The Opioid Epidemic

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Objectives

- Look at what the opioid epidemic is and how we got here
- Understand the basics of what is now understood about addiction
- Take a high level view of the efforts going on in Washington State to help with this crisis
- Gain some empathy for our patients struggling with addiction
- Better understand the role we're helping play in the opioid crisis inside and outside our jobs

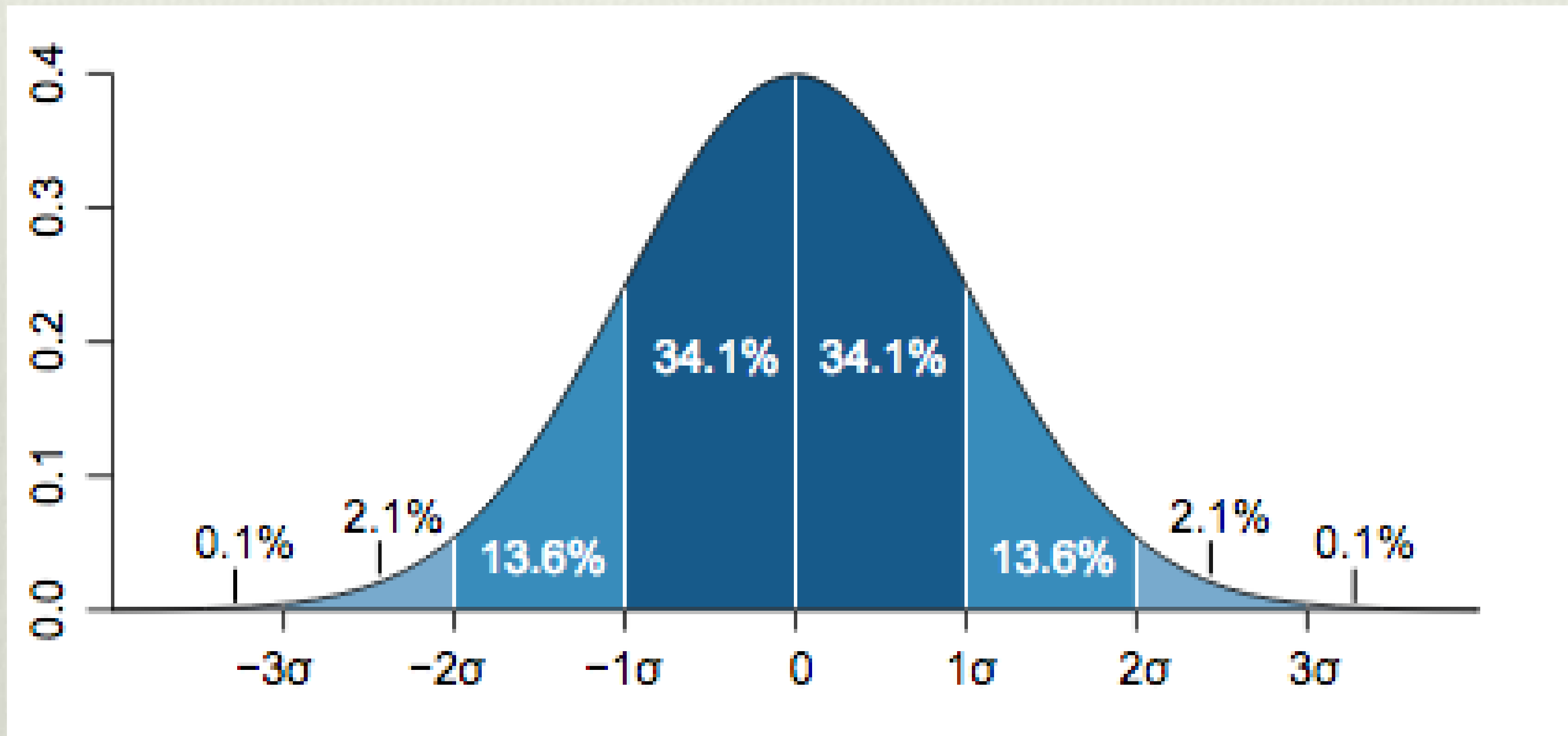
What are opiates?

- Morphine or morphine-like derivatives
- Can be raw, manufactured and/or synthetic
  - Oxycontin, Vicodin, Duragesic, MS Contin, Dilaudid, Suboxone, Methadone
- Raw Forms
  - Codeine, Morphine —> (refined) Diacetlymorphine(Heroin)
- Controlled substances (Over)used for treatment of pain, misused/abused and used as recreational drugs

What is pain?

- Pain is "what the patient says it is"
- Nociception: Central nervous system's response to noxious stimuli which are either actually tissue damaging, or potentially tissue damaging
- You have to have a brain to have pain
- Pain is good, tells us to not do that again
- Pain is blunted by natural chemicals "endogenous opioids"

The Bell-Shaped Curve



- Biological and Statistical Phenomenon
- Intelligence, Height, Weight, Pain Tolerance, Addiction Potential

Treatment Benefit
Net Benefit
more
Treatment Harm
Net Harm
less
Severe
Mild
Spectrum of Baseline Risk
severe hypertension
borderline hypertension

How do opiates work?

- Ligands (drug chemicals) bind to an already existing receptor in the body. Drugs only modify existing physiological pathways
- Opiates bind to several different types of receptors, primarily in the central nervous system
- Most notably the mu-receptor of which the endogenous ligand is Beta-endorphin and Enkephalins (opioids)
- Other receptors include Kappa and Delta receptors with significant "cross-talk" between all
- Pain signaling pathways are still not fully understood
    - Each opioid has a unique collective activity on these receptors

Beta-Endorphins

- Neuropeptides involved in pain management and natural reward circuits such as feeding, drinking, exercise, sex (morphine-like effects)

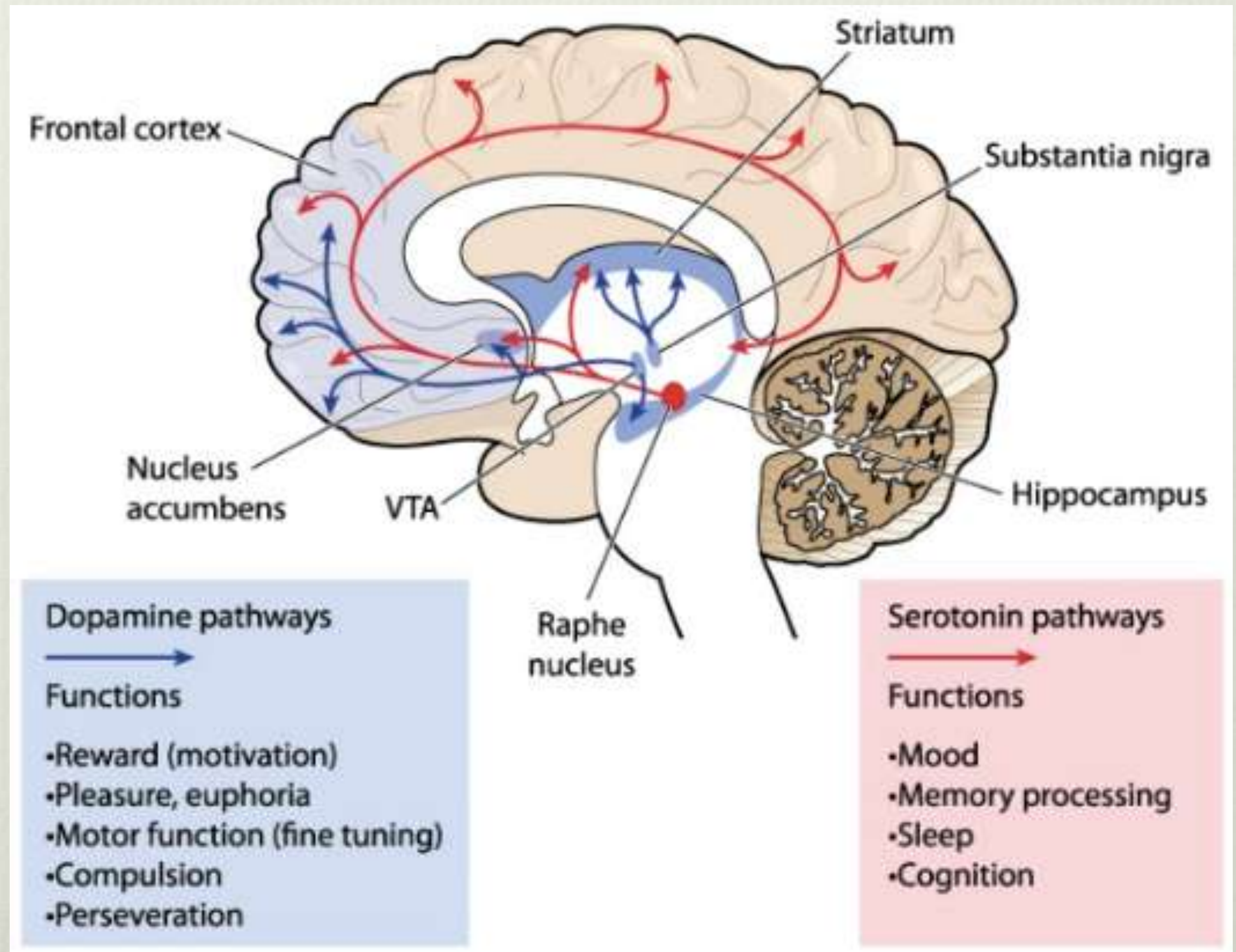
- Peripheral Activity
  - Presynaptic binding results in inhibition of the release of tachykinins, namely substance P, a key protein involved in pain transmission

- Central Nervous System:
  - Binding inhibits the release of GABA which ultimately results in excess production of dopamine. Dopamine is associated with pleasure and reward

- https://www.youtube.com/watch?v=NDVV_M__CSI

Dopamine Pathway

The reward center of the brain is meant to reinforce positive experiences so that you'll engage in those activities again. Eating, sex, exercise



Addiction

- Complex condition characterized by compulsive substance use despite known harmful consequences
- The defining public health issue of our time- Vivek Murthy
- Customarily stigmatized as moral failure
- Now known as a chronic relapsing disease of the brain
- Adaptations to the central nervous system occur after repeated exposure to certain chemicals
    - Alcohol, marijuana, PCP, inhalants, opioids, sedatives, cocaine, methamphetamine, tobacco
- Drugs effectively hijack and usurp the brains neurobiology, taking over essential neural pathways that allow the pursuit of a safe and satisfying life

- https://www.drugabuse.gov/publications/drugfacts/heroin
- https://www.facingaddiction.org/surgeon-general-report?gclid=CjwKCAjws6jVBRBZEiwAkIfZ2mwQyZCstPeAZz_XHE-40cZs6VKasQ7TwgtJfVnjr3AeffoL8TVAaBoCmsIQAvD_BwE

Addiction

- Frontal cortex: Damaged over time. This area of the brain involved in judgment and controlling our emotions and desires. Allows us to change behaviors in response to changing environment. If you're very hungry, the value of food is very high, but as you eat food, the value of the food goes down and your body needs to be able to focus on other things.

- People admit the inability to stop using a substance even when the substance no longer even gives them pleasure

- Can a brain recover from addiction? Yes, but it can take months to years and even after long periods of time the brain's circuitry still exhibits abnormal firing

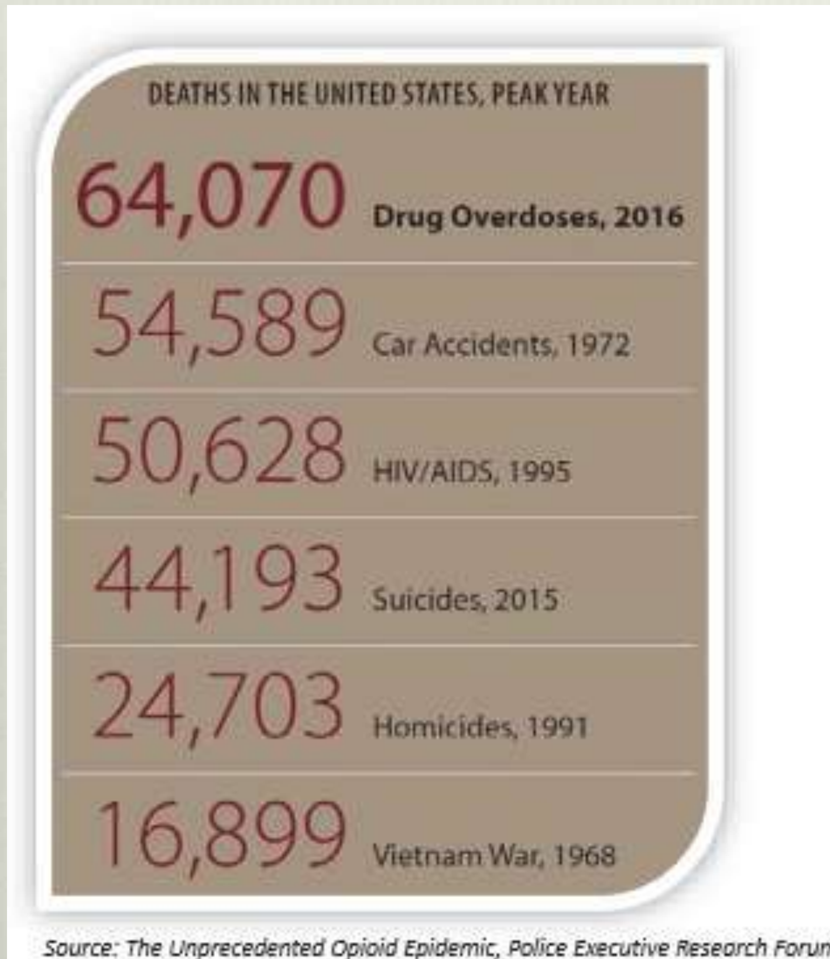
What is the Opioid Epidemic?

- The Epidemic Numbers
  - 1 in 4 receiving long-term opioid therapy (in primary care) struggle with opioid addiction
  - 300% increase in opioid prescription sales since 1999- without overall change in reported pain
  - Over 249,000,000 prescriptions written for opioids in 2013. This is enough for every adult in America to have a bottle
  - U.S. constitutes 5% of the worlds population and consumes 80% of the worlds opioids
  - Nearly 80 percent of Americans using heroin (including those in treatment) reported misusing prescription opioids first

Unlike Other Epidemics

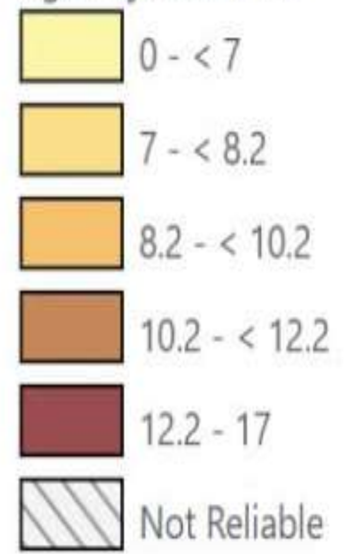
- Effects Rural Communities (Hillbilly Heroin)
- Iatrogenesis, Greek “brought forth by the healer”
  - Refers to any effect on a person, resulting from any activity of one or more persons acting as healthcare professionals or promoting products or services as beneficial to health, that does not support a goal of the person affected.
- Paid for by the Government and insurance providers

Drug Overdoses



- More than motor vehicle deaths
- Greatest killer of people aged < 50
- Decreased overall life expectancy in the U.S.
- 2017 data also shows >60,000 Americans died from drug overdose
- 142 Americans dying every day
- Death toll equal to Sept. 11th every 3 weeks

Fatal Overdoses - All Opioids



Source: Washington Tracking Network, Washington Department of Health
Time Period: 2011-2015 (not specific to Medicaid only)

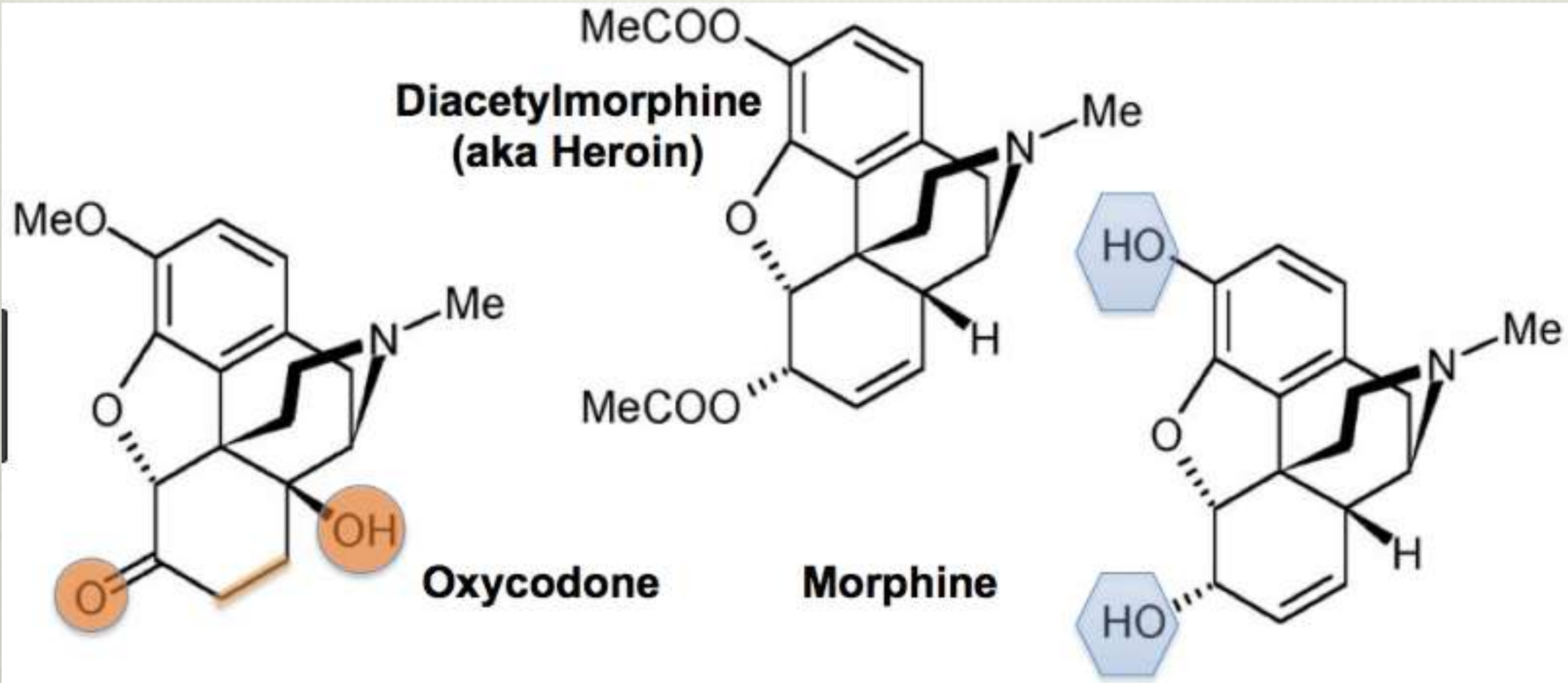
North Central Accountable Community of Health

OxyContin

- Purdue Pharmaceuticals
- In 2001, spent $200 million marketing Oxycontin
- American Pain Society: Pain the fifth vital sign, paid speakers
- People were taught that if you prescribed opioids to someone who had real pain, they could not become addicted. This is untrue
- In 2002, sales were at the $1.5 billion mark
- In 2012, OxyContin represented ~30% of painkiller market
- Can be snorted, smoked, injected, ingested
- Purdue sued for misbranding the abuse potential of the drug. Pleaded guilty in 2007 and paid over $600 million in fines
- States now suing drug manufacturers. Will this give money back to states to fight the epidemic?

Art Van Zee. The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy. Am J Public health. 2009; 99(2): 221-227

Opioid Molecular Structure



Do Opiates Work for Treating Pain?

- Acute Pain: Yes
- Chronic Pain: Questionable efficacy compared to other readily available conventional therapies and/or nontraditional therapies
- Cancer-Related and End-of-Life: Yes

Original Investigation

March 6, 2018

Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain

The SPACE Randomized Clinical Trial

Erin E. Krebs, MD, MPH[1,2]; Amy Gravely, MA[1]; Sean Nugent, BA[1]; et al

» Author Affiliations

JAMA. 2018;319(9):872-882. doi:10.1001/jama.2018.0899

SPACE Trial

For the opioid group:

- The first step was immediate-release morphine, hydrocodone/acetaminophen, or immediate-release oxycodone
- The second step was sustained-action morphine or sustained-action oxycodone
- The third step was transdermal fentanyl.

For the non-opioid group:

- The first step was acetaminophen (the generic version of Tylenol) or a nonsteroidal anti-inflammatory drug
- The second step was adjuvant oral medications—such as nortriptyline, amitriptyline, or gabapentin—and topical analgesics, such as capsaicin or lidocaine
- The third step was pregabalin, duloxetine, and tramadol

SPACE Trial Cont.

- No difference in pain scores
- VA patients
- mostly male (87%), mostly white (86%) average age of 58
- ~2/3 chronic back pain, 1/3 hip or knee osteoarthritis pain
- Patients had experienced such pain for at least six months, and the pain interfered with their day-to-day activities and quality of life
- Conclusions: Study isn’t representative of country as a whole, but the findings should make us reassess use of opioids as first-line treatment for chronic musculoskeletal pain. Adds to the existing body of literature showing opioids don’t have any advantages in terms of pain relief that may outweigh the known harmful consequences we know them to cause

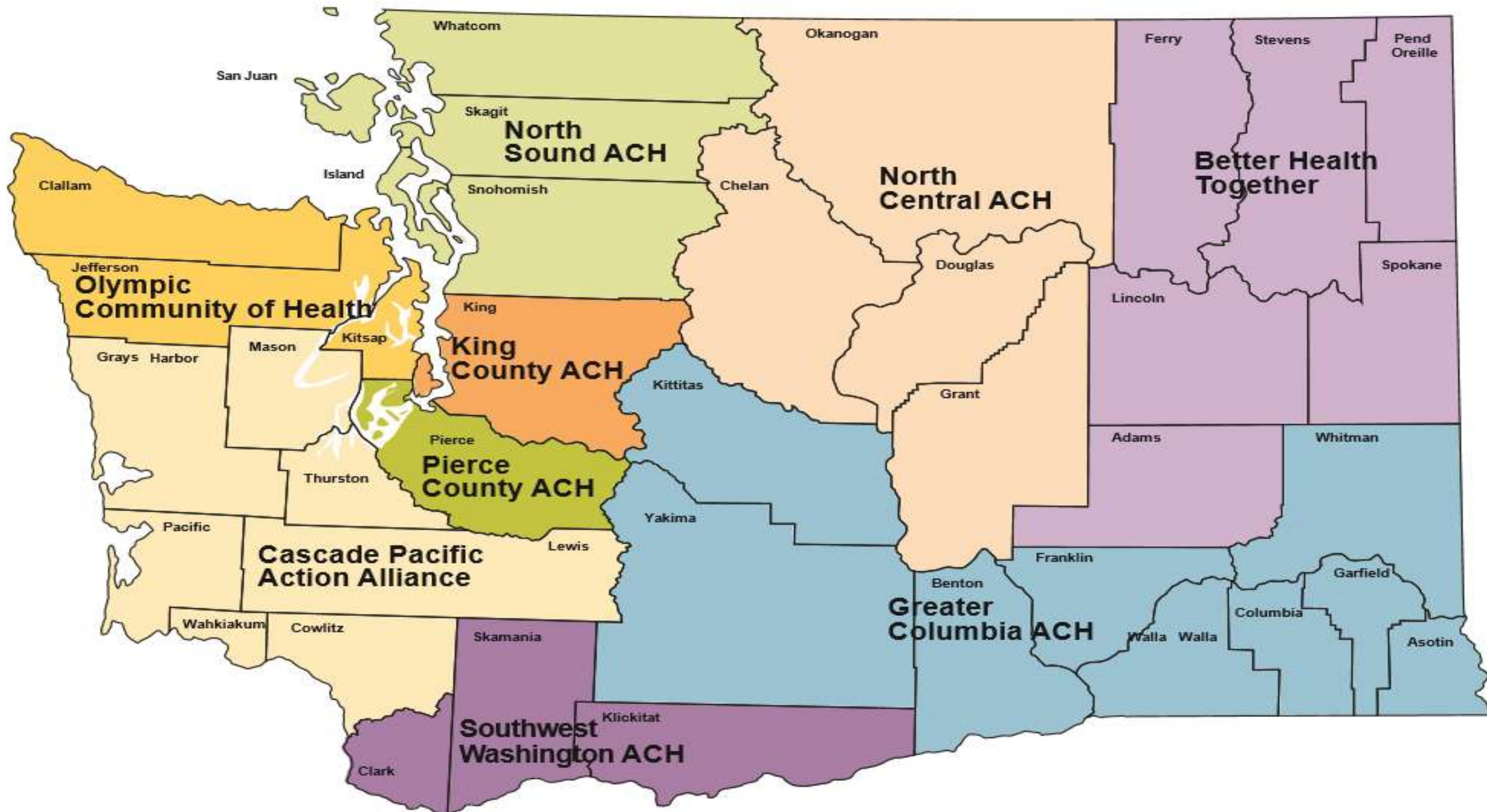
Discussion Question:

How do we fix the opioid epidemic?

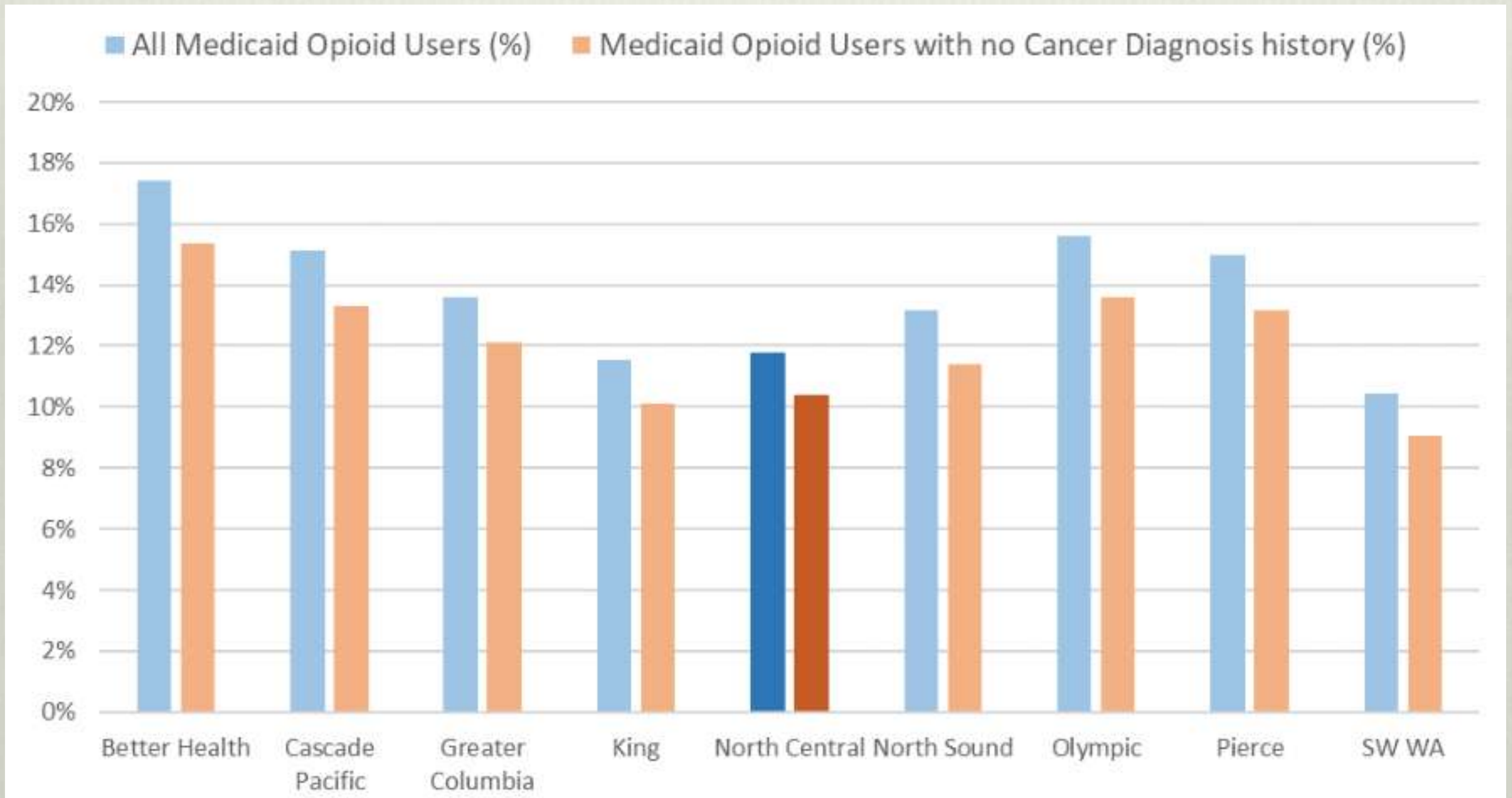
WA State Interagency Opioid Working Plan

- State plan for reducing morbidity and mortality associated with opioid use
- 4 Primary Focus Areas
  - Prevent opioid misuse and abuse
  - Identify and treat opioid use disorders
  - Prevent death from overdose
  - Use data to identify opioid use disorders, monitor morbidity and mortality, evaluate interventions

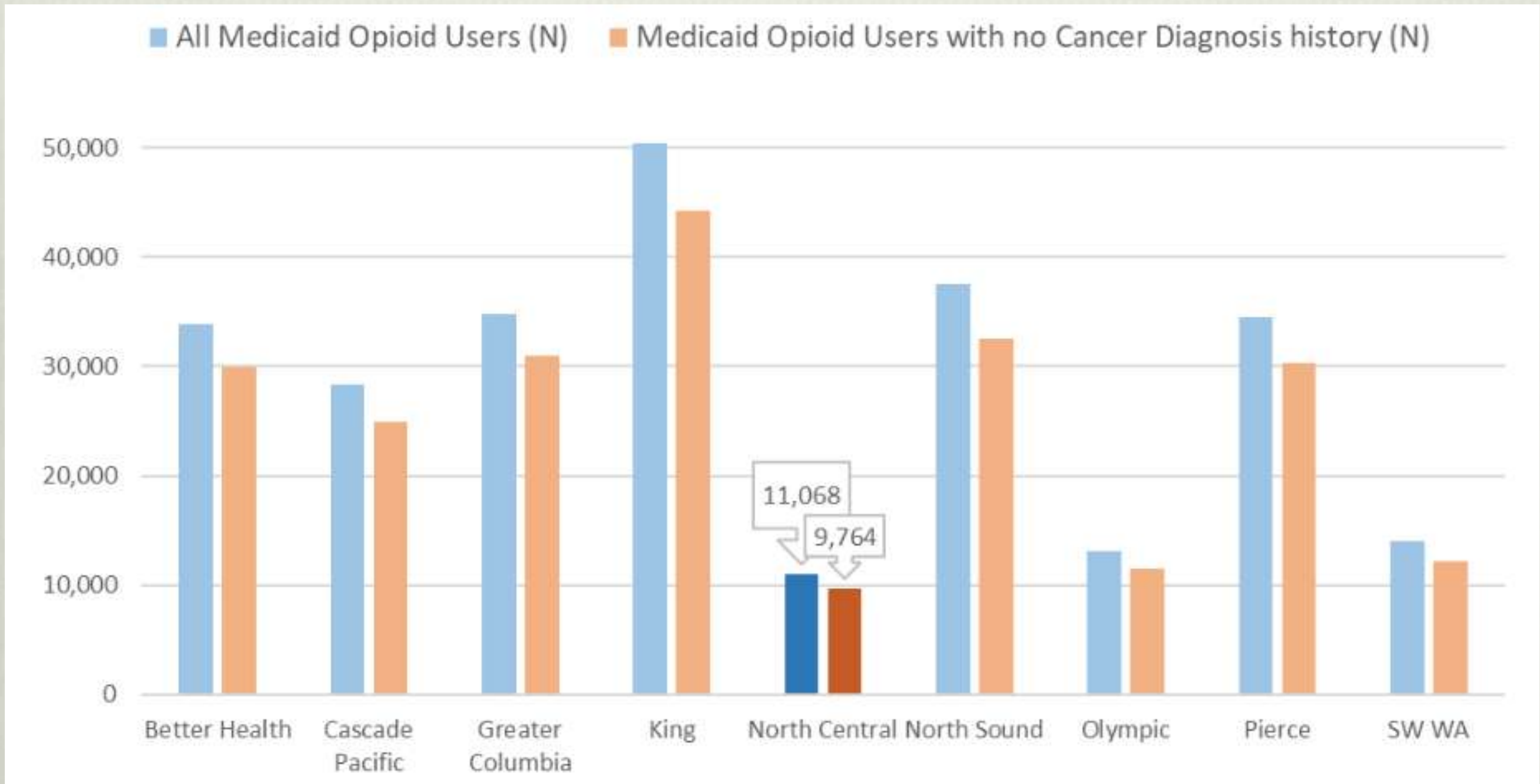
Accountable Communities of Health



Opioid Use Amongst Medicaid Population in Washington



Medicaid Volume



Source: Health Care Authority *Drawn from fiscal year 2016 claims data and ICD coding (Medicaid only population with full medical eligibility)*

Prevent Opioid Misuse/Abuse

- Improve prescribing practices
- Educate health care providers on the 2015 Agency Medical Directors' Group Interagency Guideline for Prescribing Opioids for Pain, the Washington Emergency Department Opioid Prescribing Guidelines and the CDC Guideline for Prescribing Opioids for Chronic Pain to ensure appropriate opioid prescribing.
- Align financial coverage with best practices and include non-opioid pain therapies under coverage
- Limit access to opioids
  - Take back programs
- Identify outlier physicians
- Leverage EMR to default smallest volume of opioids based on procedure type, etc
- Decrease supply of illegal drugs in the state (DEA working on this too)
- Youth education

Trump Poised To Roll Out Opioid Plan On Monday.

NBC News (3/15, Snow) reports President Trump "is set to roll out new plans to tackle the nation's opioid crisis on Monday that are expected to call for tougher penalties, potentially including the death penalty for traffickers." NBC reports Trump is expected "to propose changes in the areas of treatment and recovery for those dependent on opioids, focusing on substance abuse prevention and education efforts."

Politico (3/15, Diamond) reports the "ambitious plan, which the White House has quietly been circulating among political appointees this month, could be announced as soon as Monday" when Trump visits New Hampshire. The latest version of the policy "proposes to change how the government pays for opioid prescriptions" and "calls on Congress to change how Medicaid pays for treatment, seeking to make it easier for patients with addictions to get inpatient care."

Treatment of Opioid Use Disorders

- A small number of patients who want and need treatment are able to receive
- Increase # of providers eligible for prescribing suboxone, methadone, naltrexone
- Build capacity of health care providers to recognize signs of possible opioid misuse, effectively screen for opioid use disorder, and link patients to appropriate treatment resources. (not many docs even ask about abuse/misuse with pt.)
- Increase capacity of syringe exchange programs (SEP) to effectively provide overdose prevention and engage clients in support services, including housing.
- Identify and treat opioid abuse during pregnancy to reduce withdrawal symptoms in newborns

Prevent Deaths From Overdose

- People who overdose once are more likely to overdose again
- Educate individuals who use heroin and/or prescription opioids, and those who may witness an overdose, on how to recognize and appropriately respond to an overdose
- Make system-level improvements to increase availability and use of naloxone
- Naloxone access
  - Pharmacy through CDTA
  - Needle exchange programs
  - Parents
  - EMS programs

Naloxone

- In 2013, more than 80% of naloxone use was for heroin overdose, although there were twice as many deaths from prescription-opioid overdose as from heroin overdose. Several U.S. federal agencies have therefore recommended increasing access to naloxone, particularly for prescription-opioid users.
- Price Hikes- Evzio Two-Dose auto injector. $690 in 2014 —> $4500 in 2016. Call for transparency. Price jumped the month before CDC coprescription guidelines released. Government is promoting naloxone use. What is their responsibility to ensure the drug is affordable?
- Can this be affordable?
  - OTC status, waive new manufacturer application fees? Government contract with a manufacturer to act on their behalf?

Ravi Gupta, B.S, et al. Rising Price of Naloxone- Risks to Effort to Stem Overdose Deaths. N Engl J Med. 2016; 375:2213-2215

Use data and information to detect opioid misuse/abuse, monitor morbidity and mortality, and evaluate interventions

- Improve PMP functionality to document and summarize patient and prescriber patterns to inform clinical decision making
- Utilize the PMP for public health surveillance and evaluation
- Continue and enhance efforts to monitor opioid use and opioid-related morbidity and mortality
- Monitor progress towards goals and strategies and evaluate the effectiveness of our interventions

Vivek Murthy, Surgeon General

Letter From the Surgeon General

Dear Colleague,

I am asking for your help to solve an urgent health crisis facing America: the opioid epidemic. Everywhere I travel, I see communities devastated by opioid overdoses. I meet families too ashamed to seek treatment for addiction. And I will never forget my own patient whose opioid use disorder began with a course of morphine after a routine procedure.

It is important to recognize that we arrived at this place on a path paved with good intentions. Nearly two decades ago, we were encouraged to be more aggressive about treating pain, often without enough training and support to do so safely. This coincided with heavy marketing of opioids to doctors. Many of us were even taught – incorrectly – that opioids are not addictive when prescribed for legitimate pain.

The results have been devastating. Since 1999, opioid overdose deaths have quadrupled and opioid prescriptions have increased markedly – almost enough for every adult in America to have a bottle of pills. Yet the amount of pain reported by Americans has not changed. Now, nearly 2 million people in America have a prescription opioid use disorder, contributing to increased heroin use and the spread of HIV and hepatitis C.

I know solving this problem will not be easy. We often struggle to balance reducing our patients' pain with increasing their risk of opioid addiction. But, as clinicians, we have the unique power to help end this epidemic. As cynical as times may seem, the public still looks to our profession for hope during difficult moments. This is one of those times.

That is why I am asking you to pledge your commitment to turn the tide on the opioid crisis. Please take the pledge. Together, we will build a national movement of clinicians to do three things:

First, we will educate ourselves to treat pain safely and effectively. A good place to start is the Turn the Tide Pocket Guide with the CDC Opioid Prescribing Guideline. Second, we will screen our patients for opioid use disorder and provide or connect them with evidence-based treatment. Third, we can shape how the rest of the country sees addiction by talking about and treating it as a chronic illness, not a moral failing.

Years from now, I want us to look back and know that, in the face of a crisis that threatened our nation, it was our profession that stepped up and led the way. I know we can succeed because health care is more than an occupation to us. It is a calling rooted in empathy, science, and service to humanity. These values unite us. They remain our greatest strength.

Thank you for your leadership.

Vivek H. Murthy, M.D., M.B.A.
19th U.S. Surgeon General

Suboxone

- "Partial opioid agonist" buprenorphine combined with naloxone
  - Less Euphoria
  - Less Respiratory Depression
  - Antagonist at the Kappa receptors
- Used for pain in some cases but primarily to get off other opioids
- Holds street value

Suboxone

- Can be initiated to help with withdrawal from opiates, heroin etc.
  - Withdrawal from Suboxone is a reality too
- Similar Efficacy as methadone for treating addiction
- Addictive on its own
  - Ceiling effect ~ 16 mg
- Can be weaned over time
- MD with proper credentials can prescribe
  - Requires 8 hour training course

Methadone

- Use for opioid addiction is housed in methadone clinics
- Once daily dosing
- Dose titrate up to a “blocking dose”
  - Diminishes euphoric high
- 1930s and 1940s
- Synthetic chemical → cheap

Naltrexone

- Opioid antagonist
- Once per month injection (more effective than PO)
  - When taken PO, can skip dose then go get high
- Cannot be started until full detoxification has taken place
- Reduces cravings after a few weeks
- Reduces risk of overdose
- Less well-studied than methadone and Suboxone
- Also used for alcohol dependence (taken before drinking to reduce pleasure from drinking)

Abstinence

- Ideological Battle
- Once the addiction is under control, you can stop?
- Can be achieved by some
- Short courses for detoxification often result in high relapse rate

Why is fentanyl in heroin?

- Highly potent synthetic opioid
- First mixed with heroin and desired by users
- Now, being sold straight up in some cases instead of heroin
- Supply is quicker, easier and cheaper (synthesized in a lab)
- Chasing the dragon. Long-time addicted users of heroin want the more potent drug
- China —> mexico —> U.S.
- Ordered easily off the dark web. Delivered right to your home.

http://www.newsweek.com/fentanyl-unseats-heroin-sold-alone-opioid-crisis-693985

Are there better ways to treat pain?

- Prescription society, harmful
  - Are we addicted to prescriptions?
- Social Connection (Support Networks)
- Exercise
- Acupuncture
- Cognitive Behavioral Therapy
- Rehabilitation

Conclusions

- Drug Manufacturers downplayed the harm potential of opioid medications and poorly trained physicians overprescribed these medicines
- Contrary to what drug manufacturers were purporting as truth, opioids are highly addictive substances that should be used with the utmost care
- Now, doctors poorly trained in how to handle drug addiction are being asked to treat it
- The road to recovery from this epidemic will be long and hard. The effort must include a new understanding of what addiction is, how to prevent it and how to treat it.
- Drugs are not the answer to all of our ailments. We still do not take full advantage of all the things we know to be healthy, true social connection, exercise, good food
- Naloxone can save lives
- We have a history lesson on our hands. We should be thinking about what we can learn from the current opioid situation in which we have created and now must combat.

Resources

- Turn the tide: https://turnthetiderx.org
- UW alcohol and drug abuse institute: http://adai.uw.edu/wastate/
- CDC, Drug Overdose: https://www.cdc.gov/drugoverdose/index.html
- stopoverdose.org
- Surgeon general report: https://www.facingaddiction.org/
- https://www.samhsa.gov (substance abuse and mental health services administration