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INDIANA UNIVERSITY
RICHARD M. FAIRBANKS SCHOOL OF PUBLIC HEALTH

INSIGHTS & INNOVATIONS

Welcome
We will begin shortly...



IUPUI

RICHARD M. FAIRBANKS
SCHOOL OF PUBLIC HEALTH

INDIANA UNIVERSITY
Indianapolis

Public Health Insights and Innovations

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A pregnant woman wearing a white long-sleeved sweater is shown from the chest down. Her hands are held out in front of her belly. Her right hand is open and facing up, while her left hand is holding a small pile of white, round pills. The background is a plain, light color.

Opioid Use Disorder in Pregnancy

Tara Benjamin, MD, MS, FACOG
Assistant Clinical Professor
Department of Obstetrics & Gynecology
Division of Maternal-Fetal Medicine
Indiana University School of Medicine

Disclosure

- I have no disclosures

Learning Objectives

At the end of this presentation, participants should be better able to...

- Identify disease defining pathophysiologic changes of Opioid Use Disorder.
- Describe therapeutic options available for treatment in pregnant and non-pregnant patients.
- Understand the challenges in caring for pregnant women with Opioid Use Disorder.





Updates from Addiction Medicine



Jane Deaux

- 36yo G3P3 presents for annual exam.
- She has fibromyalgia managed with oxycodone.
- Her diagnosing physician retired.
- She's worried about not having a prescriber.

Is this chronic pain or a substance use problem?





Terminology

- The (DSM-V) replaced “abuse” & “dependence” with **Substance Use Disorder (SUD)**.
- **SUD**- primary, chronic, & neurobiological disease with genetic, psychosocial & environmental factors influencing its development and manifestations.
- _____ Use Disorder (i.e. Alcohol, Cannabis).
- Is this chronic pain AND Opioid Use Disorder?



Substance Use Disorder Diagnostic Criteria

IMPAIRED CONTROL	RISKY USE
1. Using more or for longer than intended	8. Recurrent use in physically hazardous situations.
2. Desire to cut down/failed quit attempts	9. Continued use despite negative physical or psychological consequences
3. Lots of time spent using or recovering	
4. Intense desire to use or cravings	
SOCIAL IMPAIRMENT	PHARMACOLOGIC DEPENDENCE*
5. Failure to fulfill work, school, or home obligations	10. Tolerance
6. Use causes or exacerbates interpersonal problems.	11. Withdrawal symptoms with cessation
7. Reduction in important social, occupational, or recreational activities	*Diagnosis cannot be based on #s 10 & 11 alone. At least one other is required.

Diagnosis requires the presence of at least 2 criteria over the past 12 months.

Mild SUD = 2-3 criteria Moderate SUD = 4-5 Severe SUD = 6 or more

ASAM Handbook of Addiction Medicine, 2016.





Jane Deaux-

- At her 2 week f/u, she signed a narcotic treatment agreement with you.
- You agreed to provide prescriptions & assess her bimonthly until her appt with pain mngmt.
- Today, 1 month later, she is accompanied by her significant other who is worried about her.
- You evaluate her for addictive behaviors.
- He informs you of the following:





Addictive Behaviors-since last visit

- Used illicit drugs
- Has hoarded meds
- Used more narcotic than prescribed
- Ran out of meds early
- Has increased use of narcotics
- Used analgesics PRN when prescription is for time limited use (i.e. used old Rx).
- Received narcotics from more than one provider
- Purchased meds from others.

Ms. Deaux's behaviors

Addictive Behaviors- cont.

- Appears sedated or confused
- Worries about addiction
- Strong preference for a specific analgesic or route of admin.
- Concerned about future availability of narcotic.
- Worsened family relationships.
- Misrepresented analgesic or prescription use.
- “Needs” or “must have” meds.
- Discussion of meds was the predominant issue of visit.
- Lack of interest in rehab or self-management.
- Inadequate relief from analgesic.
- Indicated difficulty with using medication agreement.
- Significant others express concern over use of analgesics

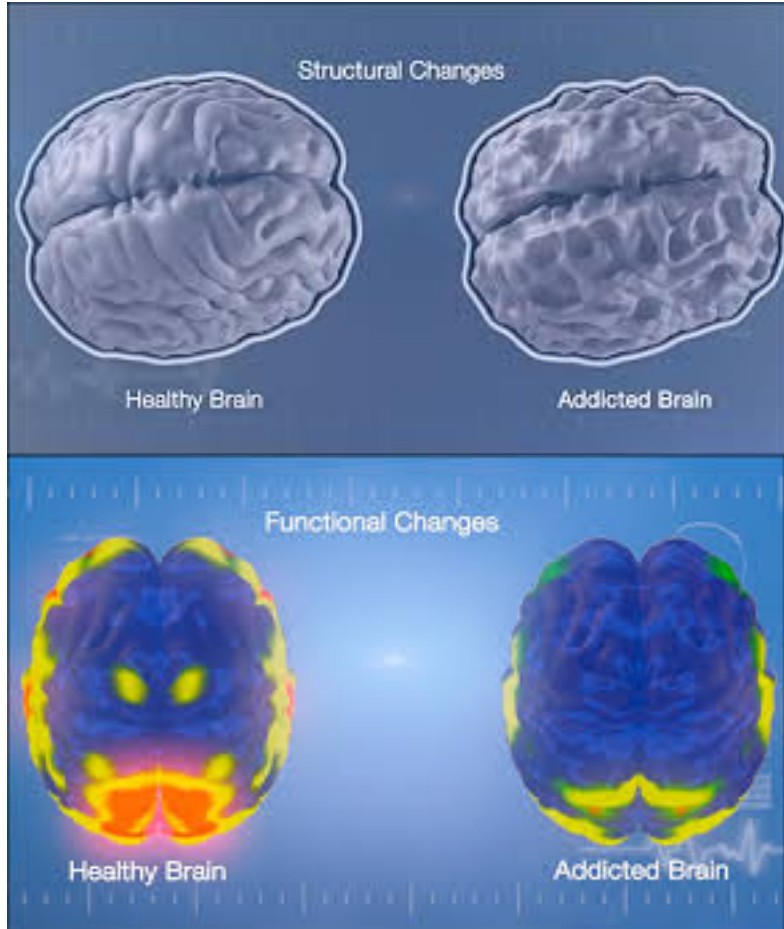
Ms. Deaux’s behaviors



Jane Deaux

- Gets upset with her husband and abruptly leaves the office.
- Later that evening, the ER calls informing you that she is in severe acute opioid withdrawal.
- She was brought in by the police after arrest for shoplifting a breast pump she planned to exchange for heroin.
- Why has she behaved this way?





Chronic Disease

Binge and Intoxication

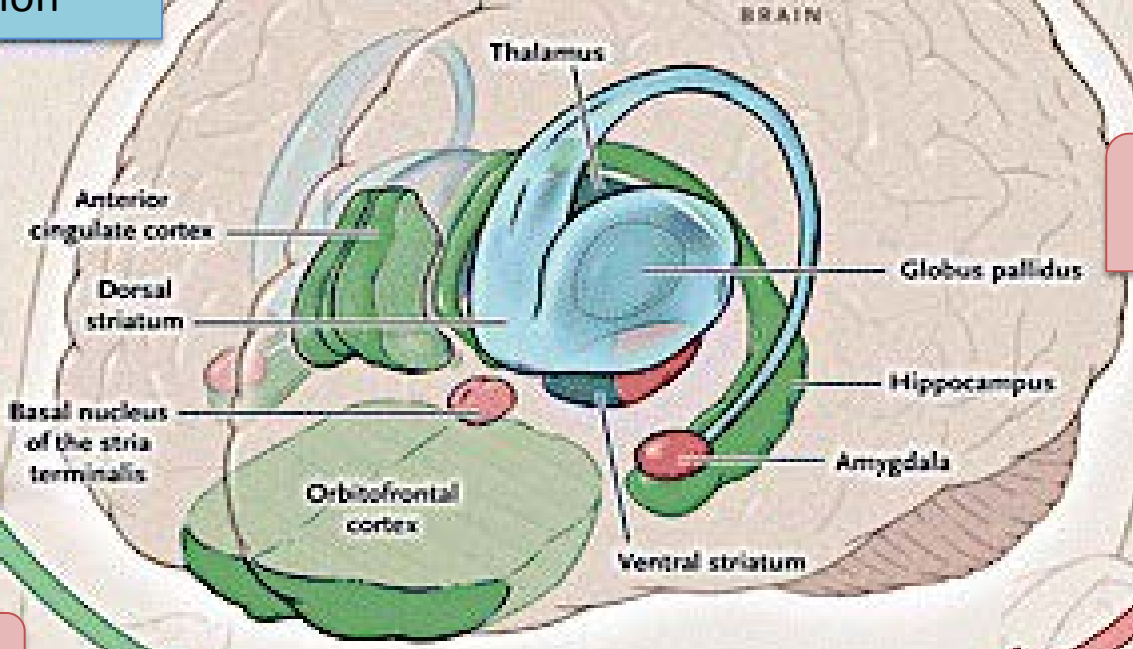
Withdrawal & negative affect

Response to drug

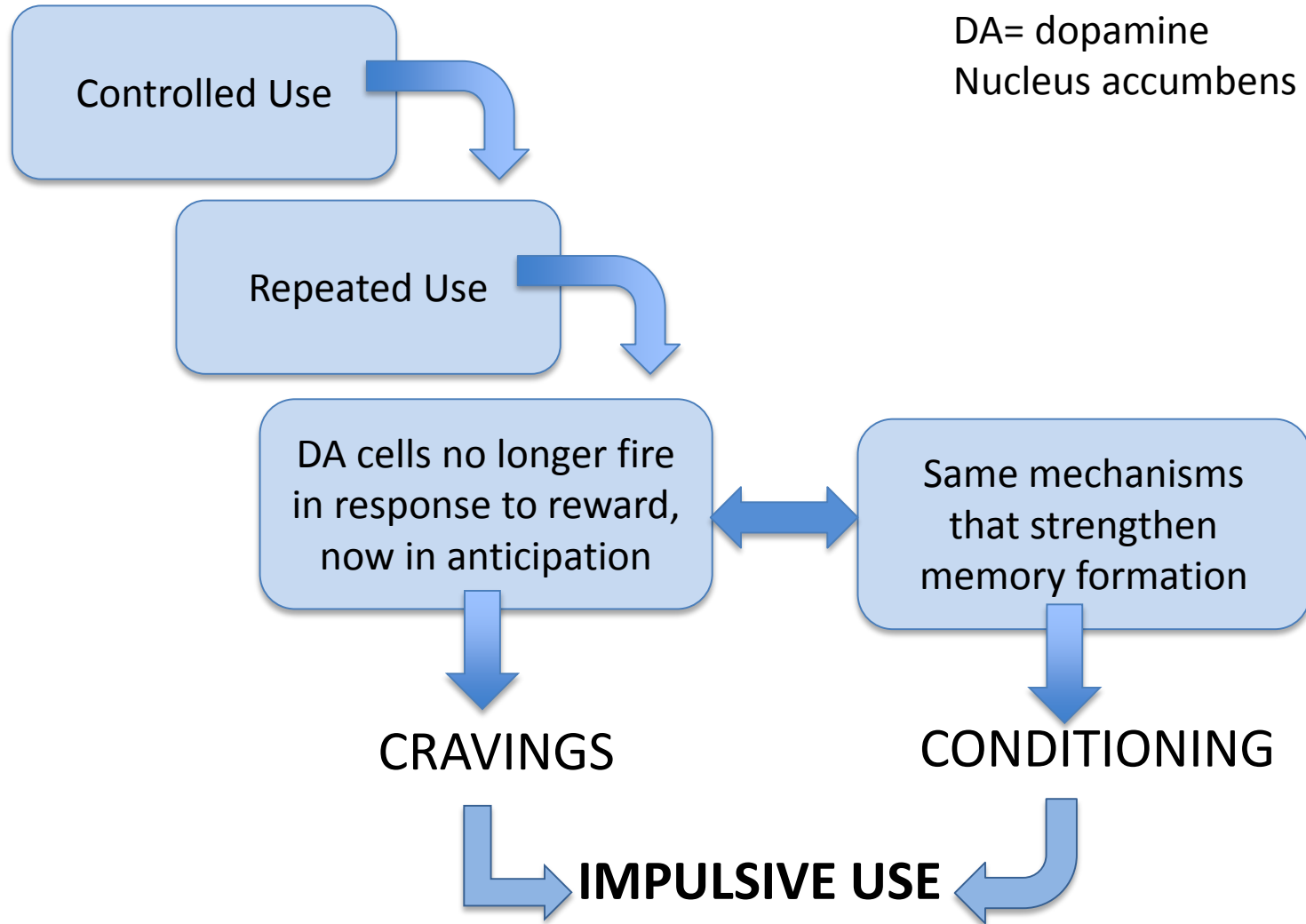
Stress & reward

Preoccupation & anticipation

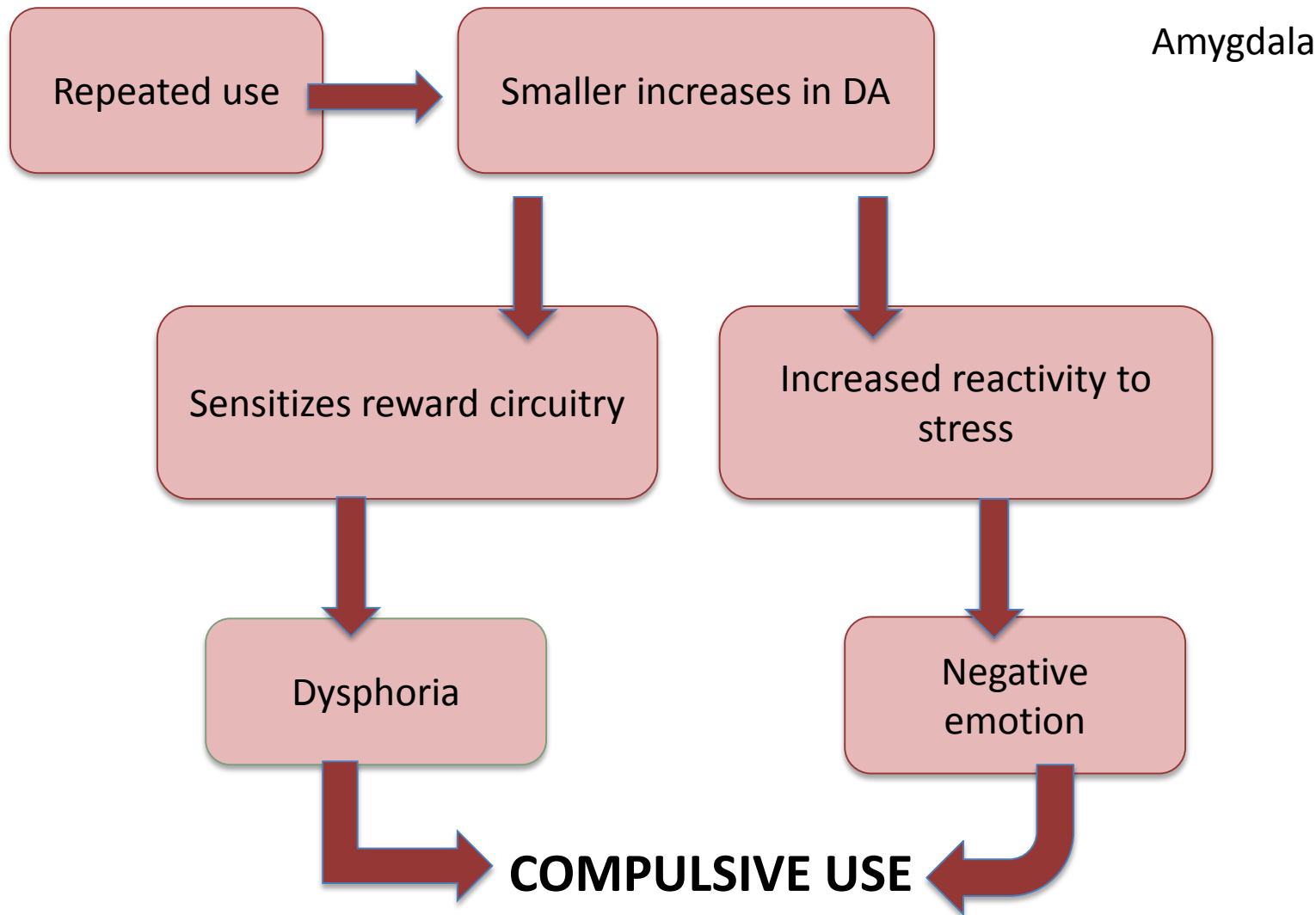
Stages of Addiction



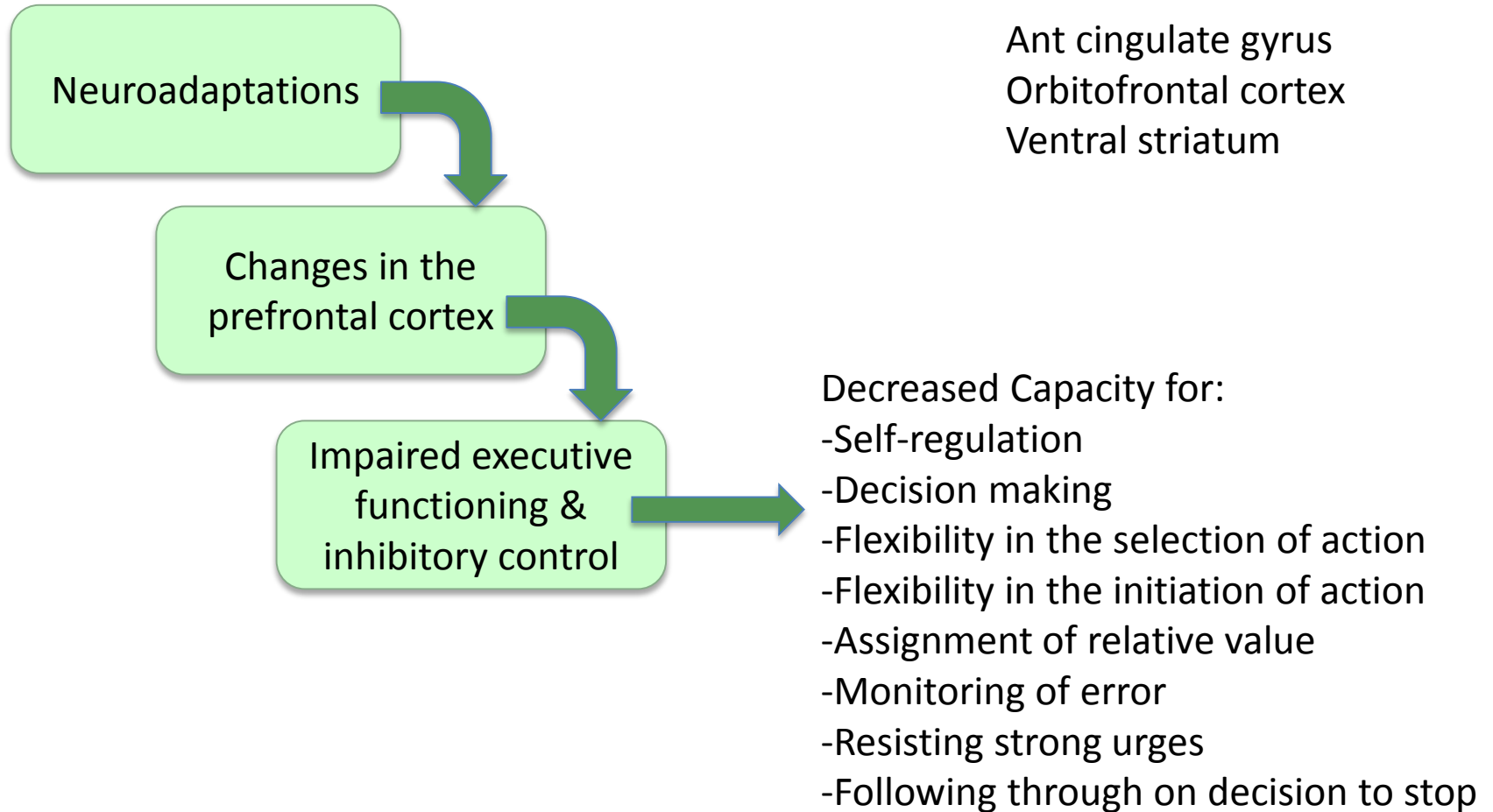
Binge & Intoxication



Withdrawal & Negative Affect



Preoccupation & Anticipation

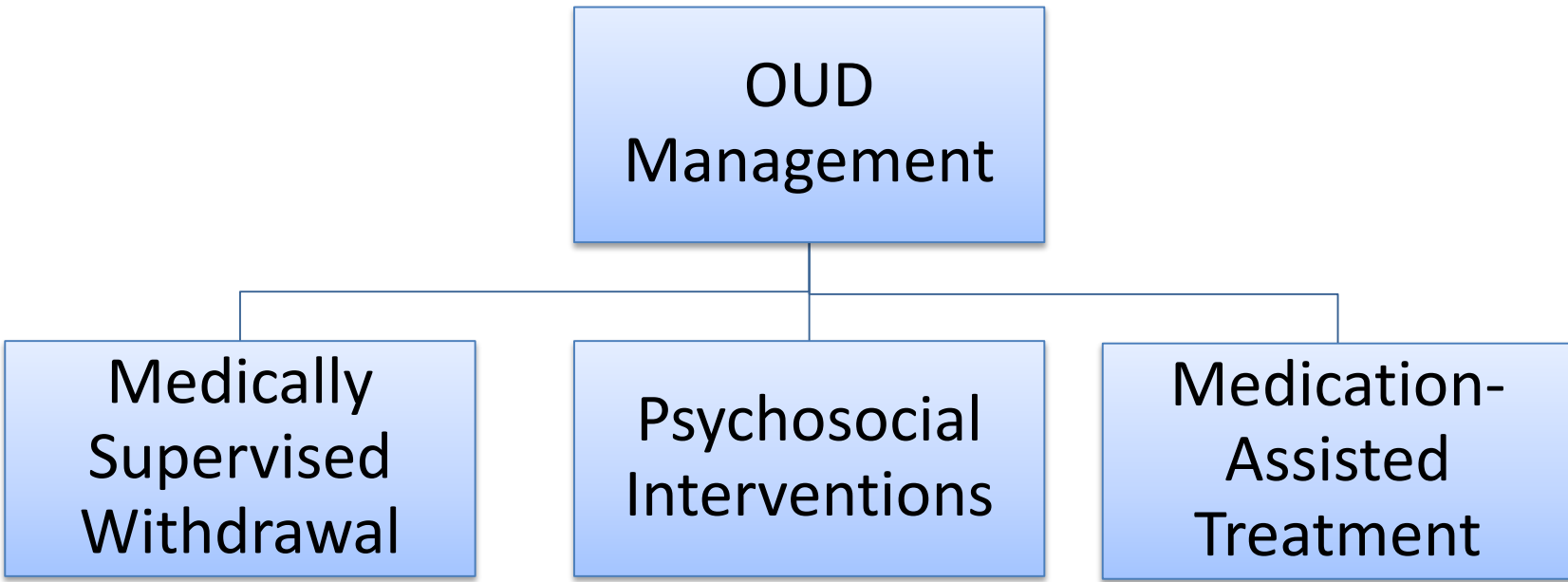


Management of Opioid Use Disorder

Jane Deaux

- Admits to having a problem
- Asks for help







Medically Supervised Withdrawal

- Cessation or dramatic opioid dose reduction.
- Spontaneous withdrawal*.
- Meds-opioid agonists, alpha-2 adrenergic agonists**.
- Titrate to dose that controls symptoms.
- Taper.
- Protocols available
- Immediate goals:
 - (1) Safe withdrawal
 - (2) Protect patient dignity
 - (3) Prepare for ongoing treatment
- **One component of a comprehensive, ongoing treatment strategy.**
- High relapse rate

*Objective withdrawal scales are available.

**Not FDA approved for withdrawal management.

ASAM Handbook of Addiction Medicine, 2016.



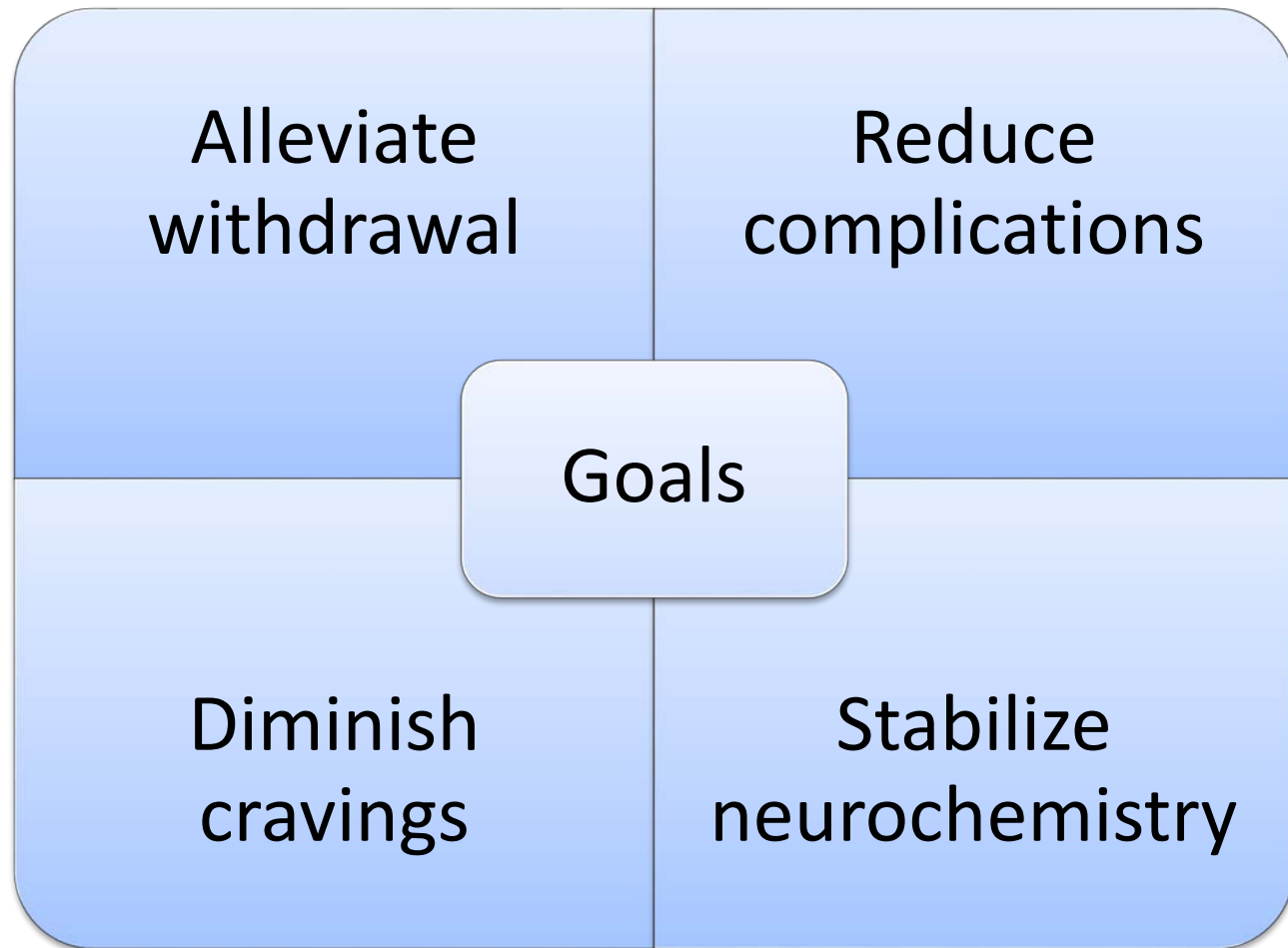


Psychosocial Treatment

- Brief interventions
- Motivational enhancement
- Self-Help Groups
- Drug Counseling
- Drug Courts
- Residential Treatment
- Analytic Psychotherapy
- Behavioral Therapy
- Cognitive-behavioral tx
- Coping skills tx
- Relapse prevention tx
- Network tx
- Mindfulness-based tx
- Contingency mngmt
- Community reinforcement

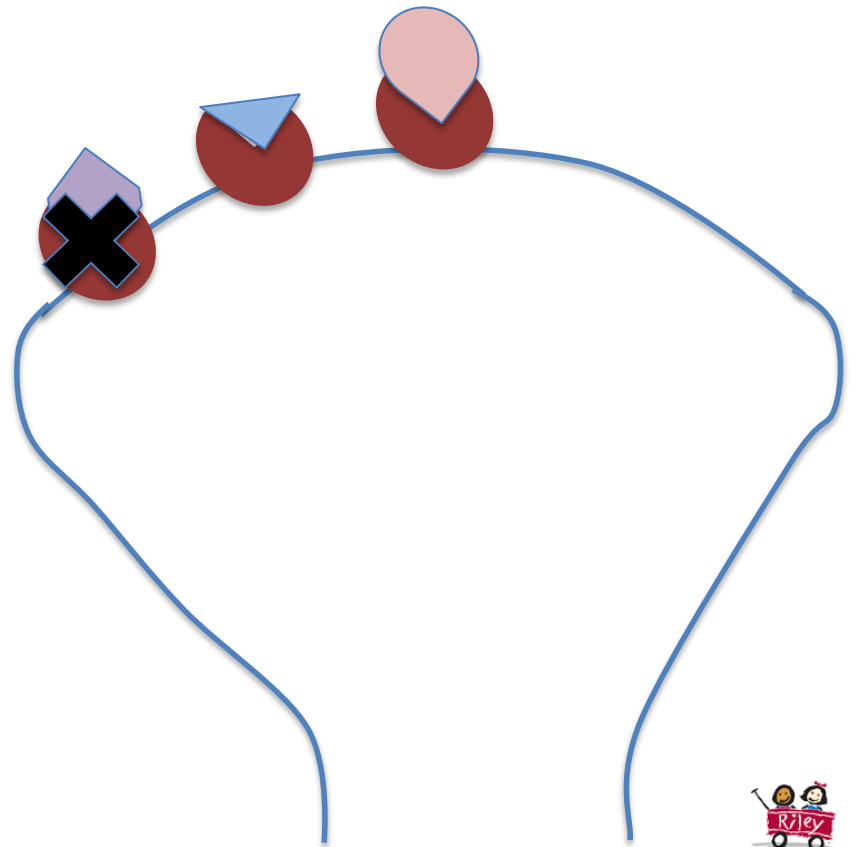


Medication-Assisted Treatment (MAT)

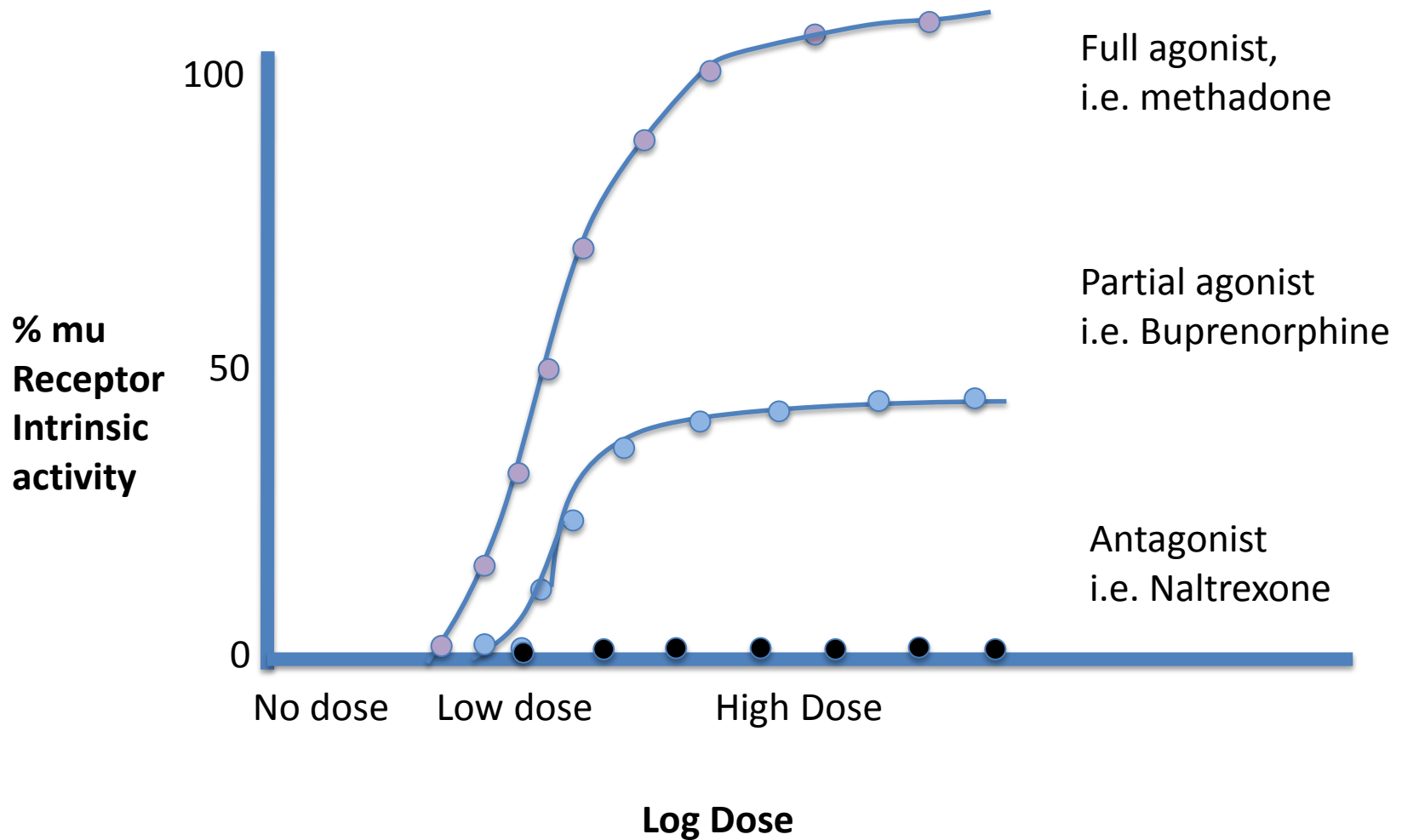


Medication Assisted Treatment

- **Methadone**
 - Long-acting, **full opioid agonist** that is slowly metabolized and has high fat solubility.
- **Buprenorphine**
 - Short-acting, **partial opioid agonist** with high affinity, low intrinsic activity, and slow dissociation.
- **Naltrexone**
 - **Opioid antagonist** that blocks opioid receptors, preventing opioid binding & effects.



Dose-response effect



Methadone

- Oral onset of action 30-60 min
- Duration of action
 - 24-36 hours to treat OUD
 - 6-8 hours to treat pain.
- Dosing-Acute Withdrawal:
 - 10-30mg then 5 mg q6 prn.
 - Not to exceed 40mg in first 24hrs.
 - Administer 24hr requirement as a single dose the next day.
- Dosing-Maintenance:
 - Increase every 2-5 as needed
 - Goal of treatment is to reduce cravings and illicit use.
- Dispensing for OUD limited to licensed facilities.
- Daily nursing assessment, weekly counseling, random supervised drug testing, & psych services available.
- Low overdose risk.
- Abuse potential with prescriptions for pain.
- Pregnant women on higher doses are less likely to relapse.

Buprenorphine

- Sublingual tablets and films.
- “**Combo**” (bup/naloxone).
- “**Mono**” (buprenorphine only).
 - Approved for mod-severe OUD
 - **OFF LABEL** for pain
- Parenteral and transdermal patch.
 - Approved for pain
 - Not approved for OUD
- Standard urine drug screen won’t be opioid positive.
- Prescribers required to complete 8hr CME & apply for a DEA waiver.
www.samhsa.gov
- Overdose risk minimal.
- Abuse potential less than with full opioid agonists.
- Most illicit use is to prevent or treat withdrawal and cravings.
- Buprenorphine and high-potency benzodiazepines...DEATH.
- Less NAS

Comer, S, Addiction. 2010.

Lofwall MR, et al. J Addic Med. 2014.


Yokel MA, et al. Curr Drug Abuse Rev. 2011





Buprenorphine Dosing

- **Acute Withdrawal:**
 - Optimal regimen not established.
- **Induction:**
 - 4mg when COWS \geq 8
 - Increase by 2mg q2-4h as needed.
- Day 2-
 - If day 1 total was 8-12mg, give 8mg. If symptoms, give 12mg.
- If symptoms return later in the day, give 4mg.
- Try not to dose beyond 16mg during induction.
- DC with 1 week f/u
- Continue titration outpatient
- Max dose may exist in some states
- Research needed



Purpose of Naloxone in Combination Product

- Limited oral & sublingual bioavailability
- Active when injected (SQ, IM, or IV).
- If the combo product is crushed, dissolved, and injected:
 - Naloxone will block the opioid agonist effect of buprenorphine.
 - This causes withdrawal if opioid dependent.
 - Decreases misuse.
 - Safer if diverted.

Pregnancy: Myths & Management



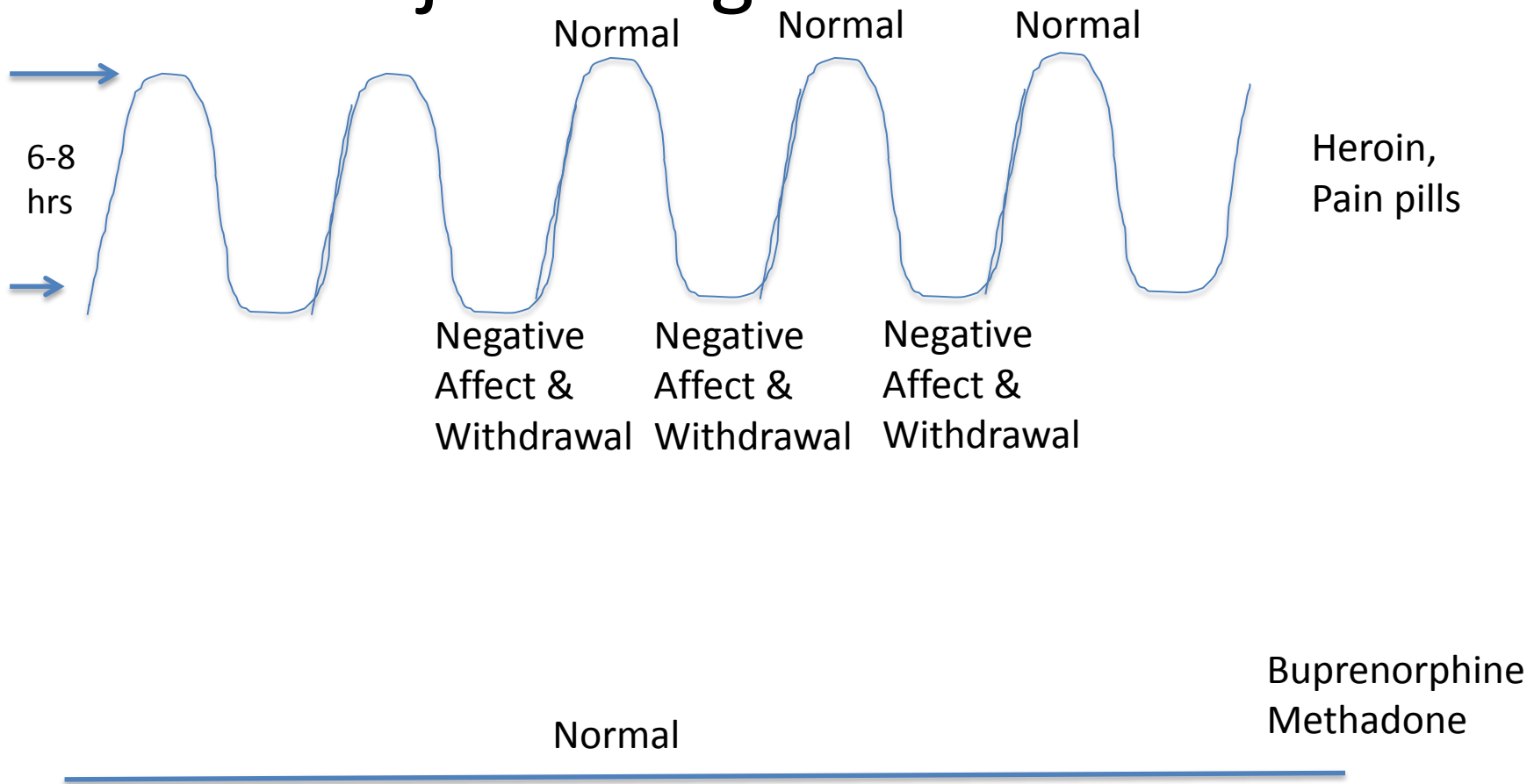
Jane Deaux

- Positive urine pregnancy test during admission.
- Discharged with a prescription for buprenorphine instead of buprenorphine/naloxone.
- She calls with questions about “detox” due to neonatal concerns.
- She also desires detox because her family has told her:
- Bup is just a legal form of heroin.
- Baby will be born addicted.
- If she cares about her baby, she would just stop using anything.



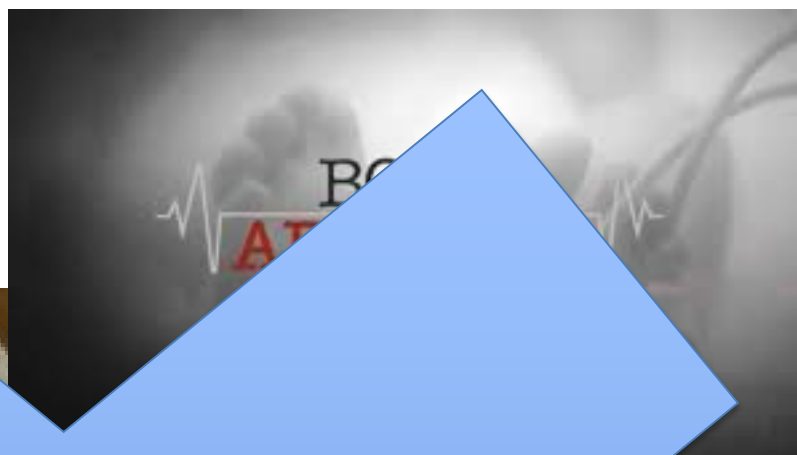
MYTH ONE

MAT is just a legal form of heroin





MYTH TWO



MYTH



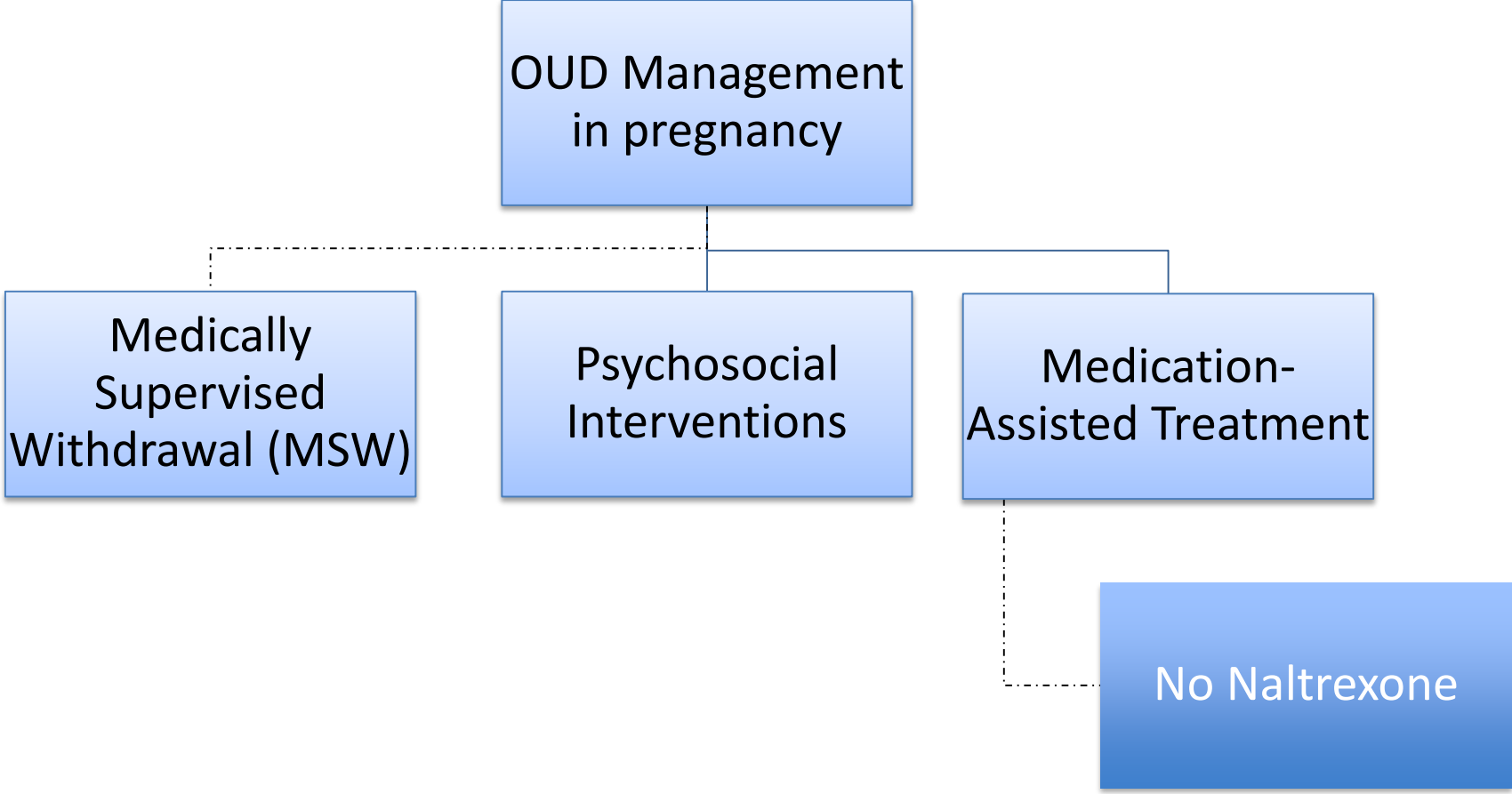
Neonatal Opioid Withdrawal Syndrome

- Aka Neonatal Abstinence Syndrome (NAS)
- Symptoms that occur in newborns with in utero exposure to opioids.
- MAT dosage does not correlate with onset or severity.
- Mild symptoms can be managed with supportive care measures, while more severe symptoms require pharmacologic intervention.
- Can result in NICU admission (though not required) and prolonged hospital stay.
- Self-limited condition with no PROVEN long term effects.

MYTH THREE

...If she cares about her baby, she should just stop (detox).





Historically, why has detox not been recommended in pregnancy?





1964

Narcotic withdrawal in pregnancy: Stillbirth incidence with a case report

JOSÉ LUIS REMENTERÍA, M.D.

NEMESIO N. NUNAG, M.D.

Bronx, New York

A stillborn infant was born to a drug-addicted mother who had withdrawal symptoms shortly before delivery. Mechanisms are presented to help explain the possible relationship between the maternal withdrawal and the fetal death. Statistics are also presented to show an increased stillborn and neonatal mortality rate in the over-all pregnant drug-addicted population.





1974

Fetal stress from methadone withdrawal

FREDERICK P. ZUSPAN, M.D.

JANIS A. GUMPEL, M.D.

ALFONSO MEJIA-ZELAYA, M.D.

JOHN MADDEN, M.D.

ROY DAVIS, D.M.N.

With the technical assistance of

MARGARET FILER, B.A.

ADEL TIAMSON, B.A.

Chicago, Illinois

A pregnant patient in the midtrimester of pregnancy was begun on a methadone detoxification program. The fetal neurobiologic response was monitored by serial amniotic fluid amines (epinephrine and norepinephrine). The detoxification program showed a marked fetal response of the adrenal gland (E) and sympathetic nervous system (NE) that was blunted when the methadone dose was increased. Detoxification during pregnancy is not recommended unless the fetus can be biochemically monitored.



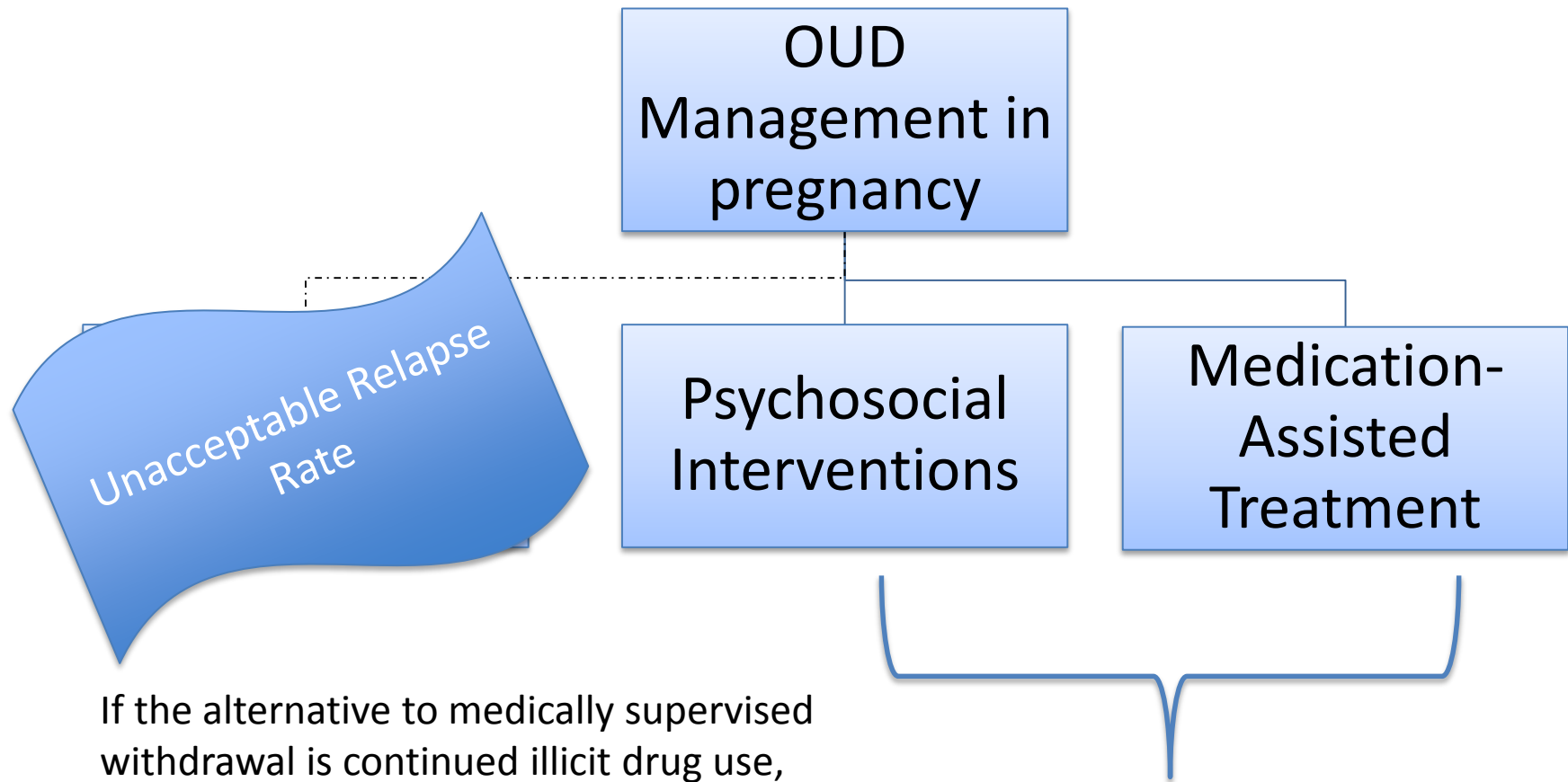
Medically Supervised Withdrawal in Pregnancy: Contemporary Data

	# pts / # yrs	Outcomes: Methadone Detoxification in Pregnancy
Maas et al, 1990	57 / 7	17 (30%) became drug free. No adverse outcomes due to detox reported.
Dashe et al, 1998	34 / 7	20 (59%) successful. No fetal distress or demise. 4 went into labor (3 at 36wks, 1 at 37wks).
Luty et al, 2003	101 /12	One 1 st trim SAB. 2 perinatal deaths. 34 neonates <2500g. One delivery <37wks. (50% of pts were actively using heroin.)
Jones et al. 2008	175 / 4	No increased risk in preterm birth or fetal loss.
Stewart et al, 2013	95/ 6	53 (56%) successful. No fetal distress or demise.
Bell et al, 2016	301	53 (17.6%) prior to 37 weeks. No adverse outcomes.



Contemporary Data Shows

- Detox may be safe in pregnancy, BUT...
- Low rates of detox completion.
- High rates of post-treatment relapse.
- Relapse is associated with increased risk for HIV, hepatitis, overdose, and death.
- Detox for prevention of NAS is not supported.



If the alternative to medically supervised withdrawal is continued illicit drug use, Then detox is preferable.

ACOG Committee Opinion No. 524, 2012.

Preferred





Other Management Considerations: Antepartum

- Coordinated care between OB, Addiction medicine, Behavioral health → MFM not required!
- Increased or split dosing may be required.
- Avoid benzodiazepines, and other CNS depressants.
- Overdose education/Narcan kit.
- Counsel on measures for NAS reduction, contraception, breastfeeding
- Screen for: Intimate partner violence (IPV), adverse childhood events (ACE)
- Assess social determinants of health
- Ultrasound
- Growth scan 28-32 weeks (unless an indication for serial scans exists)

Expert Opinion, President's Workshop on OUD in Pregnancy, SMFM, 2018

Other Management Considerations: Antepartum

- TB skin testing
- Test for Hepatitis C
- Assess Hepatitis A/B immunity → vaccinate if necessary
- EKG if methadone dose \geq 120mg
- Echo for history of endocarditis
- Dental care
- GI referral for Hepatitis C
- Consider anesthesia consult, pediatrics consult
- Shared decision making: postpartum pain management
- Use ASAM Criteria to establish level of care → residential, intensive outpatient, partial hospitalization, outpatient

Other Management Considerations: Intrapartum

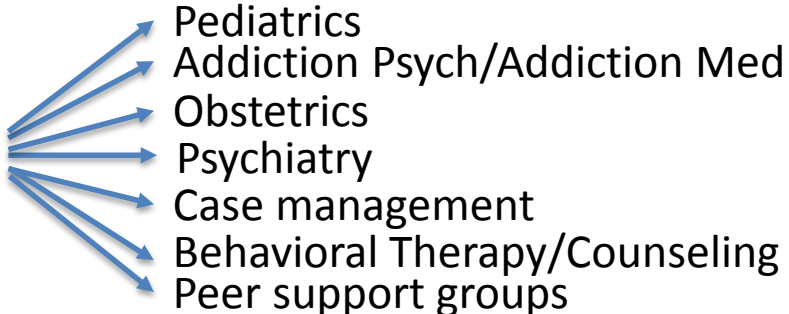
- Timing of delivery:
- Deliver for obstetric indications if stable in treatment.
- Consider early term delivery for ongoing illicit use & non-adherence.
- Continue MAT
- Avoid mixed opioid agonist-antagonists (butorphanol, nalbuphine, pentazocine).
- Neuraxial anesthesia recommended.

Expert Opinion, President's Workshop on OUD in Pregnancy, SMFM, 2018

Other Management Considerations: Postpartum

- Best practice for dosing reduction is undetermined (research needed).
- Ensure maternal stability in recovery.
- Ensure smooth transition of care.
- Ensure postpartum f/u with GI for Hepatitis C.
- Consider expanding Medicaid for up to a year postpartum.

Optimal Care

- Highlights the chronic nature of the disease
 - Woman-centered
 - Trauma-informed
 - Family support
 - Comprehensive
 - Mother-infant dyad
 - Co-location of services
- 
- Pediatrics
Addiction Psych/Addiction Med
Obstetrics
Psychiatry
Case management
Behavioral Therapy/Counseling
Peer support groups



Challenges in Care

- Late prenatal care
- Lack of Addiction Psychiatrists, Addiction Medicine Specialists, and providers with waivers to prescribe buprenorphine in IN.
- Few providers who will prescribe buprenorphine for pregnant women.
- Few providers who will accept “pregnancy medicaid.”
- Few Methadone Clinics/Inhibitory practices.



Challenges in Care

- Treating co-occurring psych diagnoses.
- Transitioning to a postpartum provider.
- Few inpatient rehabilitation facilities that will accept pregnant women or newly delivered women with their newborns.
- Substance use disorders are still viewed by many as a moral failure rather than a chronic disease.



Jane Deaux

- Delivers a 7lb. Boy at 38+9 weeks.
- Hospital stay is 13 days due to Neonatal Abstinence Syndrome.....

That's a talk for another day!





Take home points

- Opioid Use Disorder
 - Relapsing, remitting chronic disease
 - Pathophysiologic changes in the brain
 - Treatment available
- Medication Assisted Treatment is effective, safe, and preferred during pregnancy.
- There are challenges to care for all patients, but particularly for pregnant patients.





Take home points

- Opioid Use Disorder
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- There are challenges to care for all patients, but particularly for pregnant patients.



Questions

- www.samhsa.gov for more information on:
- Obtaining a DEA waiver.
- Physicians with DEA waivers by state.
- Treatment programs by state.

