

# SACRED HEART

Everybody deserves a chance. 

# SUBSTANCE USE DISORDER IN PREGNANCY

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# DISCLOSURES

- No conflicts of interests or disclosures relevant to the content of this presentation.

# UNIQUE CONSIDERATIONS FOR PREGNANT PATIENTS

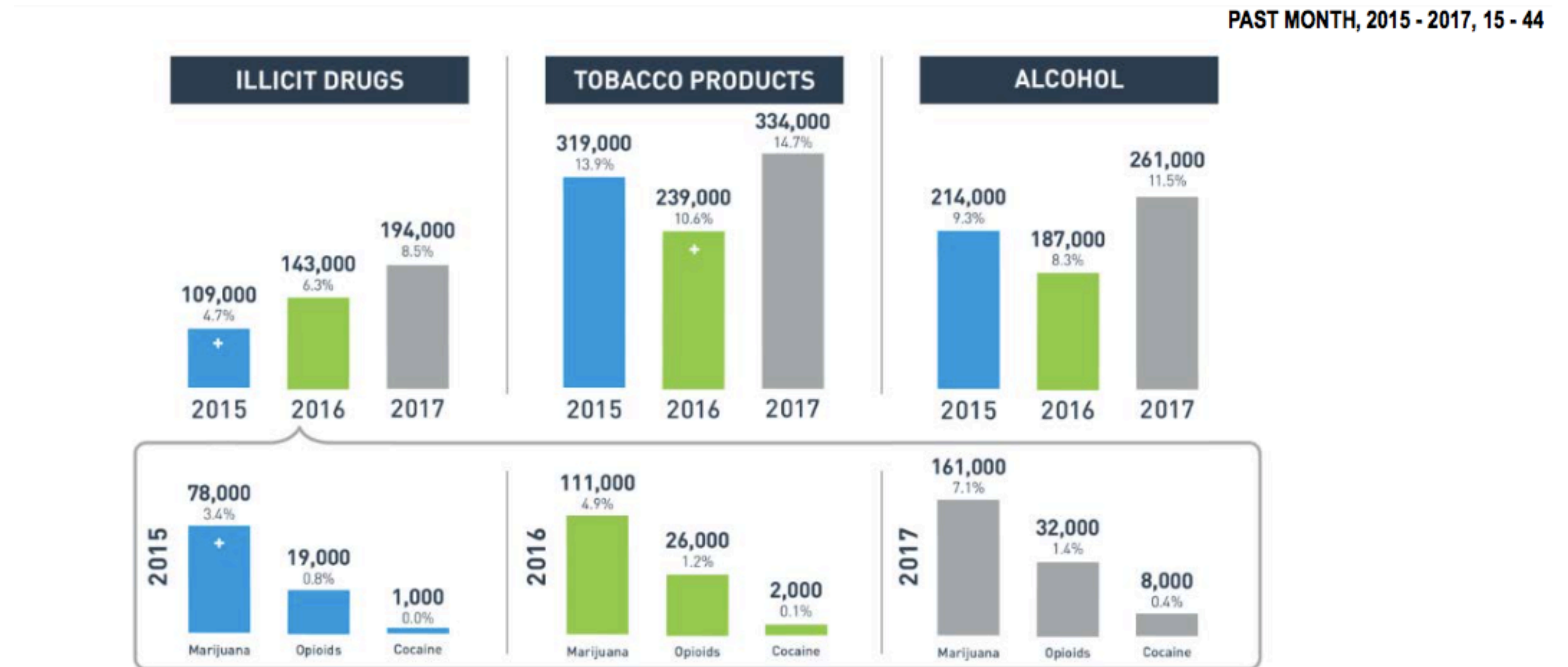
- Higher rates of domestic violence
- Fear of CPS intervention
- Childcare issues
- Stigma — high levels of shame and guilt
- Transportation issues
- Employment issues/Financial concerns
- Delayed realization of pregnancy (due to irregular menses)

# COMMON CHARACTERISTICS OF PREGNANT SUD PATIENTS

- Tend to be younger
- Emotionally labile/easily overwhelmed
- Highly Motivated to change
- Less ambivalent with willingness to change
- Shorter progression of disease
- Family support for treatment

# PREVALENCE IN PREGNANCY

- NSDUH illicit drug use INCREASED in pregnancy to 8.5% in 2017 (from 4.7% in 2016)
- 18-25y increase 8.6% to 11%
- 26-44y increase 5.2% to 7.2%



Special analysis of the 2017 NSDUH Report.

+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.

# ALCOHOL USE IN PREGNANCY

- NSDUH (2017) overall increase from 8.3% (2016) to 11.5% (2017) in past month alcohol usage
  - 18-25y increased 6.5% (2016) to 10.6% (2017)
  - 26-44y increased 9.1% (2016) to 11.7% (2017)
    - 1st Trimester 16.5% (2016) to 24.3% (2017)
    - 2nd Trimester 3.7% (2016) to 4.8% (2017)
    - 3rd Trimester 4.8% (2016) to 3.5% (2017)



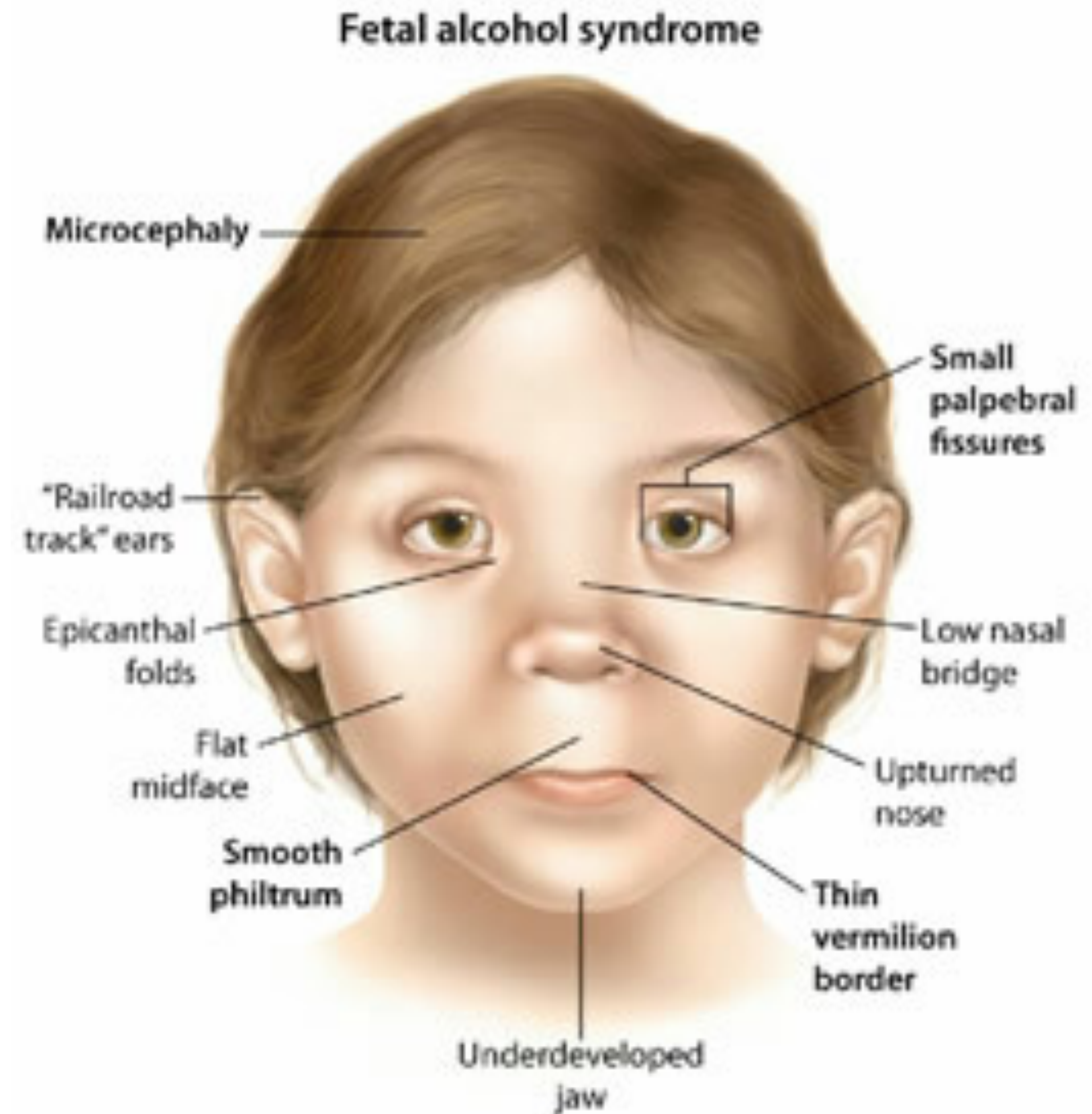
# FETAL ALCOHOL SPECTRUM DISORDERS

- Broad range of effects and symptoms from prenatal alcohol exposure
- Under diagnosed due to the difficulty of practitioners to distinguish from other developmental disorders
- More likely to suffer from mental health disorders — ADHD, Depression, Anxiety, Impulse control
- Neurodevelopmental disabilities/Cognitive Impairment/Behavioral Impairment
  - Communicating and socializing
  - Controlling emotions and impulsivity (misinterpret intentions-hit others)
  - Learning and remembering (Learning disabilities/cannot recall information)
  - Performing daily life skills (feeding, bathing, counting money, telling time)
  - Difficulty minding personal safety (do not perceive danger)
  - Shifting attention



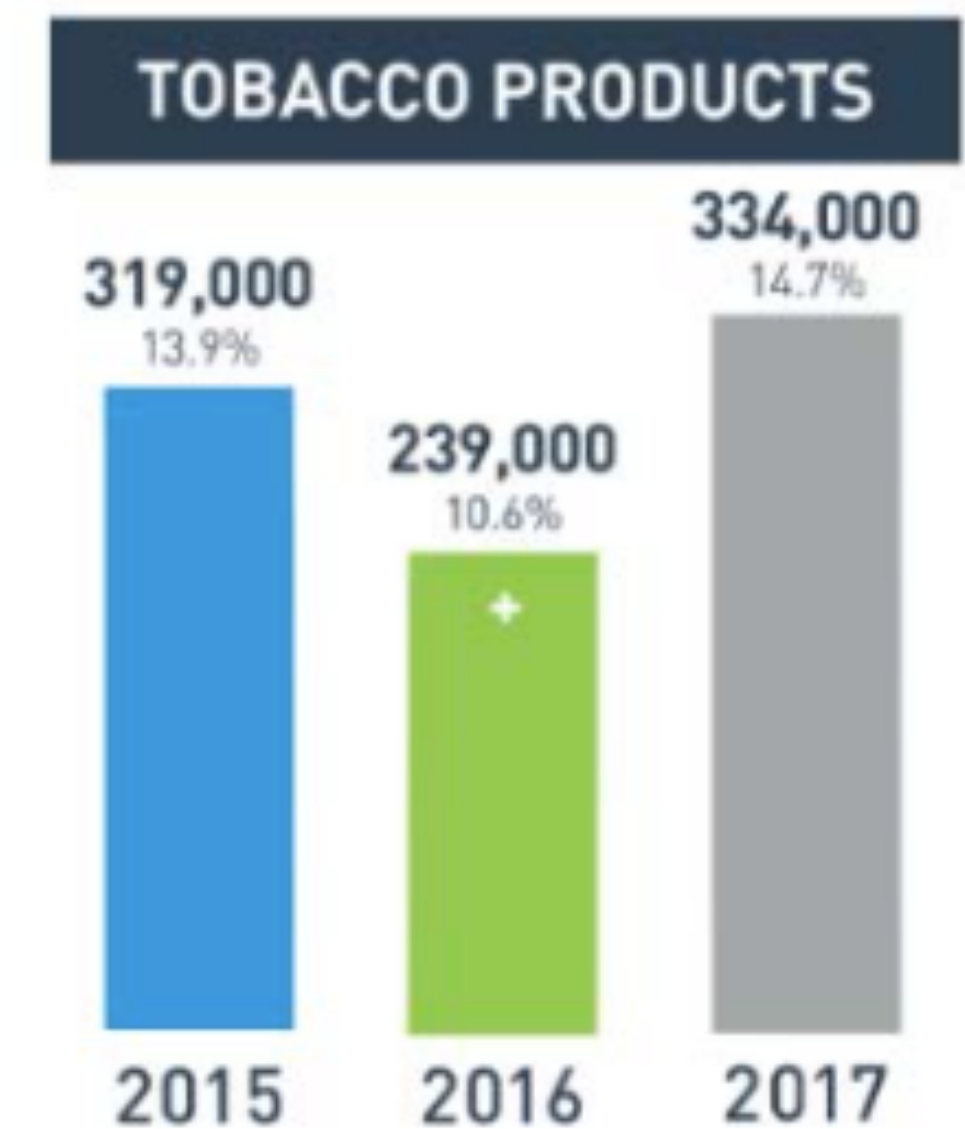
# FETAL ALCOHOL SYNDROME

- 2-5% of live births in the US
- Evidence of CNS abnormalities
- Growth deficiencies — short stature
- Abnormal facial features
  - Narrow eye openings
  - Smooth area between lip and nose
  - Thin upper lip



# TOBACCO USE IN PREGNANCY

- NSDUH overall increase from 10.6% (2016) to 14.7% (2017) in past month tobacco usage
  - 18-25y increased 13.5% (2016) to 21.2% (2017)
  - 26-44y increased 9.5% (2016) to 11.7% (2017)
    - 1st Trimester 13.7% to 18.8%
    - 2nd Trimester 12% to 11.9%
    - 3rd Trimester 6.4% to 13.8%



# TOBACCO USE IN PREGNANCY

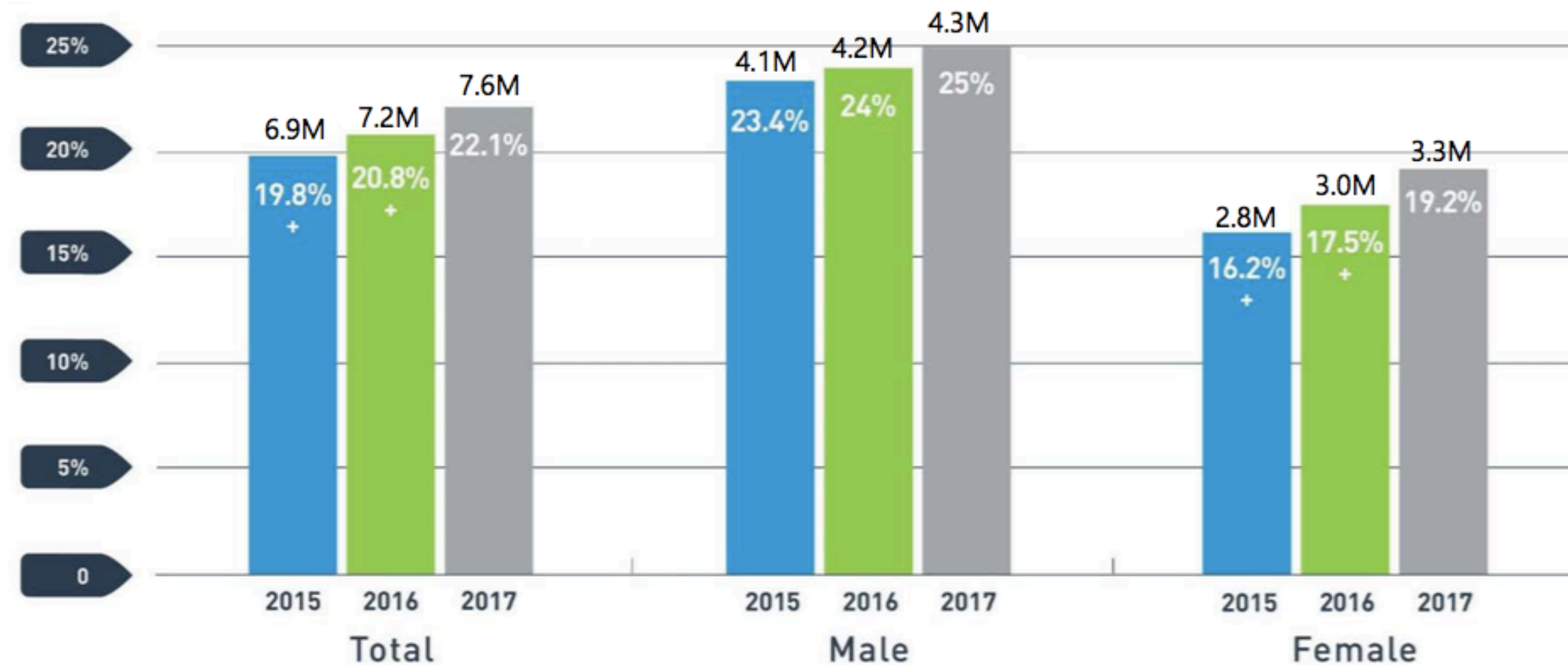
- Remains the most important modifiable cause of poor pregnancy outcomes in the US
- Quitting smoking before 15 weeks of gestation yields the greatest benefit
- Smoking cessation before the third trimester can eliminate much of the reduction in birth weight
- Adverse effects
  - Intrauterine growth restriction (IUGR)
  - Abruptio placentae
  - Placenta previa
  - Preterm premature rupture of membranes (PPROM)
  - Low birth weight

# INFANT OUTCOMES WITH TOBACCO EXPOSURE

- Preterm delivery/Prematurity — 5-8%
- SIDS — 23-34%
- Low Birth Weight — 13-19%
- Preterm deaths (Stillborn) — 5-7% (1.8-2.8 greater risk than nonsmokers)
- Increased childhood risks
  - Asthma
  - Infantile Colic
  - Childhood obesity

# CANNABIS USE IN FEMALES

PAST MONTH, 2015 - 2017, 18 - 25



Special analysis of the 2017 NSDUH Report.

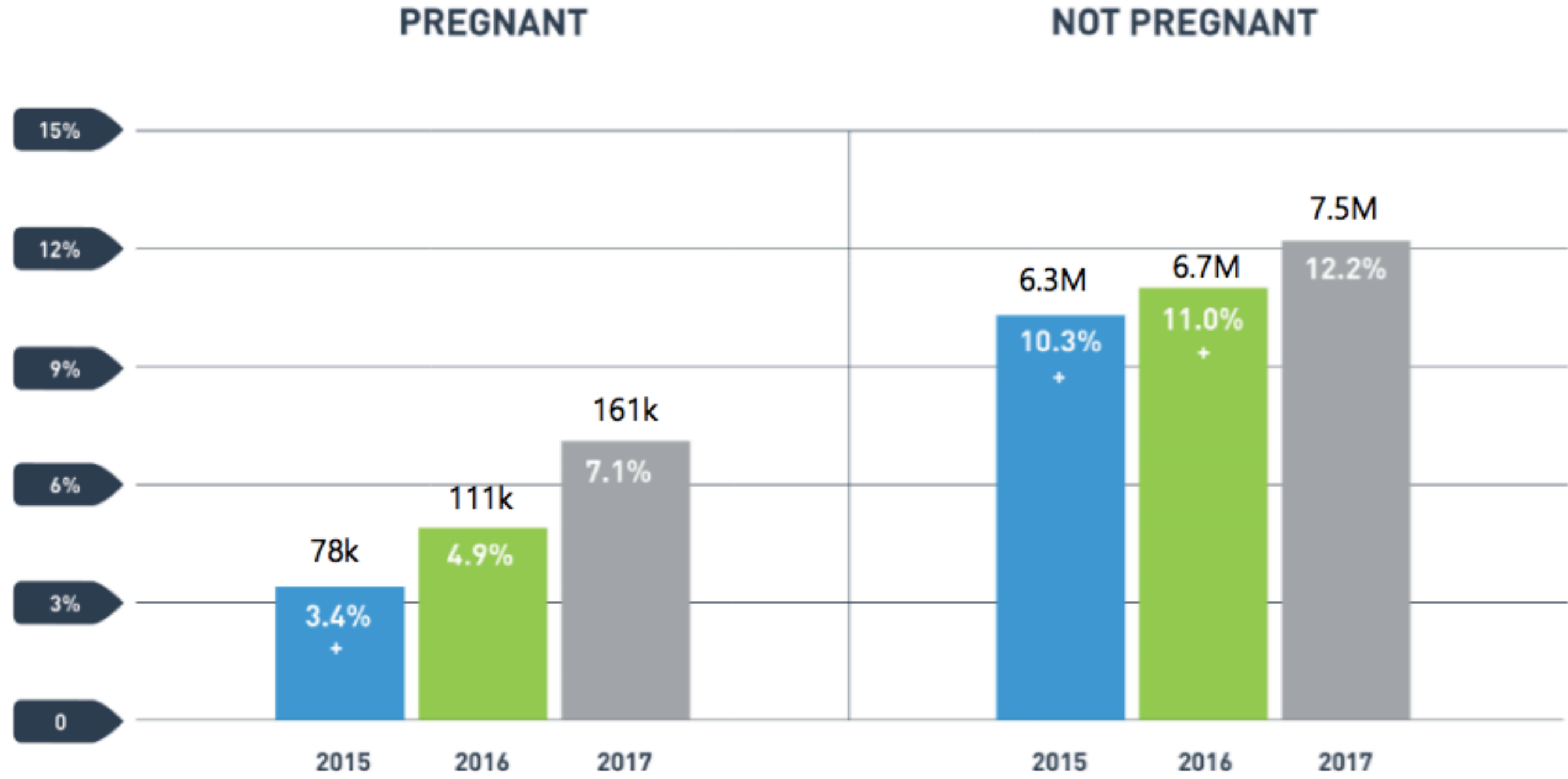
+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.



- Marijuana use among young adults (18-25): Significant INCREASES in Women from 16.2% (2015) to 19.2% (2017)

# CANNABIS USE IN PREGNANCY

PAST MONTH, 2015 - 2017, 15 - 44



Special analysis of the 2017 NSDUH Report.

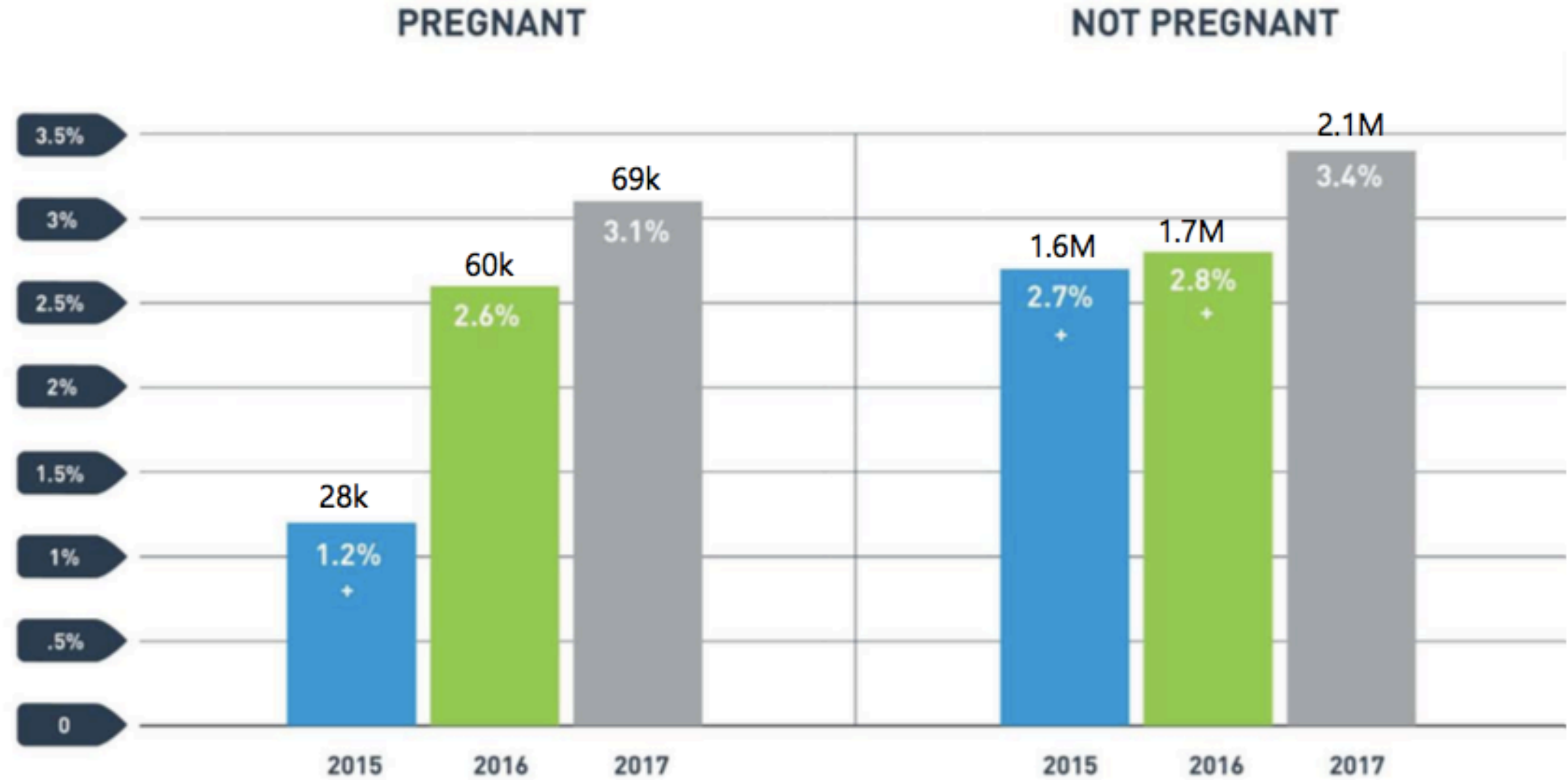
+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.



- Past month marijuana use in pregnancy 18-25y has INCREASED from 3.4% (2015) to 7.1% (2017)

# CANNABIS USE IN PREGNANCY

PAST YEAR, 2015 - 2017, 15 - 44



Special analysis of the 2017 NSDUH Report.

+ Difference between this estimate and the 2017 estimate is statistically significant at the .05 level.



- Past Year Daily Marijuana use in pregnancy 15-44y has INCREASED from 1.2% (2015) to 3.1% (2017)

# CANNABIS USE IN PREGNANCY

- Women contemplating pregnancy should be encouraged to discontinue use
- Women using marijuana weekly or more (especially during the 1st and 2nd trimester) are at an increased risk of
  - Smaller birth lengths and head circumference
  - Lower birth weights
  - Increased risk of preterm birth
  - Stillbirths (interpret with caution, could not adjust for tobacco use)
- Concurrent tobacco use may be an important mediator for some adverse pregnancy outcomes



# INFANT OUTCOMES WITH CANNABIS EXPOSURE

- Limitations to the data on cannabis use during pregnancy due to heavy polysubstance use (tobacco, alcohol, or illicit), lifestyle issues, and adverse socioeconomic conditions (poverty/malnutrition)
- Marijuana smoke contains many of the same respiratory disease carcinogenic toxins as tobacco smoke, often in concentrations greater than tobacco smoke
- Children exposed to marijuana in utero
  - Lower scores on tests of visual problem solving
  - Difficulties with visual motor coordination and visual analysis
  - Decreased attention span and behavioral problems
- Marijuana users were less likely to supplement folic acid

# OPIOID USE DISORDER IN PREGNANCY

- NSDUH annual average in 2017 of 32,000 pregnant women aged 15-44 misused opioids in the past month (increased from 26,000 in 2016)
- Past month opioid misuse increased from 0.3% (2016) to 1.2% (2017) in pregnant women age 18-25y and those aged 26-44y remained at 1.5% (2016) and 1.4% (2017)
  - 1st trimester (0.9%)
  - 2nd trimester (1.4%)
  - 3rd trimester (2%)

# OPIOID DEPENDENCE IN PREGNANCY-MATERNAL RISKS

- Overdose
- Infectious Disease
  - HIV
  - Hepatitis B and Hepatitis C
  - Infections-cellulitis, endocarditis
- Psychosocial challenges occurring with opioid use-prostitution, theft, violence, domestic violence, incarceration, poor engagement in prenatal care, legal consequences
- STI

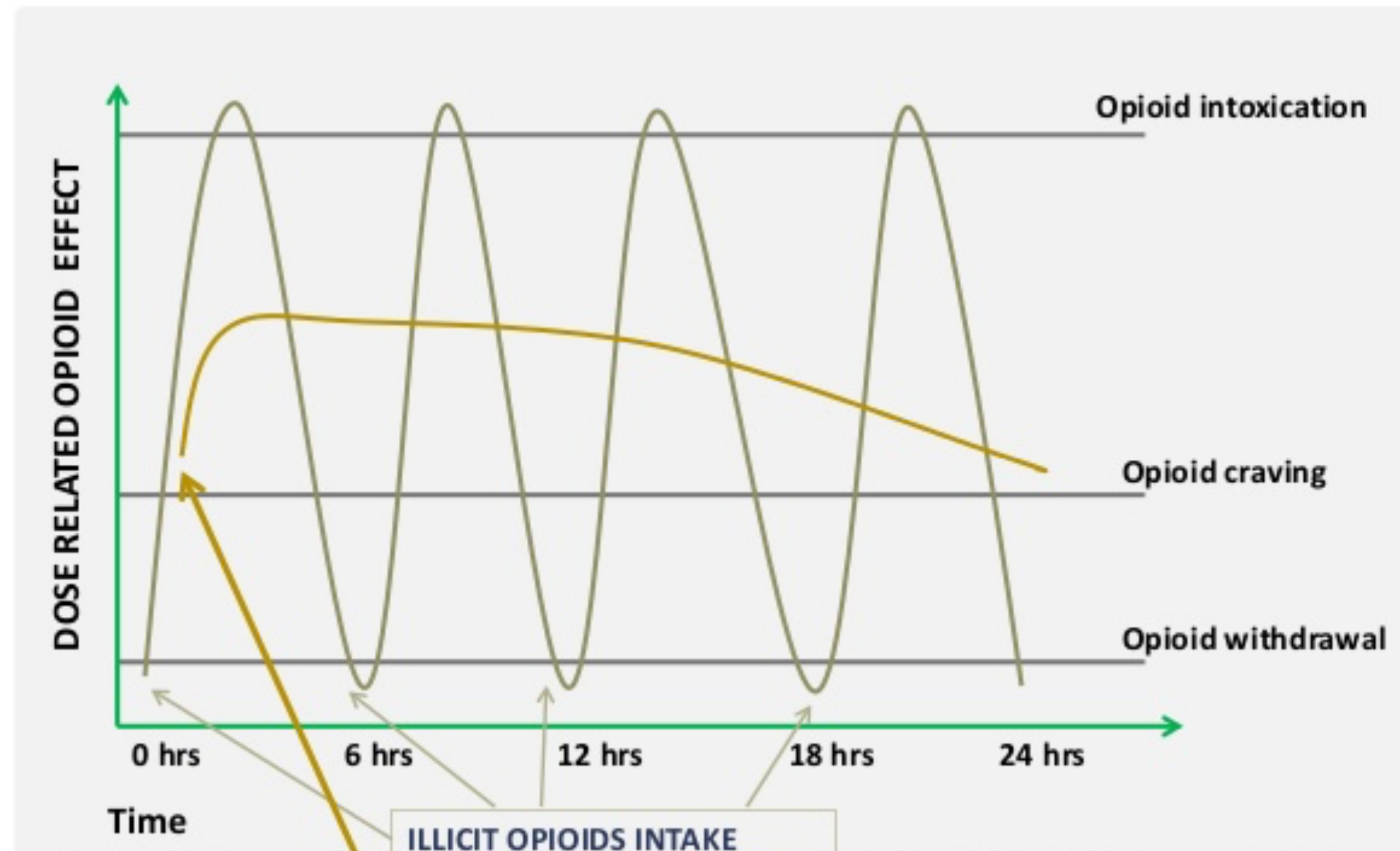
# OPIOID DEPENDENCE IN PREGNANCY-FETAL RISKS

- Fetal hypoxia
- Fetal growth restriction
- Abruptio Placenta
- Fetal death
- Intrauterine aspiration of meconium
  - Possibly related to cycles of maternal withdrawal/intoxication

# OPIOID DEPENDENCE IN PREGNANCY

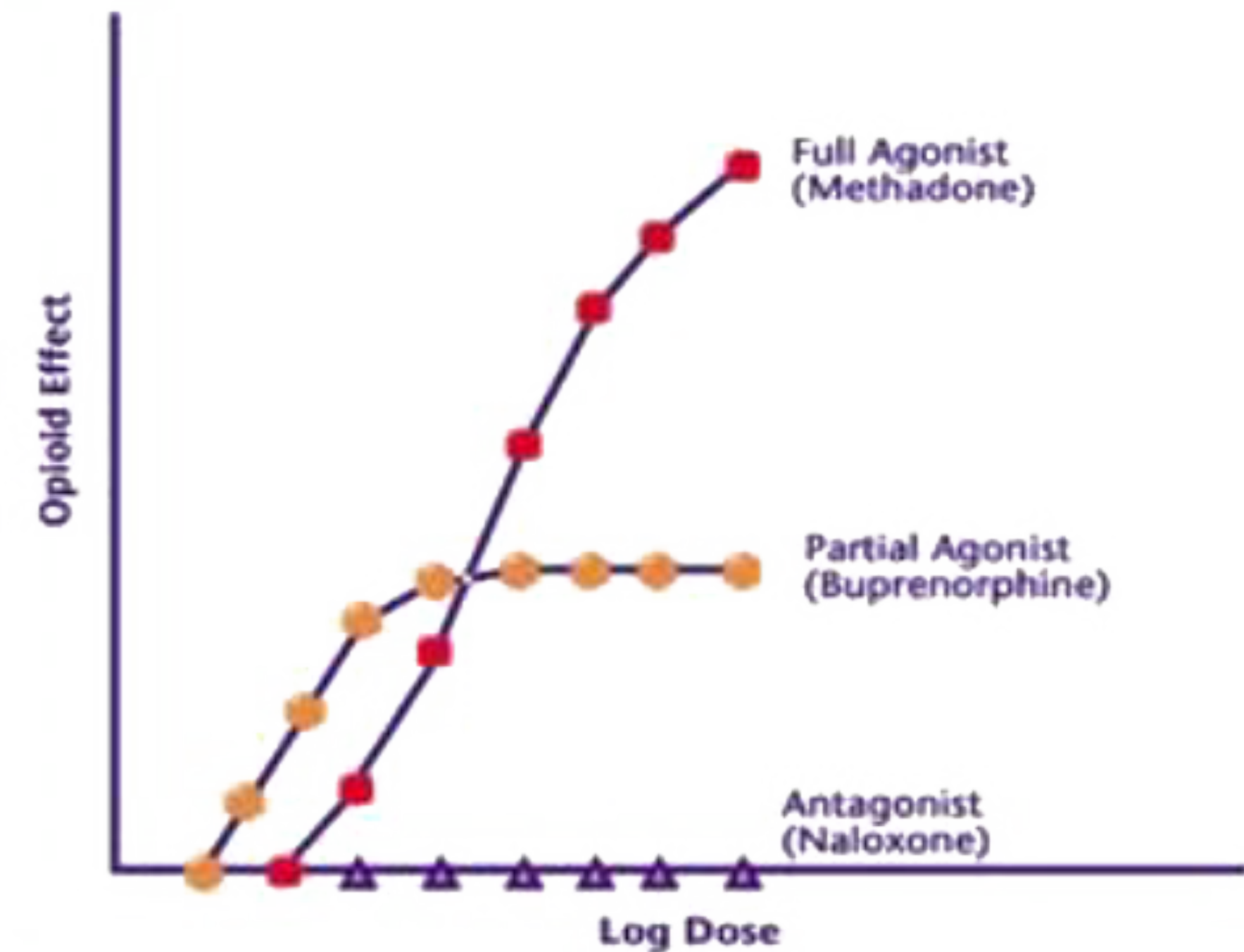
PICTORIAL REPRESENTATION OF LEVELS OF OPIOIDS IN BLOOD AT DIFFERENT TIME POINTS IN 24-HOURS CYCLE

- Postulated related to cycles of maternal withdrawal/intoxication



# MEDICATION ASSISTED TREATMENT- OPIOID DEPENDENCE IN PREGNANCY

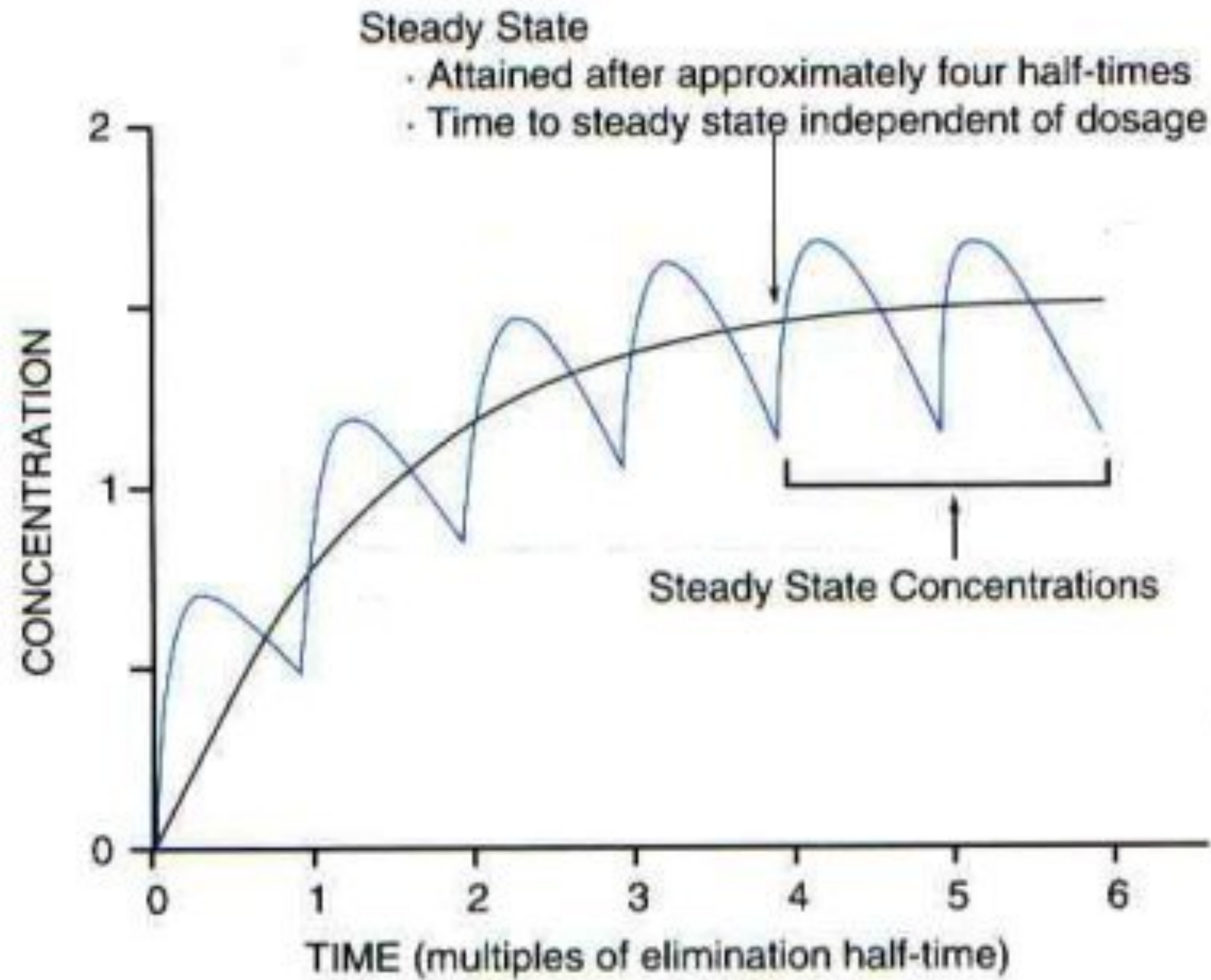
- Medication Assisted Treatment
  - Methadone
  - Buprenorphine
  - Naltrexone



# METHADONE

- Mu opioid receptor agonist and NMDA receptor antagonist
- Suppresses opioid withdrawal symptoms for 24 to 36 hours without causing sedation or intoxication
- Category C; Schedule II
- Blocks withdrawal symptoms, cravings, and reinforcing effects of opioids
- Requires 3-6 months to achieve stability
- Can correct many biological abnormalities present in opioid dependent individuals
- Start 20-40 mg (START LOW, GO SLOW)
- Adjustments in 5-10 mg increments every 3-7 days
- Daily dosing (half life 24-36 hours)
- Average dosage **80-120 mg** (150 mg)

# STEADY STATE ATTAINED AFTER 4-5 HALF-TIMES





# METHADONE DISTRIBUTION

- Methadone is distributed for MAT through licensed narcotic treatment program registered by the state (OTP)
- Requires physician to manage dosage
- Nurses to dispense methadone
- Dispensed as a liquid
- Set hours for administration
- Initial attendance to methadone program location daily
- Counseling/Psychosocial services
- Periodic toxicology screens (urine)

# METHADONE DOSING IN PREGNANCY

- Consider split dosing in pregnancy (in 2nd and 3rd trimester)
- Half life of methadone decreases from 22-24 hours in non pregnant woman to 8 hours in pregnant woman (Albright 2011)
  - Increased maternal weight
  - Increased intravascular volume (expanded volume of distribution)
  - Increased hepatic clearance and renal elimination
  - Decreased protein binding
- Dosage DOES NOT determine severity of NAS

# METHADONE

- Pros
  - Structured recovery environment
  - Medication and therapy at same place-OTP
  - More frequent monitoring
  - Decrease risk of IVDA associated diseases
  - Decreased criminal activity
  - Decreased overdose risk
  - Improved family stability
  - Improved pregnancy outcomes
  - Long track record of efficacy and safety
  - Reduction in other drug use
  - Allows the methadone-maintained person to function normally at work or in the home
  - Reduces relapse
  - No evidence of harm with long term use

# METHADONE

- Cons
  - Restriction in time and place
  - Stigma
- Side effects
  - Constipation
  - Increased appetite/weight gain
  - Excess sweating
  - Drowsiness during stabilization

# METHADONE TREATMENT SELECTION

- Previous failed attempts at failed buprenorphine treatment
- More available data on long term developmental and behavioral outcomes
- Access to methadone treatment center
- Daily oversight
  - Polysubstance abuse
- Limited social support
- Lower dropout rate (18%) relative to buprenorphine (33%) (Jones 2010)

# BUPRENORPHINE

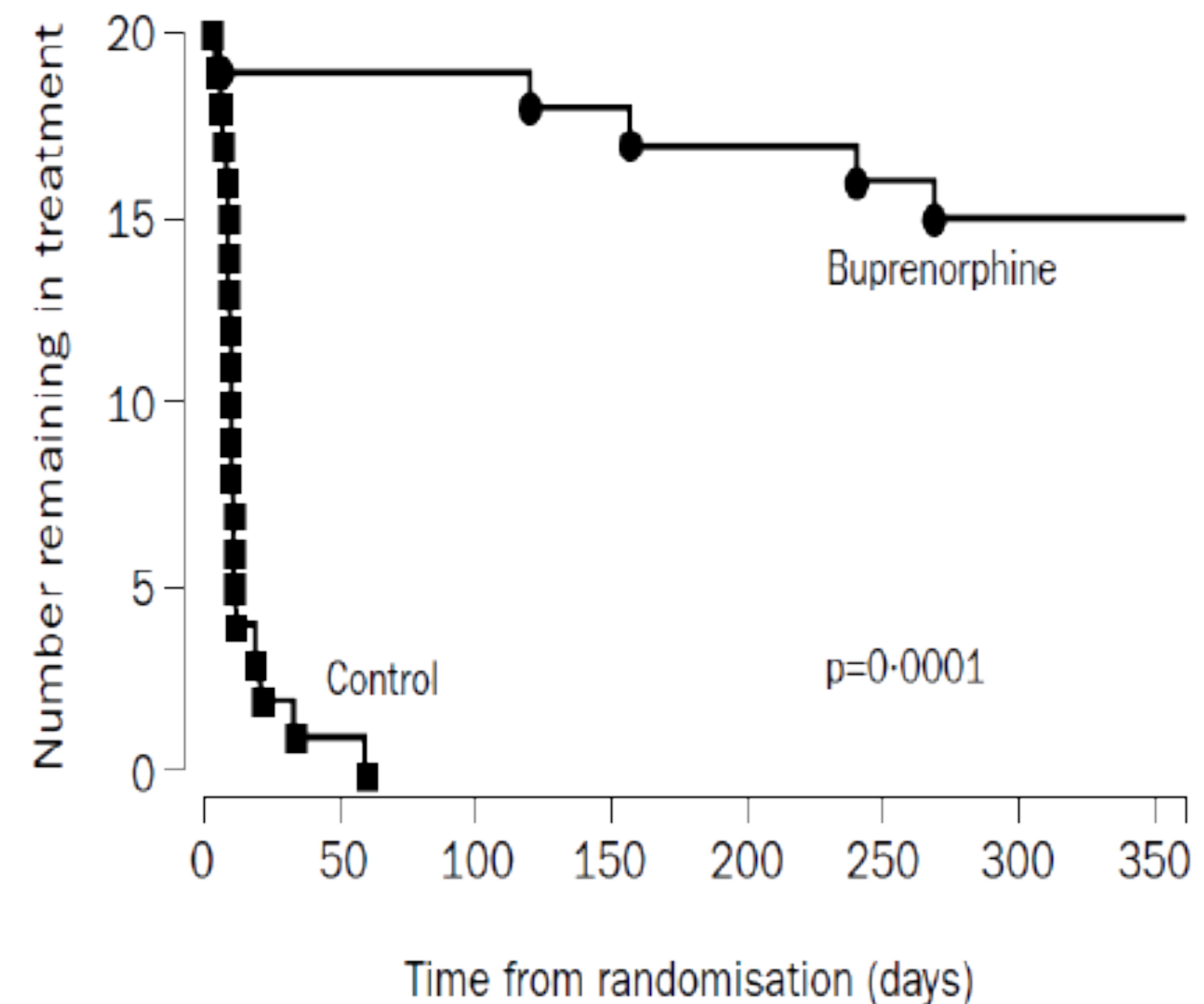
- Partial opioid agonist (less opioid activity)
- Slow onset and long duration of action blocking withdrawal symptoms (duration 72 hours)
- Can be dosed out of an office based setting (DATA 2000) or an OTP
- Provider must complete an 8 hour training course and apply to have the “X” designation added to DEA license
- Goal is to provide buprenorphine in a primary care practice (as opposed to creating specialized clinics)
- Average daily dosing 16 mg
- Favorable safety profile
  - Less respiratory depression

# BUPRENORPHINE

- Concurrent use of benzodiazepines
  - Refer to methadone
- Concurrent use of other CNS depressants (including alcohol)
- Polysubstance abuse may need daily oversight of MMT
- Impairment is not clinically significant
- Ceiling effect
- Side effects
  - Nausea, vomiting, constipation

# BUPRENORPHINE-TREATMENT (KAKKO 2003)

- RCT (Sweden)
- 40 patients, >1 year heroin addiction, not meeting criteria for methadone treatment
- Buprenorphine 16 mg vs placebo (12 mths)
- Both groups intensive psychosocial therapy
  - CBT groups, weekly individual sessions
  - 3 weekly supervised UDS
- Outcome: 1 year retention in treatment
  - 75% buprenorphine vs 0% placebo
  - Those remaining in tx- 75% negative UDS
  - 4 of 20 patients died in the placebo group, while no deaths in the buprenorphine group



## Number at risk

20	19	18	17	17	16	15	15
20	1	0	0	0	0	0	0



# BUPRENORPHINE TREATMENT SELECTION

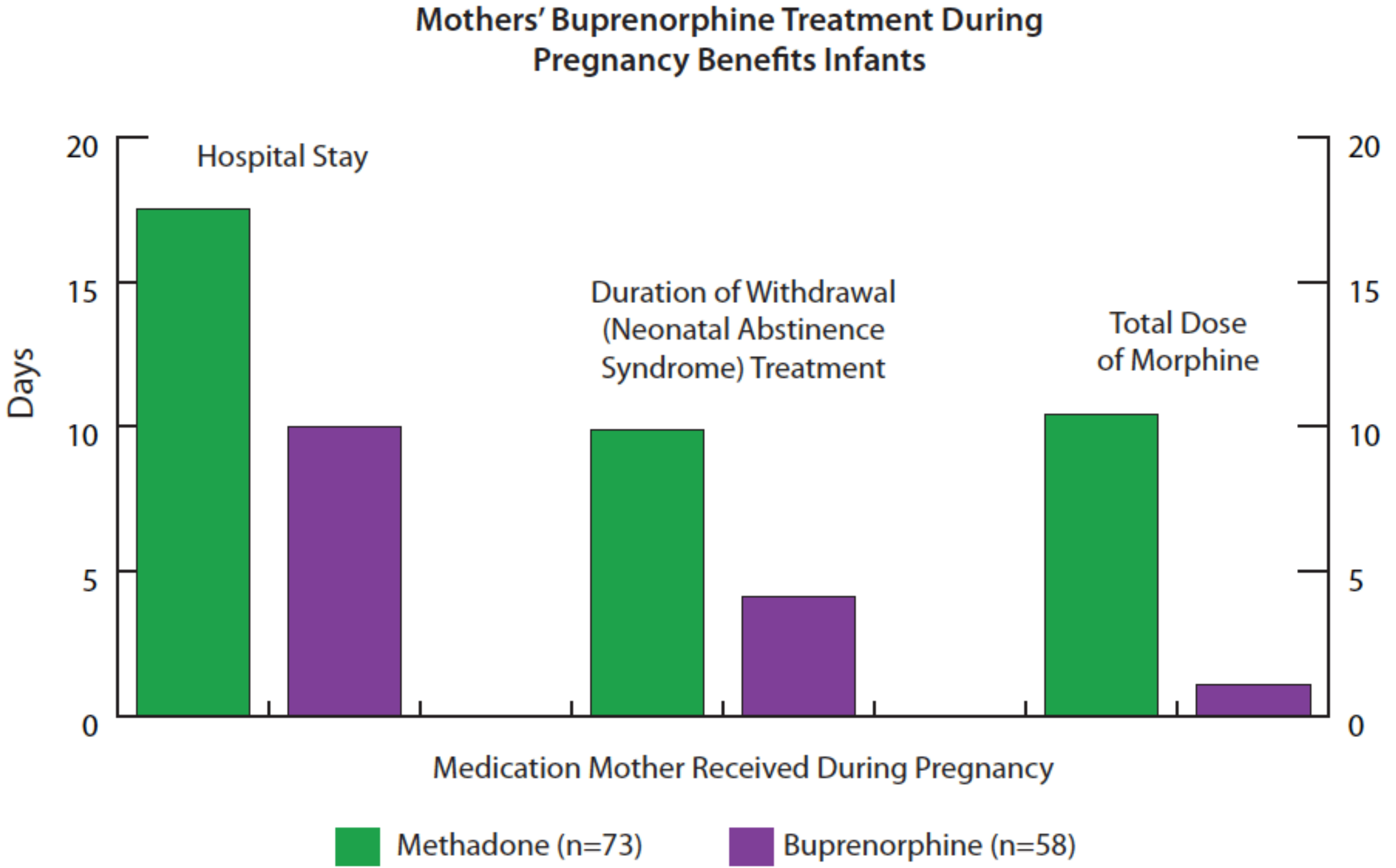
- Access to a buprenorphine waived physician
- Access to counseling center
- Moderate level of social support available
- Fewer dose adjustments needed during third trimester
- Office based treatment
- Multiple medical comorbidities
  - Decreased drug-drug interactions
- Less NAS leads to shorter hospital stays (MOTHER study)

# MATERNAL OPIOID TREATMENT: HUMAN EXPERIMENTAL RESEARCH (MOTHER)

- Double blinded, RCT occurring at 8 international sites of 175 gravid women (Jones 2010)
- Compared Methadone and Buprenorphine
- Both are effective at preventing relapse to illicit opioid use
- No significant difference in overall rates of NAS
- Higher dropout rate with buprenorphine (33%) vs. methadone (18%)

# MOTHER STUDY

- Buprenorphine group had less severity of NAS among neonates
  - Less morphine for symptoms (89% less)
  - Shorter hospital stay (43% shorter)
  - Shorter duration of treatment for NAS (58 % shorter)
- Jones 2010



# NALTREXONE

- Opioid Antagonist binds to the opioid receptor causing complete blockade
- Antagonist properties impact the midbrain dopamine release within the VTA and NA, leading to decreased rewarding properties and decreased usage
- Can be used for both opioid dependence and alcohol dependence
- Must be opioid free for 7-10 days (may vary depending on opioid)
- MUST BE THROUGH DETOXIFICATION PRIOR TO INITIATION
- No physical dependence

# NALTREXONE

- NOT CURRENTLY RECOMMENDED IN PREGNANCY
- Benefits
  - No risk of NAS
  - No special license to prescribe needed
- Risks
  - Long-term effects on fetal development due to blockade of opioid receptors in not well known. Animal studies have shown developmental and behavioral changes in adult rats exposed to naltrexone in utero, but human studies on developmental and behavioral sequelae are lacking ( Farid 2012/White 2013)
  - Requires detoxification from opioids
  - High rates of relapse/dropout from treatment (Waal 2013)
  - Possible complications for pain management at delivery

# OPIOID DEPENDENCE TREATMENT -PREGNANCY

- Methadone maintenance is considered the gold standard
- Buprenorphine has been shown to be an effective choice (Jones 2010)
- Removes mother from poor environment
- Improved access to comprehensive prenatal obstetric care
- Improved maternal nutrition
- Improves maternal/fetal outcomes
- Increases birth weight
- Increased psychosocial support
- Decreases polysubstance abuse

# NEONATAL ABSTINENCE SYNDROME

- Disorder characterized by behavioral and physiologic signs and symptoms from substance withdrawal
- Occurs in 60-90% of infants exposed to opioids in utero (Luty 2003)
- Usually beginning at 24-96 hours after birth
- Severity can be measured by the Finnegan score (neonatal withdrawal scoring system)
- Benefit of treatment outweigh risk

# NEONATAL ABSTINENCE SYNDROME

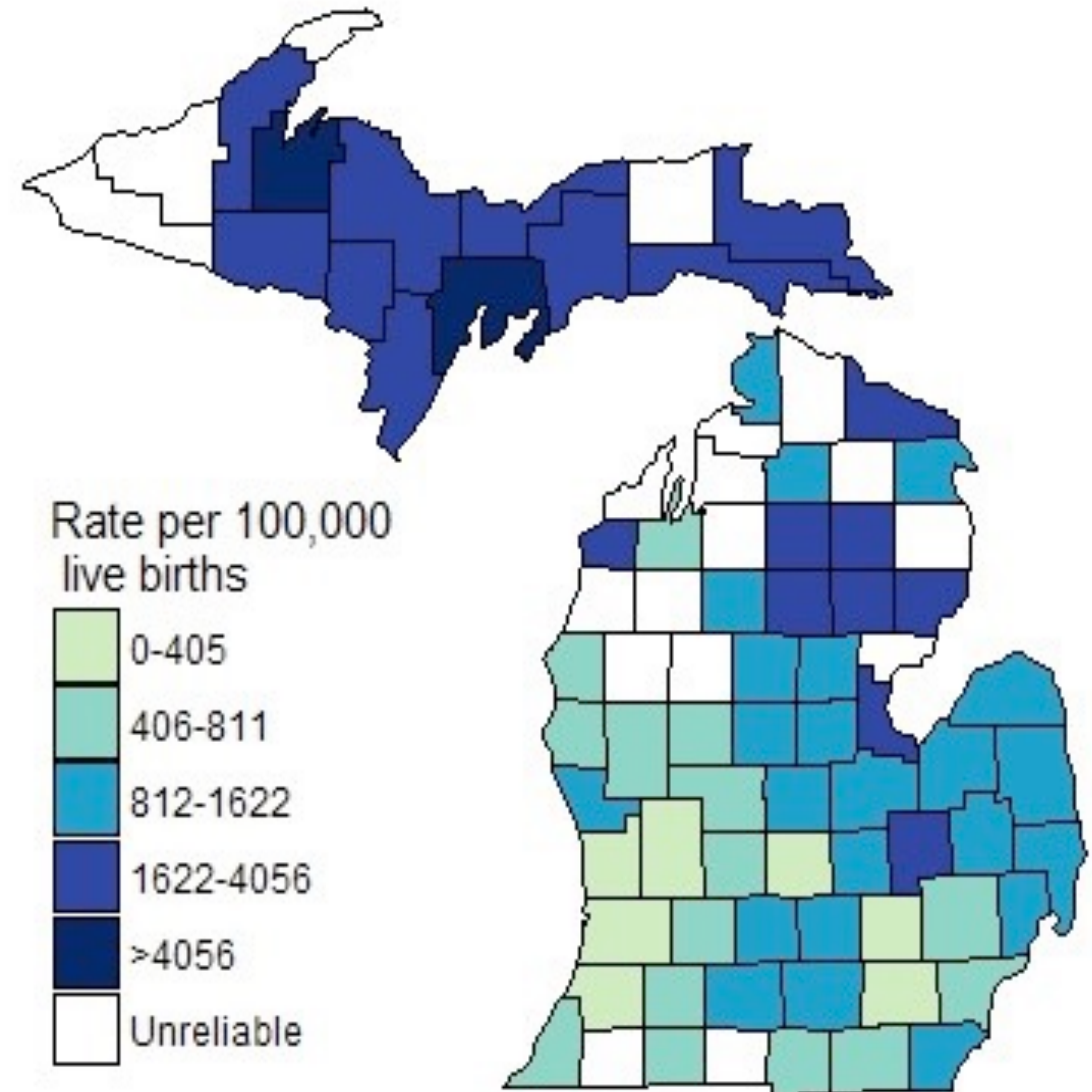
- CNS Effects
  - Irritability, Hypertonia, Hyperreflexia (increased muscle tone), abnormal suck, poor feeding, seizures (1-3%)
- GI Effects
  - Diarrhea, vomiting
- Respiratory Effects
  - Tachypnea (increased respiratory rate)
- Autonomic Effects
  - Sneezing, lacrimation, yawning, sweating, hyperpyrexia (increased temperature)
- Delayed effects seen for 4-6 months





# MICHIGAN 2016 NAS RATES

- Rate of NAS among MI infants peaked at 846.2 per 100,000 (2015) and decreased to 761.2 (2016)
- Highest county rates were in northern portion of the Lower Peninsula and in the Upper Peninsula (decreased SUD services in rural areas)
- NAS infants have longer hospital stays with costs near \$2 billion nationally



Note: Counties in white indicate that rate could not be calculated due to low reported numbers of hospitalizations of infants with NAS.

# ACCESS TO SUD FACILITIES FOR PREGNANT WOMEN (SAMHSA 2017)

- Facilities offering special programs for Pregnant/Postpartum women
  - Total 3,040 (22.4%)
  - Michigan 97 (21.3%)
- Offer Childcare for clients
  - Total 874 (6.4%)
  - Michigan 30 (6.6%)
- Offer Residential beds for clients children
  - Total 385 (2.8%)
  - Michigan 13 (2.9%)

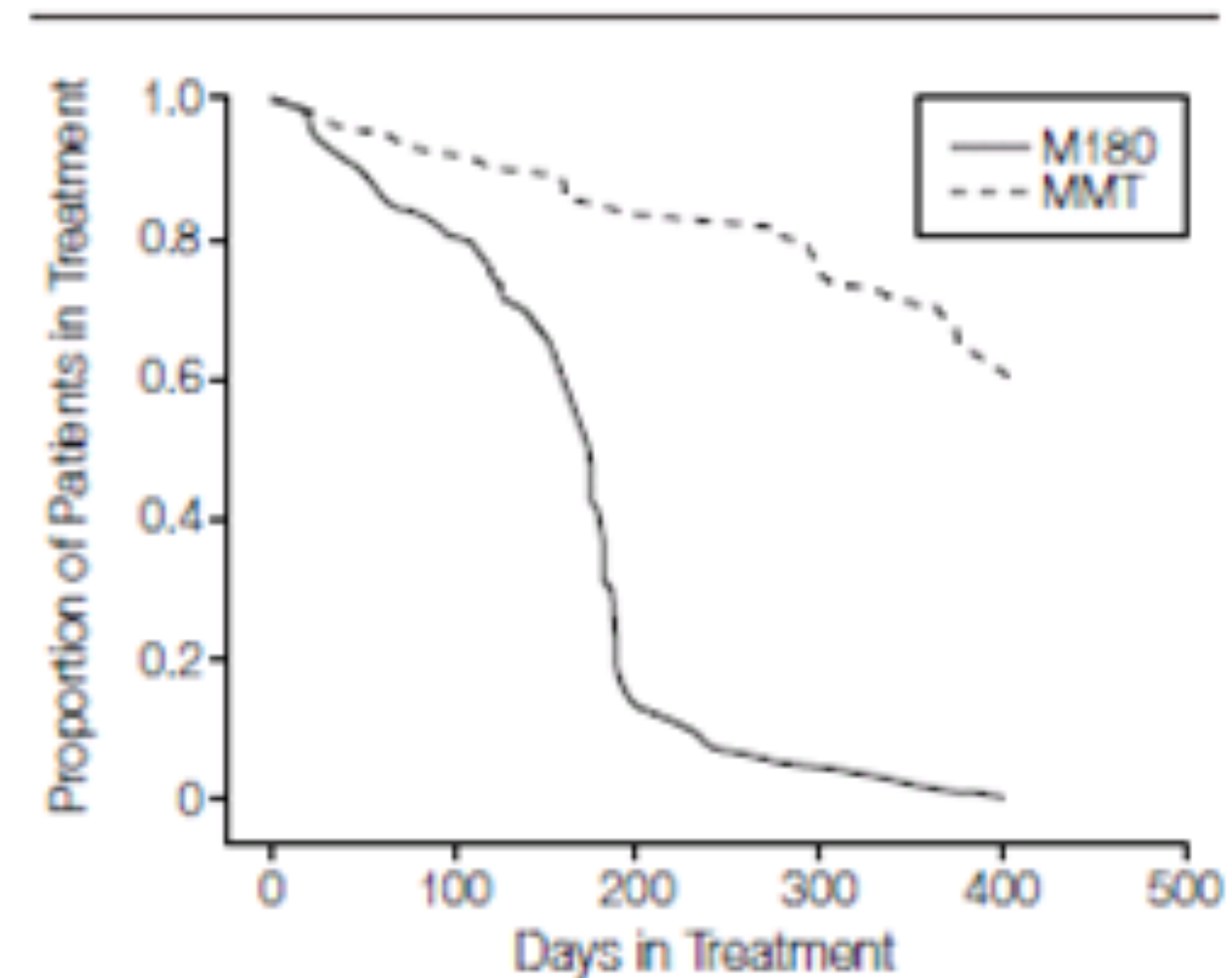
# SHOULD PREGNANT PATIENTS UNDERGO DETOXIFICATION?

- Opioid detoxification can be accomplished safely during pregnancy (Dashe 1998, Luty 2003)
- Very few women who complete detoxification remain abstinent-MOST WILL RELAPSE 80-90%
- Studies have shown relapse rates are similar to non pregnant patients at 80-90%

# METHADONE MAINTENANCE VS TAPER

- MMT vs. 180 Day Psychosocial Detoxification (Sees 2000)
- Methadone maintenance
  - Psychosocial services 2 hr/week
- 180 day methadone detoxification
  - Psychosocial services 3 hr/week
  - 14 Education sessions
  - 1 hour cocaine group therapy
  - Dose reduction beginning on day 120
- **INCREASED TREATMENT RETENTION**

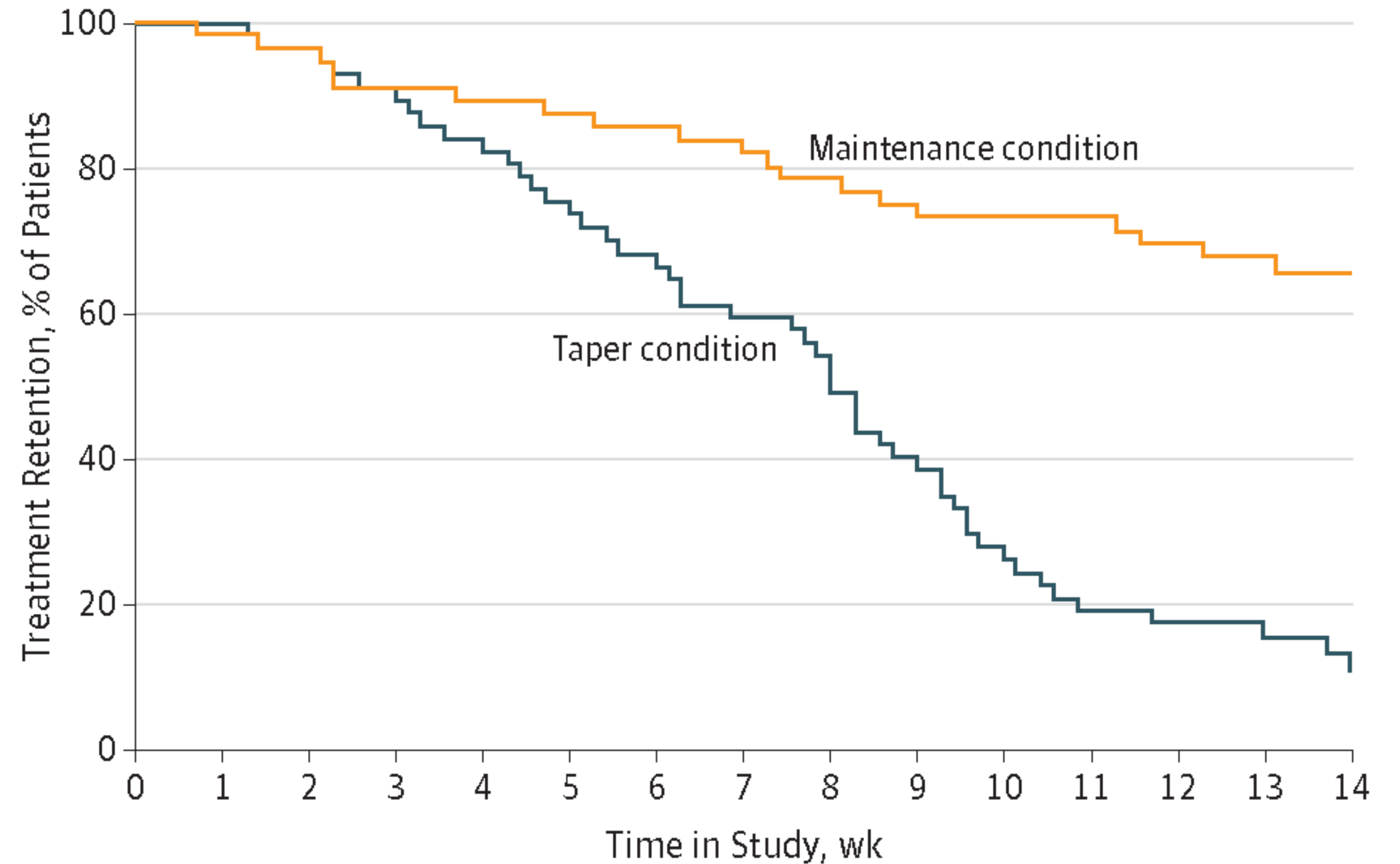
**Figure 3.** Survival Function by Treatment Group



Proportion of study participants in treatment by group over time. M180 indicates 180-day methadone-assisted detoxification; MMT, methadone maintenance treatment. For significant differences between conditions, Wilcoxon  $\chi^2_1$ , 85.0 ( $P < .001$ ).

# BUPRENORPHINE MAINTENANCE VS TAPER

- Completion of 14 week taper after 6 weeks stabilization (taper 3 weeks)
  - Taper 11% vs Maintenance 66%
- Mean percentage of urine negative for opioid
  - Taper 35% vs Maintenance 53%
- Tapering is LESS EFFICACIOUS than ongoing maintenance in prescription opioid dependence (Fiellin 2014)



Mean buprenorphine dosage, mg/d

Maintenance condition	14.9	15.1	15.2	15.3	15.3	16.0	15.9	16.2	16.2	16.6	16.8	16.2	16.1	15.8	14.6
Taper condition	15.6	15.6	15.4	15.3	14.2	9.7	5.7	3.1	0.6	0.2	0	0	0	0	0

# INFANT OUTCOME IN OPIOID EXPOSURE

- Data on long term outcomes of infants with in utero opioid exposure is limited
- Earlier studies have not found significant difference in cognitive development between children up to 5 years of age exposed to methadone in utero and control groups matched for age, race, and socioeconomic status (ACOG 2012)
- Preventative interventions focusing on enriching early experiences of such children and improving quality of home environment are likely to be beneficial (refer to Early On program)

# KEY POINTS

- Tobacco Cessation is one of the most modifiable causes of poor pregnancy outcomes in the US
- Improved maternal and fetal outcomes are associated with medication assisted treatment for OUD in pregnancy
- Maternal support throughout and after pregnancy is essential
- TREATMENT IMPROVES OUTCOMES

QUESTIONS



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