OPIOID USE DISORDER: HISTORY, IMPACT AND RECOVERY

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Sledge – Hammer to Pain

- *" Among the remedies which it has pleased the Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium."*

Dr. Thomas Sydenham

(1624 – 1689)

“Oh, jab me with your needle a hundred times and a hundred times I will thank you, Saint Morphine.”

Jules Verne (1828-1905)

Substance Use Disorders

- Alcohol
- Cannabis
- Phencyclidine
- Other Hallucinogen
- Inhalants
- Opioids
- Sedative, hypnotic, or anxiolytic
- Stimulant: Specify amphetamine or cocaine
- Tobacco

ADDICTION

- Impaired Control
- Social Impairment
- Risky Use
- Tolerance and Dependence

Percentage of U.S. Consumption of World's Opioid Production

- Hydrocodone- 99%
- Oxycodone – 80%
- Methadone- 58%
- Hydromorphone- 54%
- Fentanyl- 49%
- Meperidine- 43%

International Narcotics Control Board

“Morphine, Though It Could Cure Little, It Could Relieve Anything”

Civil War Surgeon

Pendulum Swings

- 1860's-Civil War 400,000 with "soldiers disease".
- 1920's- "Nearly 80% of the morphine addicts have acquired the habit from legitimate medications."
  - Dr. Alexander Lambert, AMA President
- 1930-1950's- Opioids illegal, "unnecessary, dangerous.

Pendulum Swings

- "Use of narcotics in terminal cases is to be condemned…Dominant on the list of these unfortunate effects is addiction."
  - American Medical Association Consensus Paper 1940

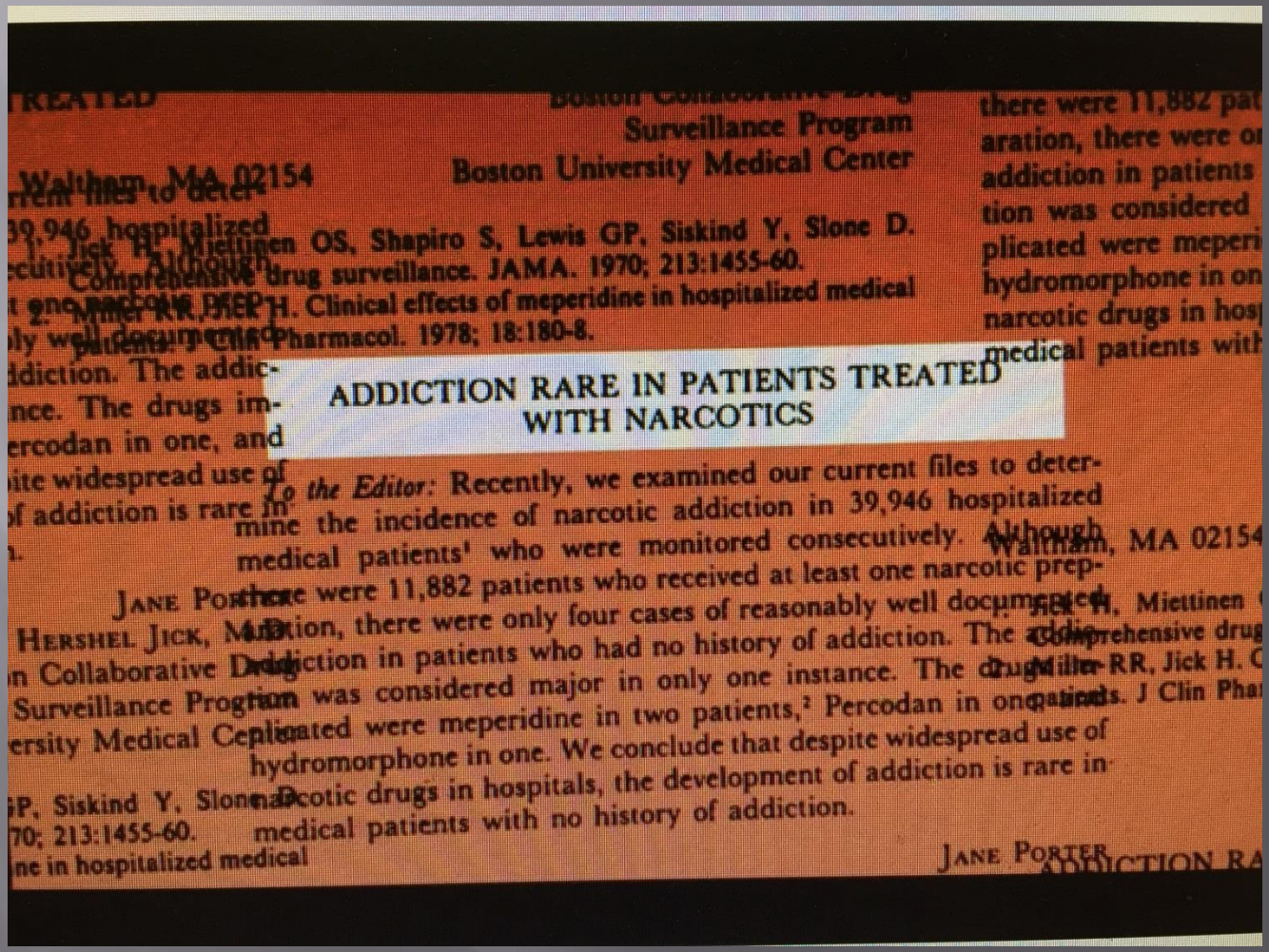
- 1960's 1970's-Hospice Movement: Death with dignity
  - 1967-first living will
  - 1969-Kubler-Ross, On Death and Dying
  - 1973-Patient Bill of Rights

How a NEJM 1980 Correspondence Letter Became a Runaway Train

- "Recently, we examined current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients who were monitored consecutively. Although there were 11,882 patients who received at least 1 narcotic preparation, there were only 4 cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only 1 instance. The drugs implication were meperidine in 2 patients, Percodan in 1, and hydromorphone in 1. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction."

Porter, Jicks. NEJM, Jan. 10, 1980; 302:123

Boston Collaborative Drug Surveillance Program Boston University Medical Center



Surveillance Program
Boston University Medical Center

Waltham, MA 02154

Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.

H. Clinical effects of meperidine in hospitalized medical
Pharmacol. 1978; 18:180-8.

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
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1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

Opioid Maintenance Therapy for Non-Malignant Pain

- 38 patients on opioids for NM pain.
- Retrospectively evaluated for safety and efficacy.
- 19 > 4 years, 6 > 7 years.
- 24 patients-partial or fully adequate relief.
- 14 patients- inadequate relief.
- Few substantial gains in employment or function.
- Conclusion of study- Opioid maintenance therapy can be a safe, salutary and a more humane alternative to surgery or no treatment with intractable NM pain.

Portenoy R, Foley K. Pain. 1986 May;25(2): 171-86

"Adverse Effects of Systemic Opioid Analgesics"

- Adverse effects of long term opioid use are overestimated.
- Systemic toxicity is negligible.
- Development of tolerance is minimal.
- Pain control, addiction and withdrawal do not pose a problem
- Their use should not be unduly limited by unfounded fears.

Drug Safety. May 1992, V 7, Issue 3, pp 200-2013

Boston Collaborative Drug Surveillance Program, Boston University Medical Center

- *Scientific American* 1990
  - Porter/Jicks- an " extensive study"
- *Institute for Clinical Systems Improvement Paper*
  - Porter/Jicks- "a landmark report"
- *Time Magazine 2001 Story*
  - "Less Pain, More Gain,"- Called Porter/Jicks a "landmarks study" showing that the "exaggerated fear that patient's would become addicted" as "basically unwarranted. "

Opioids and Chronic Pain

- 1996- Purdue launches Oxycontin
- 1999 – JCAHO released pain management standards as part of the accreditation standards for hospitals and other health care settings. *Pain as the "5th vital sign".*
- 2000 – Congress passed into law a provision that declared the ten year period beginning January 1, 2001 as the "Decade of Pain Control and Research."

What We Know

- Roughly 21-29% of patients prescribed opioids for chronic pain misuse them.
- Between 8 and 12% develop an opioid use disorder
- An estimated 4-6% who misuse prescription opioids transition to heroin
- About 80% of people who use heroin, first used prescription opioids

NIH National Institute on Drug Abuse

Boston Collaborative Drug Surveillance Program Boston University Medical Center

- "I am essentially mortified that that letter to the editor was used as an excuse to do what these drug companies did."

Hershel Jick ,MD

"I just minimized or dismissed the issues…of abuse, addiction and diversion…

we recognize that was a big error...we need to talk about the use of opioids and other prescription drugs from the perspective of two skill sets…how to prescribe, but at the same time, (doctors) have to have a skill set in addiction medicine, how to assess the risk of abuse and diversion and addiction…or they shouldn't use them."

Dr. Russell Portenoy

Drug Overdose Deaths

- Deaths involving opioids continue to rise
- Leading cause of death for Americans under 50 years of age
- Roughly 52,000 people in U.S. in 2015, and 64,000 in 2016- a 22% increase.
- 72,000 overdose deaths in 2017.

CDC: National Center for Health Statistics

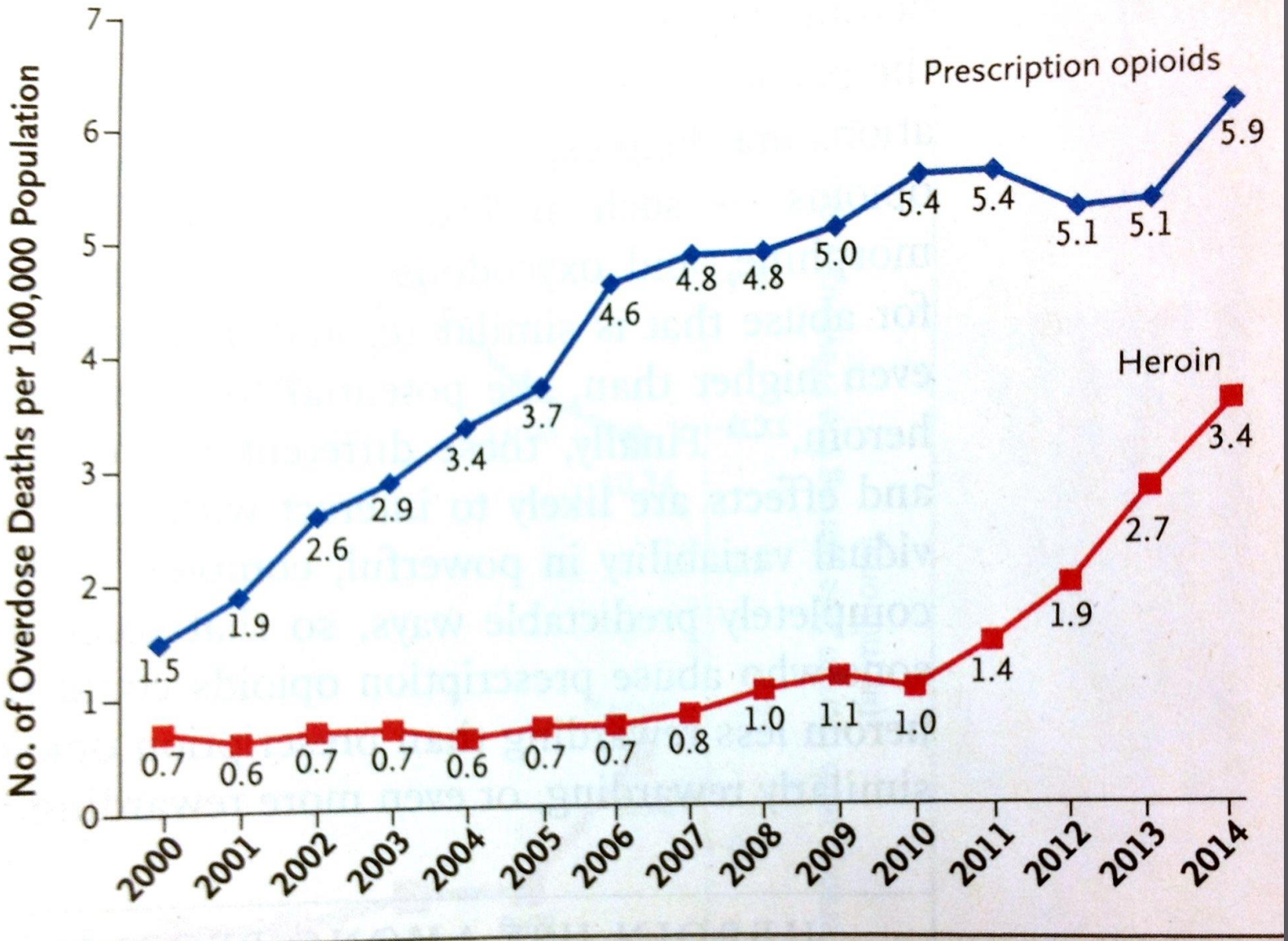


Figure 1. Age-Adjusted Rates of Death Related to Prescription Opioids and Heroin Drug Poisoning in the United States, 2000–2014.

Data are from the Centers for Disease Control and Prevention.[5]

PREMATURE DEATH TRENDS BY METHOD OF INJURY, 2006-2015

SOURCE: COUNTYHEALTHRANKINGS.ORG

TRENDS IN PREMATURE DEATH FROM DRUG OVERDOSE BY COMMUNITY TYPE, 2006-2015

YEARS OF POTENTIAL LIFE LOST PER 100,000

SOURCE: COUNTYHEALTHRANKINGS.ORG

Economic Burden

- The opioid epidemic has cost United States $ 115, 000,000,000 in 2017
- The opioid epidemic has cost the U.S. more than $1,000,000,000,000 since 2001
- May exceed another $500 billion over the next three years.

Altarum's Center for Value and Health Care,

Concepts and Definitions

- Substance use disorder
  - A cluster of cognitive, behavioral and psychological symptoms indicating that an individual continues to use a substance despite significant substance related problems. A diagnosis based on pathological pattern of behaviors related to the use of the substance.
- Tolerance
  - A state in which markedly increased drug doses are required to achieve desired effect or exposure results in diminution of 1 or more opioid effects over time
- Physical dependence
  - A state of adaptations manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level the drug, and/or administration of antagonist

Opioid Tolerance & Physical Dependence

Both tolerance and physical dependence are physiological adaptations to chronic opioid exposure

Tolerance:

- Increased dosage needed to produce specific effect
  - Develops readily for CNS and respiratory depression

Physical Dependence:

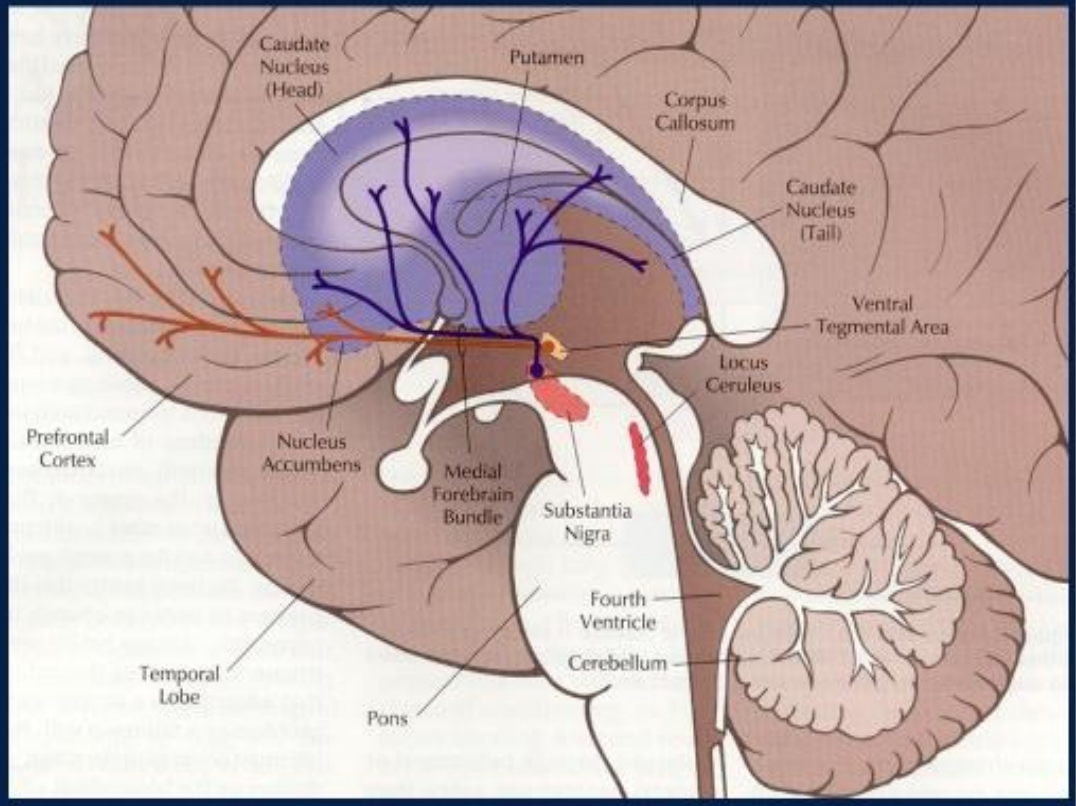
- Signs and symptoms of withdrawal by abrupt opioid cessation, rapid dose reduction

Concepts and Definitions

- Addiction
  - a primary, chronic, neuro biologic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

Reward/Reinforcement

- Reward/Reinforcement is in part controlled by mu receptors in the Reward Pathway:
  - Ventral Tegmental Area (VTA)
  - Nucleus Accumbens with projections to Prefrontal Cortex
  - Dopaminergic system



Criteria For Substance Use Disorders

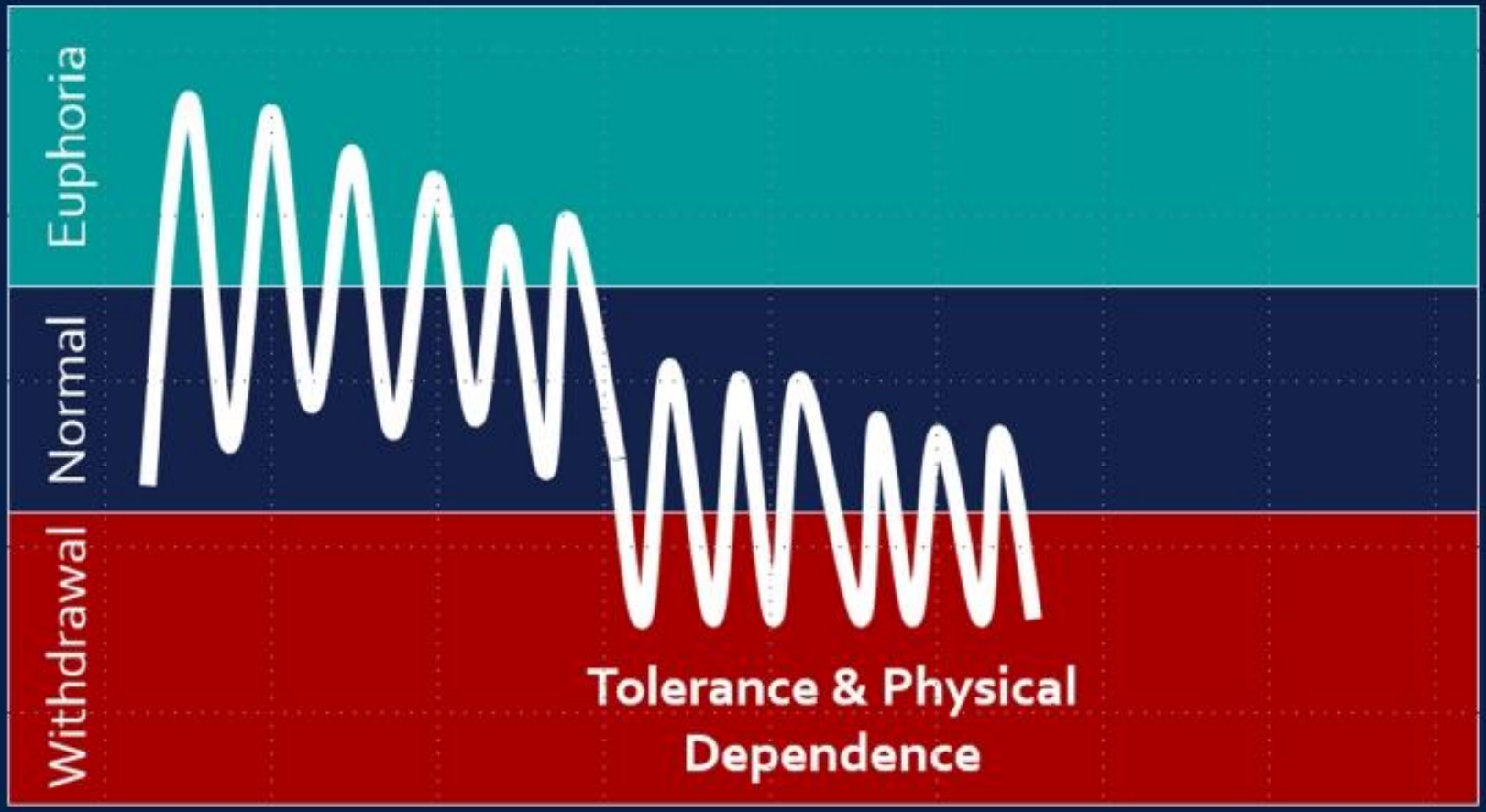
- Taking the substance in larger amounts or for longer than you're meant to.
- Wanting to cut down or stop using the substance but not managing to.
- Spending a lot of time getting, using, or recovering from use of the substance.
- Cravings and urges to use the substance.
- Not managing to do what you should at work, home, or school because of substance use.
- Continuing to use, even when it causes problems in relationships.

2-3 Mild, 4-5 Moderate, More than 6 Severe

Criteria for Substance Use Disorders

- Giving up important social, occupational, or recreational activities because of substance use.
- Using substances again and again, even when it puts you in danger.
- Continuing to use, even when you know you have a physical or psychological problem that could have been caused or made worse by the substance.
- Needing more of the substance to get the effect you want (tolerance).
- Development of withdrawal symptoms, which can be relieved by taking more of the substance.

Natural History of Opioid Use Disorder



Spontaneous Acute Opioid Withdrawal

- Develops spontaneously in a physically dependent person suddenly stops, or markedly decreases, the opioid
- Severity is usually less with longer half-life drugs
- Duration depends on half-life of opioids person is physically dependent on

	Onset	Peak	Duration
Heroin	4 - 6 hours	~3 days	4 - 7 days
Methadone	1 - 2 days	~7 days	12 - 14 days

Acute Opioid Withdrawal

Grade	Symptoms / Signs
0	Anxiety, Drug Craving
1	Yawning, Sweating, Runny nose, Tearing eyes, Restlessness Insomnia
2	Dilated pupils, Gooseflesh, Muscle twitching & shaking, Muscle & Joint aches, Loss of appetite
3	Nausea, extreme restlessness, elevated blood pressure, Heart rate > 100, Fever
4	Vomiting / dehydration, Diarrhea, Abdominal cramps, Curled-up body position

Clinical Opiate Withdrawal Scale (COWS):

pulse, sweating, restlessness & anxiety, pupil size, aches, runny nose & tearing, GI sx, tremor, yawning, gooseflesh

5-12 mild,
13-24 moderate
25-36 moderately severe
>36 severe

Precipitated Acute Opioid Withdrawal

- Precipitated in a physically dependent person, by administration of either:
  - an opioid antagonist (e.g. naloxone, naltrexone) or
  - an opioid partial agonist (e.g. buprenorphine)
- Qualitatively similar to spontaneous withdrawal but faster onset
- Duration depends upon half-life of medication causing the withdrawal

	Onset	Peak	Duration
Naloxone	minutes	minutes	~20 minutes
Naltrexone	minutes	minutes	1 – 2 days
Buprenorphine	minutes	minutes	1 – 2 days

Drug Addiction Symptoms or Behaviors Include Among Others

- Feeling that you have to use the drug regularly — daily or even several times a day
- Having intense urges for the drug that block out any other thoughts
- Over time, needing more of the drug to get the same effect
- Taking larger amounts of the drug over a longer period of time than you intended
- Making certain that you maintain a supply of the drug
- Spending money on the drug, even though you can't afford it
- Not meeting obligations and work responsibilities, or cutting back on social or recreational activities because of drug use

Drug addiction symptoms or behaviors include among others

- Continuing to use the drug, even though you know it's causing problems in your life or causing you physical or psychological harm
- Doing things to get the drug that you normally wouldn't do, such as stealing
- Driving or doing other risky activities when you're under the influence of the drug
- Spending a good deal of time getting the drug, using the drug or recovering from the effects of the drug
- Failing in your attempts to stop using the drug
- Experiencing withdrawal symptoms when you attempt to stop taking the drug

Recognizing unhealthy drug use in family members

- Sometimes it's difficult to distinguish normal teenage moodiness or angst from signs of drug use. Possible indications that your teenager or other family member is using drugs include:
- **Problems at school or work** — frequently missing school or work, a sudden disinterest in school activities or work, or a drop in grades or work performance
- **Physical health issues** — lack of energy and motivation, weight loss or gain, or red eyes

Recognizing unhealthy drug use in family members

- **Neglected appearance** — lack of interest in clothing, grooming or looks
- **Changes in behavior** — exaggerated efforts to bar family members from entering his or her room or being secretive about where he or she goes with friends; or drastic changes in behavior and in relationships with family and friends
- **Money issues** — sudden requests for money without a reasonable explanation; or your discovery that money is missing or has been stolen or that items have disappeared from your home, indicating maybe they're being sold to support drug use

Strategies for Addressing the Opioid Epidemic

- Decrease supply
  - Wholesale
  - Take back programs/ disposal boxes
- Change/influence prescribing practices
  - Education-medical school, residency
  - Prescription drug monitoring programs
    - Mandatory vs voluntary
  - Insurance based policies

National Academies of Science.Engineering.Medicine
Consensus Study Report, July 2017
Pain Management and the Opioid Epidemic

Strategies for Addressing the Opioid Epidemic

- Reduce demand
  - Educate public/patients
    - Risks and benefits
    - Goals and expectations
- Reduce harm
  - Naloxone
  - Increasing access to treatment
- FDA oversight/monitoring
  - Systems approach versus product specific approach
- Research

National Academies of Science .Engineering .Medicine
Consensus Study Report . July 2017

Pain and Opioid Dependence and Tolerance

- Clinically not unrelated phenomena*
- Presence of one condition seems to influence the expression of the other.
- The presence of addictive disease seems to worsen the experience of pain.**

* Savage SR. J Pain Symp Manage. 1993;8:265-78

** Savage SR. Pharm Therapies Drug and Alcohol Addictions. New York: Dekker; 1995. pp373-409

Medically Supervised Withdrawal "Opioid Detoxification"

- Low rates of retention in treatment
- High rates of relapse post-treatment
  - < 50% abstinent at 6 months
  - < 15% abstinent at 12 months
- "Detox" is not treatment, it is just the start of treatment
- Increased rates of overdose due to decreased tolerance

O'Connor PG. *JAMA*. 2005.
Mattick RP, Hall WD. *Lancet*. 1996.
Stimmel B et al. *JAMA*. 1977.

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