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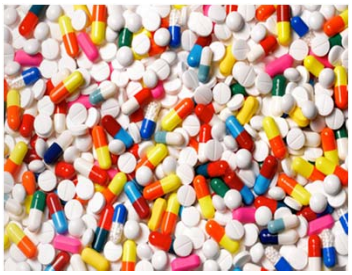
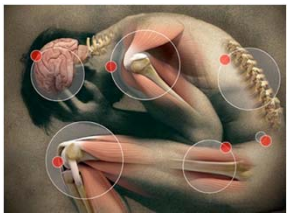
My background

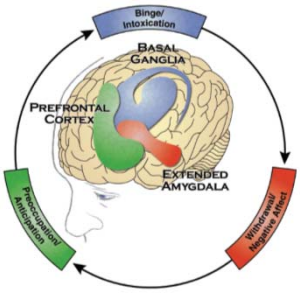
- Primary Care physician in a rural setting for 30 years
- Public Health Physician for Josephine then Jackson County
- Medical Director for a Medication Assisted Treatment program for 25 years
- Currently a consultant to the Oregon Health Authority concerning opioids.
- Member of the governor's task force on Opioids

Outline

- Despair
- Pills
- Pain
- Addiction
- Paradigm shift





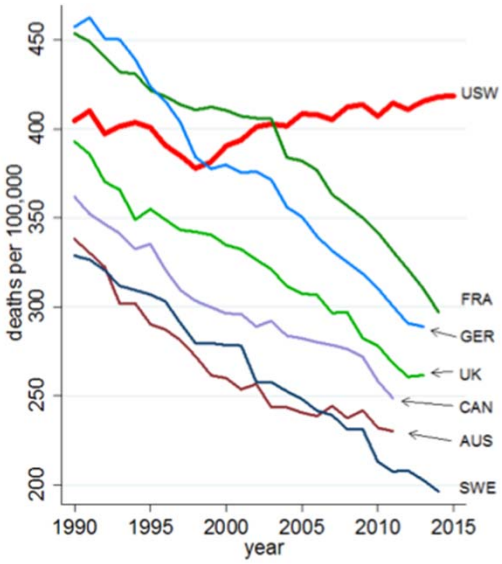


I no longer accept gifts, lunches, or anything “free” from pharmaceutical companies.

Acknowledgements: Those whose slides I have used or borrowed heavily from…we stand on the shoulder of giants:

- Paul Coelho
- Paul Lewis
- Dan Clauw
- Katrina Hedberg
- Lisa Millet
- Erin Krebs
- John Loeser
- David Tauben
- Lisa Shields
- Elizabeth white
- Melissa Weimer

US all-cause mortality rates, ages 45-54



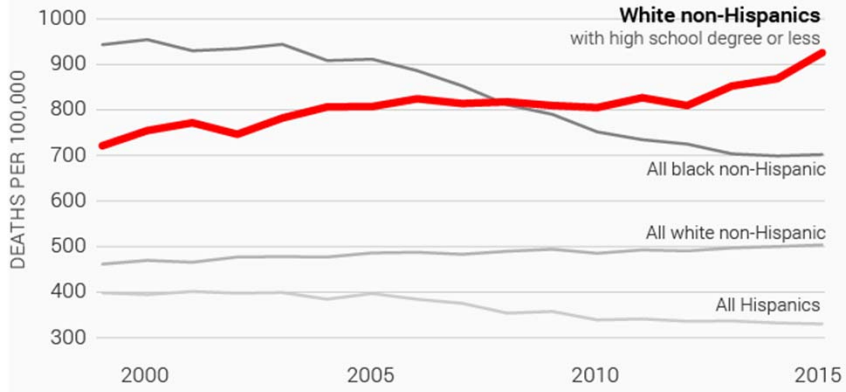
Professors Ann Case, Angus Deaton.
Princeton University

Source: "Mortality and morbidity in the 21st century" by Anne Case and Angus Deaton, Brookings Papers on Economic Activity, Spring 2017.

B | Economic Studies at BROOKINGS

Midlife mortality by all causes in the U.S.

Men and women ages 50-54, death by all causes



Source: "Mortality and morbidity in the 21st century" by Anne Case and Angus Deaton, Brookings Papers on Economic Activity, Spring 2017.

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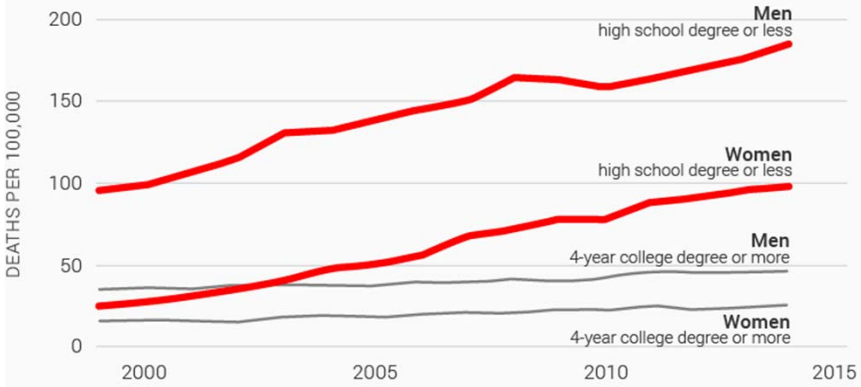
White non-Hispanic midlife mortality from "deaths of despair" in the U.S. by education

Ages 50-54, deaths by drugs, alcohol, and suicide



Source: "Mortality and morbidity in the 21st century" by Anne Case and Angus Deaton, Brookings Papers on Economic Activity, Spring 2017.

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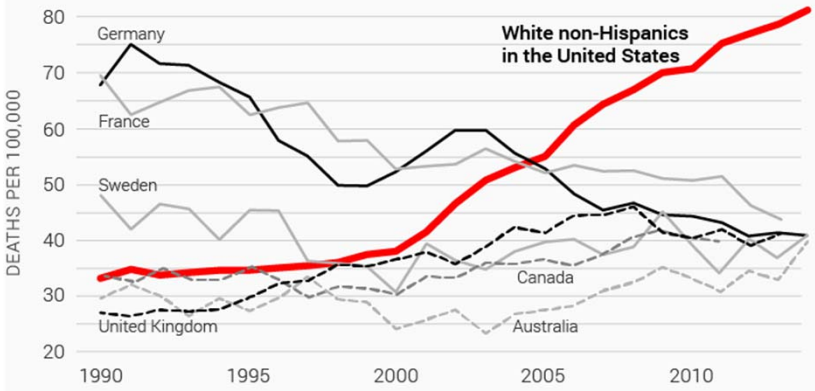
Midlife mortality from "deaths of despair" across countries

Men and women ages 50-54, deaths by drugs, alcohol, and suicide



Source: "Mortality and morbidity in the 21st century" by Anne Case and Angus Deaton, Brookings Papers on Economic Activity, Spring 2017.

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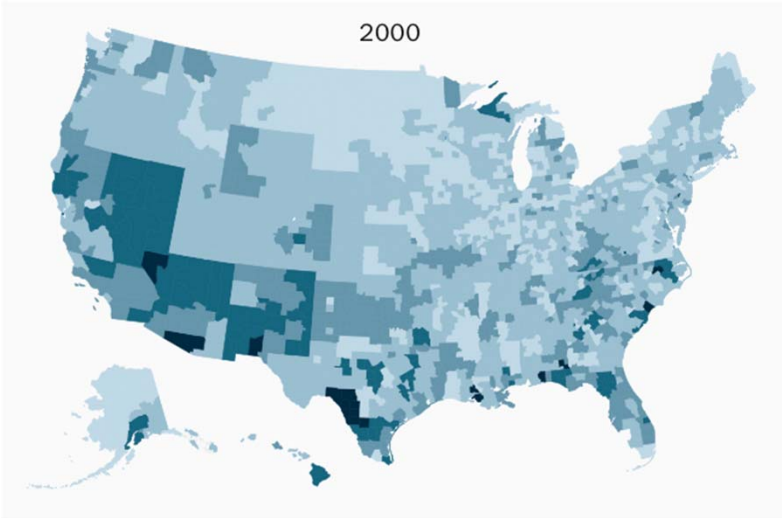
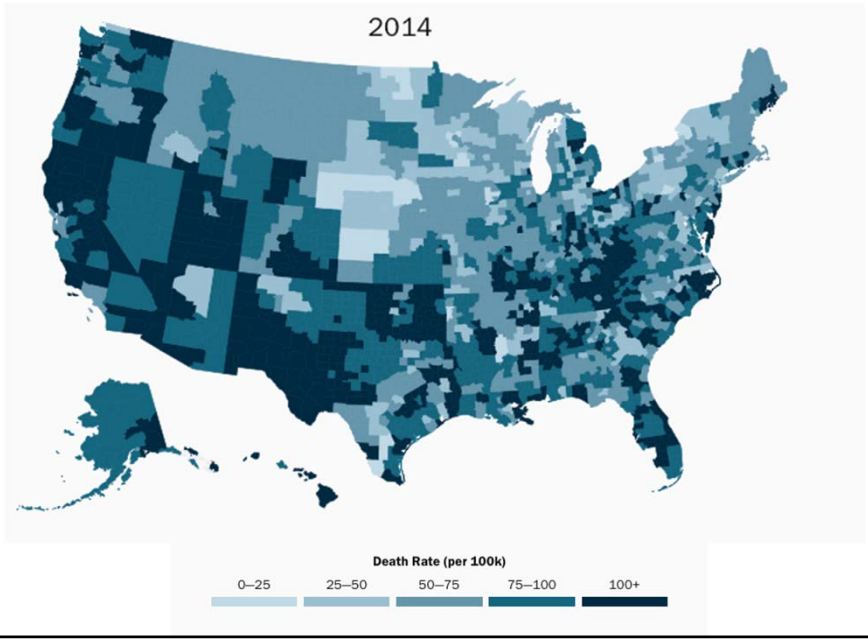
"Deaths of Despair" for white non-Hispanics, Ages 45-54



"Deaths of Despair" for white non-Hispanics, Ages 45-54



Angus / Deaton hypothesis:

Why?

- Decline in blue collar jobs since 1970s, especially for those with less than a college degree
  - Major impact on white working class men
    - Fewer jobs, lower wages, lower returns on experience
    - Reduced marriage rates, higher divorce, worse family lives
    - Increases in reports of poor health
    - Increasing poor mental health
    - Increased incidence of chronic pain
      - Loss of economic supports
      - Loss of social supports
        - Increased suicide
        - Increasing substance use
          - Alcohol
          - Drugs

"This process was unfolding before heavy-duty prescription opioids flooded the market, but their presence has heightened its impact."

Why do people use drugs?

Paradigm Shift:

From: What is wrong with you?

To: What has happened to you?

Testing the hypothesis

What if we actually asked: "What happened to you?"

- What are the **life experiences** that lead to these bad outcomes?
  - **Formal qualitative study of "Adverse Life Events"**
- Can this help us figure out what to do?

Why do people use drugs ….

Adverse Childhood Experiences (ACE) Study

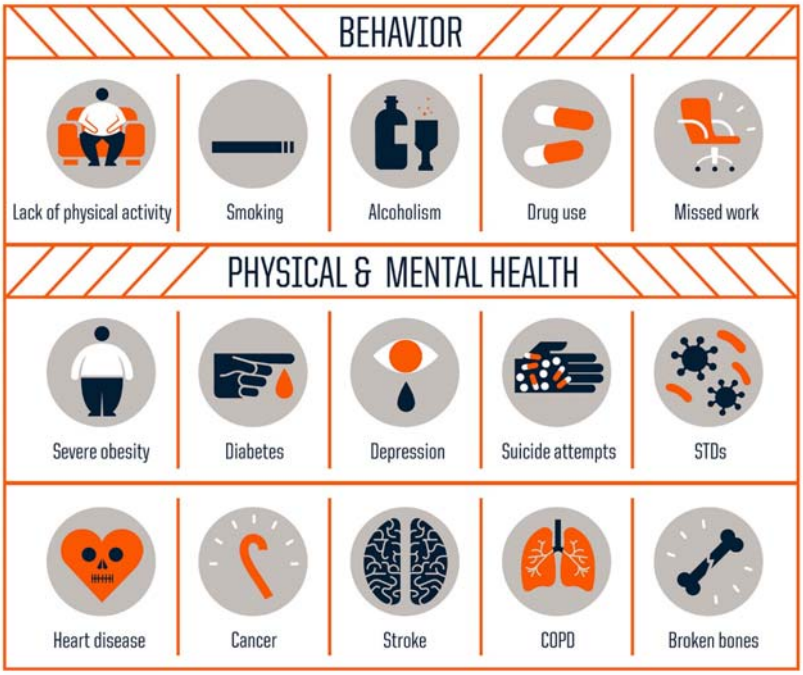
Adverse Childhood Events / Rate:

- Substance Abuse 27%
- Parental Separation/Divorce 23%
- Mental Illness 17%
- Battered Mother 13%
- Criminal Behavior 6%
- Psychological Abuse 11%
- Physical Abuse 28%
- Sexual Abuse 21%
- Emotional Neglect 15%
- Physical Neglect 10%

What are Adverse Childhood Experiences (ACEs)?

- Abuse
  - Emotional
  - Physical
  - Sexual
- Neglect
  - Emotional
  - Physical

- Household Challenges
  - Mother treated violently
  - Household substance abuse
  - Mental illness in household
  - Parental separation or divorce
  - Criminal household member

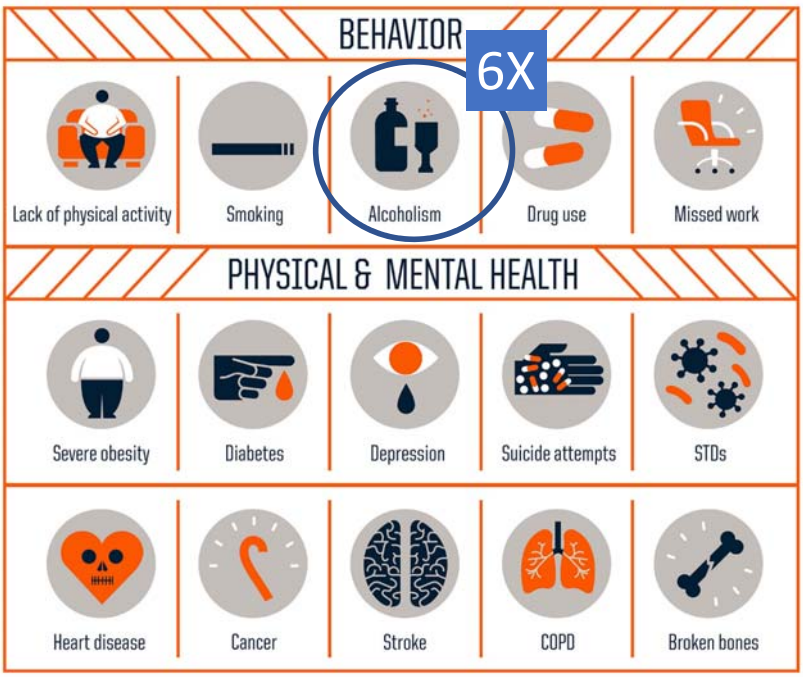


https://www.npr.org/sections/health-shots/2015/03/02/387007941/take-the-ace-quiz-and-learn-what-it-does-and-doesnt-mean

ACEs are not Destiny

ACES are Risk Factors
- Health Behavior
- Health Outcomes

High (>=4) vs Low (0)
- Alcoholism 6X
- SUD 10 X



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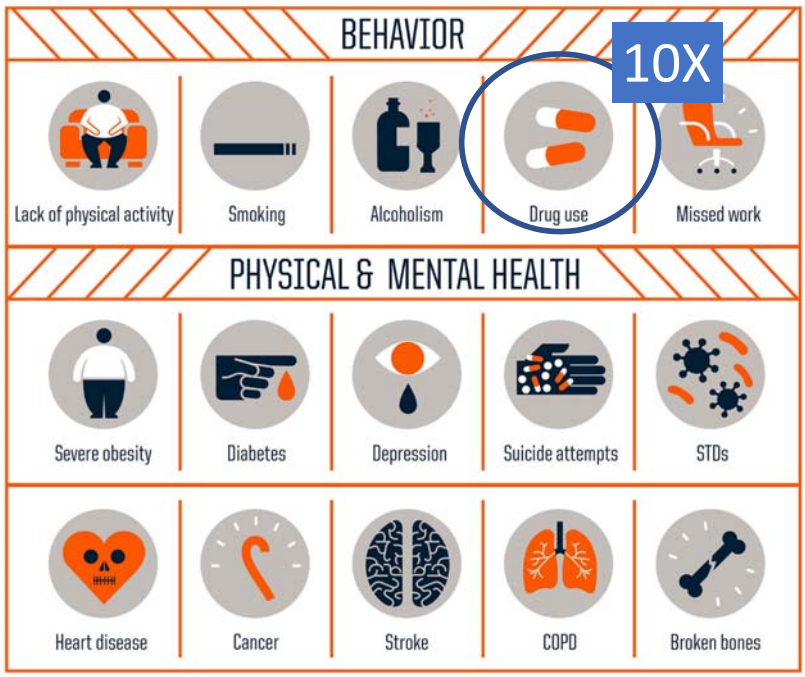

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ACEs are not Destiny

ACES are Risk Factors
- Health Behavior
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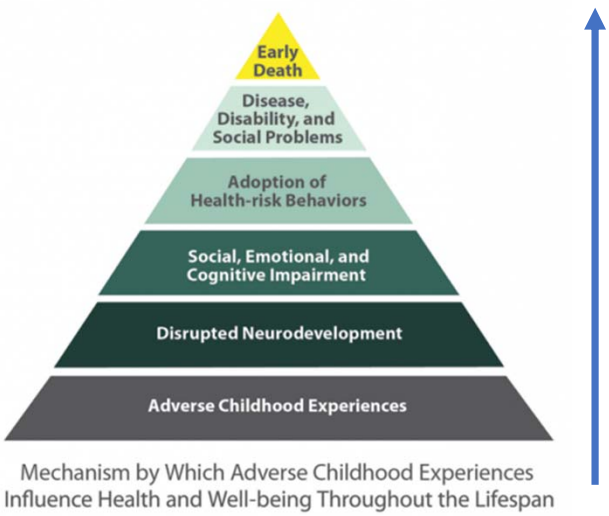
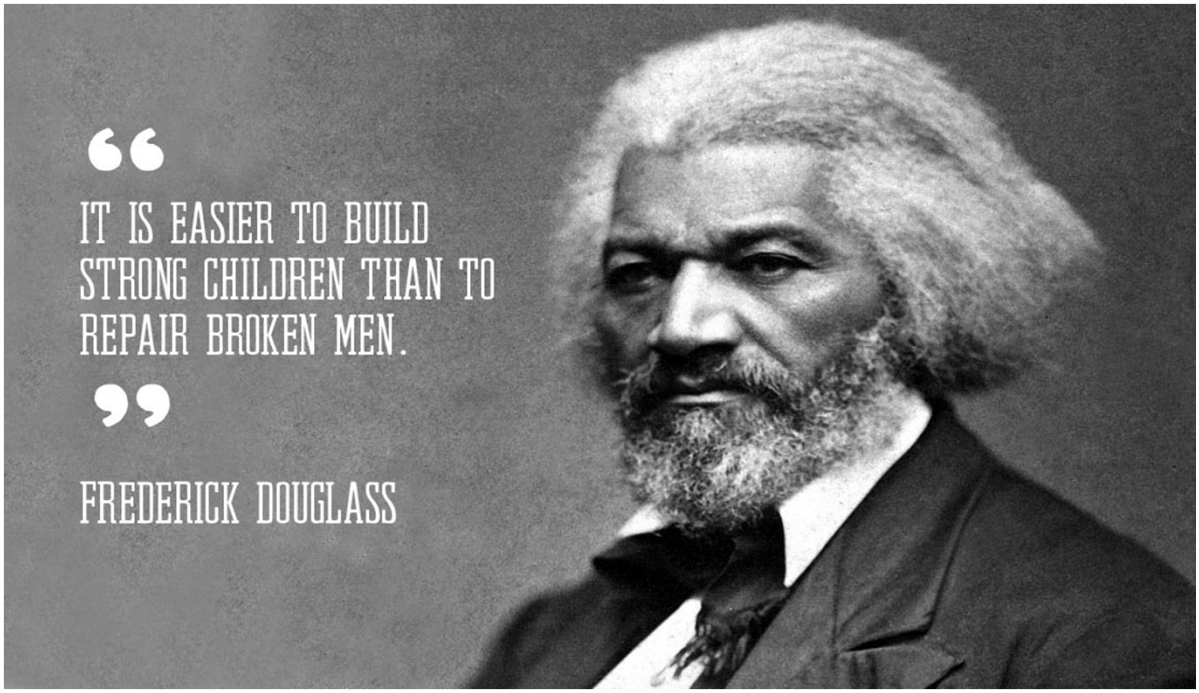
High (>=4) vs Low (0)
- Alcoholism 6X
- SUD 10 X

How do Adverse Childhood Experiences (ACEs) Hurt?



Mechanism by Which Adverse Childhood Experiences Influence Health and Well-being Throughout the Lifespan

Pediatrics March 2003, VOLUME 111 / ISSUE 3

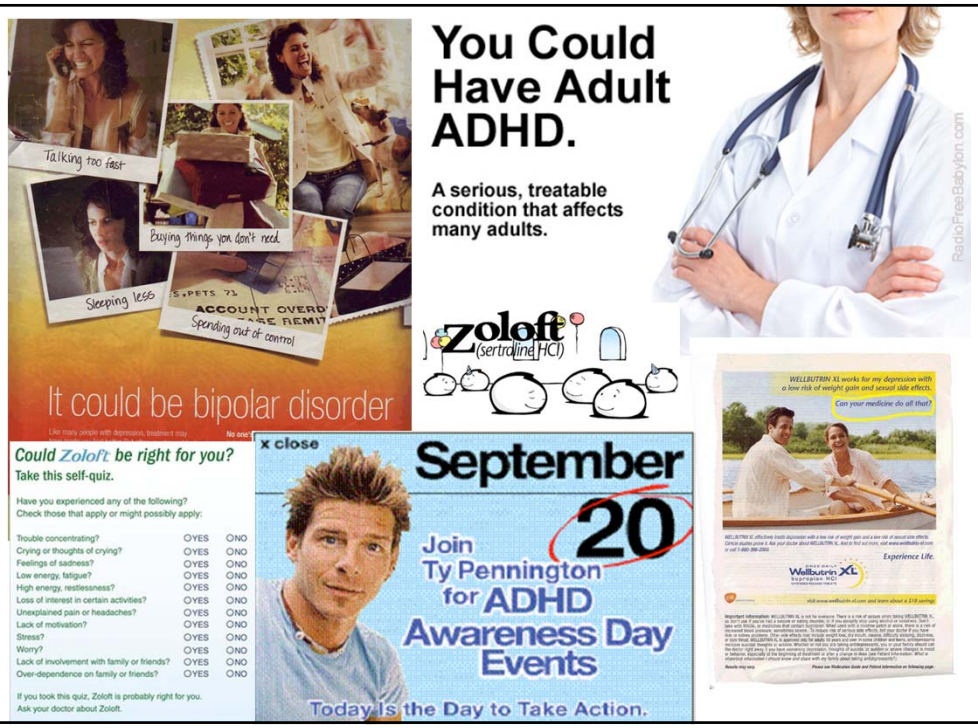

IT IS EASIER TO BUILD
STRONG CHILDREN THAN TO
REPAIR BROKEN MEN.
FREDERICK DOUGLASS

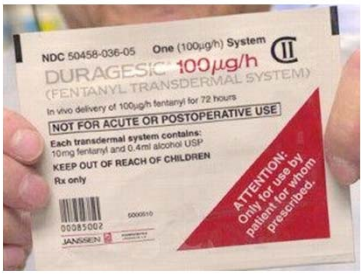

Too many pills!
How did we get here?

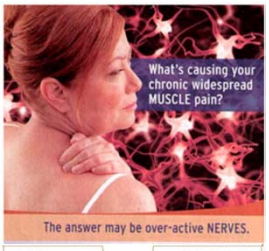
The Recent Past

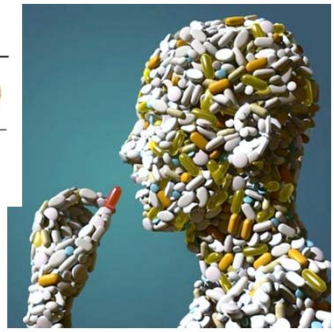
In 1991, 88% of Medical Board members believed that extended opioid prescribing for chronic non cancer pain was ***unlawful*** and ***unacceptable*** medical practice. [1]

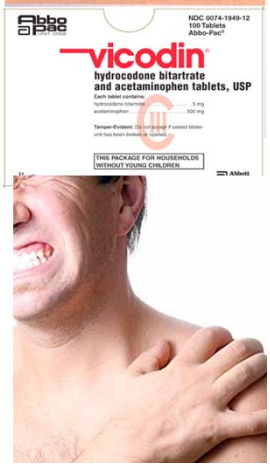
1. Gilson AM, Joranson DE. Controlled substances and pain management: changes in knowledge and attitudes of state medical regulators. J Pain Symptom Manage 2001;21(3):227–37.









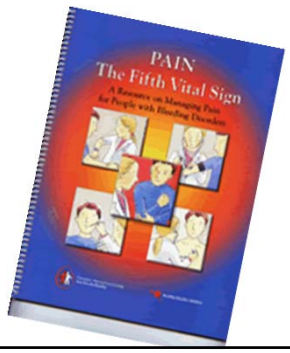


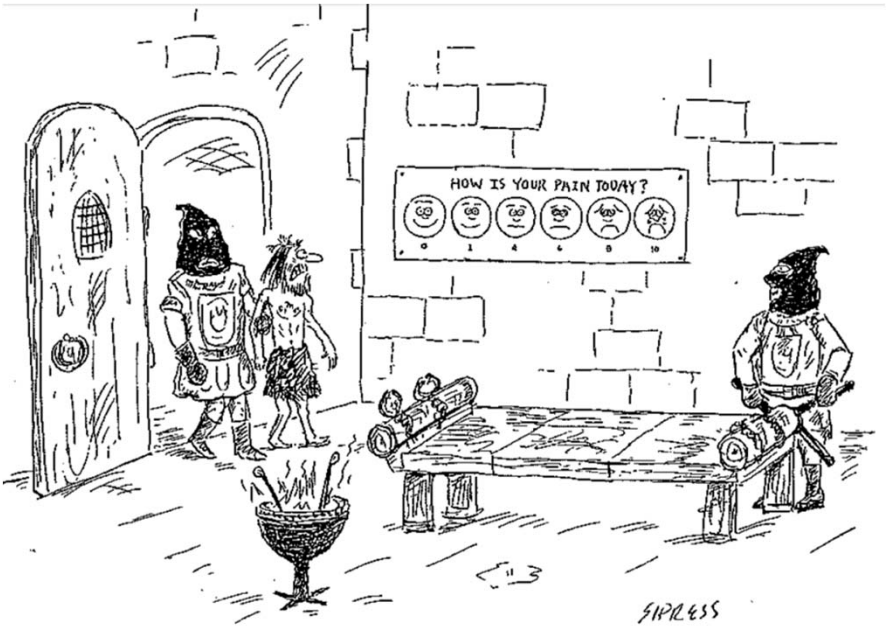
Pain Treatment

Changes in Medical Practice

- Providers have less time with their patients
- They are more reliant on pharmaceuticals for their treatments
- The patient and physician expect a “pill” transaction.

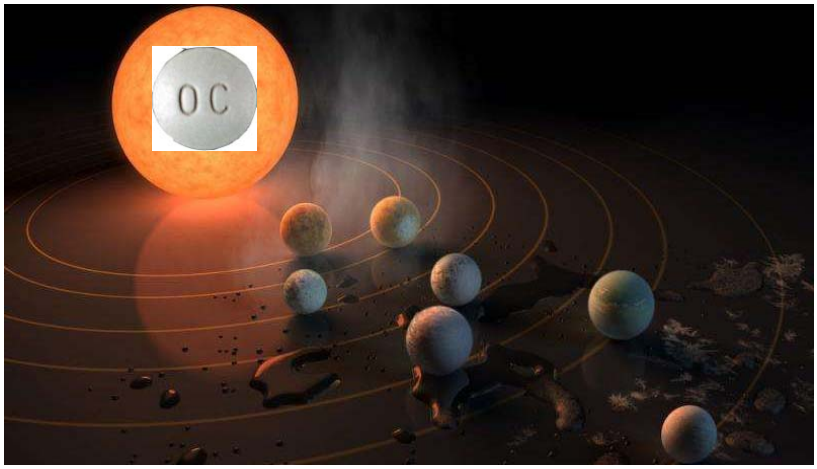
We were told that we needed to be more “compassionate” in the treatment of chronic pain.



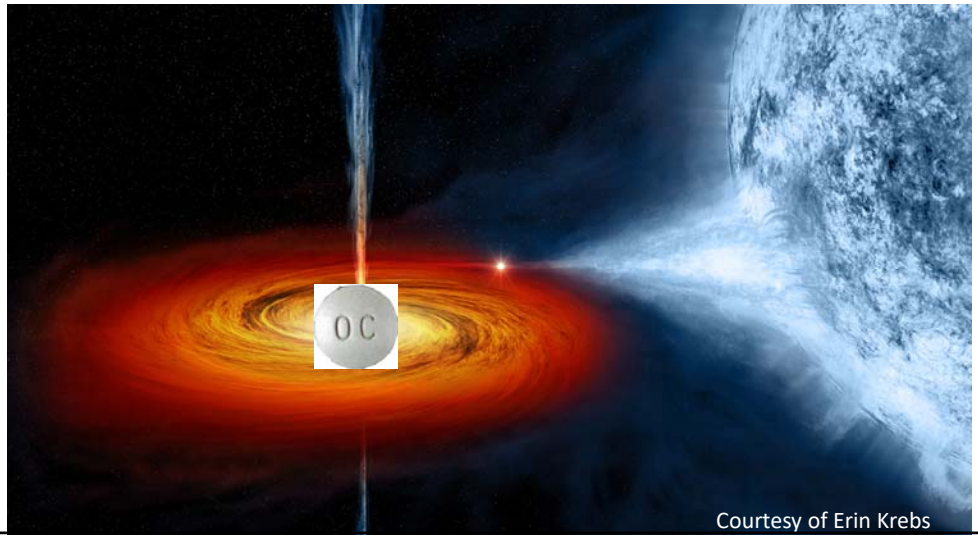


29

Opioids became the center of our pain management universe

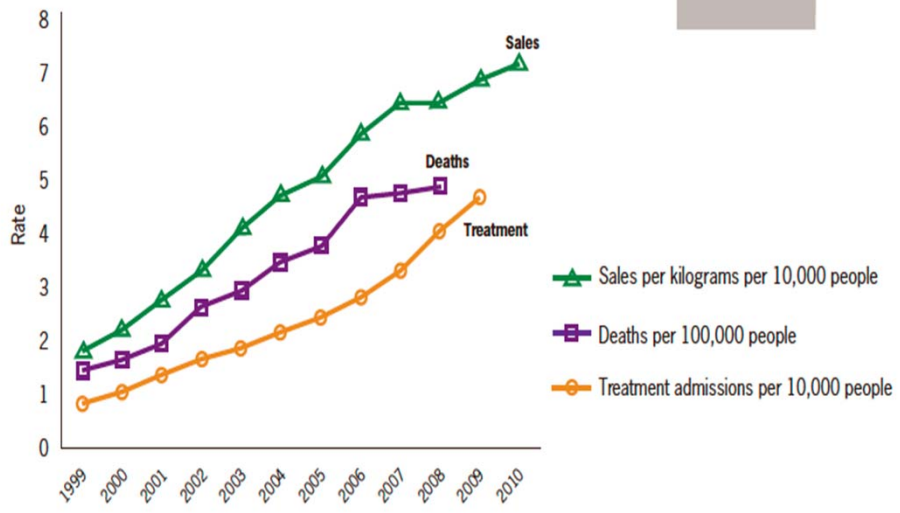


It became a black hole, sucking all other treatment modalities out of existence



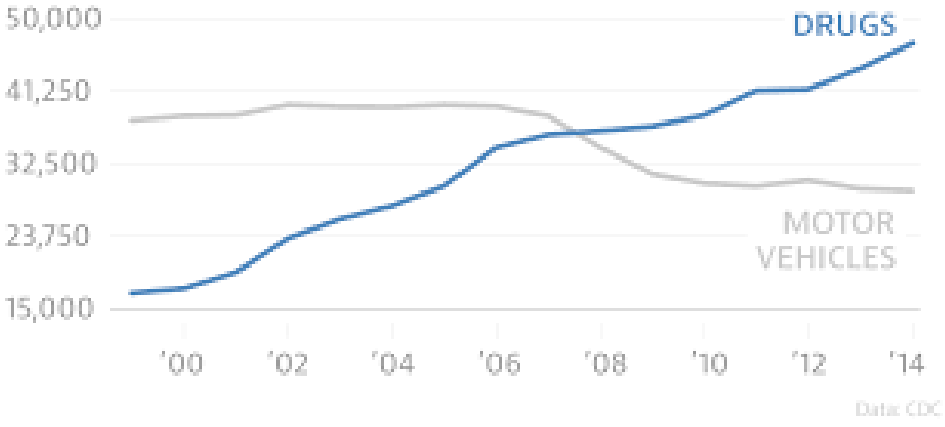
And it became a moral imperative to use opioids to relieve suffering

Rates of prescription painkiller sales, deaths and substance abuse treatment admissions (1999-2010)

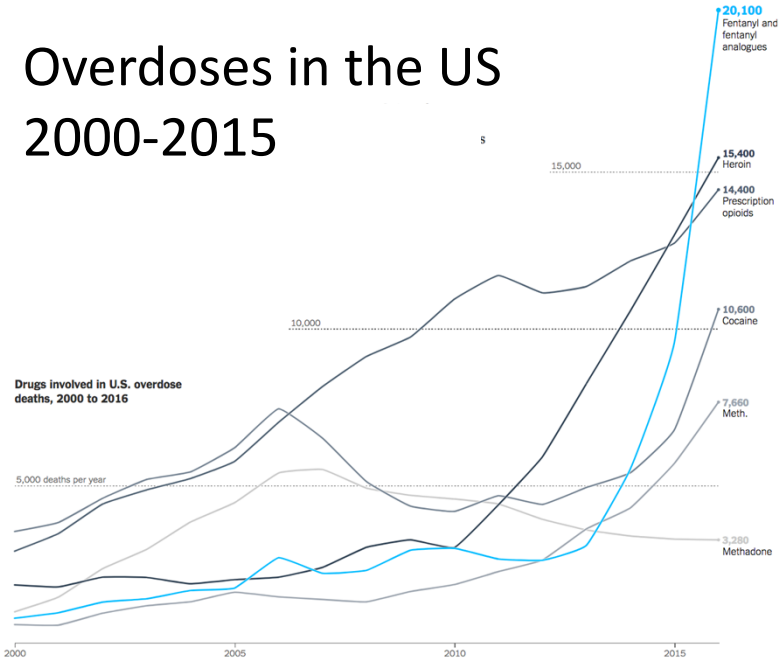


SOURCES: National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 1999-2010; Treatment Episode Data Set, 1999-2009

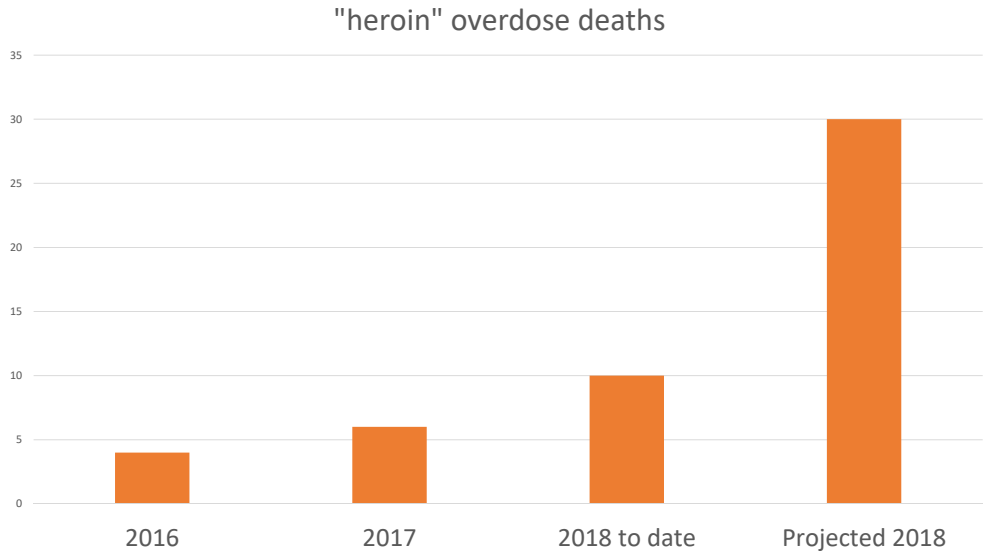
Drug Overdose & Motor Vehicle Accident Deaths



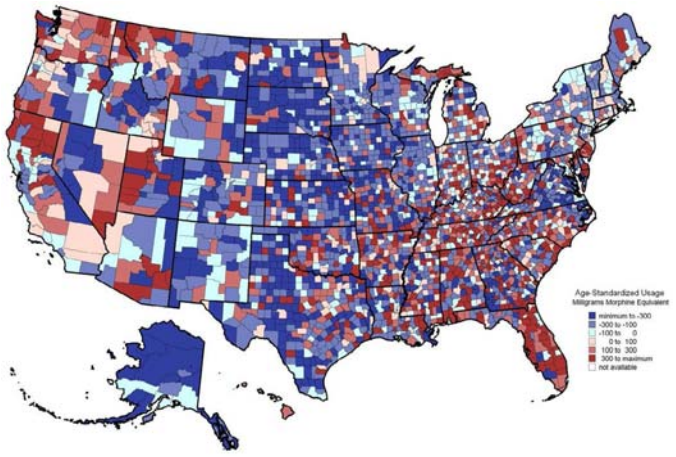
Overdoses in the US 2000-2015



What is happening now in Jackson County



Our prescribing practices are extremely inconsistent

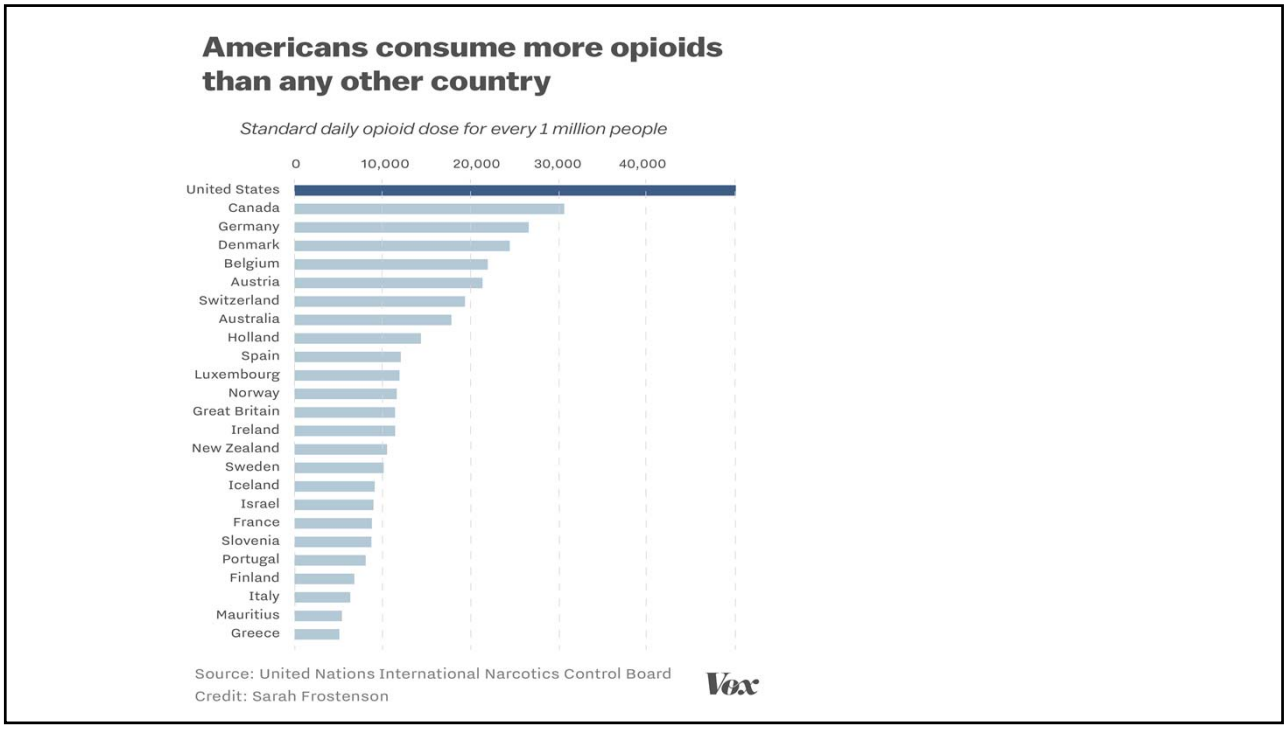


J Pain: Oct 13, 2012

Inconsistencies

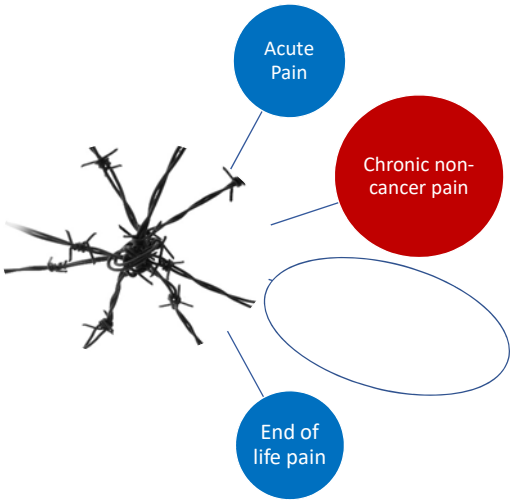
- Medicaid clients are prescribed opioids at twice the rate as non Medicaid clients[1]
- Their rate of overdose is 6X that of non-Medicaid patients[1]
- Individuals with high ACES scores (Adverse Childhood Events) are prescribed opioids at consistently higher rates

1. Mack K, Zhang K, Paulozzi L, Jones C. Prescription practices involving opioid analgesics among Americans with Medicaid, 2010 J Healthcare involving opioid analgesics among Americans with Medicaid, 2010. J healthcare Poor Underserved. 2015;26(1)


Americans consume more opioids than any other country
Standard daily opioid dose for every 1 million people
0
10,000
20,000
30,000
40,000
United States
Canada
Germany
Denmark
Belgium
Austria
Switzerland
Australia
Holland
Spain
Luxembourg
Norway
Great Britain
Ireland
New Zealand
Sweden
Iceland
Israel
France
Slovenia
Portugal
Finland
Italy
Mauritius
Greece
Source: United Nations International Narcotics Control Board
Credit: Sarah Frostenson
Vox


Pain

Pain Can Be Divided Into 3 Classes



Oregon Health Authority

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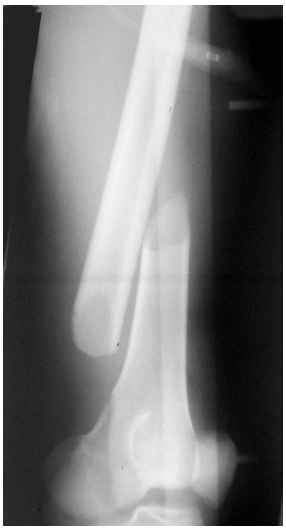
ACUTE PAIN



- Due to injury or surgery
- Tissue damage stimulates the pain
- Nature usually will heal the problem
- Alleviating the pain is the short term goal, followed by return of function

CHRONIC PAIN

- Poor correlation to pathology
- Greatly influenced by emotional overlay
- Management and functional improvement are the goals
- We cannot eliminate the pain

CANCER and END OF LIFE PAIN

- Shares many features of acute pain
- Demands prompt, effective intervention
- The goal is to provide comfort

We do need to provide compassionate care to those with certain painful conditions

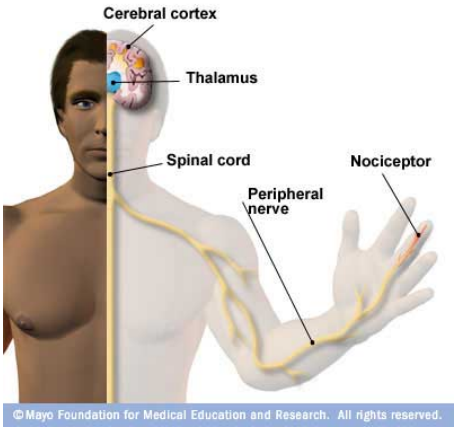
We don't want to throw the baby out with the bathwater

Opioids have a role to play

- In the treatment of acute and post surgical pain
- In cancer and other deteriorating painful conditions
- In some chronic conditions, when utilized at safe doses

How we used to think about pain

Nociceptive or injury related pain

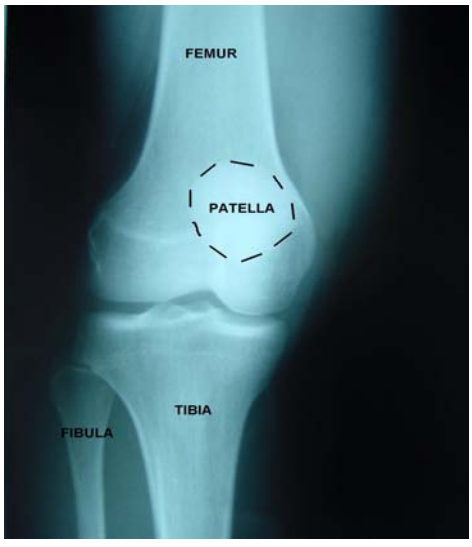


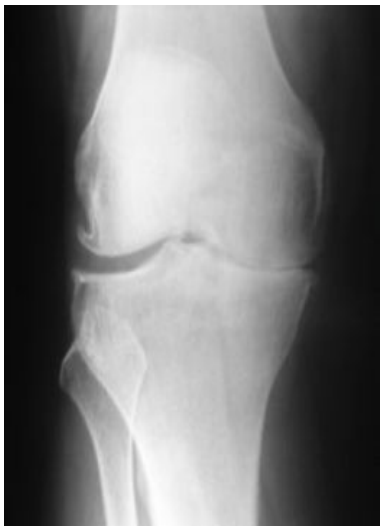
neuropathic or "nerve pain"

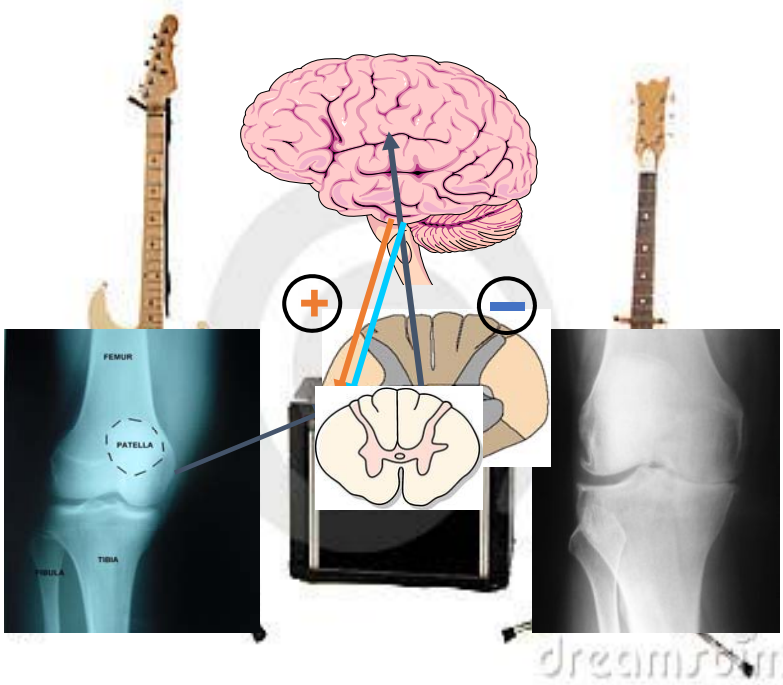
2017: More expansive view of pain

	Nociceptive	Neuropathic	Centralized
Cause	Inflammation or damage	Nerve damage or entrapment	CNS or systemic problem
Clinical features	Pain is well localized, consistent effect of activity on pain	Follows distribution of peripheral nerves (i.e. dermatome or stocking/glove), episodic, lancinating, numbness, tingling	Pain is widespread and accompanied by fatigue, sleep, memory and/or mood difficulties as well as history of previous pain elsewhere in body
Screening tools		PainDETECT	Body map or FM Survey
Treatment	NSAIDs, injections, surgery, ? opioids	Local treatments aimed at nerve (surgery, injections, topical) or CNS-acting drugs	CNS-acting drugs, non-pharmacological therapies
Classic examples	Osteoarthritis Autoimmune disorders Cancer pain	Diabetic painful neuropathy Post-herpetic neuralgia Sciatica, carpal tunnel syndrome	Fibromyalgia Functional GI disorders Temporomandibular disorder Tension headache Interstitial cystitis, bladder pain syndrome

Which person has pain?







CHRONIC PAIN TREATMENT
"COMPARATIVE EFFECTIVENESS"

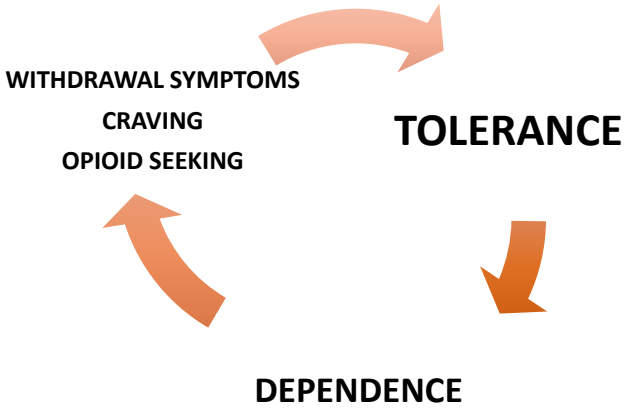
Extrapolated averages of reduction in *Pain Intensity*

Opioids:	≤ 30%
Tricyclics/SNRIs:	30%
Anticonvulsants:	30%
Acupuncture:	≥ 10⁺%
Cannabis:	10-30%
CBT/Mindfulness:	*≥ 30-50%*
Graded Exercise Therapy:	*variable*
Sleep restoration:	*≥ 40%*
Hypnosis, Manipulations, Yoga:	*"+ effect"*

Turk, D. et al. Lancet 2011; Davies KA, et al. Rheum. 2008; Kroenke K. et al. Gen Hosp Psych. 2009; Morley S Pain 2011; Moore R, et al. Cochrane 2012; Elkins G, et al. Int J Clin Exp Hypnosis 2007.

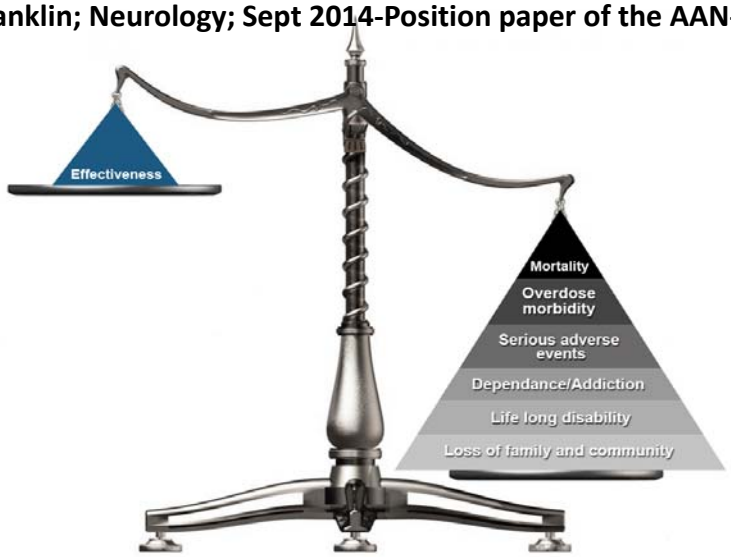
UW Medicine
PAIN MEDICINE

Dose Escalation with Opioid Use



Risk/Benefit of Opioids for Chronic Non-Cancer Pain

-Franklin; Neurology; Sept 2014-Position paper of the AAN-



We have assumed that we are being compassionate by prescribing opioids for chronic pain. But are we?

- Pharmaceutical industry influence
- Flimsy scientific evidence
- Chronic pain treatment concepts inappropriately based on acute pain
- New information suggests non opioid modalities safer and more effective
- Worsening of pain with chronic opioids is common

- HURT AND HARM ARE NOT SYNONYMS

- "No pain…no gain"

Guidelines give us “external” courage

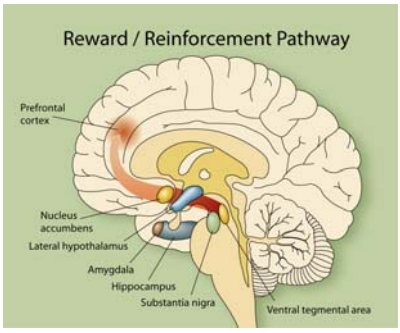
"Tell your wife that the X-ray shows that you do have a backbone."

CDC/OPG/OHA guidelines

1. Begin with non-pharmacologic/non-opioid Rx
2. Establish treatment goals
3. Weigh risks and benefits
4. IR to start
5. Keep dose low
6. Limit amounts for acute pain
7. Episodic risk/benefit discussions
8. Co-prescribe naloxone
9. PDMP
10. UDS
11. Don’t mix with benzos
12. MAT when necessary

Opioid Use Disorder

- Think of it as a chronic disease
- Taking the opioid in larger amounts and for longer than intended
- Wanting to cut down or quit but not being able to do it
- Spending a lot of time obtaining the opioid
- Craving or a strong desire to use opioids



Addiction: 5Cs

- **C**hronic
- **C**ompulsive use
- **C**ontrol—impaired
- **C**raving
- **C**ontinued use despite harm

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Addiction is not Dependence

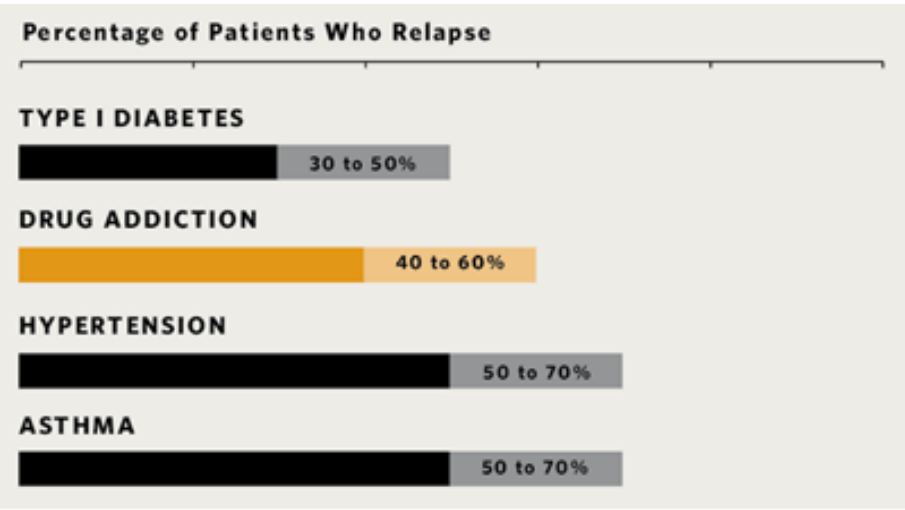
- If the definition of addiction was that you needed a drug to avoid being physically ill, then Prozac would qualify as an addictive drug and cocaine would not.
- The root problem with addiction is ***craving,*** driving compulsion to use drugs despite the harm they cause.

Opioid Use Disorder is a Chronic Disease

- Illness not moral failing
- Life long
- Treatable
- Compare with asthma or diabetes

Factor	Type II Diabetes	Opioid Use Disorder
Individual	Genetic susceptibility	Genetic Susceptibility
Social	Mother's prenatal diet Home food options On-going diet choices Friends and Family	Family exposure to substances ACEs
Curable vs Treatable	Treatable>curable	Treatable>curable
Environment		Neighborhood substance availability
Chronic vs Short term	Chronic	Chronic
Medication is standard of care	Yes	Yes
Relapses	Yes	Yes

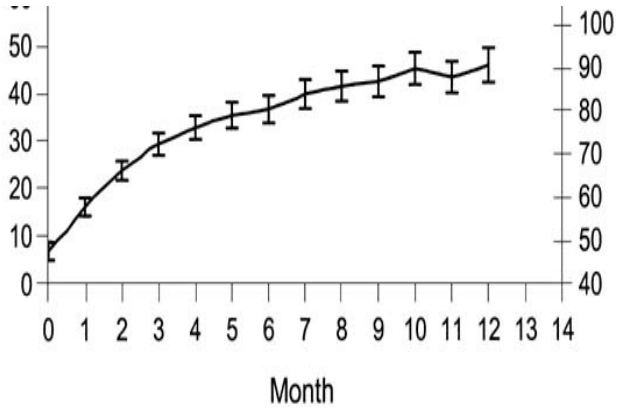
OUD is a Chronic Disease



	Genetic factors	Environ Factors	Chronic	Various Meds
	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes

https://www.drugabuse.gov/publications/media-guide/science-drug-abuse-addiction-basics

Problem 2: Higher opioid dose needed over time for same effect



Dose of Fentanyl

Miligan et al Evaluation of long-term efficacy and safety of transdermal fentanyl in the treatment of chronic noncancer pain
The Journal of Pain, Volume 2, Issue 4, August 2001, Pages 197-204

Problem 3, Chronic Use causes Physical Dependence; Halting Drug causes Withdrawal, an Illness

https://opiateaddictionsupport.com/heroin-withdrawal-symptoms/

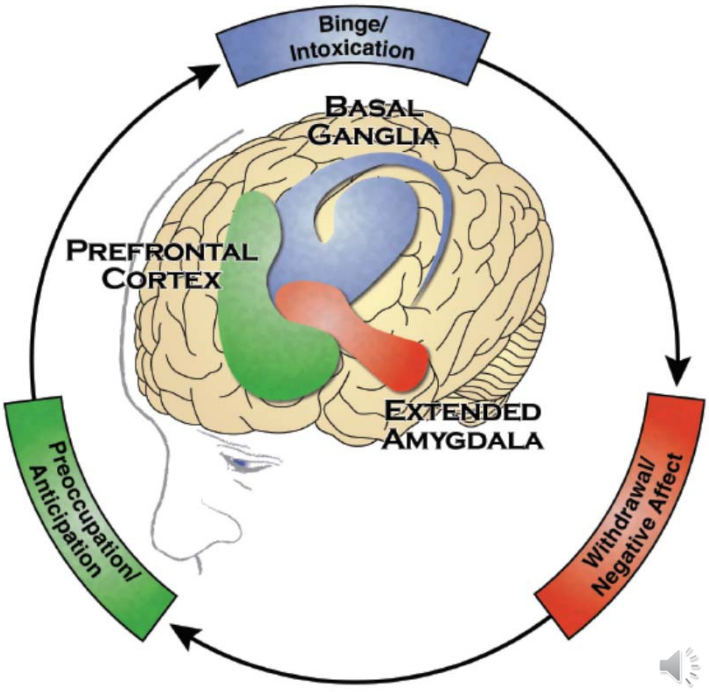
Mood Swings
Anxiety
Shakes, Chills, Sweats
Tears, Runny Nose
Bone Pain
Vomiting
Diarrhea
3-7 day duration

Problem 4,
The Opioid Use Disorder Cycle,
The Primitive Brain in Charge

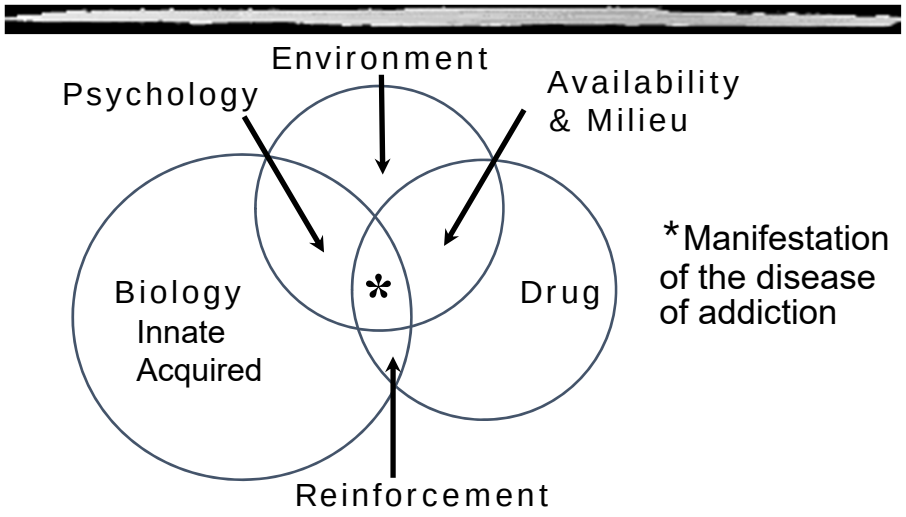
The addiction cycle is triggered by intoxication and pleasure (blue)

When intoxication wears off, the Individual feels worse (red)

More substances are sought(green) to relieve distress, the cycle continues



Addiction:
A Multi-factorial Disease State



We must de-stigmatize this condition

- Terms we need to avoid: Get clean, dirty urine, drug abuse.
- The opioid epidemic in the US today is largely an iatrogenic (physician caused) condition, and healthcare professionals must humbly and safely offer treatment to patients.

Reducing risks and providing treatment for OUD

- Risk reduction: Syringe exchange, Safe injection sites, providing basic fundamentals for a quality of living (housing, employment, etc).
- Medication Assisted Treatment (MAT): Buprenorphine (Suboxone), methadone, sustained release naltrexone (Vivitrol)
- 12 Step and other abstinence based treatments (providing community and personal responsibility)

Medication Assisted Treatment MAT

Perhaps it's time to change the name to Medication Assisted Recovery

I'll tell you why

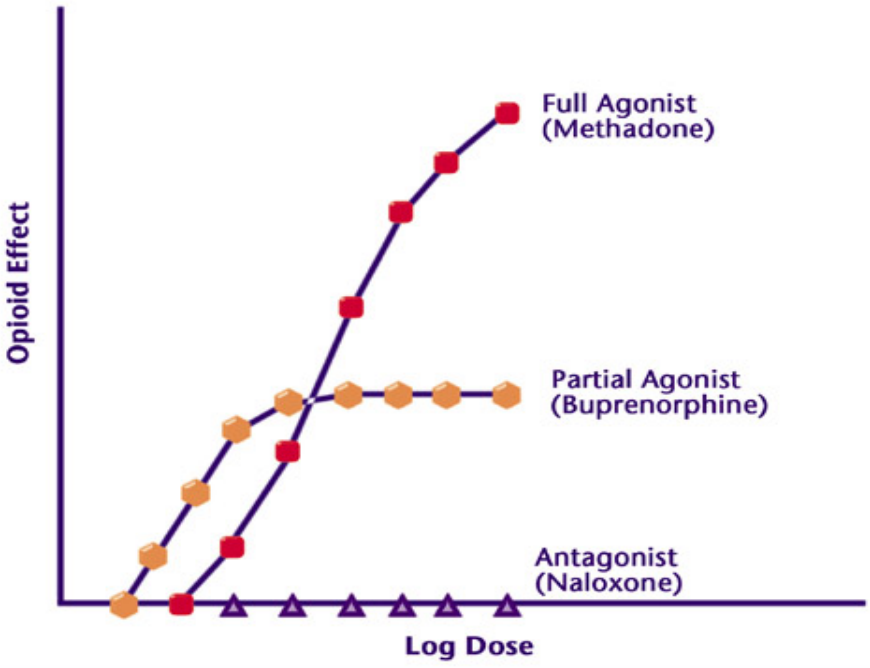
Medication Assisted Recovery

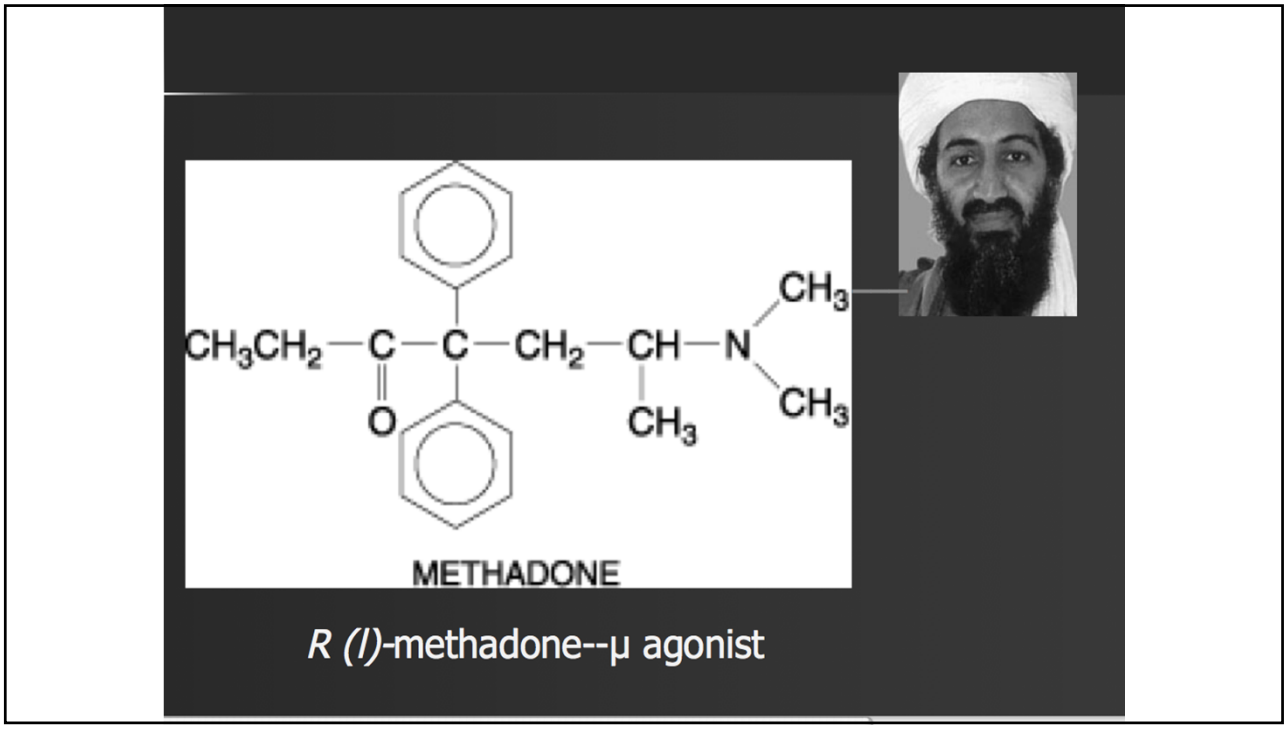
- Methadone: Has a 50+ year track record. Reduces health risks, morbidity and mortality. "Harm reduction" but also genuinely keeps many from using any illicit drugs. Has overdose risk and is very inexpensive.
- Buprenorphine (Suboxone): A very safe drug. Relieves cravings, like methadone, offers pain relief, quite expensive. Can be prescribed for addiction in a provider's office (unlike methadone).
- Naloxone injectable (Vivitrol): Can only be used when an individual is opioid free. More limited utility. Very expensive

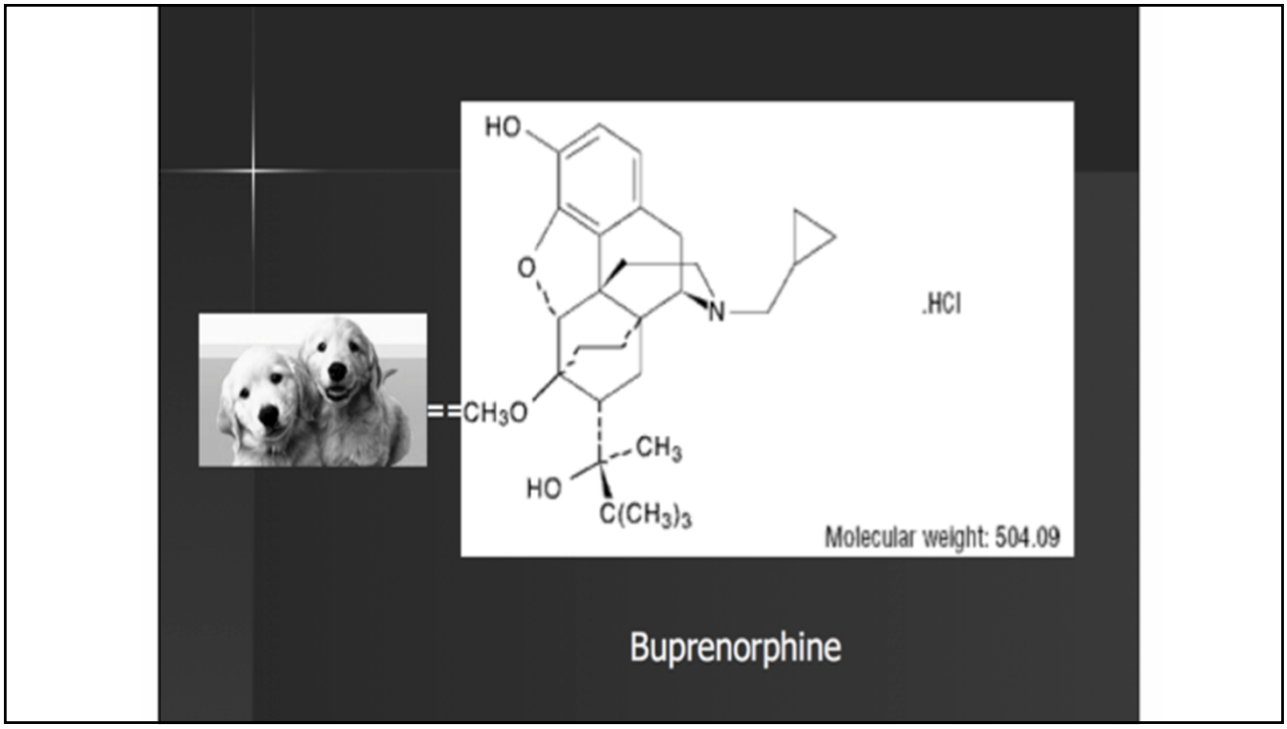
Buprenorphine + naloxone (Suboxone)

What is Buprenorphine?

- A very long lasting synthetic opioid
- It has a high affinity (attaches very strongly) for the pain receptors in the brain.
- It is a sublingual drug
- When buprenorphine (Subutex) is combined with naloxone (to discourage IV use) = Suboxone. Buprenorphine without naloxone is recommended in pregnancy.
- Can be prescribed in an office setting by prescribers with special training
- Fills the receptor site but has a partial opioid effect



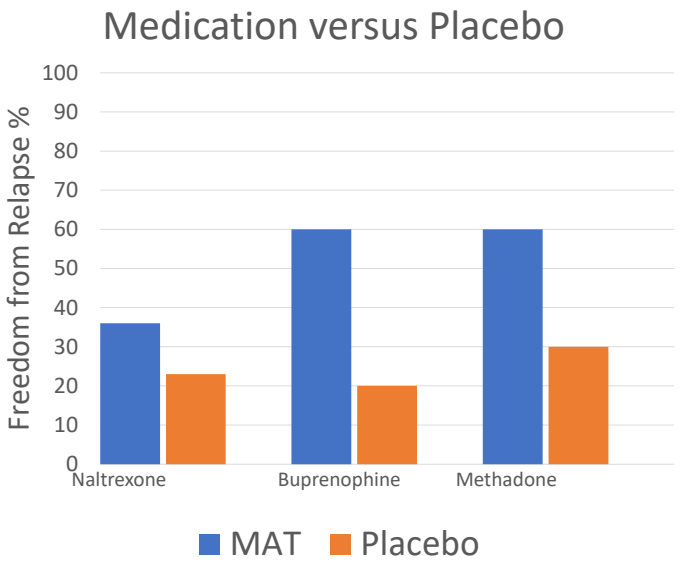

CH3CH2
C
C
CH2
CH
N
CH3
CH3
CH3
O
METHADONE
R (l)-methadone--μ agonist


HO
O
N
.HCl
CH3O
CH3
HO
C(CH3)3
Molecular weight: 504.09
Buprenorphine

MAR is not substituting one drug from another

- The pattern of taking the same dose at the same time every day means there is no high or intoxication. The drug is not reinforcing.
- With MAR, addiction (obsessive craving) is replaced by physical dependence only. This is similar to the role of antidepressants or insulin.
- When a drug's benefit outweighs its risks, continued use is healthy, not addictive.

Everyone Needs to Know that Medication Aids Recovery



Connery, Harvard review of psychiatry. , 2015, Vol.23(2), p.63-75

What do you call people on MAT who have re-engaged with their families, are re-employed, and regain control of their lives?

Role Models!

Opioids and pregnancy

Principles of Medication Assisted Treatment in Pregnancy

- Avoiding erratic maternal opioid blood levels and protecting the fetus from repeated episodes of withdrawal
- Decreasing risks to the fetus of infections from HIV, Hepatitis, Sepsis, and STIs.
- Reducing the incidence of Obstetrical and fetal complications.

MAT in pregnancy, summary:

- It is the treatment of choice for opioid dependent pregnant women.
- Lowers risk of concurrent disease for the mother
- Serum blood levels hard to predict based on dose of drug
- Neonatal abstinence may be independent of dose for MTD, and lowered for buprenorphine
- Higher dose protects against illicit drug use

NEJM 12/10 & Addiction Medicine 10/10

- **NIH: Babies of addicted moms do better when taking methadone or buprenorphine**

  - "buprenorphine was found to be superior to methadone in reducing withdrawal symptoms in the newborns"
  - "This study found that, compared to methadone, buprenorphine resulted in similar maternal and fetal outcomes, yet had lower severity of NAS symptoms, thus requiring less medication (1.1 versus 10.4 milligrams) and less time in the hospital for their babies (10 versus 17.5 days). "

What about tapering from illicit drug use to sobriety during pregnancy?

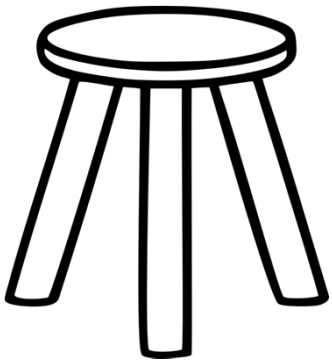
- Difficult to do safely
- Risk of relapse is high
- Puts the fetus at risk

Breastfeeding

- Buprenorphine passes into breast milk at a plasma to milk ratio of 1:1. The infant will be exposed to 1/5 – 1/10 of the total buprenorphine available
- "…it is the consensus of the panel that any effects of [buprenorphine] on the breastfed infant would be minimal and that breastfeeding is not contraindicated." *SAMHSA, 2004*
- Concentrations of methadone in breast milk were low (range: 21.0–462.0 ng/mL) and not related to maternal dose
- Results contribute to the recommendation of breastfeeding for methadone-maintained women. *AAP 2007*

Integrated Components of Successful OUD Treatment

- Medication to break the intoxication-withdrawal-craving cycle
- A Safe Place to Call Home
- Living Wage Employment
- Meaningful Relationships
- Behavioral Therapy



Opioid Misuse: Risk Factors

Fixed	Changeable
• Male> Female • Youth> Older Adult • Genetic Variants • Dopamine, GABA, serotonin, opioid receptors, enzymes, transporters	• Education • Poverty • Length of exposure to opioids • Adverse Childhood Experiences

Opioid Misuse: Risk Factors

Fixed	Changeable
• Male> Female • Youth> Older Adult • Genetic Variants • Dopamine, GABA, serotonin, opioid receptors, enzymes, transporters	• Education • Poverty • Length of exposure to opioids • Adverse Childhood Experiences

Opioid Crisis

Causes

- Abundant, cheap opioids
- Human susceptibility
- A small overdose can kill
- Opioid Use Disorder (OUD) is a chronic, relapsing disease
- Poverty, genetics and adverse childhood experiences (ACEs) underlie OUD

Opioid Crisis

Causes

- Human susceptibility
- Poverty, mental illness, genetics and adverse childhood experiences (ACEs) underlie OUD
- Opioids are abundant and cheap
- A small overdose can kill
- Opioid Use Disorder (OUD) is a chronic, relapsing disease

Consequences

- Suffering: Individual, families, intergenerational, community
- Business: Lost productivity
- Costs: Healthcare, social service, law enforcement
- Justice system overload
- Community livability
- Urgent need for effective treatment and prevention

"I'm afraid you've had a paradigm shift."

The Paradigm Shift