

Treatment of opioid addiction during pregnancy

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In a nutshell: opioid addiction in pregnancy –

- general considerations
- how does maintenance work ?
- what is a good outcome?
- what are the options?



Medication-assisted treatment (MAT) for addiction during pregnancy

- Most evidence is related to heroin addiction vs. methadone maintenance.
- No MAT benefit documented for stimulant abuse
- In general, monitored symptomatic treatment of withdrawal for addictive substances other than opioids.
- Relapse is the main practical issue.

Opioid abuse

Prevalence

3,744,000 persons in US reported using heroin at least once in their lifetime (2003 NSDUH)

149,000 new users (1999)

980,000 persons using heroin at least weekly (1998)

810,000 to 1,000,000 chronic users of heroin (ONDCP 2003)

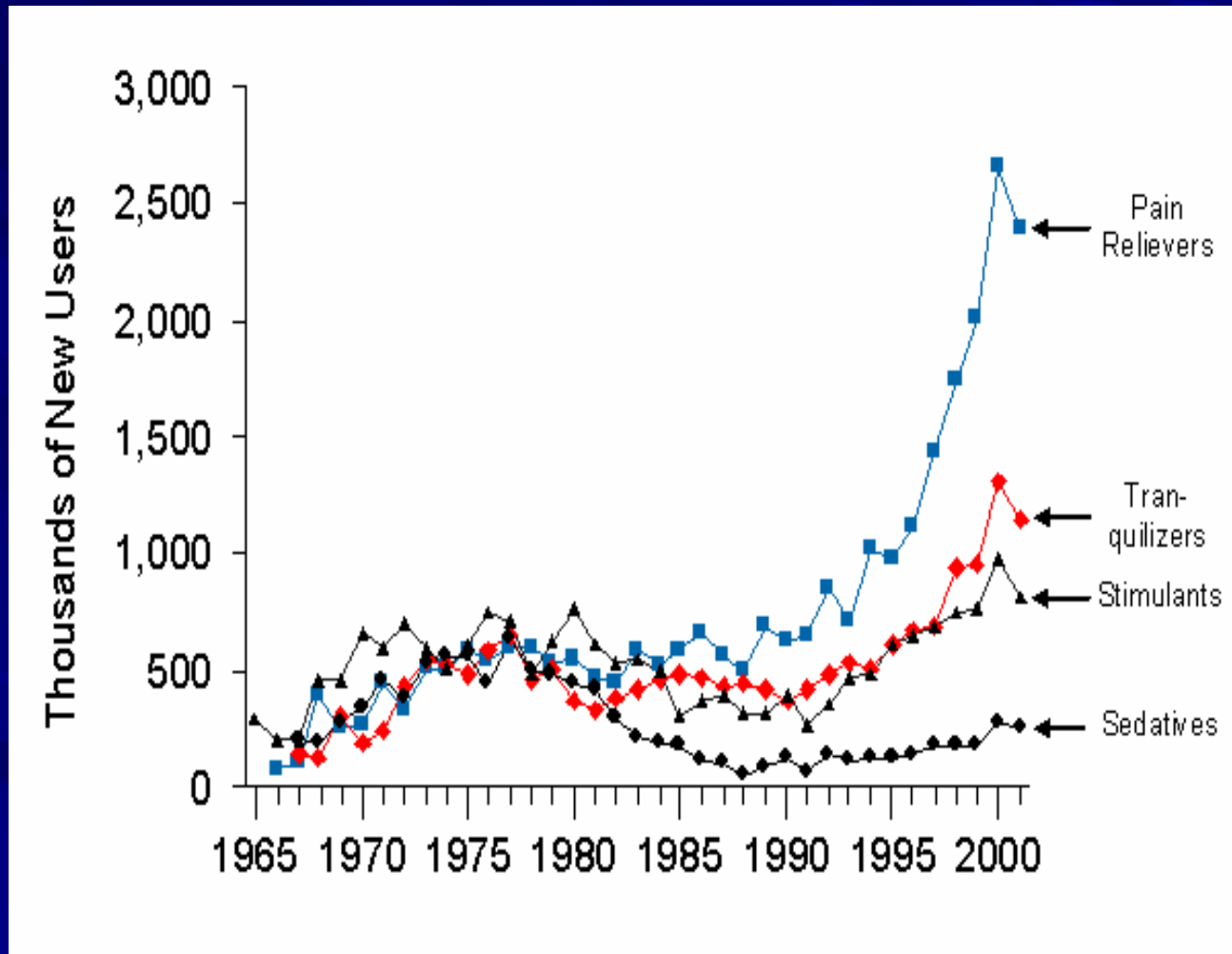
Gaps in current treatment of opioid dependence

810,000 to 1,000,000 chronic users of heroin

200,000± patients receiving methadone maintenance treatment

1998 NIH Consensus Statement on Appropriate Treatment of Opiate Dependence called for increased access to pharmacotherapy.

Number of new non-medical users of therapeutics



PREGNANCY AND OPIOID ABUSE

- Considered a “high risk” pregnancy.
- Medication: Both intake and withdrawal have fetal effects. **Withdrawal effects considered more serious.**
- Psychosocial: High motivation to change, guilt about being a ‘bad mother.’
- Legal: implications related to parenting and custody.

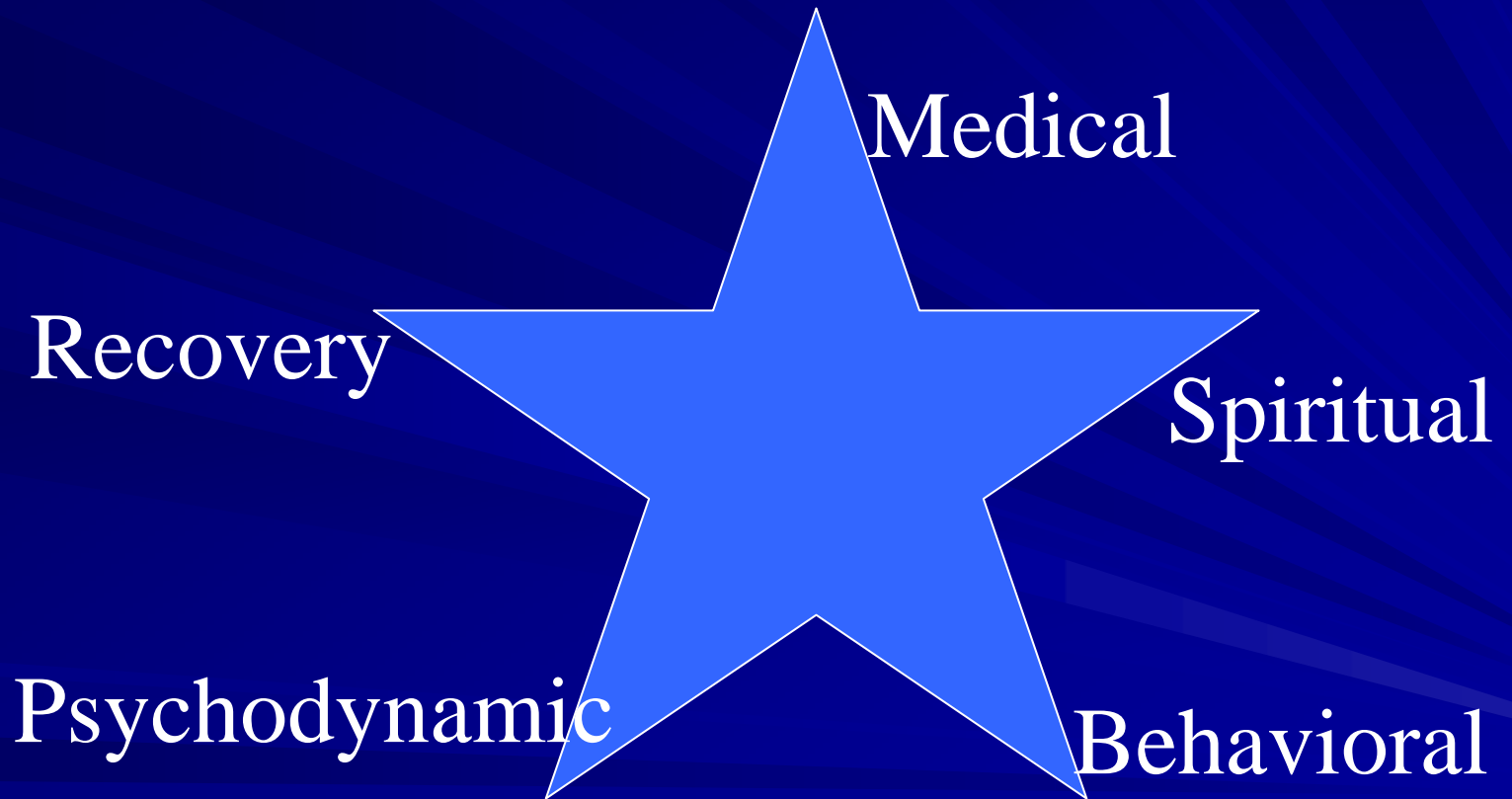
Possible Neonatal effects of heroin

- Low birth weight
- Meconium aspiration (fetal stress)
- STDs
- Neonatal withdrawal syndrome (60-80%)
- Delayed effects, 4-6mos (jittery)
- No effect

METHADONE AND PREGNANCY

- Improvement in outcomes overall over heroin.
- Fetal growth more normal than with heroin
- Perinatal mortality less than with heroin
- NAS predictable and at least 45% need treatment
- Breastfeeding OK

Models of addiction treatment



ADDICTION AS A CHRONIC ILLNESS

Chronic relapsing condition
which untreated
may lead to severe
complications
and death.

ADDICTION AS CHRONIC DISEASE: IMPLICATIONS

- It is treatable but not curable.
- Adjustment to diagnosis is part of patient's task.
- There is a wide spectrum of severity.

ADDICTION AS CHRONIC DISEASE, CONT.:

- Retention in treatment is key.
- Behavior changes needed.
- Adherence around 30%, like asthma, diabetes, hypertension.
- Medication-assisted treatment (MAT) is indicated in some cases, methadone maintenance is one evidence-based medical treatment.

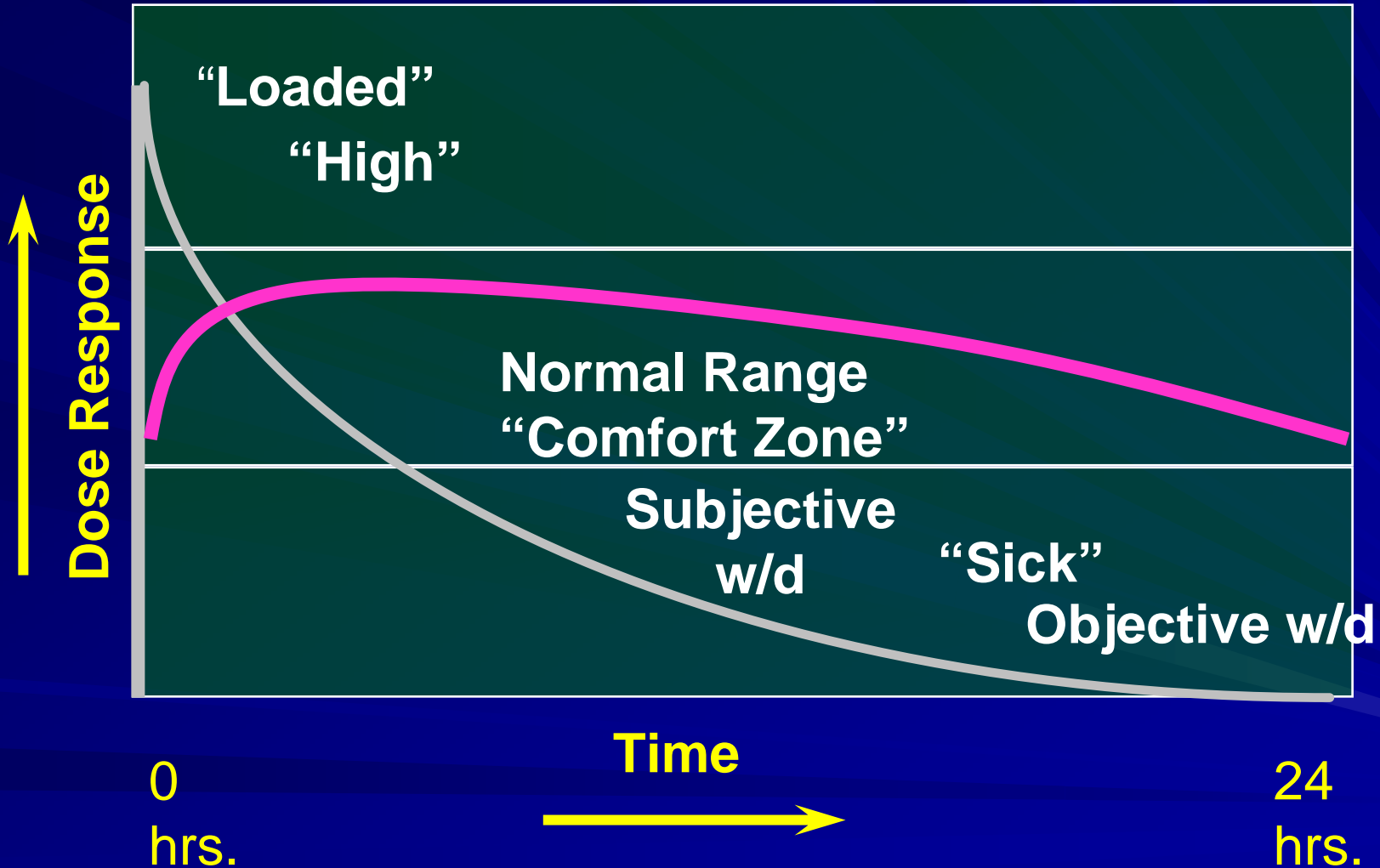
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THE DOSING WINDOW

Counseling Staff

Medical Staff

Methadone Simulated 24 Hr. Dose/Response At steady-state in tolerant patient



NEONATAL WITHDRAWAL (NAS, NWS) with MMT.

- Predictable, usually within 72 hours of birth
- Treatable, opiates vs phenobarbital, etc
- Monitor for spasms/seizures
- May have trouble gaining weight at first
- Normal development after first year
- Not dose-related, split dose may be helpful.

Baby at
bedside:
not likely

Maternal visits are the norm

Pregnant women and MMT:

- Admission is expedited
- May be admitted even without current physical dependence
- Monitoring requirements intensified
- Education about NAS, and about avoiding withdrawal during pregnancy
- Education about other substances.

TALKING WITH PREGNANT PATIENTS about MMT

- Fear about methadone
- Dose-related issues
- CPS, legal issues
- Self-concept and hormones
- Parenting
- Polysubstance abuse

Medical facts for pregnant patients on MMT

- Good overall pregnancy outcomes with maintenance.
- Avoid withdrawal during pregnancy, some women need split doses.
- NO NUBAIN during labor! (partial agonist anesthetic)
- Neonatal withdrawal is treatable

Coordination of care: when the delivery happens

- Hospital calls OTP clinic nurse to document current methadone dose, and last date and time of ingestion.
- Usually regular daily dose is maintained.
- Patient discharged with documentation of last dose: mg, date and time dispensed, and any home medications, to bring to the clinic the next day
- Clinics open 365, but may have limited hours.

What is a good outcome for MAT in pregnancy?

- Maternal abstinence during pregnancy, with steady blood levels of methadone.
- Regular prenatal visits with clinician who knows about MAT and methadone.
- Attention to surrogate markers of fetal withdrawal (increased motion, maternal craving or withdrawal)
- Baby stays at least 5 days, NAS controlled.
- Mother continues MMT after delivery, dose may decrease, may breastfeed.

Example of good outcome:

- McCarthy et al: Am J Obstet Gynecol, September 1, 2005; 193(3 Pt 1): 606-10.

High-dose methadone maintenance in pregnancy: maternal and neonatal outcomes.

Retrospective case series of 81 women on MMT in Sacramento.

McCarthy et al, cont

- Average maternal dose 101mg, most of them split dosing.
- 81% negative toxicologies at birth
- 45% treated for NAS
- Subgroup with best outcome was women already on MMT who became pregnant.

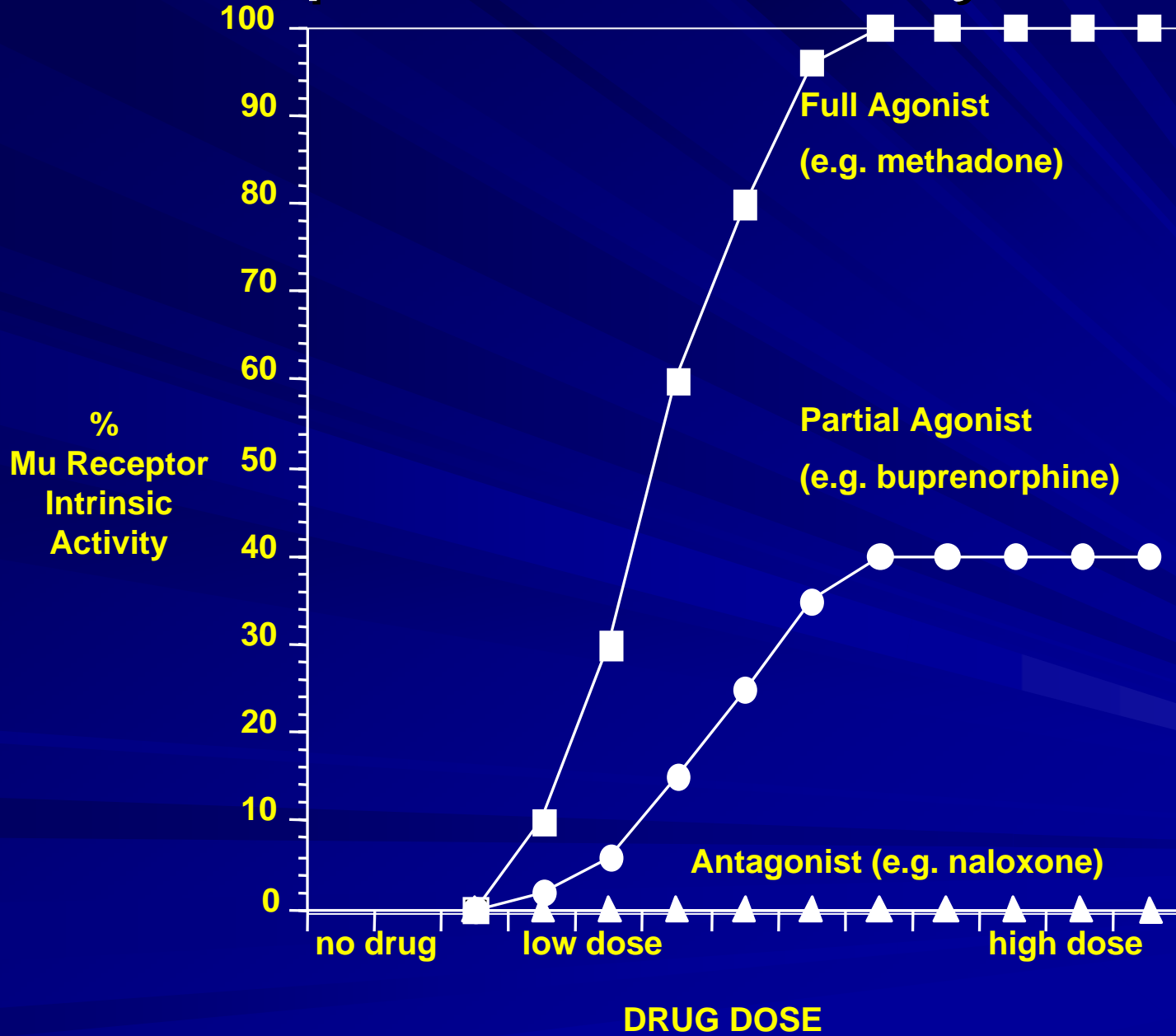
MAT and pregnancy, options:

- Methadone maintenance is the current treatment of choice for pregnant opioid addicted women
- Limited studies suggest that buprenorphine may be useful, possibly even reducing neonatal withdrawal days (partial agonist).
- No information about prescription drug abusers (one warning about OxyContin causing NAS)
- Detoxification or Medically Supervised Withdrawal (MSW) requires monitoring, usually done in second trimester.

Buprenorphine

- New formulation of a partial mu agonist, in sublingual tablets.
- New legislation (DATA 2000) enabling office opioid maintenance treatment with some restrictions.
- Suboxone® combined with naloxone to discourage injected abuse

Comparison of Activity Levels



Por cortesía de Reckitt Benkiser

Buprenorphine and pregnancy

- Case series in France: safe and effective, possibly reducing NAS

- One preliminary study in US:

Jones et al; Drug Alcohol Depend, July 1, 2005; 79(1): 1-10.

Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: effects on the neonatal abstinence syndrome.

Jones et al, 2005, cont

- Head to head randomized blinded comparison between methadone and buprenorphine in pregnant women
- Women admitted during second trimester
- One statistically significant finding: shorter stay for bup
- Other trends for bup: fewer infants treated for NAS, less NAS medication used.
- Multi-site trial in progress now.

Practical considerations about buprenorphine and pregnancy

- Labeled category C (not enough information)
- Probably better to use mono product
- Informed consent for legal reasons
- Label says no breastfeeding, but probably safe (not orally very bio - available)
- In the initial survey of use of buprenorphine, women with prescription opioid abuse were a significant population.

What about detoxification and MSW?

- First and third trimester generally considered more dangerous
- Studies show if inpatient, monitored can technically be achieved safely
- Practical consideration is relapse.

What about pregnancy in prescription opioid drug abusers?

- Not directly studied
- Methadone shown safe, may consider induction onto methadone, split doses if patient has chronic pain.

Summary: Opioid abuse and pregnancy

- Methadone maintenance is still the treatment of choice and standard of care in the US.
- Buprenorphine treatment is possible, evidence still lacking.
- Detoxification is relatively contraindicated unless done in hospital with monitoring.