



**FASEB**

Federation of American Societies  
for Experimental Biology

# The Impact of IDeA Funding in Mississippi

June 26, 2024

# Speakers



**Jane Reckelhoff, PhD**



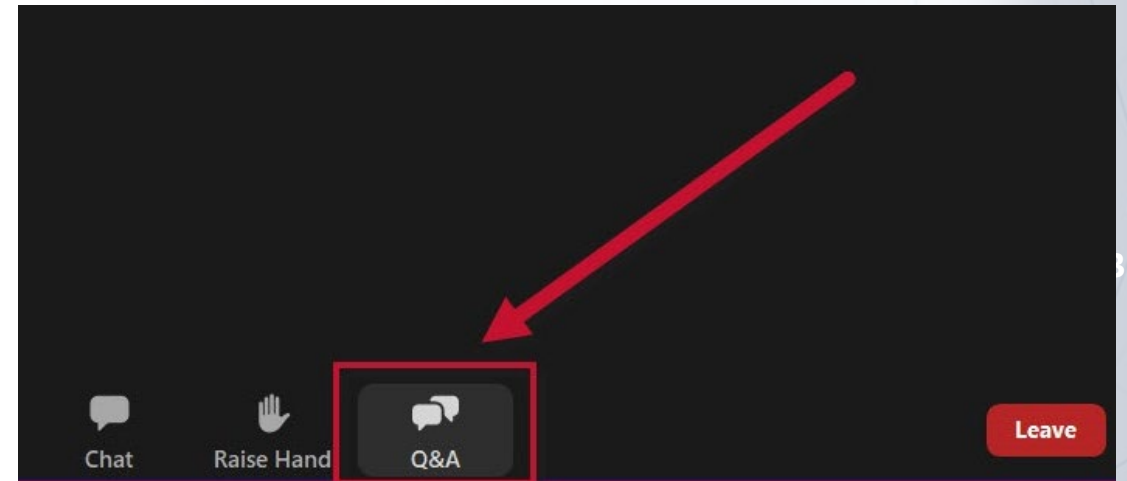
**Licy Yanes Cardozo, MD**



**Kedra Wallace, PhD**

# A Few Announcements

- Webinar format
- Chat and “Raise Hand” functions are disabled; please use the Q&A to type in your questions
- We will address as many questions as possible at the end
  
- Webinar is being recorded for on-demand viewing (to be posted on the FASEB website)





# **Mississippi Center of Excellence In Perinatal Research**

**Funded by NIGMS  
P20GM121334**

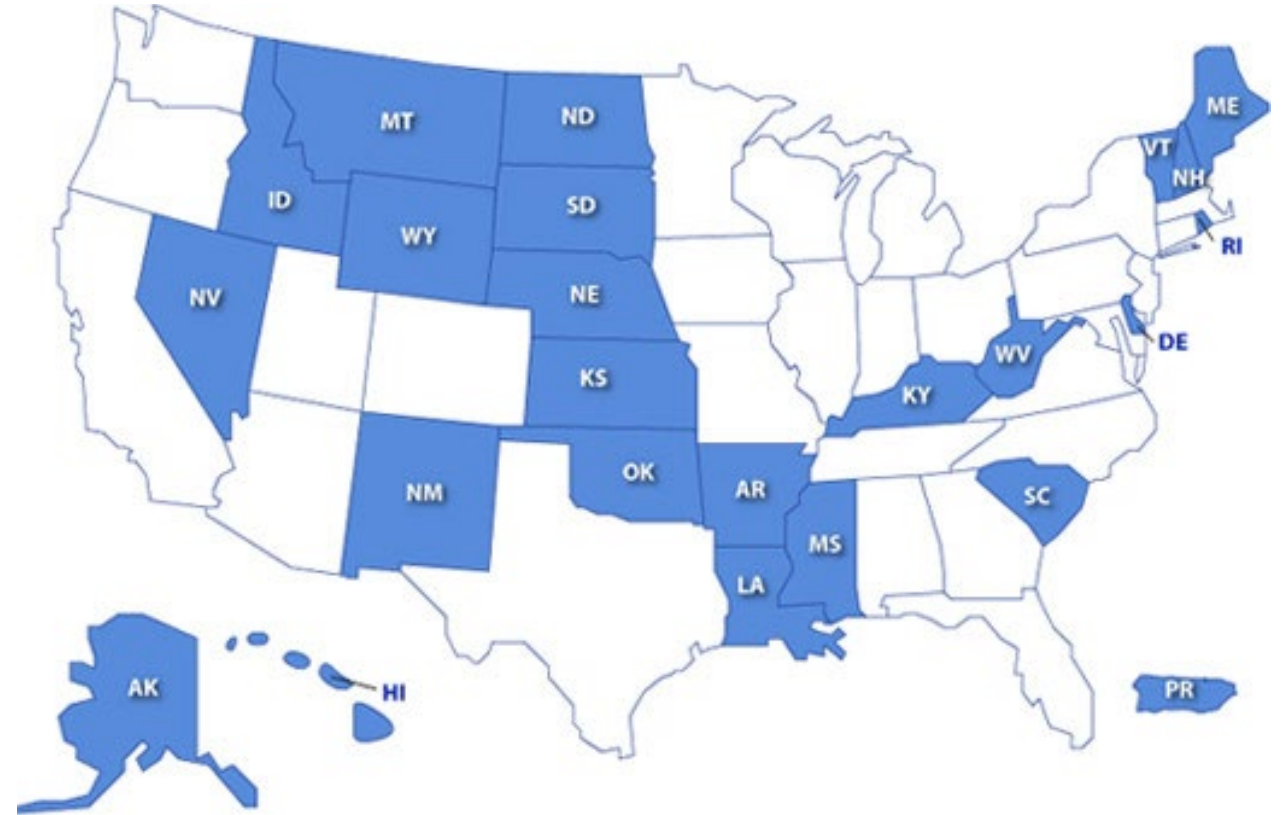
**Jane F. Reckelhoff, Ph.D.  
COBRE PI**

# Mississippi Center of Excellence in Perinatal Research

Supported by NIGMS

**Centers of Biological  
Research  
Excellence (COBRE)**

IDeA States  
(Institutional Development  
Awards)



**Purpose:** To augment and strengthen biomedical research capacity

# Mississippi Center of Excellence in Perinatal Research

The purpose of the MS CEPR is to promote research into understanding the mechanisms responsible for any health issues that initiate during pregnancy

Now in Phase 2 (Phase 1: 2017-2022; Phase 2: 2022-2027)



## **Executive Committee**

**Barbara Alexander, Ph.D., Director of Basic Research**

**Babbette LaMarca, Ph.D., Director of Clinical Research**

**Damian Romero, Ph.D., Director of the Research Resources**

## **External Advisory Committee**

**Vesna Garovic, M.D., Ph.D., Mayo Clinic**

**Sandra Davidge, Ph.D., University of Alberta**

**Nina Stachenfeld, Ph.D., Yale University**

# Mississippi Center of Excellence in Perinatal Research Provides

- Research Project grants to investigators who have never had NIH R01 level funding, or are changing directions of their research (50% effort-\$150,000-200,000 per year, 3-4 years)
- Pilot Project grants (1 year, \$50,000; no effort requirement)
- State-of-the-art research cores to assist RPLs/PPLs in research
- Provide mentorship in research design, grant writing and submission, and career mentoring



# Research Resources Core

(Director: D. Romero)

**Animal and Telemetry Sub-Core:** animal surgery, BP, HR, activity in conscious, unrestrained rats in their home cages (Dr. Damian Romero)

**Mitochondrial Research Sub-Core:** mitochondrial function (Drs. Kristin Edwards)

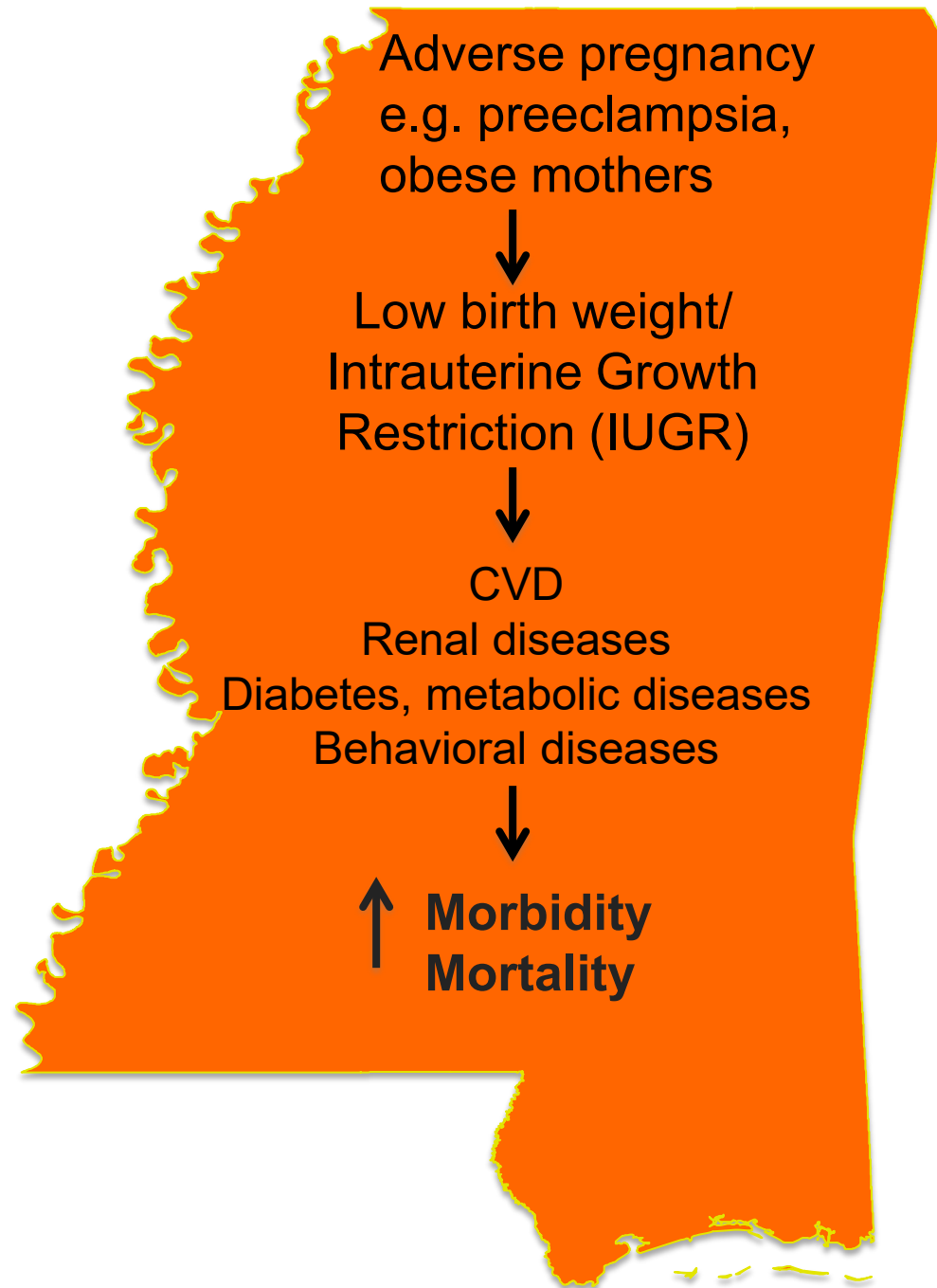
**Confocal Imaging Sub-Core:** cell microscopy, protein trafficking (Dr. David Brown)

**Fluorescence Activated Cell Sorting (FACS)/Bioplex:** (Dr. Eva Bengten)

**Clinical Research:** Nurse coordinator, LC/MS, lab (Dr. George Booz)

**Statistical Analyses Sub-Core:** assistance with experimental design, manuscript and grant submission (Dr. Seth Lirette)

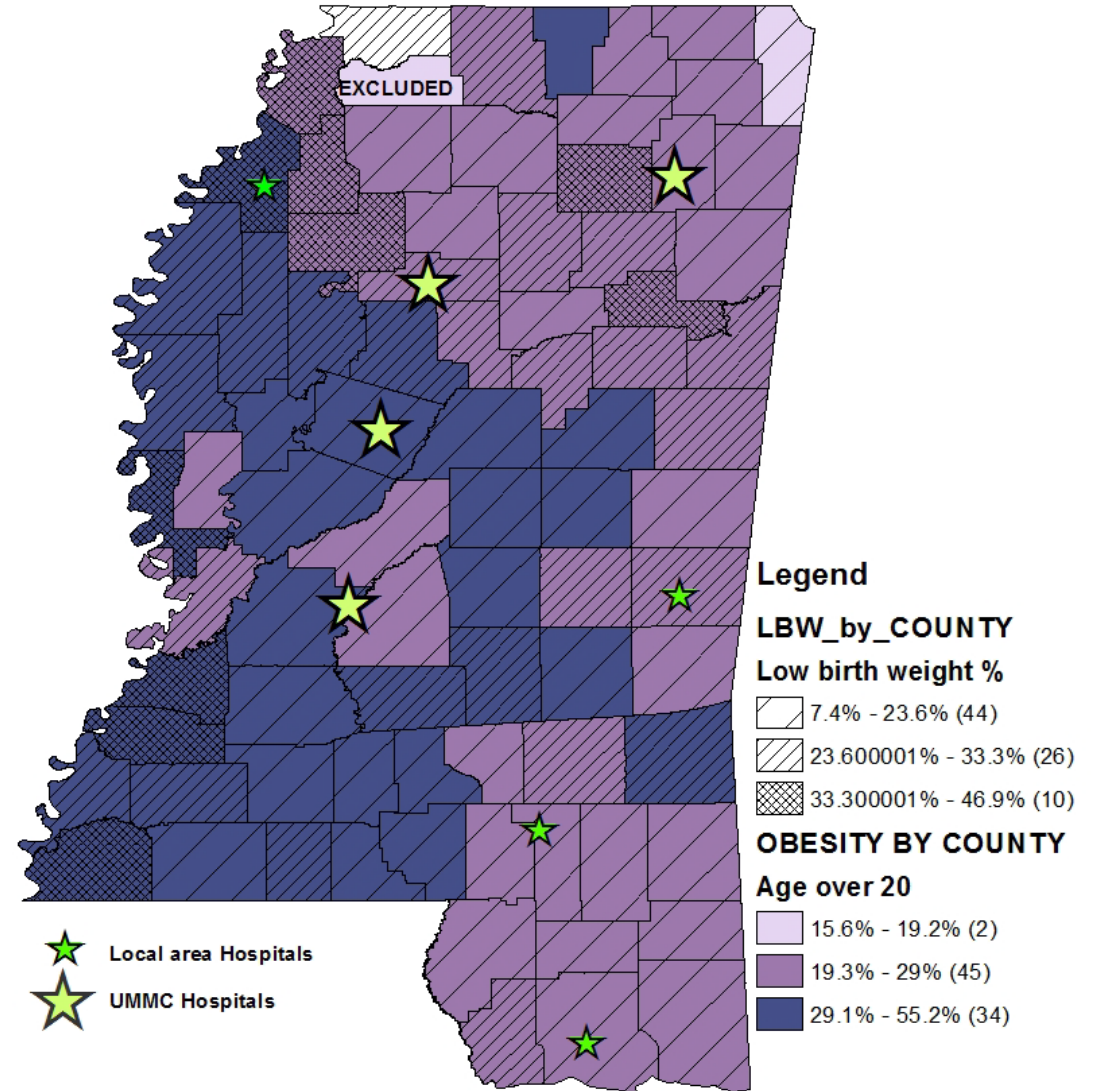
**MS CEPR**  
**Overall**  
**Hypothesis:**



# Why do we need to support perinatal research?

Mississippi has:

- highest incidence of obesity in US
- highest incidence of low birth weight in US
- highest incidence of preeclampsia
- highest incidence of diabetic pregnancies



Rates from UMMC's patient population

# **MS CEPR SUCCESS – over past 7 years (2017-24)**

**Research Project Leaders supported: 11 (5 funded)**

**Pilot Project Leaders supported: 11 (4 funded)**

**NIH Grants: R01s, R21s, COBRE Supplements**

**Other grants: AHA (CDA), DoD**

**Total amount of funding: >\$11 million**

**(RPLs, PPLs who started in Phase 2: 3 R01s submitted this cycle)**

# Two of the MS CEPR Stars:



**Licy L. Yanes Cardozo, M.D.**  
**Professor of Endocrinology *and***  
**Pharmacology and Toxicology**

**Kedra Wallace, Ph.D.**  
**Professor of Obstetrics and Gynecology**  
***and* Pharmacology and Toxicology**



# **Licy Yanes Cardozo, M.D.**

MD -- Univ of Asuncion, Paraguay

Postdoctoral fellow – UMMC

Assistant Professor – AHA SDG

Resident, UMMC Fellowship, Endocrinology, UMMC

Professor, Endocrinology; Pharmacology and Toxicology,  
UMMC



**COBRE funding, RPL -- 2017-22**

**Current funding:** PI: R01; Pilot Project, NIH- NIMHD/Forged AHEAD Center/UAB;  
COBRE supplement (JIT)

**Research interests:** Mechanisms of elevated BP and CVD in women with Polycystic Ovary Syndrome (PCOS)

# **Kedra Wallace, Ph.D.**



Ph.D. –Neuroscience, UMMC

Postdoctoral Fellow, Obstetrics and Gynecology, UMMC

Professor, OB-GYN and Pharmacology and Toxicology,  
UMMC

**COBRE funding, PPL: 2017-18; COBRE Supplement  
2020-21**

**Current Funding:** PI, 2 R01s; site PI, 3 R01s; Co-I, R01

**Research interest:** Consequences of hypertensive pregnancy  
in mothers and offspring: neurological, behavioral, CV-renal;  
treatment options for uterine fibroids



# *Thank you!*

## **RPLs**

### **Phase 1**

Licy Yanes Cardozo, M.D.

Aimee Parnell, M.D.

Rodrigo Maranon, M.D.

Frank Spradley, Ph.D.

Bernadette Grayson, Ph.D.

Damian Romero, Ph.D.

Omar Logue, Ph.D.

Daniela Ruedi-Bettschen, Ph.D.

### **Phase 2**

Lorena Amaral, Ph.D.

Noha Shawky, Ph.D.

Kristin Edwards, Ph.D.

## **PPLs**

### **Phase 1**

Kedra Wallace, Ph.D.

Lorena Amaral, Ph.D.

Yee Pang, Ph.D.

Daniela Ruedi Bettschen, Ph.D.

Lorena Amaral, Ph.D.

Frank Spradley, Ph.D.

Michael Hebert, Ph.D.

Kathy Yee, Ph.D.

### **Phase 2**

Samar Rezq, Ph.D.

Amy Kohtz, Ph.D.

Pier Paolo Claudio, Ph.D.

**NIH NIGMS**

# Cardiometabolic Complications in Polycystic Ovary Syndrome

Licy L. Yanes Cardozo, MD

Professor

Director, Women's Health Research Center

Depts. of Pharmacology & Toxicology and Medicine (Endocrinology)

University of Mississippi Medical Center

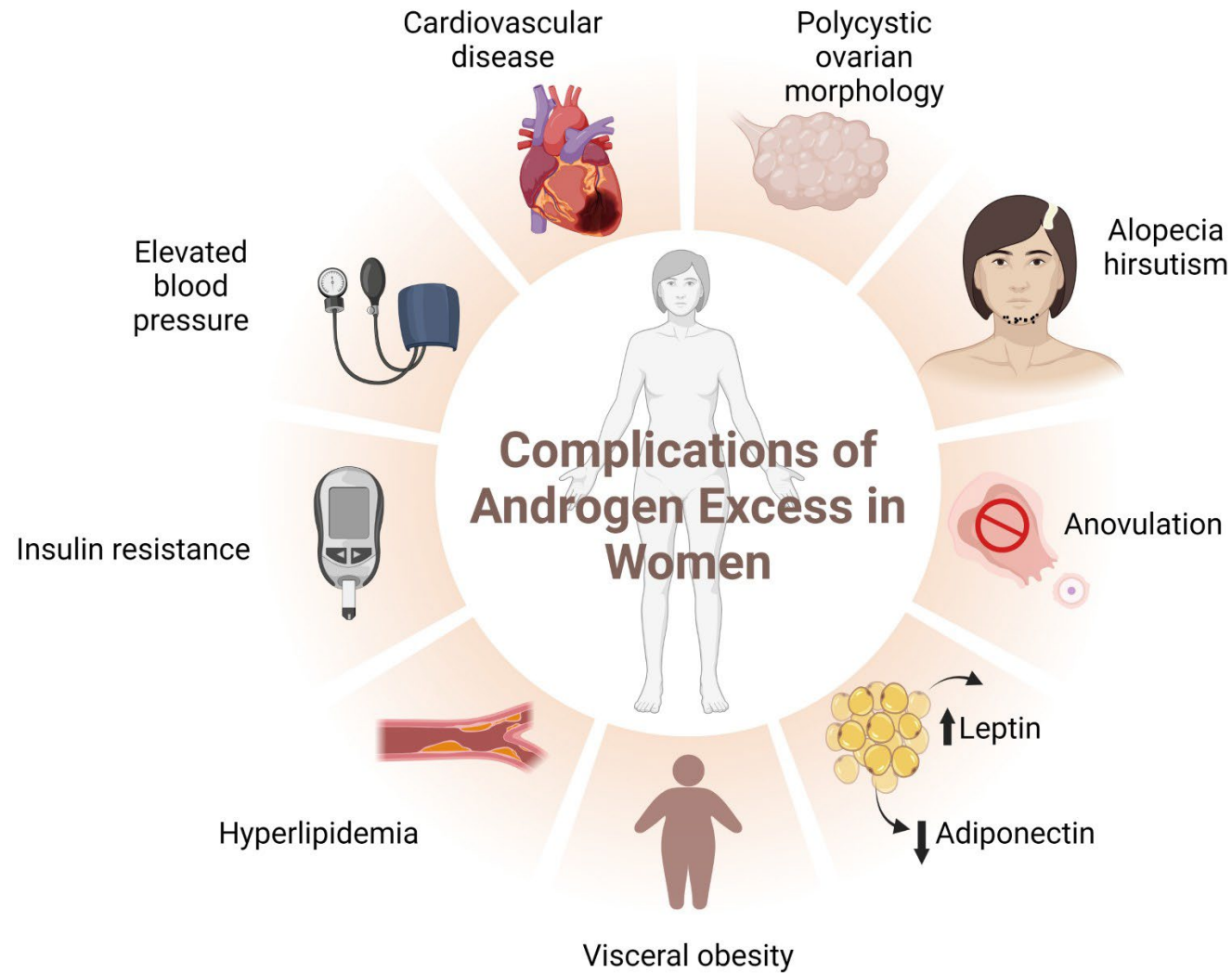
# Polycystic Ovary Syndrome (PCOS)

PCOS is the most common endocrine disorder in reproductive-age women.

There is not a single or specific test for diagnosis.

Unknown etiology and there is no cure for it.

# Cardiometabolic Complications in PCOS



# Case Presentation

Endocrine office visit in 2017

29 y.o. female with **Polycystic Ovary Syndrome** diagnosed around puberty

## **Obesity**

Inability to lose weight since puberty

Body Mass Index: 41 (obesity >30)

## **Hypertension**

Diagnosed three years ago

On Lisinopril (Renin Angiotensin System Blocker) + Hydrochlorothiazide

Blood pressure: 123/68

## **Type 2 Diabetes Mellitus**

Diagnosed two years ago

On metformin (insulin sensitizer) 1,000 mg orally twice a day since puberty.

Hemoglobin Glycosylated (A1c) : 9.3% (pre-pregnancy goal <6.5%)

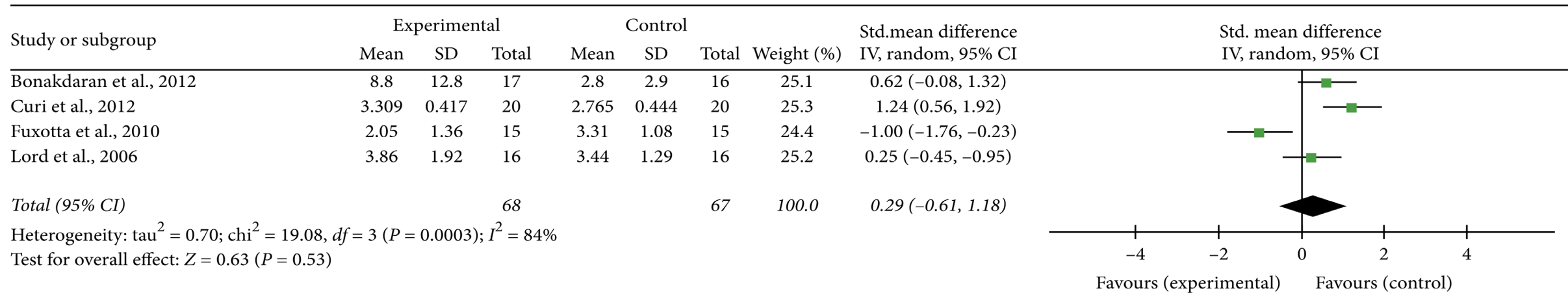
## **Wants to conceive soon**

# PCOS and Diabetes

More than **50%** of women with PCOS will become diabetic or prediabetic before age 40

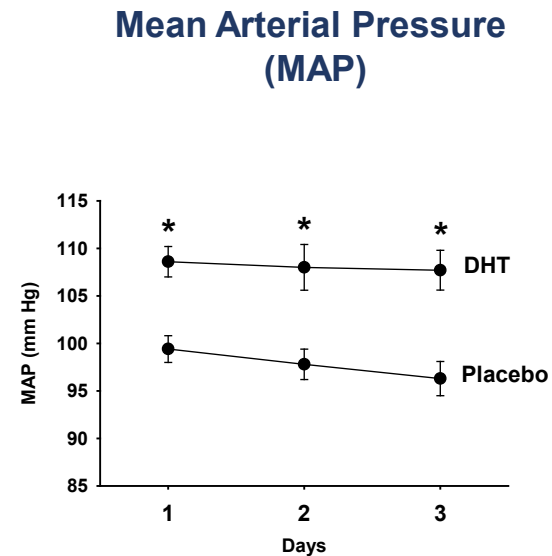
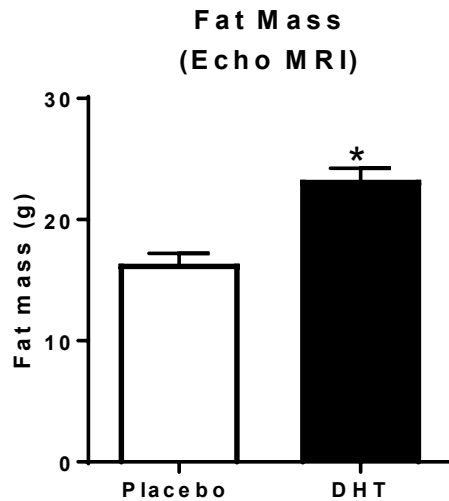
## The Effect of Metformin on Polycystic Ovary Syndrome in Overweight Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

### Insulin Resistance

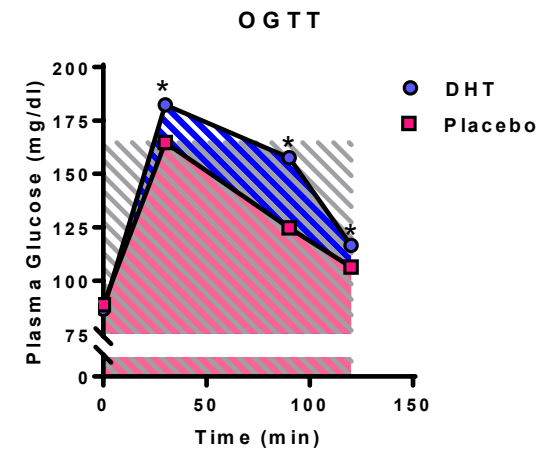


# Experimental Model of PCOS

## Excess of Androgens in female rats

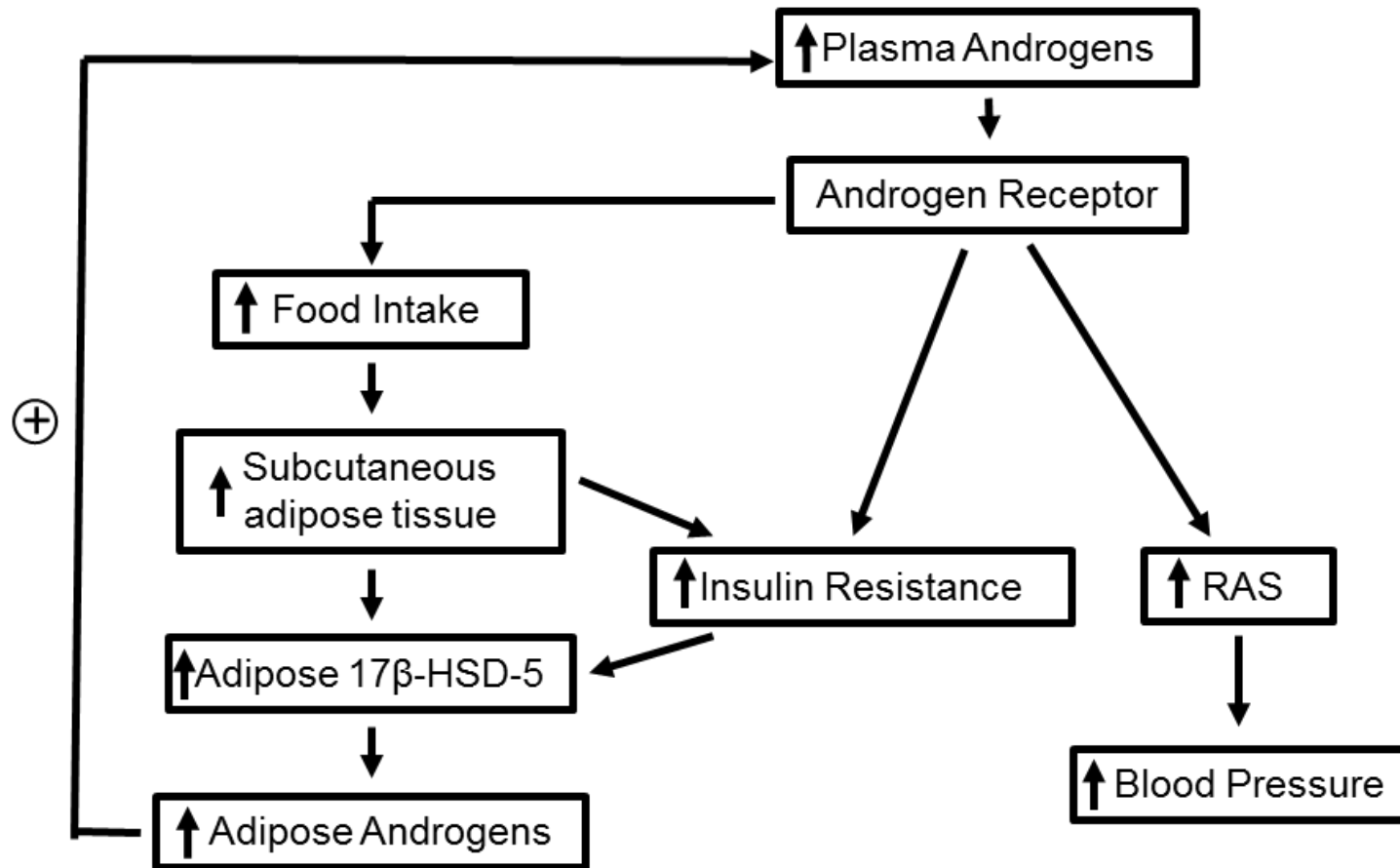


### Oral Glucose Tolerance Test

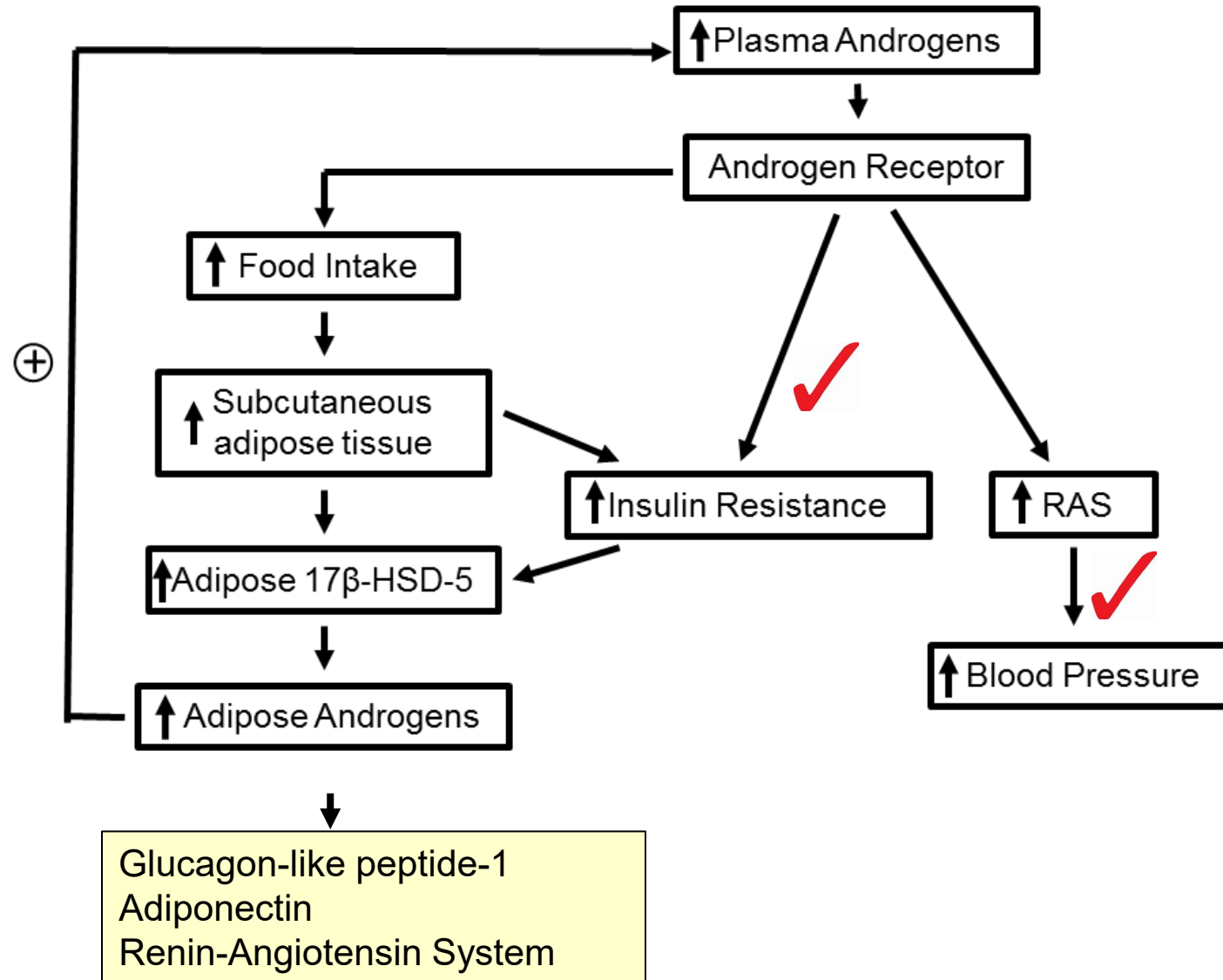




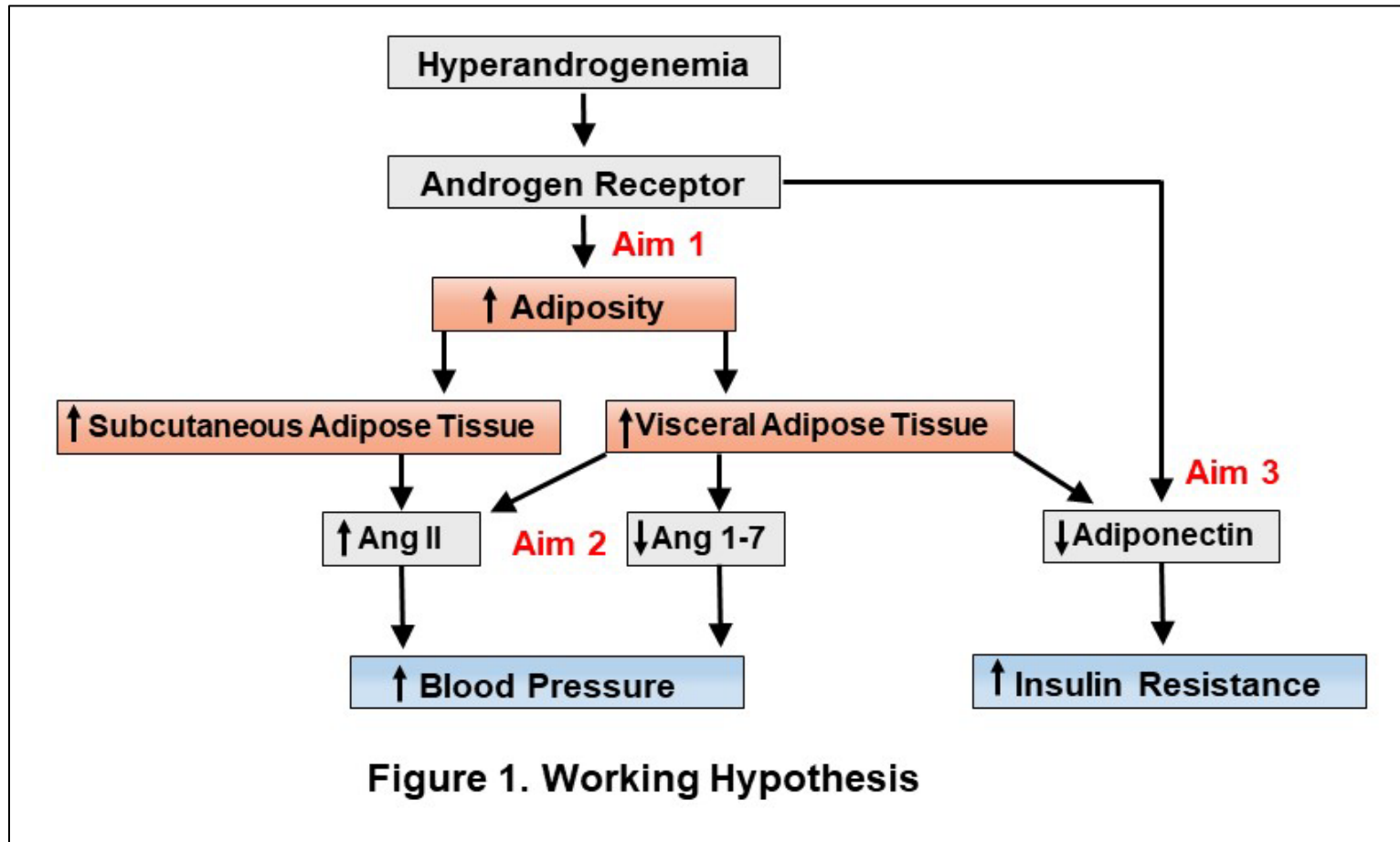
# Working Hypothesis MS-CEPR Grant



# MS-CEPR Grant-Working Hypothesis

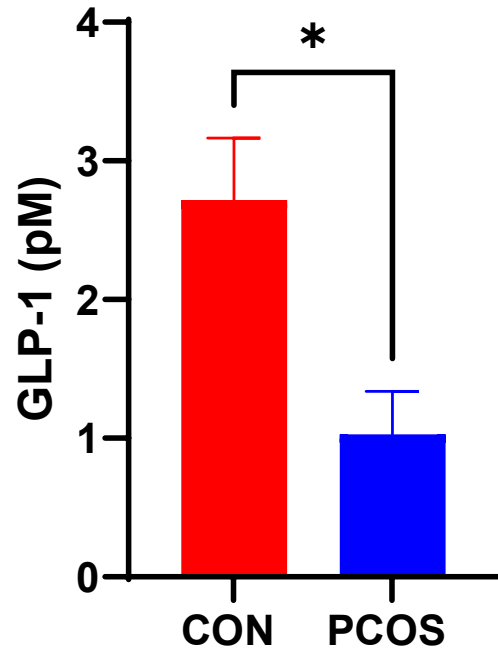


# R01- Working Hypothesis

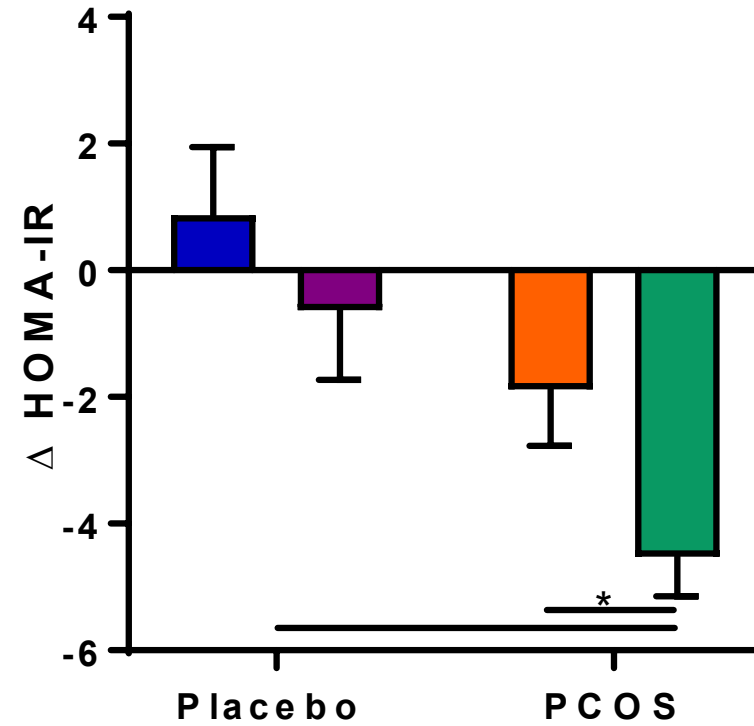


# Towards effective and safe therapeutics agents to treat Type 2 Diabetes in PCOS

GLP-1 levels are decreased in PCOS



GLP-1 RA improves IR in PCOS



# 3 months later...

## **Type 2 Diabetes Mellitus**

A1c: down to 5.3% from 9.3% on GLP-1 receptor agonist.

Several questions about GLP-1RA and pregnancy and prefers to stop it.

## **Hypertension**

Lisinopril was stopped by OB-GYN due to possible teratogenic effects.

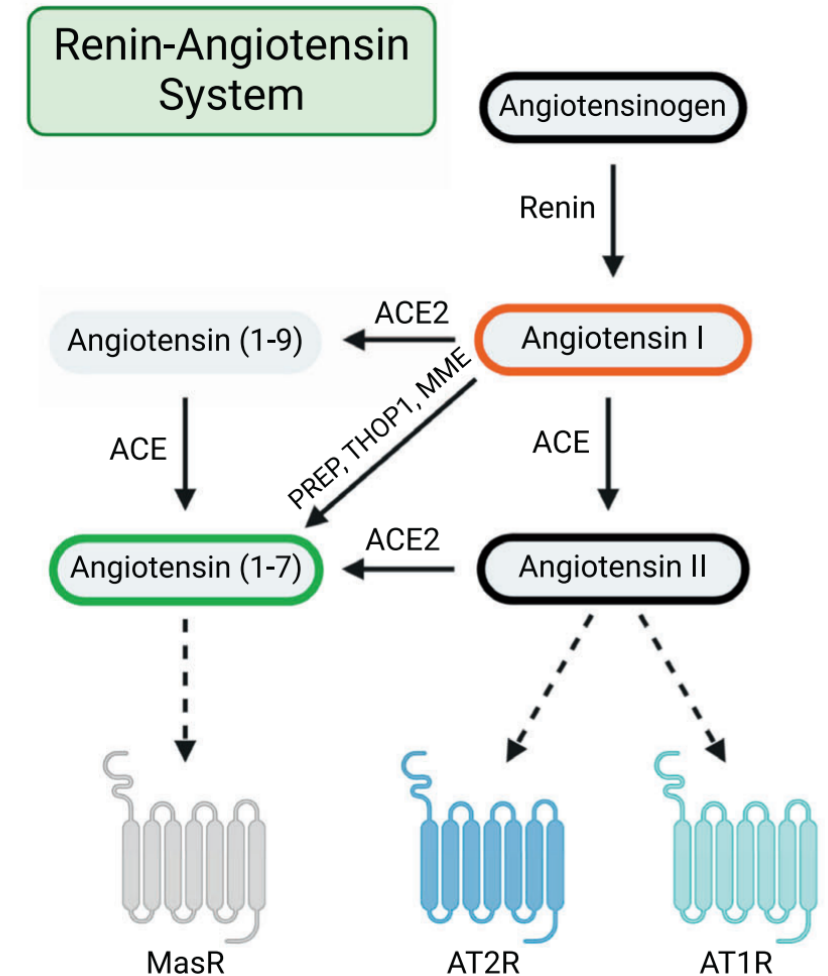
Blood Pressure 150/120

# Blood pressure regulation in PCOS

PCOS diagnosis is associated with a **37%** greater risk of hypertension even after adjustment, including age, BMI, and T2DM

## Blood pressure

- 123/68 (ON Lisinopril)
- 150/120 (OFF Lisinopril)



# Back to our patient...

After two unsuccessful IVFs got pregnant.  
3/2022: Fetal demise at 23 weeks of pregnancy  
12/2022: Pregnancy test positive  
8/2023: C-section, delivered at 38w healthy baby boy

## Diabetes regimen before delivery

Metformin 1,000 mg twice a day.  
Long-acting insulin 34 U at AM, 62 U at PM.  
Prandial Insulin 15 U with breakfast, 25 U with lunch, 35 U with dinner.

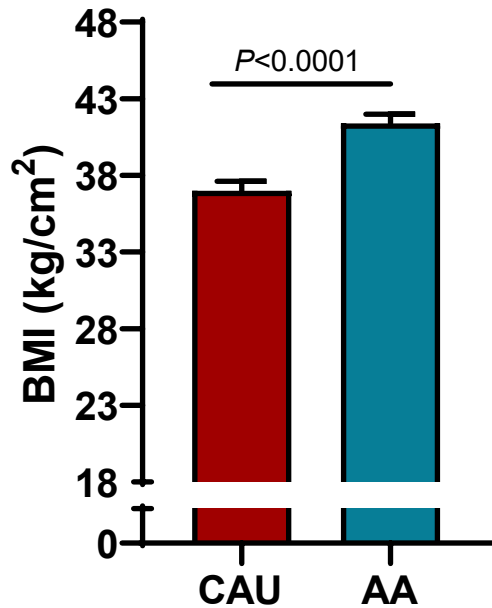
## Diabetes regimen 7 days after delivery

Metformin 1,000 mg twice a day.  
Long-acting insulin 20 U daily.  
Prandial insulin was discontinued.  
Desired not to breastfeed to restart GLP-1RA.

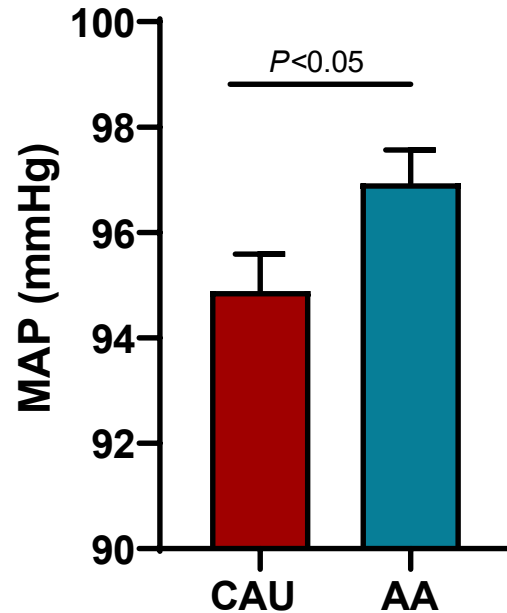


# African-American women with PCOS have worse cardiometabolic profile

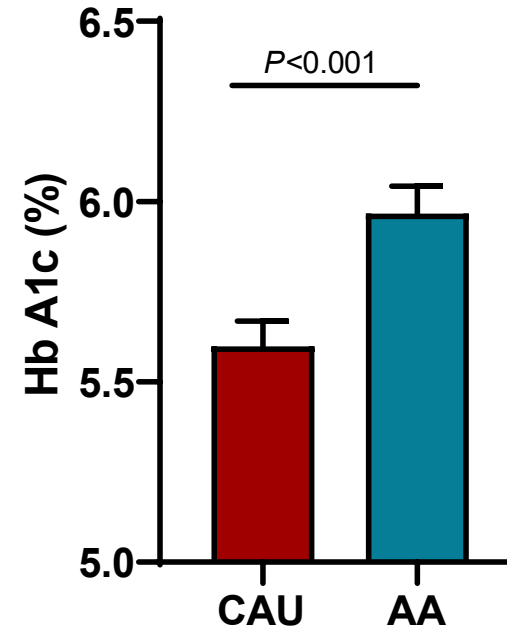
## Body Mass Index



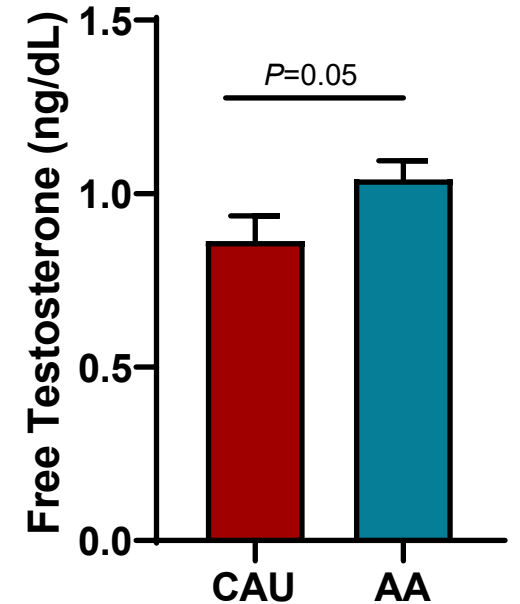
## Mean Arterial Pressure



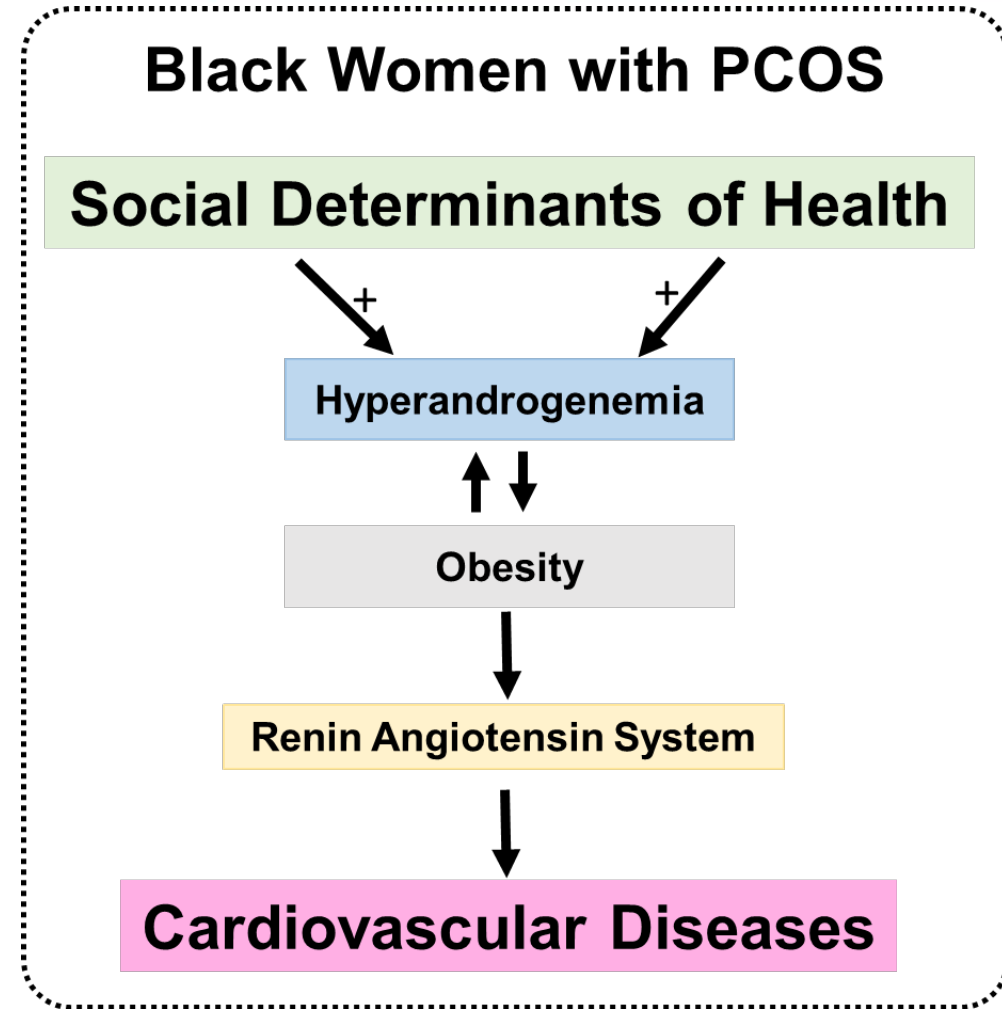
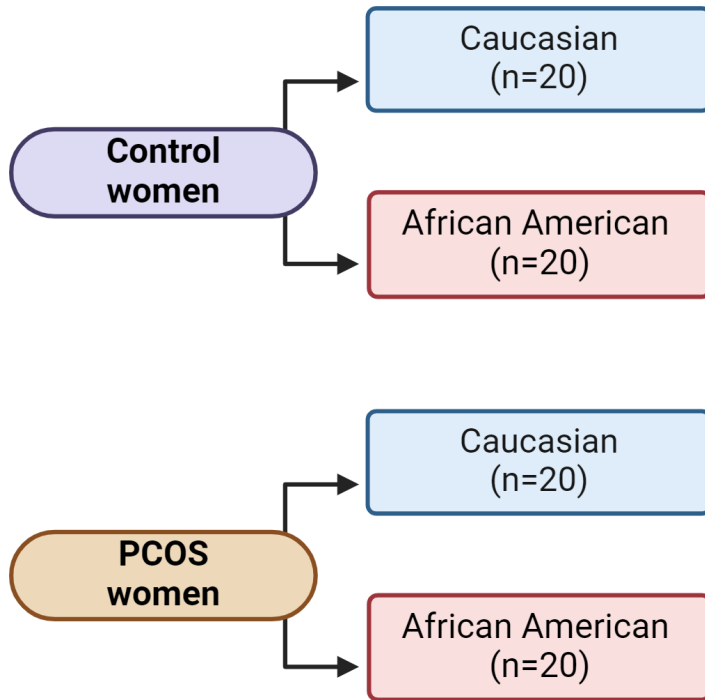
## Hemoglobin A1c



## Free Testosterone



CAU: Caucasian  
AA: African-American



# Race, Obesity and Renin-Angiotensin System in PCOS women

## Social Determinants of Health

Annual Family Income	Education	Health care access / experiences
Birthplace	Employment	Health Literacy
Current Address	Ethnicity and Race	Health Insurance Coverage
Current Age	Food Insecurity	Marital Status

## Main outcomes

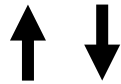
Aim 1	Aim 2	Aim 3
Plasma total testosterone	Body weight and height	Angiotensinogen
Plasma free testosterone	Body Mass Index (BMI)	Angiotensin-Converting Enzyme
Plasma SHBG	Waist and hip circumference	Angiotensin-Converting Enzyme 2
	Blood pressure and heart rate	Angiotensin II (All)
	Hemoglobin A1c	Angiotensin (1-7)
	Glucose	Plasma Renin Activity
	Lipid panel	Urinary angiotensinogen
		Urinary ACE2

# COBRE supplement-Working Hypothesis

Social Determinants of Health



Hyperandrogenemia



Obesity



Hypertension

Ambulatory Blood Pressure Monitoring (ABPM)

Home Blood Pressure Monitoring (HBPM)

Office Blood Pressure (OBP)

Bioelectrical Impedance Analysis (BIA)

# Acknowledgements

Edgar Torres Fernandez  
Jacob E. Pruetz  
Ahmed M. Abdelhameed  
Steven J. Everman  
Katie Thompson  
Victoria Wilson  
Alessandro Subauste  
Giuliana Cattivelli  
Savannah Stockton  
Stephanie A. Ye  
Sally McClung  
Logan Ryals  
Faridah Salau  
Raksha N. Chatakondi  
Natasha Burrell  
Lauren E. Peters  
Jemyllie Grace Morato  
Andrea Milton  
Aurea Toledo  
Trinity Star  
Astha Banga  
Luz Luna

## **MS-CEPR COBRE Director**

Jane F. Reckelhoff

## **MS-CEPR COBRE Research Resource Director**

Damian G Romero

## **MS-CEPR COBRE Clinic Research Director**

Babette Lamarca

## **Clinical Research Core**

Cameronne Dodd

Sheila Belk

Crystal Collins

Yelena Neely

## **Mitochondrial Research Core**

Kristin Edwards

Ngoc Hoang

## **Histology Core**

Heather Drummond

## **Analytical and Assay Core**

Barbara Alexander

Elizabeth Flynn

## **Animal and Telemetry Core**

Damian Romero

Salma Begum

## **Biostatistics/Bioinformatics Core**

Seth Lirette

## **Radiology-UMMC**

Candace Howard-Claudio

## **Samar Rezq**

Joseph Flaherty

## **Damian Romero**

Jelina Basnet

Alexandra Huffman

## **Noha Elsayed**

Kacey Davenport

Ruth Wilson

## **Medicine-UMMC**

Lampros Papadimitriou

Lilian Lien

Vishnu Garla

Calvin Thigpen

Michael Hall

Sharon Beard

Funding



# How IDeA Funding has helped shape my career

Kedra Wallace, PhD

Professor - Department of Pharmacology & Toxicology

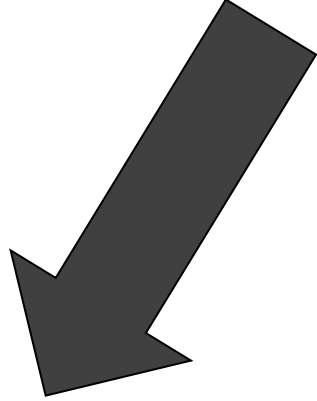
Professor - Department of Obstetrics & Gynecology

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University of Mississippi Medical Center

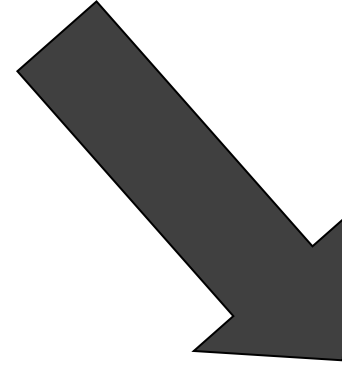
**Mississippi  
IDeA**



**DIRECT RESEARCH  
OPPORTUNITIES**

**CEPR  
Administrative  
Supplements**

**CEPR Pilot  
Project**



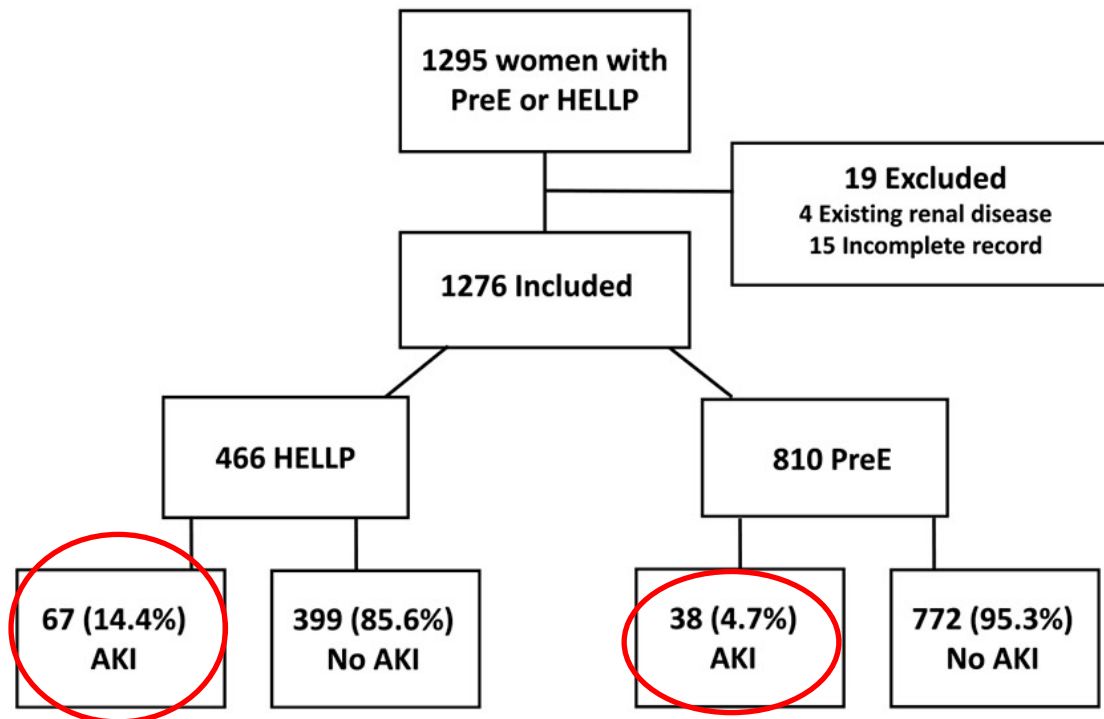
**INDIRECT RESEARCH  
OPPORTUNITIES**

**IDeA grant  
Co-Funding**

**CEPR  
Mentorship  
Core**



# CEPR Pilot Project



- Develop animal model of pregnancy-related acute kidney injury
- Induce AKI in HELLP rats
- Evaluate cognition in the post-partum period

PMC7517692

PMC10419049

PMC7020199

Chan Zuckerberg Initiative  
(5yr) 12/2022

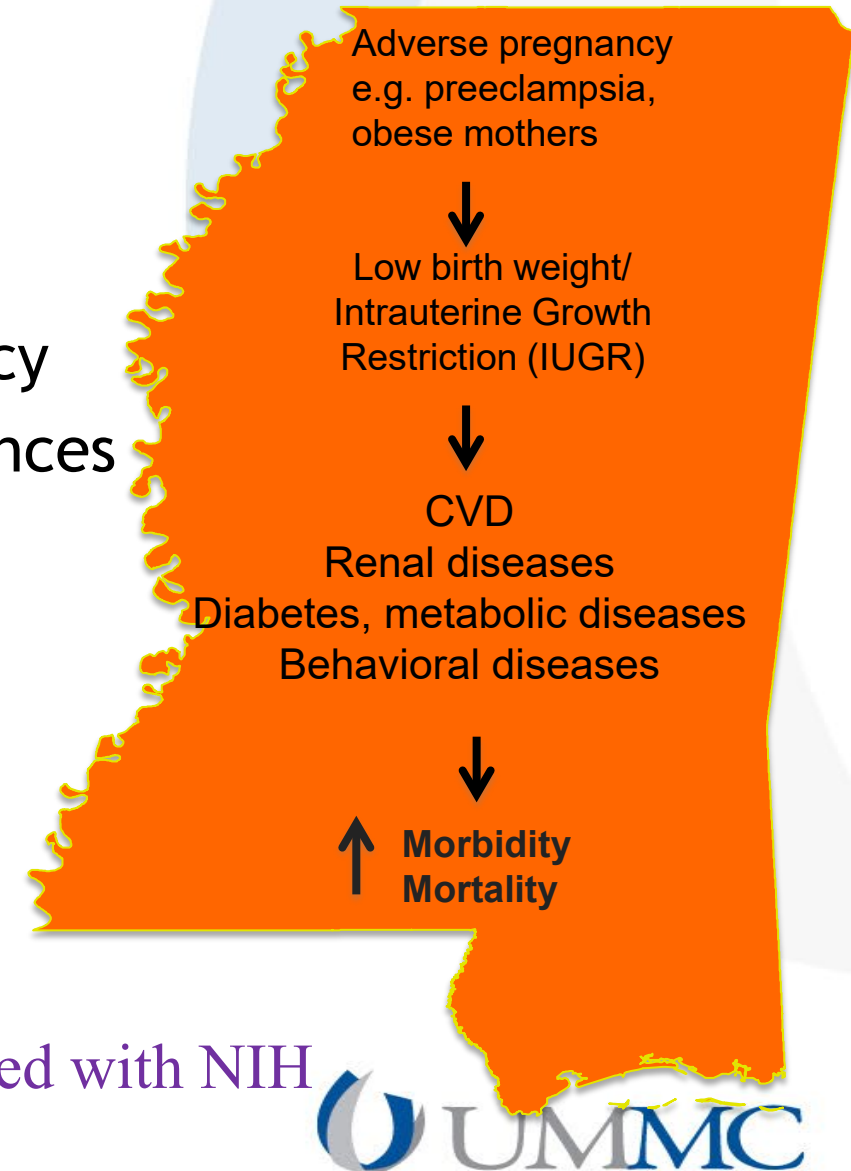
MS Graduate 5/2020

PhD Graduate 5/2024

PMC8945252

# CEPR - Mentorship Core

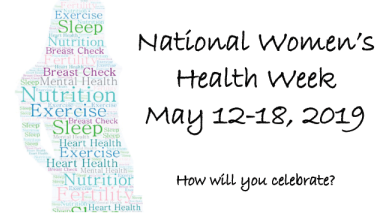
- Sponsorship and Networking
- **Society for Women's Health Research**
  - GOAL: Advance women's health through science, policy and education while promoting research on sex differences to optimize women's health



2 Patient Tool Kits  
2 White papers

Capital Hill Webinar co-sponsored with NIH





- Waiting rooms across the hospital
- Public areas in the Medical Mall
- Public areas in the WIC offices around Jackson
- Electronic copies to former Ob/Gyn residents practicing in Mississippi

**From the Chair . . .**

Spring is definitely in the air! With that being said, I can see the dawn of some new opportunities for the department and each of its members. During the winter months, the department has scored a number of achievements that will positively effect its future. The medical students who rotate in the department have increasingly had positive feedback regarding their experiences and we have had yet another successful match, acquiring five new residents and one new fellow to challenge us. In addition, two of our senior residents have matched into competitive fellowships. On a really positive note, we have received the official letter from the Accreditation Council for Graduate Medical Education awarding continued accreditation of our residency program . . . a big congratulations to our educational team!

Meanwhile, the clinical enterprise remains stable with everyone working in overdrive to sustain the well-being of their patients. Recruiting efforts are still under way as we continue to grow the educational, research and clinical mission areas of the department and the institution.

Jermaine Gray, M.D.  
Assistant Chair  
Department of Ob-Gyn

**Health Corner**

From the Division of Female Pelvic Medicine and Reconstructive Surgery (Urogynecology)

Paul Moore, M.D.  
Division of Urogynecology

**Stress Urinary Incontinence**

**Urinary incontinence is an all-too-common problem for women.**

- More than 13 million women in the United States have urinary incontinence.
- Severe incontinence can cost women up to \$900/year in supplies and care.
- Approximately \$12 billion is spent on female incontinence each year in the United States.

**Let's review stress urinary incontinence.**  
(urine leakage with a cough, sneeze, laughter or other physical activity)

- What a woman should do if she suspects she has stress urinary incontinence?**
- Explain the symptoms to a doctor
    - Diagnosis can often be made at the time of a physical exam.
    - Sometimes a bladder test may be necessary if the diagnosis is unclear.
  - Go over treatment options
    - Pelvic Floor Muscle Exercises are routines that can be done at home, with biofeedback or with a pelvic floor therapist. Most studies show improvement in symptoms when these are done correctly and routinely.
    - Incontinence pessary is a silicon ring that is inserted into the vagina and positioned under the urethra. Most women can manage the pessary themselves and find it comfortable and helpful in improving their symptoms.
    - Outpatient Surgery in which a sling or strap is placed around the urethra to help prevent leakage. These surgeries have a high success rate.
    - A woman may opt for no treatment if she decides her symptoms aren't bothersome. She could wait until her symptoms become more bothersome.
- 

Women suffering from urinary incontinence can get help from the physicians and nurses in the UMMC Division of Urogynecology. Call us or talk to a primary physician about whether a referral would be the right course of action. Women do not have to suffer with this embarrassing problem, as effective treatments do exist!

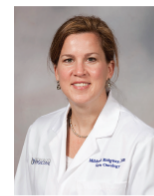
Call us at (601) 984-5314 or visit [www.umm.edu/urogyn](http://www.umm.edu/urogyn)

**Upcoming Event**

*Save the Date - June 1, 2019*  
**Free Cervical and Breast Cancer Screenings – Jackson Medical Mall**  
 8 a.m.–1:30 p.m. • Jackson Medical Mall • (601) 815-3572

For the third year, the UMMC Cancer Center and Research Institute will offer "See, Test and Treat." Women between the ages of 21-64 can receive free cervical and breast cancer screenings with same-day results at the annual event.

Women participating in this event will also receive education about available community resources, healthy eating, exercise and continued cancer screening recommendations. Last year, more than 100 participants were seen and 23 abnormal mammograms, five abnormal pap smears and 10 abnormal dermatological screenings were identified.



Mildred Ridgway, M.D.  
Division of Gyn. Oncology

One success story from this event happened during the first year. A participant who had recently moved to the Jackson area but had not established care with a gynecologist came to the event. She had a history of abnormal pap smears, but had not followed up appropriately since moving. Cervical cancer was noted on her pap smear at the See, Test and Treat event. She has since received appropriate treatment and follow-up. She is currently cancer free and is enjoying life! She loves to help promote this event and encourages women to receive the appropriate Gyn care/screening they need!

**Did you know?**

- Mississippi is No. 5 in the United States for new cases of cervical cancer?
- The cervical cancer death rate is about 50 percent higher among African-American women compared to Caucasian women?
- The American Cancer Society estimates 13,170 new cases of cervical cancer will be diagnosed in the United States in 2019.
- Routine pap screening can help detect changes in the cervix before cancer develops and can help detect cervical cancer in its early stage.
- Women may be at risk if they:
  - Have a history of sexually transmitted diseases,
  - Smoke,
  - Have multiple sex partners,
  - Practice unprotected sex and
  - Have sexual intercourse at an early age.

**HPV VACCINATION IN MISSISSIPPI**

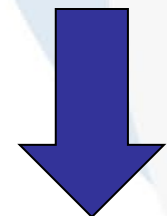
Human Papillomavirus causes almost 75 percent of cervical cancers in women. Women can get vaccinated against HPV – offering protection against cervical cancer.

In a recent study by Dr. Mildred Ridgway and her colleagues, the barriers to HPV vaccination among providers in Mississippi were examined. Among the findings: not enough parents and patients know enough about the vaccination's potential benefits in reducing cervical and anal cancers.

[https://issuu.com/jmsmamanagering/editor/docs/january\\_2019\\_jmsma\\_epub](https://issuu.com/jmsmamanagering/editor/docs/january_2019_jmsma_epub)

# SPONSORING RELATIONSHIPS

SWHR co-sponsored webinar  
(rural health and challenges)



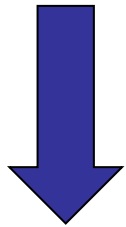
P50 Application  
June 2023



# NIGMS CEPR - Administrative Supplements

## SPONSORING RELATIONSHIPS

Guest Speaker

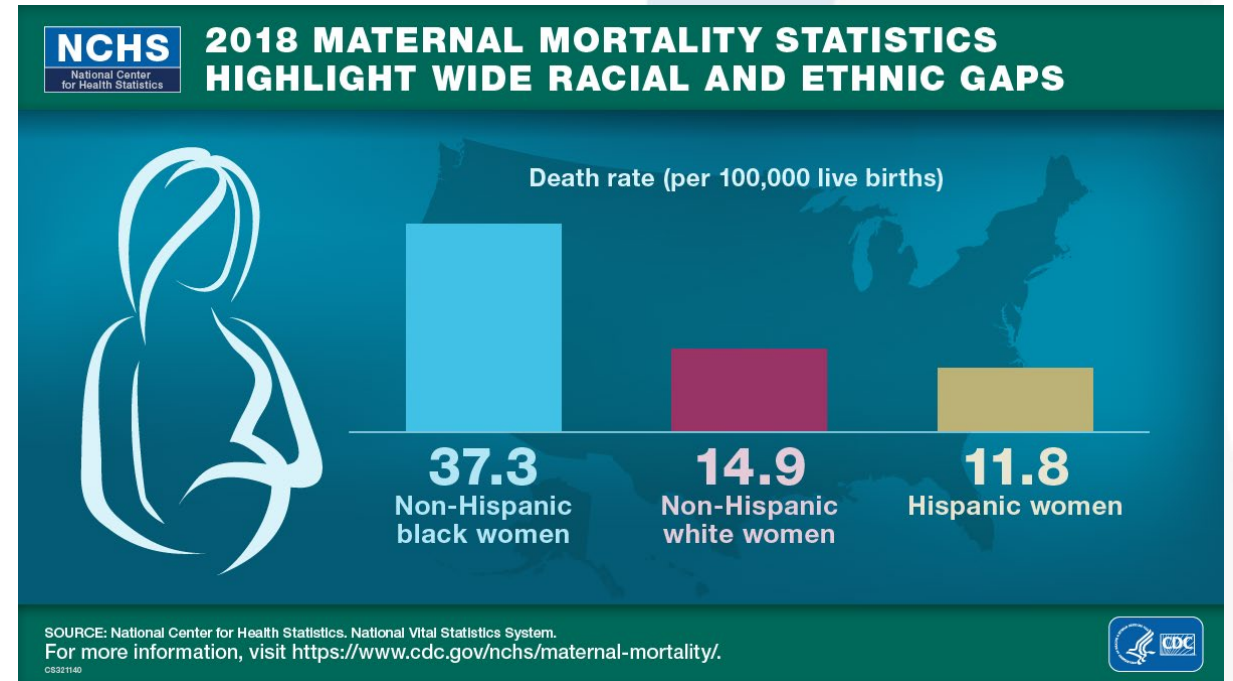


**PMID34619718**

Hypertension Innovator Award  
Competition (Phase I, II)

Clinical Trial Roche

PCORI Application (In  
progress)





# NIGMS CEPR - Administrative Supplement



38%

While pregnant

**Medical records are not automatically shared among clinics/providers**

**Women may not remember what they were diagnosed with**



University of Mississippi M



 UMMC

# IDeA Grant Co-Funding

- ESI R01 (RFA) Submission History:

- 01	February 2016	Impact Score: 36	Percentile: 33%
- 01A1	November 2016	Impact Score: 32	Percentile: 21%
- 01	June 2017	Impact Score: 40	Percentile: 34%
- 01A1	December 2017	Impact Score: 31	Percentile: 17%

- IDea Co-Funding

- PI and performance site(s) must be in an IDeA state
- NIH IC nominate application for IDeA co-funding

- R01 Funded - 9/5/2018

# Mississippi IDeA

## DIRECT RESEARCH OPPORTUNITIES

## INDIRECT RESEARCH OPPORTUNITIES

### NIGMS CEPR Administrative Supplements

### NIGMS CEPR Pilot Grant

### IDeA grant Co-Funding

### NIGMS CEPR Mentorship Core

- \*PMC11067202
- \*MS MFM Graduate  
5/2023
- \*R01 Submission  
Early 2025

- \*PMC7517692
- \*PMC10419049
- \*PMC7020199
- \*MS MFM Graduate 5/2020
- \*PhD Graduate 5/2024
- \*CZI Funding (5yr)
- \*Manuscript under review
- \*R01 Submission  
Early 2025

- \*PMC10967052
- \*PMC8869594
- \*PMC8492499
- \*Manuscript under review
- \*MS MFM Graduate 5/2021

- \*PMID34619718
- \*PMID30790565
- \*2 Patient tool kits
- \*NOA P50



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# Q & A

