OPIOID USE DISORDER: SCREENING AND INTERVENTION

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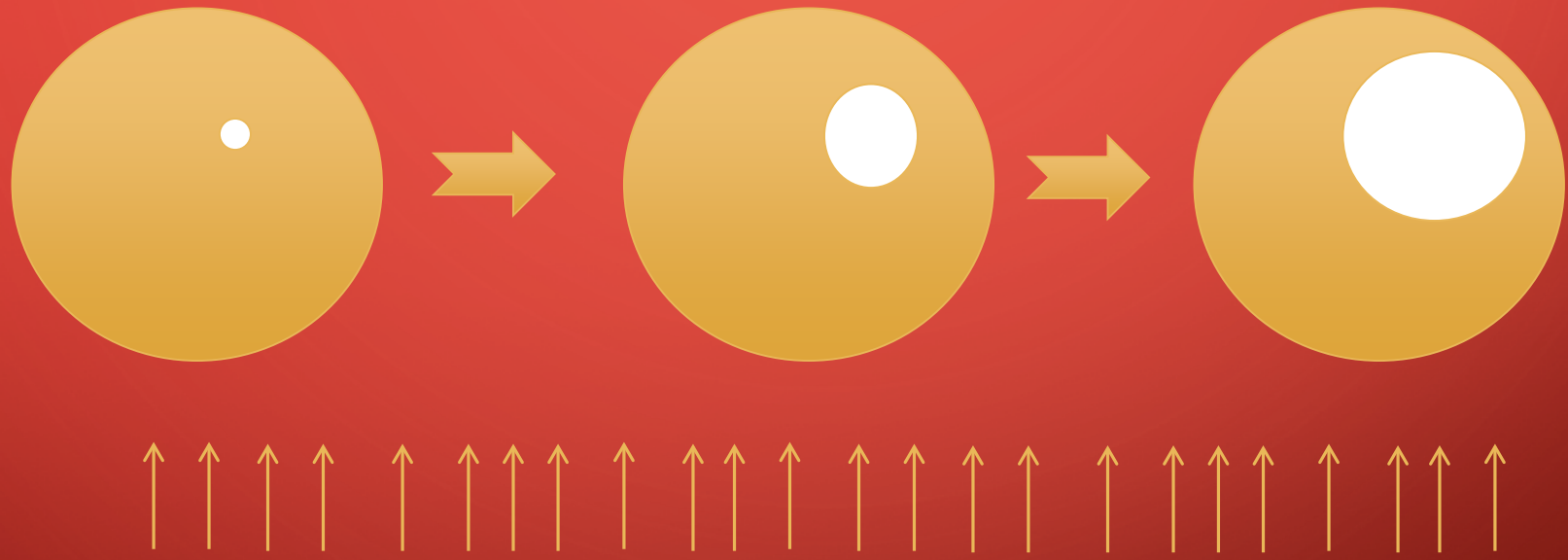
DISCLOSURES

- I have no pertinent disclosures.

LEARNING OBJECTIVES

- Discuss how to asses and identify stages of change
- Discuss drug metabolism and pharmacokinetics during pregnancy
- Discuss proposed recommendations for MAT prescribing during pregnancy

ADDICTION OVERTAKES MOTIVATION



Adapted from Emily Zarse, M.D. and Andrew Chambers, M.D.

STAGES OF CHANGE

- Pre-contemplative - "I don't need to/want to change."
- Contemplative – "I am considering making a change."
- Planning – "I am thinking/planning my how to change."
- Action – "I executing my plan for change."
- Maintenance – "I am using skills to continue my behavior."

STAGES OF CHANGE

- Pre-contemplative - "I don't need to/want to change."
- Contemplative – "I am considering making a change." Where the patient is!
- Planning – "I am thinking/planning my how to change."
- Action – "I executing my plan for change." Where we as treaters go.
- Maintenance – "I am using skills to continue my behavior."

DON'T FORGET PLANNING

- There is some urgency with pregnant patients due to dyadic relationship between mother and fetus
- However, women still need to be in the planning to action stage of change before starting MAT
- Women who are still contemplative; will be less likely to achieve sobriety
- Don't be held hostage by the fetus

MOTIVATIONAL ENHANCEMENT THERAPY

- Open, curious, supportive demeanor
- Help create dissonance and increase perceived need for treatment
  - "On the one hand I hear you saying that you enjoy using heroin, but on the other hand you say that it has certain costs for you?"
- Remember the patient has some degree of ambivalence
- Bolster the change side of ambivalence by using "change talk"
  - "It sounds as if you have taken some steps already in curbing your opioid use."
- Your goal is to move from 1 stage to the next and not more

INTERVENTION: HOW DOES IT LOOK IN PRIMARY CARE?

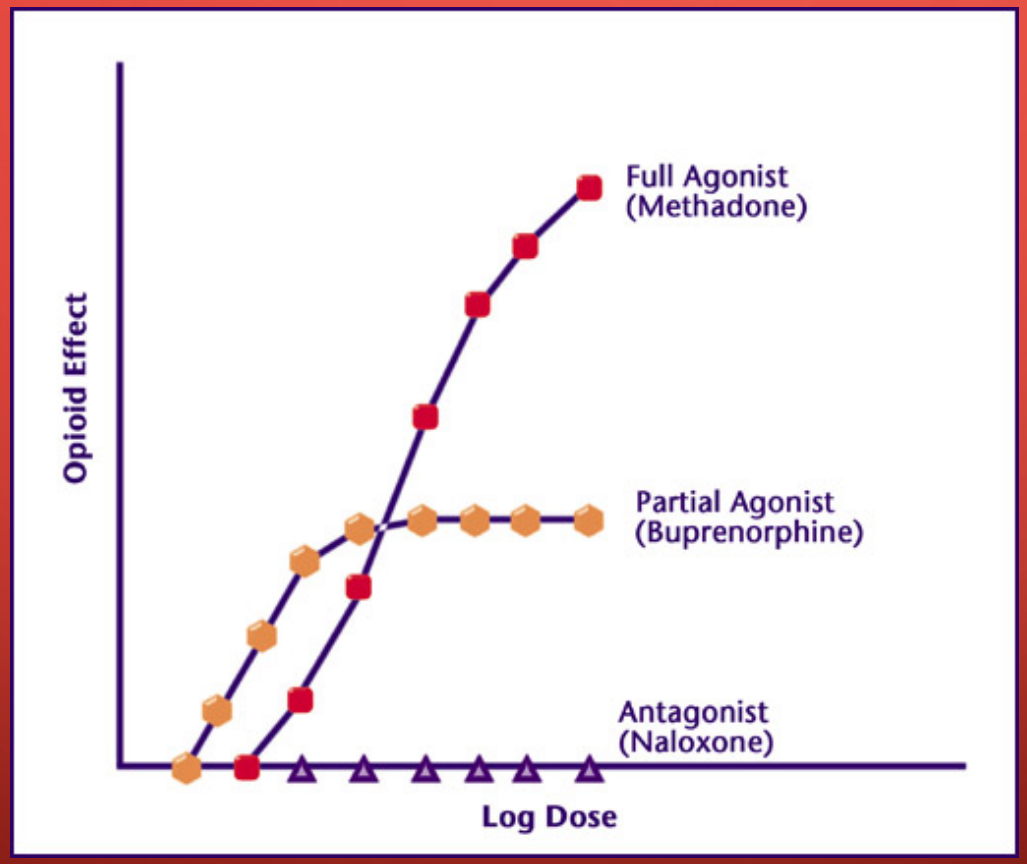
- Pharmacotherapy with buprenorphine or naltrexone;
- Provider and community educational interventions (e.g. in-person, web-based, and telehealth provider CME activities, community-based advertising campaigns, stakeholder conferences);
- Coordination/integration of OUD treatment with other medical/psychological needs;
- Psychosocial services (e.g. counseling on-site or by referral)
- Models varied in the degree of component implementation.

Korthuis P.T., McCarty D., Weimer M., et al: Primary care-based models for the treatment of opioid use disorder: a scoping review. Ann Intern Med 2017; 166: pp. 268-278

PHARMACOTHERAPY FOR OPIOID USE DISORDER

- Methadone – “gold standard” in pregnancy; but must be administered I highly regulated clinics;
- Buprenorphine – not FDA approved in pregnancy, but efficacy comparable with methadone treatment, produces less NAS (MOTHER study);
- Naltrexone – not approved in pregnancy and not widely used in pregnancy

AGONIST/ANTAGONIST



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BUPRENORPHINE IN PREGNANCY

- Buprenorphine mono product (without naloxone) is generally preferred
- Originally used to to fears that of precipitated withdrawal if buprenorphine-naloxone was used IV by pregnant women
- Newer studies with Bup/Naloxone combo have shown comparable safety and efficacy without increase in adverse effects; (reference)
- Of note, dosing scheme based on adult dosing regimen where daily dosing is usually sufficient

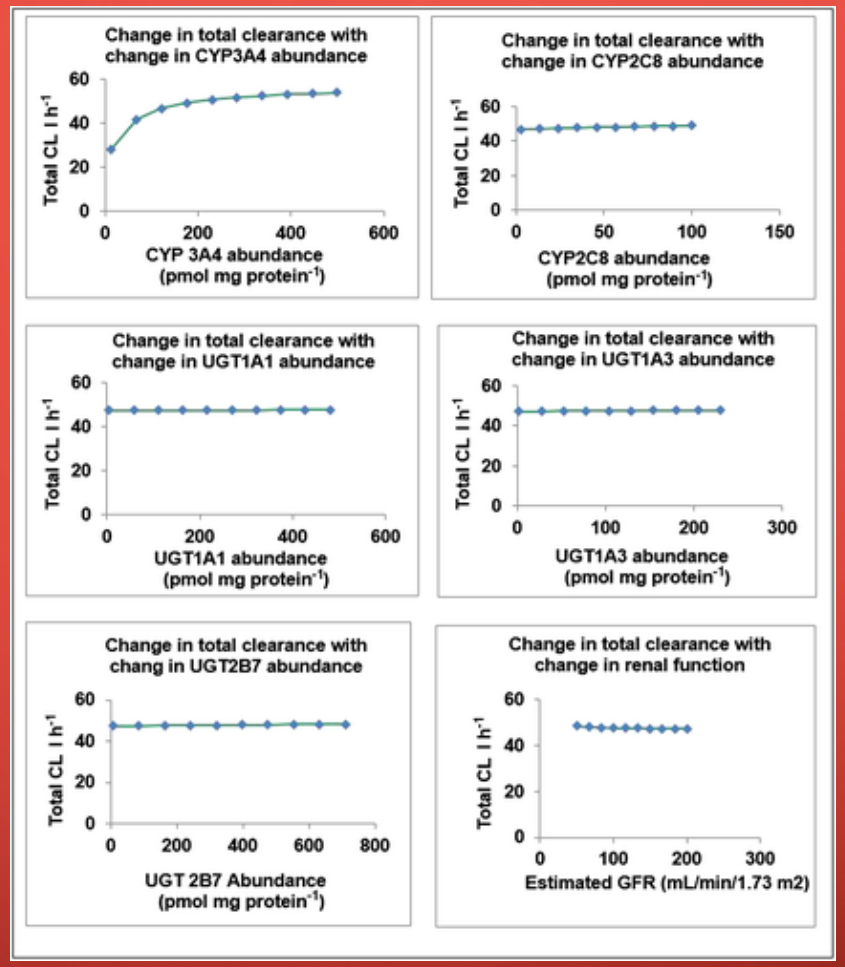
Jones HE, Heil SH, Baewert A, et al. Buprenorphine treatment of opioid-dependent pregnant women: a comprehensive review. Addiction. November 2012:5-27.

BUPRENORPHINE METABOLISM

- Response to buprenorphine appears to be related to dose
- Pregnancy leads to a number of changes in the woman's body that lead to changes in how medicines are processed
- Liver metabolized via CYP3A4 is the main avenue for buprenorphine metabolism

Zhang, H., Kalluri, H. V., Bastian, J. R., Chen, H., Alshabi, A., Caritis, S. N., and Venkataramanan, R. (2018) Gestational
changes in buprenorphine exposure: A physiologically-based pharmacokinetic analysis.
Br J Clin Pharmacol, 84: 2075–2087.

Gestational changes in buprenorphine exposure: A physiologically-based pharmacokinetic analysis



British Journal of Clinical Pharmacology, Volume: 84, Issue: 9, Pages: 2075-2087, First published: 05 June 2018, DOI: (10.1111/bcp.13642)

BUPRENORPHINE LEVELS IN PREGNANCY

- Small cohort study showed pregnant had lower blood concentrations than non-pregnant women at same doses (ref.)
- A correlation exists between response to buprenorphine and blood concentration
- Recent work looking at changes in blood concentration of buprenorphine in each trimester

Zhang, H., Kalluri, H. V., Bastian, J. R., Chen, H., Alshabi, A., Caritis, S. N., and Venkataramanan, R. (2018) Gestational
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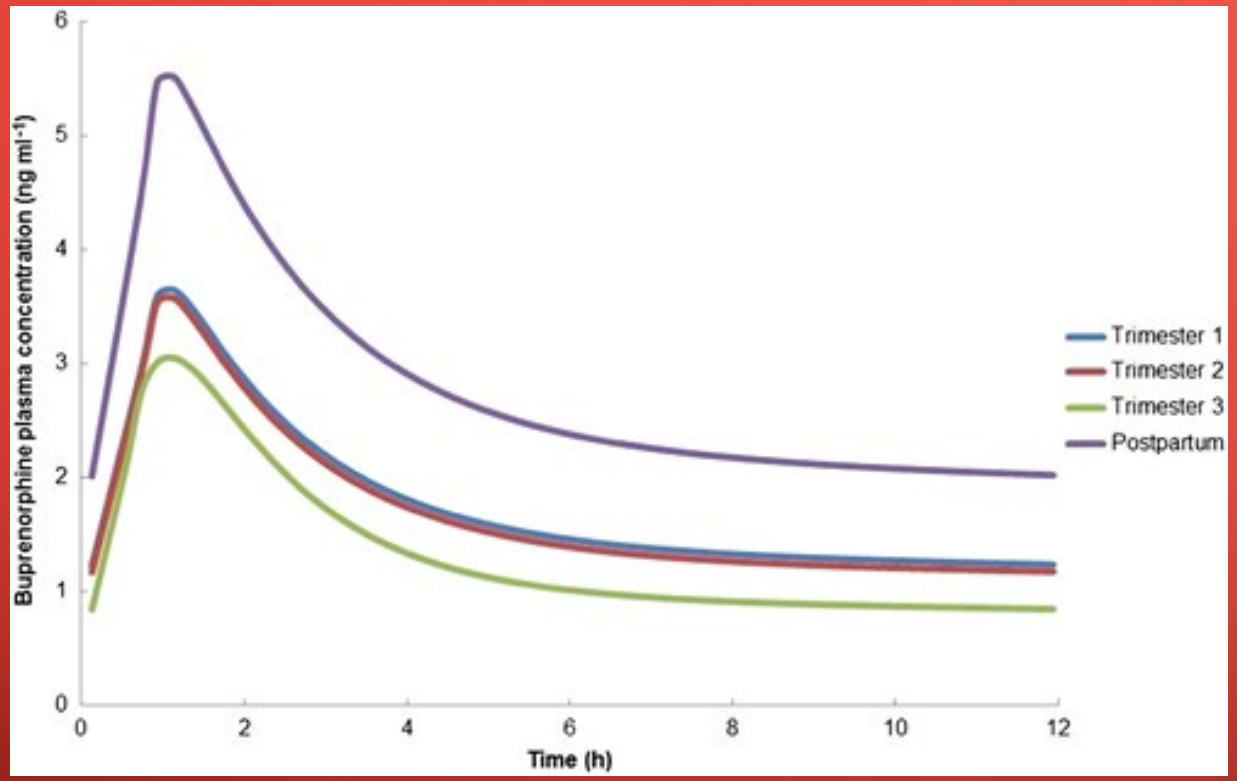

Observational studies suggest plasma concentrations remain above 1 ng/mL during an entire dosing interval.

British Journal of Clinical Pharmacology, Volume: 84, Issue: 9, Pages: 2075-2087, First published: 05 June 2018, DO: (10.1111/bcp.13642)

M.K. Greenwald, C.E. Johanson, D.E. Moody, *et al.* **Effects of buprenorphine maintenance dose on mu-opioid receptor availability, plasma concentrations, and antagonist blockade in heroin-dependent volunteers**
Neuropsychopharmacology, 28 (2003), pp. 2000-2009

M. Greenwald, C.E. Johanson, J. Bueller, *et al.* **Buprenorphine duration of action: mu-opioid receptor availability and pharmacokinetic and behavioral indices**
Biol Psychiatry, 61 (2007), pp. 101-110

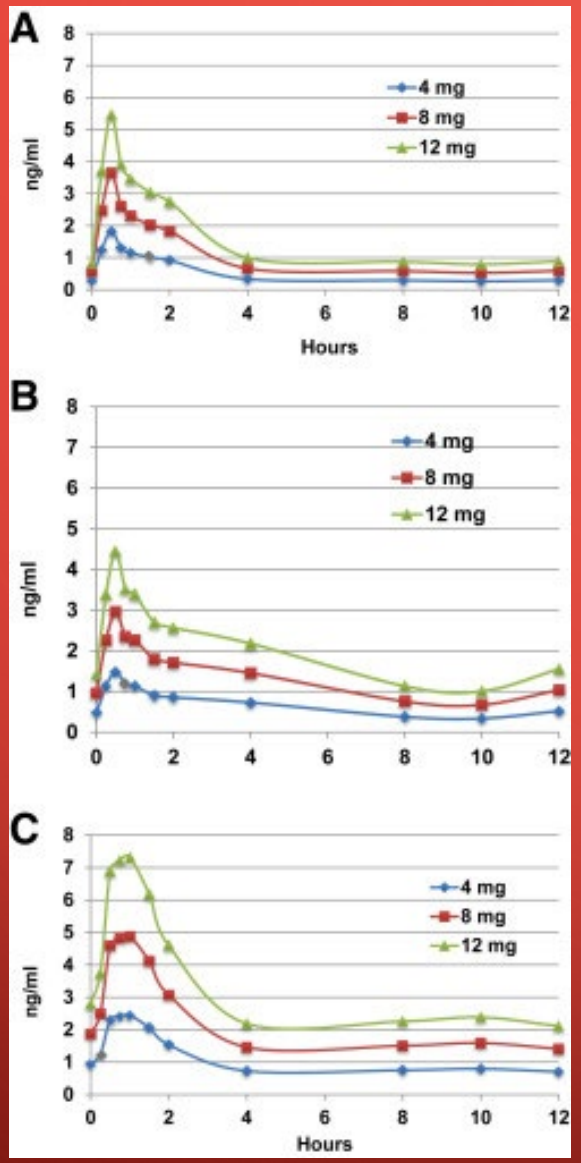

Figure 1. Median buprenorphine concentrations

Median buprenorphine concentrations according to dose in second (**A**) and third trimesters (**B**) and postpartum period (**C**) after sublingual dose of 4, 8, or 12 mg BID. All subjects were at steady state.

Caritis et al. Dosing recommendations for buprenorphine during pregnancy. Am J Obstet Gynecol 2017.

DOSING RECOMMENDATIONS

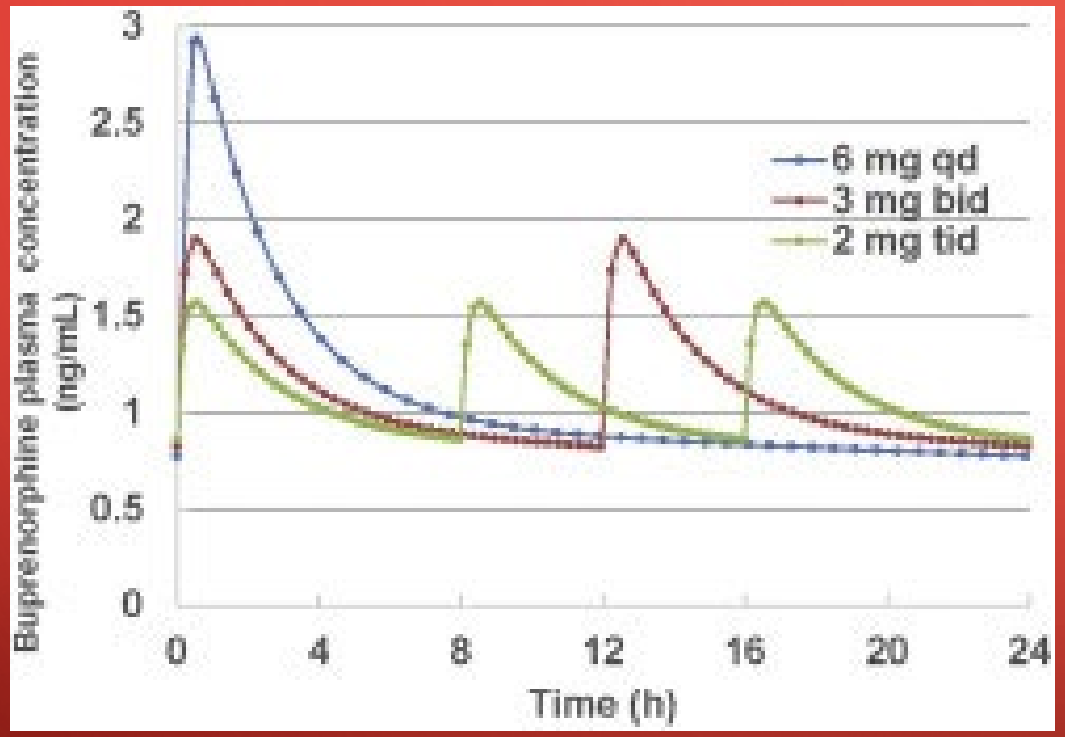

Figure 3. Simulated plasma concentrations of buprenorphine in nonpregnant subjects Simulated plasma concentrations of buprenorphine in nonpregnant subjects utilizing physiologically based pharmacokinetic modeling. Values are means. Frequency of dosing includes 6 mg daily, 3 mg BID, and 2 mg TID.

Caritis et al. Dosing recommendations for buprenorphine during pregnancy. Am J Obstet Gynecol 2017.

CONCLUSIONS

- Addiction to opioids during pregnancy is a still growing problem in the US

REFERENCES

- Zhang, H., Kalluri, H. V., Bastian, J. R., Chen, H., Alshabi, A., Caritis, S. N., and Venkataramanan, R. (2018) Gestational changes in buprenorphine exposure: A physiologically-based pharmacokinetic analysis. Br J Clin Pharmacol, 84: 2075–2087.