North Dakota Medical Association
10/4/19

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Disclaimer

- Nothing to declare, nothing to hide…
After the presentation, the participant should be able to:

• Describe general criteria used in diagnosing substance use disorders

• Understand the impact of substance misuse and substance use disorders on individual and population health

• Describe available treatments for substance use disorders.
Format

• **Brief** overview…

• Won’t be discussing: Physicians and substance use issues

• Will be emphasizing marijuana use issues
First, a question!

- What is the most widely abused substance in the world?
The Onset of “Addiction”

- Genetics
- Chippers vs “Addicts”
Formal Diagnosis

- Symptoms
- Time
- Impact
- Differential
Example-Substance X
Pattern of use, number of concerns (>2), time-frame (within a 12 month period), length of remission/maintenance

1. Larger amounts used, or for longer than intended
2. Can’t cut down/control use
3. Focus/time spent on obtaining drug or recovering
4. Craving
5. Recurrent issue with fulfilling obligations/roles due to use
6. Using despite ongoing problems re: above
7. Important activities are given up/reduced (social, occupational, etc...)
8. Recurrent use despite physical hazards
9. Recurrent use despite medical/psychological impact from use
10. Tolerance
11. Withdrawal
Substance Use Disorders Continuum

Withdrawal Management

Treatment/Rehabilitation

Maintenance

Relapse
Comorbidity is the rule
General Categories

• Depressants (alcohol, benzodiazepines, barbiturates, etc…)

• Opioids (prescription pain meds, heroin, codeine, methadone, buprenorphine…)

• Stimulants (amphetamines, cocaine, methylphenidate, as well as caffeine, nicotine, etc…)

• Cannabinols

• New Psychoactive Substances (Synthetics)

• Hallucinogens

• Inhalants
Reward System

**Alcohol (depressant)**
- GABA receptor
- NMDA receptor

**Cocaine (stimulant)**
- Monoamine transporters

**Mesolimbic Dopamine System**
(Ventral tegmental area, Nucleus accumbens, medial prefrontal cortex)

**Morphine (opioid)**
- Opioid receptors

Cellular and Molecular Mechanisms of Addiction
Nestler, E. Neurobiology of Mental Illness
Depressants
(alcohol, benzodiazepines, barbiturates, etc...)

- High: Silly, laid back. Occasionally disinhibition
- Decrease in anxiety
- Decrease in blood pressure, temperature. At high doses, respiratory depression.
- Sedation, dysarthria, ataxia
- Muscle relaxation

- Overdose: Dangerous
Withdrawal

• More or less, opposite of intoxication symptoms.

• With alcohol, also risk of convulsions, delirium tremens.
Alcohol. What is “a drink?”

- Beer: 12 fluid ounces (355 milliliters)
- Wine: 5 fluid ounces (148 milliliters)
- Distilled spirits (80 proof): 1.5 fluid ounces (44 milliliters)
• “Low risk,” per the National Institute on Alcohol Abuse and Alcoholism:

For women: (or men > 65) No more than 3 drinks on any single day
No more than 7 drinks per week

For men: No more than 4 drinks on any single day
No more than 14 drinks per week.

Risk of alcohol use disorder within this group: 2/100
alcohol use that brings the BAC up to 0.08 g/dL in about 2 hours.
Average number of drinks when binge drinking...

Intensity of Binge Drinking Among US Adults, 2015
1. North Dakota

- Adults drinking excessively: 24.7%
- Alcohol-related driving deaths: 46.7% (the highest)
- Adults in fair or poor health: 13.4% (9th lowest)
- Drunkest metro area: Fargo, ND-MN

The state with the highest share of adults drinking excessively is North Dakota, with nearly 25% of adults reporting binge drinking or drinking heavily. Not surprisingly, the state with the highest drinking rate also has the highest rate of alcohol-related driving deaths. A total of 46.7% of all roadway fatalities are attributable to alcohol consumption, much higher than the national share of 30%.
“Misuse”

- Excessive drinking can increase the risk of serious health problems, including:
  - Certain cancers, including breast cancer and cancers of the mouth, throat, esophagus and liver
  - Pancreatitis
  - Sudden death if you already have cardiovascular disease
  - Heart muscle damage (alcoholic cardiomyopathy) leading to heart failure
  - Stroke
  - High blood pressure
  - Liver disease
  - Suicide
  - Accidental serious injury or death
  - Brain damage and other problems in an unborn child
  - Alcohol withdrawal syndrome
Stimulants
Stimulants

• INTAKE
• Oral
• Snorting
• Smoking
• Injection
Stimulants

• Intoxication: “rush”, euphoria, decreased sleep, appetite, increased stereotypic behavior. Paranoia may occur. Increased pulse, BP, temp. Risk of stroke.

• Withdrawal: opposite symptoms- Crash. Peaks in couple of days, over by day five. But lingering symptoms such as moodiness, cognitive difficulty. High relapse risk. Cues, euphoric recall.
Methamphetamine

- Telescoping/Compression
- Physical
- Mental
- Social
Methamphetamine

- In addition: Easy to make
- Scarring (crank bugs)
- Increased risk for STDs
- Dental complications
- Tweaking (Run)
- The Wall (roughly half a year)
- Cognitive difficulties might last months, sometimes indefinitely
- Psychosis....
Misuse of stimulants

• Study of college-age students’ reasons for illicit use:
  • Improve concentration: 28.8%
  • Increase alertness: 23.4%
  • Get high: 6.3%
  • Control appetite: 4.2%
  • Lose weight: 3.6%
  • Enhance exercise: 2.6%
  • Counteract other drugs: 2.1%
  • Experiment: 1.2%

Risks (not all-inclusive)
  • Tachycardia
  • Hypertension
  • Stroke
  • Anxiety
  • Agitation
  • Confusion
  • Paranoia

Nicotine binds predominantly to nicotinic acetylcholine (nACh) receptors in the CNS; the primary is the α4β2 nicotinic receptor in the Ventral Tegmental Area (VTA).

After nicotine binds to the α4β2 nicotinic receptor in the VTA, it results in a release of dopamine in the Nucleus Accumbens (nAcc) which is believed to be linked to reward.
Nicotine

Quitting is obviously good. However...

Know what medication or over-the-counter substances people taking when planning/starting tobacco/nicotine cessation

Nicotine (and Caffeine) stimulate 1A2 liver enzyme system:
Common substrates: *
  Amitriptyline, Theophylline, Warfarin, Propranolol, Olanzapine, Clozapine
Inhibitors: fluvoxamine, grapefruit juice, quinolones
Additional inducers: omeprazole, phenobarbital, phenytoin, rifampin
Long-term and short-term benefits to quitting smoking

After quitting for:

20 minutes
An individual’s heart and blood pressure decrease.

2-3 weeks
Circulation and lung functionality improve.

1 year
The risk of coronary heart disease and heart attack is reduced.

10 years
The risk of mortality from lung cancer is 50% less likely compared with a current smoker’s risk. Pancreas and larynx cancer risks are also decreased.

12 hours
The body’s carbon monoxide levels return to healthy levels.

1-9 months
Lungs continue to improve and heal, reducing coughing and shortness of breath.

5 years
The risk of mouth, throat, esophagus and bladder cancer are decreased by half. The risk of cervical cancer and stroke decline to that of a nonsmoker’s.

15 years
The risk of coronary disease equates to that of a nonsmoker’s.
What about Vaping?

- A moving target…
- NEJM published British study showed:
  - Tobacco free after 1 year using e-cigarettes: (Not FDA approved)
    - People who try to quit on own-3% successful
    - People using nicotine patches, gum, etc…10% successful
    - People using e-cigarettes…18% successful
  - Risks:
    - Nicotine is toxic: with e-cigs you can increase nicotine concentration by cartrages or voltage
    - Cardiovascular concerns
    - Vape burns can occur
    - Addiction
Vaping and youth

Estimated at least 40% never smoked cigarettes prior to vaping.
However…

• Well publicized recent lung problems associated with vaping.
  
  • “No common thread” (FDA Director for Tobacco Products-9/26/19)
  
  • Many involve THC use, but not all (some CBD, some nicotine).
  
  • Many, but not all, involve illicit cartridges.
  
  • While damage originally was thought to be similar to lipoid pneumonia, with vitamin E acetate a potential contributor; Mayo autopsy study indicates chemical injury, not oil, may be cause.
Caffeine: A socially acceptable psychoactive drug…

➢ Avg. US consumption 300mg per day (2-4 cups)

➢ Over 400mg per day linked with insomnia, irritability, tachycardia, migraine headache, restlessness, frequent urination, G.I. upset, tremors. (Mayo Clinic)

➢ Arrhythmias can occur

➢ Rare--seizures
What are opioids?

• Opiates - drugs derived from opium.

• Opioids - term previously used to describe synthetic opiates.

• Now it is common to refer to all as “opioids.”
Opioids

Rush of euphoria, tranquility, then drowsiness, mood changes, mental clouding, motor slowing.

Constipation

Overdose: respiratory collapse

Coma

(potent effects on brainstem and spinal cord)
How is opioid misuse a different type of problem than misuse of other substances?

• The good news - withdrawal is usually not potentially life-threatening, as opposed to withdrawal from alcohol, some CNS depressants.

• Depending on supply and demand, some individuals cycle from prescription misuse to street use.

• Bad news - for unknown quantities (particularly with heroin, “counterfeit” pills, and synthetic analogues/fentanyl) one time use can result in death. In other words, a person might not even have time to become “addicted…”
Marijuana refers to the dried leaves, flowers, stems, and seeds from the *Cannabis sativa* or *Cannabis indica* plant.

- There are hundreds of compounds in marijuana
CB1 receptors
mainly localized in the brain
(hippocampus, cerebellum and cerebrum)

CB2 receptors
mainly situated in the periphery
(spleen, tonsillar and immune cells)
Marijuana

- Can have both stimulant and sedative properties.
- Antiemetic properties*
- Anticonvulsant effects
- Muscle-relaxing effects
- Reduction of intraocular pressure
THC vs CBD

Tetrahydrocannabinol

Cannabidiol

Image from FarmaPDX.com
THC vs. Cannabidiol (CBD)

**THC**
- Dronabinol as Marinol
- Approved for AIDS associated anorexia or treatment-resistant nausea/vomiting secondary to cancer chemotherapy

**CBD**
- FDA Approved as Epidoliex for:
  - Lennox-Gastaut Syndrome and
  - Dravet Syndrome

*Synthetic THC analogue*

Nabilone as Cesamet

“last resort” chemotherapy anti-emetic
THE THERAPEUTIC EFFECTS

In adults with chemotherapy-induced nausea and vomiting, oral cannabinoids are effective antiemetics.

In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms.

In adults with multiple sclerosis (MS)-related spasticity, short-term use of oral cannabinoids improves patient-reported spasticity symptoms.

For these conditions, the effects of cannabinoids are modest; for all other conditions evaluated, there is inadequate information to assess their effects.

CANCER

The evidence suggests that smoking cannabis does not increase the risk for certain cancers (i.e., lung, head, and neck) in adults.

There is modest evidence that cannabis use is associated with one subtype of testicular cancer.

There is minimal evidence that parental cannabis use during pregnancy is associated with greater cancer risk in offspring.

CARDIOMETABOLIC RISK

The evidence is unclear as to whether and how cannabis use is associated with heart attack, stroke, and diabetes.

RESPIRATORY DISEASE

Smoking cannabis on a regular basis is associated with chronic cough and phlegm production.

Quitting cannabis smoking is likely to reduce chronic cough and phlegm production.

It is unclear whether cannabis use is associated with COPD, asthma, or worsened lung function.
Concerns

• See Surgeon General’s report

• Article on adolescent use: threshold age 17…
  • Renard et al...Front. Neurosci., 10 November 2014
Absorption and bio-availability

• **Smoking or vaporizing** allows for pulmonary first-pass metabolism with direct systemic blood stream absorption across lung lining. THC bio-availability ~ 30%

• Similarly, **sublingual** (i.e., use of oils, etc...) absorption also avoids first-pass metabolism, with slightly less rapid absorption than above. Bio-availability~20%?

• **Edible** use-absorbed via intestinal mucosa and transported to the liver and metabolized prior to reaching other organs, such as the brain. THC bio-availability ~10%

• Only about 1% of administered TCH dose reaches the brain.

• **However**- THC variability in marijuana plants can range from 0.3-30% or higher
Acute effects:
Usually temporary and reversible, and do not present a risk of harm (outside of risk of activities when intoxicated).

Pleasant:  Euphoria and relaxation.

Sleepiness

Unpleasant:
Anxiety
Paranoia/Psychotic symptoms, depending on genetic and vulnerability characteristics
Study of Canadian medical marijuana users

- Subjective acute reduction in anxiety, depression and stress
- Subjective increase in depression over time

Edible vs. inhaled and ER visits

• Colorado study-approx. 10,000 patients

• While cannabinoid hyperemesis syndrome was twice as likely with inhaled vs. ingested cannabis, the opposite was true for acute psychiatric symptoms, intoxication and cardiovascular symptoms.

• Cannabis-attributed presentations involving edible use-10%
• Edible Products as percent representation of state total cannabis sales:
• 0.32%
MANY individual factors will impact how long THC/metabolites will stay in the system.
Cannabis Withdrawal Syndrome
Bonnet and Preuss, *Subst Abuse Rehabil.* 2017; 8: 9–37

O= none, 1=mild, 2=moderate, 3=heavy

[Graph showing symptoms over days]
Formulations

• We have so much yet to learn…

• Are effects related to:

  • THC/CBD ratio?
  • THC/CBD strength?
  • Sativa vs. Indica genomics?
  • Terpenes?
  • Other?
ND, infraction and fine for < ½ oz. of marijuana. Not completely decriminalized...
These are the qualifying condition under Measure 5 to get a North Dakota Medical Marijuana Card.

Qualifying conditions include:

- Cancer
- HIV/AIDS
- Hepatitis C
- ALS
- PTSD under certain circumstances
- Agitation of Alzheimer’s disease
- Dementia
- Crohn’s disease
- Fibromyalgia
- Spinal stenosis
- Chronic back pain (including neuropathy or damage to the nervous tissues of the spinal cord with objective neurological indication of intractable spasticity)
- Glaucoma
- Epilepsy
- A medical condition that produces cachexia or wasting, severe and debilitating pain that has not responded to previously prescribed medication or surgical measures for more than three months or for which other treatment options produced serious side effects
- Intractable nausea
- Seizures
- Severe and persistent muscle spasms
New Psychoactive Substances (NPS)

- Synthetic Cannabinoids ("K2," "Spice"). Binds to CB1 receptors at five times the affinity of THC.
  - JW Huffman, chemist and research developer: Likened using it to playing “Russian Roulette,” and that those who try it “must be idiots…”

- Synthetic Cathinones ("bath salts") such as MDPV--synthetic derivative of khat. Excited delirium not uncommon.
# Hallucinogens

## Classic:
1) Serotonin-like
   (indole alkylamines)
   LSD, psilocybin, etc…

2) Resemble norepinephrine/dopamine
   (phenylalkylamines)
   Mescaline

- Ecstasy “Molly,” methylenedioxymethamphetamine (NDMA) somewhat similar.
  Unfortunately often adulterated

## Dissociative:
- Phencyclidine (PCP)
- Ketamine
- Dextromethorphan
- Salvia
Hallucinogens-short term effects:

- Visual illusions, “trails” or “tracers”
- Expansive, “religious” sense
- “Trading senses” (synesthesia)
- Change in sense of time
- Depersonalization/derealization/
- Increased pulse, BP, temp
- Can approach delirium/seizures if high doses
Hallucinogens-Rare Long-term effects:

Classic types:

1) Persistent psychosis

2) Hallucinogen Persisting Perception Disorder (hallucinations, visual disturbances such as “tracers/trails”)

Dissociative drugs:

• speech problems
• memory loss
• weight loss
• anxiety
• depression and suicidal thoughts
Suspicion re: Prescription Drug misuse?

• SCREENING TOOLS

Patient Request

Patient Info

First Name*  Last Name*

☐ Partial Spelling  ☐ Partial Spelling

Date of Birth*  
MM/DD/YYYY

Phone Number

Prescription Fill Dates

No earlier than 3 years from today
What is SBIRT?

• Screening
  • Universal, quick assessment for use/severity
  • Occurs in a variety of settings (e.g., public health, primary care settings, social service)

• Brief Intervention
  • Brief motivation and awareness-raising
  • 1-5 sessions lasting 5 minutes to an hour

• Referral to Treatment
  • Specialty care
  • 5-12 sessions

Osborne & Benner (2012), SAMHSA (2012)
<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristic</th>
<th>Strategy (MI)</th>
<th>Processes (MI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-contemplation</td>
<td>Need for change is either not on the radar or the individual is not interested in change</td>
<td>Education (risks/benefits)</td>
<td>Engaging/Eliciting</td>
</tr>
<tr>
<td>Contemplation</td>
<td>Ambivalence</td>
<td>Identify discrepancies, misconceptions as well as potential supports.</td>
<td>Focusing</td>
</tr>
<tr>
<td>Preparation</td>
<td>Planning to experiment with small changes</td>
<td>Develop realistic goals</td>
<td>Processing/planning</td>
</tr>
<tr>
<td>Action</td>
<td>Taking definitive action</td>
<td>Positive reinforcement</td>
<td></td>
</tr>
<tr>
<td>Maintenance/Relapse Prevention</td>
<td>One day at a time, yet long-term approach</td>
<td>Encouragement/Support</td>
<td></td>
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</tbody>
</table>
Within the five broad levels of care (0.5, 1, 2, 3, 4), decimal numbers are used to further express gradations of intensity of services. The decimals listed here represent benchmarks along a continuum, meaning patients can move up or down in terms of intensity without necessarily being placed in a new benchmark level of care.
Treatments and Supports

- Addiction Counseling*
- Cognitive/Behavioral Therapies
- Peer Supports
- Support Programs (12-step, other)
- MAT
- Other
Team Players

- Patient
- Addiction counselor(s)
- Care/Case Managers
- Nurses
- Lab staff
- Receptionists
- Prescribers
- Pharmacists
<table>
<thead>
<tr>
<th>Medication Assisted Treatment:</th>
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<tbody>
<tr>
<td><strong>We have MAT</strong></td>
</tr>
<tr>
<td>• Tobacco</td>
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<tr>
<td>• Alcohol</td>
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<tr>
<td>• Opioids</td>
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<tr>
<td><strong>We don’t have MAT</strong></td>
</tr>
<tr>
<td>• Marijuana</td>
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<tr>
<td>• Cocaine</td>
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<tr>
<td>• Methamphetamine</td>
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<td>• Synthetics</td>
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<td>• Inhalants</td>
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</table>
MAT for Tobacco Use Disorder

Most successful with a smoking cessation program.

• **Nicotine replacement**
• **Gum, nasal spray, patch, lozenge, etc…**

  • **Bupropion** (Zyban/Wellbutrin)
  • **Varenicline** (Chantix)

• Many other non-pharmacologic treatments including acupuncture, hypnosis, etc…

• **Vaping** – not FDA approved;
MAT-Alcohol

- **Disulfiram** (Antabuse) Aversive therapy.  
  - 1500mg/week

- **Naltrexone** (Revia)  
  - 50mg/day
  - (Vivitrol)- monthly injection 380mg – issue of pain meds*

- **Acamprosate** (Campral) (2) 333mg tabs T.I.D

- Others-
**Replacement Therapies:**
- **Methadone:** Special outpatient treatment center
- **Buprenorphine:** (partial agonist)/naloxone (antagonist) =
  - Indicated for maintenance treatment in opioid use disorder. Office-based
  - 1) Induction 2) Stabilization 3) Maintenance

**Opiate blockade:**
- Naltrexone (Revia/Depade) and monthly injection Vivitrol
What about for withdrawal?

No longer use the term “Detox”
Use “Withdrawal Management.” We have “social,” we have “ambulatory,” we have “medically monitored,” we have “medically managed,” etc…

- Alcohol
- Benzodiazepines
- Anti-convulsants

- Opiates
  - Opiates
  - Buprenorphine/other*
  - δ-2 agonisist (clonidine/lofexidine)
What did we just talk about again?

- Definition of substance use disorders
- Burden of illness as well as misuse.
- Potential treatments
Hope