

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

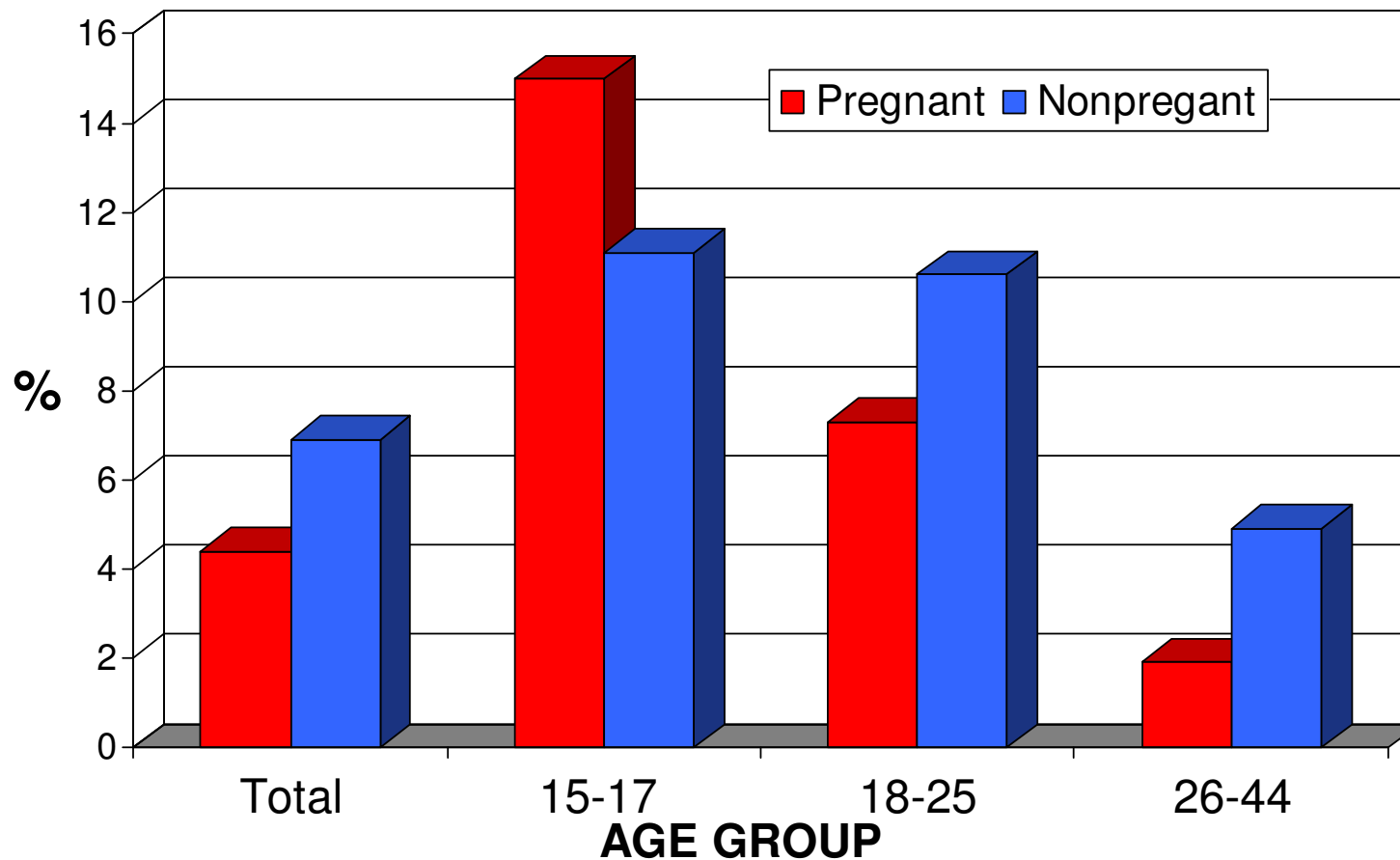
- A universal public health problem
- Alcohol, tobacco and illicit drugs
- There is an absence of systematic solid prevalence data

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., 2005)

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 choices appropriate for a healthy pregnancy

Drug use during pregnancy elicits strong opinions

- Treating drug dependence with medications during pregnancy elicits even *stronger* 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

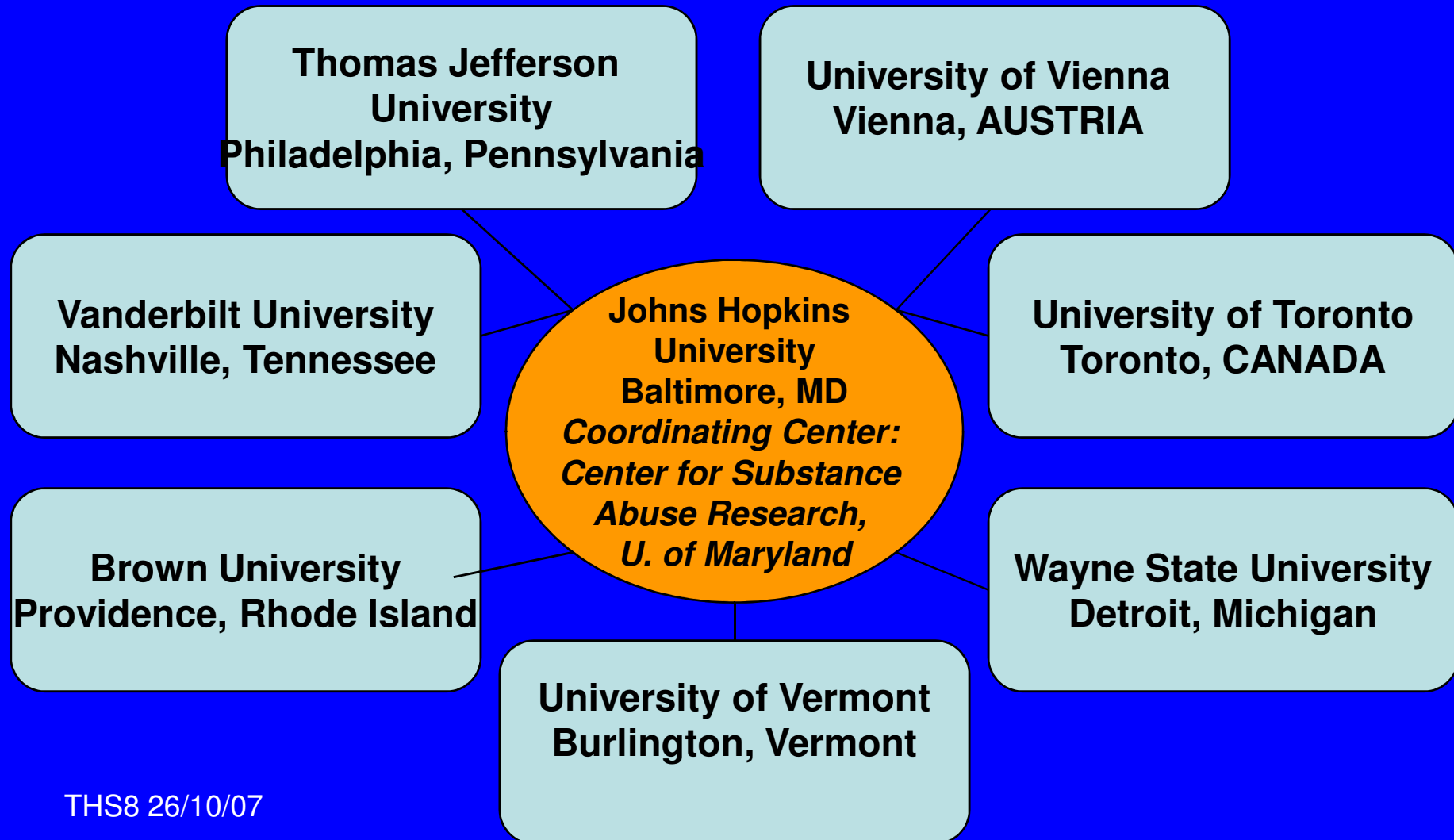
- Untreated maternal opioid addiction is associated with adverse medical and environmental circumstances that can negatively impact birth outcomes
- Methadone maintenance is associated with better prenatal care compliance and birth outcomes
- Available reports suggest buprenorphine is similar to methadone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

Background

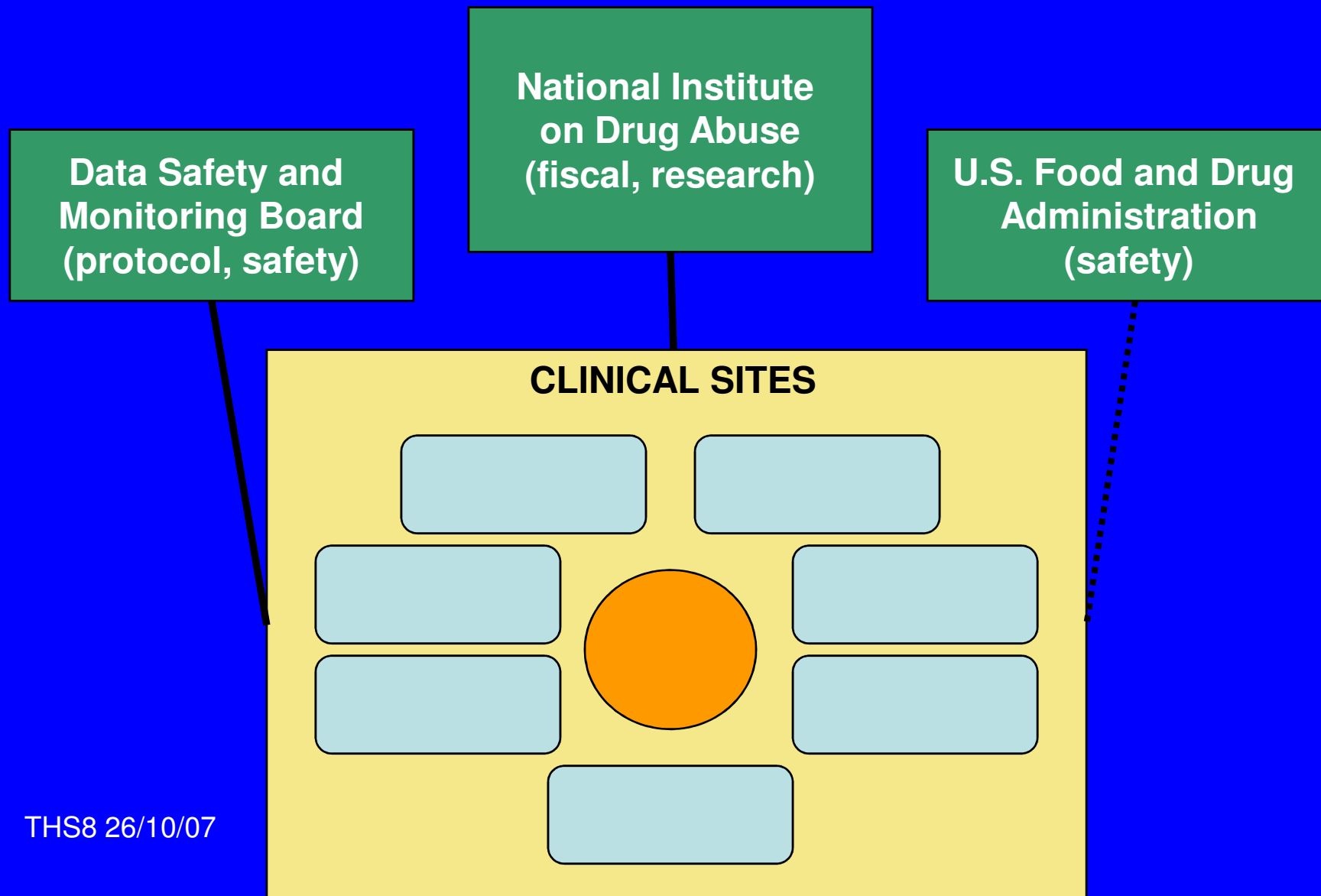
Gaps in our understanding

- Buprenorphine vs. methadone?
- Neonatal Abstinence Syndrome
- Co-factors related to outcomes

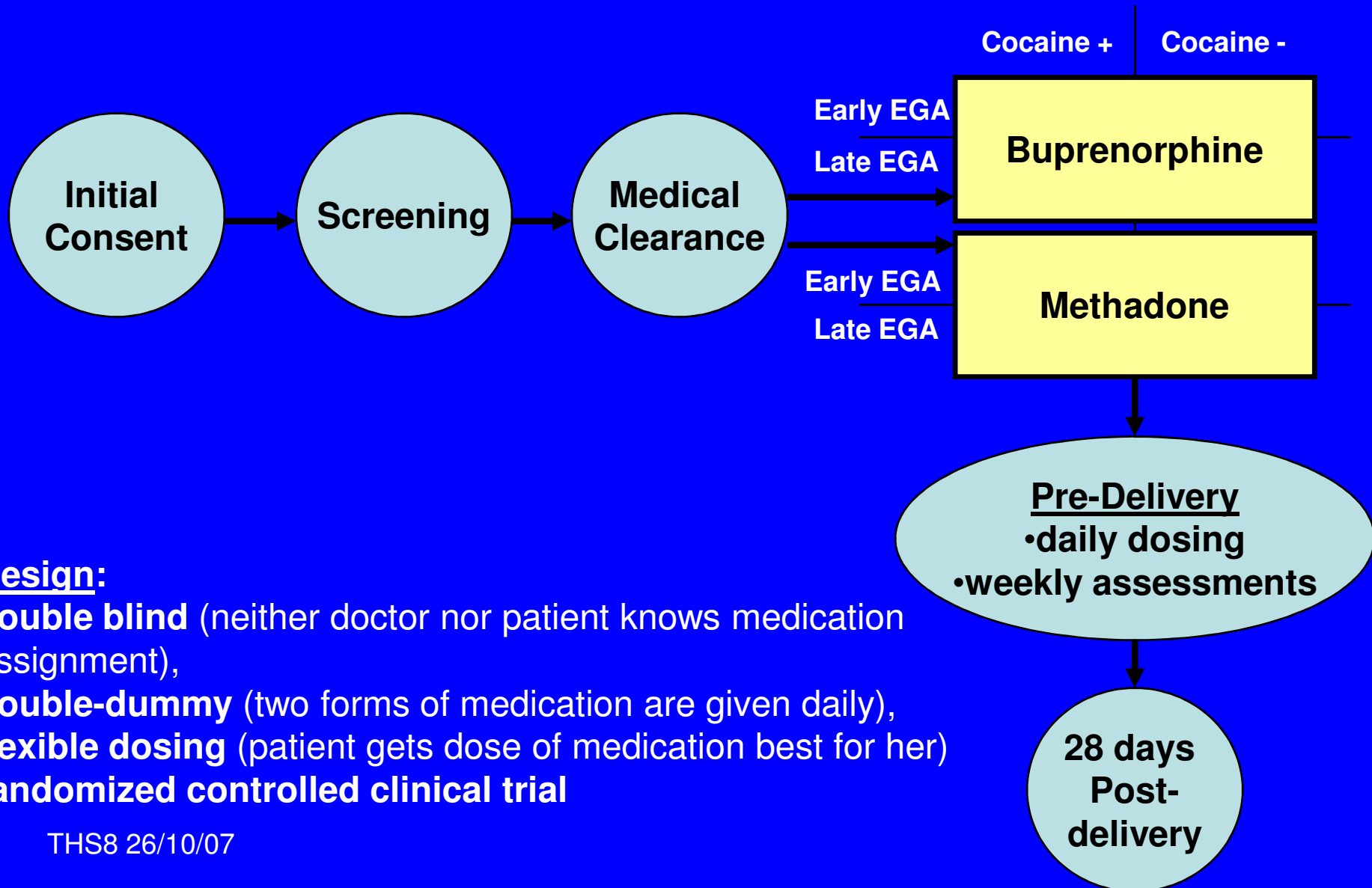
MOTHER Study Clinical Sites



MOTHER Study Oversight



MOTHER: Experimental Design



Design:

double blind (neither doctor nor patient knows medication assignment),

double-dummy (two forms of medication are given daily),

flexible dosing (patient gets dose of medication best for her)

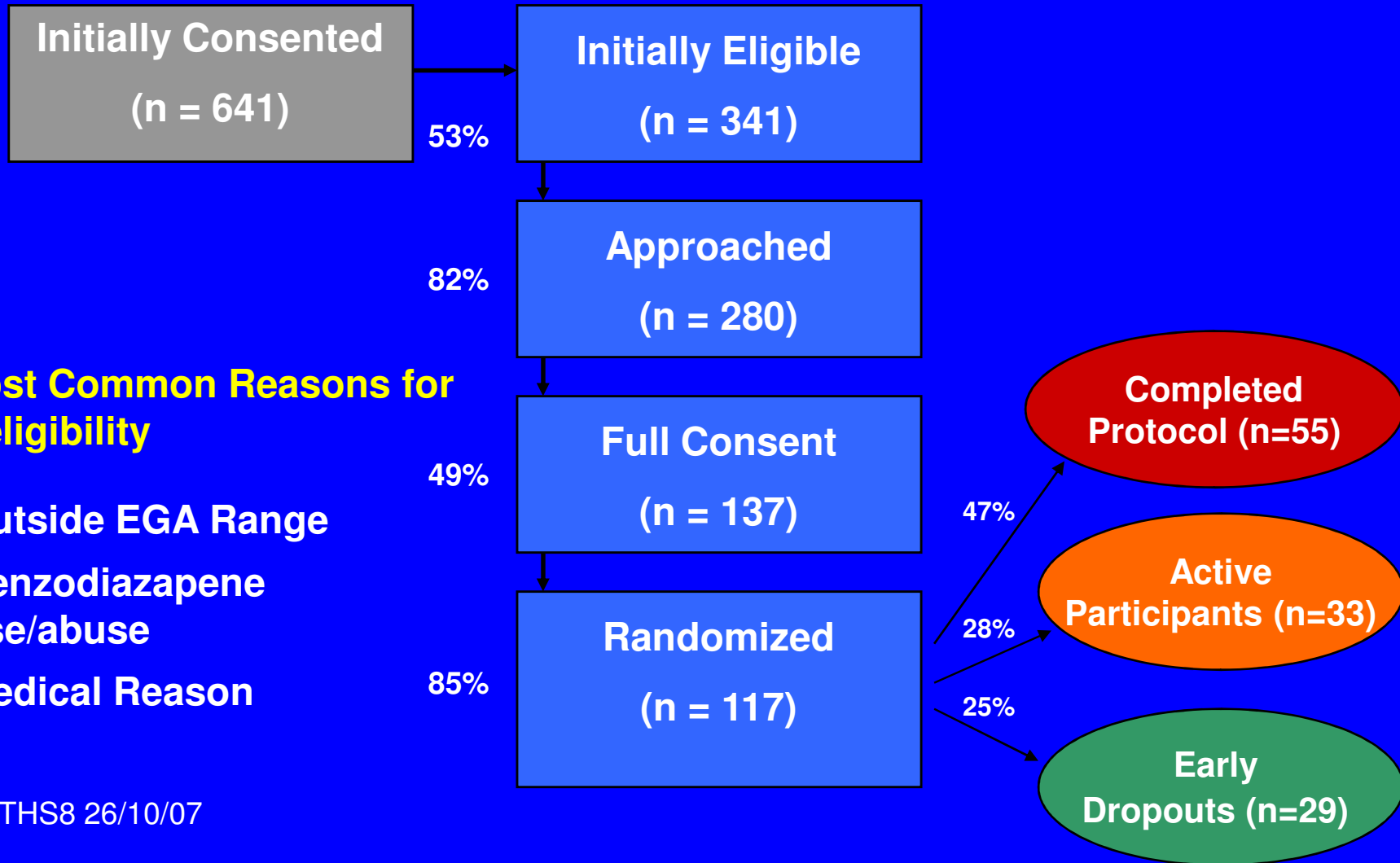
randomized controlled clinical trial

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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)



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

Opportunities for Research in Drug Addiction and Pregnancy

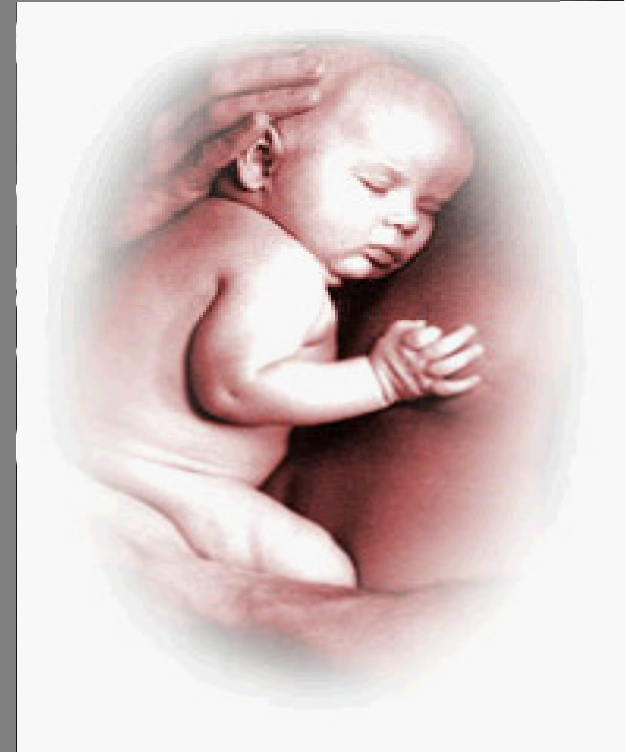


Maternal

Fetal

Neonate

Child



Future Research

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

Future Research

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

Future Research

Fetal

- Systematic evaluation of fetal safety with different medications, dosing regimens and medication-assisted 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

Future Research

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



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Roger Carver