



OPIOID USE DISORDER: SCREENING AND INTERVENTION

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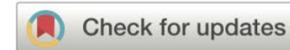
AUGUST 21, 2019

DISCLOSURES

- I have no pertinent disclosures.

LEARNING OBJECTIVES

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

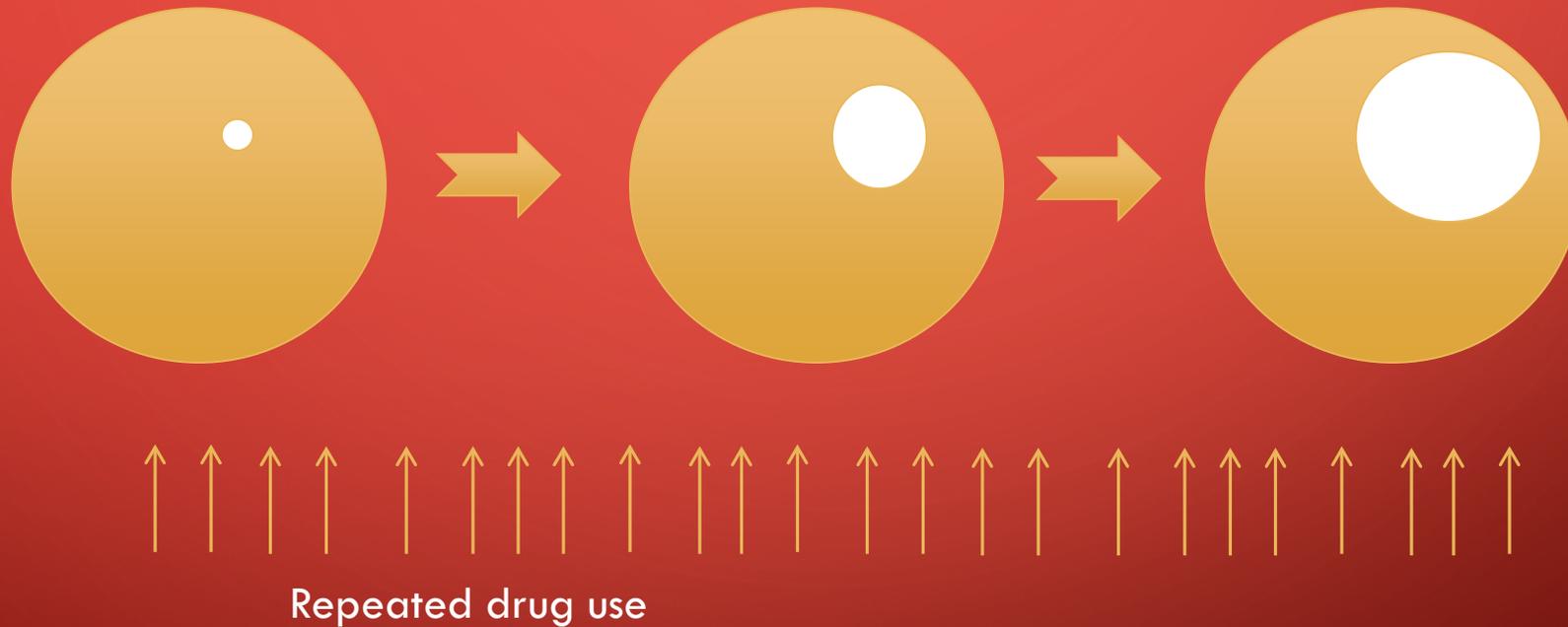


Substance use disorders in pregnancy: clinical, ethical, and research imperatives of the opioid epidemic: a report of a joint workshop of the Society for Maternal-Fetal Medicine, American College of Obstetricians and Gynecologists, and American Society of Addiction Medicine

Jeffrey Ecker, MD; Alfred Abuhamad, MD; Washington Hill, MD; Jennifer Bailit, MD; Brian T. Bateman, MD; Vincenzo Berghella, MD; Tiffany Blake-Lamb, MD; Constance Guille, MD; Ruth Landau, MD; Howard Minkoff, MD; Malavika Prabhu, MD; Emily Rosenthal, MD; Mishka Terplan, MD; Tricia E. Wright, MD; Kimberly A. Yonkers, MD

The American College of Obstetricians and Gynecologists supports the value of this clinical document as an educational tool, March 2019.

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

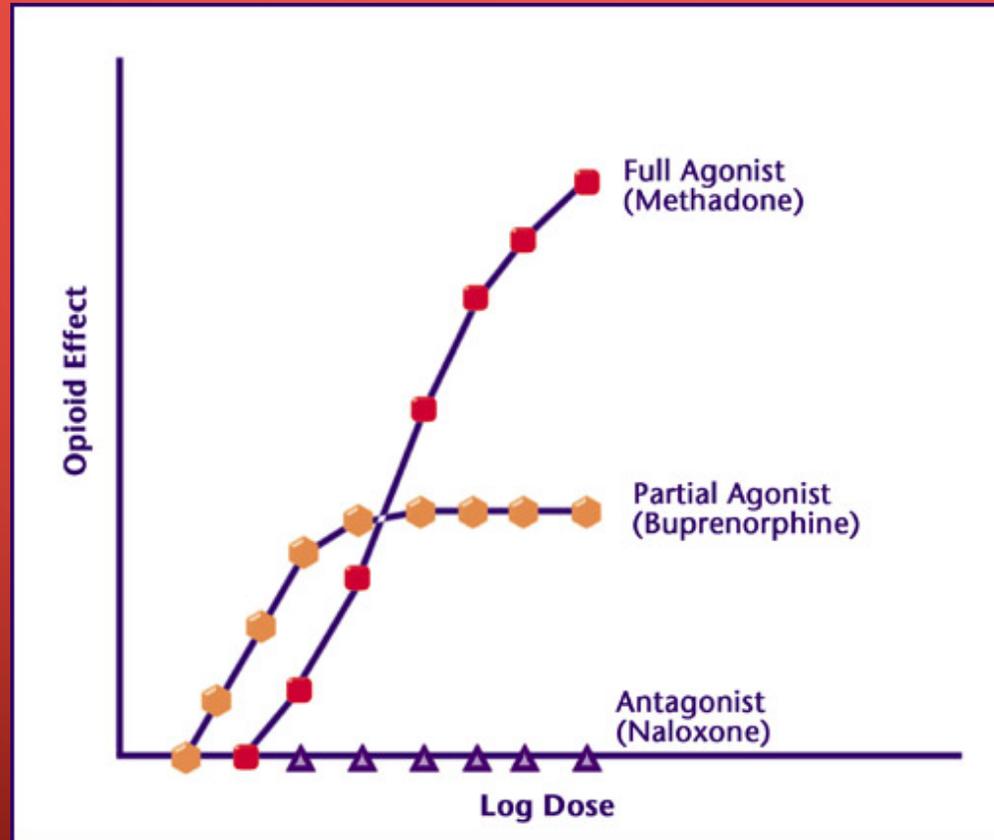
INTERVENTION: HOW DOES IT LOOK IN PRIMARY CARE?

- 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.

PHARMACOTHERAPY FOR OPIOID USE DISORDER

- Methadone – “gold standard” in pregnancy; but must be administered in 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



BUPRENORPHINE IN PREGNANCY

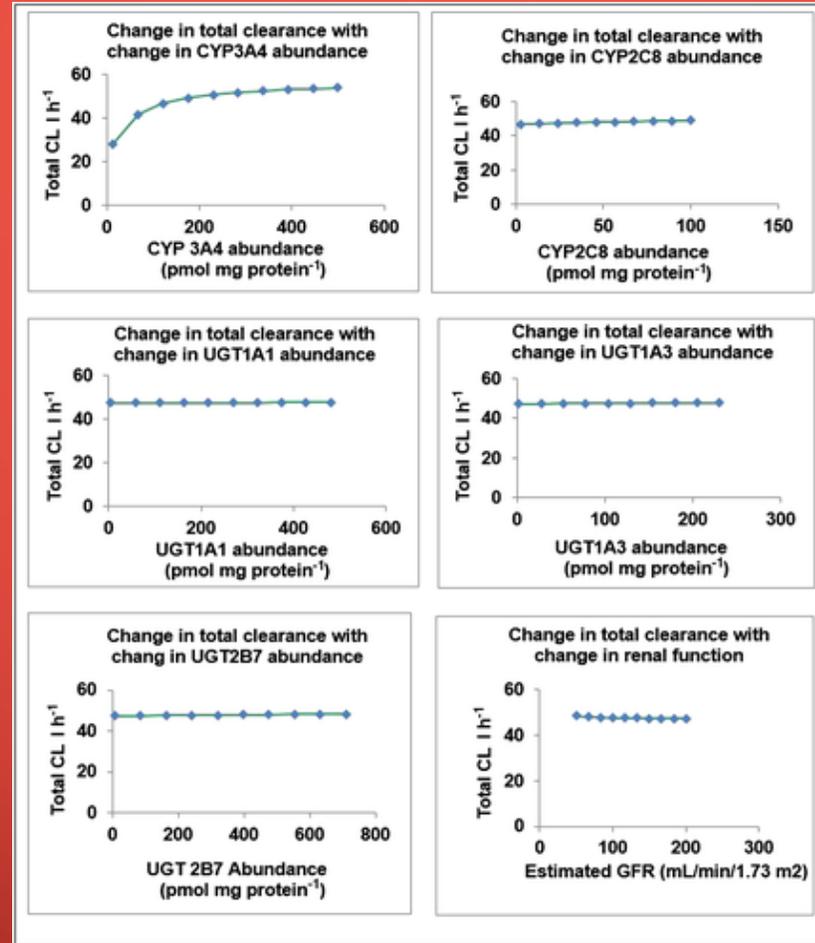
- Buprenorphine mono product (without naloxone) is generally preferred
- Originally used to to fears that of precipitated withdrawal if buprenorphine-naloxone was used IV by pregnant women
- Newer studies with Bup/Naloxone combo have shown comparable safety and efficacy without increase in adverse effects; (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.



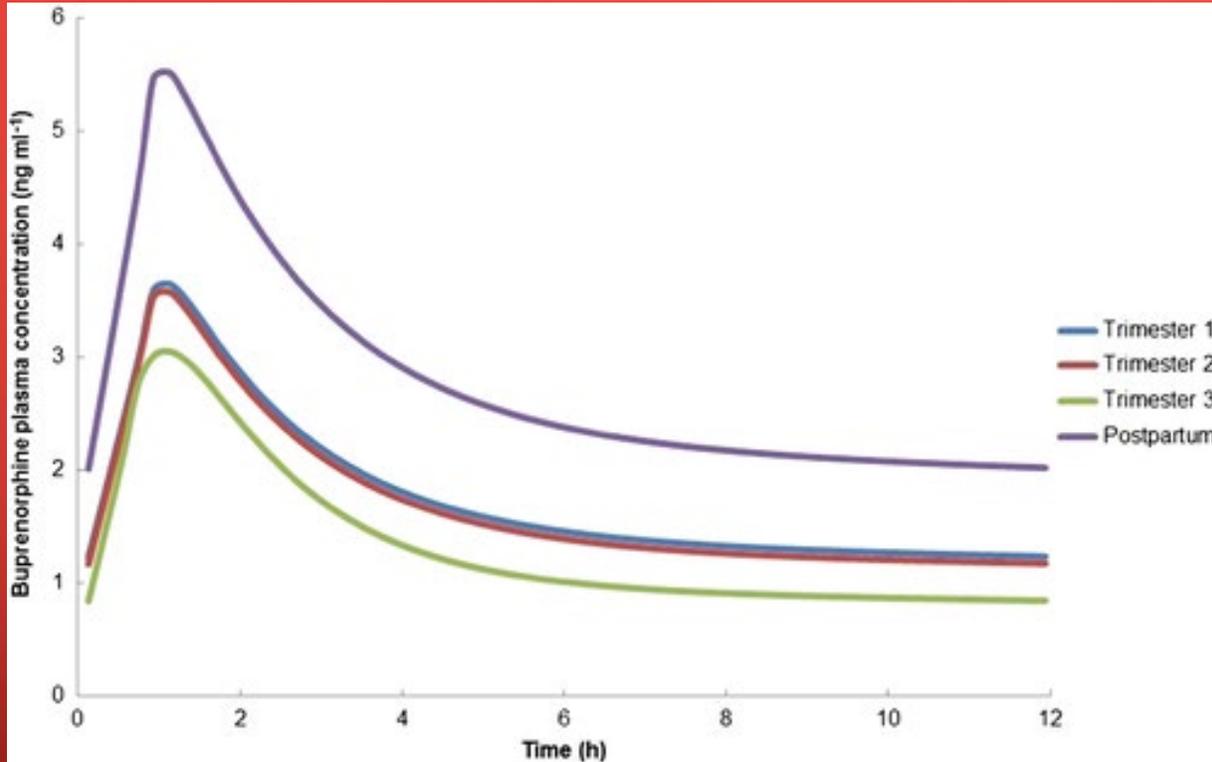
British Journal of Clinical Pharmacology, Volume: 84, Issue: 9, Pages: 2075-2087, First published: 05 June 2018, DOI: (10.1111/bcp.13642)

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 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



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**
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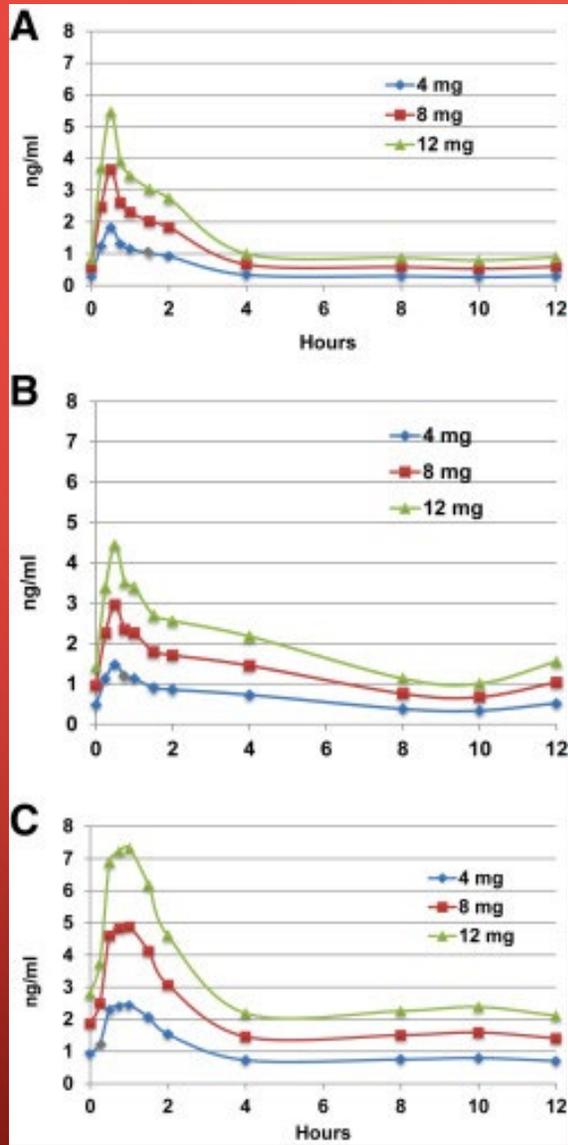


Figure 1. Median [buprenorphine](#) concentrations

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](#).

DOSING RECOMMENDATIONS

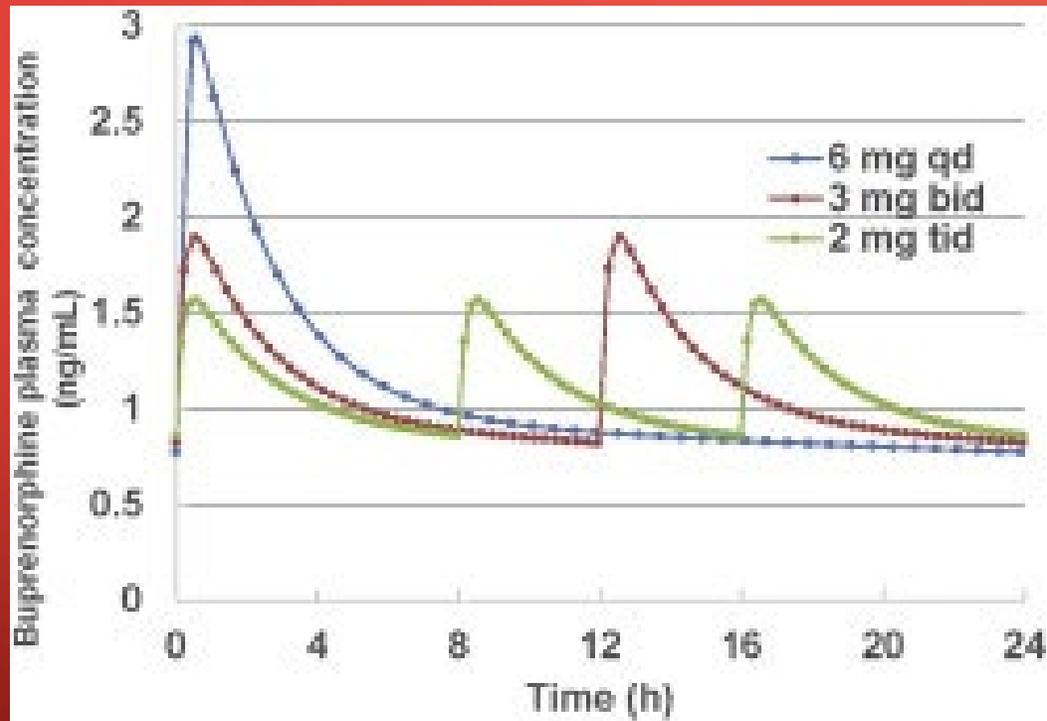


Figure 3. Simulated plasma concentrations of [buprenorphine](#) in nonpregnant subjects utilizing physiologically based [pharmacokinetic](#) modeling. Values are means. Frequency of dosing includes 6 mg daily, 3 mg BID, and 2 mg TID.

CONCLUSIONS

- Addiction to opioids during pregnancy is a still growing problem in the US
- Pregnancy does provide a window of opportunity for women to make changes in their health promoting behavior and address their addictive illnesses
- OUD is an illness and by definition this means women are not able to automatically stop using opioids due being pregnant
- Motivational Enhancement Therapy is a helpful harm reduction tool to aid women in maintaining sobriety during their pregnancy

CONCLUSION (CONT.)

- Medication Assisted Treatment using methadone or buprenorphine are currently recommended treatments for pregnant women with OUD
- Dosages and administration regimen changes during pregnancy due to changes to women's liver metabolism during pregnancy
- Women on MAT should be provided doses that maintain them free from withdrawal symptoms helping to reduce cravings

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- 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.
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