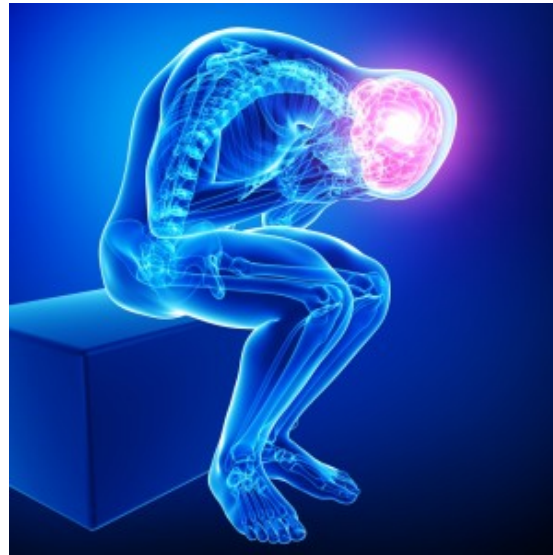


Buprenorphine and the Treatment of Opiate Addiction in Primary Care



Yukon-Kuskokwim Health Corporation
February 2017

Catherine Arnatt, PharmD, MS, NCPS
Southcentral Foundation/Alaska Native Medical Center

Road Map

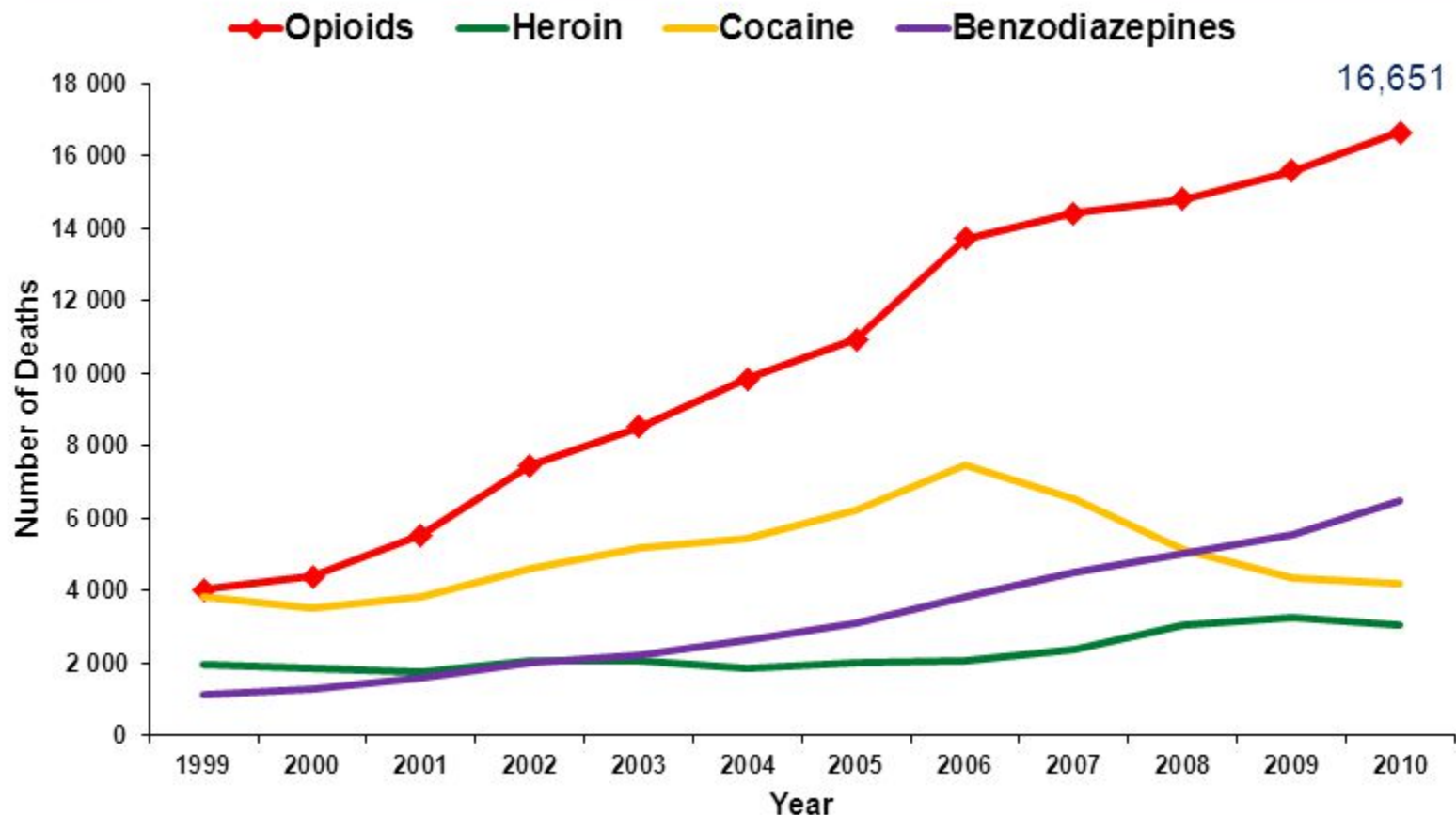
- Opioid statistics
- The nature of addiction
- Basic overview of buprenorphine
- Medication Assisted Treatment
 - Key components
- Legal Aspects: DEA & credentialing
- Medication Management
 - Suboxone induction, maintenance, discontinuation
 - Naltrexone, Naloxone, ancillary medications for withdrawal
- Pharmacist's role & responsibilities
- Questions & Discussion

Opiates/Opioids

- Opiates: alkaloids derived from the opium poppy
- Opioids: any endogenous compound including natural, synthetic and semi-synthetic drugs, which acts as an agonist at any of several receptors

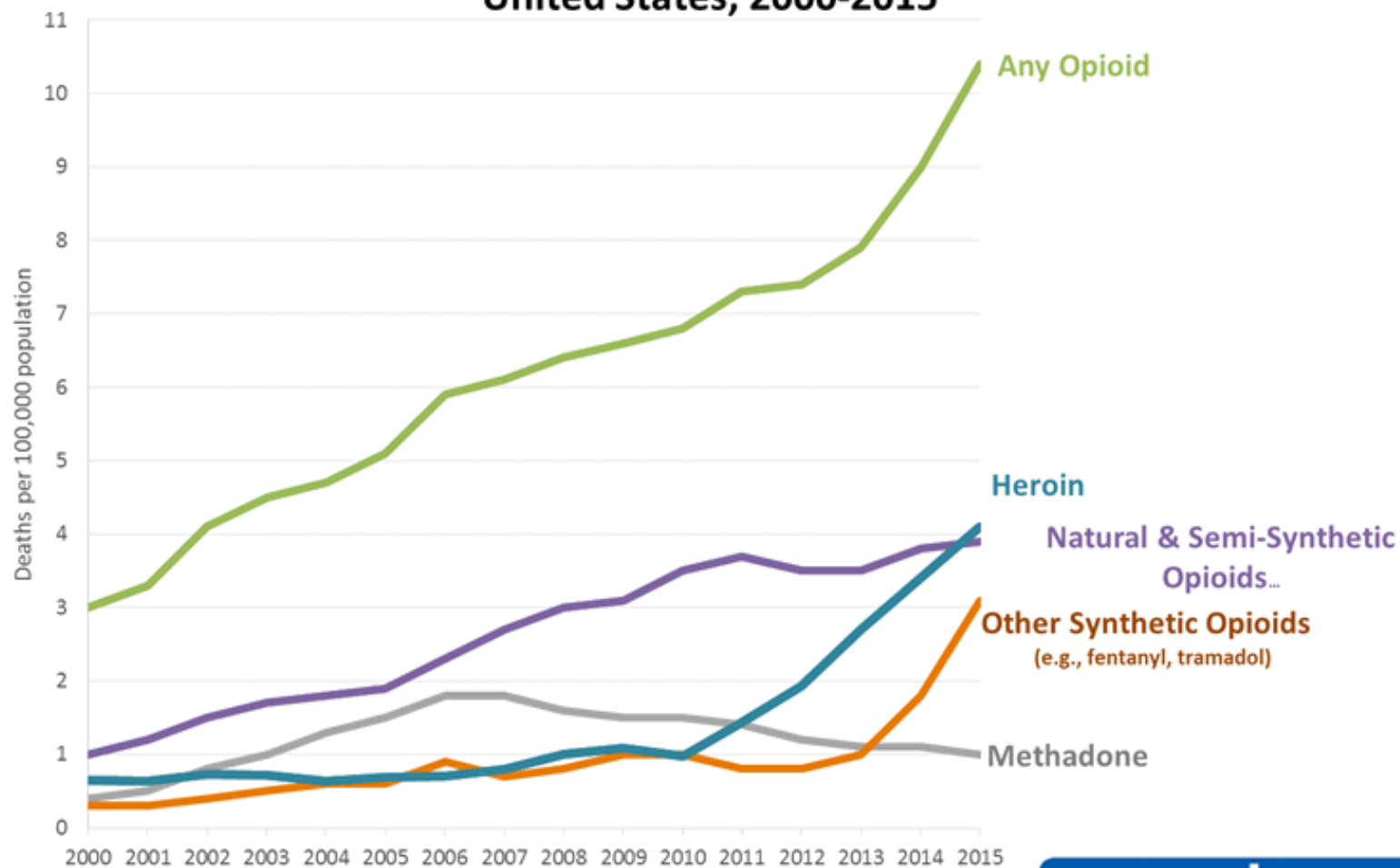


Drug overdose deaths by major drug types in the US, 1999-2010



CDC/NCHS National Vital Statistics System. CDC Wonder. The reported 2009 numbers are underestimates. Some overdose deaths were not included in the total for 2009 because of delayed reporting of the final cause of death.

Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2015



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <https://wonder.cdc.gov/>.

www.cdc.gov
Your Source for Credible Health Information

Turn the Tide Champaign



- <http://turnthetiderx.org/>

"WE, AS CLINICIANS, ARE UNIQUELY POSITIONED TO TURN THE
TIDE ON THE OPIOID EPIDEMIC."

— U.S. SURGEON GENERAL VIVEK MURTHY

TURN
THE
TIDE



PRESCRIBING OPIOIDS FOR CHRONIC PAIN

ADAPTED FROM CDC GUIDELINE

Opioids can provide short-term benefits for moderate to severe pain. Scientific evidence is lacking for the benefits to treat chronic pain.

IN GENERAL, DO NOT PRESCRIBE OPIOIDS AS THE FIRST-LINE TREATMENT FOR CHRONIC PAIN (for adults 18+ with chronic pain > 3 months excluding active cancer, palliative, or end-of-life care).

BEFORE PRESCRIBING

1 ASSESS PAIN & FUNCTION

Use a validated pain scale. Example: PEG scale where the score = average 3 individual question scores (30% improvement from baseline is clinically meaningful).

Q1: What number from 0 – 10 best describes your PAIN in the past week?

(0 = "no pain", 10 = "worst you can imagine")

Q2: What number from 0 – 10 describes how, during the past week, pain has interfered with your ENJOYMENT OF LIFE? (0 = "not at all", 10 = "complete interference")

Q3: What number from 0 – 10 describes how, during the past week, pain has interfered with your GENERAL ACTIVITY? (0 = "not at all", 10 = "complete interference")

2 CONSIDER IF NON-OPIOID THERAPIES ARE APPROPRIATE

Such as: NSAIDs, TCAs, SNRIs, anti-convulsants, exercise or physical therapy, cognitive behavioral therapy.

3 TALK TO PATIENTS ABOUT TREATMENT PLAN

- Set realistic goals for pain and function based on diagnosis.
- Discuss benefits, side effects, and risks (e.g., addiction, overdose).
- Set criteria for stopping or continuing opioid. Set criteria for regular progress assessment.
- Check patient understanding about treatment plan.

4 EVALUATE RISK OF HARM OR MISUSE. CHECK:

- Known risk factors: illegal drug use; prescription drug use for nonmedical reasons; history of substance use disorder or overdose; mental health conditions; sleep-disordered breathing.
- Prescription drug monitoring program data (if available) for opioids or benzodiazepines from other sources.
- Urine drug screen to confirm presence of prescribed substances and for undisclosed prescription drug or illicit substance use.
- Medication interactions. AVOID CONCURRENT OPIOID AND BENZODIAZEPINE USE WHENEVER POSSIBLE.

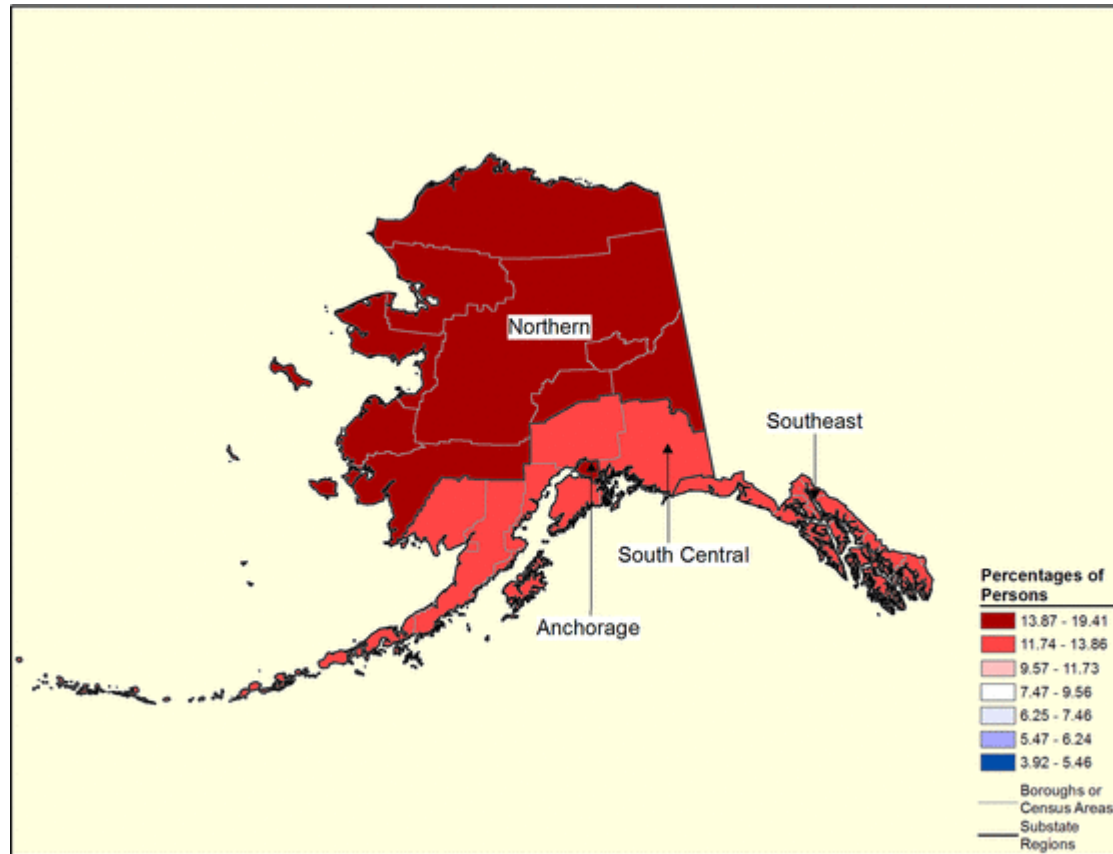
WHEN YOU PRESCRIBE

START LOW AND GO SLOW. IN GENERAL:

- Start with immediate-release (IR) opioids at the lowest dose for the shortest therapeutic duration. IR opioids are recommended over ER/LA products when starting opioids.
- Avoid ≥ 90 MME/day; consider specialist to support management of higher doses.
- If prescribing ≥ 50 MME/day, increase follow-up frequency; consider offering naloxone for overdose risk.
- For acute pain: prescribe < 3 day supply; more than 7 days will rarely be required.
- Counsel patients about safe storage and disposal of unused opioids.

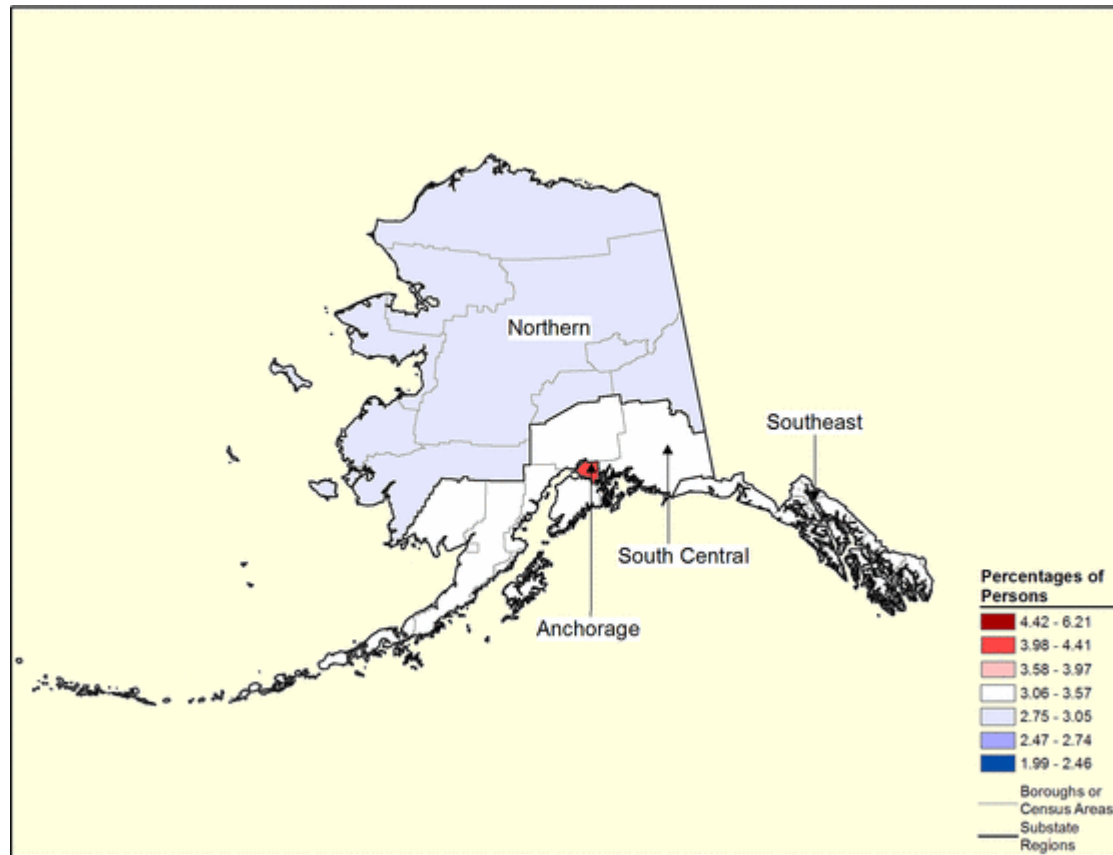
Illicit Drug Use in Alaska

based on 1 month averages 2010-2012



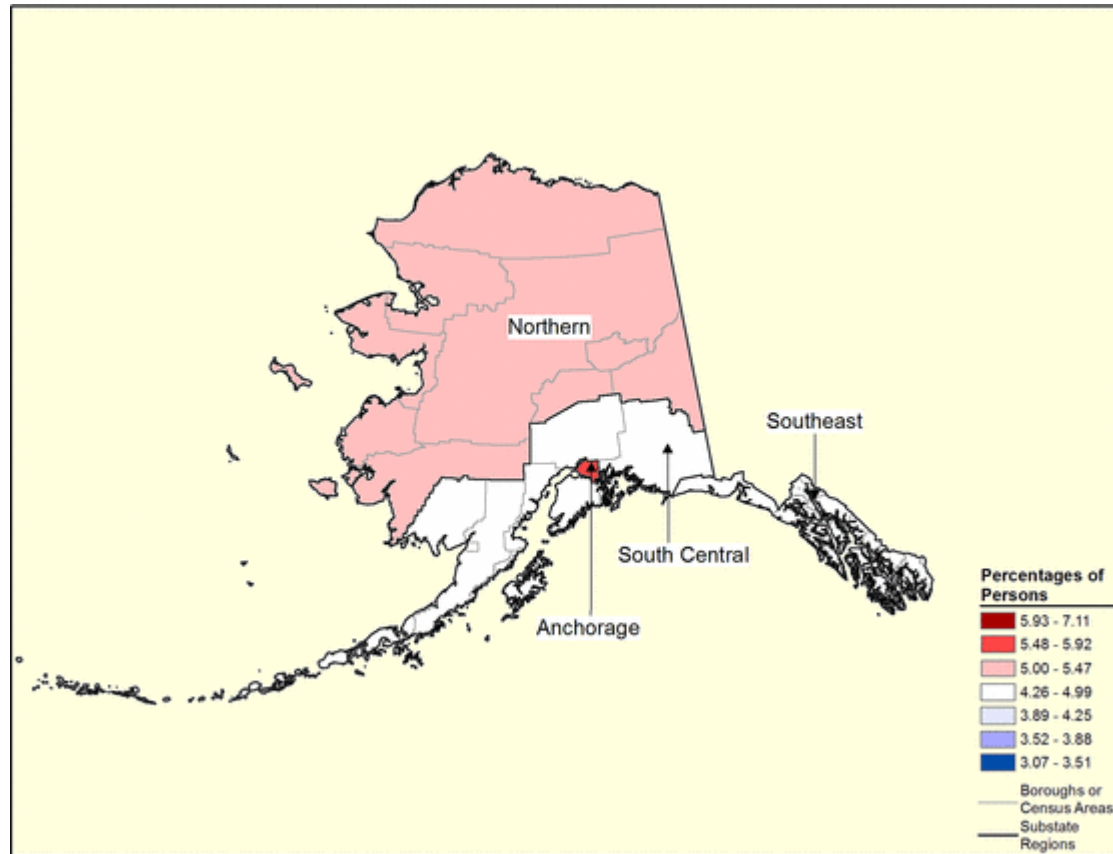
- An Alaska map showing illicit drug use in the past month among persons aged 12 or older, by substate region: percentages, annual averages based on 2010, 2011, and 2012 NSDUHs.

Illicit Drug Use Other than Marijuana among Persons Ages 12 or Older in AK



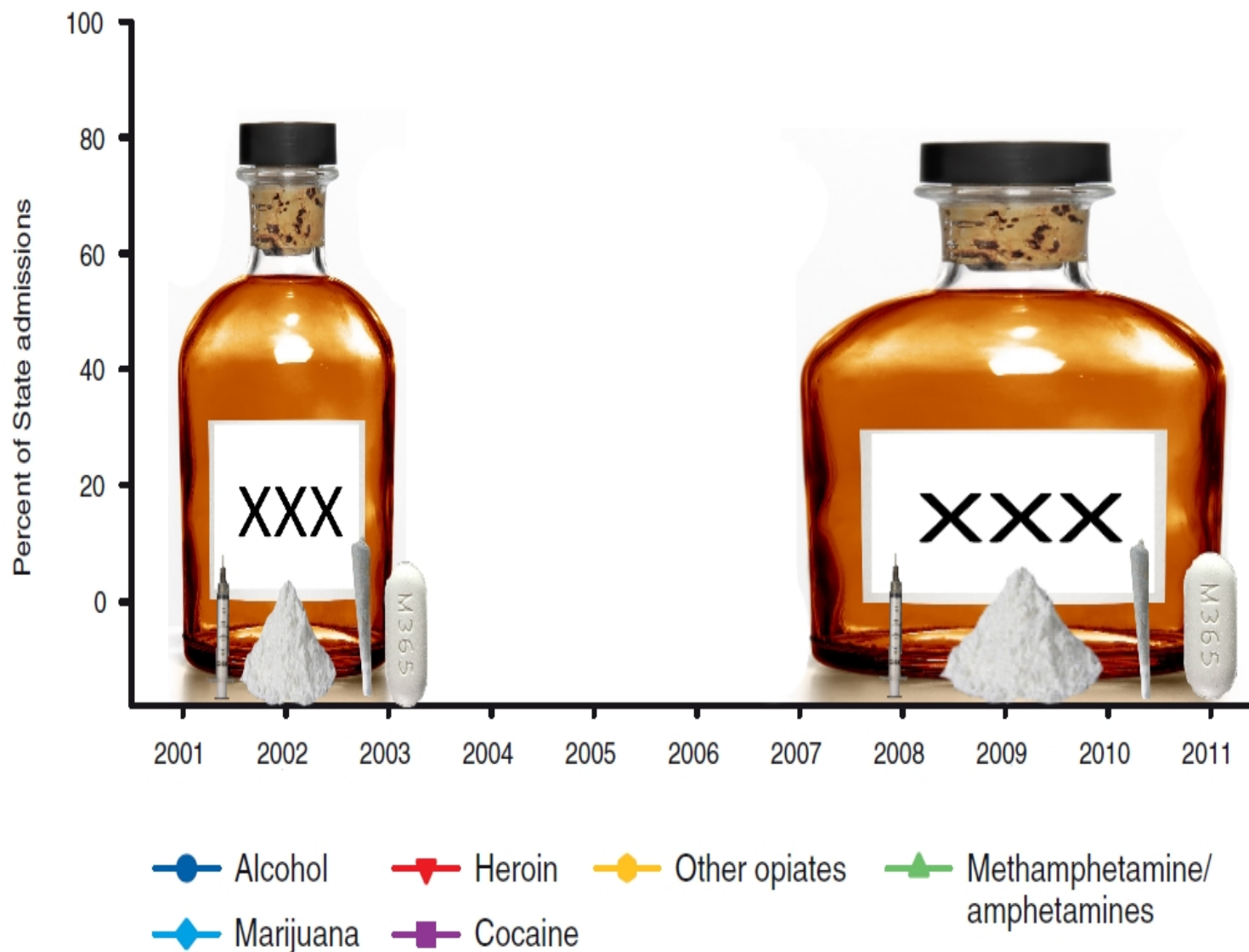
- An Alaska map showing illicit drug use other than marijuana among persons aged 12 or older, by substate region: percentages, annual averages based on 2010, 2011, and 2012 NSDUHs.

Nonmedical Use of Pain Relievers among Persons Ages 12 or Older in AK

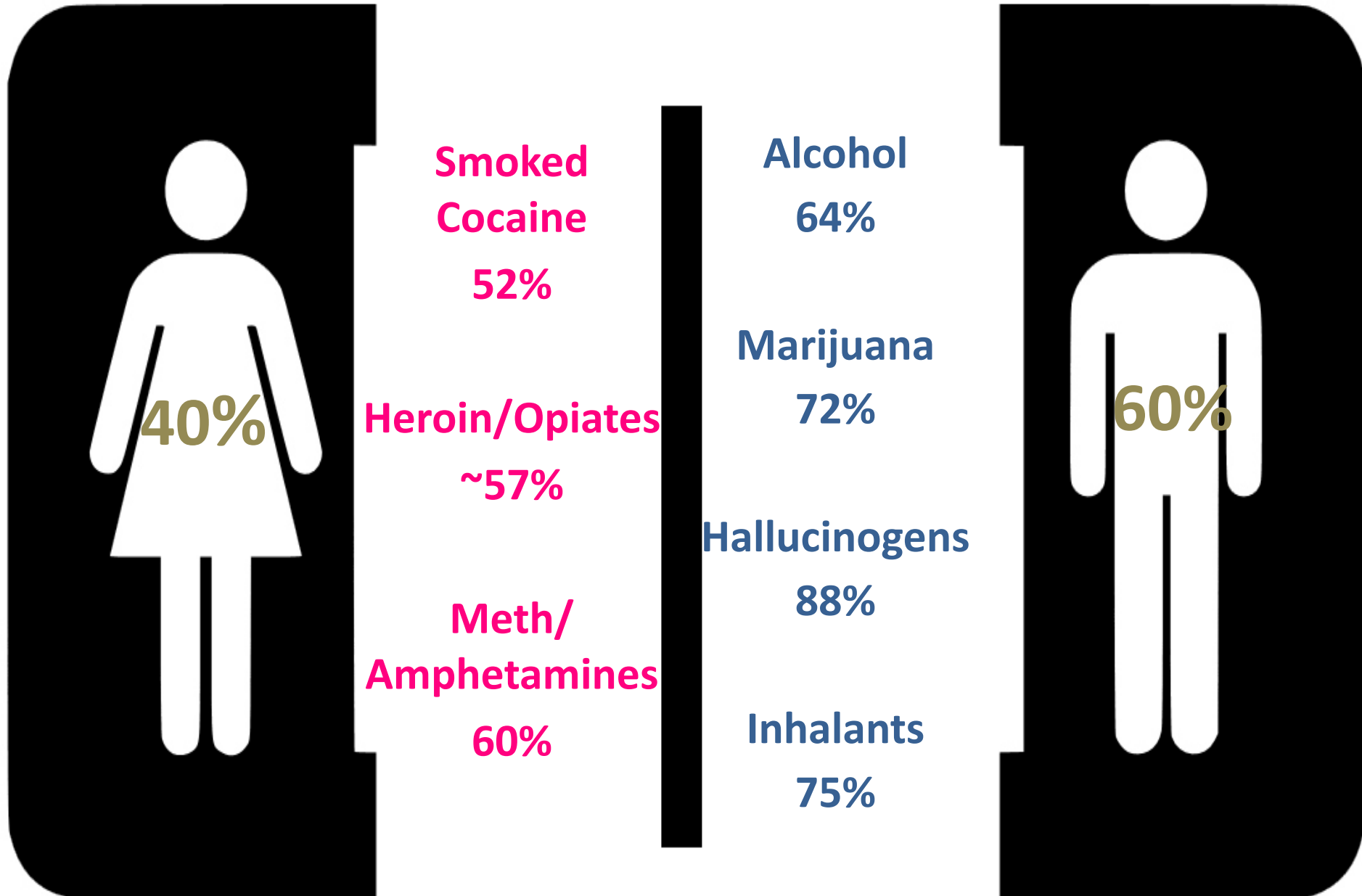


- An Alaska map showing nonmedical use of pain relievers in the past year among persons aged 12 or older, by substate region, annual averages based on 2010, 2011, and 2012 NSDUHs.

**Figure 9. Alaska admissions aged 12 and older,
by primary substance of abuse: 2001-2011**



2013 Treatment Admissions



Treatment Facilities and Services in Alaska

- 76 substance abuse treatment facilities in Alaska
- 2,840 clients
- 294 clients under the age of 18
- 67.1% are for profit
- 7.9% are non-profit
- 5.3% are local, county or community government
- 3.9% federal government
- 15.8% of facilities are Native Corporation/IHS



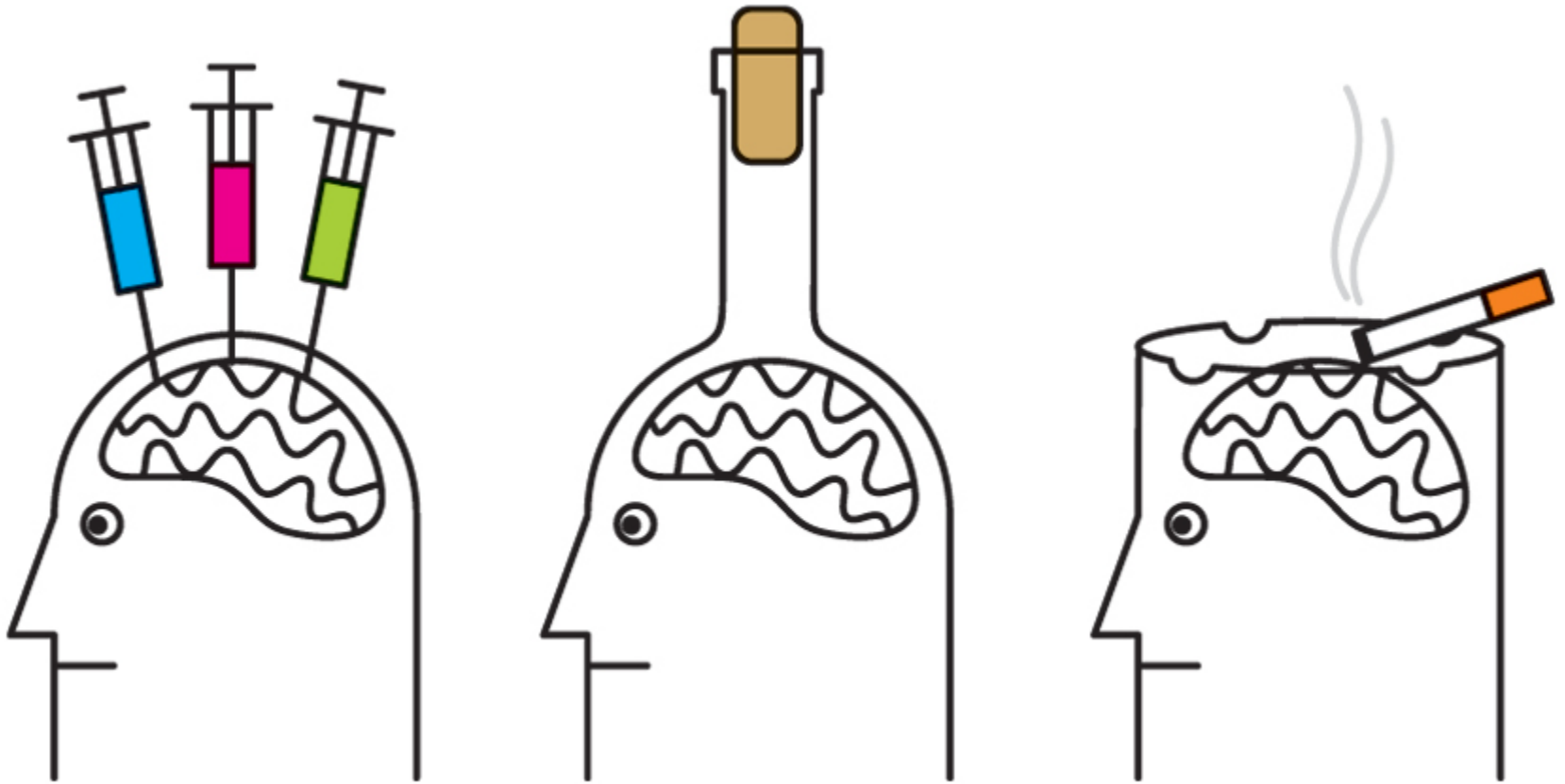
Scope of the Problem

- Escalating Opiate epidemic nationwide: leading cause of substance related deaths in US,
- Estimated opiate addiction costs > \$55 billion to society
- Use highly associated with HIV, Hep B and C transmissions
- Use associated with unemployment, criminality, childhood mental health issues, etc.
- Significant neonatal impact to developing fetus
- In Anchorage opiate dependence related to increased rates of prostitution
- High percentage of pregnant opiate abusers
- Long term users develop abstinence syndrome



Group Exercise

Empathy in substance use disorder.



“The brain has remarkable plasticity in response to drugs of abuse.”

Opioid Use Disorder

DSM-5 Diagnostic Criteria

- A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by **at least two** of the following, occurring **within a 12-month period**:
 - Opioids are often taken in larger amounts or over a longer period than was intended.
 - There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
 - A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects
 - Craving, or a strong desire or urge to use opioids
 - Recurrent opioid use resulting in failure to fulfill major role obligations at work, school, or home.
 - Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
 - Important social, occupational, or recreational activities are given up or reduced because of opioid use.
 - Recurrent opioid use in situations in which it is physically hazardous.
 - Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
 - Tolerance, (as defined)
 - Withdrawal, (as manifested)
 - *Criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision.*

Tolerance vs Withdrawal

Tolerance

- A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
- A markedly diminished effect with continued use of the same amount of an opioid.

Withdrawal

- The characteristic opioid withdrawal symptoms.
- Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.

- Dependence: sudden discontinuation of medication results in withdrawal symptoms
- Addiction: Maladaptive behaviors around the use of the substance

Intoxication vs Withdrawal

Intoxication

- ▣ **Pupillary constriction** and one or more of the following shortly after opioid use:
 - ▣ Drowsiness, stupor or coma
 - ▣ Slurred speech
 - ▣ Impaired memory/attention
 - ▣ Shallow or slow respiration
 - ▣ Bradycardia
 - ▣ Hypothermia

Withdrawal

- ▣ Peak withdrawal occurs **between 36 to 72 hours after last use** and should be **complete within 5 to 8 days** depending on the opioid used.
- ▣ Symptoms include:
 - ▣ **Pupillary dilation**
 - ▣ Dysphoric mood
 - ▣ Nausea or vomiting
 - ▣ Muscle aches
 - ▣ Lacrimation or rhinorrhea
 - ▣ Diarrhea
 - ▣ Fever, piloerection, sweating
 - ▣ Insomnia

Medication Assisted Treatment

- Opiate Replacement Therapy
 - Not an Abstinence Model
- Risk-Reduction Model
- Research based
- Basics:
 - Induction – Start the medication
 - Stabilization – Get the patient's life stable
 - Maintenance – Living life, not the addiction
 - Discontinuation – Stopping the medication

MAT Team

- Partnership between Behavioral Health & Primary Care Teams
 - Behavioral Health Provider
 - Primary Care Provider
 - Nurse Case Managers
 - Integrated Pharmacist
 - Chemical Dependency Counselors (CDCs)
 - Behavioral Health Consultants (BHC)
 - Support Clinic

Behavioral Health & Primary Care

- Treatment Groups**
 - Outpatient Substance Use Program (intensive)
- Regular meetings with CDC/BHC/PCP
- Community Support groups (mandatory)
- Establishment of community sober support system (mandatory)
- Medication Management
- Pill Counts
- Utox (advanced urinalysis) & Buprenorphine screens
- On going evaluation of other substance use: THC, EtOH, etc

Program Components

- Assessment
 - Behavioral Health & Primary Care Teams
- Contract/ Agreement: Clear cut expectations
 - Commitment to program requirements: Phase 1-4
 - What ifs: stolen/lost meds, relapse, prn pain, etc.
 - Who to contact when

Suboxone: A Basic Overview

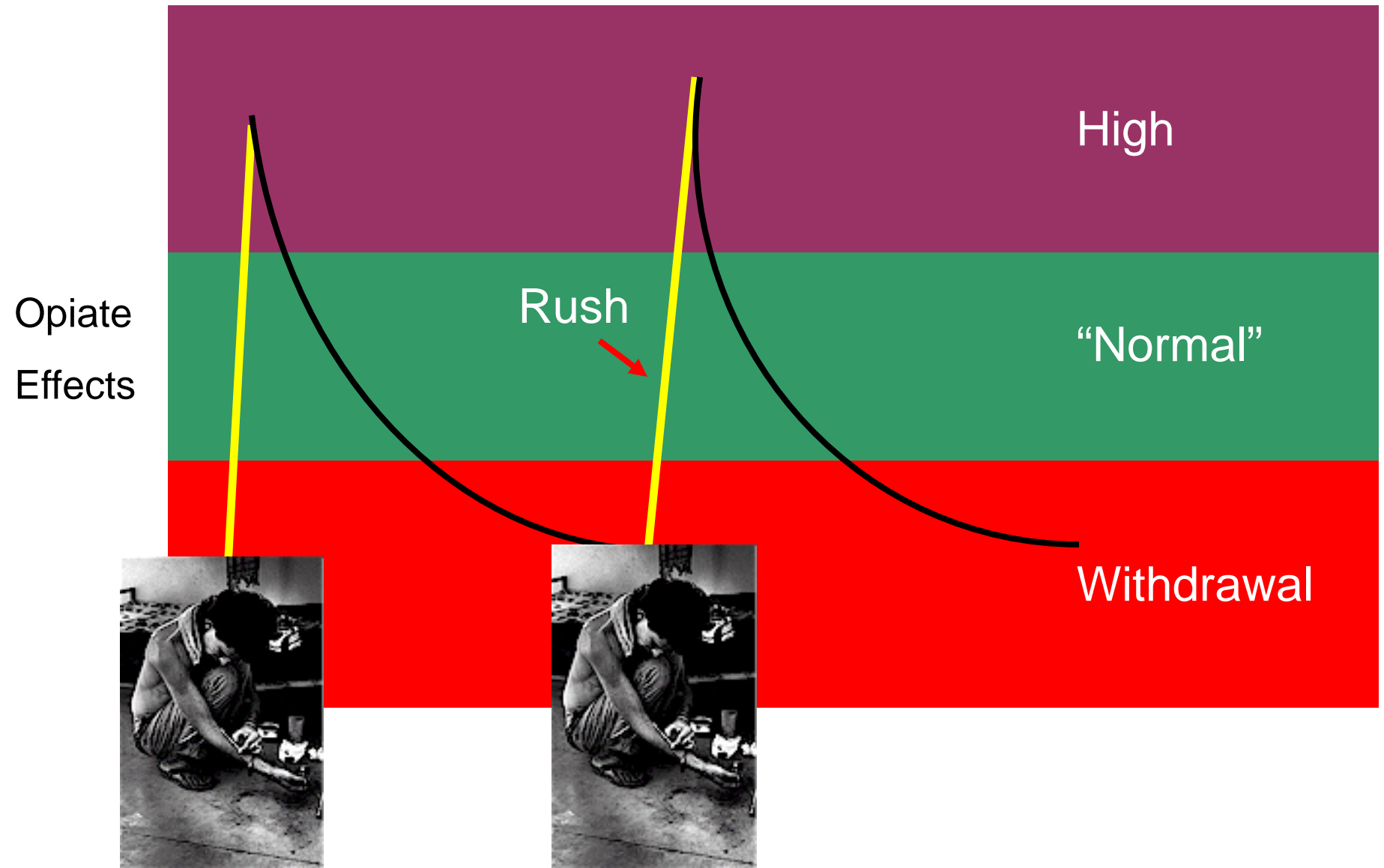
- **Suboxone (buprenorphine/naloxone) – CIII**
 - Buprenorphine/naloxone sublingual film
 - 2mg/ 0.5mg, 4mg/1mg, 8mg/2mg, 12mg/3mg
 - Buprenorphine/naloxone sublingual tablet
 - 2mg / 0.5mg, 8mg / 2mg
- The ratio of buprenorphine to naloxone in Suboxone® is 4:1

- **Subutex (buprenorphine) - CIII**
 - Buprenorphine sublingual tablet
 - 2mg, 8mg
- Used in pregnancy



- **Buprenorphine** is a mu-opioid receptor partial agonist & kappa-opioid receptor antagonist
- **Naloxone** is a mu-opioid receptor antagonist

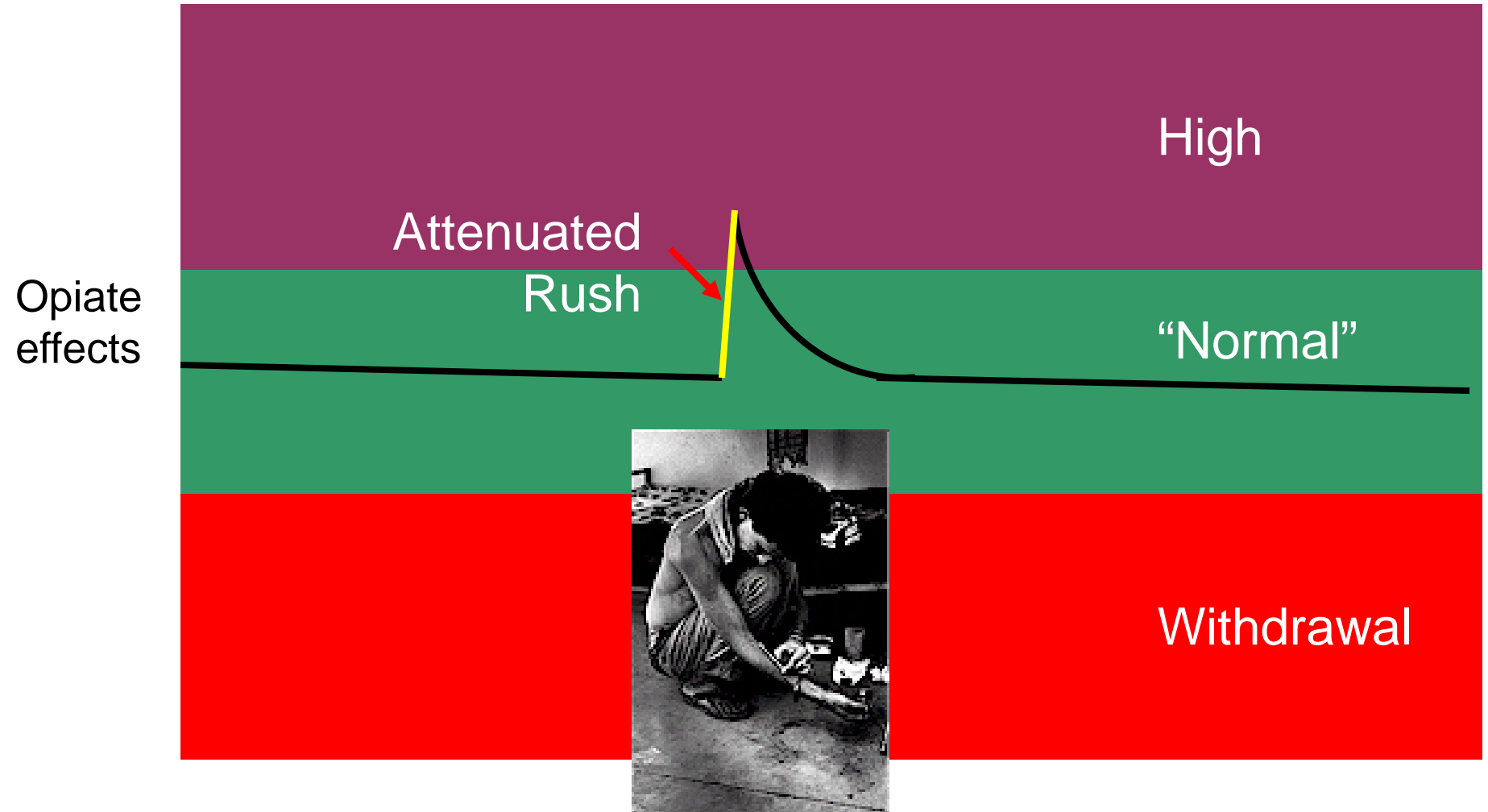
Effects of IV Heroin without Buprenorphine



Usual Effect of Buprenorphine Induction in an Opiate Dependent Patient



Effects of Using Heroin while on Buprenorphine




Buprenorphine

- Relatively long acting (24-60 hours)
 - Blocks other opiates
 - Low risk of overdose
 - Limited to no euphoria (no high when using)
 - Keeps person from getting sick
-
- Lower doses may be used to treat moderate chronic pain (without XDEA waiver)

Buprenorphine Side Effects

- Headache
- Numb/inflamed mouth and/or swollen or painful tongue
- Attention disturbance
- Blurred vision
- Back pain
- Fainting
- Dizziness
- Sleepiness
- Drug withdrawal syndrome: includes: shaking, sweating, diarrhea, vomiting, muscle aches, runny nose, hot/cold temp

Legal aspects: DEA & Credentialing



U.S. DEPARTMENT OF JUSTICE ★ DRUG ENFORCEMENT ADMINISTRATION

DIVERSION CONTROL DIVISION

DEA Registration Validation Login:

Important: Please enter *your* DEA information to login (not the DEA # you are attempting to validate)

DEA Number (Required - Not Case Sensitive)

- The Drug Addiction Treatment Act (DATA) of 2000 requires prescribers be certified for addiction treatment.
- DEA website → validate XDEA for Suboxone prescribing:
 - <https://apps.dea diversion.usdoj.gov/webforms/validateLogin.jsp>
- DATA waived physicians may treat 30 or 100 patients at any one time, dependent on individual authorization from the Center for Substance Abuse Treatment (CSAT).
 - "PRACTITIONER-DW/30" or "PRACTITIONER-DW/100"



U.S. DEPARTMENT OF JUSTICE ★ DRUG ENFORCEMENT ADMINISTRATION

DIVERSION CONTROL DIVISION

DEA Registration Validation Result:

DEA Number: BA1234567

This DEA Number is ACTIVE

Name (Last, First): Doe, Prescriber, MD

Business Activity: PRACTITIONER-DW/100

Business Address 1: SOUTH CENTRAL FOUNDATION

Business Address 2: 4501 DIPLOMACY DR.

Business Address 3:

City: ANCHORAGE

State: AK

Zip: 99508

Schedules: Schedule II Narcotic, Schedule II Non Narcotic, Schedule III Narcotic, Schedule III Non Narcotic, Schedule IV, Schedule V

Fee Status: Paid

Expire Date: 03-31-2017

The U.S. Department of Justice, Drug Enforcement Administration, Diversion Control Division maintains registrant data and is considered the primary source of information on DEA registrants. The website <https://www.deadiversion.usdoj.gov> is the official location for real time online verification.

DEA Registration Validation:

DEA Number to be validated (Required - Not Case Sensitive)

Validate

Logout

Induction

- Type of Opioids (Long or short acting)
 - Abstain from short-acting opiates for 16 to 24 hours prior to induction
 - Abstain from long-acting opiates for 24 to 48 hours prior to induction
- Time Since Last Use
 - Avoid precipitating opioid withdrawal syndrome, by starting 1st dose of buprenorphine/naloxone only when objective signs of moderate withdrawal appear → COWS score
 - 1st dose not less than 6 hours after patient's last use (heroin or short acting opioid)
- Degree or Level of Dependence

Clinical Opiate Withdrawal Scale (COWS)

Howsheet for measuring symptoms over a period of time during buprenorphine induction.

For each item, write in the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal.
For example: If heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.

Patient Name: _____		Date: _____			
Buprenorphine Induction: _____					
Enter scores at time zero, 30 minutes after first dose, 2 hours after first dose, etc.		Times of Observation:			
Resting Pulse Rate: Record Beats per Minute					
Measured after patient is sitting or lying for one minute					
0 = pulse rate 80 or below					
1 = pulse rate 81-100					
2 = pulse rate 101-120					
3 = pulse rate greater than 120					
Sweating: Over Past 1/2 Hour not Accounted for by Room Temperature or Patient Activity					
0 = no report of chills or flushing					
1 = subjective report of chills or flushing					
2 = flushed or observable moistness on face					
3 = beads of sweat on brow or face					
4 = sweat streaming off face					
Restlessness Observation During Assessment					
0 = able to sit still					
1 = reports difficulty sitting still, but is able to do so					
2 = frequent shifting or extraneous movements of legs/arms					
3 = Unable to sit still for more than a few seconds					
Pupil Size					
0 = pupils pinned or normal size for room light					
1 = pupils possibly larger than normal for room light					
2 = pupils moderately dilated					
3 = pupils so dilated that only the rim of the iris is visible					
Bone or Joint Aches if Patient was Having Pain Previously, only the Additional Component Attributed to Opiate Withdrawal is Scored					
0 = not present					
1 = mild diffuse discomfort					
2 = patient reports severe diffuse aching of joints/muscles					
3 = patient is rubbing joints or muscles and is unable to sit still because of discomfort					
Runny Nose or Tearing Not Accounted for by Cold Symptoms or Allergies					
0 = not present					
1 = nasal stuffiness or unusually moist eyes					
2 = nose running or tearing					
3 = nose constantly running or tears streaming down cheeks					
GI Upset: Over Last 1/2 Hour					
0 = no GI symptoms					
1 = stomach cramps					
2 = nausea or loose stool					
3 = vomiting or diarrhea					
4 = multiple episodes of diarrhea or vomiting					
Tremor Observation of Outstretched Hands					
0 = no tremor					
1 = tremor can be felt, but not observed					
2 = slight tremor observable					
3 = gross tremor or muscle twitching					
Yawning Observation During Assessment					
0 = no yawning					
1 = yawning once or twice during assessment					
2 = yawning three or more times during assessment					
3 = yawning several times/minute					
Anxiety or Irritability					
0 = none					
1 = patient reports increasing irritability or anxiousness					
2 = patient obviously irritable/anxious					
3 = patient so irritable or anxious that participation in the assessment is difficult					
Gooseflesh Skin					
0 = skin is smooth					
1 = piloerection of skin can be felt or hairs standing up on arms					
2 = prominent piloerection					
Score:					
5-12 = Mild					
13-24 = Moderate					
25-36 = Moderately Severe					
More than 36 = Severe Withdrawal					
Total score					
Observer's initials					

Suboxone Induction

Day 1

- Induction dosage of up to 8mg/2mg Suboxone film is recommended
 - Start with initial dose of 2mg/0.5mg or 4mg/1mg buprenorphine/naloxone and titrate in 2 or 4 mg increments of buprenorphine at 2 hour intervals under supervision, to 8mg/2mg based on control of acute withdrawal symptoms

Day 2

- A single daily dose of up to 16mg/4mg Suboxone film is recommended
 - Medication should be prescribed in consideration of frequency of visits.
 - Multiple refills not advised early in treatment or without appropriate follow-up
 - Maintenance dose should be achieved as rapidly as possible for clinical effectiveness to prevent high drop-out rate

Maintenance









- Dosage of Suboxone from Day 3 onwards should be adjusted in up or down increments of 2mg/0.5mg or 4mg/1mg buprenorphine/naloxone to a level that maintains patient in treatment and prevents signs and symptoms of opioid withdrawal
- Maintenance dose typically range from 4mg/1mg to 24mg/6mg buprenorphine/naloxone based on clinical response
- Recommended target dose varies, can be ~16mg/4mg
- Doses higher than 24mg/6mg have not been demonstrated to provide clinical advantage
- Recommend plan in place to manage treatment and prevent relapse
 - Urinalysis: weekly, monthly, etc
 - Film/Tablet counts
 - Follow up with MAT Team

Discontinuation

- Individualized based on treatment goals
- No guideline for duration of therapy, may be long term
- When discontinuing, taper patients to avoid signs and symptoms of opioid withdrawal
 - Can tapering to very low doses minimize withdrawal?
 - Dose decreases of 25% every 10 or more days have been reported to be tolerable**
 - Suboxone film can be cut into very small pieces
 - Ancillary medications can help with withdrawal symptoms
- In 1 study of individuals terminating buprenorphine pharmacotherapy for opioid dependence, there appeared to be no advantage in prolonging the duration of taper.
 - Better success with patient buy in, working together

Suboxone Relative Size



			
8mgs.	4mgs.	2mgs.	
			
1mg.	0.5mgs.	0.25mgs.	0.13mgs.

Post Suboxone Taper

- > 90% relapse after taper
- Consider Naltrexone/Vivitrol
 - Naltrexone 380 mg ER IM Injection (Vivitrol)
 - Recommended dosage form**
 - Naltrexone 50 mg tablets
- Generally recommended that naltrexone be initiated 3-5 days after the last dose of Suboxone/Subutex following dose taper.

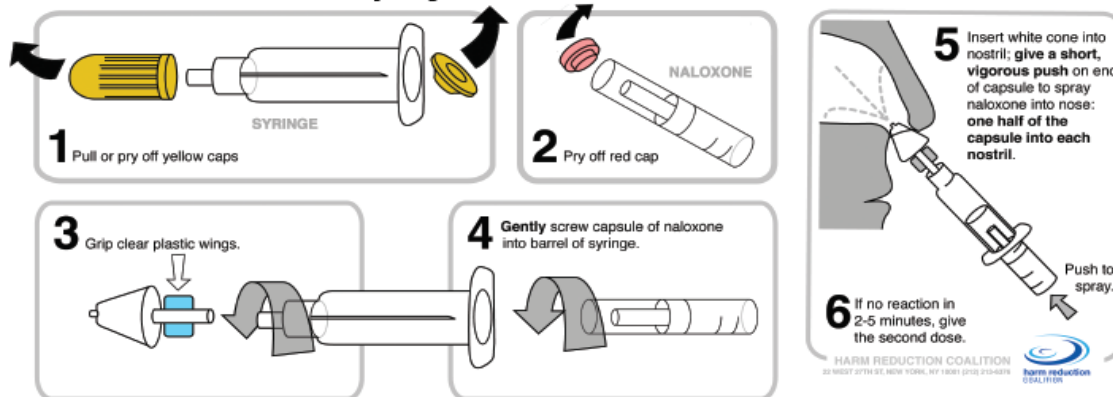
Naltrexone (Vivitrol)

- Opiate antagonist
 - 30 day injectable form (IM), painful if not administered well
 - Person needs to be detoxed from opiates
 - 1+ weeks for short acting
 - 2+ weeks for long acting
 - High relapse rate due to poor compliance
 - First month is hard, as person still has withdrawal symptoms
 - Second month better – cravings dissipate
 - Third month – person doing great
- No medicine is a cure all!

Naloxone (Narcan®)

- Dispense to:
 - Individuals at risk of overdose, 3rd party prescribing allowed
- Treatment administration for acute life threatening opioid overdose
 - Give 0.4mg IV or IM every 2-3 minutes (not to exceed 10mg)
 - Give intranasally (dependent on selected product)
 - 4mg once as a single spray in nostril; may repeat every 2-3 minutes in alternating nostrils
 - 2mg divided into each nostril; may repeat in 2-5 minutes if needed

How to Give Nasal Spray Naloxone



Adverse Effects (withdrawal symptoms) and Symptomatic Options

- Hypertension, Hypotension, Tachycardia, Chills/Sweats, etc.
 - Clonidine: 0.1mg up to 5 times/day prn chills/sweats
- Nausea/Vomiting
 - Phenergan: 25mg every 6 hours prn nausea/vomiting
 - Ondansetron: 4mg by mouth q 6 to 8 hours prn nausea/vomiting
- Loose Stools
 - Loperamide: 2 capsules with first loose stool and 1 capsule following every additional loose stool; max 8 capsules/day
- Muscle Aches/ Pain
 - Ibuprofen: 400-800mg by mouth q 6 to 8 hours prn aches/pains
 - Dicyclomine: 20mg by mouth QID prn GI cramping
 - Epsom Salt baths
 - Magnesium Citrate 1 teaspoon three times daily as needed for muscle relaxation
- Anxiety, Insomnia
 - Hydroxyzine, Benadryl: 25-50 mg q 4-8 hours prn

Pharmacist's Role & Responsibilities

- Verify that the prescriptions you receive are from DATA waived prescribers
- Remind patients who are picking up induction doses to return as directed to the doctor's office so that they can be supervised while taking the medication
- Be vigilant in detecting fraudulent prescriptions or simultaneous prescriptions for the same patient from multiple suppliers
- Suboxone Risk Evaluation and Mitigation Strategy (REMS)
- 42 CFR part 2
- Pharmacist opportunities in Medication Assisted Treatment

Treatment Effectiveness

- Treatment failure rate for opiate addiction ~ 80 -90%
 - Regrettably standard psycho-social treatment is less effective for Opiate addicts than addicts of any other substance
 - Co-morbidities, environmental factors, the nature of addiction, etc.
 - Relapse rate after psycho-social treatment completion tops 90%
 - Includes non-medication assisted options (e.g. outpatient, inpatient, long term residential, incarceration)
- Differential characteristics of opiate dependence:
Neurophysiological CNS changes induced by high dose opiate use
 - Chronic withdrawal/abstinent state
 - Physiological effects of chronic opiate use → severe cravings, ultra high relapse rate



Success Stories

Alaska News

Alaskans battling opioid epidemic get audience with U.S. surgeon general

✍ Author: **Zaz Hollander** ⌚ Updated: September 15, 2016 📅 Published August 4, 2016



U.S. Surgeon General Vivek Murthy listens to a comment from Kim Whitaker, the mother of a heroin addict, during the Wellness Summit at the Glenn Massay Theater on Thursday. The summit was convened by Sen. Dan Sullivan to address the opioid epidemic. (Loren Holmes / Alaska Dispatch News)



Catherine Arnatt, PharmD, MS, NCPS
LT, United States Public Health Service
Pharmacist
Alaska Native Medical Center/Southcentral Foundation
4320 Diplomacy Drive
Anchorage, AK 99508
907-729-2140 (work)
443-243-6782 (cell)
carnatt@SouthcentralFoundation.com