


***Hidden connections:  
Opioid use disorder and  
depression***

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***Disclosures***

The presenter has declared that she does not, nor does her family has, any financial relationship in any amount occurring in the last 12 months with a commercial interest whose products or services are discussed in the presentation. The presenter has declared that she does not have any relevant non-financial relationships. Additionally, all planners involved do not have any financial relationships.

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***Learning objectives***

Upon completion of the instructional program, you should be able to:

1. Summarize the relationship between opioid use disorder, depression and suicide.
2. Evaluate the risks and benefits of both controversial and conventional interventions for the treatment of opioid use disorder.
3. Utilize evidence-based treatments for co-occurring depression and opioid use disorder.

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**Agenda**

- The scope of the opioid use crisis
- Complex factors impacting treatment
- Current prevention, treatment and recovery initiatives
- The role of depression in opioid use disorder
- Complex, conventional, and controversial techniques

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***The long, winding road:  
The statistics behind the opioid crisis***

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***How did we get here? - Polling question #1***

**Motor vehicle accidents**

- Do you wear your seat belt every time you get in the car?



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**How did we get here? – Polling question #2**

- What if you are only going *less than one mile?*



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**How did we get here?**

**Societal norms**

- No one expects to become addicted
- Genetic predisposition – how does this factor into the story?
- Adolescent experimentation is normal
- 90% of substance use disorders began in adolescence

DuPont, et al., 2018

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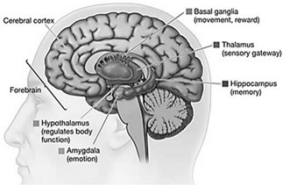
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**How did we get here?**

Let's talk about how the brain develops...



DuPont, et al., 2018

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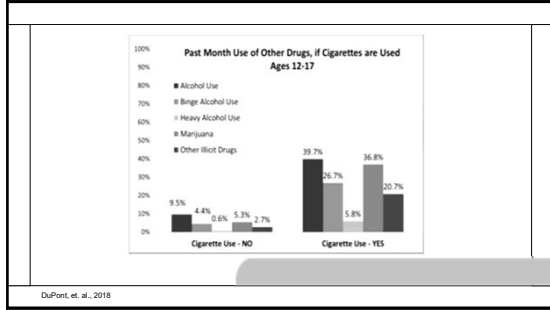
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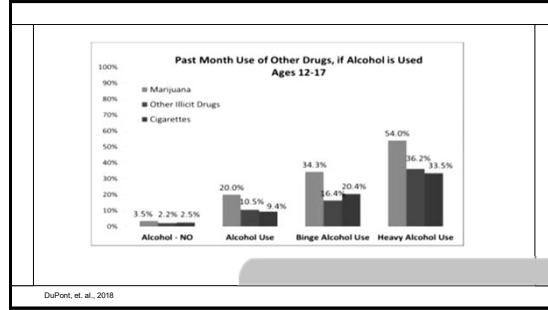
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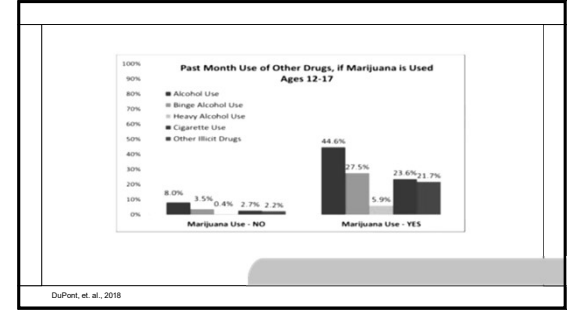
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*How did we get here?*

**Reality check**

- 20.8 million individuals 12 years and older have been diagnosed with substance use disorder
- 27.1 million individuals report using some substance over the last year
- 89% of individuals who need treatment do not receive treatment
- Currently, more people die from overdoses than motor vehicle accidents

SAMSHA, 2017; DuPont, et. al., 2018

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*So... Polling question #3*

Should we continue to promote adolescent substance experimentation as normal?

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**2009**

Here's what we were reading at the beginning of the opioid crisis...

Story	Followed very closely %
1. Condition of U.S. economy (Jan 23-26)*	57
2. Barack Obama's inauguration (Jan 23-26)	52
3. Congress passes stimulus plan (Feb 13-16)*	50
4. Big bonuses to AIG employees (Mar 20-23)	50
5. Debate over health care reform (July 27-Aug 3)	49
6. Obama unveils budget plan (Feb 27-Mar 2)	47
7. Rising unemployment rate (Jan 9-12)*	45
8. Deadly shootings at Fort Hood (Nov 6-9)*	44
9. US Airways plane lands in Houston (Jan 16-19)	44
10. Swine flu and the vaccine (May 1-9)*	43
11. Obama's Afghanistan strategy (Dec 4-7)*	43
12. Attacks on ships by Somali pirates (Apr 17-20)*	41
13. Obama proposes health care fund (Mar 16-19)	41
14. Obama plan for troops in Iraq (Feb 27-Mar 2)	40
15. Stock market ups and downs (Mar 13-16)*	38

Dates show survey field period.  
\* Interest in these stories was tracked over several weeks and months; highest reported interest shown here.

LaBelle, 2019

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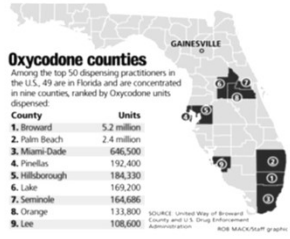
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### The impact of prescriptions

Prescription opioids increased by 300% from 1991 to 2009 in the United States



LaBelle, 2019

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### The costs ...

#### 2009 – the start of the crisis

- \$24 billion are spent on substance use treatment
- 100 people per day were dying from overdoses

Coye, 2019; SAMHSA, 2017; DuPont, et al., 2018; CDC, 2018

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### The costs ...

#### Today

- \$100 billion dollars are spent on purchasing illegal drugs
- \$34 billion are spent on substance use treatment
- \$800 million in grants
- 70,237 people die from substance use disorder each year
- Over 30,000 people die from opioid overdoses – 24% are from prescriptions
- 174 people die each day

Garcia, et al., 2019; CDC, 2018; Hedegaard, Warner & Minino, 2017

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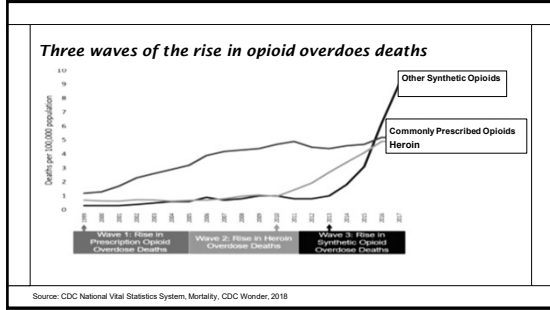
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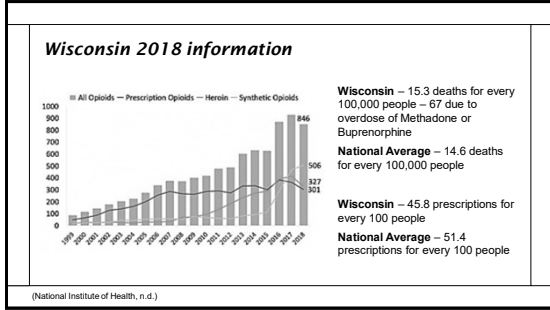
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*Complex factors impacting treatment of opioid use disorder*

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### Stigma... It still exists

Non-Stigmatized Conditions ← Perceived Fault / Perceived Control → Stigmatized Conditions

*As Perceived fault and perceived control decrease, the patient feels less stigma; whereas as perceived fault and perceived control increase, the patient feels more stigma.*

**Far too often we...**

- Treat patients with substance use differently
- Expect patients to have poorer outcomes
- Inadvertently use stigmatizing language

(SAMHSA, 2017)

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### Complex factors - why is it difficult to treat?

- Codependence with alcohol, cocaine, benzodiazepine or other substances is frequent
- Overdose deaths involve more than one drug
- 14 of the top 15 counties in the USA (by percentage) are rural counties
- Demographics of opiate deaths may surprise you
- Recent studies of opioid-addiction patients, showed that:
  - 34% relapse within 3 days
  - 45% relapse within 7 days
  - 50% relapse within 14 days
  - 60% relapse with 90 days

Garcia, et. al., 2019; Podesta, 2018; Kiang et. al., 2019

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### Complex factors - Are all opioids the same?

Direct comparison study between heroin use and prescription opioids: Eight weeks of CBT therapy and suboxone

<b>Demographics:</b>	<b>Retention:</b>
• Average age for both groups: 22	• Heroin 64.7%
• Heroin 3.7 years of use	• Prescription 82.5%
• Prescription 3 years of use	<b>Medication compliance:</b>
	• Heroin 96%
	• Prescription 99%

Romero-Gonzalez, et. al., 2019

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**Complex factors - Chronic pain**

- Interconnections between obesity, chronic pain, co-occurring medical conditions, depression and substance use.
- 1990's – American Pain Society advocated for the recognition of pain as the 5<sup>th</sup> vital sign – Joint Commission added standards in 2001
- Increase in Oxycontin sales from 48 million in 1996 to 2.4 billion in 2012.

Baker, 2017

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**Complex factors - Moms and infants**

- Neonatal abstinence syndrome is increasing at alarming rates
- Costs have increased more than six times since 2004
- Barriers
- 2018 – only 19 states had specialized services for pregnant women who has a substance use disorder
- Fear of losing their child – many states have laws regarding babies born with NAS
- 2016 – 92,107 children in foster care

LaBelle, 2019

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**Complex factors - Older adults**

- The emerging population is the older adults
- By 2020 the number of adults 50+ with a substance use disorder will double
- Depression is the single most significant risk factor for suicide among the elderly
- 27% of older adults have major depression

CDC, 2018; NABH, 2019

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**Complex factors - Other epidemics**

- Hepatitis C is quickly becoming another epidemic stemming from opiate use – has increased by 622%
- Foster system
- Criminal Justice system

CDC, 2018; NABH, 2019

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**Solving the crisis:  
Current prevention, treatment and  
recovery initiatives**

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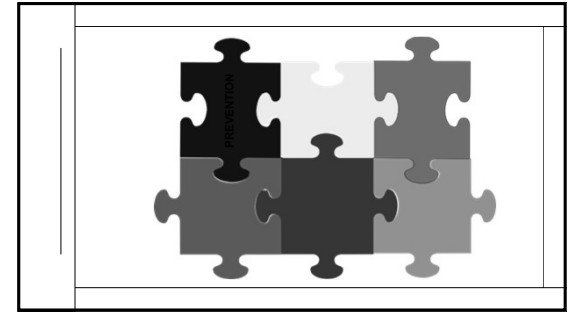
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**Treatment approaches - Prevention**

- Overdose prevention
- School-based prevention
- One-choice
- Include all substances when discussing prevention
- More education for medical students and residents in training

Onechoiceprevention.org, 2019

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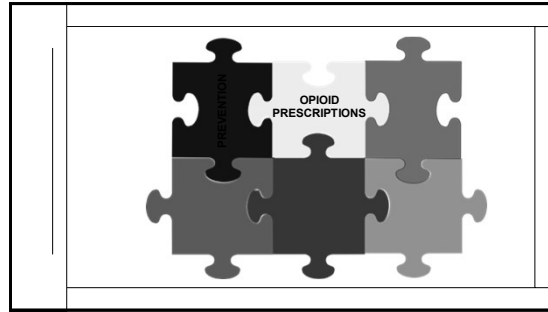
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**Treatment approaches - Opioid prescriptions**

- Approach to prescribing is changing
- Better awareness of potential misuse and addiction
- Prescription drug monitoring programs
- Not the magic bullet
- Between 2012 and 2015, opioid prescriptions dropped by 15% yet overdose rates increased by 38%

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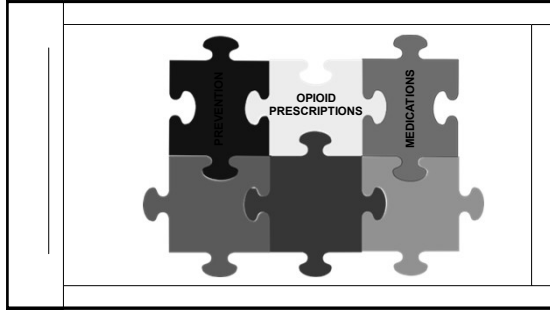
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**Treatment approaches - Medications**

- Naloxone
- Methadone
- Buprenorphine
- Naltrexone

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**Treatment approaches - Why use medications?**

- Total healthcare costs are 30% lower for those patients who receive MAT
- Increases retention
- Reduces:
  - Drug use
  - Cravings
  - High risk behaviors
  - Crime

National Academy of Sciences, 2019

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**Treatment approaches - Medications**

Medications along with psychosocial services is considered the gold standard.



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**Treatment approaches - Medication barriers**

- Stigma
- Inadequate education for professionals
- Current regulations

National Academy of Science, 2019; Wattenberg, 2018

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**Treatment approaches - Medication barriers**

**Access to care**

- Sober living
- 2016 – 27% of inpatient or residential addiction providers offered BUP and 21% offered injectable naltrexone
- 2016 – 21% of outpatient addiction providers offered BUP or injectable naltrexone
- 2016 – only 1/2 of US counties had a BUP provider
- 2016 – 60% of rural US counties did not have any BUP provider

National Academy of Science, 2019; Wattenberg, 2018

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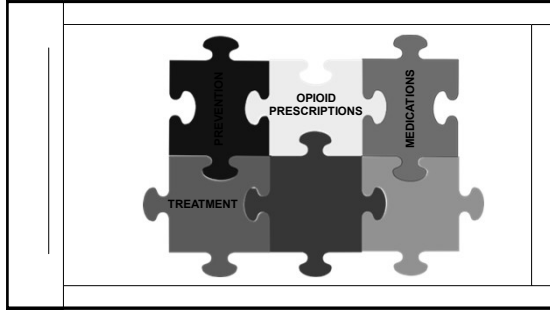
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**Treatment approaches - Evidence-based practices**

*Evidence-based practices (EBP) are comprised of scientific research, physician's clinical judgement, and the patient's values and preferences.*

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**Use of technology**

How will digital and AI impact treatment?

Coye, 2019

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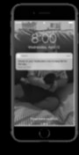


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**Treatment approaches - Use of technology**

TRIGGER	BEHAVIOR	REWARD
		

Coye, 2019

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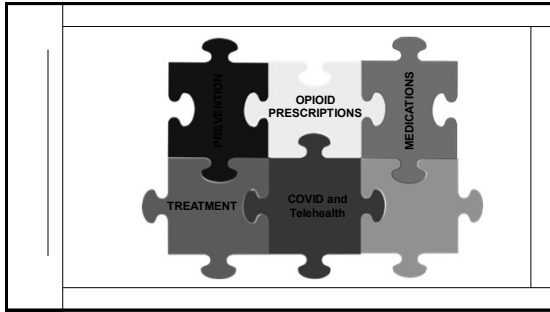
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**Stigmatizing factors to consider - Misdiagnosis**

**Could be due to...**

- Clinician level of comfort with treating SUDs
- Perception of "moral defect" instead of medical diagnosis
- Ineffective treatment interventions
  - Lack of adequate assessment
- Telehealth specific
  - Clinicians only have patient report to rely on for initial clinical information
  - Inability to provide assessments, drug testing, etc.

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***Stigmatizing factors to consider***

**Other factors...**

- Translating empathy across a technology platform
  - Research shows that empathy is a mediating factor for treatment success among SUD populations
- Less resources to engage
  - no computer
  - no internet access
  - no video capabilities
- Essential worker
- Financially unable to miss work

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***Intake process - Differences and limitations***

**Traditional intakes**

- Multidisciplinary team available (nurse, psychiatrist, psychologist, therapist, dietitian, etc.)
  - Allows for flexibility if assessment takes longer
  - Provides real-time feedback/results if drug tests are administered
  - Beneficial for rapid treatment planning and intervention as needed
- Varying forms of assessment available
- Drug testing
- Protocol for intoxicated patients

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***Intake process - Differences and limitations***

**Virtual intakes**

- Specific risks increased due to telehealth
- Time delay for providing patient detoxification medications if patient needs detox
- Less accuracy in assessing if patient is currently intoxicated
  - Higher risk of patient overdose
- More challenging to obtain baseline UTOX screen
- Patient quality of care diminished
  - Time constraints due to other scheduled virtual appointments
  - Less ability to ask someone to let your patient know if you are running behind

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***Culturally responsive care***

**Awareness of ones' cultural identity**

- Telehealth specific
  - May require more detailed questions during assessment
  - Can provide insight to other aspects of their substance use
- Apprehensiveness to treatment
- Function of substance use behavior
- Motivation for change

(Vaeth et al., 2017)

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***Vulnerable populations***

**Race/ethnic background considerations**

- Psychosocial stressors
- Racism
  - Posttraumatic Slave Syndrome (PTSS)
  - Intergenerational trauma
- Pre-existing health conditions/disparities
- Lack of community/increased isolation
- Perception of risk regarding use
  - May be lower depending on environment

(Swann et al., 2020; Williams et al., 2016; Unger et al., 2020)

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***Vulnerable populations***

**Socioeconomic status considerations**

- Finances
  - Lack of financial resources to receive treatment
  - Difficulty obtaining drug tests
  - Appointment frequency = increased cost
  - COVID-19 may have cost them their job
  - Financial issues can contribute to increased presence of mental health issues and increase in substance use behaviors to cope

(Vaeth et al., 2017)

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***Vulnerable populations***

**Socioeconomic status considerations**

- Living environment
  - Family members needing a place to stay due to COVID-19
  - Lack of privacy/confidentiality
- Isolation due to COVID-19
  - Living alone, higher risk for relapse/overdose
  - Lack of accountability from sober peers or support groups
- Homelessness
  - Inability to pay rent due to COVID-19 layoffs, leading to homelessness and increased mental health issues and increased substance use
  - Possible increase in higher risk substance use

(Martinez et al., 2020)

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***Home environment considerations***

**Family**

- Is there anyone in the home with patient?
  - Possible safety issues
- Do family members in the home use substances?
  - Increased risk of relapse
- Are their children in the home?
- Does the patient have any support in their home environment?

**Substances**

- It may be more difficult for the patient to remove all substances from the home if there is a family member who also uses substances

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***Increased access to substances***

**COVID-19 pandemic**

- Created deliverable alcohol from restaurants in some states
- Companies like "Eaze" and "Drizzly" conduct home deliveries of alcohol and/or cannabis
- Buying alcohol from the store
  - Higher risk of "buying in bulk" and having access at home all day every day
- Fewer options for activities
  - Playing sports, attending events
  - Increases likelihood of use due to "boredom"

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***Other things we didn't anticipate***

- What we see on camera
- Lack of drug availability
- The impact of hand sanitizer
- Increased patient attendance

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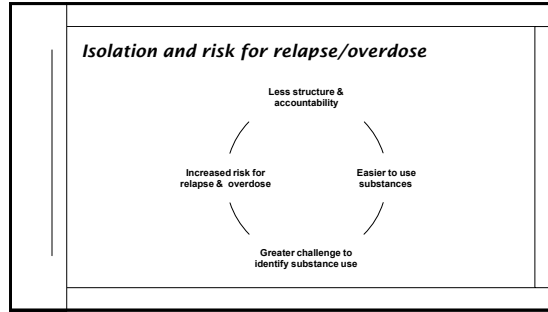
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***Logistics of providing care in a virtual world***

**Abstinence approach**

**Difficulty tracking abstinence**

- Depending on the substance a patient is using, it may be out of their system by the time they complete a drug test
- Make efforts to utilize random in-home testing for most accurate information

**Reduced motivation for abstinence**

- Reduction in ability to engage in out-of-home activities may increase difficulty of remaining abstinent during program
- Work with patient to create a list of safe activities to engage in that may still be in the home
- Discuss having them find an accountability partner or have someone in the house assist them with remaining abstinent

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***Logistics of providing care in a virtual world***

**Harm-reduction approach**

- Logistics
  - Providing accurate information regarding amount consumed may be more difficult to obtain
  - Focus more on family dynamics, environment, and motivation for use
    - Approach emphasizes change talk more than abstinence
  - Utilize worksheets to have patient track their use
    - In some cases, this can be used as an intervention

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***Drug screening***

- New challenges for drug screening during pandemic
- Consider screening as an opportunity to recognize individual's hard work in recovery
- Relapse is part of recovery
- Consider different methods for screening

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***Monitoring for success***

**Drug screen testing**

- Urine or salivary testing
- Salivary point of care/instant screening during telehealth

**Contingency management**

- Positive reinforcement
- Rewards for engaging in pro-social activities, negative drug screens, attending appointments

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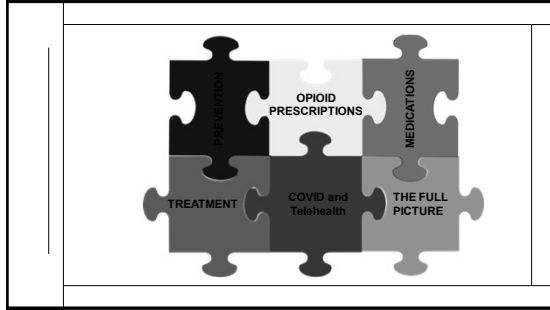
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*If we have all of the puzzle pieces, why don't we seem to be making progress?*

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*The role of depression in opioid use disorder*

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**Complex factors - Suicide rates**

- Suicide rates have been rising in nearly every state
- Nearly 45,000 Americans age 10 or older die by suicide
- There were more than 6,000 Veteran suicides each year from 2008 –2016
- There is one elderly suicide every 80 minutes
- 10<sup>th</sup> leading cause of death in the United States
- Suicide rate may be underreported in regards to overdose deaths

CDC, 2018; Ahmadi, et al., 2018; NIDA, 2020

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**How prevalent is the connection?**

**Higher risk for suicide than rest of the population**

- If OUD, 40 – 60% increased risk of suicidal ideation
- If IV OUD, 13% more likely to die of suicide than general population
- In 2017, opiates were involved in 40% of all suicide and unintentional overdose deaths
- June 2019 – OTPs are now required to follow standards from the National Action Alliance for Suicide Prevention
- few studies are available on the use of tricyclic antidepressants and opiate use disorder

Astrafroun, et al., 2017; CDC, 2018; National Action Alliance, 2019

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**Link between depression and OUD**

- Depression has been a significant predictor of long-term opioid use
- Individuals with moderate depression are 2-3 times more likely to misuse/abuse opioids.
- In individuals with depression, 19% also have an opioid use disorder compared to 5% of those with other mental health disorders
- Patients diagnosed with a mood disorder account for the majority of opioid prescriptions in the United States
- Recent study shows that individuals who survive an overdose are 18 times more likely to commit suicide within one year and 100 times more likely to succumb to overdose

Pecina, et al., 2018; CDC, 2018; NIDA 2020

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**Link between depression and OUD**

- Recent studies suggests the risk of a new onset of depression increases with longer duration of opioid analgesic use
- Dose or amount of opioids do not appear to have an effect
- Longer use of opiates also increases the risk of treatment resistant depression
  - 25% of patients who used opiates for 31-90 days
  - 52% of patients if longer than 90 days

Scherrer, et. al., 2016; 2013

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**Link between depression and OUD**

Treatment resistant depression			
Opioid duration (days)	Overall (n=6,169)	NO (n=4,623)	YES (n=1,546)
1-30	4631 (75.1)	3541 (76.6)	1090 (70.5)
31-90	802 (13.0)	578 (12.5)	224 (14.5)
> 90	736 (11.9)	504 (10.9)	232 (15.0)
Opioid dose > 50 mg	431 (7.0)	312 (6.7)	119 (7.7)

Scherrer, et. al., 2016

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**Link between depression and OUD**

- A different study found that 12% of individuals prescribed opiates longer for 30 days developed new onset depression
- Speculated causes:
  - Hyperalgesia
  - Changes in neuroanatomy - Amygdala and nucleus accumbens changes – reduced gray matter in amygdala was found with 30 days of use
  - Low testosterone
  - Changes last on average 4.7 months after opioid use has stopped

Cicford, 2010

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***The chicken or the egg....?***

- *Debate in the industry continues*
- Mood disorders also arise during detoxification from an opiate
- *Hyperkatifeia* - increased intensity of negative emotional/motivational symptoms and signs observed during withdrawal from abused drugs.
- Two ideas – both are accurate:
  - How to best induce abstinence
  - How to best maintain it

Maremmani, et al., 2018; ASAM, 2019

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***The potential science behind the link***

- Endogenous opioid system is comprised of three different protein couple receptors –  $\mu$  and  $\kappa$  and  $\delta$ .
- These receptors are widespread in central and peripheral nervous system.

Pecina, et al., 2018; Serafini, et al., 2018

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***The potential science behind the link***

- Rat studies – behavioral despair known as forced swim test – rats are placed in a narrow, inescapable cylinder of water
- Vigorous activity at first and then the rat does only the minimum necessary movement – this immobility is similar to a depressive like state
- Opioids decrease the immobility
- Differences between the rats and humans – there are less  $\delta$ -opioid receptor binding and more  $\kappa$ -opioid receptor binding

Pecina, et al., 2018;

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***The potential science behind the link***

- Differences between the rats and humans – there are less  $\delta$ -opioid receptor binding and more  $\kappa$ -opioid receptor binding
- Human neuroimaging studies have established a link between opioids and processing social cues
- Studies have shown that the  $\mu$  – opioid receptor system is involved in regulating non-painful stressor – social pain
- Patients with depression had reduced opioid releases
- Post-mortem studies revealed an increase in  $\mu$ -opioid receptor

Pecina, et al., 2018; Serafini, et al., 2018; Semenkevich, et al., 2014

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***Other possible links...***

- PTSD is another disorder where beginning research is showing that it may benefit from the modulation of opioid receptor systems.
- One study showed that morphine prevented the development of stress-enhanced fear learning in animals
- Study using US military personnel showed that the use of or morphine during early resuscitation and trauma care significantly lowered the risk of PTSD.
- Studies are also beginning using borderline personality disorder

Pecina, et al., 2018;

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***Link between depression and OUD***

*Would it surprise you.....?*

Until the 1950s, opium was the primary pharmacologic treatment for melancholia.

*Are we coming full circle?*

Ehrlich, et al., 2015

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**Treatment approaches - Naltrexone?**

- Enhances the effects of antidepressants
- Although studies have been able to duplicate this, the reason for this is unknown

Pecina, et al., 2018;

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**Treatment approaches - Buprenorphine?**

- Improves symptoms and reduces illicit opiate use while on a waitlist
- Use of buprenorphine has increased 300% to 1.2 million since 2014
- 35 times more likely to be prescribed in whites; while overdose deaths/suicides are increasing faster in blacks
- Payer sources are a significant factor
  - 40% cash
  - 35% private insurance
  - 25% Medicaid/Medicare

Streck, et al., 2018; Lagisetty, et al., 2019

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**Treatment approaches - Buprenorphine?**

Balanced agonist-antagonist opioid modulation represents a novel and potentially clinically important approach to the treatment of MDD and other psychiatric disorders.

- 2015 study: Combination of BUP and SAM showed antidepressant activity in subjects with MDD
- 2018 study: Low dose buprenorphine reduced emotional reactivity and improved negative affect
- 2018 study: Buprenorphine shown to be effective in reducing suicidal ideation

Ehrich, et al., 2015; Serafini, et al., 2018; Ahmadi, et al., 2018; Pecina, et al., 2018

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**Treatment approaches - Buprenorphine?**

- Summary: 13 studies have shown reduction in depression symptoms, self-injurious behaviors, and suicidal ideation in both treatment resistant depression and opioid dependent patients
- Studies have varied in outcome rates from 50% to 75% improvement in the first week

Ehrlich, et al., 2015; Serafini, et al., 2018; Ahmadi, et al., 2018; Pecina, et al., 2018

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**Treatment approaches - Methadone?**

- Both fluoxetine and fluvoxamine may increase methadone blood levels
- Patients who show an unsatisfactory response to methadone at 100–150 mg/day can benefit from the addition of fluvoxamine

Maremmani, et al., 2019

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**Treatment approaches**

**So, what does all this mean?**

- Beta-endorphins, in two trials, were successful in treating depression in a few non-addicted depressed patients but were not significantly more substantial than placebo.
- SSRIs are not useful during the detoxification of patients with HUD.
- Long-acting opiates have antidepressant properties
- Over-standard dosages of methadone (up 120 mg/day) are needed.
- Craving increases during manic phases.

Maremmani, et al., 2019

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*Complex, conventional, and controversial techniques*

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**Treatment approaches**

- Less than 10% of individuals nationally receive treatment for both opioid use disorder and depression
- Harm reduction is beneficial if it gets to the ultimate goal of abstinence
- Screen all depressed patients for opioid use
- Perform psychiatric evaluations on all opioid use disorder patients at the onset of treatment and once the symptoms have stabilized
- Gold standard – medications in combination with psychosocial therapy and services

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**Treatment approaches**

Think back to the 80's and the AIDS epidemic – how was that treated?  
Are we currently in the same place with the opioid crisis?

**The cascade of care model:**

- Identify 90% of individuals with an OUD
- Link 90% of identified individuals to treatment
- Retain 90% of treatment individuals for six months
- Provide post-treatment support efforts

Wattenberg, 2018

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**Treatment approaches - Innovative or controversial? - Polling question #4**

First responder initiative



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**Treatment approaches - Innovative or controversial? - Polling question #5**

New York State is providing a tax credit to employers for each individual they hire that has a substance use/opioid disorder in remission.



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**Treatment approaches - Innovative or controversial?**

**The Bridge Device -**

- approved by the FDA to help reduce symptoms of opioid withdrawal
- sends gentle electrical impulses to areas of the brain and branches of nerves



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***Innovative or Controversial - Polling Question #6***



- Is the Bridge Device innovative or controversial?

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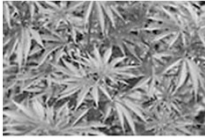
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***Innovative or Controversial - Polling Question #7***



shutterstock - 200379260

- Should marijuana be used to treat opioid use disorder?

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***Treatment approaches - Innovative or controversial?***

- Using marijuana to treat opioid use disorder – several states have recently enacted laws
- 2014 study found that states with medical marijuana laws slowed the overdose opioid deaths
- 2019 study did not have the same findings



Bachhuber et al., et. al., 2014; Shover, et. al., 2019; Otison, et. al., 2018

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**Treatment approaches - Use of marijuana**

- 2018 study found that cannabis use appears to increase rather than decrease the risk of developing non-medical prescription opioid use and opioid use disorder
- Other results of study:
  - Younger
  - More likely to be male
  - Past history of substance use disorder
  - Past history of mood disorder
  - Family history of substance use disorder

Olson et al., 2018

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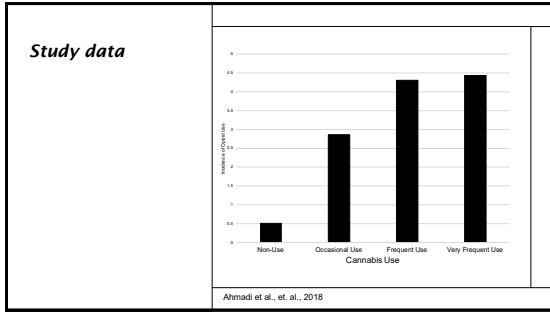
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**Treatment approaches - Factors that may contribute**

- Heroin and tetrahydrocannabinol have similar effects on dopamine transmission
- Cannabis use can lead to behavioral disinhibition which can increase the risk of using other substances
- Increased availability and social exposure to other drugs

Ahmadi et al., et. al., 2018

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**Million dollar question - Polling question #8**

- If increased cannabis use leads to increased opioid use
- More states are legalizing marijuana and therefore availability increases

**Is the worst still yet to come in regard to the opioid crisis??**



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**Treatment approaches - What can you do?**

- Implementation of screening tools
- Treating women – incorporating conversations on pregnancy and options for all women of child-birthing age
- Partnering with primary care physicians
- Long term treatment – recovery groups
- Integrated treatment approach
- Use of technology
- Staying current with the new information

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**Thank you for coming**

We'll use any remaining time for questions and answers...



**Q&A**

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