The PReclampsia Early Determination for Intervention, Cure, and Therapeutics by Vasopressin (PREDICTV) Study

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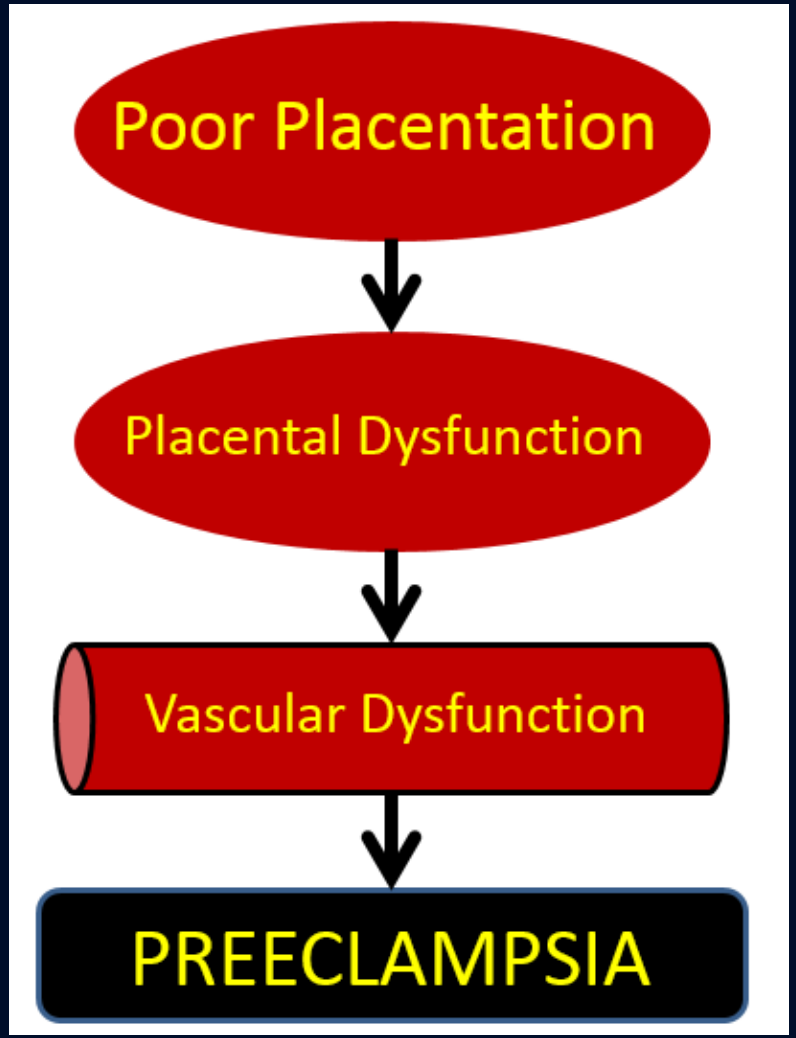
What is Preeclampsia?

- Pregnancy Complication
- Symptoms
  - Headaches/Blurred Vision
  - High Blood Pressure
  - Kidney Damage
- Health Issues
  - For Child and Mother
  - Eclampsia
  - HELLP
- 20 weeks into gestation – 6 weeks postpartum

26 Weeks
0.5 Pounds
Delivered due to
Severe Preeclampsia

What is PreE? Cont'd

- Diagnosis
- No Known Treatment
- No Known Direct Cause
- Biomarkers Aid in Detection

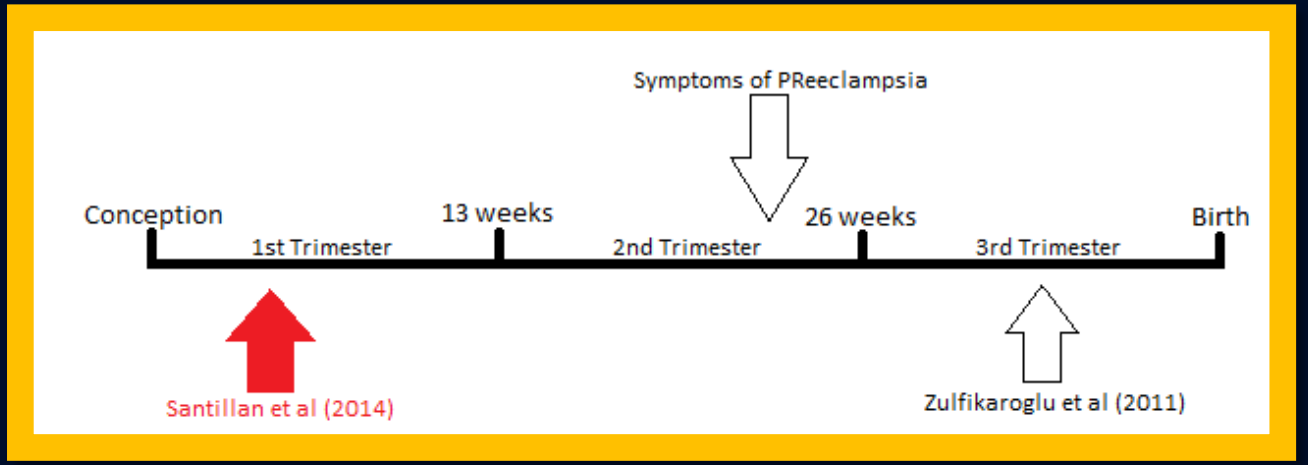


What are Vasopressin & Copeptin?

- Previous Research (Morgenthaler et al, 2006)
  - Vasopressin
    - Hormone
    - Not stable
  - Copeptin
    - Protein
    - Surrogate biomarker of Vasopressin
- High levels Vasopressin/Copeptin in Preeclamptic Women (Zulfikaroglu et al, 2011)

Why Copeptin?

- Statistically Significant in the First Trimester (Santillan et al, 2014)
  - Sensitivity
  - Specificity
  - Positive Predictive Value
  - Negative Predictive Value
- Additional Benefits
  - Easy to Measure
  - Early Detection
  - Cheap
  - Simple Blood Test



Why Study Preeclampsia?

- One of the Leading Causes of Death in Pregnancy
  - Mother and Child
  - 100,000 and 500,000 deaths respectively each year
  - 5-10% pregnancies affected
- **Delay in diagnosis caused 92% of deaths (Snydal, 2014)**
- If early detection is possible…
  - Helps decrease mortality and complications

Objectives

- What factors play a role in Preeclampsia?
  - Race
  - Diabetes
  - Multiple Gestation
  - Age
  - BMI
  - History of Preeclampsia
- What level of plasma copeptin is a good classifier of Preeclampsia?
- Can urine samples be a good measure early Preeclampsia detection?
  - More Efficient
  - Cheaper → Home Tests

What is Logistic Regression?

- The response variable is dichotomous (success; failure)
  - Preeclamptic or Non Preeclamptic
- Estimates the probability of success (π)
  - 1 = success; 0 = failure
- Logit:
  - Log of the Odds of success = $\log(\frac{\pi}{1-\pi}) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_n X_n = \text{logit}(\pi)$
  - Logit linearizes the problem

Logistic Regression Cont'd

- How is the logit used in fitting a logistic regression model?
  - $\text{logit}(\pi) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_k X_k \rightarrow \frac{e^{\text{logit}(\pi)}}{1 + e^{\text{logit}(\pi)}} = \pi$
  - $\pi = \frac{e^{\beta' X}}{1 + e^{\beta' X}}$
- Three Components for a Logistic Regression Model:
  1. Data:
     - Number of successes in total number of observations
     - Has predictors
  2. Randomness:
     - Trials are independent
     - Depends on the Bernoulli distribution
  3. Fixed: $\frac{e^{\text{logit}(\pi)}}{1 + e^{\text{logit}(\pi)}}$

Coefficients

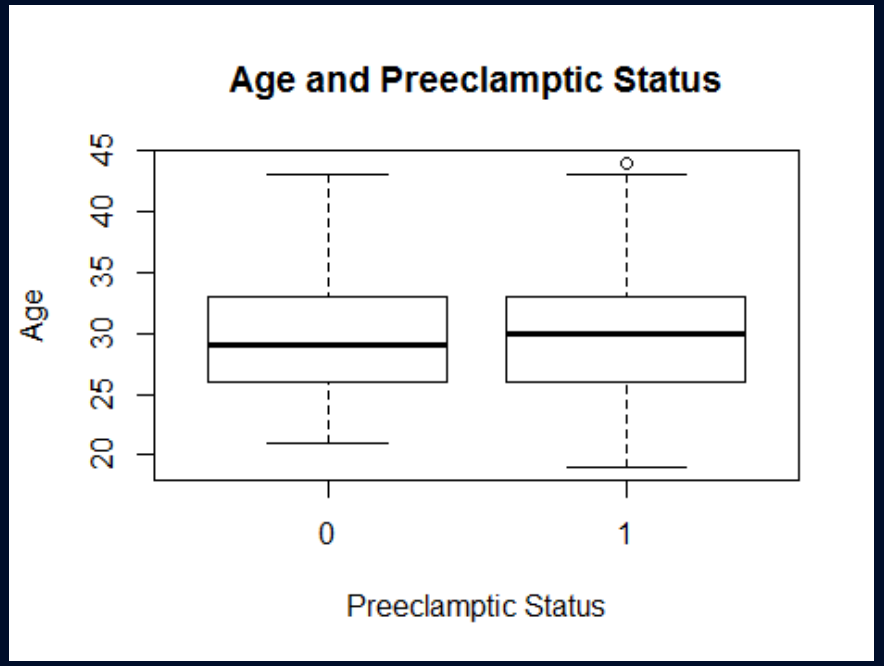
- Log(odds of success) = logit = $\beta_0 + \beta_1 X_1$, where $X_1 = 0$ or 1
  - If $X_1 = 0$, e^{β_0} = odds of success
  - If $X_1 = 1$, $e^{\beta_0 + \beta_1}$ = odds of success
- Log(odds of success) = logit = $\beta_0 + \beta_1 X_1$, where X_1 is continuous
  - If X_1 increases by 1, $(e^{\beta_0 + \beta_1 X_1})(e^{\beta_1})$ = odds of success

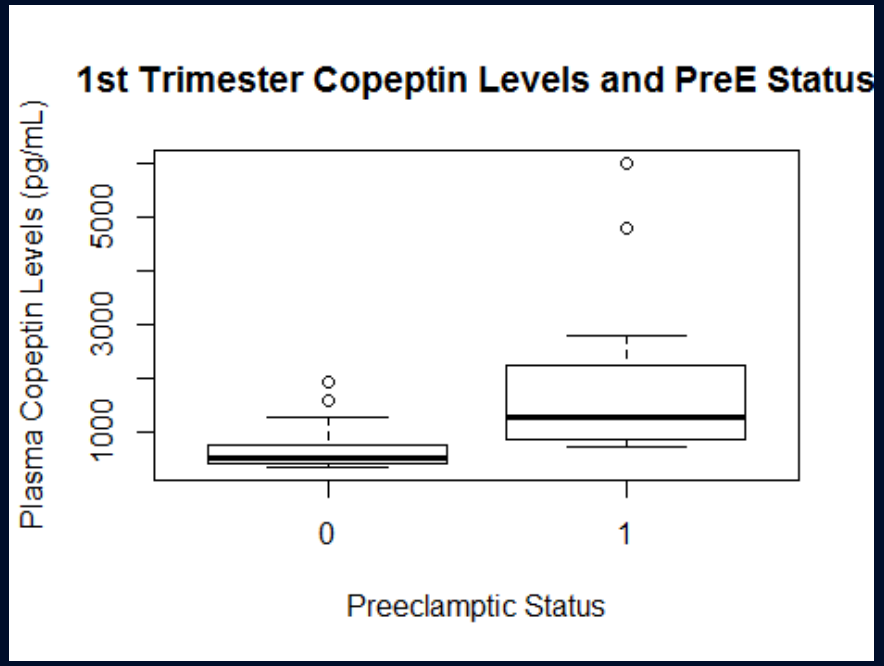
Data

- Cohort of 104 women (Preeclamptic and nonpreeclamptic)
  - 68 Prognostic Variables
    - Univariate analysis
  - Success = Having Preeclampsia

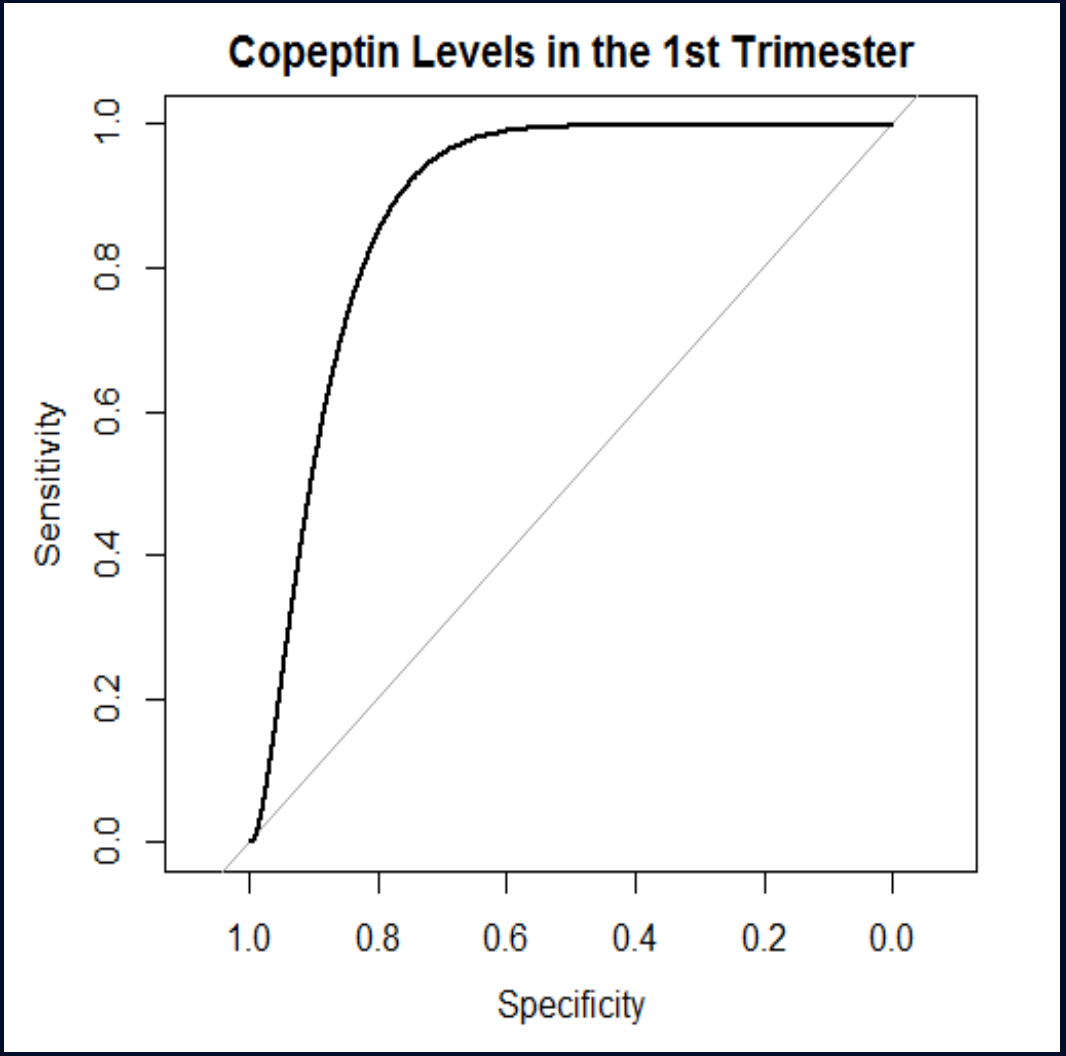
Results

- Variables not Significant:
  - BMI
  - Age
  - Multiple Gestation
  - Race
  - Diabetes
- Significant Variables:
  - Copeptin
  - History of Preeclampsia





Results



Logit(π) = -3.19 + 0.003*Copeptin

- As copeptin level increases by 100, then the probability of getting preeclampsia increases by ~2%

Copeptin Level: 811 pg/mL

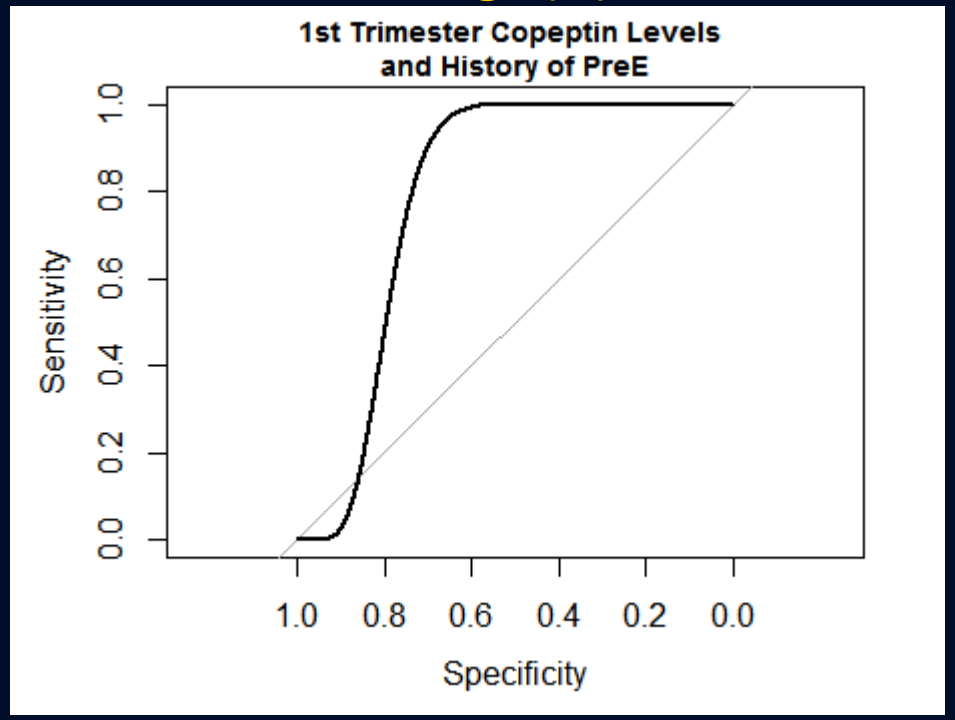
Specificity: 0.81

Sensitivity: 0.94

AUC: 0.90

Results

Logit(π) = -4.21 + 0.005*Copeptin – 3.23*History

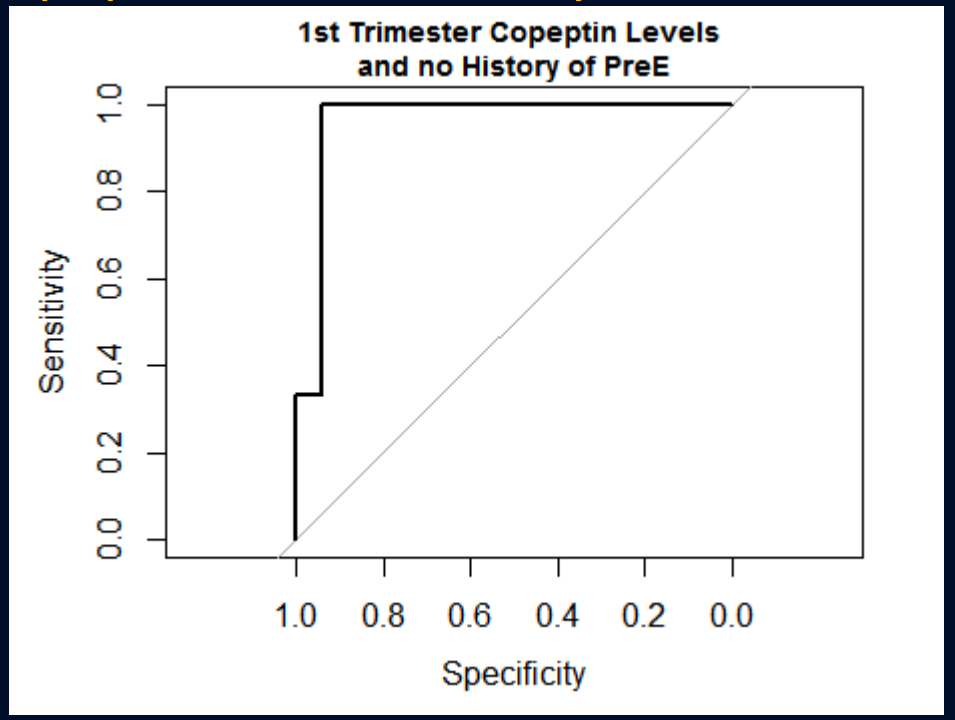


With History of Preeclampsia:

As copeptin level increases by 100, then the probability of preeclampsia increases by 0.06%

AUC: 0.85

Copeptin Level with History: 1138 pg/mL



Without History of Preeclampsia:

As copeptin level increases by 100, then the probability of preeclampsia increases by 3%

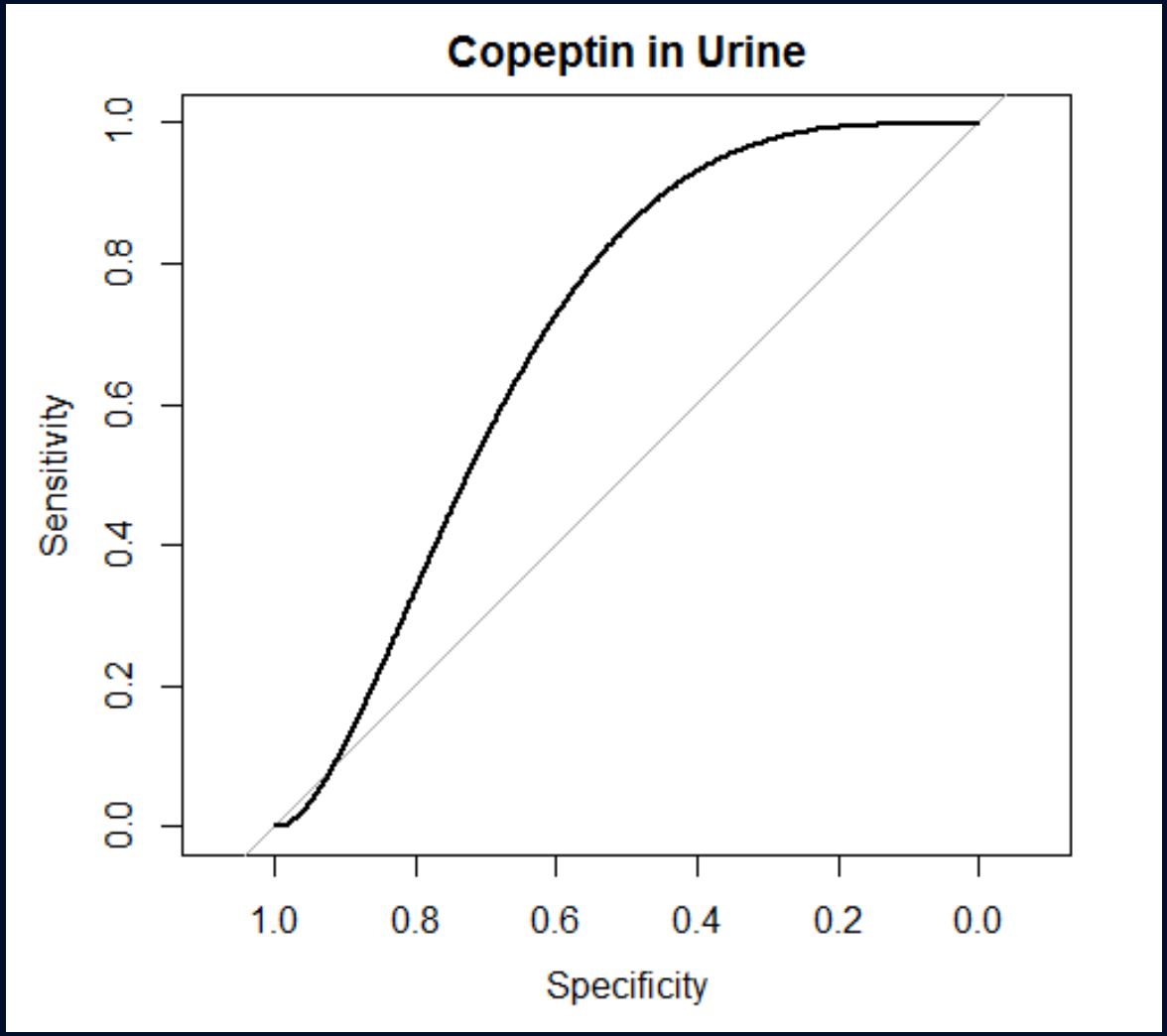
AUC: 0.963

Copeptin Level without History: 684 pg/mL

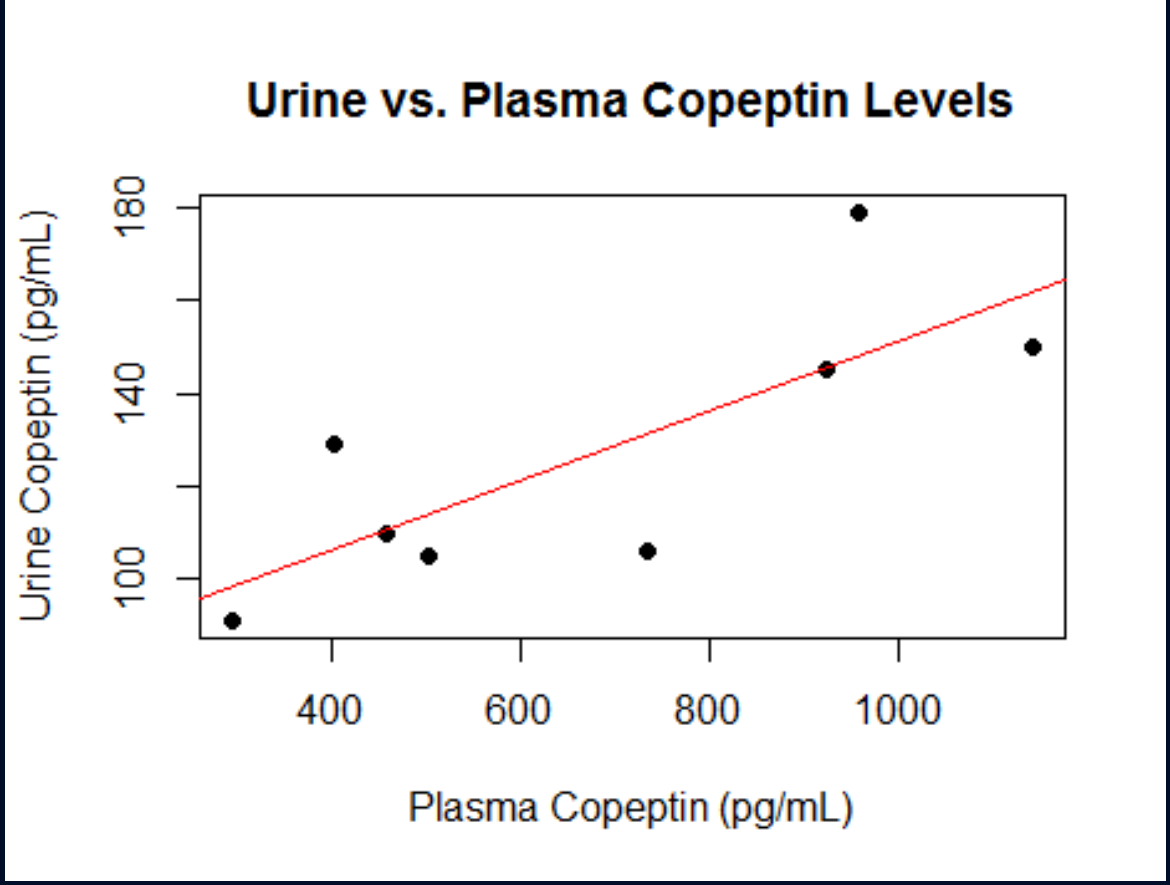
Data

- Cohort of 8 women (Preeclamptic and nonpreeclamptic)
  - Urine and plasma copeptin levels
  - Interested in finding relationship between Plasma and Urine Copeptin

Results


Copeptin in Urine
Sensitivity
0.0
0.2
0.4
0.6
0.8
1.0
1.0
0.8
0.6
0.4
0.2
0.0
Specificity

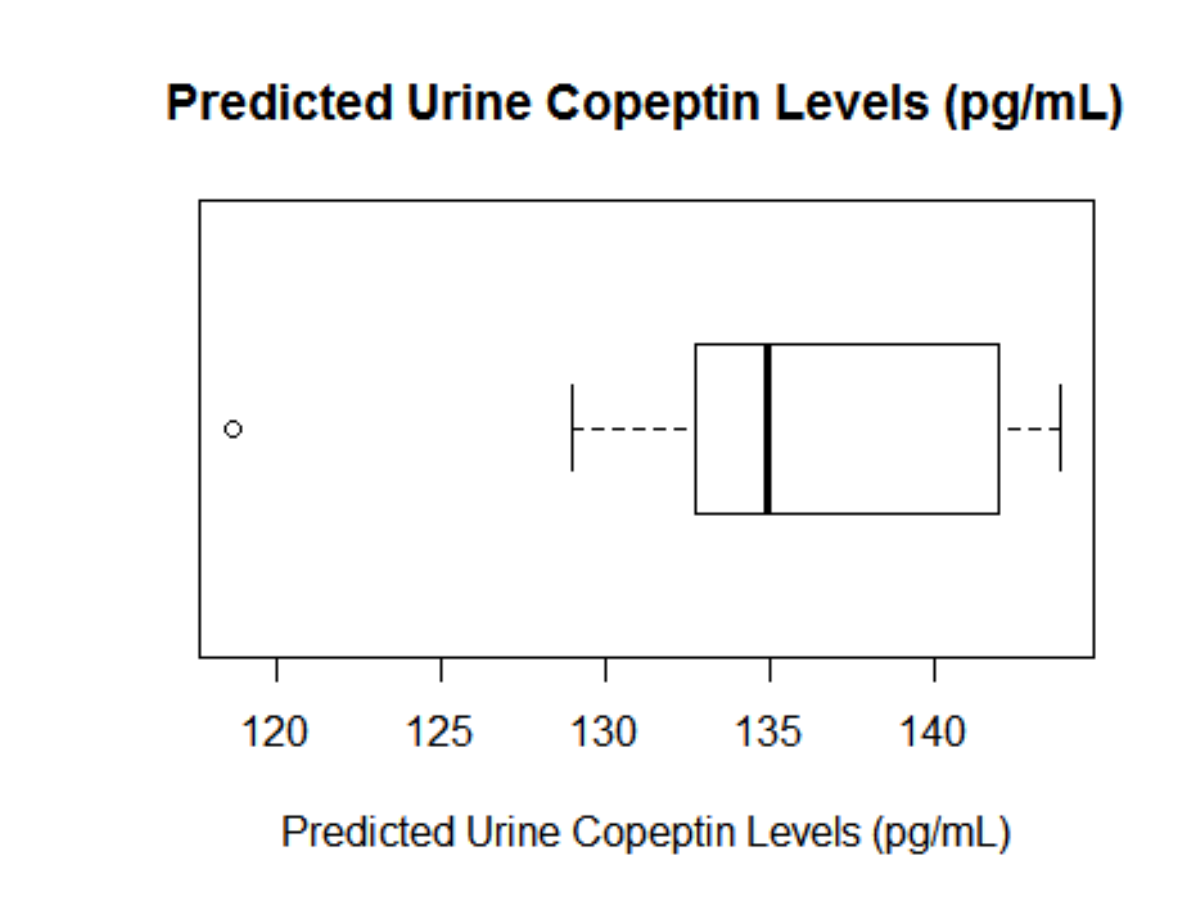
Results



Urine Copeptin= 76.2 + 0.07*Plasma Copeptin

t_7=3.041; p=0.0228; R-sq=0.6065

Results



Monte Carlo simulation

Median = 134.9 pg/mL

Mean= 134.8 pg/mL

Discussion/Conclusion

- Conclusions
  - History of PreE and 1st Trimester Copeptin levels
    - ~800 pg/mL
  - Urine Copeptin
    - ~130 pg/mL
    - Could be used as an at-home diagnostic test
- Limitations
  - Small sample size
  - Lack of diversity
  - Lack of studies involving plasma and urine copeptin

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