Precision Maternity Care: A biosocial research program

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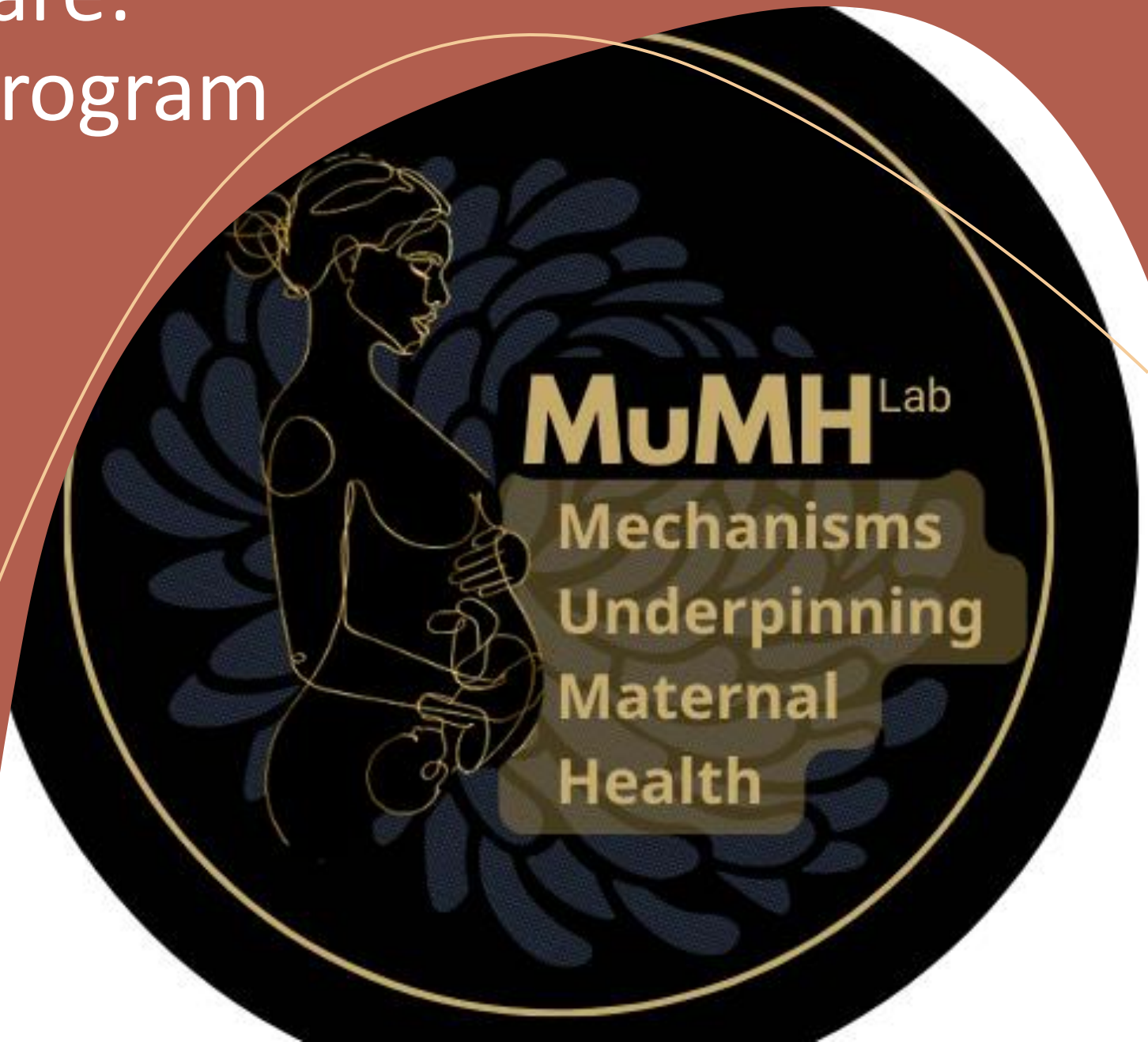


Primary Studies
www.mumhlab.com

Oxytocin response & function/ variation contributing to PPH

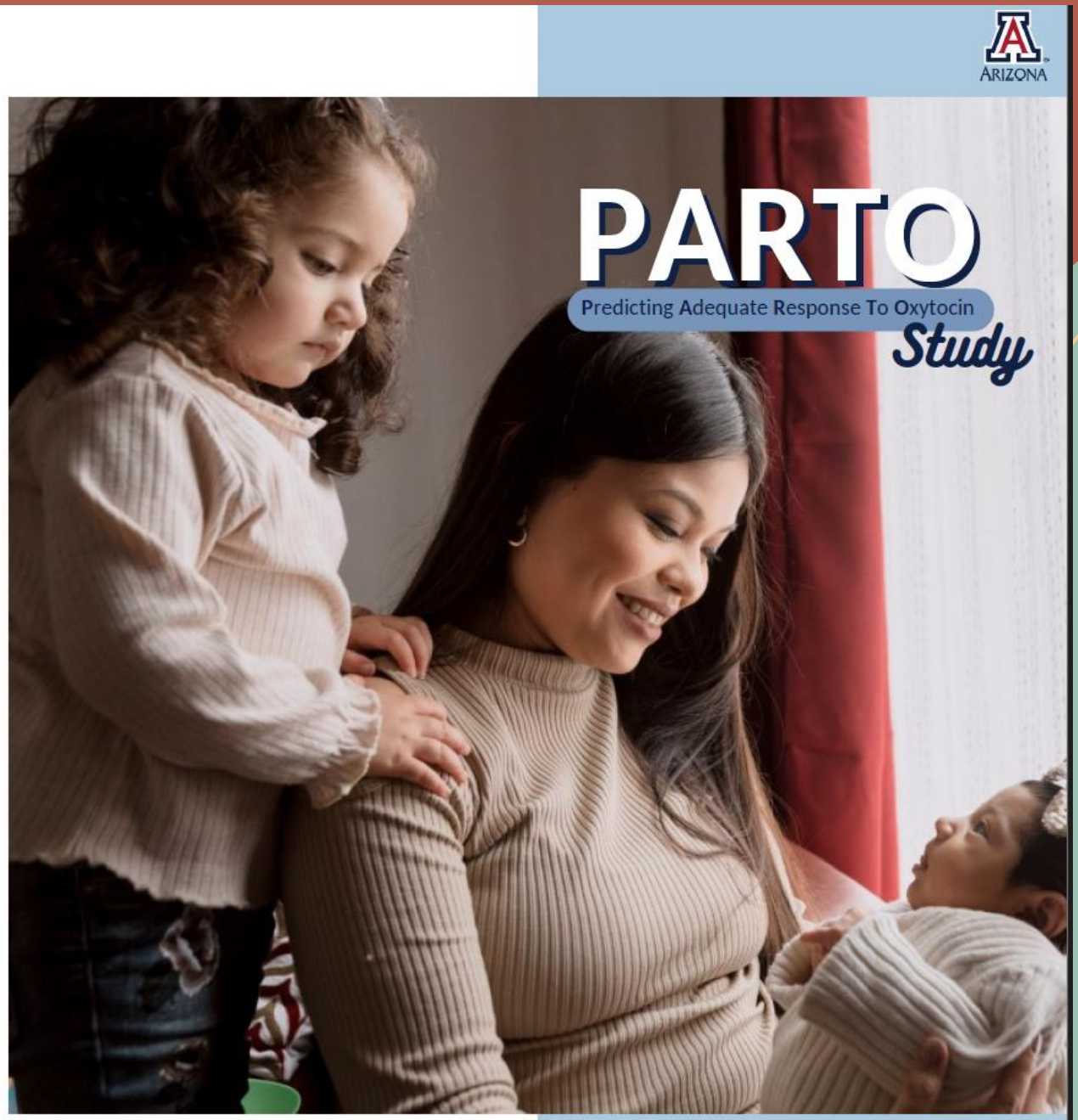
Physiological timeseries data and prediction of labor before symptoms

Midwifery-led care and obstetric outcomes (latent mixture modeling)

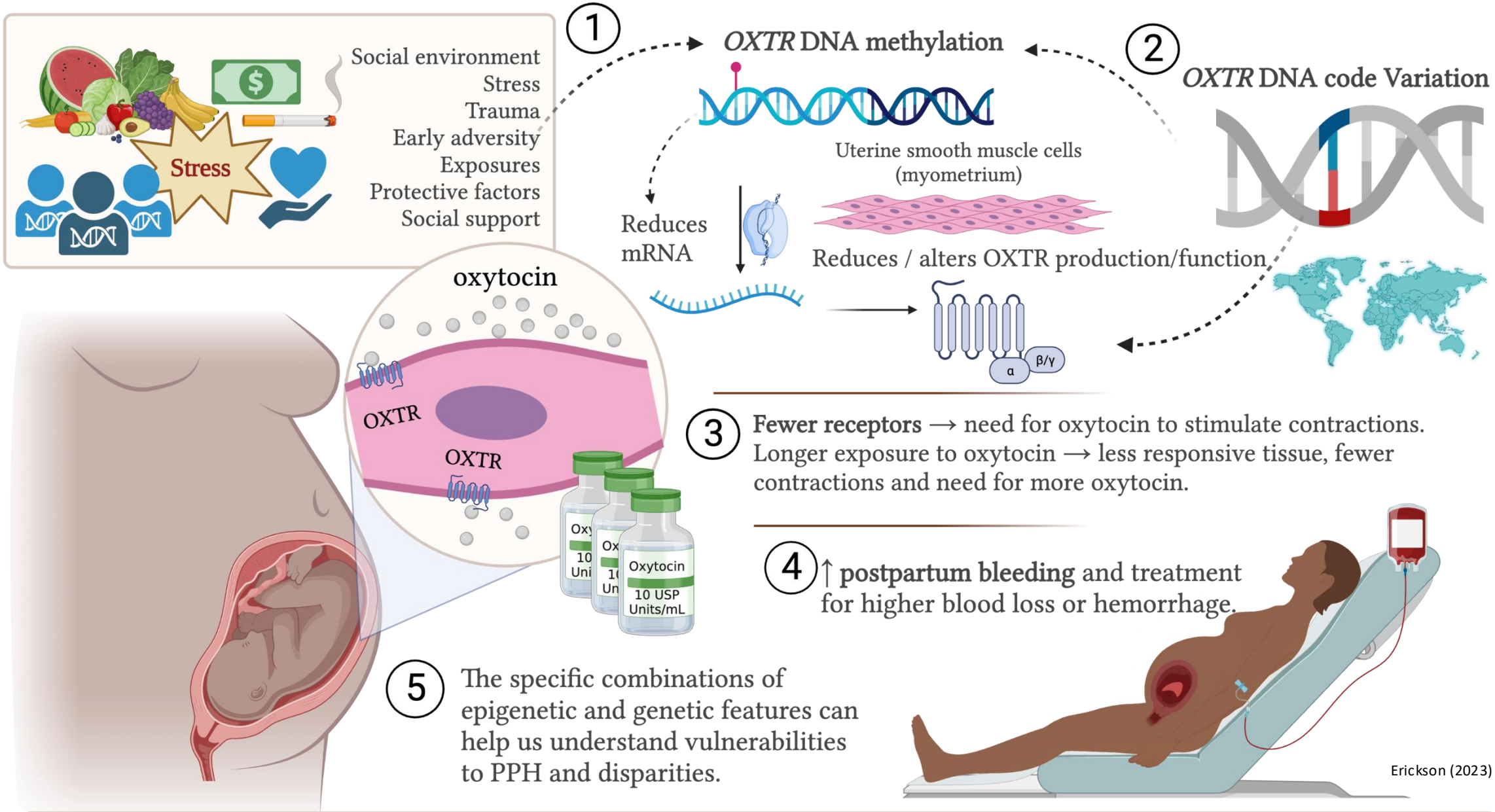
ARIZONA

- Most people giving birth receive a medication called oxytocin either during labor/ after birth.
- Oxytocin causes the uterus to contract.
- We are studying why oxytocin may work better for some people than others, leading to easier labor or less bleeding postpartum.

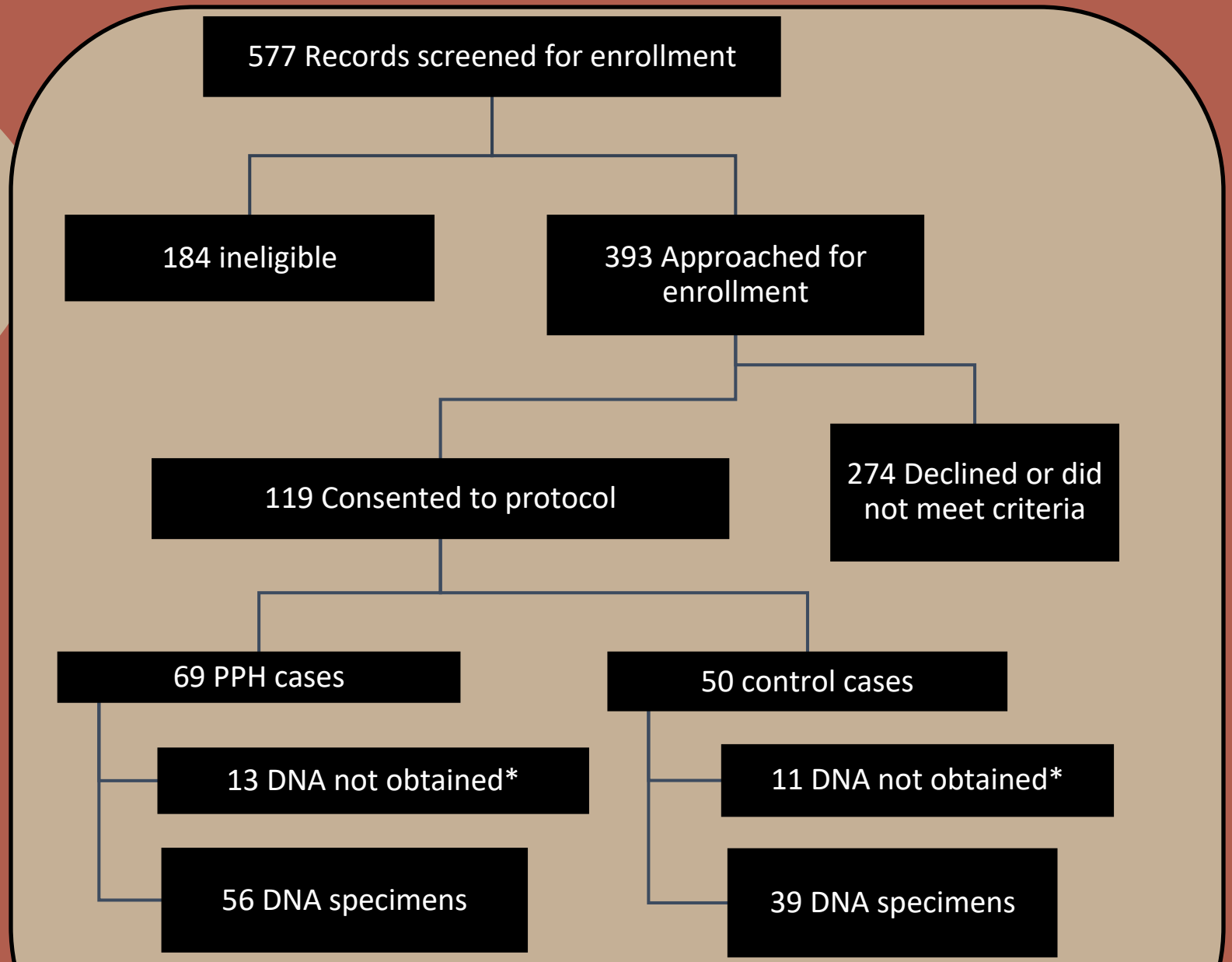
Scan for an informational video



40% of PPH events are among people who are deemed "low risk" for PPH



Genetic and epigenetic perspectives on oxytocin use during labor:
This conceptual model demonstrates how studying oxytocin receptor (*OXTR*) DNA methylation or genetic variation has clinical significance for maternal health during and after childbirth.



*DNA not obtained due to COVID-19 pandemic restrictions after enrolling in study (n=6), lost to follow-up/no-show (n=17), blood not able to be drawn (n=1).

Case Control Study

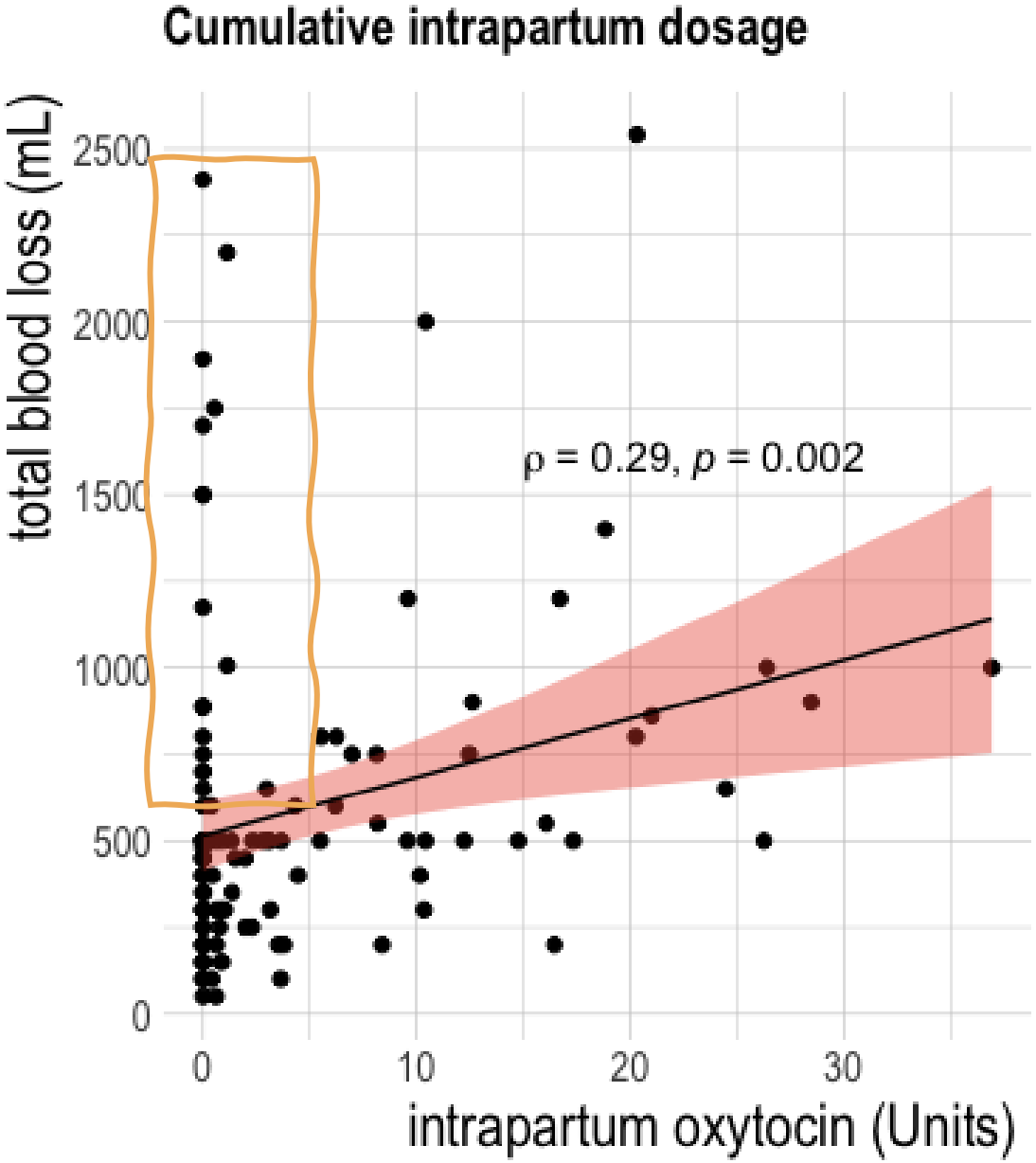
- Cases defined as >1000 blood loss or use of 2nd uterotonics + atony
- Vaginal births
- Equal # induced/ spontaneous

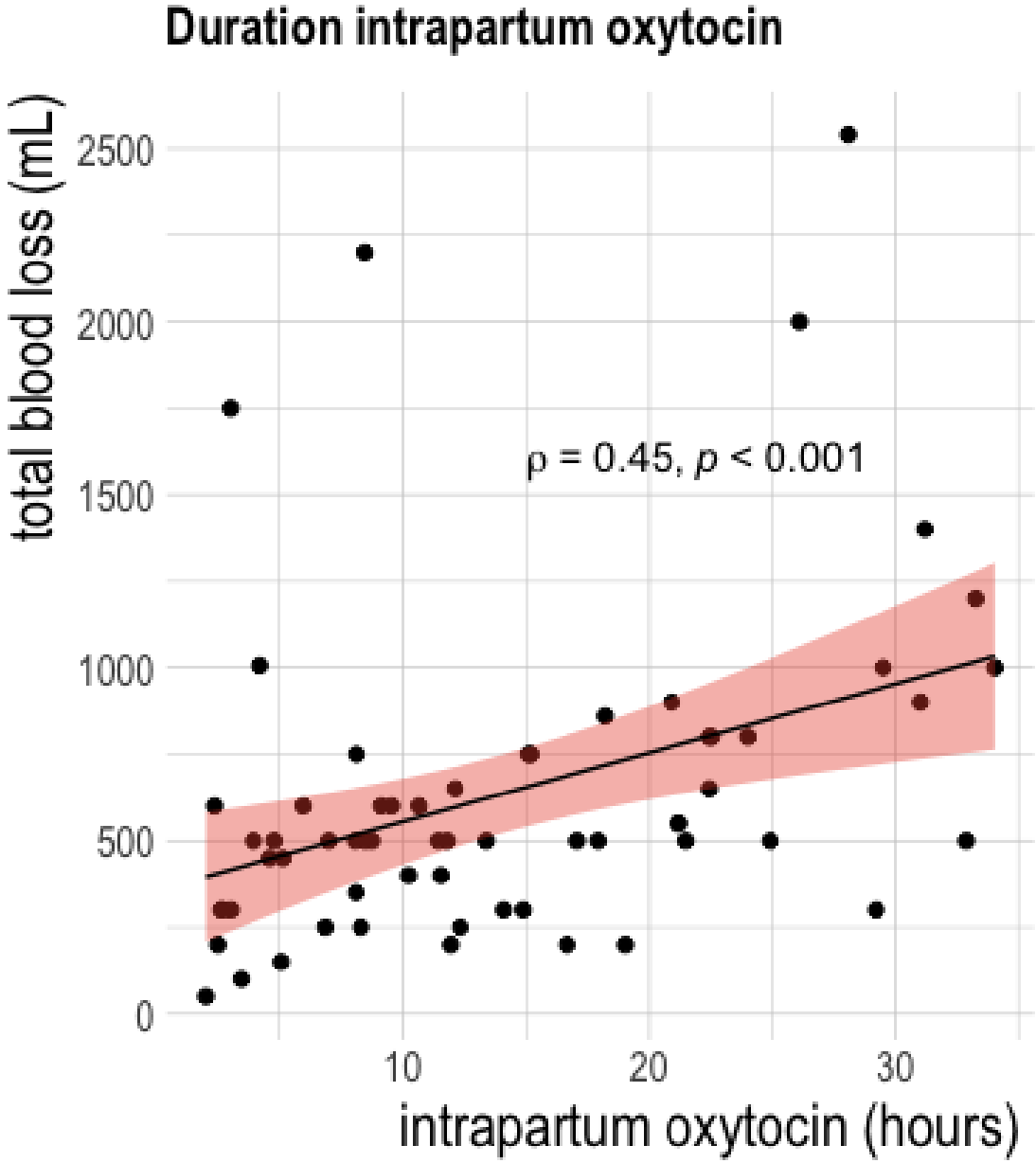
Exclusions

- Known coagulopathy
- HELLP
- DIC
- Mag Sulfate
- Accreta
- Low platelets
- Severe bleeding from laceration

Sample Characteristics

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


Cumulative intrapartum dosage
total blood loss (mL)
2500
2000
1500
1000
500
0
ρ = 0.29, p = 0.002
0
10
20
30
intrapartum oxytocin (Units)

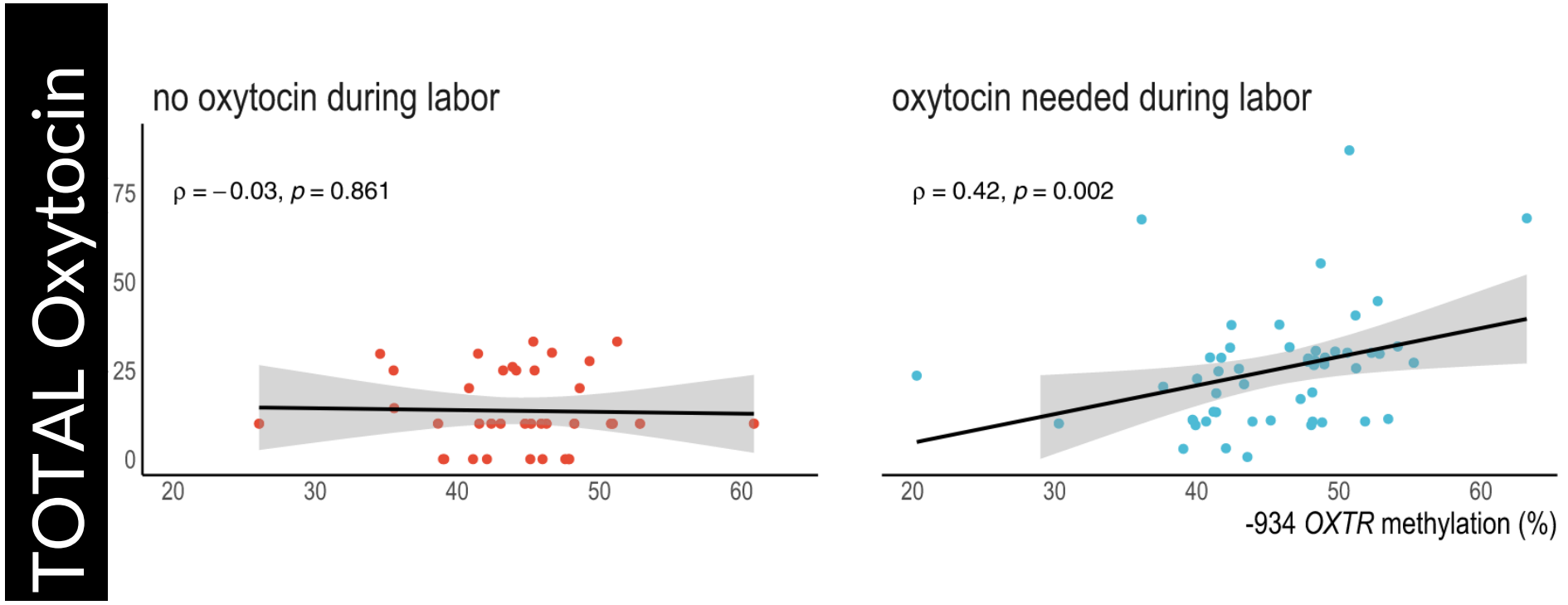

Duration intrapartum oxytocin
total blood loss (mL)
2500
2000
1500
1000
500
0
ρ = 0.45, p < 0.001
10
20
30
intrapartum oxytocin (hours)

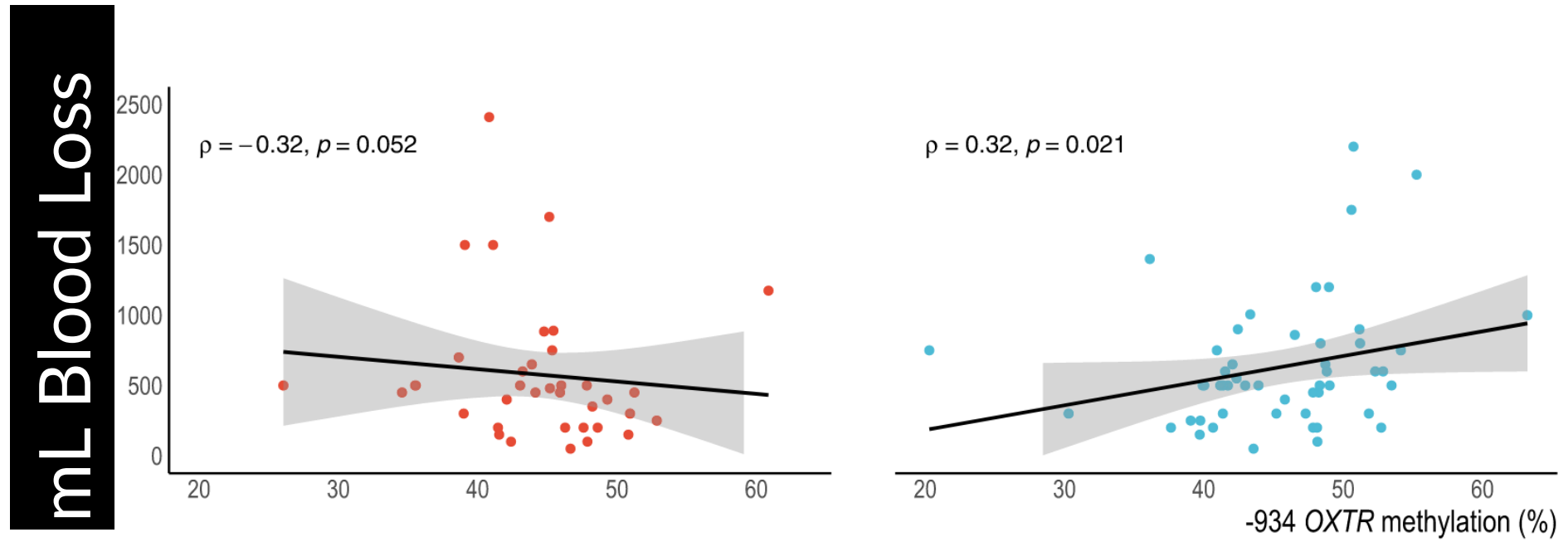
Higher DNA methylation

greater total oxytocin use

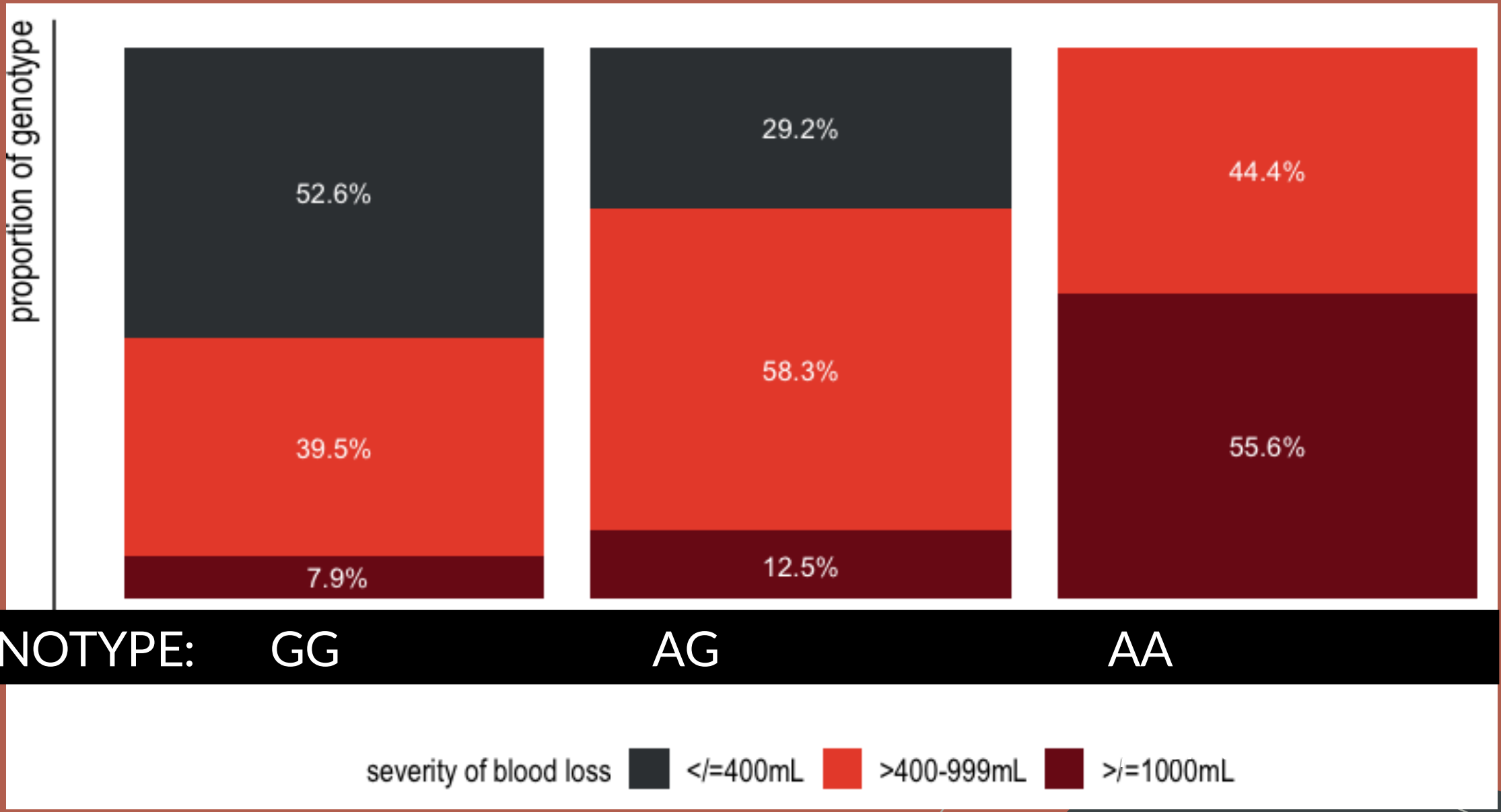
greater overall blood loss

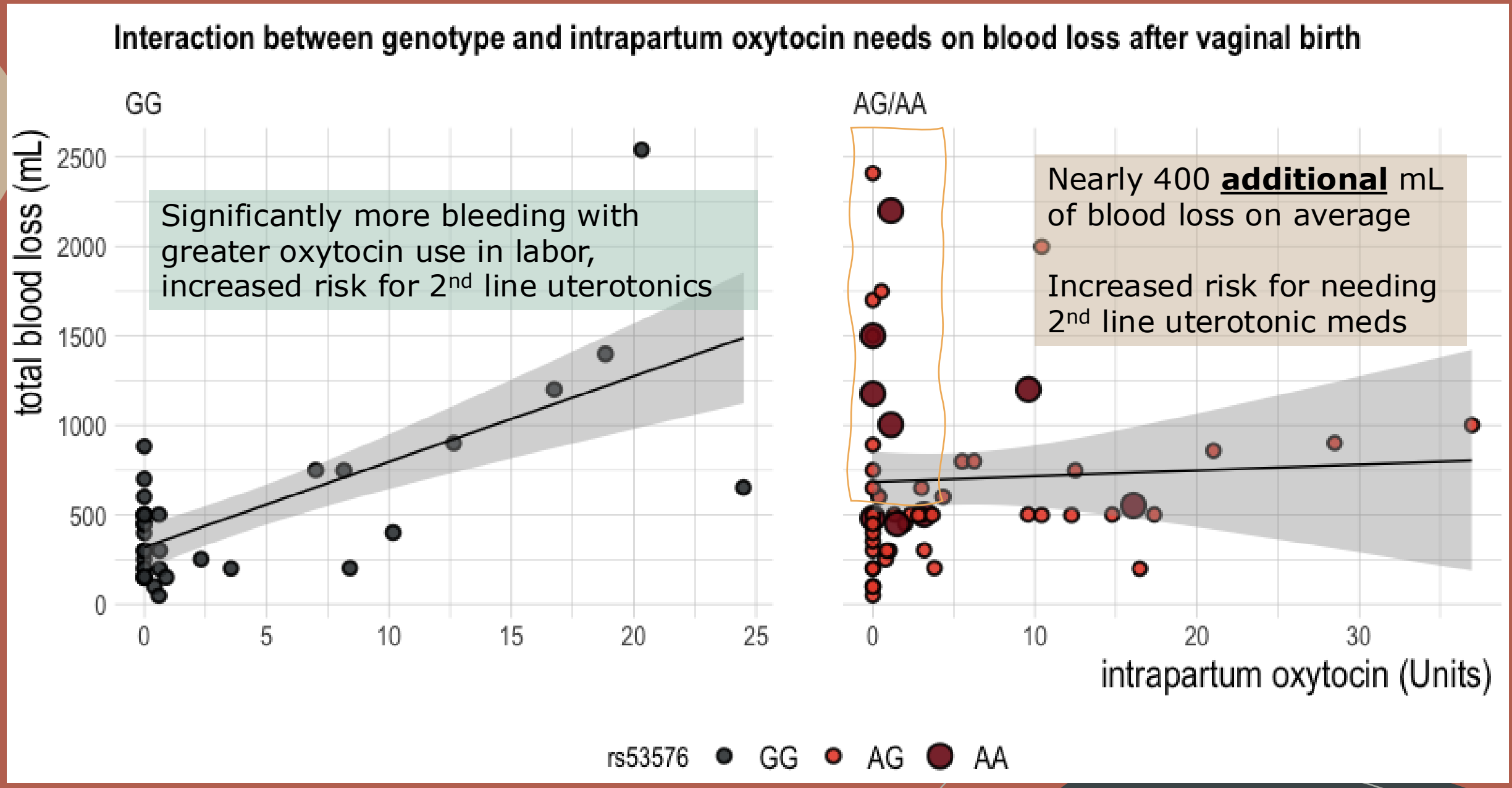
195% RR for 1000mL blood loss





Severity of Blood Loss is Associated with rs53576 Genotype




Interaction between genotype and intrapartum oxytocin needs on blood loss after vaginal birth
GG
AG/AA
total blood loss (mL)
2500
2000
1500
1000
500
0
0
5
10
15
20
25
0
10
20
30
intrapartum oxytocin (Units)
Significantly more bleeding with greater oxytocin use in labor, increased risk for 2nd line uterotonics
Nearly 400 additional mL of blood loss on average
Increased risk for needing 2nd line uterotonic meds
rs53576
GG
AG
AA

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. Krol[3], Allison M. Perkeybile[3], Jessica J. Connelly[3] and Leslie Myatt[2]

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 Myatt[1], Joshua S. Danoff[3], Kathleen M. Krol[3] & Jessica J. Connelly[3]

THE UNIVERSITY OF ARIZONA

Reproductive Sciences
https://doi.org/10.1007/s43032-024-01621-9

PREGNANCY: ORIGINAL ARTICLE

A Common *OXTR* Risk Variant Alters Regulation of Gene Expression by DNA Hydroxymethylation in Pregnant Human Myometrium

Joshua S. Danoff[1,2] · Travis S. Lillard[1] · Leslie Myatt[3] · Jessica J. Connelly[1] · Elise N. Erickson[4]

GG:

- ↑ HYDROXYmethylation
- ↑ gene transcription in myometrial tissue
- ↓ Pitocin use
- ↓ odds for PPH

AG/ AA:

- ↑ true methylation
- ↓ gene transcription in myometrial tissue
- ↑ Pitocin use
- ↑ odds for PPH

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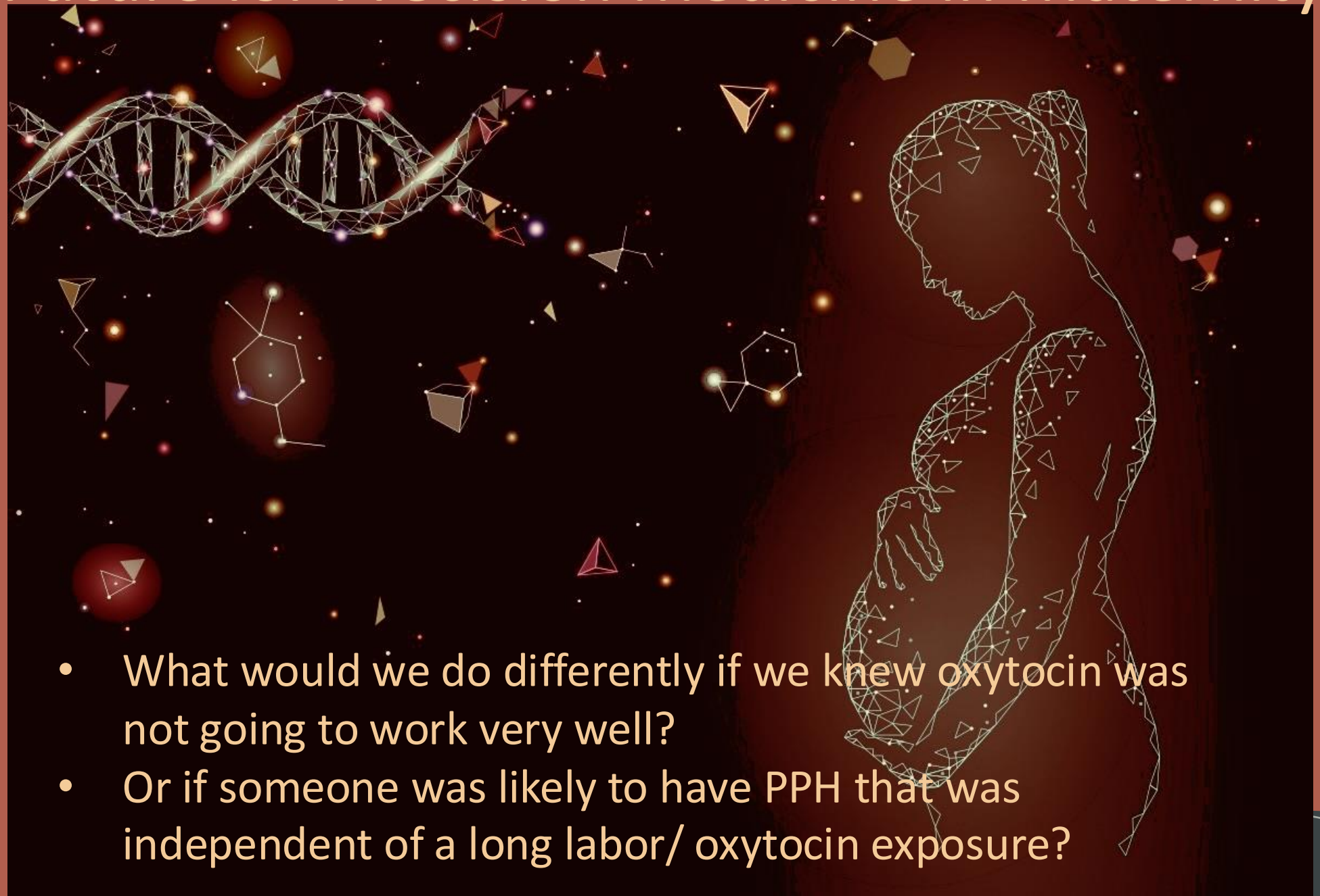
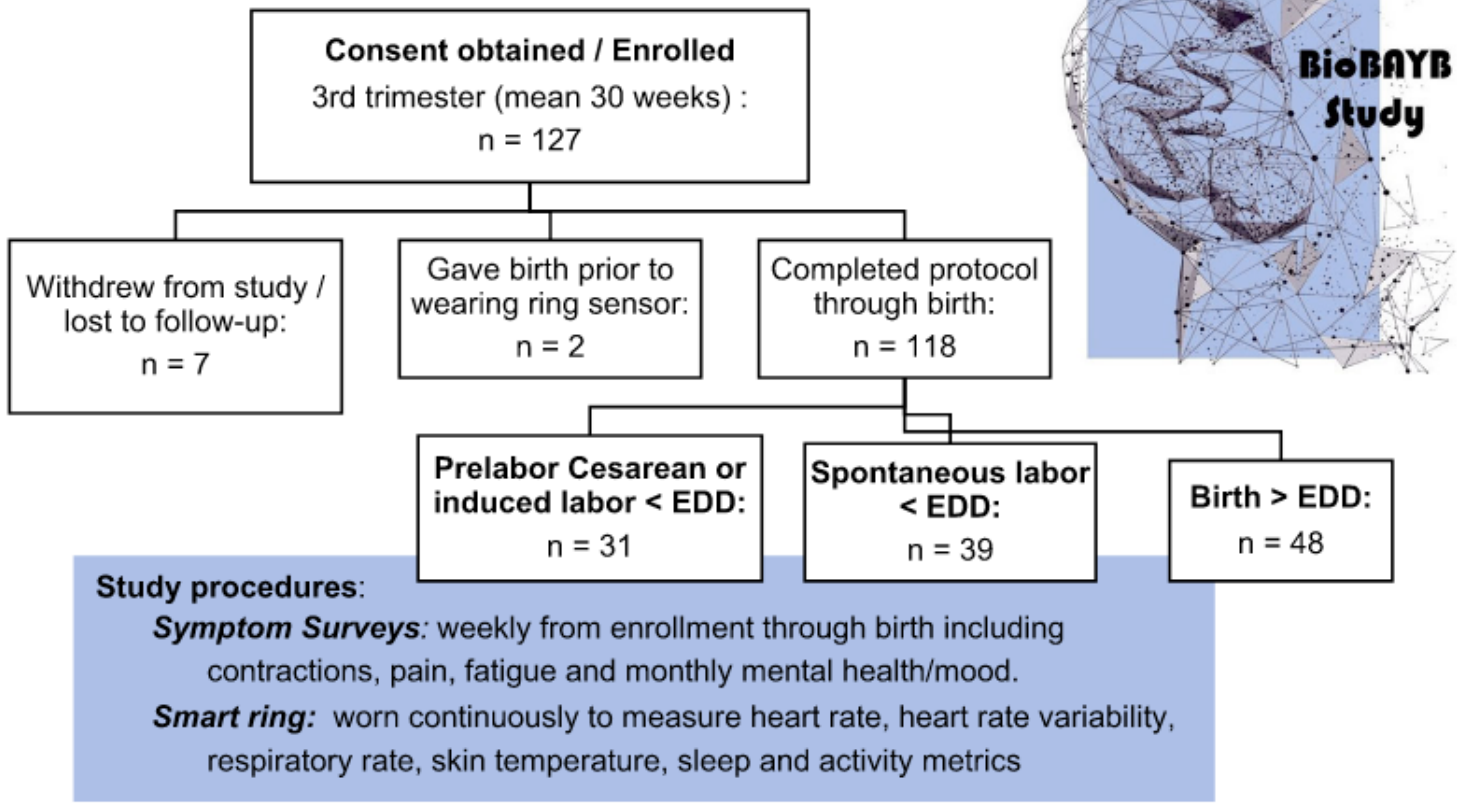
A Future for Precision Medicine in Maternity?



- What would we do differently if we knew oxytocin was not going to work very well?
- Or if someone was likely to have PPH that was independent of a long labor/ oxytocin exposure?



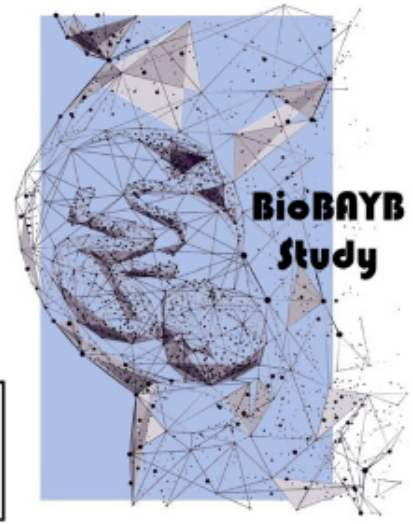
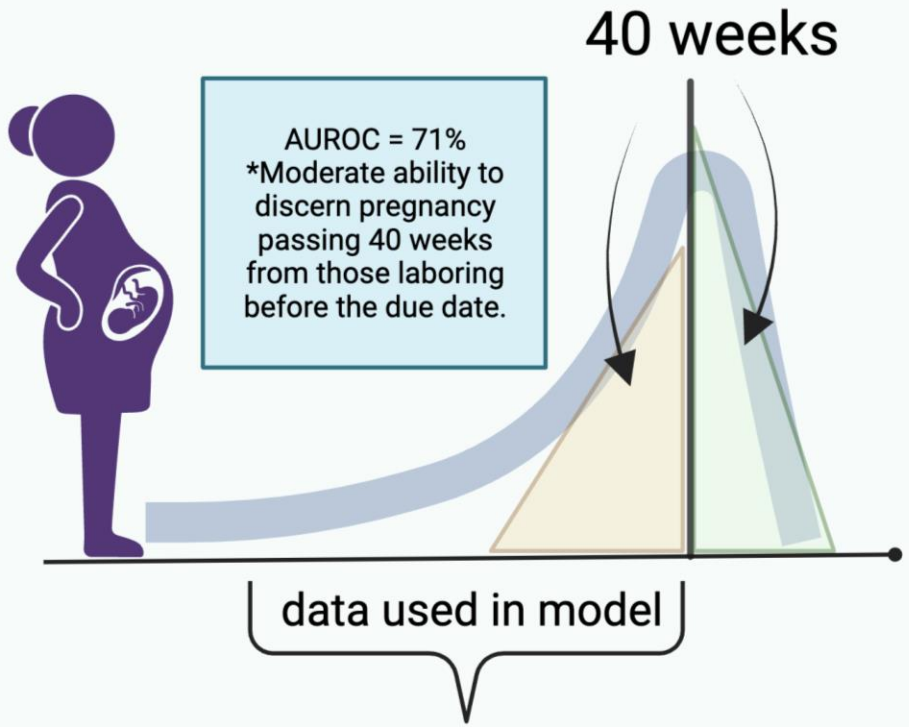


Fig. 1 Flow diagram of participants and study procedures for BioBAYB study. Of the 127 participants gave consent and enrolled into the study, 118 completed data collection with prelabor/birth data from the wearable smart ring. Comparison groups for analysis included those who gave birth prior to the Estimated Date of Delivery (EDD) through planned prelabor Cesarean or induced labor, those who experienced labor starting before the EDD and those whose pregnancies lasted beyond the clinical EDD. Study procedures listed in blue box, sent via REDCap questionnaires, smart ring metrics gathered.

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



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)

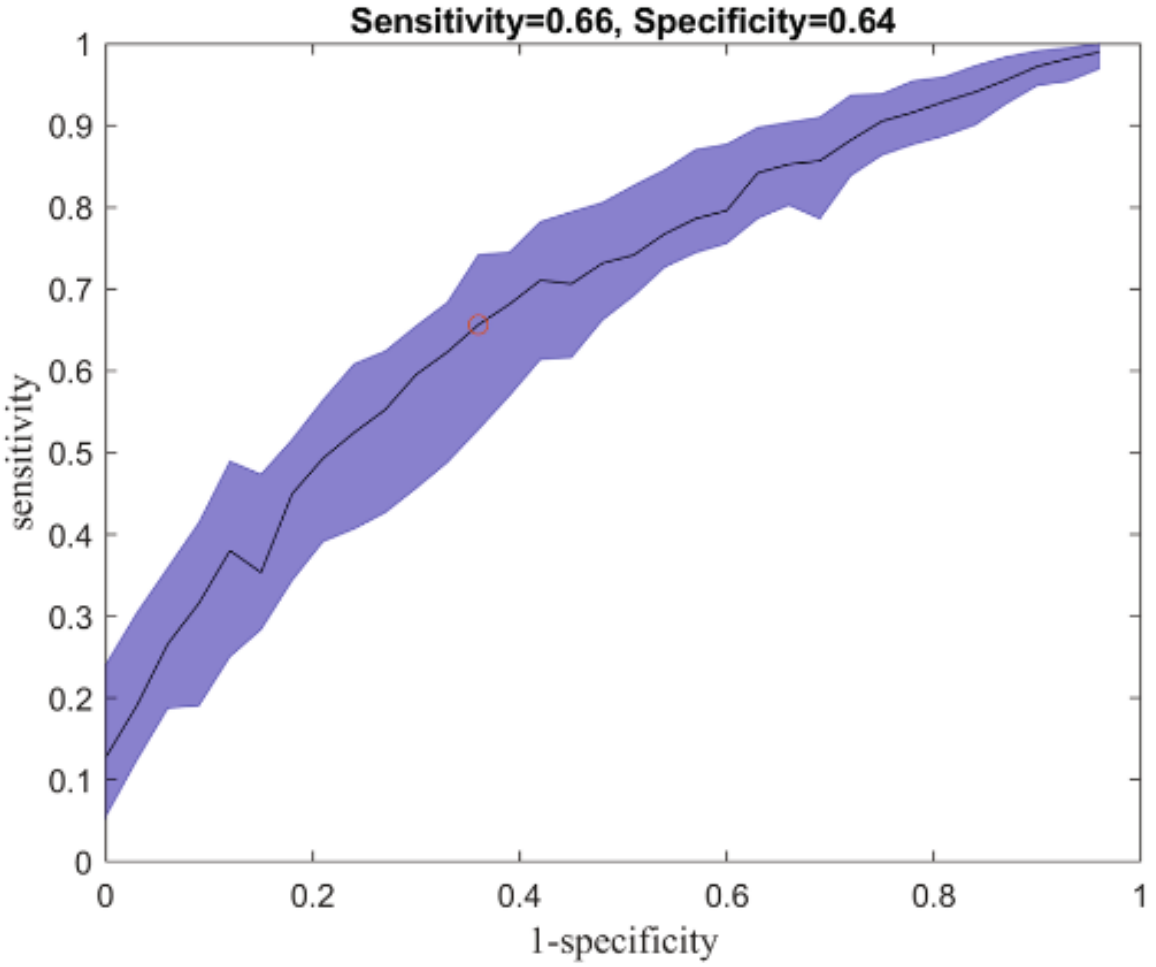


Fig. 5 Receiver operating characteristic (ROC) curve showing the sensitivity vs. 1-specificity for predicting if a pregnancy would pass the EDD. The area under the curve on average across the five folds was 0.71 with a sensitivity of 0.66 and specificity of 0.64.

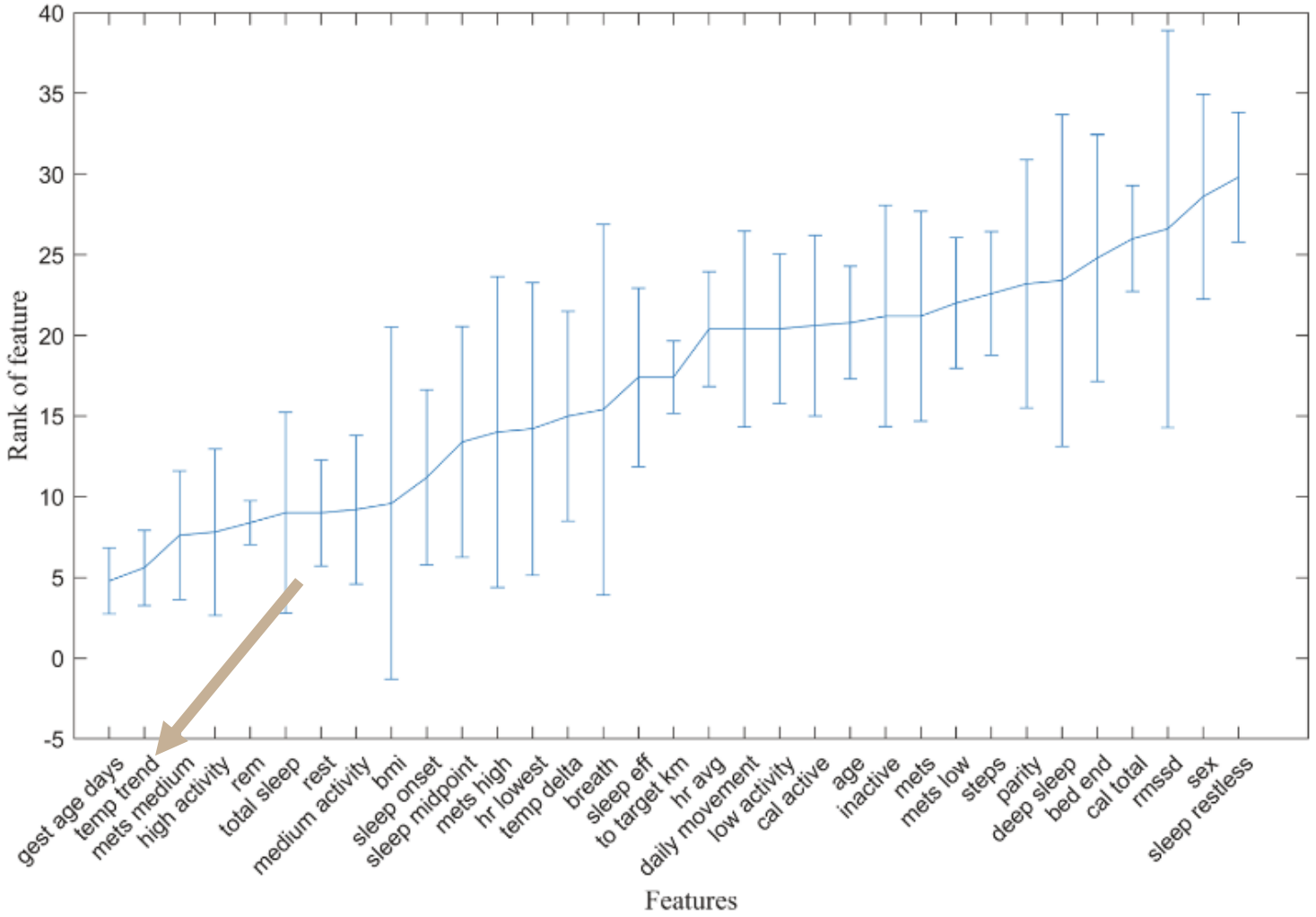
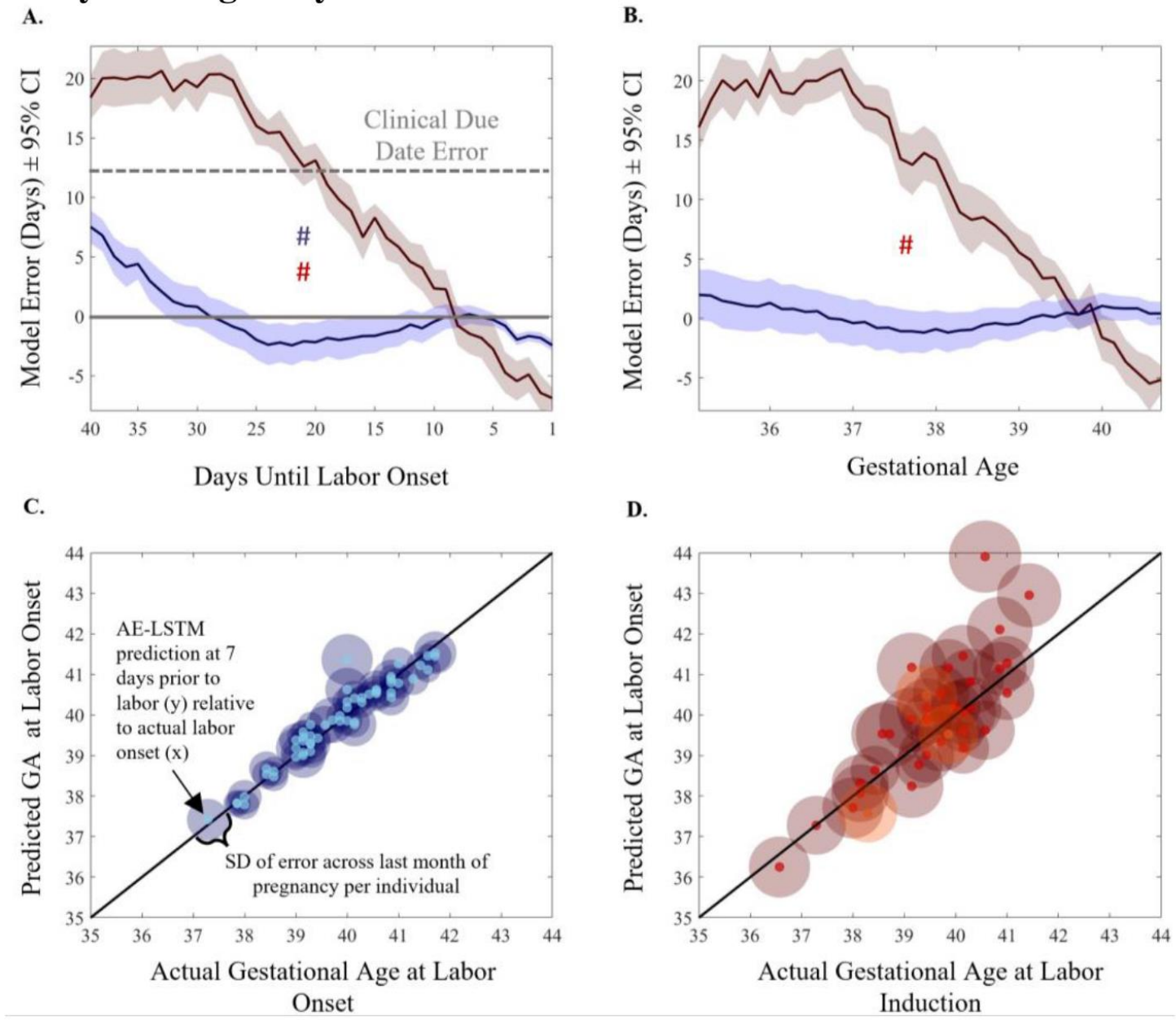


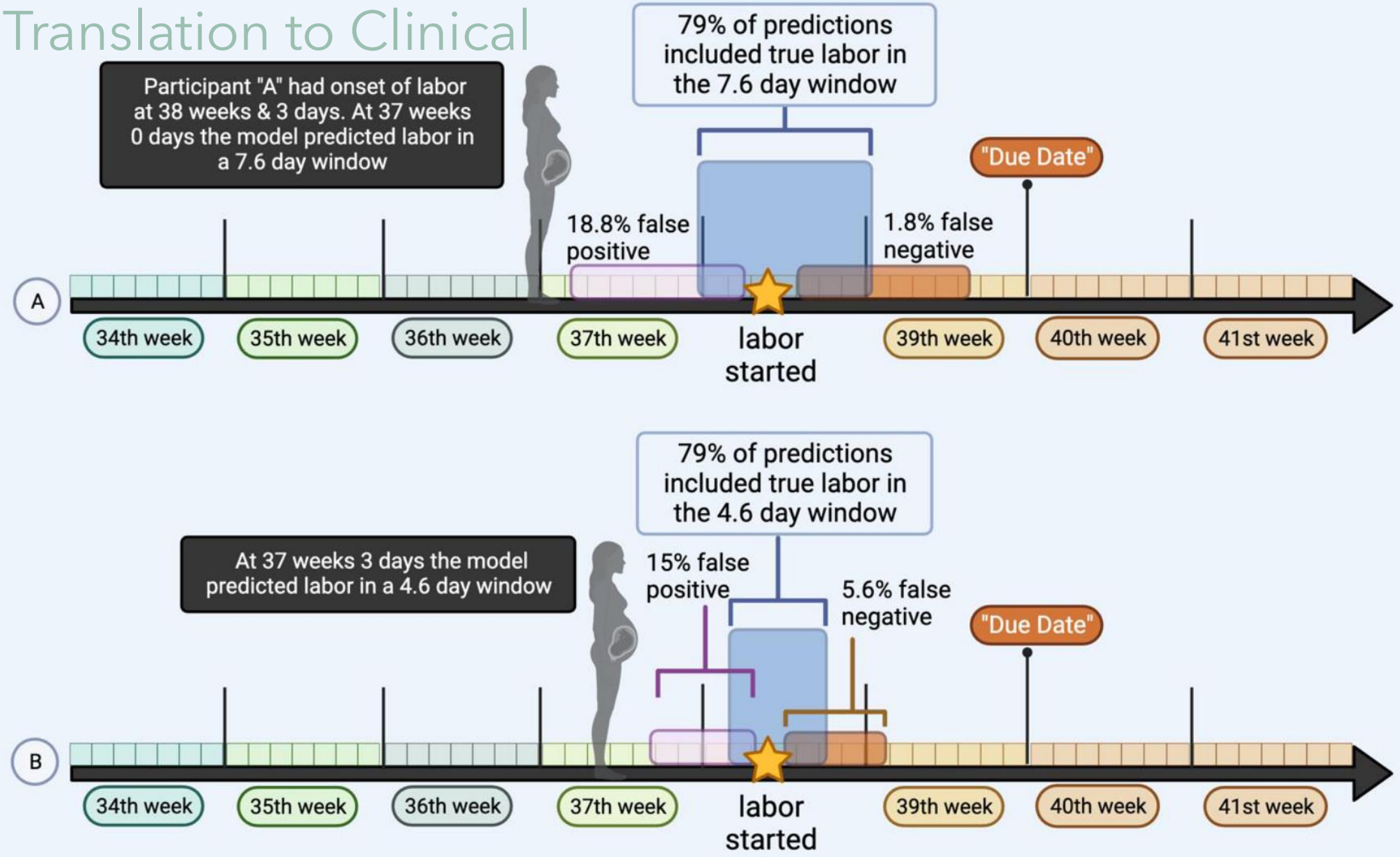
Fig. 4 Average predictive rank of features used in boosted random forest model across five runs. Features are shown based on their rank as determined by greedy search in predicting that a pregnancy would pass the EDD. The rank of the feature within the greedy search is shown on the *y*-axis while *x*-axis lists the features from left (best) to worst (right) based on the average of their rank across the five-fold cross validation. The error bars show the standard deviation of each feature's rank, indicating its consistency at that rank across the five folds.

AI/ML for predicting days until labor

Figure 6. AE-LSTM Predicts Spontaneous Labor Onset With < 2 Days of Error in the Last 8 Days of Pregnancy.



Translation to Clinical



Thank you, Team Science!

Study Participants & Funders!

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