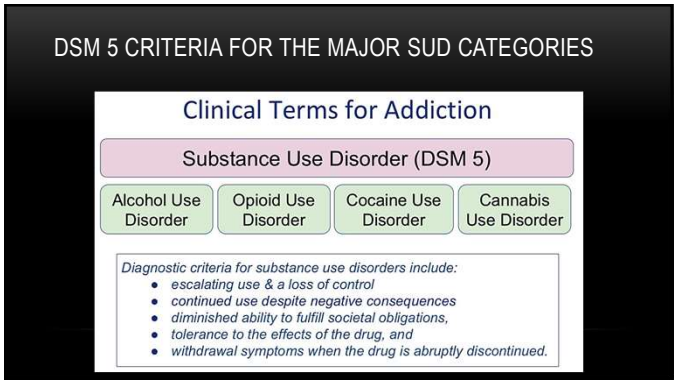

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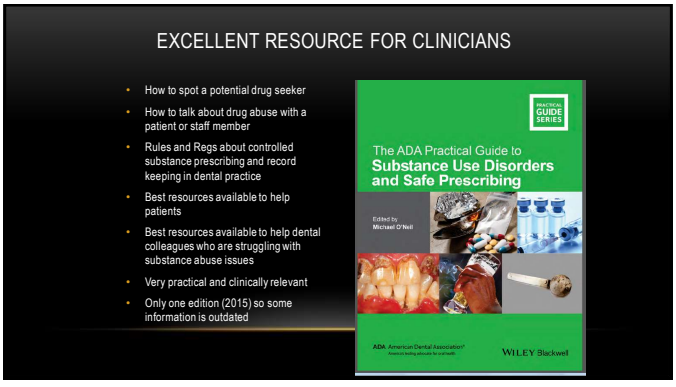
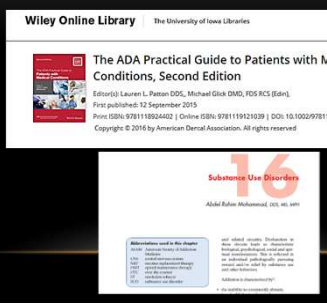


210

THE ADA PRACTICAL GUIDE TO PATIENTS WITH MEDICAL CONDITIONS-NOT AS DETAILED FOR SUD



211

Table 5: CNS Depressants	
General Effects	• Slow down nervous system activity • Decrease anxiety • Drowsiness • Relax muscles • Sedation • Dilated blood vessels • Dilated pupils
Method(s) of Administration	• Ingested • Injected • Smoked • Snorted
Withdrawal Symptoms	• Seizures • Hallucinations • Tremors • Agitation • Irritability • Sweating • Anxiety

212

Table 6: Opiates & Opioids (Narcotics)	
Action & Use	These drugs (along with amphetamines and cocaine) offer the most powerful activation of the drug reward system. Activation of opiate receptors in the brain produces sensations of pleasure (reward) and pain relief (analgesic). Opiates may also be used as antidiarrheal and **antitussive** agents.
Method(s) of Administration	• Oral (ingested and transmucosal) • Snorted • Smoked • Injected (increased risk of hepatitis, HIV and blood poisoning)
Effects	• Vomiting • Drowsiness • Depressed respiration • Constricted (pinpoint) pupils
Prolonged Use/Abuse	• Physical and psychological dependence • Constipation • Congested lungs • Peptic and duodenal ulcers • Diabetes • Liver disease* • Death *narcotics pain relievers are commonly made with acetaminophen; abuse of these drugs expose the user to prolonged doses of acetaminophen

213

Table 7: CNS Stimulants [3]	
General Effects	• Increase nervous system activity • Increase heart rate and blood pressure • Increase gastric and adrenal secretions • Nausea, vomiting, diarrhea • Xerostomia • Headache • Fever • Loss of coordination • Mood swings • Loss of appetite • Dilated pupils • Long periods without sleep (24-120 hours) followed by long periods of sleep (24-48 hours) (methamphetamine)
Method(s) of Administration	• Snorted • Smoked • Injected • Ingested • Rubbed into gums • Rectal insertion
Withdrawal Symptoms	• Depression • Severe hunger • Exhaustion
Mental Symptoms	• Paranoia • Anxiousness • Nervousness • Agitation • Extreme Mood Swings • Hallucinations • Delusions

214

Table 8: Hallucinogens	
General Effects	• Visual and/or auditory distortions • Rapid emotional swings • Delusions • Sexual dysfunction • Decreased muscle coordination • May develop chronic mental disorders following long term use
Method(s) of Administration	• Injected • Ingested • Swallowed (e.g., paper soaked with LSD) • Ocular (LSD dropped into eyes with an eyedropper) • Smoked • Sniffed
Withdrawal Symptoms	Although psychological dependence is likely, no withdrawal symptoms occur when use is discontinued.

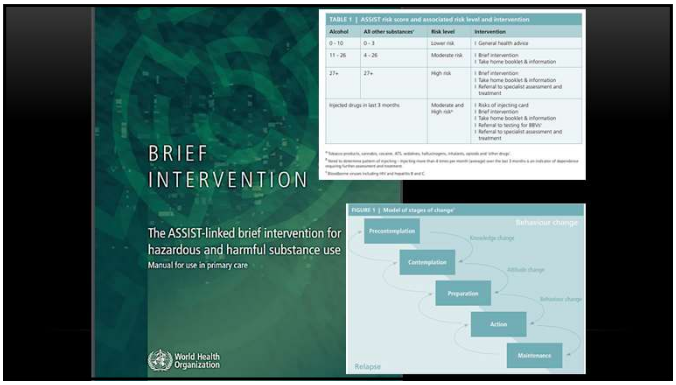
215

Table 9: Cannabis [8, 9, 11]	
General Effects	• Increased pulse rate • Bronchial passages relax and expand • Blood vessels of eyes dilate • Xerostomia • Increased appetite • Apathy • Impaired immune symptoms • Confusion • Impaired coordination • Increased risk of lung cancer, chronic bronchitis • Impaired memory (temporary and permanent)
Method(s) of Administration	• Smoked • Oral ingestion
Withdrawal Symptoms	• Irritability • Sleeplessness • Anxiety • Increased aggression has been displayed peaking approximately one week after the last use of the drug

216

Table 11: Screening and Intervention	
ASK about drug and alcohol use	Use the health history and verbally inquire about drug and alcohol use. CAGE or other screening inventories may be used.
ASSESS for drug and alcohol related problems	*Determine whether there is a* maladaptive pattern of alcohol use, *causing* clinically significant impairment *or* distress. Note any behavioral or clinical manifestations of substance abuse such as premalignant oral lesions or unexpected drug interactions.
ADVISE and ASSIST	State your conclusion and recommendation clearly: "You are drinking more than is medically safe." Relate to patient's concerns and medical findings. "I am concerned that that the sore you brought to my attention may be related to your smoking and alcohol intake; we will refer you for a biopsy. I strongly recommend that you quit.") **Gauge readiness** to change abuse status "Are you willing to consider making changes in your drinking and or smoking?"
At Follow-up: Continue Support	Provide ongoing support for the patient. Monitor efforts to cut down or abstain. Reinforce positive behavior.

217



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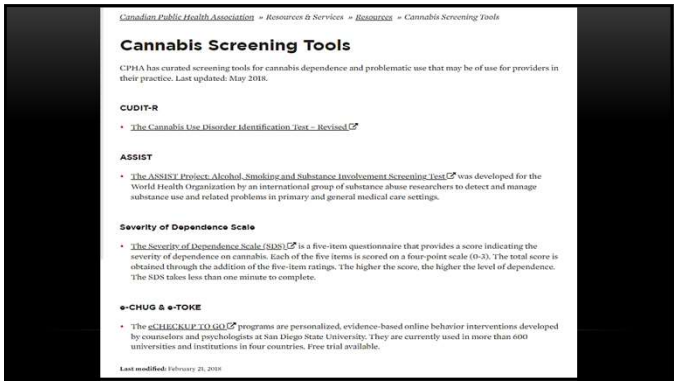

Canadian Public Health Association » Resources & Services » Resources » Cannabis Screening Tools

Cannabis Screening Tools

CPHA has curated screening tools for cannabis dependence and problematic use that may be of use for providers in their practice. Last updated: May 2018.

CUDIT-R

- The Cannabis Use Disorder Identification Test – Revised

ASSIST

- The ASSIST Project: Alcohol, Smoking and Substance Involvement Screening Test was developed for the World Health Organization by an international group of substance abuse researchers to detect and manage substance use and related problems in primary and general medical care settings.

Severity of Dependence Scale

- The Severity of Dependence Scale (SDS) is a five-item questionnaire that provides a score indicating the severity of dependence on cannabis. Each of the five items is scored on a four-point scale (0-3). The total score is obtained through the addition of the five-item ratings. The higher the score, the higher the level of dependence. The SDS takes less than one minute to complete.

e-CHUG & e-TOKE

- The eCHECKUP TO GO programs are personalized, evidence-based online behavior interventions developed by counselors and psychologists at San Diego State University. They are currently used in more than 600 universities and institutions in four countries. Free trial available.

Last modified: February 21, 2018

219


The Cannabis Use Disorder Identification Test - Revised (CUDIT-R)

Have you used any cannabis over the past six months? Yes_____ No _____

If you answered "Yes" to the previous question, please answer the following questions about your cannabis use. Circle the response that is most correct for you in relation to your cannabis use over the *past six months.*

1. How often do you use cannabis?
Never 0 | Monthly or less 1 | 2-4 times a month 2 | 2-3 times a week 3 | 4+ times a week 4

2. How many hours were you "stoned" on a typical day when you had been using cannabis?
Less than 1 0 | 1 or 2 1 | 3 or 4 2 | 5 or 6 3 | 7 or more 4

3. How often during the past 6 months did you find that you were not able to stop using cannabis once you had started?
Never 0 | Less than monthly 1 | Monthly 2 | Weekly 3 | Daily/almost daily 4

4. How often during the past 6 months did you fail to do what was normally expected from you because of using cannabis?
Never 0 | Less than monthly 1 | Monthly 2 | Weekly 3 | Daily or almost daily 4

5. How often in the past 6 months have you devoted a great deal of your time to getting, using, or recovering from cannabis?
Never 0 | Less than monthly 1 | Monthly 2 | Weekly 3 | Daily/almost daily 4

6. How often in the past 6 months have you had a problem with your memory or concentration after using cannabis?
Never 0 | Less than monthly 1 | Monthly 2 | Weekly 3 | Daily or almost daily 4

7. How often do you use cannabis in situations that could be physically hazardous, such as driving, operating machinery, or caring for children?
Never 0 | Less than monthly 1 | Monthly 2 | Weekly 3 | Daily/almost daily 4

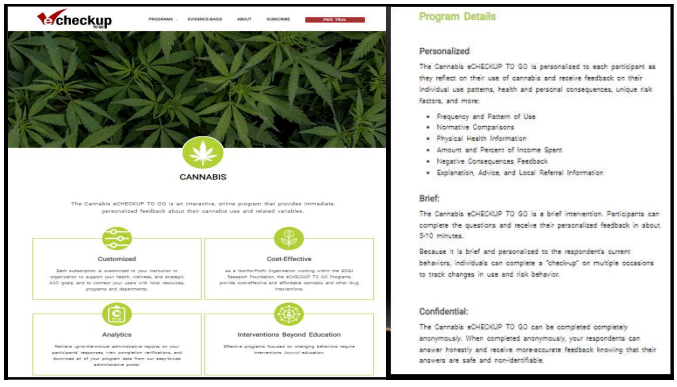
8. Have you ever thought about cutting down, or stopping, your use of cannabis?
Never 0 | Yes, but not in the past 6 months 2 | Yes, during the past 6 months 4

This questionnaire was designed for self-administration and is scored by adding each of the 8 items:
Question 1-7 are scored on a 0-4 scale
Question 8 is scored 0,2, or 4

Score:_____

Scores of 8 or more indicate hazardous cannabis use, while scores of 12 or more indicate a possible cannabis use disorder for which further intervention may be required.

220



221

Table 12: Intraoral Findings	
Drug	**Intraoral Manifestations**
alcohol Abuse and alcoholism	• Oral cancer • Leukoplakia and other premalignant conditions • Oral mucosal changes • Inflammation of one or both parotid glands • Oral ulceration • Glossitis • Angular chelitis • Candidiasis • Glossodynia • Prolonged bleeding • Facial tics • Oral and facial • High dental caries rate [25] • Dental erosion [25] • Bruxism • Increased calculus deposits • Halitosis (fruity acetone breath) • Delayed wound healing and unpredictable treatment response • Reduced tolerance to pain [25]
Stimulants	• Xerostomia • Clenching, grinding bruxism
Methamphetamine	• Xerostomia • Clenching, grinding bruxism • Extensive and severe dental caries • Tooth loss

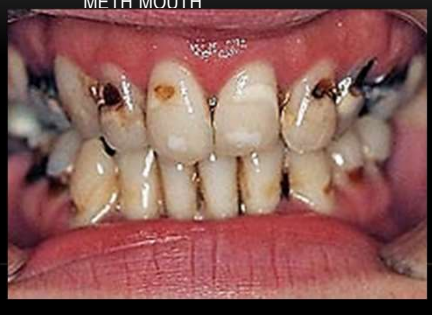
222

WHAT IS "METH MOUTH"??

- Rampant and severe decay which is common among methamphetamine addicts
  - Severity depends on frequency and type of use
  - Smoking meth is more destructive than other types of use because the acidic drug vapors are heated and held in contact with the teeth.
- Early cases present as shallow Class V lesions
- Lesions progress to cavitating buccal destruction

223

METH MOUTH



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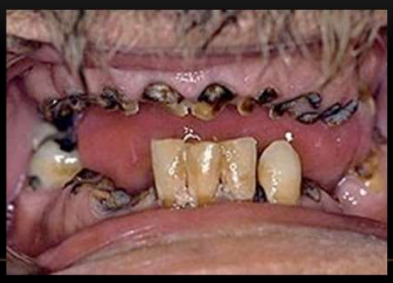
METH MOUTH



225

WHY ARE TEETH DEVASTATED BY METH?

- Poor Oral Hygiene
- Significant Xerostomia
- Consumption of Sugary Acidic Beverages
- Lack of Professional Care

226

POOR ORAL HYGIENE

- Meth has a long duration of action
  - User is euphoric for 12 hours at a time
  - User "crashes" when meth wears off
  - User becomes depressed and despondent
- Meth "takes over" the user's thoughts
  - Seeking and using meth is the most important activity for the meth addict
  - Self care of any kind is virtually ignored

227

XEROSTOMIA

- Meth is a potent constrictor of salivary gland blood flow
- Meth reduces saliva during prolonged waking hours and then patient sleeps
- Xerostomia resembles that of head and neck radiation and cancer chemotherapy patients
- Heavy plaque deposits are usually grey which indicates staining with tobacco smoke

228

BRUXISM

- Meth promotes increased muscle activity
- Meth increases anxiety levels
- Meth addicts are much more likely to grind and clench their teeth
- Meth-induced bruxism may cause oblique cleaving of canine and premolar clinical crowns
  - Occlusal plane and structure of teeth are weakened by deep Class V decay

229

DRINKING SUGARY/ACIDIC BEVERAGES

- Meth addicts have dry "cotton" mouths
  - Continuous drinking of Mountain Dew and other sugared/acidic sodas relieves dry mouth feeling – phosphoric, citric and malic acids
  - Meth users also have very poor nutrition and use high fructose corn syrup and caffeine as nutrition!
- Combination of no buffering capacity and constant pH of 2.8-3.4 cause severe erosion

230

LACK OF PROFESSIONAL CARE

- Meth Addicts Generally Avoid Dental Care
  - They don't seek treatment for pain
  - They seek treatment due to inability to chew or due to aesthetic concerns
- Meth Addicts Often Defer Dental Treatment
  - They want to avoid detection and identification
  - Often present for treatment only when irreversible and advanced damage has already occurred

231

HOW TO IDENTIFY METH SUD

- Unexplained and accelerated decay in teenagers and young adults
- Distinctive pattern of decay on buccal smooth surface and interproximal surfaces of anteriors
- Excessive tooth wear due to grinding/clenching
- Malnourished appearance and skin lesions
- Dilated and reactive pupils

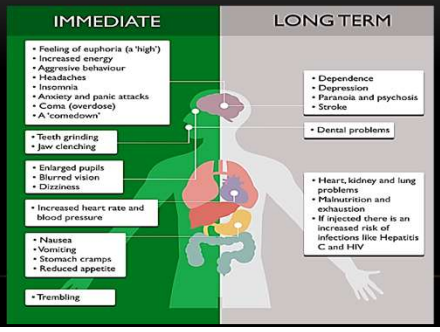
232

SPECIAL TREATMENT CONSIDERATIONS

- Strategies to Combat Poor Compliance
  - Encourage the use of a powered toothbrush with a 2 minute timer (costs $17-$100)
  - Use of sugar-free antacid after smoking meth
  - Using lozenges or gum with xylitol or Recaldent
  - Addition of an antimicrobial in toothpaste
    - Stannous fluoride, zinc, essential oils
  - Use of high concentration fluoride toothpaste

233

EFFECTS OF METHAMPHETAMINE USE



234

SPECIAL TREATMENT CONSIDERATIONS

- Methamphetamine Interacts with Dental Drugs
  - Most significant interaction is with epinephrine
  - Limit epinephrine to 4-6ml of 1:100,000
  - Meth can trigger transient hyperalgesia
- General Anesthetic Inhaled Gases Interact
  - Recent Meth use with general anesthesia can trigger seizures or cardiac arrhythmias

235

SPECIAL TREATMENT CONSIDERATIONS

- Habitual Meth Users are Called "Tweakers"
- Patient May Appear Normal At First
  - Awake for extended time periods
  - Sudden paranoid or violent reactions

- Evaluate further to determine severity of stimulatory symptoms and whether to use safety precautions

236

SPECIAL TREATMENT CONSIDERATIONS

- If Patient's eye movements are 10x normal, voice has a quiver, and jerky movements:
  - Keep your distance so as not to threaten
  - Do not use bright lights
  - Slow your speech and lower your voice
  - Slow your movements
  - Keep your hands visible
  - Keep the tweaker talking as much as possible

237

SPECIAL TREATMENT CONSIDERATIONS

- A Tweaker who becomes silent can be EXTREMELY DANGEROUS:
  - Silence may indicate that the patient's paranoid thoughts have taken the place of reality
  - Anyone present in the office can become part of the patient's paranoid delusions.
  - These patients cannot be seen for elective care.
  - The police should be summoned if the patient threatens anyone. Take the threats seriously.

238

TREATMENT FOR METH SUD

- Ongoing research is intensifying
- Use of antidepressants is common
- Cognitive behavioral interventions
  - Modify patient's thinking, expectations
  - Modify long-term behaviors
  - Increase coping skills
- Recovery support groups are very helpful
  - www.crystalmeth.org

239

METHAMPHETAMINE SUD IS VERY DIFFICULT TO TREAT

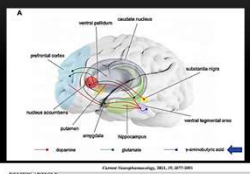

The NEW ENGLAND JOURNAL of MEDICINE

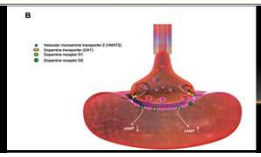
ORIGINAL ARTICLE

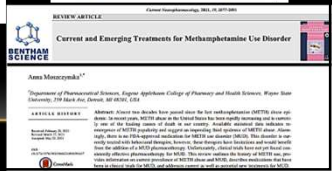
Bupropion and Naltrexone in Methamphetamine Use Disorder

M.H. Trivedi, R. Walker, W. Ling, A. dela Cruz, G. Sharma, T. Carmody, U.E. Ghitza, A. Wahle, M. Kim, K. Shores-Wilson, S. Sparenborg, P. Coffin, J. Schmitz, K. Wiest, G. Bart, S.C. Sonne, S. Wakhlu, A.J. Rush, E.V. Nunes, and S. Shoptaw

ABSTRACT







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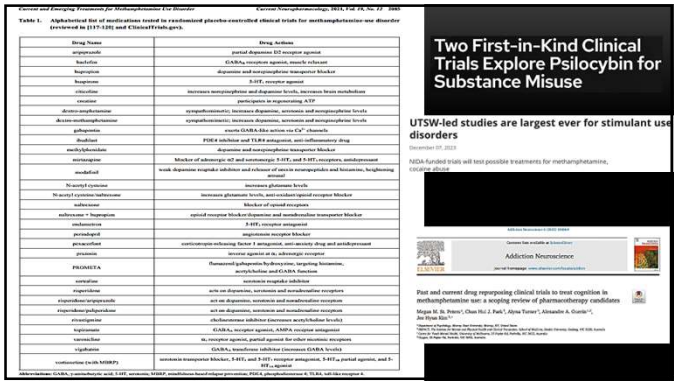


Table 1. Alphabetical list of medications tested in randomized placebo-controlled clinical trials for methamphetamine-use disorder (reviewed in [117-120] and ClinicalTrials.gov).

Drug Name	Drug Actions
aripiprazole	partial dopamine D2 receptor agonist
baclofen	$GABA_B$ receptor agonist, muscle relaxant
bupropion	dopamine and norepinephrine transporter blocker
buspirone	5-HT$_{1A}$ receptor agonist
citicoline	increases norepinephrine and dopamine levels, increases brain metabolism
cocaine	participates in regenerating ATP
dextro-amphetamine	sympathomimetic; increases dopamine, serotonin and norepinephrine levels
dextro-methamphetamine	sympathomimetic; increases dopamine, serotonin and norepinephrine levels
gabapentin	exerts GABA-like action via Ca^{2+} channels
ibudilast	PDE4 inhibitor and TLR4 antagonist, anti-inflammatory drug
methylphenidate	dopamine and norepinephrine transporter blocker
mirtazapine	blocker of adrenergic α2 and serotonergic 5-HT$_2$ and 5-HT$_3$ receptors, antidepressant
modafinil	weak dopamine reuptake inhibitor and release of orexin neuropeptides and histamine, heightening arousal
N-acetyl cysteine	increases glutamate levels
N-acetyl cysteine/naltrexone	increases glutamate levels, anti-resident/opioid receptor blocker
naltrexone	blocker of opioid receptors
naltrexone + bupropion	opioid receptor blocker/dopamine and noradrenaline transporter blocker
ondansetron	5-HT$_3$ receptor antagonist
perindopril	angiotensin receptor blocker
pexacerfont	corticotropin-releasing factor 1 antagonist, anti-anxiety drug and antidepressant
prazosin	inverse agonist at α_1 adrenergic receptor
PROMETA	flumazenil/gabapentin/hydroxyzine, targeting histamine, acetylcholine and GABA function
sertraline	serotonin reuptake inhibitor
risperidone	acts on dopamine, serotonin and noradrenaline receptors
risperidone/aripiprazole	act on dopamine, serotonin and noradrenaline receptors
risperidone/gabapentine	act on dopamine, serotonin and noradrenaline receptors
rivastigmine	cholinesterase inhibitor (increases acetylcholine levels)
topiramate	$GABA_A$ receptor agonist, AMPA receptor antagonist
varenicline	$\alpha_4\beta_2$ receptor agonist, partial agonist for other nicotinic receptors
vigabatrin	$GABA_A$ transferase inhibitor (increases GABA levels)
vortioxetine (with MSRP)	serotonin transporter blocker, 5-HT$_1$ and 5-HT$_7$ receptor antagonist, 5-HT$_{1B}$ partial agonist, and 5-HT$_{1A}$ agonist

Abbreviations: GABA, γ-aminobutyric acid; 5-HT, serotonin; MSRP, mindfulness-based relapse prevention; PDE4, phosphodiesterase 4; TLR4, toll-like receptor 4.

Two First-in-Kind Clinical Trials Explore Psilocybin for Substance Misuse

UTSW-led studies are largest ever for stimulant use disorders

December 07, 2023

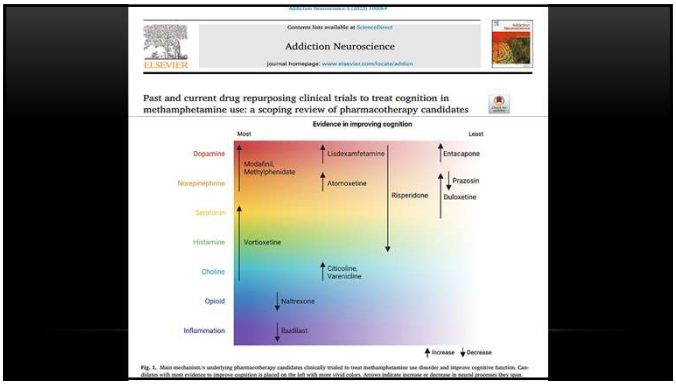
NIDA-funded trials will test possible treatments for methamphetamine, cocaine abuse

Addiction Neuroscience

Past and current drug repurposing clinical trials to treat cognition in methamphetamine use: a scoping review of pharmacotherapy candidates

Megan M. St. Peters[a], Chan Hui J. Park[a], Alyna Turan[a], Alexandre A. Gorin[a,c], Jee Hyun Kim[a,b]*

241



Addiction Neuroscience 4 (2024) 100047

Contents lists available at ScienceDirect

Addiction Neuroscience

journal homepage: www.elsevier.com/locate/addicn

Past and current drug repurposing clinical trials to treat cognition in methamphetamine use: a scoping review of pharmacotherapy candidates

Evidence in improving cognition

Most Least

Dopamine: Modafinil, Methylphenidate; Lisdexamfetamine; Entacapone

Norepinephrine: Atomoxetine; Risperidone; Prazosin; Duloxetine

Serotonin: Vortioxetine

Histamine: Vortioxetine

Choline: Citicoline, Varenicline

Opioid: Naltrexone

Inflammation: Ibudilast

Increase Decrease

Fig. 1. Main mechanism/s underlying pharmacotherapy candidates clinically trialed to treat methamphetamine use disorder and improve cognitive function. Candidates with most evidence to improve cognition is placed on the left with more vivid colors. Arrows indicate increase or decrease in neural processes they exert.

242

Cocaine, crack cocaine	• Xerostomia • Dental caries • Tooth loss • Localized attachment loss (cocaine testing-rubbing on gingival to test potency)[26]
Heroin	• Dental erosion associated with frequent vomiting
Long term opiate or opioid use	• Xerostomia • Clenching, grinding bruxism
Marijuana	• Stains often greenish gold in appearance, xerostomia, halitosis, • Increased caries? (Due to increased appetite and consumption of highly cariogenic foods)

243

TREATMENT OF PATIENTS ON STIMULANTS

- Do not administer local anesthetic with or without vasoconstrictor if the patient has used cocaine in the past 6-8 hours.
- Administer up to 3 carpules of LA with 1:100,000 epinephrine if the patient has had no methamphetamine for the past 8-12 hours. Large doses persist for up to 24 hours.
- Propranolol is the treatment of choice for anxiety in these patients.
- Monitor blood pressure and pulse if the patient is a chronic stimulant user.
- Avoid mood-altering analgesics and use maximum dosages of NSAIDs with acetaminophen to manage dental pain.
- Major damage to dentition may occur due to high sugar diet, bruxism, xerostomia and poor self care.
- Frank discussion and referral to treatment facility if patient is receptive.

244

TREATMENT OF PATIENTS ON DEPRESSANTS

- Record blood pressure and pulse as well as respiratory rate initially and upon dismissal. Utilize continuous monitoring if possible.
- Amide local anesthetic liver clearance may be impaired to limit dosage to 3 carpules or 2% lidocaine with 1:100,000 epinephrine.
- Log onto prescription monitoring program and assess recent use of depressant drugs. https://iowa.pmpaware.net/login
- Prescribe scheduled NSAIDs with or without acetaminophen for acute pain.
- Do not honor patient requests for specific opiates such as "Percocet" or "Dilaudid". True allergy to one but not all morphine-like drugs is improbable.
- Consult patient's primary care physician with patient's permission.
- Refer to treatment program if patient is receptive.

245

COD HEALTH HISTORY QUESTIONS ON SUD

YES NO DK Do you use or have you used tobacco products? If yes, please specify type:
CIGARETTES E-CIGARETTES CIGARS PIPES HOOKAH SNUFF CHEW OTHER:_____
☐ PAST: When did you stop:_____ How many years of use:_____
☐ CURRENT: ☐ > 10 per day ☐ < 10 per day ☐ Occasionally For how many years:_____
How interested are you in stopping? VERY SOMEWHAT NOT INTERESTED

YES NO DK Do you drink alcoholic beverages? If yes, daily? YES NO DK How many drinks per week?_____

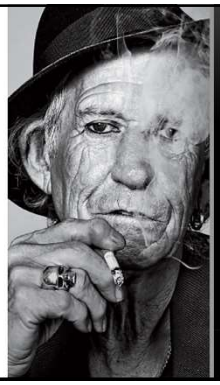
YES NO DK Do you use or have you used prescription, street drugs or other substances for recreational purposes? (Specify):
☐ PAST ☐ CURRENT Are you drug dependent? YES NO DK
(Specify): COCAINE ECSTASY HEROIN MARIJUANA METH OPIOIDS Other:_____

246

How to identify drug seeking behavior?

- **Drug being requested:** opioids, benzodiazepines, methylphenidate, dexamphetamine, anabolic steroids, anti-psychotic drugs
- **Asking for a specific drug by name or brand name**
- **Claiming allergy to alternative drugs**
- **Doctor shopping**
- **Anger when questioned about symptoms such as pain**
- **Unscheduled clinic visits for refills**
- **Unauthorized dose escalation**
- **Claiming to be unable to afford dental work needed to manage dental pain**
- **Multiple visits for the same complaint**
- **More concerned about the drug than medical/dental problem**

How can we identify vulnerability for developing an SUD prior to Rx?



247

DENTAL TREATMENT OF THE SUD PATIENT

Table 2.4 Clinical Considerations Prior to Administering or Prescribing to Patients with a History of SUD

Is the medication in the class of medications or substances that was/is the patient's preferred substance of abuse? If yes, do you absolutely need to administer or prescribe this medication? (Addiction IS NOT a contraindication to prescribe the medication if the benefits outweigh the risks.)

Is the patient in a treatment program for drug or alcohol addiction or under a treatment center/prescriber contract for pain or anxiety management? If yes, dental practitioners optimally should consult with the treatment center or practitioner enforcing the contract to discuss preferred treatment options.

Will the medication being administered result in a positive drug screen that potentially could compromise treatment contracts? If yes, dental practitioners *and patients* should discuss this issue with personnel responsible for the treatment contract *before* the procedure when possible.

NSAIDS remain the first-line oral agents of choice for the management of acute pain in dental procedures unless otherwise contraindicated.

For patients with a history of alcohol, benzodiazepine, or barbiturate addiction, controlled substances such as benzodiazepines or barbiturates are not recommended for light sedation or anxiolysis due to the *potential* for stimulating similar pathways in the brain that promote craving. Alternative agents, such as antihistamines (diphenhydramine or hydroxyzine), may be considered if light sedation is required. Anecdotally, patients in recovery from alcohol or benzodiazepine addiction have reported a significant increase in cravings after receiving nitrous oxide inhalation for light sedation or anxiolysis.

248

Definitions

- **Pseudo-addiction**-a healthcare induced condition in which health professionals misinterpret a patient's request for more medication due to inadequate treatment of a condition (e.g., pain, anxiety or sedation).[1]
- **Opioid Maintenance Therapy (OMT)**-aka opioid substitution therapy (OST), office based opioid treatment (OBOT), opioid replacement treatment (ORT), medication assisted treatment (MAT) or methadone maintenance programs (MMT) are part of a comprehensive opioid addiction management strategy targeting illegal opioid abuse, the treatment of opioid addiction and other negative social consequences.
- **Hyperalgesia** may be defined as a patient's increased detection or hypersensitivity to painful stimulus that previously was not perceived as painful without other known causes. This increased sensitivity to pain is most commonly associated with chronic opioid therapy for nonmalignant pain.[2]
- **Cross-tolerance** is a pharmacological phenomenon that may be characterized as an inability to achieve a specific pharmacological effect due to prolonged exposure of a similar pharmacologic substance (B). Higher doses are required to achieve the same desired pharmacological effect. Cross-tolerance is most commonly associated with the sedative, analgesic, respiratory depressant, or euphoric effects of a substance.[3]

References
(1) www.whocancerpain.wisc.edu › Index › Volume 11, No. 3 – 1998. Accessed August 2014
(2) Pain Physician. 2011 Mar-Apr;14(2):145-61A comprehensive review of opioid-induced hyperalgesia. Lee Ms, Silverman SM, Hansen H, Patel VB, Manchikanti L.
(3) http://www.dhcs.ca.gov/services/medi-cal/Documents/SBI_glossary.pdf. Accessed August 2014

249

COMMON SUBSTANCE USE DISORDERS

- Alcohol-treated with disulfiram (Antabuse), acamprosate (Campral), **Naltrexone (ReVia 50mg oral tab, Vivitrol-380mg SR IM injection)**
- **Opioids-treated with methadone, buprenorphine (CS III), naltrexone, Suboxone (buprenorphine/naloxone-also CS III)**
- Stimulants – no specific treatment for meth and cocaine
- Hallucinogens – no specific treatment
- Cannabis – no specific treatment

Full Agonist		Full Antagonist
Heroin Morphine Methadone	Buprenorphine	Naloxone Naltrexone

Opioid receptor activation/inactivation.

250

TREATING THE ALCOHOLISM HISTORY PATIENT

Pharmacologic Cautions

Although little evidence based data exists, caution should be taken when administering NO, benzodiazepines or barbiturates to alcoholics in recovery since these agents ***may*** stimulate similar receptors in the brain that provoke cravings.

10

251

Patients Receiving Naltrexone

Naltrexone – ReVia®

-Opioid antagonist - blocks reinforcing properties of alcohol

-Usual daily dose is 50 mg orally

-Side effects - nausea, vomiting, headache, anxiety, fatigue, insomnia, elevated liver function tests (LFT's)

Depo-naltrexone – Vivitrol®

-Opioid antagonist – blocks reinforcing properties of alcohol

-One injection of 380mg IM every month

-Side effects - nausea, vomiting, headache, anxiety, fatigue, insomnia, elevated LFT's, pain or redness at injection site

Ask patients if you do not see it on the profile……monthly injections are frequently not reported

11

252

Considerations for Acute Pain Management in Patients Receiving Naltrexone

- Discontinue daily Naltrexone 72 hours before the procedure
- Reassure the patient the intent to adequately treat pain, NOT deny treatment of pain
- Establish specific post procedure pain management goals/expectations before the procedure (e.g., pain scores 1-3 not "0")
- Educate and emphasize optimal nonpharmacological therapy post-procedure (ice packs, oral rinses, hygiene, compliance with eating instructions, etc.)
- Consider preemptive strike with NSAIDs then scheduled NSAID therapy
- Consider long acting topical anesthetics like bupivacaine prior to discharge from the office
- Use of combination analgesics with NSAIDS + acetaminophen may add additional analgesia. (Caution is recommended since these agents may be contraindicated for patients with a history of renal or hepatic impairment.)
- Consider adjunct corticosteroid therapy in cases with major inflammation (multiple extractions)

12

253

Active Alcoholics

Clinical Considerations

Procedures should be postponed whenever possible in an impaired patient

1. Cross tolerance to sedation medication

   -Nitrous Oxide frequently the preferred agent
   -benzodiazepines may have minimal effects
   -opioids (e.g. morphine/fentanyl) *may* be helpful for mild sedation

2. Coagulopathies (end stage/cirrhosis)
3. Alcohol withdrawal

   -can actually start within an hour of admission or treatment
   -patients in withdrawal should be stabilized before treatment

4. Analgesia

   -NSAIDs and acetaminophen / or both preferred
   -acetaminophen may still be used even in patients with liver disease but doses should not exceed 3 grams/day and consulting with the patients GI/IM doctor is always recommended
   -In end-stage liver disease NSAIDS and acetaminophen should be avoided
   -Opioids morphine/fentanyl are reasonable considerations

14

254

Acute Dental Pain in Opioid Addiction

1) opioid addicts in recovery in abstinence-based programs (nonpharmacological management)
2) opioid addicts in recovery receiving OMT
3) opioid addicts in recovery receiving naltrexone therapy
4) opioid addicts still using.

While evidence-based studies are limited regarding acute pain management of dental patients with opioid addiction, there is ample evidence to support clinical considerations that are key when treating acute pain in patients with opioid addiction who are also receiving OMT.

15

255

Common Misperceptions Regarding Opioid Addiction with Acute Pain

- Addicts *in recovery* always lie about their pain
- Opioid medications used for chronic pain adequately treat acute pain
- Patients receiving opioid maintenance treatment with methadone or buprenorphine are adequately treated for acute pain
- Opioid addicts in recovery receiving opioids for acute pain have a higher risk of relapse than opioid addicts in recovery NOT receiving opioids
- Patients reporting high chronic pain scores (6+ on 0-10 scale)should be demonstrating visible symptoms such as increased HR, BP, grimacing or diaphoresis.
- Patients receiving chronic opioids for pain or OMT are "drug seeking" if they complain of inadequate analgesia.

16

256

Opioid Addicts in Recovery in Abstinence Programs

- NSAIDS and/or acetaminophen *are always* first line unless otherwise contraindicated
- Dentists are usually appropriately concerned about causing a relapse. "Relapse is a process *not an instantaneous event*"
- If opioids are necessary, respect the patients right to deny opioid treatment.
- The goal is to minimize pain…that doesn't mean the patient should expect "0" pain

17

257

Checklist for Optimizing Acute Pain Management in Patients in Abstinence Programs

Reassure the patient the intent to adequately treat pain, NOT deny treatment of pain
Establish specific pain management goals/expectations *before the procedure (e.g., pain scores 1-3 not "0") to prevent prescriber-patient analgesia mismatch*
Respect a patient's wishes to NOT receive or be prescribed opioid analgesics or "extra doses" if they are adamant.
Educate and emphasize optimal nonpharmacological therapy post-procedure (ice packs, oral rinses, hygiene, compliance with eating instructions, smoking discontinuation or reduction, etc.)
Document in chart all opioids and sedatives administered
Consider preemptive strike with NSAID 1 hour before the procedure then *scheduled* NSAID or NSAID + acetaminophen pain treatment around the clock and not *as needed*.
Consider long-acting topical anesthetics like bupivacaine prior to discharge from the office
Use of combination analgesics with NSAIDs or acetaminophen may add analgesia. (*Caution is recommended since these agents may be contraindicated for patients with a history of renal or hepatic impairment. Doses of acetaminophen should not exceed 3.0 grams per day*)
Do not prescribe excessive doses of medications or in quantities expected to be left over.
Consider (with the patient's consent) that a responsible family member or friend control pain medications
Encourage the patient to use their support services such as counselors, narcotics anonymous/Alcoholics Anonymous groups if cravings increase

258

Opioid Addicts in Recovery in Opioid Maintenance Programs (methadone/buprenorphine)

Buprenorphine – CIII

- generic mono-buprenorphine tablets (often referred to as "Subutex®" though brand name discontinued by manufacturer in 2011)
- Buprenorphine/naloxone tablets (4/1ratio) – generic tablets, buprenorphine/naloxone film (4/1 ratio) – Suboxone®
- All forms of buprenorphine approved for opioid treatment are to be used sublingually.
- Usually dosed daily or bid

Methadone – CII

The average daily oral dose of methadone is 7omg-120mg/day

19

259

Checklist for Optimizing Acute Pain Management in Patients Receiving OMT

Reassure the patient the intent to adequately treat pain, NOT deny treatment of pain
Establish specific pain management goals/expectations *before the procedure (e.g., pain scores 1-3 not "0") to prevent prescriber-patient analgesia mismatch*
Respect a patient's wishes to NOT receive or be prescribed opioid analgesics or "extra doses" if they are adamant.
Confirm doses of buprenorphine/methadone or chronic opioid doses with the treatment facility or patient's primary pain specialist and discuss *preferred* plans of treatment with treatment providers.
Educate and emphasize optimal nonpharmacological therapy post-procedure (ice packs, oral rinses, hygiene, compliance with eating instructions, smoking discontinuation or reduction, etc.)
Document in chart all opioids and sedatives and report information to the OMT treatment center or primary pain specialist as soon as possible.
Consider preemptive strike with NSAID 1 hour before the procedure then *scheduled* NSAID or NSAID + acetaminophen pain treatment around the clock and not *as needed*.
Consider long-acting topical anesthetics like bupivacaine prior to discharge from the office
Use of combination analgesics with NSAIDs or acetaminophen may add analgesia. (*Caution is recommended since these agents may be contraindicated for patients with a history of renal or hepatic impairment. Doses of acetaminophen should not exceed 3.0 grams per day*)
Do not prescribe excessive doses of medications or in quantities expected to be left over.
Consider (with the patient's consent) that a responsible family member or friend control pain medications
Ideally, the OMT prescriber or the chronic pain medication prescriber should manage all pain medications

21

260

Checklist for Optimizing Pain Management in Patients Receiving OMT for Acute Pain Management

- The dental practitioner should discuss with the OMT prescriber options such as addition of higher dose traditional short acting oral opioid analgesics or combination analgesics (e.g., hydrocodone/apap, hydrocodone/ibuprofen, oxycodone/apap, hydromorphone) in addition to their current maintenance dose of methadone.
- Addition of higher dosage, short-acting opioids should be limited to the anticipated duration of acute pain.
- Codeine products should be avoided since it is dependent on its demethylation to morphine to produce its major analgesic effects. Only about 10% of codeine is metabolized to this active form. Also, many common antidepressants compete with codeine metabolism which may reduce codeine's effectiveness .
- In clinical practice, emergency dental events may be managed with ***higher traditional doses*** of short acting oral opioids. Medications should be titrated daily by phone if possible to manage the acute event.
- The dental practitioner should document all medications administered or prescribed and notify the patient's OMT prescriber due to potential patient contract violations such as positive urine drug screens.
- Another option is to have the OMT prescriber add supplemental oral methadone doses every 4-6 hours for analgesia in addition to their daily OMT methadone.
- Minimal data exists regarding post-op or post-procedural acute pain management in patients receiving buprenorphine (29). Patients receiving buprenorphine for OMT may benefit by dividing the total daily dose of buprenorphine into 3-4 doses throughout the day to provided better analgesic coverage.
- Having the OMT prescriber add additional low dose sublingual buprenorphine (e.g. 2mg) at 4-6 hour intervals) is also an option.

22

261

Opioid Addicts Receiving Naltrexone Treatment

Considerations for Acute Pain Management in Patients Receiving Naltrexone

- Discontinue daily Naltrexone 72 hours before the procedure
- Reassure the patient the intent to adequately treat pain, NOT deny treatment of pain
- Establish specific post procedure pain management goals/expectations before the procedure (e.g., pain scores 1-3 not "0")
- Educate and emphasize optimal nonpharmacological therapy post-procedure (ice packs, oral rinses, hygiene, compliance with eating instructions, etc.)
- Consider preemptive strike with NSAIDs then scheduled NSAID therapy
- Consider long acting topical anesthetics like bupivacaine prior to discharge from the office
- Use of combination analgesics with NSAIDS + acetaminophen may add additional analgesia. (Caution is recommended since these agents may be contraindicated for patients with a history of renal or hepatic impairment.)
- Patients usually require higher dose opioids if opioid therapy is definitely warranted. Fentanyl or hydromorphone may be preferred agents due to their high affinity for opioid receptors.

23

262

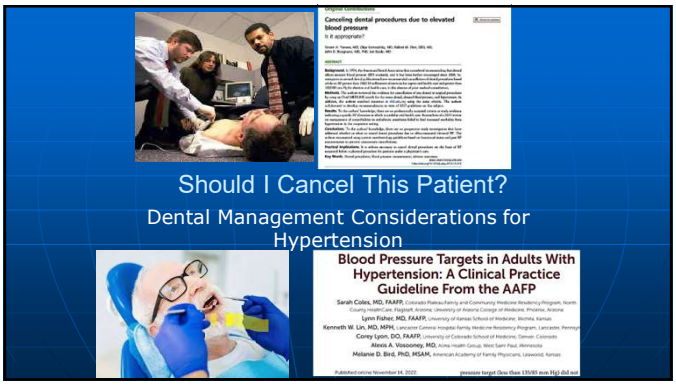
GREATEST DANGER IS RECENT COCAINE OR METH USE*

Dental Considerations with Illicit Drug Users

	Cardiovascular Effects	Respiratory Effects	Xerostomia	Interaction with local anesthesia	Interaction with vasoconstrictors	Interaction with narcotic analgesics
Cannabis	+	++	++	-	+	-
Cocaine	++	+	++	+++	+++	+++
Narcotics	++	++	++	-	-	+++
METH	+++	+	+++	-	+++	+++

- Mark Donaldson, BSP, RPH, ACP, PharmD.

263



264

Cardiovascular Diseases

- Hypertension
- Angina Pectoris
- Heart Failure
- Arrhythmias
- Hyperlipidemias
- Anticoagulation Therapy
- Antiplatelet Therapy

265

Hypertension Evaluation

- Assess lifestyle and identify other CV risk factors or comorbid conditions that affect prognosis and treatment
- Reveal identifiable causes of High BP
- Assess the presence or absence of target organ damage and cardiovascular disease (CVD)

266

What's the Damage?

- Heart – left ventricular hypertrophy, angina or prior MI, prior coronary revascularization, heart failure
- Brain – stroke or TIA
- Chronic kidney disease
- Peripheral artery disease (PAD)
- Retinopathy

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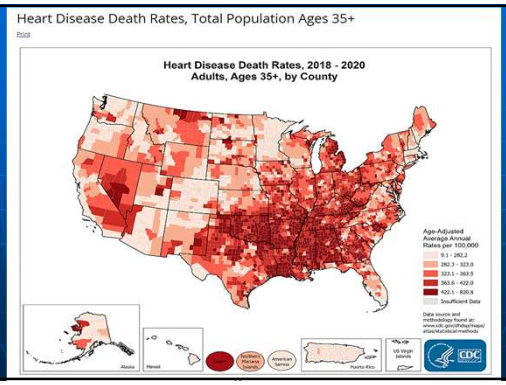

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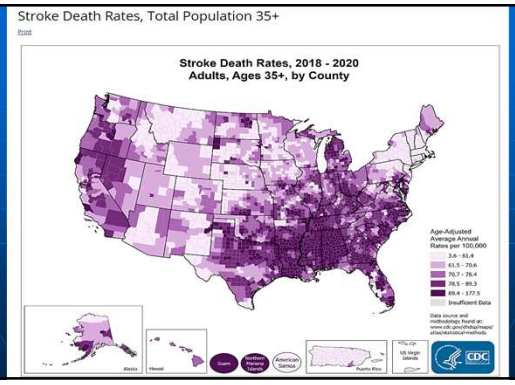


269

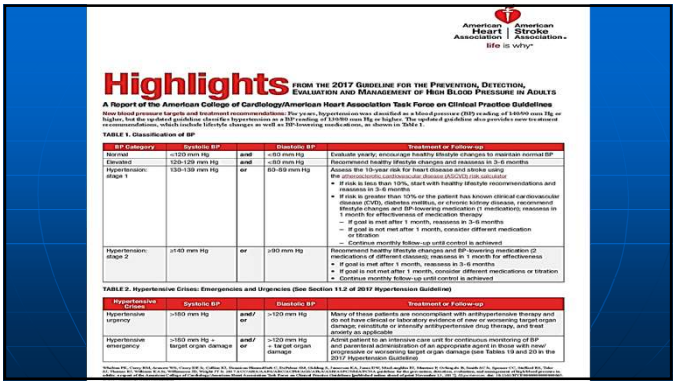
Risks with Hypertension

- Relationship between BP and CVD risk is continuous, consistent, and independent of other risk factors
- The higher the BP, the greater the chance of MI, heart failure, stroke and chronic kidney disease
- The risk of developing CVD DOUBLES for every increment of 20mm Hg Systolic (SBP) or 10mm Hg of Diastolic (DBP)
- The risk of dying of ischemic heart disease and stroke increases progressively and linearly when blood pressure exceeds 115/75 mm Hg.

270

New Hypertension Classification

271



Highlights FROM THE 2017 GUIDELINE FOR THE PREVENTION, DETECTION, EVALUATION AND MANAGEMENT OF HIGH BLOOD PRESSURE IN ADULTS

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

New blood pressure targets and treatment recommendations: The 4-year, hypertension-related disease (HRD) reading of 140/90 mm Hg or higher. The guideline identifies hypertension as a BP reading of ≥130/80 mm Hg. The updated guideline also provides new treatment recommendations, which include lifestyle changes as well as BP-lowering medications, as shown in Table 1.

TABLE 1. Classification of BP

BP Category	Systolic BP		Diastolic BP	Treatment or Follow-up
Normal	<120 mm Hg	and	<80 mm Hg	Evaluate yearly; encourage healthy lifestyle changes to maintain normal BP
Elevated	120–129 mm Hg	and	<80 mm Hg	Recommend healthy lifestyle changes and reassess in 3–6 months
Hypertension: stage 1	130–139 mm Hg	or	80–89 mm Hg	Assess the 10-year risk for heart disease and stroke using the atherosclerotic cardiovascular disease (ASCVD) risk calculator • If risk is less than 10%, start with healthy lifestyle recommendations and reassess in 3–6 months • If risk is greater than 10% or the patient has known clinical cardiovascular disease (CVD), diabetes mellitus, or chronic kidney disease, recommend lifestyle changes and BP-lowering medication (1 medication); reassess in 1 month for effectiveness of medication therapy – If goal is met after 1 month, reassess in 3–6 months – If goal is not met after 1 month, consider different medication or titration – Continue monthly follow-up until control is achieved
Hypertension: stage 2	≥140 mm Hg	or	≥90 mm Hg	Recommend healthy lifestyle changes and BP-lowering medication (2 medications of different classes); reassess in 1 month for effectiveness • If goal is met after 1 month, reassess in 3–6 months • If goal is not met after 1 month, consider different medications or titration • Continue monthly follow-up until control is achieved

TABLE 2. Hypertensive Crises: Emergencies and Urgencies (See Section 11.2 of 2017 Hypertension Guideline)

Hypertensive Crises	Systolic BP		Diastolic BP	Treatment or Follow-up
Hypertensive urgency	>180 mm Hg	and/ or	>120 mm Hg	Many of these patients are noncompliant with antihypertensive therapy and do not have clinical or laboratory evidence of new or worsening target-organ damage; reinstitute or intensify antihypertensive drug therapy, and treat anxiety as applicable
Hypertensive emergency	>180 mm Hg + target-organ damage	and/ or	>120 mm Hg + target-organ damage	Admit patient to an intensive care unit for continuous monitoring of BP and parenteral administration of an appropriate agent in those with new/ progressive or worsening target-organ damage (see Tables 19 and 20 in the 2017 Hypertension Guideline)

272

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

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273

BP Measurement Definitions

BP Measurement	Definition
SBP	First Korotkoff sound*
DBP	Fifth Korotkoff sound*
Pulse pressure	SBP minus DBP
Mean arterial pressure	DBP plus one third pulse pressure†
Mid-BP	Sum of SBP and DBP, divided by 2

*See Section 4 for a description of Korotkoff sounds.
†Calculation assumes normal heart rate .
BP indicates blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

274

Categories of BP in Adults*

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120–129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130–139 mm Hg	or	80–89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

*Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.
BP indicates blood pressure (based on an average of ≥2 careful readings obtained on ≥2 occasions, as detailed in DBP, diastolic blood pressure; and SBP systolic blood pressure.

275

Out-of-Office and Self-Monitoring of BP

COR	LOE	Recommendation for Out-of-Office and Self-Monitoring of BP
I	A^{SR}	Out-of-office BP measurements are recommended to confirm the diagnosis of hypertension and for titration of BP-lowering medication, in conjunction with telehealth counseling or clinical interventions.

SR indicates systematic review.

276

Masked and White Coat Hypertension

COR	LOE	Recommendations for Masked and White Coat Hypertension
IIa	B-NR	In adults with an untreated SBP greater than 130 mm Hg but less than 160 mm Hg or DBP greater than 80 mm Hg but less than 100 mm Hg, it is reasonable to screen for the presence of white coat hypertension by using either daytime ABPM or HBPM before diagnosis of hypertension.
IIa	C-LD	In adults with white coat hypertension, periodic monitoring with either ABPM or HBPM is reasonable to detect transition to sustained hypertension.
IIa	C-LD	In adults being treated for hypertension with office BP readings not at goal and HBPM readings suggestive of a significant white coat effect, confirmation by ABPM can be useful.

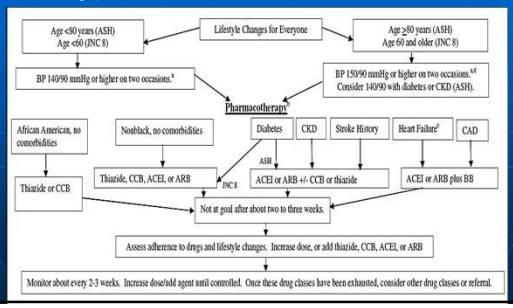
277

Masked and White Coat Hypertension (cont.)

COR	LOE	Recommendations for Masked and White Coat Hypertension
IIa	B-NR	In adults with untreated office BPs that are consistently between 120 mm Hg and 129 mm Hg for SBP or between 75 mm Hg and 79 mm Hg for DBP, screening for masked hypertension with HBPM (or ABPM) is reasonable.
IIb	C-LD	In adults on multiple-drug therapies for hypertension and office BPs within 10 mm Hg above goal, it may be reasonable to screen for white coat effect with HBPM (or ABPM).
IIb	C-EO	It may be reasonable to screen for masked uncontrolled hypertension with HBPM in adults being treated for hypertension and office readings at goal, in the presence of target organ damage or increased overall CVD risk.
IIb	C-EO	In adults being treated for hypertension with elevated HBPM readings suggestive of masked uncontrolled hypertension, confirmation of the diagnosis by ABPM might be reasonable before intensification of antihypertensive drug treatment.

278

Initial Treatment Approach for Hypertension ACC/AHA 2017



279

BP Goal for Patients With Hypertension

COR	LOE	Recommendations for BP Goal for Patients With Hypertension
I	SBP: B-R[SR]	For adults with confirmed hypertension and known CVD or 10-year ASCVD event risk of 10% or higher a BP target of less than 130/80 mm Hg is recommended.
	DBP: C-EO	
IIb	SBP: B-NR	For adults with confirmed hypertension, without additional markers of increased CVD risk, a BP target of less than 130/80 mm Hg may be reasonable.
	DBP: C-EO	

SR indicates systematic review.

280

Choice of Initial Medication

COR	LOE	Recommendation for Choice of Initial Medication
I	A[SR]	For initiation of antihypertensive drug therapy, first-line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs.

SR indicates systematic review.

281

2017 Hypertension Guideline

Summary of BP Thresholds and Goals for Pharmacological Therapy Plan of Care for Hypertension

282

BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General		
Clinical CVD or 10-year ASCVD risk ≥10%	≥130/80	<130/80
No clinical CVD and 10-year ASCVD risk <10%	≥140/90	<130/80
Older persons (≥65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥130 (SBP)	<130 (SBP)
Specific comorbidities		
Diabetes mellitus	≥130/80	<130/80
Chronic kidney disease	≥130/80	<130/80
Chronic kidney disease after renal transplantation	≥130/80	<130/80
Heart failure	≥130/80	<130/80
Stable ischemic heart disease	≥130/80	<130/80
Secondary stroke prevention	≥140/90	<130/80
Secondary stroke prevention (lacunar)	≥130/80	<130/80
Peripheral arterial disease	≥130/80	<130/80

ASCVD indicates atherosclerotic cardiovascular disease; BP, blood pressure; CVD, cardiovascular disease; and SBP, systolic blood pressure.

283

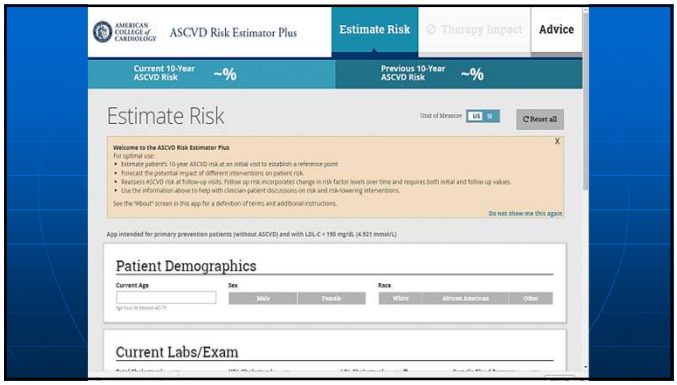
What Are the Implications?

ACC/AHA 2017 HYPERTENSION GUIDELINES (13TH NOV 2017)
New Classification for Hypertension

CATEGORY	SYSTOLIC BP (MM HG)		DIASTOLIC BP (MM HG)	COMPARISON WITH JNC 7
NORMAL	<120	AND	<80	--
ELEVATED BP	120-129	AND	<80	*Was classified as Pre-hypertension under JNC7*
STAGE 1	130-139	OR	80-89	
STAGE 2	≥ 140	OR	≥ 90	*SBP of 140-159 OR DBP of 90-99 mm Hg was classified as Stage 1 under JNC7*
HYPERTENSIVE CRISIS	≥ 180	OR	≥ 120	--

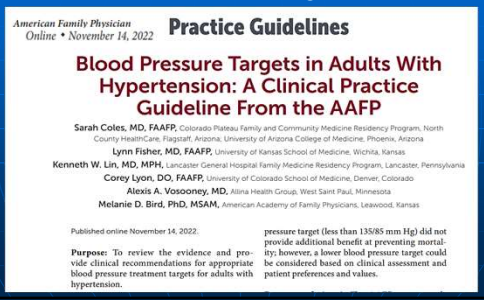
Compiled by PlexusMD

284



285

AAFP Published Different Guidelines November 2022



American Family Physician Online • November 14, 2022

Practice Guidelines

Blood Pressure Targets in Adults With Hypertension: A Clinical Practice Guideline From the AAFP

Sarah Coles, MD, FAAFP, Colorado Plateau Family and Community Medicine Residency Program, North County HealthCare, Flagstaff, Arizona; University of Arizona College of Medicine, Phoenix, Arizona
Lynn Fisher, MD, FAAFP, University of Kansas School of Medicine, Wichita, Kansas
Kenneth W. Lin, MD, MPH, Lancaster General Hospital Family Medicine Residency Program, Lancaster, Pennsylvania
Corey Lyon, DO, FAAFP, University of Colorado School of Medicine, Denver, Colorado
Alexis A. Vosooney, MD, Allina Health Group, West Saint Paul, Minnesota
Melanie D. Bird, PhD, MSAM, American Academy of Family Physicians, Leawood, Kansas

Published online November 14, 2022.

Purpose: To review the evidence and provide clinical recommendations for appropriate blood pressure treatment targets for adults with hypertension.

pressure target (less than 135/85 mm Hg) did not provide additional benefit at preventing mortality; however, a lower blood pressure target could be considered based on clinical assessment and patient preferences and values.

286

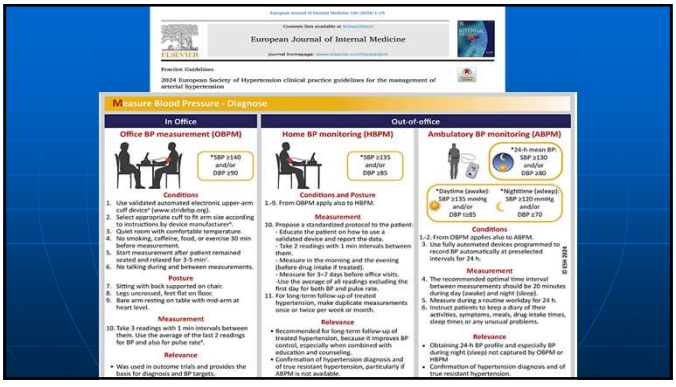
TABLE 4

Comparison of Recommended Blood Pressure Targets in Recent Guidelines

Guideline	18 to 59 years of age (mm Hg)	60 to 69 years of age (mm Hg)	70 to 79 years of age (mm Hg)	Older than 80 years (mm Hg)
2022 American Academy of Family Physicians*	< 140/90	< 140/90	< 140/90	< 140/90
2022 National Institute for Health and Care Excellence[13]	< 140/90	< 140/90	< 140/90	< 150/90
2021 European Society of Hypertension Council[14]	< 130/80†	< 130/80†	< 140/80	< 140/80
2020 International Society of Hypertension‡[44]	< 130/80	< 140/90§	< 140/90	< 140/90
2020 U.S. Department of Veterans Affairs/U.S. Department of Defense‖[15]	< 130/90¶	< 150/90	< 150/90	< 150/90
2017 American College of Cardiology/American Heart Association*[16]	< 130/80	< 130/80	< 130/80	< 130/80
2017 American College of Physicians and American Academy of Family Physicians[11]	--	< 150/90	< 150/90	< 150/90
2014 Eighth Joint National Committee[10]	< 140/90	< 150/90	< 150/90	< 150/90

*—Lower targets are reasonable based on clinical judgment and patient preferences or values.
†—A target of less than 140/90 mm Hg is recommended for patients with chronic kidney disease.
‡—Recommendation is to treat all patients to less than 140/90 mm Hg but states it is optimal to treat persons younger than 65 years and people with coronary artery disease, chronic kidney disease, heart failure, previous stroke, chronic obstructive pulmonary disease, or diabetes mellitus to less than 130/80 mm Hg (less than 140/80 mm Hg in older patients).
§—Recommendation is to transition from target of 130/80 mm Hg to 140/90 mm Hg at 65 years of age.
‖—A target of less than 140/90 mm Hg is recommended in patients with diabetes.
¶—Recommendation is to treat all patients 18 to 59 years of age (including those with diabetes) to a systolic blood pressure target of less than 130 mm Hg. For patients 30 years and older, a diastolic blood pressure target of less than 90 mm Hg is recommended.

287



288

Why Are Patients Not At Goal?

- Practitioner Factors
  - Acceptance of higher BP levels
  - Inadequate knowledge
  - Fear of inducing adverse effects
- Patient Factors
  - Noncompliance with medication regimens
    - Side effects
    - Cost
    - Lack of education regarding risks

289

Types of Drug Therapy

- Medications used for hypertension cover about six main groups
- Most drugs work on baroreceptors and the sympathetic nervous system or the renin-angiotensin-aldosterone system
- Antihypertensive drugs can be used as single agents or in combination
- Target goal BP depends on severity of the disease
- Standard doses of most antihypertensive agents reduce blood pressure by 8-10/4-7mmHg

290

Pharmacotherapeutic Agents

- Diuretics
- Beta-adrenergic blocking agents
- Angiotensin converting enzyme inhibitors
- Angiotensin II receptor antagonists
- Calcium channel blocking agents
- Alpha receptor antagonists

291

Diuretics

- MOA: initial lowering of blood pressure by decreasing plasma volume
  - Chronic effect is to decrease peripheral vascular resistance
- USES: management of edema, HTN, osteoporosis, diabetes insipidis, calcium nephrolithiasis

292

Diuretic Categories

- Thiazide-type
  - **Chlorthalidone (Hygroton, g)**
  - Hydrochlorothiazide (Hydrodiuril, g)
  - Chlorothiazide (Diuril, g)
- Loop
  - Bumetanide (Bumex, g)
  - Furosemide (Lasix, g)
  - Torsemide (Demadex)

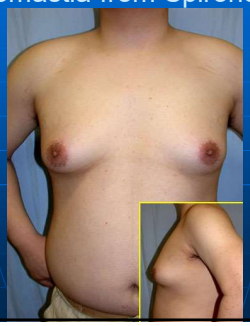
293

Diuretic Categories

- Potassium Sparing
  - Amiloride (Midamor, g)
  - Eplerenone (Inspra)
  - Spironolactone (Aldactone, g)
    - Used to treat congestive heart failure
    - May cause male breast enlargement (gynecomastia)
  - Triamterene (Dyrenium)

294

Gynecomastia from Spironolactone



295

Adverse Effects of Thiazide Diuretics

- High uric acid/high blood sugar
- Low potassium, sodium
- Slight xerostomia
- Oral mucosal lesions

296

Treatment Impact of Thiazide Diuretics

- Oral lesions possible
- Chronic NSAIDs decrease effect due to renal prostaglandin inhibition
- Best NSAID with thiazide is sulindac (Clinoril, g)

297

Adverse Effects of Loop Diuretics

- Dehydration
- Low potassium
- High uric acid/blood sugar
- Oral lichenoid lesions
- Most severe xerostomia

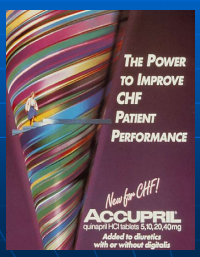
298

Treatment Impact of Loop Diuretics

- Xerostomia may require treatment
- Oral lichenoid lesions
- Chronic NSAIDs decrease effect due to renal PG inhibition
- Remember that loop diuretics are NOT used to treat hypertension. They are primarily for heart failure and/or dependent edema.

299

Angiotensin-Converting Enzymes Inhibitors (ACEi)



- Benazepril (Lotensin,g)
- Captopril (Capoten,g)
- Enalapril (Vasotec,g)
- Fosinopril (Monopril,g)
- Lisinopril (Prinivil, Zestril,g)
- Moexipril (Univasc,g)
- Perindopril (Aceon)
- Quinapril (Accupril)
- Ramipril (Altace,g)
- Trandolapril (Mavik,g)

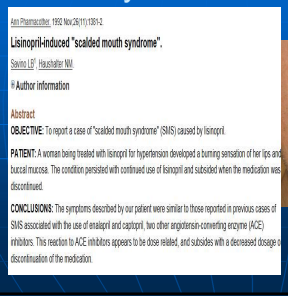
300

ACE Inhibitor Effectiveness

- Protects the kidneys from the renovascular damage caused by diabetes
- Lowers blood pressure substantially
- Eight ACE inhibitors are GENERIC!!
- ACE Inhibitors can be used for the chronic prophylaxis of vascular headaches such as migraine and cluster headache.

301

Angioedema and Scalded Mouth Syndrome from ACEIs



Am Pharmacother. 1992 Nov;26(11):1093-5.

Lisinopril-induced "scalded mouth syndrome".

Savino LP, Hauketter WJ.

Author information

Abstract

OBJECTIVE: To report a case of "scalded mouth syndrome" (SMS) caused by lisinopril.

PATIENT: A woman being treated with lisinopril for hypertension developed a burning sensation of her lips and buccal mucosa. The condition persisted with continued use of lisinopril and subsided when the medication was discontinued.

CONCLUSIONS: The symptoms described by our patient were similar to those reported in previous cases of SMS associated with the use of enalapril and captopril, two other angiotensin-converting enzyme (ACE) inhibitors. This reaction to ACE inhibitors appears to be dose related, and subsides with a decreased dosage or discontinuation of the medication.

302

Dental Impact of ACE Inhibitors

- Oral lesions possibly drug-induced
- NSAIDs decrease ACE inhibitor effects due to renal PG inhibitioin
- Position change may result in orthostatic hypotension
- "Scalded-mouth Syndrome" and angioedema can occur within the first three months of therapy
- 4-12% rate of chronic dry cough!

303

Angiotensin II Converting Enzyme Inhibitors (ARBs)

- Candesartan (Atacand)
- Eprosartan (Teveten)
- Irbesartan (Avapro)
- Losartan (Cozaar,g)
- Telmisartan (Micardis)
- Valsartan (Diovan)

304

Angiotensin II Receptor Antagonists (aka: Angiotensin Receptor Blockers)

- Losartan (Cozaar,g)
  - With HCTZ (Hyzaar,g)
- Valsartan (Diovan)

Advantage: LESS COUGH

Disadvantage: Much more expensive

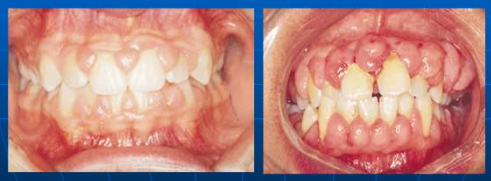
305

Calcium Channel Blockers (CCBs)

- Amlodipine (Norvasc, g)
- Bepridil (Vascor)
- Diltiazem (Cardizem, Dilacor, Tiazac,g)
- Felodipine (Plendil)
- Israpidine (DynaCirc)
- Nicardipine (Cardene)
- Nifedipine (Procardia XL, Adalat,g)
- Nimodipine (Nimotop, g)
- Nislodipine (Sular)
- Verapamil (Calan/SR, Isoptin/SR,Verelan,g)

306

Gingival Overgrowth from CCBs



307

Dental Impact of Calcium-Channel Blockers is Gingival Overgrowth!!

- Strict plaque reduction at the beginning of therapy is necessary to avoid anterior interdental papillae overgrowth
- Incidence is 5-10%
- "Power chlorhexidine" application at bedtime is very effective in controlling plaque regrowth without staining

308

Beta Adrenergic Blockers

309

Types of Beta Blockers

- Noncardioselective beta blockers
  - Block beta-1 receptors in the heart
  - Block beta-2 receptors in the smooth muscle of the peripheral vasculature
- Cardioselective beta blockers
  - Block beta-1 receptors in the heart
  - Selectivity is lost as the dose increases

310

Beta Adrenergic Blockers

- Non-Selective B-blockers
  - Carteolol (Cartrol)
  - Carvedilol (Coreg, g)
  - Nadolol (Corgard, g)
  - Penbutolol (Levatol)
  - Pindolol (Visken, g)
  - Propanolol (Inderal, g)
  - Sotalol (Betapace, g)
  - Timolol (Blocadren, g)
- Blocks beta-1 and beta-2 receptors

311

Epinephrine\Beta Blocker Interaction

Epinephrine: α-1 agonist → vasoconstriction
β-1 agonist→cardiac stimulate
β-2 agonist → vasodilation

EPI » minimal change in mean arteriole pressure
α-1, β-1, β-2 mild increase in heart rate

EPI + β-Blocker »
α-1 reflex increase in vagal tone
(BRADYCARDIA,HYPERTENSION)

312

Epinephrine/Beta Blocker Interaction

- If patient is on nonselective agents, then limit epinephrine to 2.5 carpules of 1:100,000 per two hour visit
- If patient is on cardioselective agent, then up to five carpules of 1:100,000 per two hour visit is safe
- If patient is on a 3+ beta blocker, then disease state dictates limits

313

Dental Management Considerations

- Identify hypertensive patients
  - Through drug and/or disease history
  - Realize that hypertension is generally asymptomatic
  - Always take office BP on patients with:
    - Congestive heart failure
    - Angina pectoris
    - History of hypertension
    - Other risk factors
  - Take 2 separate readings w/manual cuff several minutes apart
    - Screening function
    - Medicolegal considerations

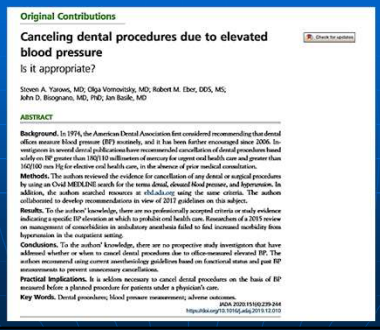
314

Dental Management Considerations

- The manifestation of end organ damage are of primary concern in dentistry so use METs
  - Stroke or myocardial infarction brought on by stress of procedure is worst case
- Disease classification by complexity of drug therapy and METs function
  - Frequent changes in dose or drugs or noncompliance are ominous signs

315

When Should You Decline To Treat?



Original Contributions

Canceling dental procedures due to elevated blood pressure

Is it appropriate?

Steven A. Yarows, MD; Olga Vornovitsky, MD; Robert M. Eber, DDS, MS; John D. Bisognano, MD, PhD; Jan Basile, MD

ABSTRACT

316

Uncontrolled BP Risk Assessment

Box 1. Questions to determine functional capacity of at least 4 metabolic equivalents.*

ACTIVITY of AT LEAST 4 METABOLIC EQUIVALENTS

- Can you do light work around the house like dusting or washing dishes?
- Can you climb a flight of stairs or walk up a hill?
- Can you walk on level ground at 4 miles per hour (6.4 kilometers per hour)?
- Can you run a short distance?
- Can you do heavy work around the house, like scrubbing floors or lifting or moving heavy furniture?
- Can you participate in golf, bowling, dancing, doubles tennis, or throwing a baseball or football?

Box 2. Risk stratification for patients whose correctly measured blood pressure is greater than 180/110 millimeters of mercury.*

RISK STRATIFICATION CATEGORY

Category A

- Is the patient taking antihypertensive medication, and did he or she take it this day?
- Does the patient have a health care provider managing his or her hypertension and has he or she been seen in the past 6 months?
- Does the patient appear anxious, acknowledge anxiety about the procedure, or have a heart rate > 100 beats per minute?

Category B

- Did the patient take public transportation or drive and walk in for the procedure?
- Does the patient take care of his or her own house or apartment?
- Does the patient state he or she can walk up a flight of stairs?

317

Patient Assessment Using METs

Table 1. Clinically Significant Key Metabolic Equivalents for Maximum Exercise

1 MET = resting
2 METs = level walking at 2 mph
4 METs = level walking at 4 mph
<5 METs = poor prognosis; usual limit immediately after MI; peak cost of basic activities of daily living
10 METs = prognosis with medical therapy as good as coronary artery bypass surgery
13 METs = excellent prognosis regardless of other exercise responses
18 METs = elite endurance athletes
20 METs = world class athletes

MET indicates metabolic equivalent or a unit of sitting, resting oxygen uptake; MI, myocardial infarction. 1 MET = 3.5 mL · kg^{-1} · min^{-1} oxygen uptake.

318

Cardiac Pre-Surgical Evaluation

Table 2. Active Cardiac Conditions for Which the Patient Should Undergo Evaluation and Treatment Before Noncardiac Surgery (Class I, Level of Evidence: B)

Condition	Examples
Unstable coronary syndromes	Unstable or severe angina* (CCS class III or IV)† Recent MI‡
Decompensated HF (NYHA functional class IV; worsening or new-onset HF)	
Significant arrhythmias	High-grade atrioventricular block Mobitz II atrioventricular block Third-degree atrioventricular heart block Symptomatic ventricular arrhythmias Supraventricular arrhythmias (including atrial fibrillation) with uncontrolled ventricular rate (HR greater than 100 bpm at rest) Symptomatic bradycardia Newly recognized ventricular tachycardia
Severe valvular disease	Severe aortic stenosis (mean pressure gradient greater than 40 mm Hg, aortic valve area less than 1.0 cm², or symptomatic) Symptomatic mitral stenosis (progressive dyspnea on exertion, exertional presyncope, or HF)

CCS indicates Canadian Cardiovascular Society; HF = heart failure; HR, heart rate; MI, myocardial infarction; and NYHA, New York Heart Association.
*According to Campeau.[19]
†May include "stable" angina in patients who are unusually sedentary.
‡The American College of Cardiology National Database Library defines recent MI as greater than 7 d but less than or equal to 1 month (within 30 d).

Downloaded from

319

Conclusions About Treating Hypertensive Patients

- Preop BP of **less than 180/110** without angina pectoris or acute heart failure signs and symptoms is NOT an indication for canceling or postponing dental procedures
- If BP is **greater than 180/110?** –assess risk using Box 2-proceed if YES to one question in each category. If not, then dismiss or contact PHCP

Box 2. Risk stratification for patients whose correctly measured blood pressure is greater than 180/110 millimeters of mercury.*

RISK STRATIFICATION CATEGORY

Category A
- Is the patient taking antihypertensive medication, and did he or she take it this day?
- Does the patient have a health care provider managing his or her hypertension and has he or she been seen in the past 6 months?
- Does the patient appear anxious, acknowledge anxiety about the procedure, or have a heart rate > 100 beats per minute?

Category B
- Did the patient take public transportation or drive and walk in for the procedure?
- Does the patient take care of his or her own house or apartment?
- Does the patient state he or she can walk up a flight of stairs?

320

Dental Management Considerations

- Morning appointments
- Avoid lengthy appointments
- Use anxiolytics when indicated
  - Benzodiazepines
  - Nitrous oxide
- Avoid intravascular injections
- Avoid retraction cord with epinephrine
- Give clonidine 0.1mg tablet?

321

TABLE 4 – DENTAL TREATMENT RECOMMENDATIONS ACCORDING TO THE MEASUREMENT OF HIGH BLOOD PRESSURE

Dental treatment Recommendations According to the Measurement of High Blood Pressure			
SBP	DBP	ORF	Recommendations
120-139	80-89	Yes/No	Routine dental care OK; discuss BP guidelines
140-159	90-99	Yes/No	Routine dental care OK; consider stress reduction, refer for medical consult
160-179	100-109	No	Routine dental care OK; consider stress reduction, refer for medical consult
160-179	100-109	Yes	Urgent dental care OK; consider stress reduction, refer for medical consult
180-209	110-119	No	No dental treatment without medical consult; refer for prompt medical consult
180-209	110-119	Yes	No dental treatment; refer for emergency medical treatment
>210	>120	Yes/No	No dental treatment; refer for emergency medical treatment
Other Risk Factors: History of myocardial infarction, angina pectoris, high coronary disease risk, recurrent stroke, diabetes mellitus, renal disease			
[Adapted from Yagiela et al[10]; Merin et al[11]; Herman et al][12]			

322

New College of Dentistry Treatment Guidelines

High Blood Pressure Clinical Guidelines

Blood pressure (BP) is a common chronic cardiovascular condition in the United States and dentistry can play an important role in screening patients for hypertension and is an important vital sign to consider in providing dental treatment.

Definitions:
- Acute Hypertension: Can result from stimuli such as physical exertion, anxiety, or stress and generally normalizes once the stimuli is gone.
- Chronic Hypertension: Is blood pressure that remains consistently higher than normal.

Blood Pressure should be taken on patients with an upper arm BP monitor (provided in clinic – manual and/or automatic). Wrist BP monitors can be used if a upper arm BP monitor is not able to be used as determined by the faculty/provider. However, wrist BP monitors/cuffs are not as accurate as the Upper Arm BP monitors and should be limited in use.
- Always utilize the appropriate size cuff (e.g., small, medium, large) based on the patient's age and size to take the BP.
- A manual and/or automatic upper arm BP cuff should be used. If an automatic BP cuff is used and high BP readings are attained, a manual upper arm BP cuff may need to be used.
- If high BP readings are obtained that would preclude treatment, the BP measurement should be repeated after the patient has sat quietly for 5 minutes with their feet flat on the floor and their arm supported at the level of their heart. If the BP decreases to a recommended level allowing treatment to proceed (see section 6.22.4.1) should be in conjunction with clinical judgement.

323

Recommendations for when to take BP
- Patient on anti-hypertensive medications and/or previous history of cardiac event, such as, but not limited to, myocardial infarction or stroke;
- Comprehensive Oral Evaluation (D0150), Periodic Oral Evaluation (D0120), or Limited Oral Evaluation (D0140);
  - Pediatric/minor patients: provider should evaluate and determine if taking BP is appropriate given review of Health History.
- Before surgical procedures and those involving sedation (oral, IV or Nitrous Oxide); and/or,
  - Nitrous Oxide: Pediatric/minor patients: provider should evaluate and determine if taking BP is appropriate given review of Health History.
- Before vasoconstrictors in local anesthetics are used in patients, especially in patients with a cardiac event history and/or taking anti-hypertensive medication(s), or contributory health history.

References: https://www.ada.org/resources/research/science-and-research-institute/oral-health-topics/hypertension#.Y0A1K9dhE6E.link

324

Category	Systolic Blood Pressure (mm Hg)		Diastolic Blood Pressure (mm Hg)	Dental Treatment recommendations	Referral to Physician
Normal	<120	and	<80	Elective care	No
Elevated	120-129	and	<80	Elective care	No
Hypertension					
Stage 1	130-139	or	80-89	Elective care	No
Stage 2	140-159	or	90-99	Elective care	No
Stage 2	>160	and/or	>100	• Wait 5 minutes and reassess. • If the BP decreases below 160/100 or within written guidance from a physician treatment may proceed in conjunction with clinical judgement. • If dental symptoms, pain, and/or anxiety contribute to HTN, initiate emergency care with BP monitoring • If BP does not decrease <160/100, utilize the Functional Capacity and Risk Stratification framework to determine if treatment can be safely completed	Yes
Hypertensive Crisis	>180	and/or	>120	• Utilize the Functional Capacity and Risk Stratification framework to determine if treatment can be safely completed • If dental symptoms, pain, and/or anxiety contribute to HTN, provider may initiate emergency care in conjunction with clinical judgement with BP monitoring. • Refer to physician as soon as possible or send for urgent medical evaluation, if symptomatic. This should be in conjunction with clinical judgement and using the Functional Capacity and Risk Stratification. • Consider deferring elective care after risk stratification.	Yes

325

Functional Capacity Determination and Risk Stratification

Patients with an elevated blood pressure, less than 180/110, with no active cardiac conditions is not an indication to cancel a dental procedure without considering the potential risks and benefits of delaying the procedure. In conjunction with the risk/benefit analysis, it is recommended that the clinician utilize the multifactorial risk stratification based on the American College of Cardiology Foundation and American Heart Association taskforce on practice guidelines to determine if the dental procedure should be delayed.

Providers should use the following risk stratification: One (1) "yes" answer in Section 1 and in Section 2 one (1) "yes" answer for both category A and B.

Section 1: Determination of Metabolic Capacity	
The patient should be "Yes" to at least one of the following	• Can you do light work around the house like dusting or washing dishes? • Can you climb a flight of stairs or walk up a hill? • Can you walk on level ground at 4 miles per hour? • Can you run a short distance? • Can you do heavy work around the house, like scrubbing floors, or lifting or moving heavy furniture? • Can you participate in golf, bowling, dancing, doubles tennis, or throwing a baseball or football?

Section 2: Risk Stratification	
Category A	• Is the patient taking antihypertensive medication and did they take it this day? • Does the patient have a health care provider managing their hypertension and have they been seen in the past 6 months? • Does the patient appear anxious, acknowledge anxiety about the procedure, or have a heart rate >100 beats per minute?
Category B	• Did the patient take public transportation or drive and walk in for the procedure? • Does the patient take care of their own house or apartment? • Does the patient state they can walk up a flight of stairs?
There must be a one (1) "yes" answer to category A and B	

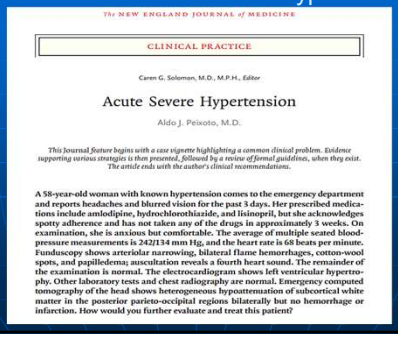
326

Other Considerations

- Recognize drugs that commonly raise blood pressure
  - Stimulants
  - Immunosuppressive drugs
  - Erythropoietin
  - Corticosteriods
- Noncompliance is a frequent cause of acutely high blood pressure readings

327

Treatment of Acute Severe Hypertension



The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

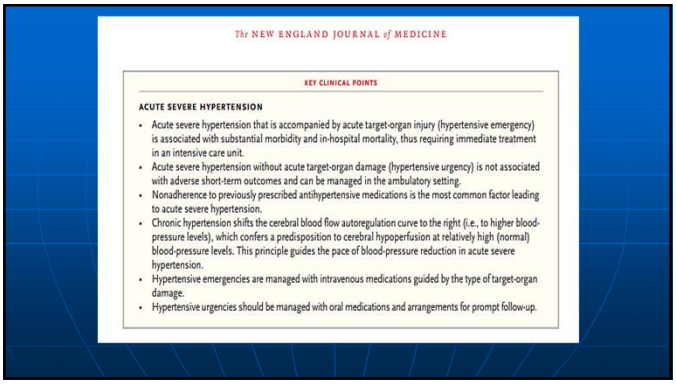
Acute Severe Hypertension

Aldo J. Peixoto, M.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

A 58-year-old woman with known hypertension comes to the emergency department and reports headaches and blurred vision for the past 3 days. Her prescribed medications include amlodipine, hydrochlorothiazide, and lisinopril, but she acknowledges spotty adherence and has not taken any of the drugs in approximately 3 weeks. On examination, she is anxious but comfortable. The average of multiple seated blood-pressure measurements is 242/134 mm Hg, and the heart rate is 68 beats per minute. Funduscopy shows arteriolar narrowing, bilateral flame hemorrhages, cotton-wool spots, and papilledema; auscultation reveals a fourth heart sound. The remainder of the examination is normal. The electrocardiogram shows left ventricular hypertrophy. Other laboratory tests and chest radiography are normal. Emergency computed tomography of the head shows heterogeneous hypoattenuation of subcortical white matter in the posterior parieto-occipital regions bilaterally but no hemorrhage or infarction. How would you further evaluate and treat this patient?

328



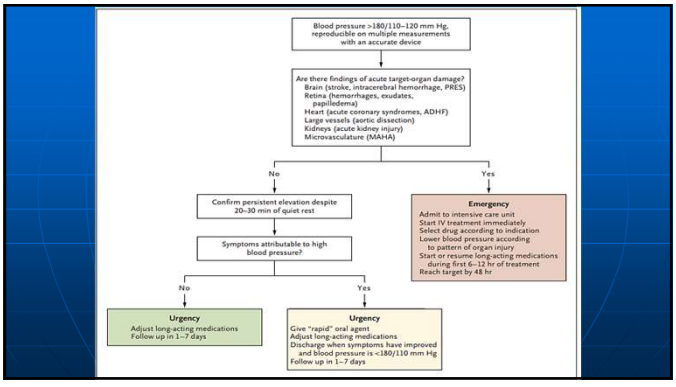
The NEW ENGLAND JOURNAL of MEDICINE

KEY CLINICAL POINTS

ACUTE SEVERE HYPERTENSION

- Acute severe hypertension that is accompanied by acute target-organ injury (hypertensive emergency) is associated with substantial morbidity and in-hospital mortality, thus requiring immediate treatment in an intensive care unit.
- Acute severe hypertension without acute target-organ damage (hypertensive urgency) is not associated with adverse short-term outcomes and can be managed in the ambulatory setting.
- Nonadherence to previously prescribed antihypertensive medications is the most common factor leading to acute severe hypertension.
- Chronic hypertension shifts the cerebral blood flow autoregulation curve to the right (i.e., to higher blood-pressure levels), which confers a predisposition to cerebral hypoperfusion at relatively high (normal) blood-pressure levels. This principle guides the pace of blood-pressure reduction in acute severe hypertension.
- Hypertensive emergencies are managed with intravenous medications guided by the type of target-organ damage.
- Hypertensive urgencies should be managed with oral medications and arrangements for prompt follow-up.

329



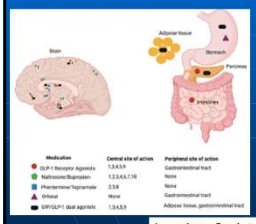
330

Figure 1. Evaluation and Management of Acute Severe Hypertension.

A focused evaluation of the targets of hypertension-mediated organ injury should be performed in every patient. With respect to the brain, inquire about focal motor or sensory deficits and speech or visual changes. Perform a neurologic examination, looking for motor deficits and gait, speech, and visual abnormalities. If there are positive findings, perform imaging with computed tomography (CT) or magnetic resonance imaging. With respect to the retina, perform funduscopy or retinal fundus photography, looking for evidence of microvascular injury (hemorrhages or exudates) or cerebral edema (papilledema). With respect to the heart, ask about chest pain, dyspnea, orthopnea, paroxysmal nocturnal dyspnea, palpitations, and edema. Look for signs of heart failure on examination (elevated jugular venous pressure, bibasilar rales, third heart sound, or edema). Perform chest radiography, electrocardiography (for ischemic changes), and troponin measurement in most patients. Acute coronary syndromes include unstable angina and myocardial infarction. With respect to large vessels (aorta), ask about chest or back pain. Obtain blood-pressure measurements in both arms and thigh, looking for asymmetry. If suspicion is aroused, obtain CT of the chest and abdomen with contrast or transesophageal echocardiography. With respect to the kidneys, measure the serum creatinine level to rule out acute kidney injury. Urinalysis may show proteinuria or hematuria as a sign of microvascular injury. With respect to the microvasculature, obtain a complete blood count, looking for anemia and thrombocytopenia suggestive of microangiopathy. ADHF denotes acute decompensated heart failure, IV intravenous, MAHA microangiopathic hemolytic anemia, and PRES posterior reversible encephalopathy syndrome. Adapted from Whelton et al.[1]

331

New Weight Loss Drugs:
Dental Treatment Considerations



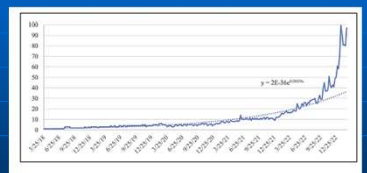


Figure 1. Relative search volume of the term "Ozempic"—March 2018 to February 2023.

American Society of Anesthesiologists Consensus-Based Guidance on Preoperative Management of Patients (Adults and Children) on Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

332

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory

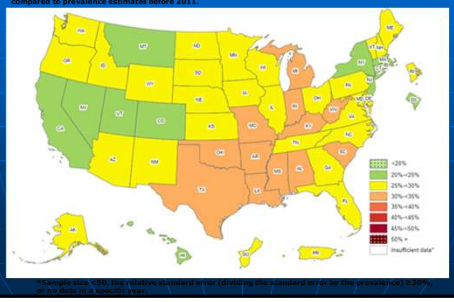
Definitions

- **Obesity: Body Mass Index (BMI) of 30 kg/m² or higher.**
- **Body Mass Index (BMI): A measure of an adult's weight in relation to his or her height, calculated by using the adult's weight in kilograms divided by the square of his or her height in meters.**

333

Prevalence[1] of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2011

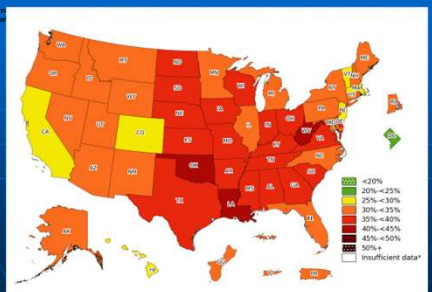
[1] Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.



*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

334

Prevalence[1] of Obesity Based on Self-Reported Weight and Height Among US Adults by State and Territory, BRFSS, 2022



*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

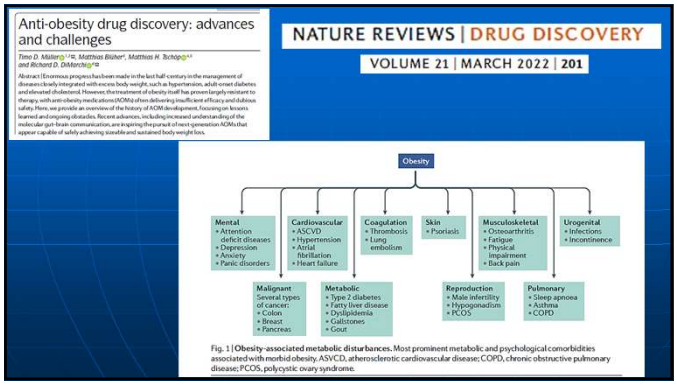
335

Prevalence[1] of Obesity Based on Self-Reported Weight and Height Among US Adults by State and Territory, BRFSS, 2022

State	Prevalence	95% Confidence Interval
Alabama	38.3	(36.3, 40.3)
Alaska	32.1	(30.4, 33.9)
Arizona	33.2	(31.6, 34.9)
Arkansas	37.4	(35.6, 39.2)
California	28.1	(26.8, 29.4)
Colorado	25.0	(23.9, 26.2)
Connecticut	30.6	(29.1, 32.1)
Delaware	37.9	(35.6, 40.2)
District of Columbia	24.3	(22.2, 26.5)
Florida	31.6	(29.9, 33.4)
Georgia	37.0	(35.4, 38.7)
Guam	32.7	(28.8, 36.8)
Hawaii	25.9	(24.4, 27.4)
Idaho	33.2	(31.7, 34.7)
Illinois	33.4	(31.5, 35.3)
Indiana	37.7	(36.4, 38.9)
Iowa	37.4	(36.0, 38.8)
Kansas	35.7	(34.4, 37.0)
Kentucky	37.7	(35.6, 39.9)
Louisiana	40.1	(38.3, 41.9)
Maine	33.1	(31.8, 34.5)
Maryland	33.2	(31.9, 34.4)
Massachusetts	27.2	(26.0, 28.5)
Michigan	34.5	(33.2, 35.8)
Minnesota	33.6	(32.6, 34.7)
Mississippi	39.5	(37.5, 41.4)
Missouri	36.4	(34.9, 38.0)

State	Prevalence	95% Confidence Interval
Montana	30.5	(29.1, 32.0)
Nebraska	35.3	(33.7, 36.9)
Nevada	33.5	(31.0, 36.2)
New Hampshire	30.2	(28.6, 32.0)
New Jersey	29.1	(27.6, 30.7)
New Mexico	32.4	(30.5, 34.4)
New York	30.1	(29.1, 31.7)
North Carolina	34.1	(32.1, 36.1)
North Dakota	35.1	(32.8, 37.5)
Ohio	36.1	(34.6, 37.6)
Oklahoma	40.0	(38.4, 41.6)
Oregon	30.9	(29.4, 32.4)
Pennsylvania	33.4	(31.2, 35.5)
Puerto Rico	34.1	(32.3, 35.9)
Rhode Island	30.8	(29.1, 32.7)
South Carolina	35.0	(33.6, 36.4)
South Dakota	36.8	(33.5, 40.1)
Tennessee	38.9	(37.1, 40.8)
Texas	35.5	(34.0, 37.1)
Utah	31.1	(29.9, 32.4)
Vermont	26.8	(25.4, 28.3)
Virgin Islands	32.1	(25.4, 39.6)
Virginia	35.2	(33.8, 36.6)
Washington	31.7	(30.9, 32.5)
West Virginia	41.0	(39.3, 42.8)
Wisconsin	37.7	(36.4, 39.0)
Wyoming	34.3	(32.3, 36.2)

336



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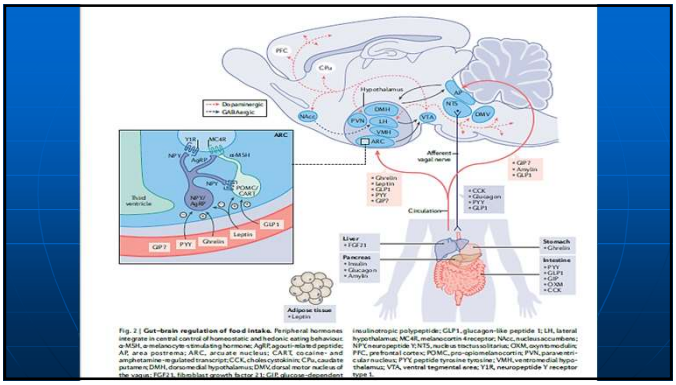

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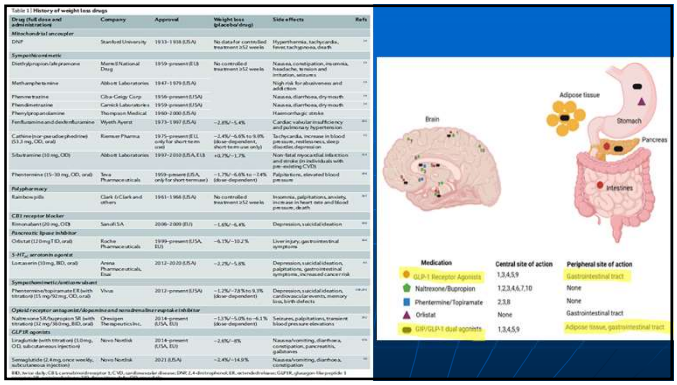

339

Pharmacotherapy of obesity: an update on the available medications and drugs under investigation

Marlene Chakhtoura,[a] Rachelle Haber,[a] Malak Ghezzawi,[a] Caline Rhayem,[a] Raya Tcheroyan,[b] and Christos S. Mantzoros[c,*]

[a]Division of Endocrinology, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon
[b]Faculty of Medicine and Medical Center, American University of Beirut, Beirut, Lebanon
[c]Beth Israel Deaconess Medical Center and Boston VA Healthcare System, Harvard Medical School, Boston, MA, USA

Summary

Obesity is an epidemic and a public health threat. Medical weight management remains one of the options for the treatment of excess weight and recent advances have revolutionized how we treat, and more importantly how we will be treating obesity in the near future. Metreleptin and Setmelanotide are currently indicated for rare obesity syndromes, and 5 other medications (orlistat, phentermine/topiramate, naltrexone/bupropion, liraglutide, semaglutide) are approved for non-syndromic obesity. Tirzepatide is about to be approved, and other drugs, with exciting novel mechanisms of action primarily based on incretins, are currently being investigated in different phases of clinical trials. The majority of these compounds act centrally, to reduce appetite and increase satiety, and secondarily, in the gastrointestinal tract to slow gastric emptying. All anti-obesity medications improve weight and metabolic parameters, with variable potency and effects depending on the specific drug. The currently available data do not support a reduction in hard cardiovascular outcomes, but it is almost certain that such data are forthcoming in the very near future. The choice of the anti-obesity medication needs to take into consideration the patient's clinical and biochemical profile, co-morbidities, and drug contra-indications, as well as expected degree of weight loss and improvements in cardio-renal and metabolic risk. It also remains to be seen whether precision medicine may offer personalized solutions to individuals with obesity, and whether it may represent the future of medical weight management along with the development of novel, very potent, anti-obesity medications currently in the pipeline.

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340

Drug (trade name)	Approval FDA/EMA (year)	Mechanism of action	Adverse events[a]	Contraindications[b]
Orlistat (Xenical, Alli)	FDA 1999 EMA 1998	Gastric and pancreatic lipase inhibitor	Oily rectal leakage, abdominal distress, abdominal pain, flatulence with discharge, fecal urgency, steatorrhea, fecal incontinence, increased defecation	Patients with chronic malabsorption syndrome or cholestasis, pregnancy
Phentermine/ Topiramate (Qsymia)	FDA 2012	NE agonist/GABA agonist, glutamate antagonist	Elevation in heart rate, mood and sleep disorders, cognitive impairment, metabolic acidosis, paresthesia, dry mouth	Glaucoma, hyperthyroidism, during or within 14 days following the administration of monoamine oxidase inhibitors, hypersensitivity to sympathomimetic amines, pregnancy
Naltrexone/ Bupropion (Contrave/ Mysimba)	FDA 2014 EMA 2015	Opioid receptor antagonist/DA and NE reuptake inhibitor	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea, sleep disorder	Chronic opioid use, acute opioid withdrawal, uncontrolled hypertension, seizure disorder, bulimia or anorexia nervosa, abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiseizure drugs; concomitant use of MAOIs, patient receiving linezolid or IV methylene blue, pregnancy
Liraglutide (Saxenda)	FDA 2014 EMA 2015	GLP-1 analogue	Increased heart rate, hypoglycemia, constipation, diarrhea, nausea, vomiting, headache	Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2, pregnancy
Semaglutide (Wegovy)	FDA 2021 EMA 2021	GLP-1 analogue	Nausea, vomiting, diarrhea, abdominal pain, constipation, headache	Personal or family history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type 2, pregnancy
Setmelanotide (Imcivree)	FDA 2020 EMA 2021	MC4R agonist	Injection site reactions, hyperpigmentation, nausea, headache, diarrhea, vomiting, abdominal pain	None
Tirzepatide[c]	Under consideration by FDA	GIP/GLP-1 dual agonist	Nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, and abdominal pain	Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2, known serious hypersensitivity to tirzepatide or any of the excipients

Abbreviations: DA, dopamine; EMA, European Medicines Agency; FDA, Food and Drug Administration; GABA, gamma-aminobutyric acid; GI, gastrointestinal; GIP, gastric inhibitory polypeptide; GLP-1, glucagon-like peptide 1; IV, intravenous; MAOIs, monoamine oxidase inhibitors; MC4R: melanocortin-4 receptor; NE, norepinephrine. [a]Adverse events presented here are those that are present in more than 10% of the population, based on the FDA approval leaflet. [b]Contraindications are based on the FDA approval leaflet. [c]Under expedited consideration for FDA approval.

Table 1: **Anti-obesity medications: approval, mechanism of action, adverse events, and contraindications.**

341

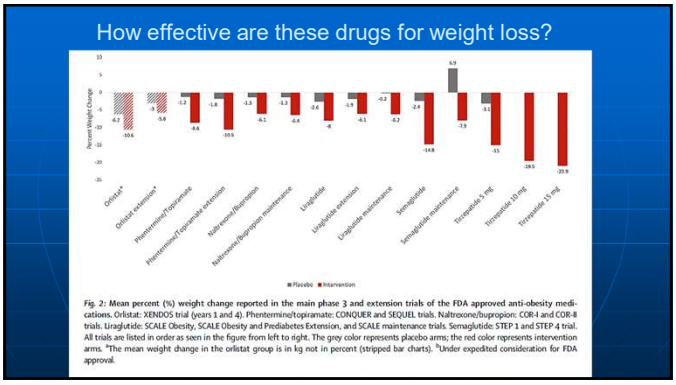
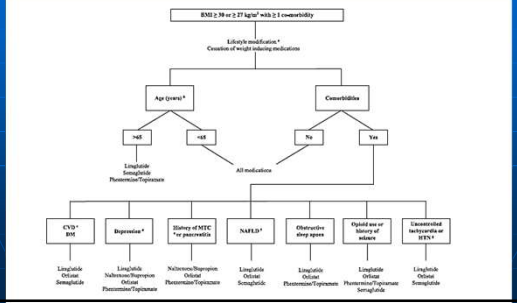


Fig. 2: Mean percent (%) weight change reported in the main phase 3 and extension trials of the FDA approved anti-obesity medications. Orlistat: XENDOS trial (years 1 and 4). Phentermine/topiramate: CONQUER and SEQUEL trials. Naltrexone/bupropion: COR-I and COR-II trials. Liraglutide: SCALE Obesity, SCALE Obesity and Prediabetes Extension, and SCALE maintenance trials. Semaglutide: STEP 1 and STEP 4 trial. All trials are listed in order as seen in the figure from left to right. The grey color represents placebo arms; the red color represents intervention arms. *The mean weight change in the orlistat group is in kg not in percent (stripped bar charts). [b]Under expedited consideration for FDA approval.

342

Suggested algorithm for patient management



343

What medications are already FDA approved for weight loss?

As of October 2023, 10 medications are FDA approved as weight loss treatments. Some are only meant for short-term use, while others can be used for weight management over time.

Medication	Dosage form	How it works
Contrave (naltrexone / bupropion)	Tablet	Lessens hunger and manages cravings
Qsymia (phentermine / topiramate ER)	Capsule	Lessens hunger and manages cravings
Orlistat (Alli, Xenical)	Capsule	Blocks fat absorption from your diet
Phentermine (Adipex-P, Lomaira)*	Tablet or capsule	Lowers appetite
Phendimetrazine*	Tablet or capsule	Lowers appetite
Diethylpropion*	Tablet	Lowers appetite
Benzphetamine*	Tablet	Lowers appetite
Wegovy (semaglutide)	Injection	Lowers appetite and food intake, helps you feel full
Saxenda (liraglutide)	Injection	Lowers appetite and food intake, helps you feel full

344

A Side-by-Side Comparison of Popular Weight Loss Drugs

	DOSAGE	DOSAGE FORM	SUITABLE FOR LONG-TERM USE	EFFICACY*
Metformin**	1-2 DAILY		YES	
Contrave*** (NALTREXONE/BUPROPION)	2 DAILY		YES	
Phentermine (ADIPEX-P)	1-3 DAILY		NO	
Diethylpropion	1-3 DAILY		NO	
Qsymia (PHENTERMINE/TOPIRAMATE ER)	1 DAILY		YES	
Saxenda (LIRAGLUTIDE)	1 DAILY		YES	
Wegovy (SEMAGLUTIDE)	1 WEEKLY		YES	
Tirzepatide** (MOUNJARO)	1 WEEKLY		YES	

* Efficacy isn't the whole picture when it comes to weight loss drugs. Having a choice of options allows you to find one that works best for you and your lifestyle.
** Currently only approved for Type 2 diabetes.
*** Dosing after initial titration.

GoodRx Health

345

FDA NEWS RELEASE

FDA Approves New Medication for Chronic Weight Management

For Immediate Release:
November 08, 2023

Today, the U.S. Food and Drug Administration approved Zepbound (https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217806s000lbl.pdf) (tirzepatide) injection for chronic weight management in adults with obesity (body mass index of 30 kilograms per square meter (kg/ m2) or greater) or overweight (body mass index of 27 kg/m2 or greater) with at least one weight-related condition (such as high blood pressure, type 2 diabetes or high cholesterol) for use, in addition to a reduced calorie diet and increased physical activity. Tirzepatide, the active ingredient in Zepbound, is already approved under the trade name Mounjaro to be used along with diet and exercise to help improve blood sugar (glucose) in adults with type 2 diabetes mellitus.

"Obesity and overweight are serious conditions that can be associated with some of the leading causes of death such as heart disease, stroke and diabetes," said John Sharretts, M.D., director of the Division of Diabetes, Lipid Disorders, and Obesity in the FDA's Center for Drug Evaluation and Research. "In light of increasing rates of both obesity and overweight in the United States, today's approval addresses an unmet medical need."

Approximately 70% of American adults have obesity or overweight, and many of those overweight have a weight-related condition. Losing 5% to 10% of body weight through diet and exercise has been associated with a reduced risk of cardiovascular disease in adults with obesity or overweight.

346

ASA Urges Withholding GLP-1 RA Therapy Prior to Elective Procedures

July 14, 2023
Patrick Campbell

News Article

With the popularity of the class skyrocketing, the American Society of Anesthesiologists has released new guidance urging patients to withhold GLP-1 receptor agonist use prior to elective surgeries or procedures based on potential risk of regurgitation and aspiration associated with delayed gastric emptying.

The American Society of Anesthesiologists (ASA) has released new guidance recommending the withholding of GLP-1 receptor agonists ahead of elective procedures or surgeries.

Michael W. Champeau, MD
Credit: American Society of Anesthesiologists

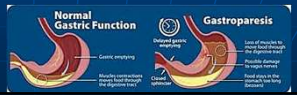
The new guidance, which was composed by of members of the ASA's Task Force on Preoperative Fasting, comes as a result of the growing popularity of agents within the class and includes recommendations addressing potential risk of regurgitation and aspiration based on available literature.

"While there is currently a lack of scientific data on how GLP-1 receptor agonists affect patients having surgery and interact with anesthesia, we've received anecdotal reports that the delay in stomach emptying could be associated with an increased risk of regurgitation and aspiration of food into the airways and lungs during general anesthesia and deep sedation," said Michael W. Champeau, MD, president of the ASA and an adjunct clinical professor of Anesthesiology, Perioperative and Pain Medicine at Stanford University.[2] "These complications can be serious, so we are providing guidance on when GLP-1 agonists should be stopped in advance of an elective procedure."

347

Full stomach precautions if no dose held

- For patients with scheduled elective procedures using GLP-1 receptor agonists is as follows:
- Day(s) Prior to the Procedure:1
- Consider holding GLP-1 receptor agonists on the day of the procedure/surgery. For patients on weekly dosing, consider holding GLP-1 receptor agonists for a week prior. The ASA notes this suggestion is irrespective of the indication, dose, or type of procedure/surgery.
- If GLP-1 receptor agonists prescribed for diabetes management are held for longer than the dosing schedule, consider consulting an endocrinologist for bridging antidiabetic therapy to avoid hyperglycemia.
- Day of the Procedure:1
- If gastrointestinal symptoms are present, including severe nausea/vomiting/retching, abdominal bloating, or abdominal pain, consider delaying the elective procedure and discuss the concerns of potential risk of regurgitation and pulmonary aspiration of gastric contents with the proceduralist/surgeon and the patient.
- If there are no gastrointestinal symptoms, and GLP-1 receptor agonists are held as advised, proceed as usual.
- If there are no gastrointestinal symptoms, but GLP-1 receptor agonists are not held, proceed with "full stomach" precautions or consider evaluating gastric volume by ultrasound. If the stomach is empty, proceed as usual. If the stomach is full of ultrasound is inconclusive or not possible, consider delaying the procedure or treat the patient as "full stomach" and manage accordingly. Discuss the concerns of potential risk of regurgitation and pulmonary aspiration of gastric contents with the proceduralist/surgeon and the patient.



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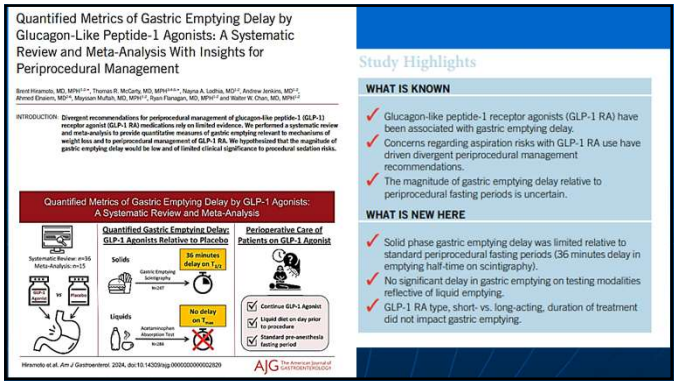

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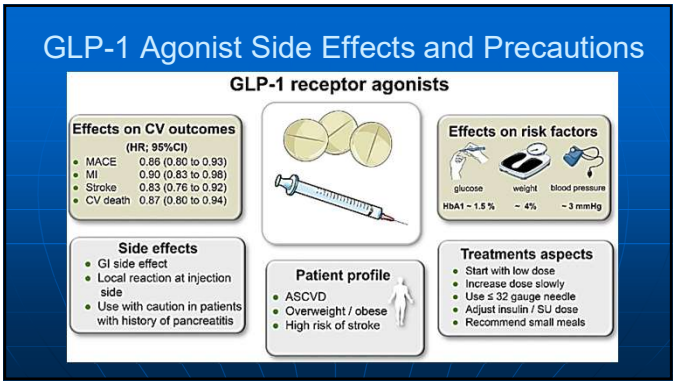

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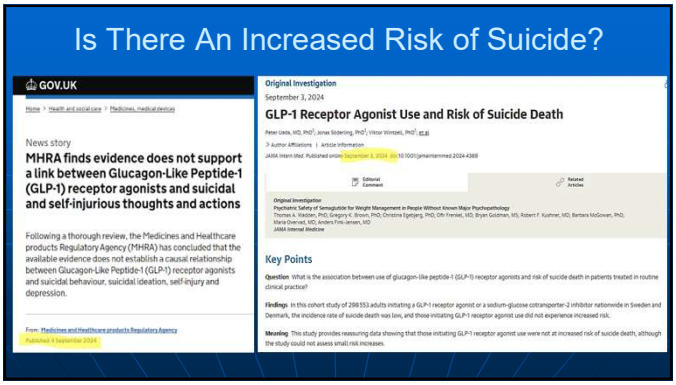

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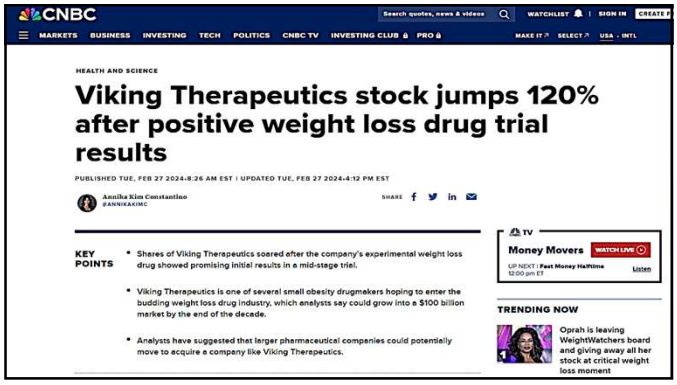

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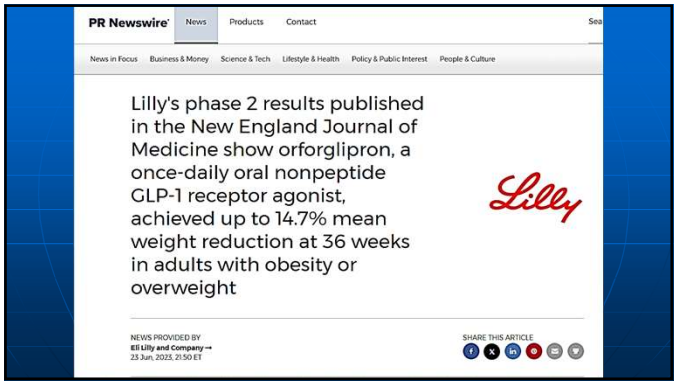
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Lilly's phase 2 results published in the New England Journal of Medicine show orforglipron, a once-daily oral nonpeptide GLP-1 receptor agonist, achieved up to 14.7% mean weight reduction at 36 weeks in adults with obesity or overweight
Lilly
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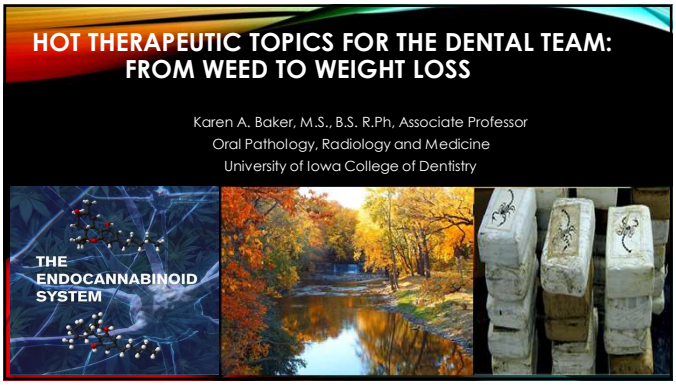
355


HOT THERAPEUTIC TOPICS FOR THE DENTAL TEAM: FROM WEED TO WEIGHT LOSS
Karen A. Baker, M.S., B.S. R.Ph, Associate Professor
Oral Pathology, Radiology and Medicine
University of Iowa College of Dentistry
THE ENDOCANNABINOID SYSTEM

356