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Disclosures & Funding

- **Funding for the research discussed today provided by**
 - Current
 - Eunice Kennedy Shriver National Institute for Child Health and Human Development (R01HD111125)
 - Arizona Biomedical Research Centre
 - The Flinn Foundation
 - The National Science Foundation
 - Prior
 - National Institute for Nursing Research (R00NR019596)
 - The American College of Nurse Midwives
 - National Center for Advancing Translational Sciences
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- **Disclosures**
 - Outside interest in Amahealth LLC. This interest has been disclosed to the University of Arizona and reviewed in accordance with its conflict-of-interest policies.

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- ✓ Grapple with a couple of long-standing questions in our field
- ✓ Share some of our work trying to address these questions in new ways
- ✓ Learn about other emerging precision tools in pregnancy care
- ✓ Envision paths that might address questions and lead us to precision/personalized care... one day
 - Hopefully... inspire **aspirations, conversations** and new research questions

OBJECTIVES

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**HOW MANY
PREGNANCIES WILL
LAST 41+ WEEKS?**

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1 in 4

AT LEAST

8

(BASED ON US / HOSPITAL BIRTH DATA)

**WHAT % OF
POSTPARTUM
HEMORRHAGES HAD
NO CLINICAL RISK
FACTORS**

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40%

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Does "risk factor" based care...

→ improve care?

→ personalize care?



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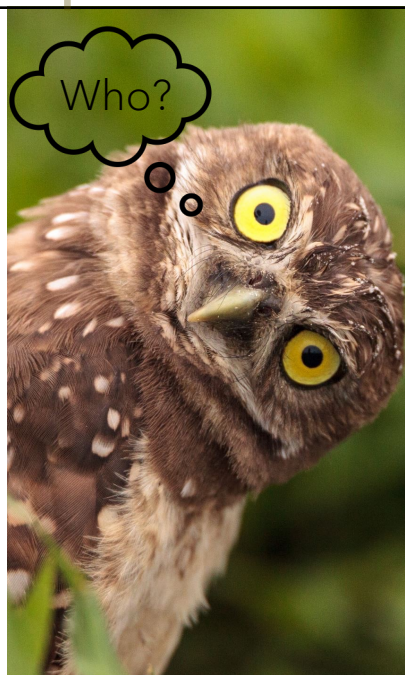
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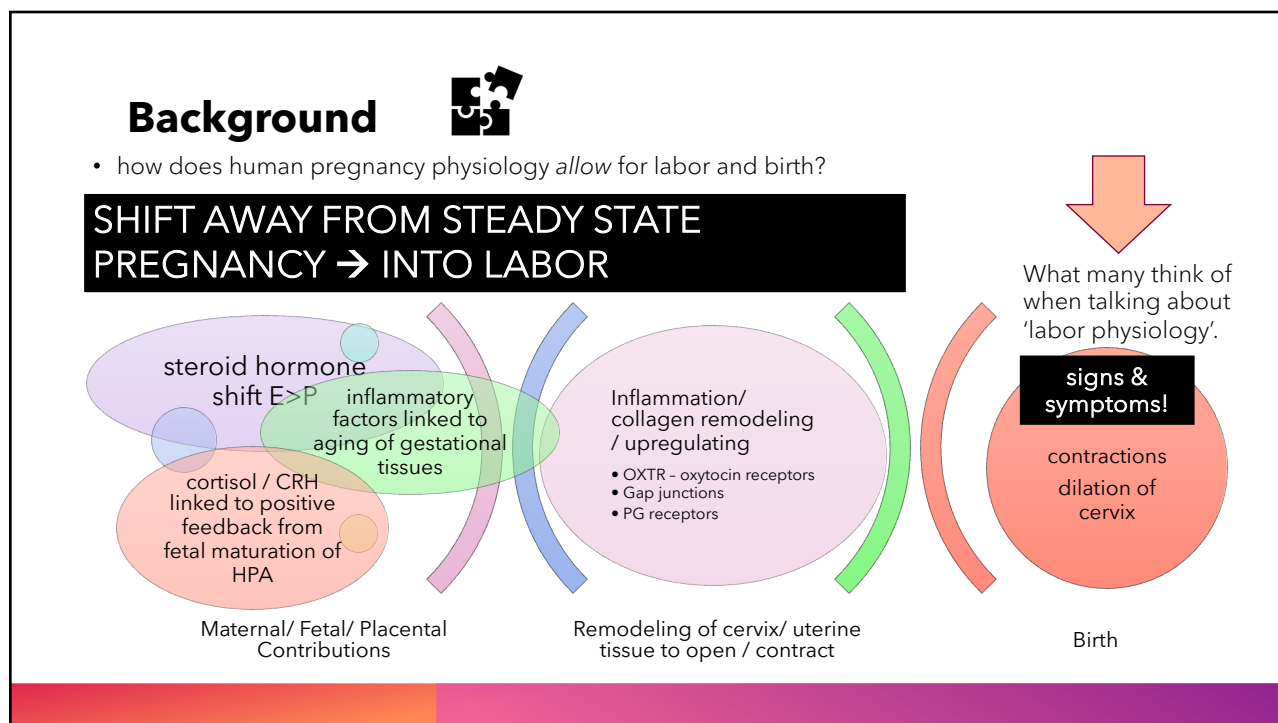
Problem 1



- Timing of labor onset is uncertain
- Even with reassuring maternal / fetal status- how long will a pregnancy last?
- Our current 'risk-factor' based approach to supporting **ongoing pregnancy** has made induction is increasingly common:
 - AMA → IOL
 - High BMI → IOL
 - Big baby/ small baby? → IOL
 - GDM → IOL
 - 41 weeks → IOL
 - 40 weeks → IOL
 - 39 weeks → IOL
 - 2 blood pressures >140/90, > 4 hours apart.... → IOL
- If we had a better understanding of **who would labor earlier or later...**
- ...Could we personalize labor induction by **decreasing uncertainty** in labor onset?



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Did you know?

WHEN ALL OF THESE ANIMALS ARE PREGNANT, SOMETHING AMAZING HAPPENS...



FORECASTING MAMMALIAN PARTURITION

IN THE DAYS BEFORE LABOR STARTS, BODY TEMPERATURE DROPS AS A FUNCTION OF FALLING PROGESTERONE

TEMPERATURE CHANGES CAN BE RELIABLE ENOUGH THAT ANIMAL CARETAKERS MAY MONITOR TEMPERATURE TO BE 'ON HAND' IN CASE THE ANIMAL NEEDS HELP WITH BIRTH.

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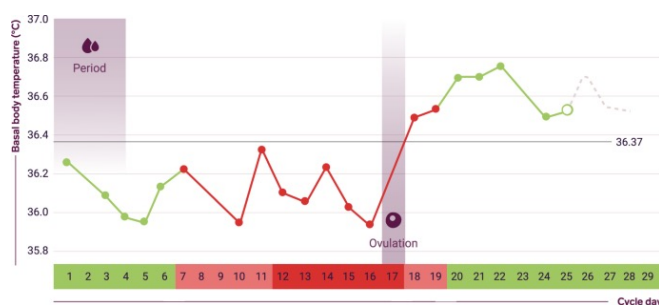
Table 1: Reported changes in body temperature (skin or core) among various mammalian species during pregnancy that have been observed prior to the onset of parturition

Species	Observed Change (T)	Time Window	Measurement Method and Frequency
lion	-1.3 C	"late gestation"	intraperitoneal, ~ continuous
squirrel	-1.2 C	-20 days	intraperitoneal, 1/min
orca whale	-0.3 C, -0.8 C	-5 days, -24 hours	rectal, 1/day
wolverine	-0.8 C	- 24 hours	intraperitoneal, 1 & 15 min
rabbit	-0.7 C	< - 24 hours	intraperitoneal, 1 & 6 min
rat	~-0.5 C	-5 to -1 days	intraperitoneal
horse	-0.5 c (-0.1)	(-24) -15 to -3 hours	rectal, 2/day
sheep	-0.5 c	-24 hours	neck and vulvar, 1 & 10 min
cow	-0.3- -0.2 C	-2.5 to 0 days	intravaginal; or ruminal
dog	≤ -0.3 C	-24 hours	intravaginal, daily means.
moose	≤ -0.2 C	-3 to 0 days	ingested logger, 1 & 5 min
mouse	<0.5 C	-72 h to -24 h	intraperitoneal, 1/min
goat	not reported	n/a	vulva, 1/day
macaque	not reported	-1 to -1.5 hours	subscapular, 1/min

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Thermogenic Effect of Progesterone



Bull, J.R., Rowland, S.P., Scherwitzl, E.B. *et al.* Real-world menstrual cycle characteristics of more than 600,000 menstrual cycles. *npj Digit. Med.* **2**, 83 (2019). <https://doi.org/10.1038/s41746-019-0152-7>

Progesterone

- inhibits heat loss (raising body temperature) by directly affecting the neurons in the hypothalamus that control autonomic body temperature.
- Raises the 'set point' for sweating, vasodilation, and cold sensation.

Baker FC, Siboza F, Fuller A. Temperature regulation in women: Effects of the menstrual cycle. *Temperature (Austin)*. 2020 Mar 22;7(3):226-262.

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Humans?

- One woman's insight in 1979
- No formal study

TEMPERATURE CHANGE WITH IMPENDING LABOUR

SIR,—I decided to monitor my daily body temperature during pregnancy because I had noticed that my temperature during labour with my first child had been much lower than usual. I wondered if the drop could be used to predict the time of labour.

At the beginning of my pregnancy, my temperature was 36.9°C, and it fluctuated between 36.7 and 37.3°C until twenty weeks when it moved into the range 36.5–36.8°C. On the Wednesday before the baby was born, my temperature dropped to 36.2°C; I started losing mucus on the Thursday and went into labour early Saturday morning.


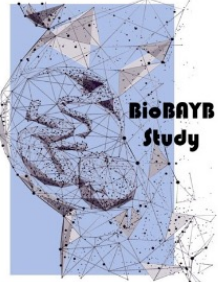
Since it would be very convenient for a woman to know that labour would start in two or three days might I suggest that a survey be done to see if the temperature changes I recorded are seen in all pregnant women?. If confirmed, the change around twenty weeks could be a simple way of fixing dates more accurately for women with irregular periods, and the drop in the last week could be useful for women who have domestic arrangements to make.

Keeper's Lodge,
Dyffryn,
Bryncoch, Neath

HELEN M. YEWLETT
The Lancet, July 14, 1979

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Biological Rhythms Before & After Your Birth (BioBAYB) Study

npj | digital medicine

www.nature.com/npjdigitalmed

ARTICLE OPEN

Predicting labor onset relative to the estimated date of delivery using smart ring physiological data

Elise N. Erickson^{1,2,3}, Neta Gottlieb³, Leonardo M. Pereira⁴, Leslie Myatt⁴, Clara Mosquera-Lopez⁵ and Peter G. Jacobs⁵

Basavaraj et al. *BMC Pregnancy and Childbirth* (2024) 24:777
<https://doi.org/10.1186/s12884-024-06862-9>

BMC Pregnancy and Childbirth

RESEARCH Open Access

Deep learning model using continuous skin temperature data predicts labor onset

Chinmai Basavaraj^{1†}, Azure D. Grant^{2†}, Shravan G. Aras^{3†} and Elise N. Erickson^{4†}

Likelihood of labor starting before 40 weeks versus passing the due date using maternal physiological data gathered from a smart ring device.

40 weeks

AUROC .71
*Moderate ability to discern pregnancy passing 40 weeks from those laboring before the due date.

data used in model

Use of a boosted random forest approach. Training and testing dataset: smart ring data gathered during the span of time from enrollment until 4 days before labor started or 40 weeks, whichever occurred first.

Erickson et al (2023)

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AI- model for encoding multiple dimensions of temperature fluctuation to predict "days until labor"

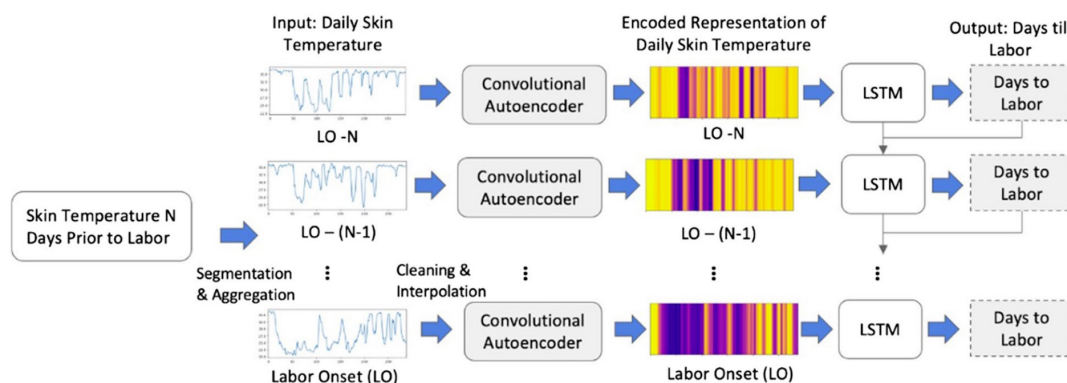


Fig. 3 AE-LSTM Model architecture extracts temperature features relevant to labor. Continuous daily skin temperature data is fed into a convolutional autoencoder, which outputs an encoded representation of length 64 for each day. Heatmaps depict the actual encoded representation of sample days of data. These are then fed into an LSTM (Long Short-Term Memory) in an autoregressive fashion to obtain a "days until labor onset" value relative to the current gestational age

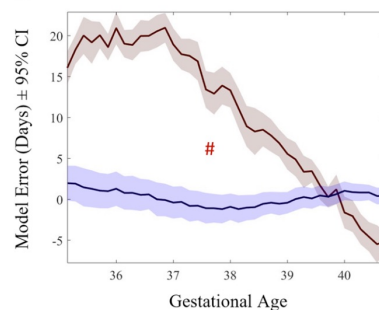
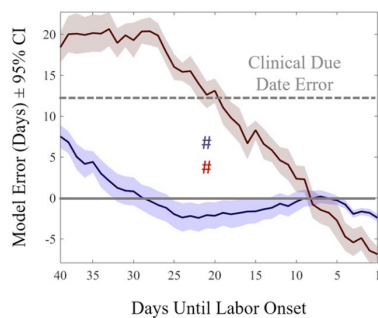
doi:10.1186/s12884-024-06862-9

19

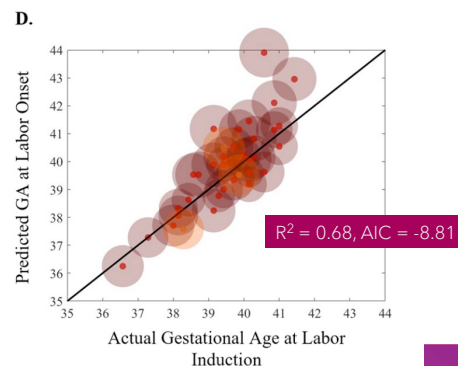
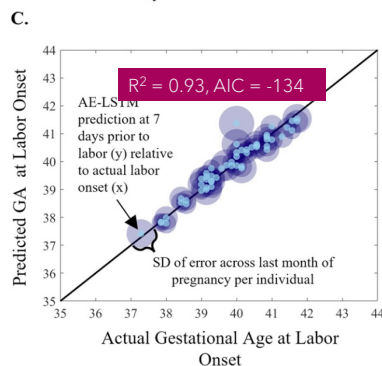
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Blue spontaneous labor "error" - predicted days until labor vs. the actual labor onset

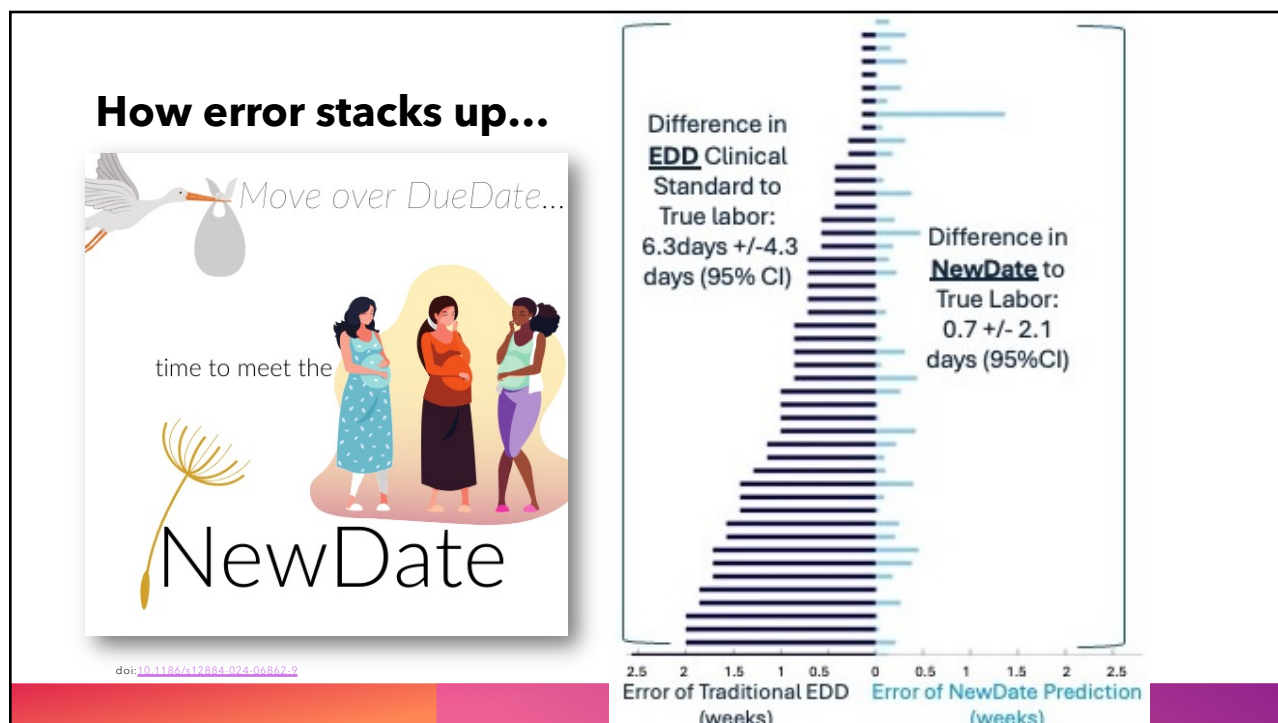


Also linked temperature changes to hormone ratios from urinary metabolites of Estrogen/Progesterone → see paper.



doi:10.1186/s12884-024-06862-9

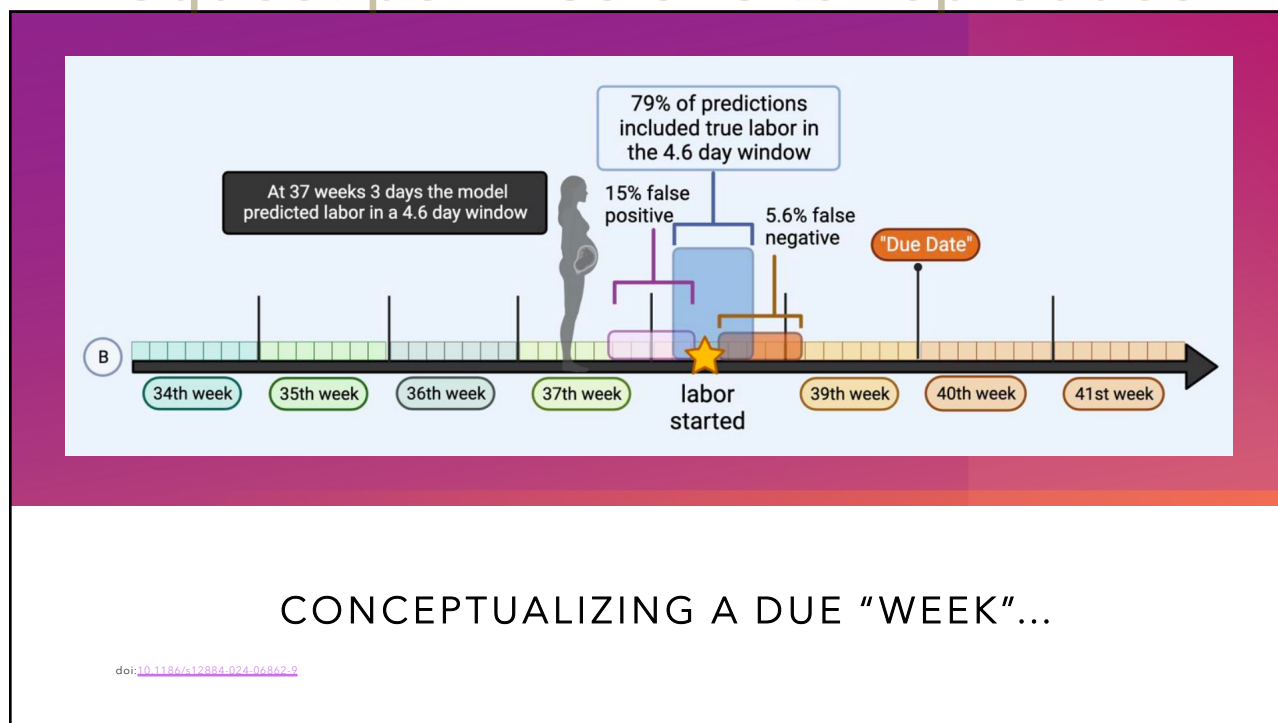
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Now Enrolling! BioBAYB₂



N =300
150 with risk factors of PTB
150 with high hopes for spontaneous term birth

<https://www.mumhlab.com/biobayb2-study>

AN INSTITUTIONAL REVIEW BOARD RESPONSIBLE FOR HUMAN SUBJECTS RESEARCH AT THE UNIVERSITY OF ARIZONA REVIEWED THIS RESEARCH PROJECT AND FOUND IT TO BE ACCEPTABLE, ACCORDING TO APPLICABLE STATE AND FEDERAL REGULATIONS AND UNIVERSITY POLICIES DESIGNED TO PROTECT THE RIGHTS AND WELFARE OF PARTICIPANTS IN RESEARCH

The Biological Rhythms Before and After Your Birth II (BioBAYB2) Study



Your body, your baby, your timeline.

Let's unlock the science of labor.

Earn up to \$400 OR devices for tracking wellness

- + Use a smart ring to get personalized insights into your sleep quality, daily readiness, activity levels, and other biometrics to optimize your overall well-being
- + Receive a summarized report of your metrics and insights



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Wearable data, remote monitoring and symptom integration:

Your Weekly Report

For the week of July 28 - August 3, 2025

21

Weeks Pregnant

89%

Ring Wear Time

5

Check-in's Completed

Avg. Sleep

7.2 hrs

52 hours this week

Resting Heart Rate

72 bpm

48.3M beats this week

Avg. Steps

6,345

200 total minutes
200 fewer steps than last week

Blood Pressure

4 readings

None over 140/90
Lower than last week

Temperature

Steady

No readings over 100.0°F
403,560 total readings

Weight Change

+3 lbs

This week

6 days

Back Pain

4 days

Indigestion

3 days

Nausea

1 day

Headache

Welcome, Shravan

Tasks

Depression Questionnaire Overview Start


Anxiety Questionnaire Overview Start

Pregnancy Experience Scale Overview Start

Connect to devices

I received my sizing kit

Click here to report your cuff and ring size



Show All Symptoms
Record No Symptoms

If you have connected Apple Health, Google Fit, Fitbit, or Garmin, check back later to view your data.

Connect Devices

Share data from your wearables, apps, and other devices.

Oura

Connect

Apple Health

Connected

Omron

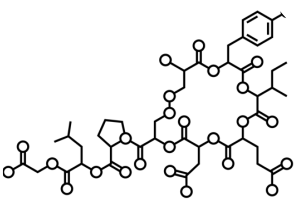
Connect

<https://www.mumhlab.com/biobayb2-study>

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Problem 2



OXYTOCIN

- PPH continues to contribute to rising maternal morbidity & health disparities
- Oxytocin is the first line medication for PPH prevention / treatment
- Most** people receive oxytocin (in **most** places in the US), yet PPH continues to be a problem

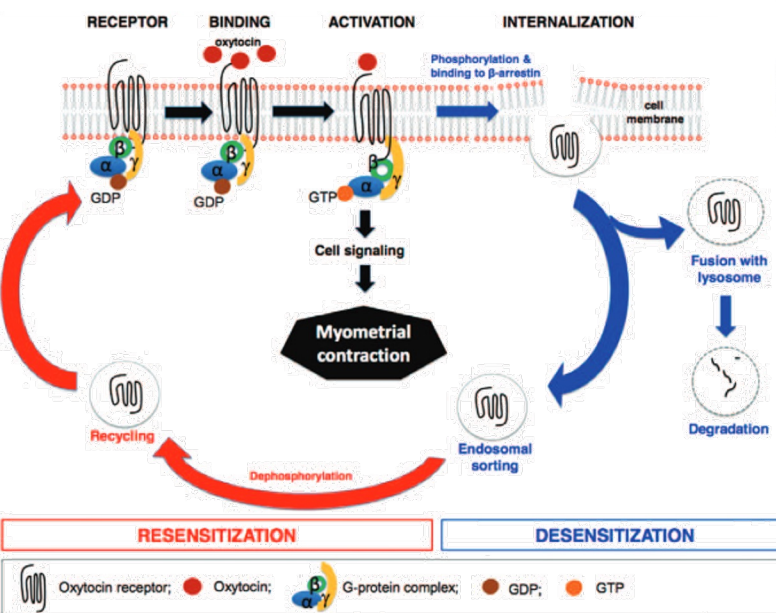
→ IF we had a better understanding of **who would / would not** respond to oxytocin, we could better prepare for or prevent PPH



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Balki M, doi:[10.1213/ANE.0000000000001268](https://doi.org/10.1213/ANE.0000000000001268)



RECEPTOR **BINDING** **ACTIVATION** **INTERNALIZATION**

Phosphorylation & binding to β-arrestin

Cell signaling

Myometrial contraction


Endosomal sorting

RESENSITIZATION **DESENSITIZATION**

Recycling Fusion with lysosome Degradation

Dephosphorylation

Legend: Oxytocin receptor; Oxytocin; G-protein complex; GDP; GTP



OXTR

(oxytocin receptor) desensitization → pharmacodynamic variability

- Greater PPH
- Higher dosage for PPH treatment
- Secondary uterotonics or interventions
- DNA OXTR can be epigenetically 'tuned' throughout the lifespan

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The diagram illustrates the process of DNA methylation. At the top left, a blue chromosome is shown, which is composed of DNA wrapped around histone cores (yellow cylinders). A label "Chromosome" points to the blue structure, and "Histone" points to one of the yellow cylinders. To the right, a DNA double helix is shown with three green boxes labeled "CH₃" attached to it, representing methyl groups. Above the DNA, a chemical reaction is shown: Cytosine (a six-membered ring with an amino group at position 4) is converted to 5-methylcytosine (5mC) by the enzyme DNA methyltransferase. The reaction adds a methyl group (CH₃) to the 5th carbon of the cytosine ring. Below the DNA helix, a detailed view of a DNA segment is shown. It consists of two horizontal lines representing the sugar-phosphate backbone, with vertical bars representing the nitrogenous bases. The bases are color-coded: G (green), C (blue), T (yellow), and A (orange). Methyl groups (M) are shown as red circles attached to the 5' carbon of the cytosine bases (C) in the top strand. The bottom strand also shows methyl groups (M) attached to the 5' carbon of the cytosine bases (C). A label "Methyl group" points to one of the red circles. The chemical structure of a cytosine base is shown on the left, with an amino group (NH₂) at position 4 and a methyl group (CH₃) at position 5. A label "Methyl group" points to the CH₃ group.

Suppresses expression → protein expression.

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1 Social environment: Stress, Trauma, Early adversity, Exposures, Protective factors, Social support. This leads to **OXTR DNA methylation** in **Uterine smooth muscle cells (myometrium)**, which **Reduces mRNA** and **Reduces / alters OXTR production/function**.

2 **OXTR DNA code Variation** (genetic variation) also leads to **Reduces / alters OXTR production/function**.

3 **Fewer receptors** → need for oxytocin to stimulate contractions. Longer exposure to oxytocin → less responsive tissue, fewer contractions and need for more oxytocin.

4 **↑ postpartum bleeding and treatment for higher blood loss or hemorrhage**.

5 The specific combinations of epigenetic and genetic features can help us understand vulnerabilities to PPH and disparities.

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Erickson et al. *BMC Pregnancy and Childbirth* (2022) 22:884
<https://doi.org/10.1186/s12884-022-05205-w>


BMC Pregnancy and Childbirth

RESEARCH **Open Access**

Oxytocin receptor single nucleotide polymorphism predicts atony-related postpartum hemorrhage

Elise N. Erickson^{1,2*}, Kathleen M. Krol³, Allison M. Perkeybile³, Jessica J. Connelly³ and Leslie Myatt²





communications medicine

ARTICLE

<https://doi.org/10.1038/s43856-023-00244-6> **OPEN**

Oxytocin receptor DNA methylation is associated with exogenous oxytocin needs during parturition and postpartum hemorrhage

Elise N. Erickson^{1,2✉}, Leslie Myatt¹, Joshua S. Danoff³, Kathleen M. Krol³ & Jessica J. Connelly³

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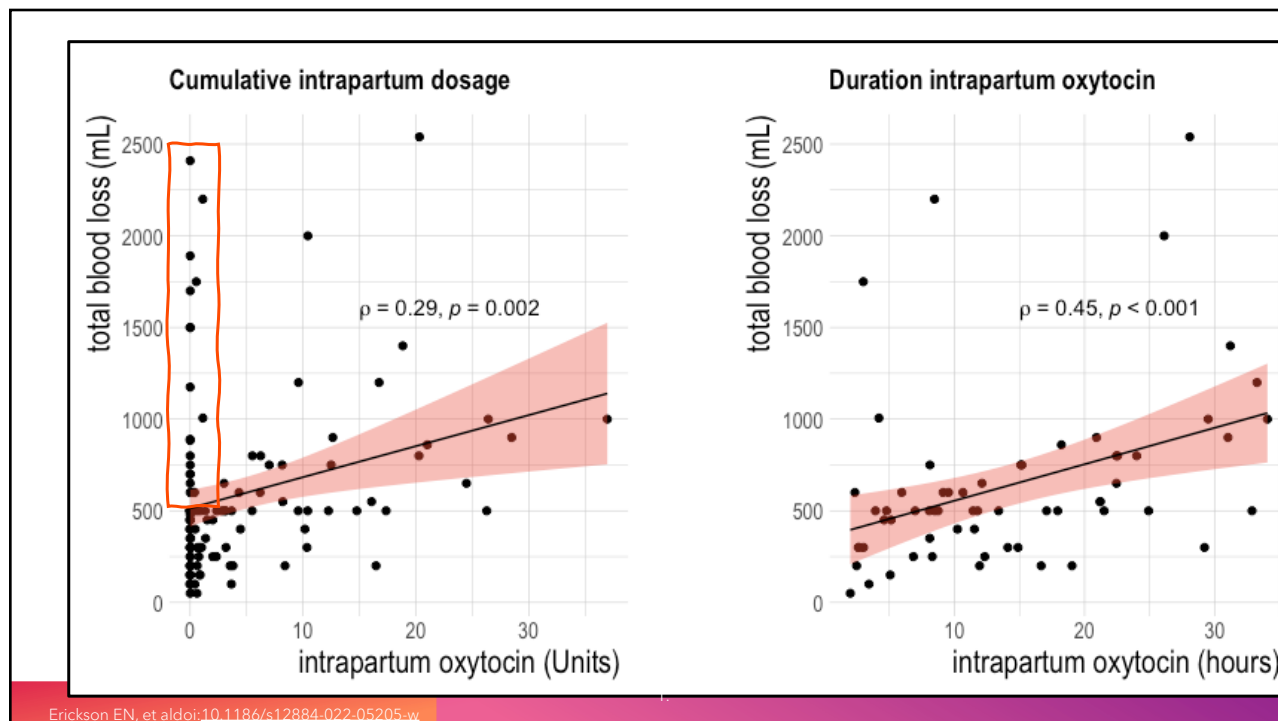
PPH Atony cases (n=69) vs. controls (n=50)

- More likely identifying as Hispanic/ Latina
- Higher BMI
- Nulliparous
- Antibiotic use (GBS+)
- Intrapartum oxytocin dosages
- Longer first stage

**Case/Control
Sample Characteristics**

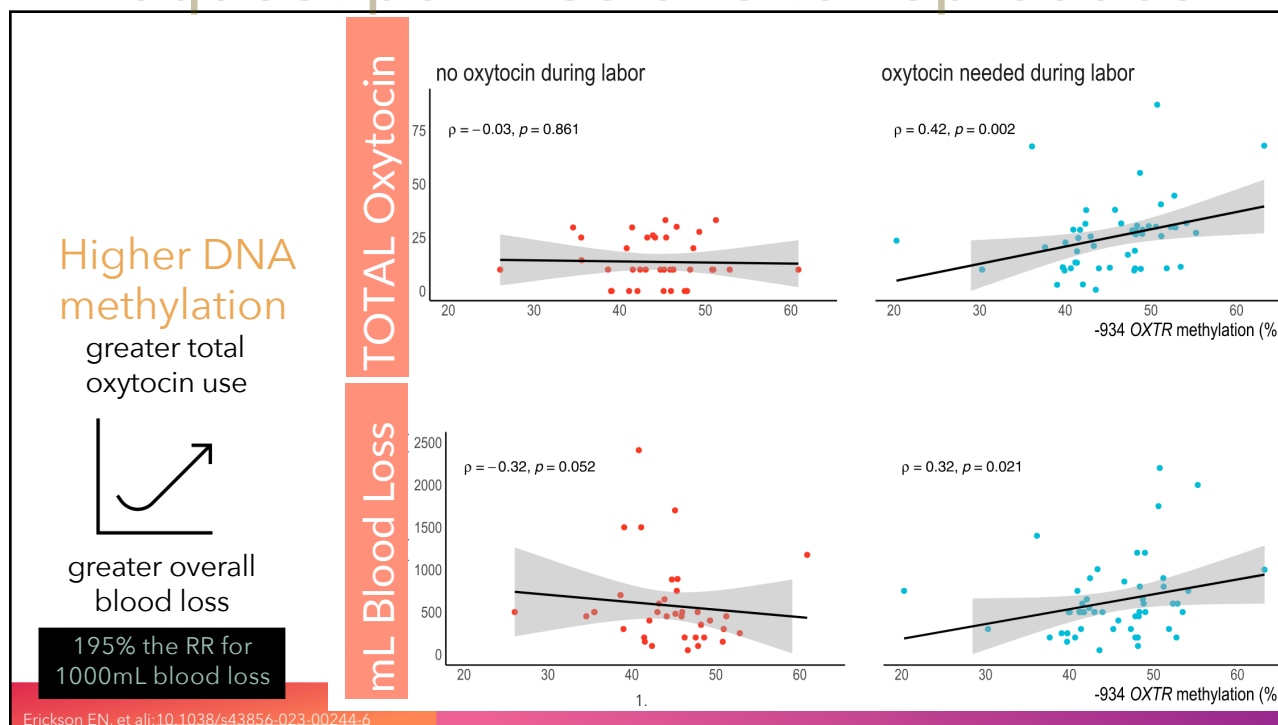
**2018-2020
Oregon, USA**

30

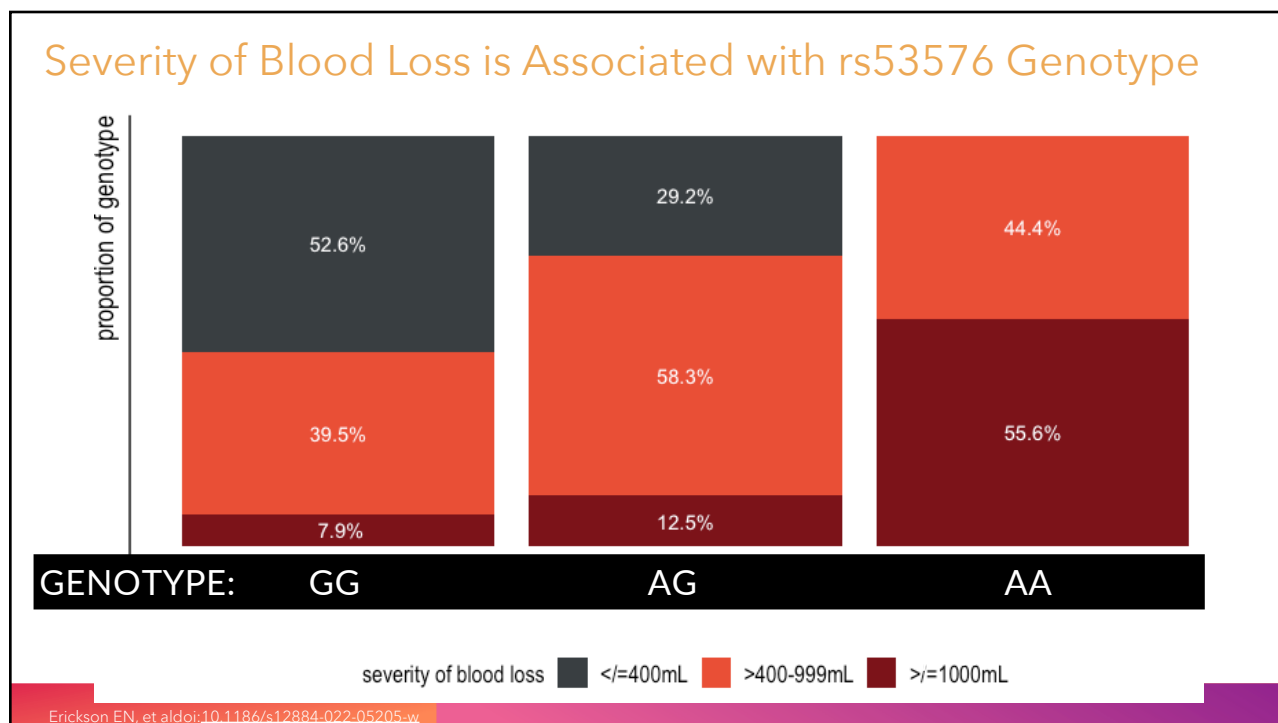


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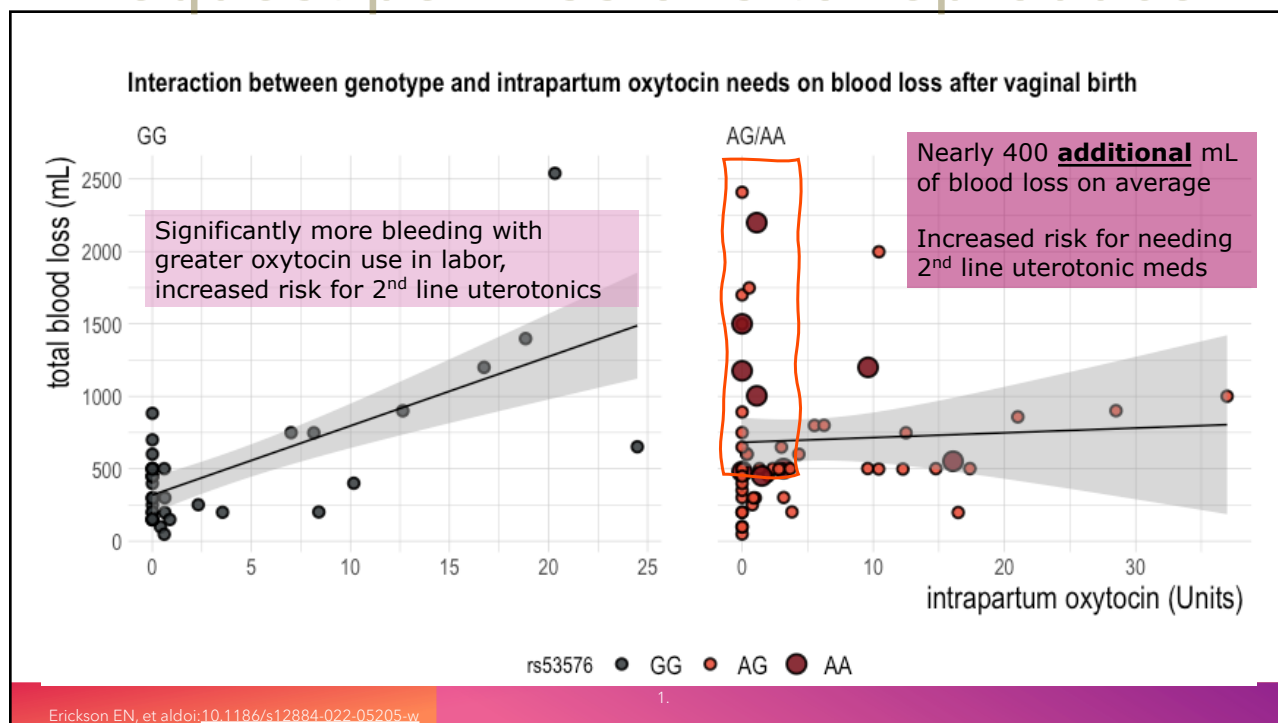


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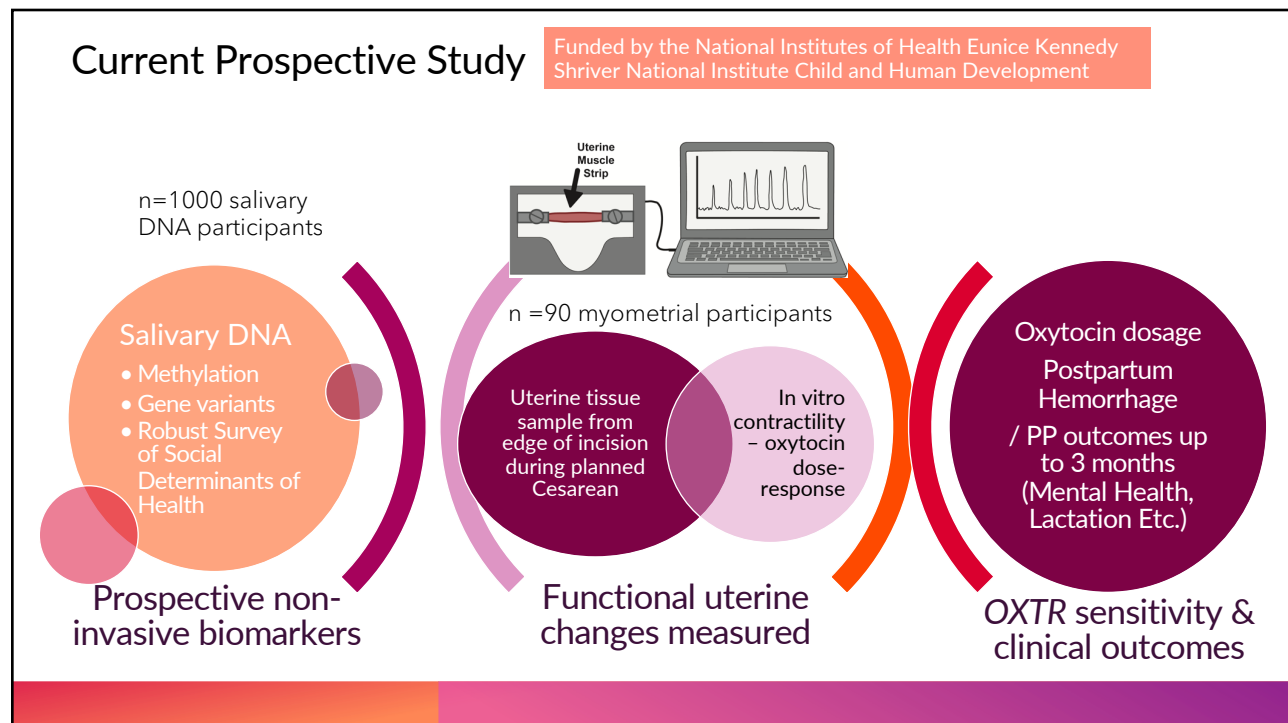


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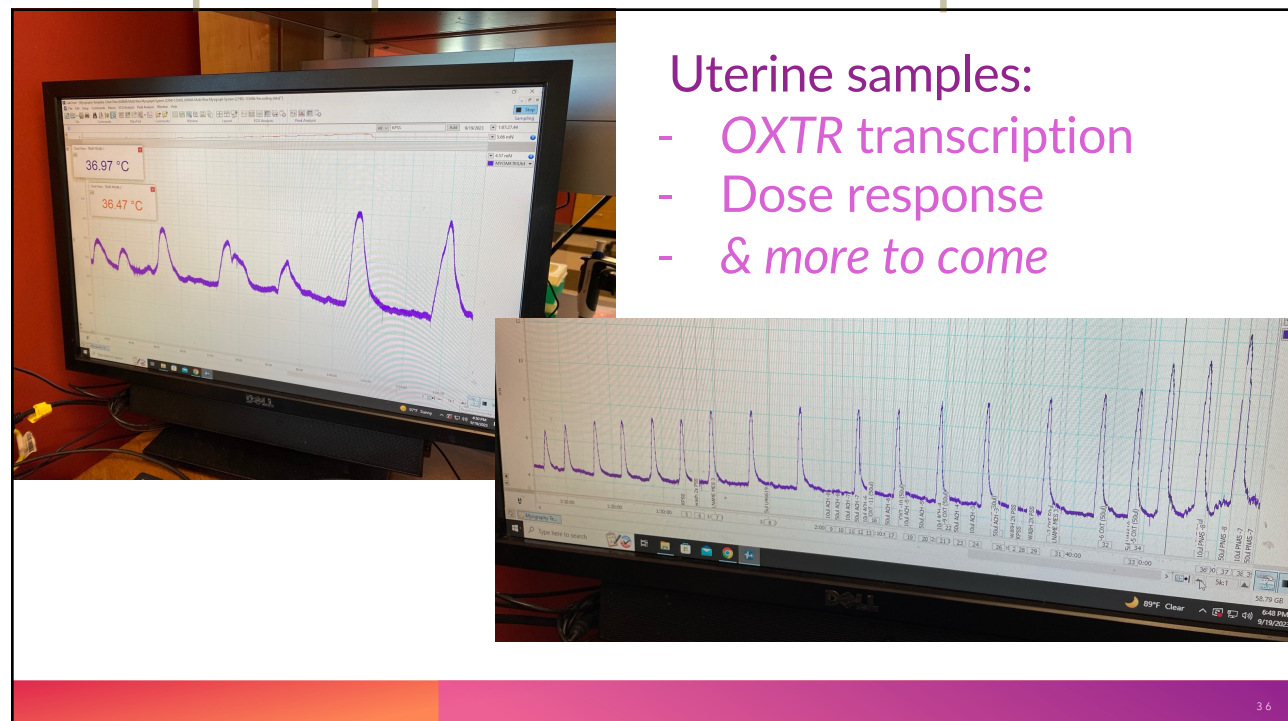


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2 years into project

n= 670 salivary DNA samples

n=65 myometrial samples



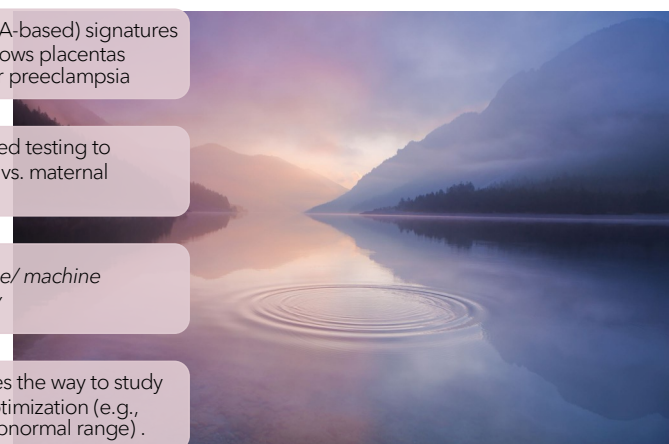
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On the horizon

- Precision Preeclampsia**
 - **Mirvie**: transcriptomic (RNA-based) signatures (from 1st / 2nd trimester) shows placentas maladapting and at risk for preeclampsia
- AMA "Biological Aging"**
 - Epigenetic / telomere-based testing to identify accelerated aging vs. maternal chronological age.
- PPH prediction during labor**
 - **Vasowatch** - maternal pulse/ machine learning based technology
- Accelerating Gestational Diabetes Monitoring**
 - **Continuous glucose**, paves the way to study new factors for glucose optimization (e.g., sleep, stress, duration of abnormal range) .



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Aspirations

- Move away from *tired* **polarized** research positions → different path to same goal or to funding
- Seek **critique** from those who disagree with you... 'get your retaliation in **first**.'
- Consider current questions through **different lenses**:
 - What is the root of the problem?
 - Ask **why/ how**... find different tools
- **Strengthen interdisciplinary partnerships**
- Learn about **emerging technology** (smartphones, machine learning, biosensors, 'omics') – can it be applied responsibly/ usefully?
 - How technology can represent the lived experience and physiology of parturition and reproductive life cycles
- Who could it help?

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Many thanks to the MuMH Lab, Participants & Funders!

Collaborators

- Jessica Connelly, PhD
- Paulo Pires, PhD
- Shravan Aras, PhD
- Chinmai Basavaraj, PhD
- Azure Grant, PhD
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- Allison Perkeybile, PhD
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