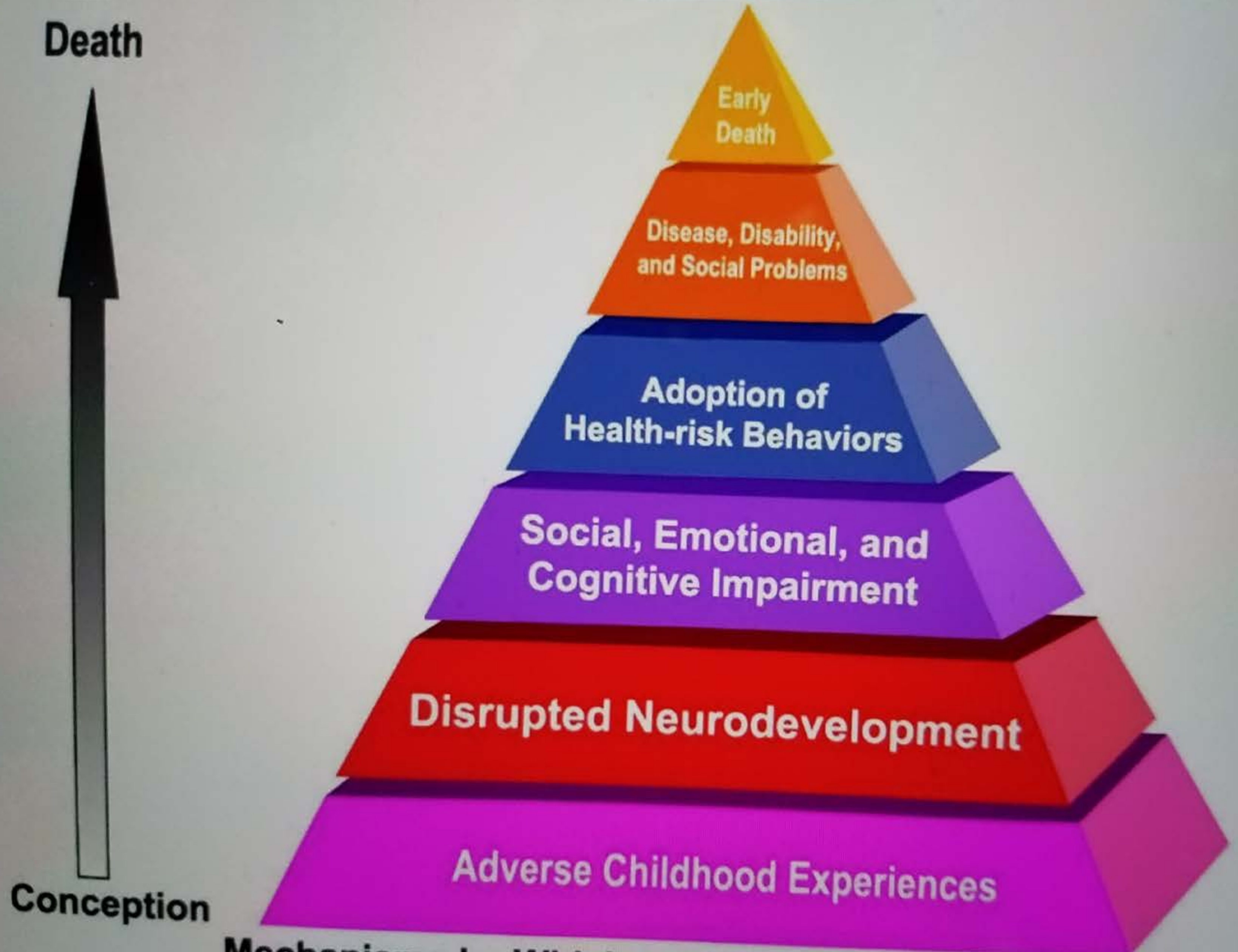
DANIEL A. NAUTS, FASAM

OPIOID-USE DISORDERS IN PREGNANCY

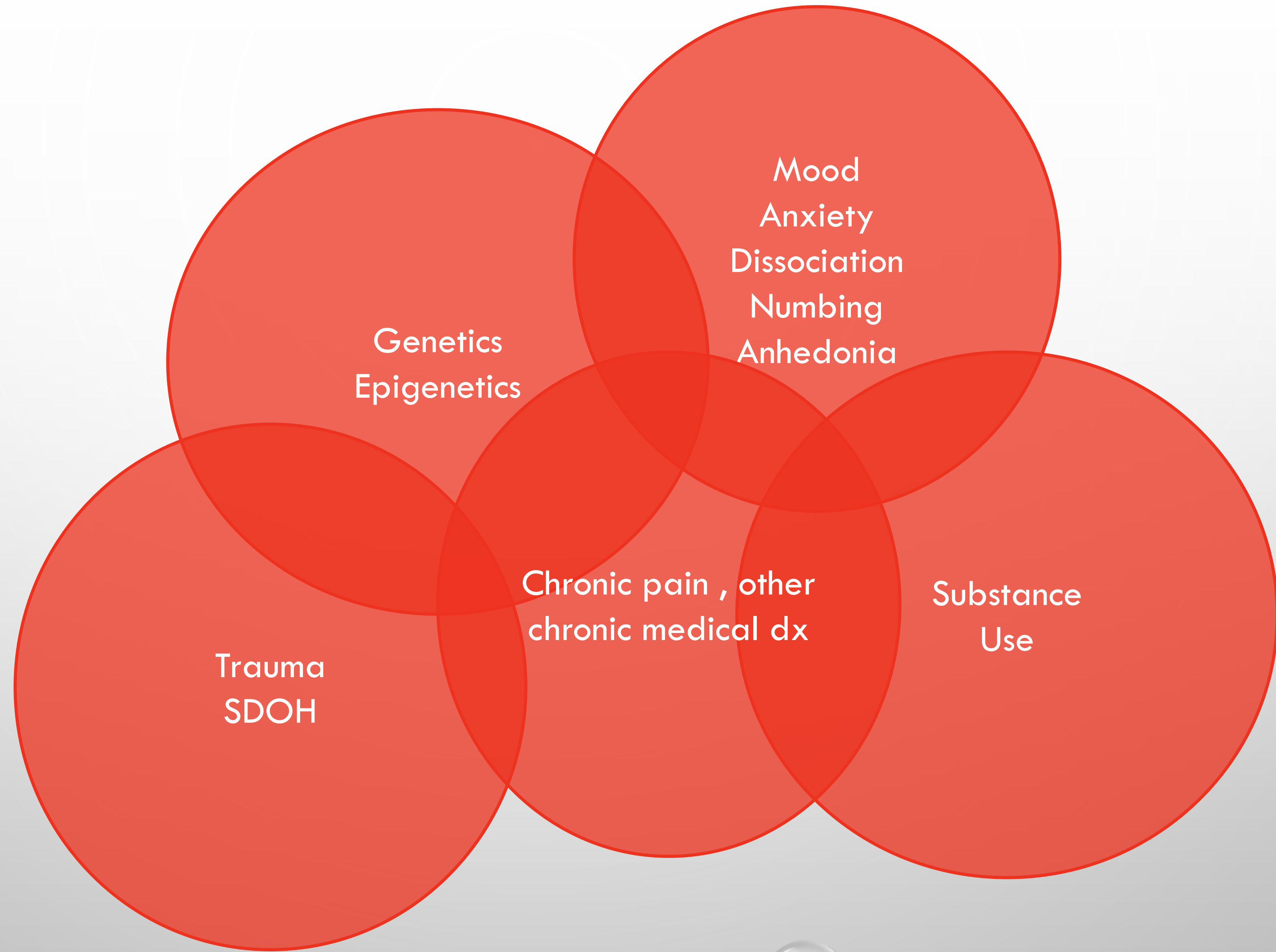
- MANAGEMENT GUIDELINES FOR IMPROVING OUTCOMES, EDITED BY TRICIA WRIGHT, CAMBRIDGE MEDICINE, 2018.

- WHY?

PEOPLE WHO HAVE ADDICTION OR A SUBSTANCE USE DISORDER ARE ILL WITH A CHRONIC BRAIN DISEASE



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


Mood
Anxiety
Dissociation
Numbing
Anhedonia
Genetics
Epigenetics
Chronic pain , other
chronic medical dx
Substance
Use
Trauma
SDOH

WHAT FACTORS CONTRIBUTE TO OUD?

Drug availability, peers who use drugs

Low hedonic tone with decreased capacity to experience pleasure

Chronic stress

Family problems

Early physical or sexual abuse

Adverse Childhood Events

TRAUMA WE DON'T TALK ABOUT

- JUDGMENTAL, MORALIZING, STIGMATIZING, AND PUNITIVE BEHAVIOR IN THE MEDICAL SYSTEM, SOCIAL SERVICES, AND LAW ENFORCEMENT
- PARADIGM SHIFT NEEDED
    - ACCEPTANCE OF HARM REDUCTION AS APPLICABLE TO ALL CHRONIC DISEASES
    - ADVOCACY OF SUBSTANCE USE DISORDERS AS CHRONIC BRAIN DISEASES WITH FREQUENT OVERLAP WITH CHRONIC PAIN, TRAUMA DISORDERS, AND MOOD AND ANXIETY DISORDERS
    - GENETIC AND EPIGENETIC VULNERABILITY
    - BELIEF IN THE SCIENCE
    - COMPASSIONATE, FRIENDLY, WARM, ENGAGING, TRUSTING, MOTIVATIONAL, LISTENING, ACCEPTING, AFFIRMING, REWARDING, POSITIVE, REASSURING, ADVOCATING, AND SO ON

DELIVERY EXPERIENCES IN THE HOSPITAL (N=11)

- PERCEIVED JUDGMENTAL TREATMENT BY HOSPITAL STAFF, RELATED TO BEING ON MAT(11)
- DESCRIBED SPECIFIC NURSE JUDGMENTAL TREATMENT OR PUNITIVE TREATMENT (6)
- MAT DOSING DELAYED OR DISRUPTED (4)

- OSTRACH, ET AL, AMBIVALENCE IN PERINATAL SUBSTANCE USE TREATMENT, J ADDICT MED, 13: 264-271, JULY/AUGUST 2019

STIGMA

- PREGNANT WOMEN WITH SUD FEEL INTENSE SHAME AND GUILT
- FEAR OF BEING "LABELED" MAY BE BARRIER TO ACCEPTING MAT, FEAR OF ATTITUDINAL CHANGE IN PROVIDERS, PHARMACISTS, PROVIDER SUPPORT STAFFS
- PREGNANT WOMEN FEAR DISCLOSURE TO SPOUSE/PARTNER, FAMILY AND HEALTH CARE PROVIDERS

WHY DO PEOPLE TAKE DRUGS?

To Feel Good

To have novel feelings, sensations, experiences, & to share them, to belong, change persona

To Feel Better

To lessen anxiety, worries, fears, depression, pain, hopelessness, & withdrawal, and to function

PREGNANCY: SUBSTANCE USE DISORDER

Women with substance use disorders often experience dysregulation of their menstrual cycle

Chronic opioid use alters dopamine/prolactin levels in hypothalamic-pituitary axis leading to amenorrhea and unpredictable cycles

Menstrual cycle alterations can lead to unplanned and often unrecognized pregnancies with delayed initiation of prenatal care

LaRose AT, Jones HE. Women's health and pregnancy. Office-Based Buprenorphine Treatment of Opioid Use Disorders. 2nd edition. 2018

PREGNANT WOMEN WITH POSITIVE URINE DRUG TEST

- ONLY 50% DISCLOSED SUCH USE TO THEIR PROVIDER DESPITE BEING SCREENED FOR USE
- A POSITIVE URINE DRUG TEST **DOES NOT EQUAL ABUSE, NEGLECT, OR ABANDONMENT**

BUT, WHAT ABOUT TOBACCO, ALCOHOL, BENZOS

- WE CAN MEASURE COTININE, ETG, ETS, BENZOS
- EVIDENCE IS CLEAR-CUT FOR SIGNIFICANT FETAL EFFECTS OF THESE SUBSTANCES AND NOT NECESSARILY FOR ILLICITS—YET GENERALLY NOT REPORTED

RACIAL DISPARITIES

- PEOPLE OF COLOR MORE LIKELY TO BE SCREENED AND REPORTED RELATIVE TO WHITE PATIENTS—IF WE SCREEN, MAKE IT UNIVERSAL IRRESPECTIVE OF COLOR, ETHNICITY, AGE, GENDER,SEXUAL IDENTITY, SOCIOECONOMIC STATUS, ETC.
- CLINICIANS HAVE AN ETHICAL RESPONSIBILITY TO INFORM PATIENTS ABOUT MANDATORY REPORTING POLICIES AND TO ADVOCATE AGAINST STATE POLICIES THAT ARE PUNITIVE IN NATURE(ACOG2015)
- AMERICAN ACADEMY OF PEDIATRICS RECOMMENDS PROVIDERS BE KNOWLEDGEABLE ABOUT MANDATORY REPORTING REQUIREMENT AND COMMUNICATE WITH FAMILIES ABOUT MANDATORY REPORTING AND THE RESOURCES AND SERVICES AVAILABLE TO SUPPORT FAMILIES

ASAM

- HEALTH CARE PROVIDERS SHOULD BE AWARE OF MANDATORY REPORTING POLICIES AND THAT PREGNANT WOMEN SHOULD NOT BE SUBJECT TO PUNITIVE LEGAL CONSEQUENCES SOLELY BASED ON SUBSTANCE USE(ASAM 2017).

EPIDEMIOLOGY: OUD AND PREGNANCY

5.4% of pregnant women ages 15-44 used illicit substances

- Higher in young women with 14.6% in women 15-17 years vs. 3.2% in women 26-44 years

~21,000 pregnant women aged 15 to 44 misused opioids in the past month

Between 2000 - 2009 the prevalence of opioid use among women who gave birth increased from 1.2 to 5.6 per 1,000 births annually

LaRose AT, Jones HE. Women's health and pregnancy. Office-Based Buprenorphine Treatment of Opioid Use Disorders. 2nd edition. 2018

PREGNANCY: OPIOID AGONIST MAINTENANCE THERAPY REMAINS THE STANDARD OF CARE

Opioid agonist pharmacotherapy (either **methadone** or **buprenorphine**) is endorsed by the American College of Obstetricians and Gynecologists (ACOG) as the optimal treatment for OUD during pregnancy

Methadone and buprenorphine are safe and effective treatment options in pregnancy

Fischer et al. 1998, 1999. Jones et al. 2010.
Terplan M, et al. Obstetrics & Gynecology. 2018.

OPIOID DETOXIFICATION

- FETAL EXPOSURE TO FLUCTUATING LEVELS OF OPIOIDS WITH REPEATED WITHDRAWAL
  - IMPAIR PLACENTAL FUNCTION WITH DECREASED NEONATAL BIRTH WEIGHT, PRETERM LABOR, CONVULSIONS, POTENTIAL FETAL DEATH
- HIGH RISK OF MATERNAL RELAPSE AND RESUMPTION OF HIGH-RISK BEHAVIORS
- STANDARD OF CARE FOR PREGNANT WOMEN WITH OUD IS MAT WITH EITHER METHADONE OR A BUPRENORPHINE PRODUCT
- NALTREXONE IS NOT RECOMMENDED BECAUSE OF UNKNOWN SAFETY PROFILE IN PREGNANCY—LIMITED EVIDENCE OF NO PROBLEMS WITH WOMEN ESTABLISHED ON NTX

PREGNANCY
BENEFITS OF OPIOID AGONIST THERAPY

Maternal Benefits

- 70% reduction in overdose related deaths
- Decrease in risk of HIV, HBV, HCV
- Increased engagement in prenatal care and recovery treatment

Fetal Benefits

- Reduces fluctuations in maternal opioid levels; reducing fetal stress
- Decrease in intrauterine fetal demise
- Decrease in intrauterine growth restriction
- Decrease in preterm delivery

Klaman SL, et al. J Addict Med. 2017

USE OF BUPRENORPHINE DURING PREGNANCY: WITH OR WITHOUT NALOXONE

Consent

BUPRENORPHINE/NALOXONE

- NO KNOWN TERATOGENIC EFFECTS IN ANIMALS
- CONTROLLED STUDIES HAVE NOT BEEN CONDUCTED IN HUMANS
- INCREASING EVIDENCE THAT BUPRENORPHINE/NALOXONE MAY BE SAFE IN PREGNANCY
- HOWEVER, BUPRENORPHINE *WITHOUT* NALOXONE IS RECOMMENDED DURING PREGNANCY

Lund et al., 2013

Stop labeling babies as 'born addicted' — it stigmatizes them and is inaccurate

BY DR. LYNN WEBSTER, OPINION CONTRIBUTOR — 06/19/18 07:00 AM EDT
THE VIEWS EXPRESSED BY CONTRIBUTORS ARE THEIR OWN AND NOT THE VIEW OF THE HILL

- Generalized disorder with dysfunction of the autonomic nervous system, GI tract and respiratory system
- Occurs in 50-80% of infants with intrauterine exposure to opioid maintenance therapy
- Infants are passively physically dependent to opioids, **NOT** addicted

COGNITIVE AND MOTOR OUTCOME OF CHILDREN WITH PRE-NATAL OPIOID EXPOSURE(POE) SYSTEMATIC REVIEW AND METANALYSIS

- ESTIMATE THAT 6.3% CHILDREN WITH POE WILL HAVE AN IQ SCORE 2 SDS BELOW NORMAL WHEN COMPARED WITH ONLY 2.3% OF CHILDREN IN A NORMALLY DISTRIBUTED POPULATION
- SUGGESTS THAT CHILDREN WITH POE ARE 3X MORE LIKELY TO HAVE SEVERE INTELLECTUAL DISABILITY
- ALREADY VULNERABLE CHILDREN
  - TENUOUS LIVING SITUATION
  - INCREASED NEGLECT AND POSSIBLE ABUSE
  - PROPENSITY TO HAVE BEHAVIORAL AND ATTENTION DEFICITS
  - CONTRIBUTES TO POORER ACADEMICS, SOCIAL AND LIFESTYLE OUTCOMES
  - SU LYN YEOH, ET AL, JAMA NETW OPEN, 2019; 2(7)

NAS MANAGEMENT

Non-Pharmacologic Approaches

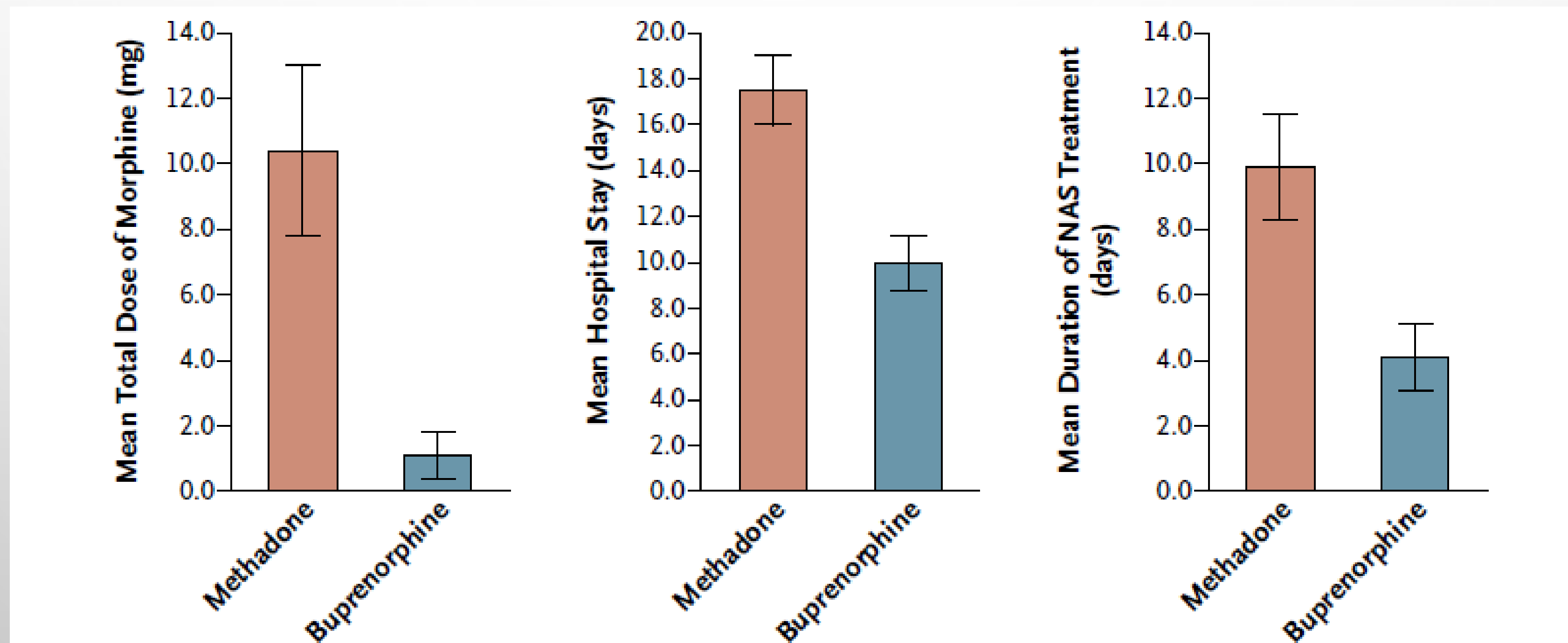
- Quiet dimly lit room, handled gently, swaddling, pacifier, gentle rocking
- Rooming In by keeping mother and baby together - reduction in NAS length of stay and cost
- Non-insertive acupuncture
- Breastfeeding recommended as it sooths agitated infants

Pharmacotherapy

- Oral morphine is preferred first-line medication

Bagley SM et al. Addiction Science & Clinical Practice. 2014

MATERNAL OPIOID TREATMENT:
HUMAN EXPERIMENTAL RESEARCH (MOTHER) STUDY



Jones et al., 2010

MAINTENANCE THERAPY IN PREGNANCY: NAS

META-ANALYSIS OF 12 STUDIES FROM 1996-2012

Showed buprenorphine exposed neonates (515) compared to methadone exposed (855) had…

- Shorter mean length of hospital stay (-7.23 days, 95% CI: -10.64, -3.83)
- Shorter NAS treatment duration(-8.46 days, 95% CI: -14.48, -2.44)
- Lower morphine dose (-3.60 mg, 95% CI: -7.26, 0.07)

Brogly et al. Am J Epidemiol. 2014;180(7):673-86

MATERNAL DOSE AND NAS SEVERITY

No correlation between maternal opioid maintenance therapy dose and the duration or severity of NAS

Women should be encouraged to report any symptoms of withdrawal through her pregnancy without fear a dose increase will affect her baby's hospital stay or need for NAS treatment

Tobacco use is strongly associated with NAS and NAS severity

Berghella et al. 2003; McCarthy et al. 2005; Cleary et al. 2010; Isemann et al. 2010; Jones et al. 2010; Seligman et al. 2011.

DOSING IN PREGNANCY—3RD TRIMESTER

- INCREASED CARDIAC OUTPUT
- INCREASED PLASMA VOLUME
- INCREASED CYP 3A4 ACTIVITY(INCREASE OF 35%)
- SALIVARY PH DECREASE MAY DECREASE ABSORPTION
- HIGHER DOSAGES AND NEED FOR SPLIT DOSING DUE TO INCREASED CLEARANCE
- MAY TAPER 4MG/WEEK POST PARTUM UNTIL AT PREVIOUS MAINTENANCE DOSE PRIOR TO PREGNANCY

- WRIGHT, ASAM, 2019

The transfer of methadone and buprenorphine into human milk is minimal and unrelated to maternal dose

Transferred amounts of methadone or buprenorphine are insufficient to prevent symptoms of NAS

Sachs et al., 2013; McCarthy JJ 2000; Begg EJ 2001; Jansson LM 2007 & 2008; Hale 2008; Grimm 2005; Lindemalm 2008; Ilett 2012.

BENEFITS OF BREASTFEEDING FOR NEWBORNS WITH NAS

30% decrease the development of NAS

50% decrease in length of neonatal hospital stay

Improved mother-infant bonding

Positive reinforcement for maternal recovery

Pritham UA et al. *J Obstet Gynecol Neonatal Nurs.* 2012. Welle-Strand GK et al. *Acta Paediatr*. 2013. Wachman EM et al. *JAMA.* 2013. Abdel-Latif ME et al. *Pediatrics*. 2006.

BREASTFEEDING

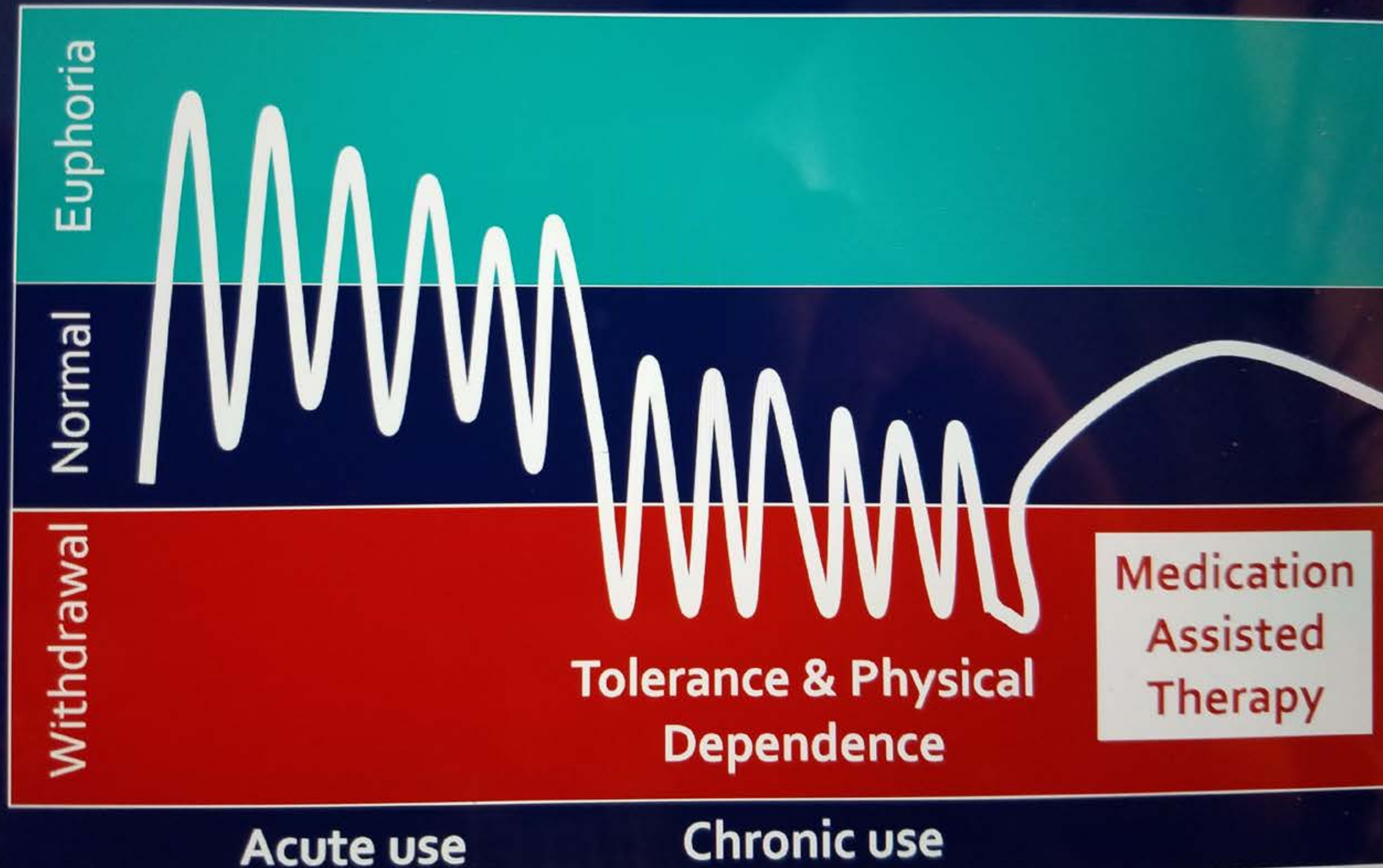
- HCV INFECTION IS NOT A CONTRAINDICATION TO BREASTFEEDING
  - UNLESS SHE DEVELOPS CRACKED OR BLEEDING NIPPLE
  - RECOMMEND TO PUMP/ DUMP UNTIL HEALED
- CONTRAINDICATIONS TO BREASTFEEDING
  - MATERNAL HIV INFECTION
  - CURRENT MATERNAL SUBSTANCE USE
  - MOTHER CURRENTLY UNDER THE INFLUENCE OF ILLICIT SUBSTANCE
  - RECENT HEAVY MARIJUANA USE
    - LIPOPHILIC, CONCENTRATION IN BREAST MILK
    - RECENT STUDY FOUND LITTLE THC IN BREAST MILK (BAKER ET AL. OB GYN. 2018)

THE 4TH TRIMESTER

- MATERNAL MORTALITY INCREASING IN THE USA—MATERNAL OVERDOSE LEADING CAUSE OF MATERNAL DEATH IN POST-PARTUM PERIOD. BLACK DEATHS 4X WHITE
- MAINTAIN THE HIGHER LEVEL OF CLINICAL ENGAGEMENT FOR AT LEAST A YEAR THOUGH MAY BE INSURANCE LIMITATIONS, ADVOCATE FOR INCREASED COVERAGE, MAINTAINING MEDICAID EXPANSION
- PROMOTE CONTRACEPTION AT LEAST FOR A YEAR AFTER DELIVERY, WOMEN WITH OUD LESS LIKELY TO USE CONTRACEPTION. IN WOMEN WITH OUD, POST-PARTUM 40% NO CONTRACEPTION
- TERPLAN, ASAM, 2019

4TH TRIMESTER

- CONTRACEPTION EMPOWERS WOMEN
  - NON-MEDICAL BENEFITS
    - EDUCATION
    - WORKPLACE PARTICIPATION
    - ECONOMIC STABILITY
- HUMAN RIGHT WHEN TO HAVE CHILDREN
- TERPLAN, ASAM, 2019


Opioid Agonist Therapy
Euphoria
Normal
Withdrawal
Tolerance & Physical Dependence
Medication Assisted Therapy
Acute use
Chronic use
ASAM
THE REVIEW COURSE
in Addiction Medicine

BUPRENORPHINE EFFICACY: SUMMARY

Studies (RCT) show buprenorphine (16-24 mg) more effective than placebo and equally effective to moderate doses (80 mg) of methadone on primary outcomes of:

- Retention in treatment
- Abstinence from illicit opioid use
- Decreased opioid craving
- Decreased mortality
- Improved occupational stability
- Improved psychosocial outcomes

Johnson et al. NEJM 2000; Fudala PJ et al. NEJM 2003; Kakko J et al. Lancet 2003; Sordo L et al. BMJ 2017; Mattick RP et al. Conchrane Syst Rev 2014; Parran TV et al. Drug Alcohol Depend 2010

IT IS NOT JUST MAT

01

Investing in community prosperity is component of efforts to counteract the effects of the opioid epidemic in remote rural counties

02

Prevention efforts must focus more broadly on reproductive age women

03

Punitive laws that discourage women from disclosing substance use during pregnancy must be amended.

04

Pregnant and postpartum women should have priority access to insurance coverage expansion programs and other programs supporting treatment continuation.

05

Increased risk for fatal and non-fatal OD postpartum