# Place of Possible Therapeutic **Choice in the Treatment of Opioid-Dependent Pregnant** Patients: What's Up with the International, Prospective, Double-Blind, Multi-Center **Trial funded by NIDA?**

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### Outline

I. World view of the problem

II. Current research

III. Future research

# Drug Addiction During Pregnancy

A universal public health problem

Alcohol, tobacco and illicit drugs

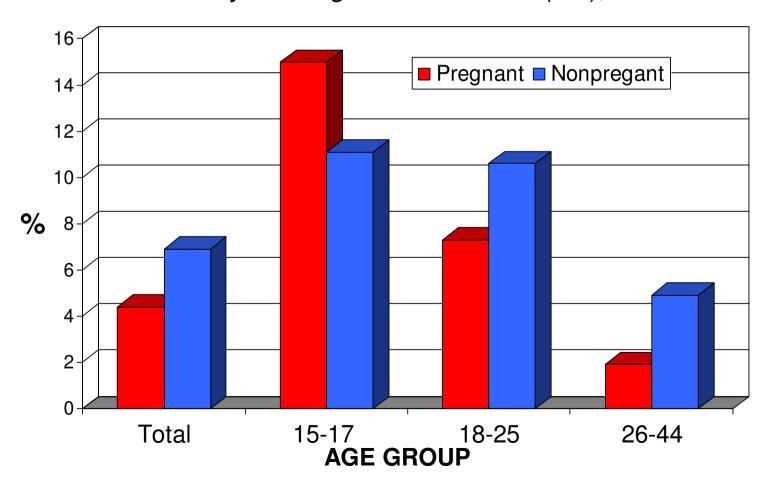
There is an absence of systematic solid prevalence data

# Examples of Data from Around the World

- France: 28% women smoke during pregnancy (Ducret 2005)
- Italy: FASD rate 20-40 per 1,000 children (2006)
- Nova Scotia: 25% smoking during pregnancy (Ebrahim et al., 2000)
- Philippines: 21% methamphetamine meconium positive rate N=393 (Ostrea et al., 2004)
- United States National Survey on Drug Use and Health 2004/5: 17% women smoke during pregnancy, 12% drink alcohol, 3% use marijuana
- South Africa: FASD rate 65-74 per 1,000 children (Viljoen et al., TH 2005) 0/07

# Nonmedical Use of Prescription Analgesics among Pregnant Women

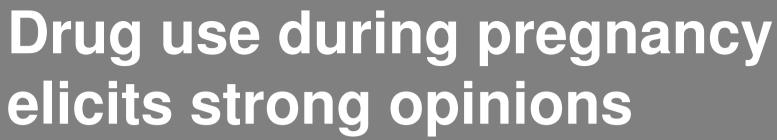
National Survey on Drug Use and Health (US), 2002-2004



# Drug Addiction During Pregnancy

- Collective goals of wanting to rid the world of drug addiction and have healthy mothers, children and families
- Approaches to achieving these goals differ
  - 1. Legal/punitive methods to prosecute women into submission
  - 2. Treatment and empowerment, providing the care and education to support women in making

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•Treating drug dependence with medications during pregnancy elicits even <u>stronger</u> opinions

•Both the mother and the child deserve our compassion and evidence-based treatments



# Current Medication Treatments Examined during Pregnancy

#### **Opioid dependence:**

- Buprenorphine
- Methadone
- Naltrexone

#### Nicotine dependence:

- Nicotine replacement products
- Bupropion

### Current Research

The advancement of treatment for opioid-dependent pregnant women is best served through a close multi-site international collaborative network able to conduct randomized controlled trials

The Maternal Opioid Treatment: Human Experimental Research (MOTHER) study is a first step in building this network

## Background to MOTHER

- Untreated maternal opioid addiction is associated with adverse medical and environmental circumstances that can negatively impact birth outcomes
- Methadone maintenance is associated with better prenatal care compliance and birth outcomes
- Available reports suggest buprenorphine is similar to methadone and relatively safe and effective during pregnancy
- Methodological limitations of previous studies

# Background Gaps in our understanding

Buprenorphine vs. methadone?

Neonatal Abstinence Syndrome

Co-factors related to outcomes

## MOTHER Study Clinical Sites

Thomas Jefferson University Philadelphia, Pennsylvania

University of Vienna Vienna, AUSTRIA

Vanderbilt University Nashville, Tennessee

Brown University 
Providence, Rhode Island

Johns Hopkins
University
Baltimore, MD
Coordinating Center:
Center for Substance
Abuse Research,
U. of Maryland

**University of Vermont Burlington, Vermont** 

University of Toronto Toronto, CANADA

Wayne State University Detroit, Michigan

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# MOTHER Study Oversight

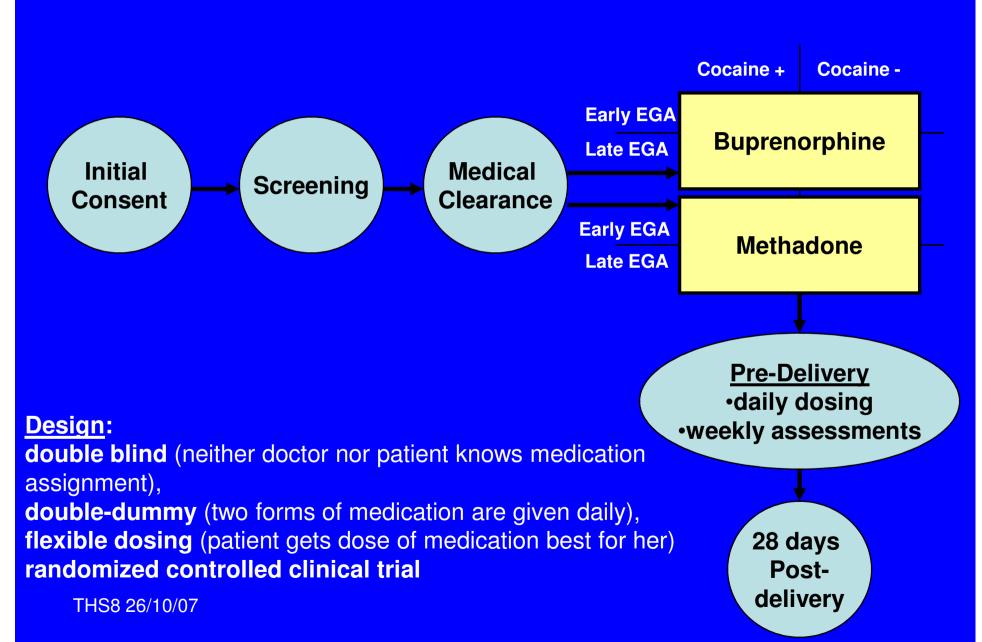
Data Safety and Monitoring Board (protocol, safety) National Institute on Drug Abuse (fiscal, research)

U.S. Food and Drug
Administration
(safety)

**CLINICAL SITES** 

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# MOTHER: Experimental Design



# Non-Pharmacotherapy Treatments

- Vouchers contingent upon drug negative biological samples
- Vouchers contingent upon compliance with treatment
- Counseling
- Medical Care
- Obstetric services
- Non-Obstetrical medical care (e.g., psychiatric)

### **MOTHER Study Enrollment Summary**

(as of 10/1/07)

**Initially Consented** 

$$(n = 641)$$

53%

**Initially Eligible** 

$$(n = 341)$$

82%

**Approached** 

$$(n = 280)$$

**Most Common Reasons for** Ineligibility

85%

49%

**Outside EGA Range** 

Benzodiazapene

use/abuse

**Medical Reason** 

(n = 137)

**Full Consent** 

Randomized

$$(n = 117)$$

Completed Protocol (n=55)

**Active** Participants (n=33)

25%

28%

47%

**Early** Dropouts (n=29)

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## Challenges

#### **Participants**

- Variability by site (type of opioid used, polydrug use patterns)
- Complicated life circumstances
- Co-existing mental health conditions

#### **Protocol**

- Standardization of procedures
- Exclusionary criteria
- Adverse event reporting procedures
- Concomitant medication reporting

#### **Coordination/Administrative**

- Participant recruitment
- Participant retention
- Staff Turnover, Training and Re-training
- Site Monitoring and Quality Control
- Communication

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# Opportunities for Research in Drug Addiction and Pregnancy

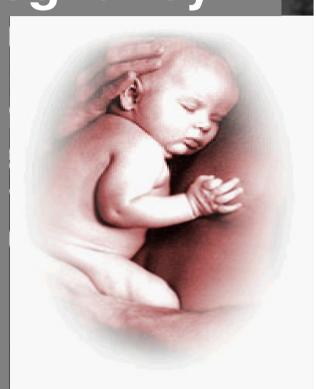


Maternal

**Fetal** 

Neonate

Child



Maternal, fetal, neonate and child

Safety and efficacy trials of other medications

 Effectiveness trials of other medications or medication combinations (e.g., NRT, SSRIs)

Post-marketing surveillance

#### **Maternal**

- Pharmacokinetics and pharmacodynamics of medications pre- and post-partum
- Matching mothers to agonist medications
- Transitioning mothers to another medication
- Pain management pre- and post-partum
- HIV risk behaviors in pregnant agonist treated patients
- Tools to better quantify drug use

#### **Fetal**

- Systematic evaluation of fetal safety with different medications, dosing regimens and medicationassisted withdrawal or transfers
- Fetal effects of medication combinations

#### **Neonate**

- Development of NAS tools for premature neonates
- Develop tools to assess and determine treatment for withdrawal from benzodiazepines, alcohol and combinations of drugs
- Compare medication protocols to treat NAS

#### **Child**

 Systematic long-term follow-up of children prenatally exposed to medications to treat drug dependence or other co-occurring conditions in this population

### **Future Direction**

- Establish a consortium of global researchers dedicated to the prevention and treatment of drug dependence and other co-occurring psychiatric disorders during pregnancy
- Utilization of a collaborative flexible network approach to develop and answer research questions
- Pool collective data, knowledge and experience to develop evidence-based best practice guidelines on a global level

## Summary

- Drug dependence during pregnancy is a public health problem that can be treated
- MOTHER may provide data for government bodies to consider labeling changes for methadone and buprenorphine
- Future studies may build upon the collaborative infrastructure to study other medications and women's health issues during pregnancy

