

## Maternal Opioid Treatment: Human Experimental Research (MOTHER)

As part of a multi-site clinical trial, each of the Maternal Opioid Treatment: Human Experimental Research (MOTHER) sites has a similar abstract in the NIH CRISP query system. For the Lead Site, we have included the complete abstract. For the other sites, we have edited the abstracts to include their unique focus. More specific information is available through the Principal Investigators and information on other research in this area is available through CRISP at <http://crisp.cit.nih.gov/>.

Maternal Opioid Treatment:Human  
Experimental Research

Johns Hopkins University  
Dept. of Psychiatry & Behavioral Sciences  
4940 Eastern Avenue, D-3 East  
Baltimore, MD 21224  
Hendree Jones, Ph.D.  
[hejones@jhmi.edu](mailto:hejones@jhmi.edu)

Though clearly beneficial, the use of methadone during pregnancy remains controversial in part due to the large percentage of newborns having signs of opioid withdrawal requiring medical intervention and extended hospitalization. Buprenorphine, a newly approved medication for the treatment of non-pregnant opioid dependent patients, produces only a mild abstinence syndrome following abrupt withdrawal. Promising preliminary data from a double-blind randomized trial at the Johns Hopkins School of Medicine (JHUSOM) have suggested that buprenorphine results in improved birth outcomes and less neonatal abstinence syndrome (NAS) relative to methadone. The current randomized, parallel group study will be the first multi-site trial to assess in opioid-dependent pregnant women the efficacy of buprenorphine for reducing NAS relative to methadone.

Coordinating Center

University of Maryland  
Center for Substance Research (CESAR)  
4321 Hartwick Road, Suite 501  
College Park, MD 20740  
Amelia Arria, Ph.D.  
[aarria@cesar.umd.edu](mailto:aarria@cesar.umd.edu)

JHUSOM is the Lead Site for this study involving six United States and two international sites. The JHUSOM team trained in addiction medicine, psychiatry, pediatrics, obstetrics, neonatology, and controlled clinical trials will assure comprehensive oversight and rigorous scientific integrity of the study. Opioid-dependent pregnant women (N=370 across 8 sites) will be randomized to optimal doses of methadone or buprenorphine and followed throughout pregnancy. The JHUSOM site will randomize 30 women each to receive methadone or buprenorphine. Treatment groups will be compared on the primary outcome measures of: Peak total NAS score; number of neonates treated for NAS; total amount of anti-withdrawal medication given to neonates treated for NAS; physical birth parameter of head circumference; and neonatal length of hospital stay. Secondary neonatal/fetal outcome measures include other physical, behavioral and safety parameters. Secondary maternal outcomes include: Treatment retention, drug use, medication safety, psychosocial functioning and dose adequacy. Overall, this study will provide pivotal data to the FDA to support an indication for the use of buprenorphine during pregnancy and potentially optimize strategies for safe and effective treatment of pregnant opioid-dependent women. Keywords: Buprenorphine, drug abuse, drug abuse chemotherapy, embryo /fetus toxicology, human therapy evaluation, pregnancy clinical trial, drug /alcohol abstinence, embryo /fetus disorder, hospital length of stay, methadone, sign /symptom

Maternal Opioid Treatment:Human  
Experimental Research

Medical University of Vienna  
Dept. of Psychiatry  
Wahringer Gurtel 18-20  
1090 Vienna  
Vienna, Austria  
Gabriele Fischer, M.D.  
[gabriele.fischer@meduniwien.ac.at](mailto:gabriele.fischer@meduniwien.ac.at)

The Vienna team skilled in addiction medicine, psychiatry, pediatrics, obstetrics, neonatology, and controlled clinical trials will assure comprehensive oversight and rigorous scientific integrity of the study. Opioid-dependent pregnant women will be randomized to optimal doses of buprenorphine (n=26) or methadone (n=26) and followed throughout pregnancy. Treatment groups will be compared on the same primary and secondary outcome measures as the Lead Site. This first study will establish an infrastructure and network with expertise in conducting controlled trials with pharmacotherapies for substance dependent pregnant women. Keywords: Buprenorphine, drug abuse, drug abuse chemotherapy, embryo /fetus toxicology, human therapy evaluation, pregnancy clinical trial, drug /alcohol abstinence, embryo /fetus disorder, hospital length of stay, methadone, sign /symptom

Maternal Opioid Treatment:Human Experimental Research

University of Vermont  
Substance Abuse Treatment Center  
1 South Prospect Street, Room 1415  
Burlington, VT 05401  
Sarah H. Heil, Ph.D.  
sarah.heil@uvm.edu

The University of Vermont (UVM) site proposes to participate in the multi-site trial led by the Johns Hopkins School of Medicine (JHUSOM) involving six sites in the U.S. and two international sites. To do so, we have brought together a multidisciplinary team trained in psychiatry, addiction medicine, obstetrics, and neonatology with the professional expertise to provide comprehensive care for the participants and rigorous scientific expertise for the study. At the UVM site, opioid-dependent pregnant women will be randomized to optimal doses of methadone (n=24) or buprenorphine (n=24) and followed throughout pregnancy. Treatment groups will be compared on the same primary and secondary outcome measures as the Lead Site. Unique to the UVM site, delay discounting will be compared between study participants and gestational age matched community volunteers. The results of this site-specific study have the potential to provide important insights into why some pregnant women abuse opiates despite the potential harm that may do to the fetus. Keywords: Buprenorphine, drug abuse, drug abuse chemotherapy, embryo /fetus toxicology, human therapy evaluation, pregnancy clinical trial, drug /alcohol abstinence, embryo /fetus disorder, hospital length of stay, methadone, sign /symptom

Maternal Opioid Treatment:Human  
Experimental Research

Thomas Jefferson University  
Dept. of Pediatrics  
1201 Chestnut Street, 9th Floor  
Philadelphia, PA 19107  
Karol Kaltenbach, Ph.D.  
karol.kaltenbach@jefferson.edu

Thomas Jefferson University (TJU) proposes to participate in the multi-site trial led by the Johns Hopkins School of Medicine (JHUSOM) involving six United States and two international sites. Maternal Addiction Treatment Education and Research (MATER) at TJU has brought together a multi-disciplinary team trained in addiction medicine, psychiatry, pediatrics, obstetrics, neonatology, and controlled clinical trials with the professional expertise to provide comprehensive care for the subjects and rigorous scientific integrity of the study. Opioid-dependent pregnant women will be randomized to optimal doses of methadone (n=30) or buprenorphine (n=30) and followed throughout pregnancy. Treatment groups will be compared on the same primary and secondary outcome measures as the Lead Site. Keywords: Buprenorphine, drug abuse, drug abuse chemotherapy, embryo /fetus toxicology, human therapy evaluation, pregnancy clinical trial, drug /alcohol abstinence, embryo /fetus disorder, hospital length of stay, methadone, sign /symptom

Maternal Opioid Treatment:Human  
Experimental Research

The Psychiatric Hospital at Vanderbilt  
1601 23rd Avenue S., Suite 3068

Nashville, TN 37232  
Peter R. Martin, M.D.  
peter.martin@vanderbilt.edu

The efficacy of buprenorphine to produce less neonatal abstinence signs (NAS) in the neonate, compared to methadone, will be assessed in opioid-dependent pregnant women. The professional expertise of a multi-disciplinary group at Vanderbilt University Medical Center and Middle Tennessee Treatment Center trained in addiction medicine, psychiatry, pediatrics, obstetrics, neonatology, and controlled clinical trials has been brought together to provide comprehensive care for the subjects and rigorous scientific integrity for the study. Subjects randomized to equivalent opioid doses of methadone (N=30) or buprenorphine (N=30) will be followed through pregnancy. Treatment groups will be compared on the same primary and secondary outcome measures as the Lead Site. This will be the first study to develop an infrastructure and network of sites with expertise in conducting controlled trials with pharmacotherapies for substance abusing and dependent pregnant women. Utilization of this network will ensure the successful accrual of study participants in a difficult to recruit population (i.e., pregnant women). Keywords: Buprenorphine, drug abuse, drug abuse chemotherapy, embryo /fetus toxicology, human therapy evaluation, pregnancy clinical trial, drug /alcohol abstinence, embryo /fetus disorder, hospital length of stay, methadone, sign /symptom

#### Maternal Opioid Treatment:Human Experimental Research

Wayne State University  
Dept. of Psychiatry & Behavioral Neurosciences  
2761 E. Jefferson  
Detroit, MI 48207  
Susan M. Stine, M.D., Ph.D.  
sstine@med.wayne.edu

The Wayne State University (WSU) Site proposes to participate in the multi-site trial led by the Johns Hopkins School of Medicine (JHUSOM) involving six U.S. and two international sites. The Substance Abuse Research division (SARD) at WSU has brought together a multi-disciplinary group trained in addiction medicine, psychiatry, pediatrics, obstetrics, neonatology, and controlled clinical trials with the professional expertise to provide comprehensive care for the subjects and rigorous scientific integrity for the study. At this site, subjects randomized to equivalent optimal doses of methadone (n=20) or buprenorphine (n=20) will be followed through pregnancy. Treatment groups will be compared on the same primary and secondary outcome measures as the Lead Site. Unique to this site, a pilot study will be conducted in which maternal salivary cortisol levels during pregnancy and labor and neonatal stressed (after heel prick blood draw) and unstressed salivary cortisol levels will be obtained. In addition, the WSU site also proposes to extend neonatal follow up to 6 months. The Wayne State site also proposes to participate in the NICU (Neonatal Intensive Care Unit) Network Neurobehavioral Scale (NNNS) as a secondary outcome measure in collaboration with the Providence, Rhode Island site and the Lead Site. Keywords: Buprenorphine, drug abuse, drug abuse chemotherapy, embryo /fetus toxicology, human therapy evaluation, pregnancy clinical trial, drug /alcohol abstinence, embryo /fetus disorder, hospital length of stay, methadone, sign /symptom

#### Maternal Opioid Treatment:Human Experimental Research

Brown University  
Dept. of Pediatrics  
79 Plain Street, 2nd Floor  
Providence, RI 02903  
Barry M. Lester, Ph.D.  
barry\_lester@brown.edu

The Johns Hopkins School of Medicine (JHUSOM), the Lead Site for this study has a team trained in addiction medicine, psychiatry, pediatrics, obstetrics, neonatology, and controlled clinical trials will assure comprehensive oversight and rigorous scientific integrity of the study. Opioid-dependent pregnant women at the Brown site at Women and Infants Hospital will be randomized to optimal doses of methadone (n=10) or buprenorphine (n=10) and followed throughout pregnancy. Treatment groups will be compared on the same primary and secondary outcome measures as the Lead Site. This first study will establish an infrastructure and network with expertise in conducting controlled trials with pharmacotherapies for substance abusing/ dependent pregnant women. Keywords: Buprenorphine, drug abuse, drug

abuse chemotherapy, embryo /fetus toxicology, human therapy evaluation, pregnancy clinical trial, drug /alcohol abstinence, embryo /fetus disorder, hospital length of stay, methadone, sign /symptom

Maternal Opioid Treatment:Human  
Experimental Research

St. Joseph's Health Centre  
Dept. of Family Medicine  
30 The Queensway  
Toronto, ON M6R 1B5  
Canada  
Peter Selby, M.D.  
peter\_selby@camh.net

St. Joseph's Health Centre (SJHC) (Toronto, CA) proposes to participate in the multi-site trial led by the Johns Hopkins School of Medicine (JHUSOM) involving six U.S. and two international sites. SJHC has brought together a multi-disciplinary group trained in addiction medicine, psychiatry, toxicology, pediatrics, obstetrics, neonatology, and controlled clinical trials with the professional expertise to provide comprehensive care for the subjects and rigorous scientific integrity for the study. At this site, subjects randomized to equivalent optimal doses of methadone (n=15) or buprenorphine (n=15) will be followed through pregnancy. Treatment groups will be compared on the same primary and secondary outcome measures as the Lead Site. Unique to this site, is the extended follow-up of both neonates and mothers for 6 months. This study will provide pivotal data on the optimal management of pregnant opioid dependent women and establish a network for future studies with this population. Keywords: Buprenorphine, drug abuse, drug abuse chemotherapy, embryo /fetus toxicology, human therapy evaluation, pregnancy clinical trial, drug /alcohol abstinence, embryo /fetus disorder, hospital length of stay, methadone, sign /symptom