VIRONIX

Remote Preventive Care

Mathematical Problems in Industry workshop
June 29, 2024

Acknowledgement

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Special thanks to Dr. Taras Lakoba for continued support and hospitality throughout the MPI.

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Are my kidneys functioning properly?

MANRAJ SINGH	0080XE008608	MALE | 26	24-05-2024 13:38:18
Name	Accession No	Basic Info	Date of Test

Kidney Profile

This panel checks the health status of your kidneys. Kidneys filter waste from your blood and produce urine. Healthy kidneys also maintain proper dilution of your blood and maintain electrolyte balance of your body.

Normal (N) Low (L) Borderline (BL) High (H)

Profile Summary

Test Name	Result unit	Range
Blood Urea Nitrogen (BUN)	13 mg/dL	6-20
Serum Creatinine	0.96 mg/dL	0.7-1.2
BUN : Creatinine ratio	13.54	5-15
Uric Acid	**7.2** mg/dL	3.4-7

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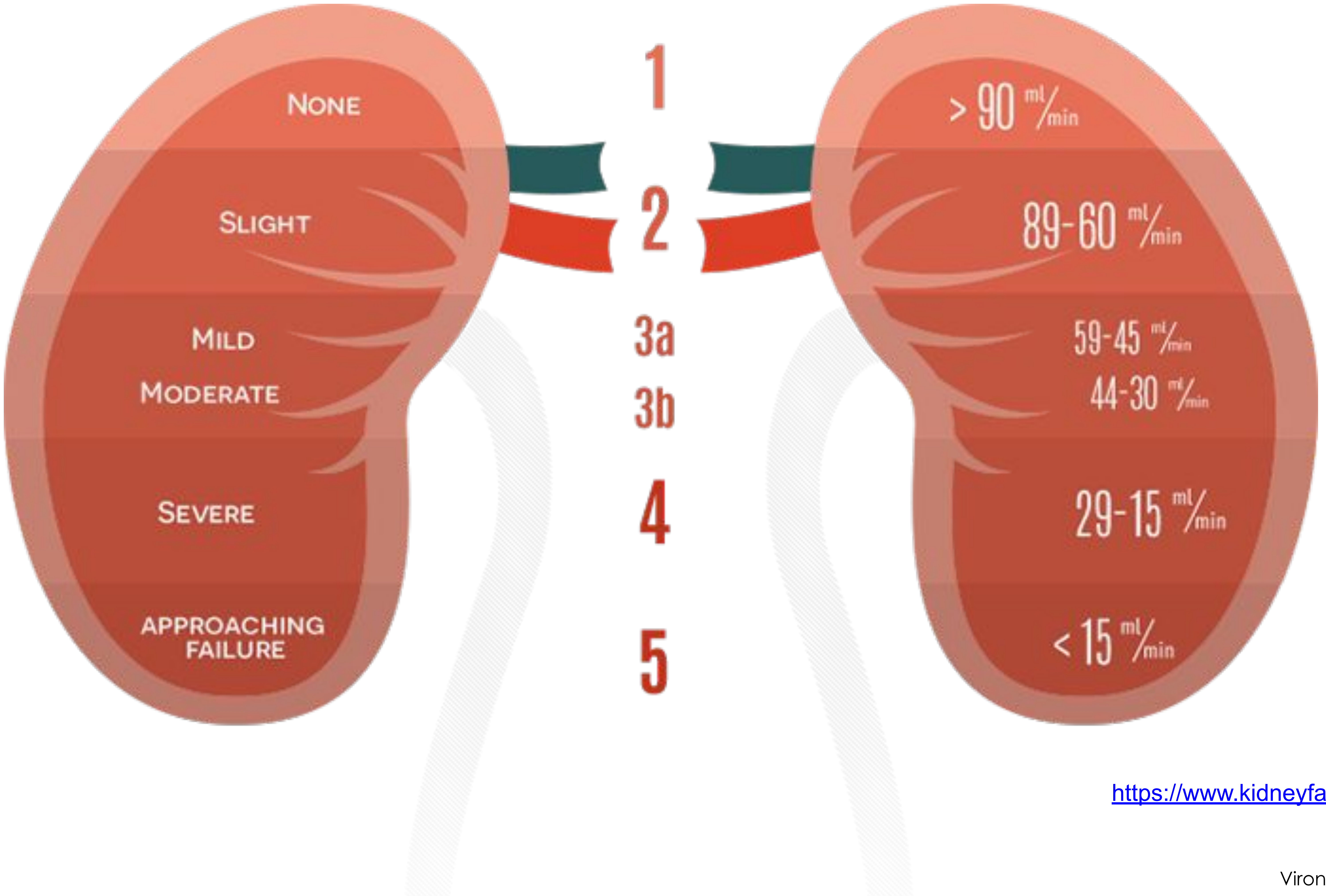
Chronic Kidney Disease (CKD)



https://www.kidneyfailurerisk.co.uk/

Why understand CKD progression?

- 2021: 15% of adults in the US – an estimated 37 million Americans (more than 1 in 7 people) have CKD.

- 2020: Nearly 808,000 people in the United States are living with ESKD, also known as end-stage renal disease (ESRD), with 69% on dialysis and 31% with a kidney transplant.

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Medicare Spending:

- 2020: Medicare spending for beneficiaries with CKD (not including ESKD) ages 66 or older exceeded $75 billion in 2020, representing 25.2% of Medicare spending in this age group.

- Medicare-related spending for beneficiaries with ESKD totaled $50.8 billion in 2020.

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Estimated Glomerular Filtration Rate (eGFR):

- Age
- Gender (K, α)
- Serum Creatinine (Scr)

$$eGFR = 142 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.200} \times 0.9938^{Age} \times 1.012$$

Manraj eGFR = 111.8 > 90!

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Predictive Modelling:

Am I getting sicker?

Do I need to get treatment?

How did I end up here?

Kidney Failure Risk Equations (KFRE):

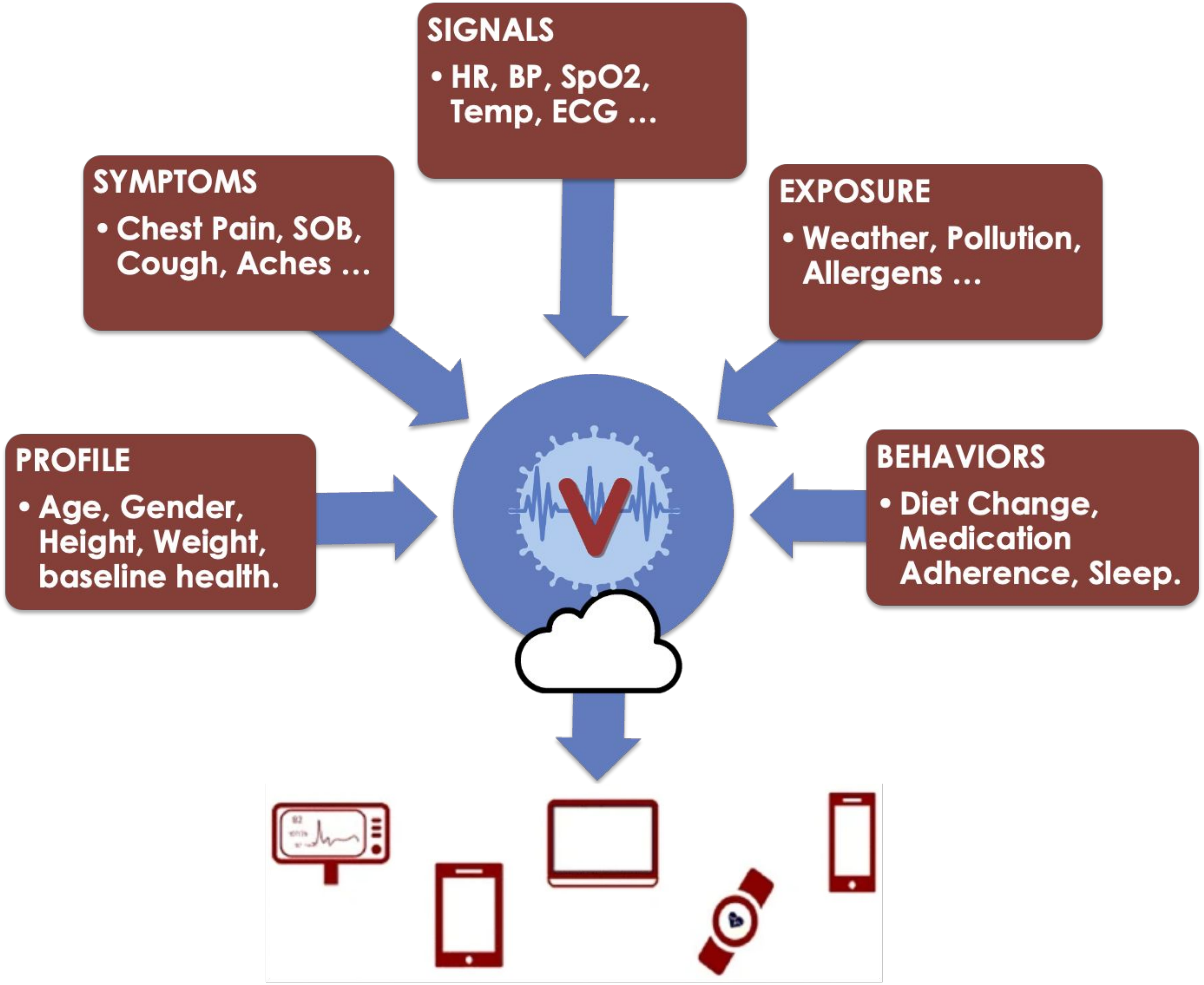
- Age
- Gender (K, α)
- eGFR
- Albumine/Creatinine

KFRE-4

- Serum Bicarbonate
- Serum Albumin
- Serum Phosphorus
- Serum Calcium

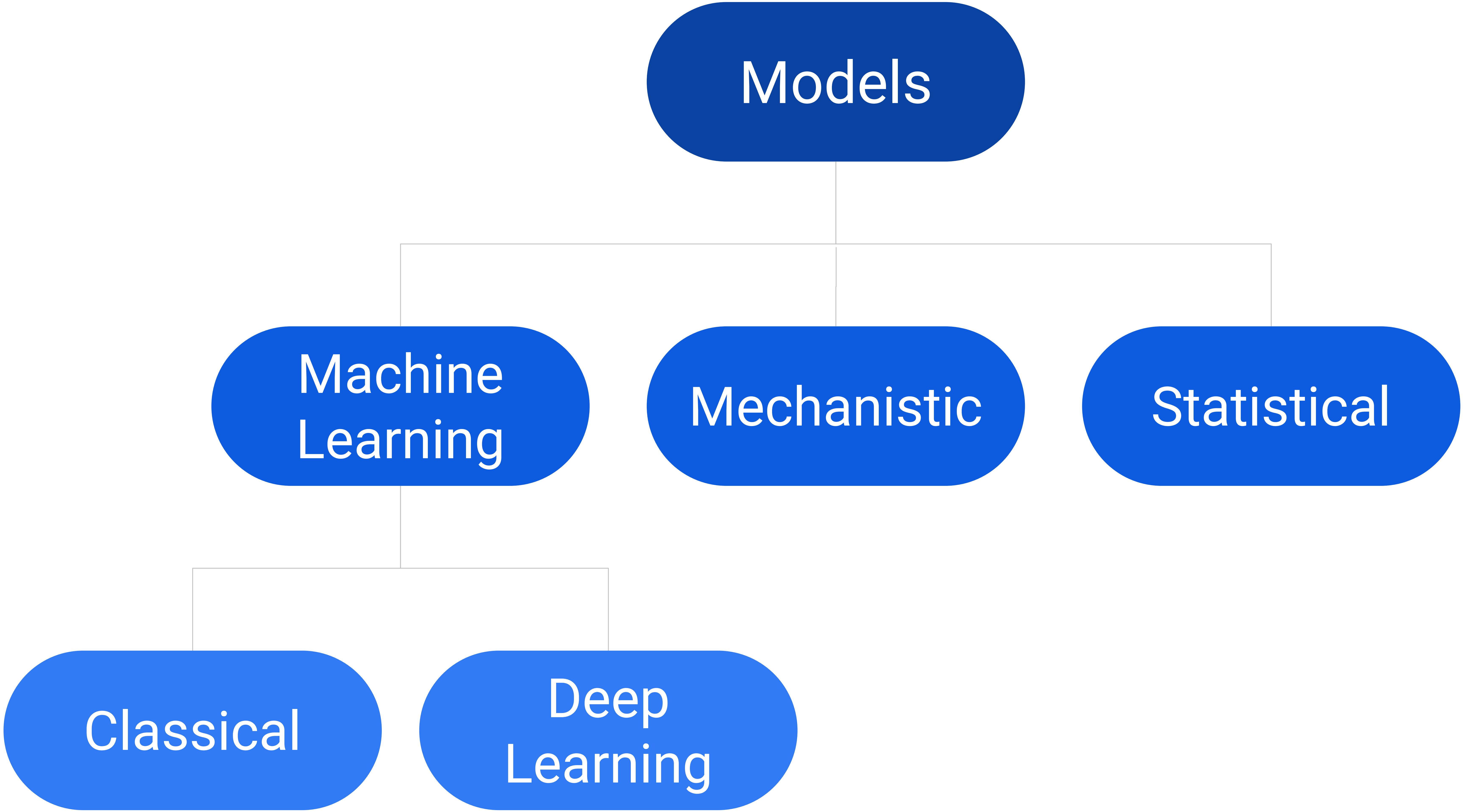
KFRE-8

The Solution: Vironix AI APIs



CKD stage progression with time

Predictive Modelling (Models):



Predictive Modelling (Data):

Literature review:

National Health and Nutrition Examination Survey (NHANES): Major program of the National Center for Health Statistics (NCHS). NCHS is part of the Centers for Disease Control and Prevention (CDC) and has the responsibility for producing vital and health statistics for the Nation.

UK biobank: De-identified data from half a million UK Biobank participants. Also contains genotype data.

Chronic Renal Insufficiency Cohort (CRIC) Study: Longitudinal dataset provided by National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) with 3288 patients.

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Group 2: Data Analysis – Datasets Introduction

I. Dataset 1: Patients' Profile
   - Demographics: Age, Gender, etc.
   - Disease History

II. Dataset 2: Observations
   - From Vironix platform
   - Body Mass, Blood Pressure, Heart Rate, and etc.

III. Dataset 3: Encounters
   - Doctor-visit records: Date, Type, and etc.

IV. Dataset 4: Questionnaire
   - Symptoms

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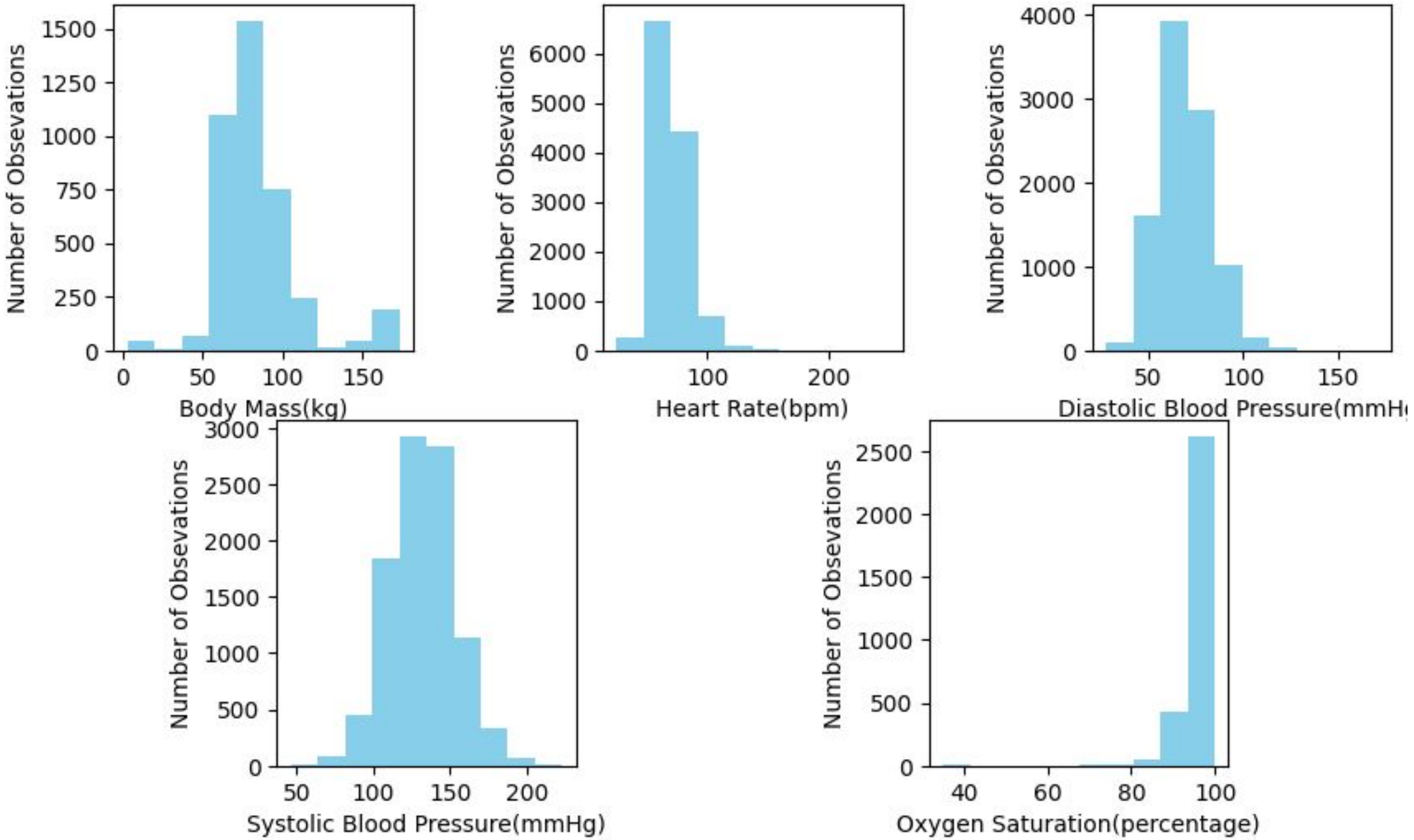
Group 2: Data Analysis – Observations



- Frequency of patient vitals observations uploaded to Vironix platform

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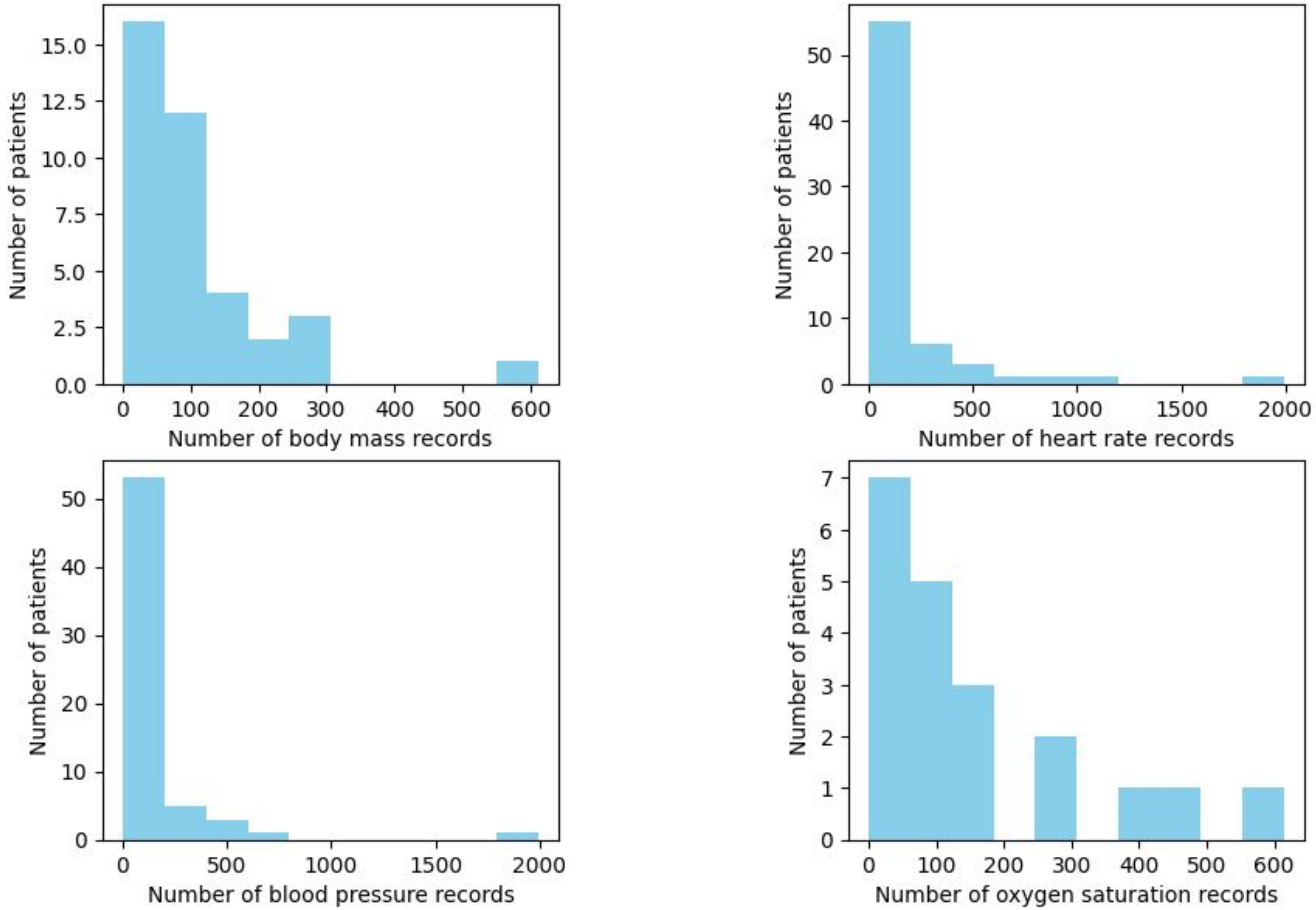
Group 2: Data Analysis – Observations



- Frequency of patient vitals uploaded to Vironix platform

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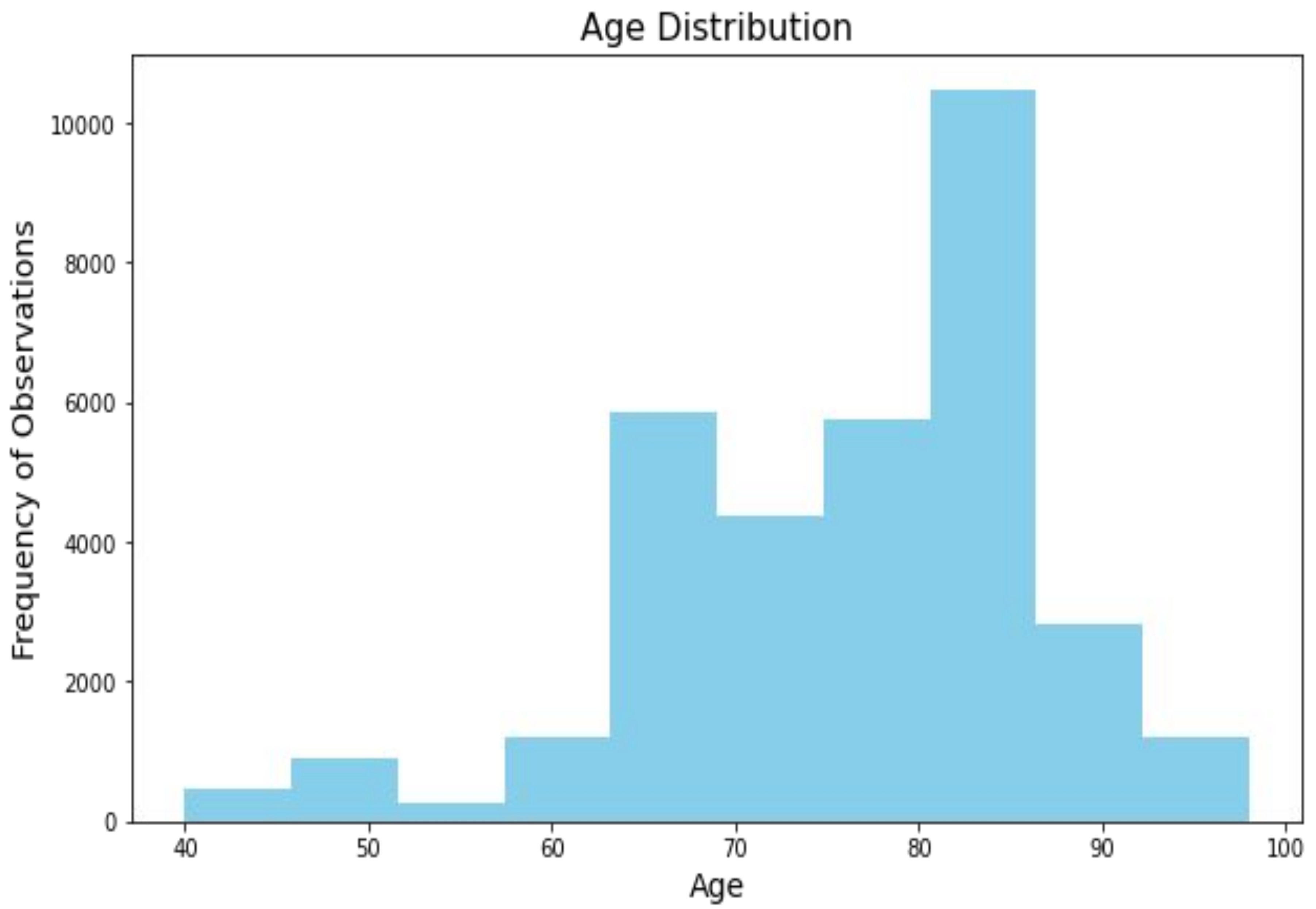
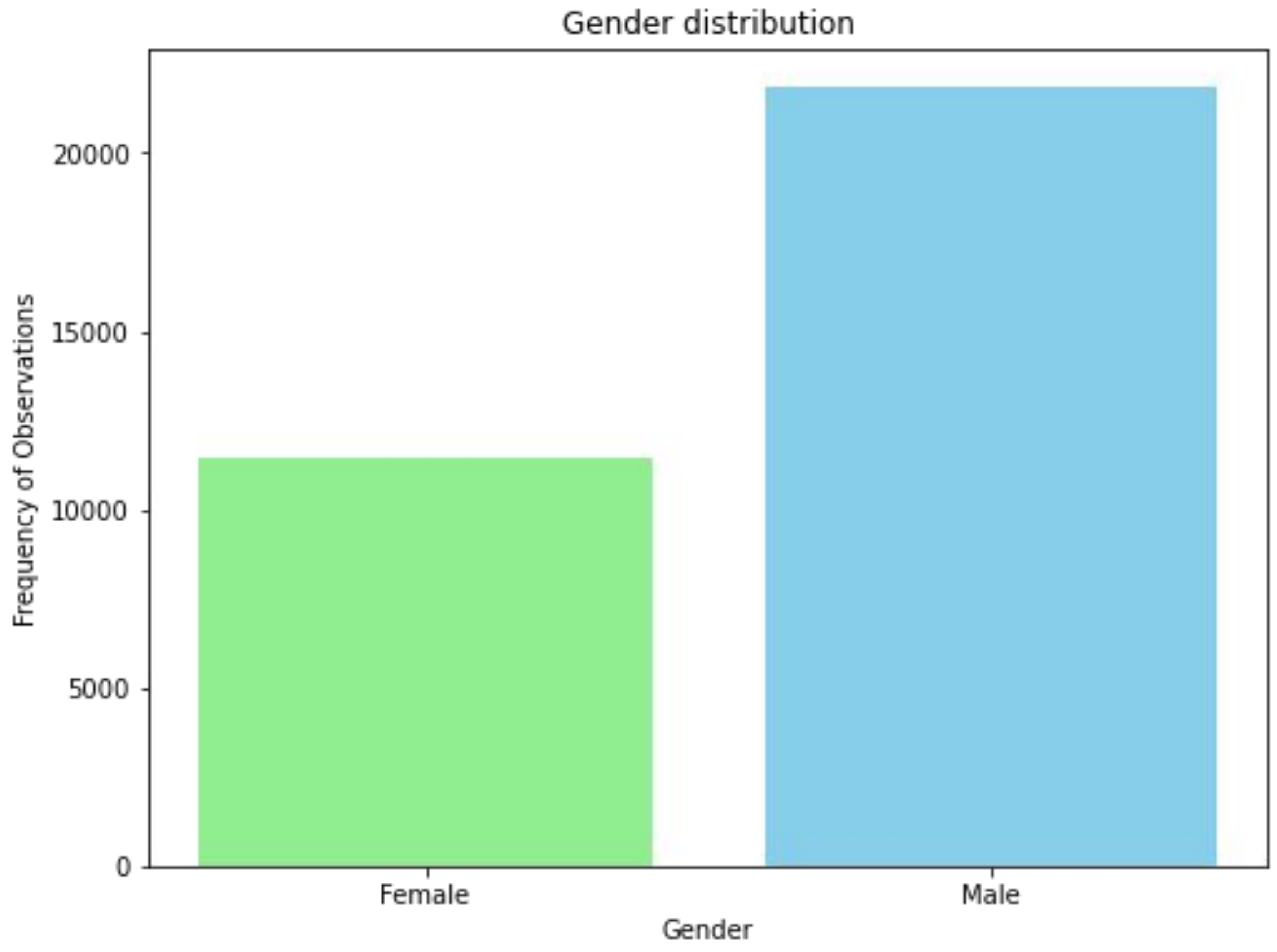
Group 2: Data Analysis – Observations with Demographics





- 75-85 age group has more observations
- Males have more observations than females

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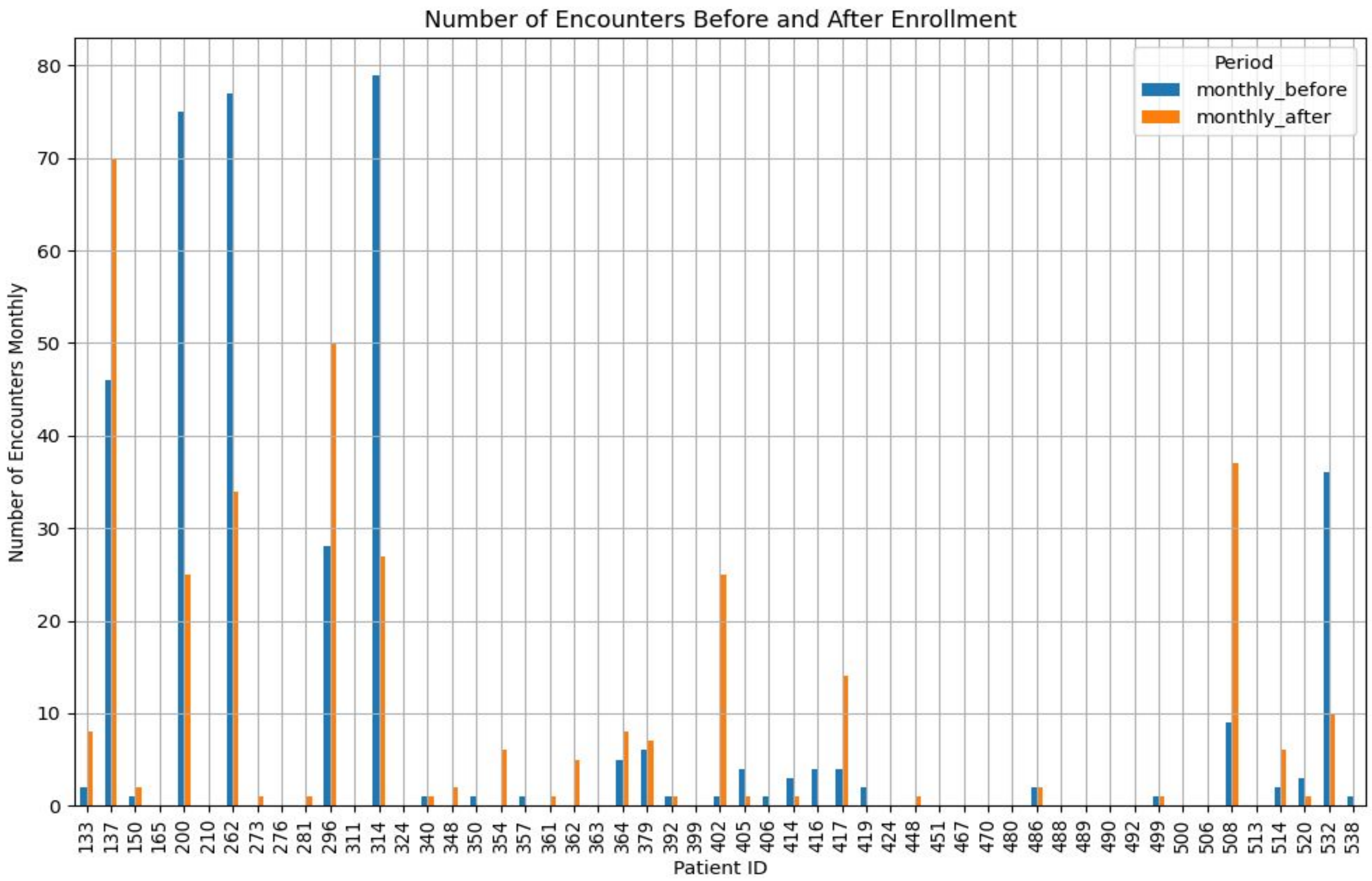
Group 2: Data Analysis – Encounter according to enrollment



- Can we see a consistent difference in medical encounter frequency before and after engaging the Vironix platform?

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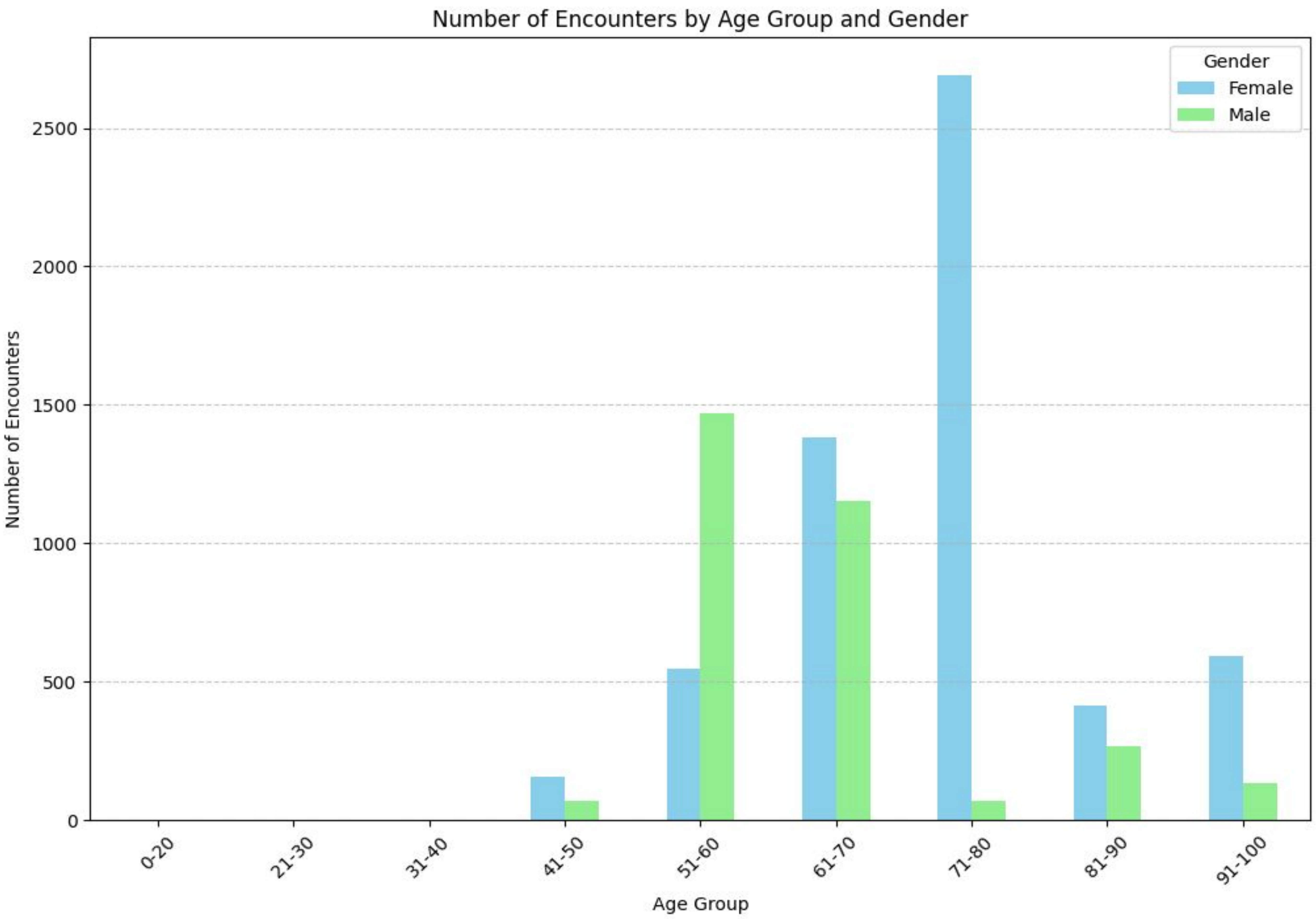
Group 2: Data Analysis – Encounters with Demographics



- Males and Females have different peaks

- Females of age group 71-80 have more encounters

- Males of age group 61-70 have more encounters

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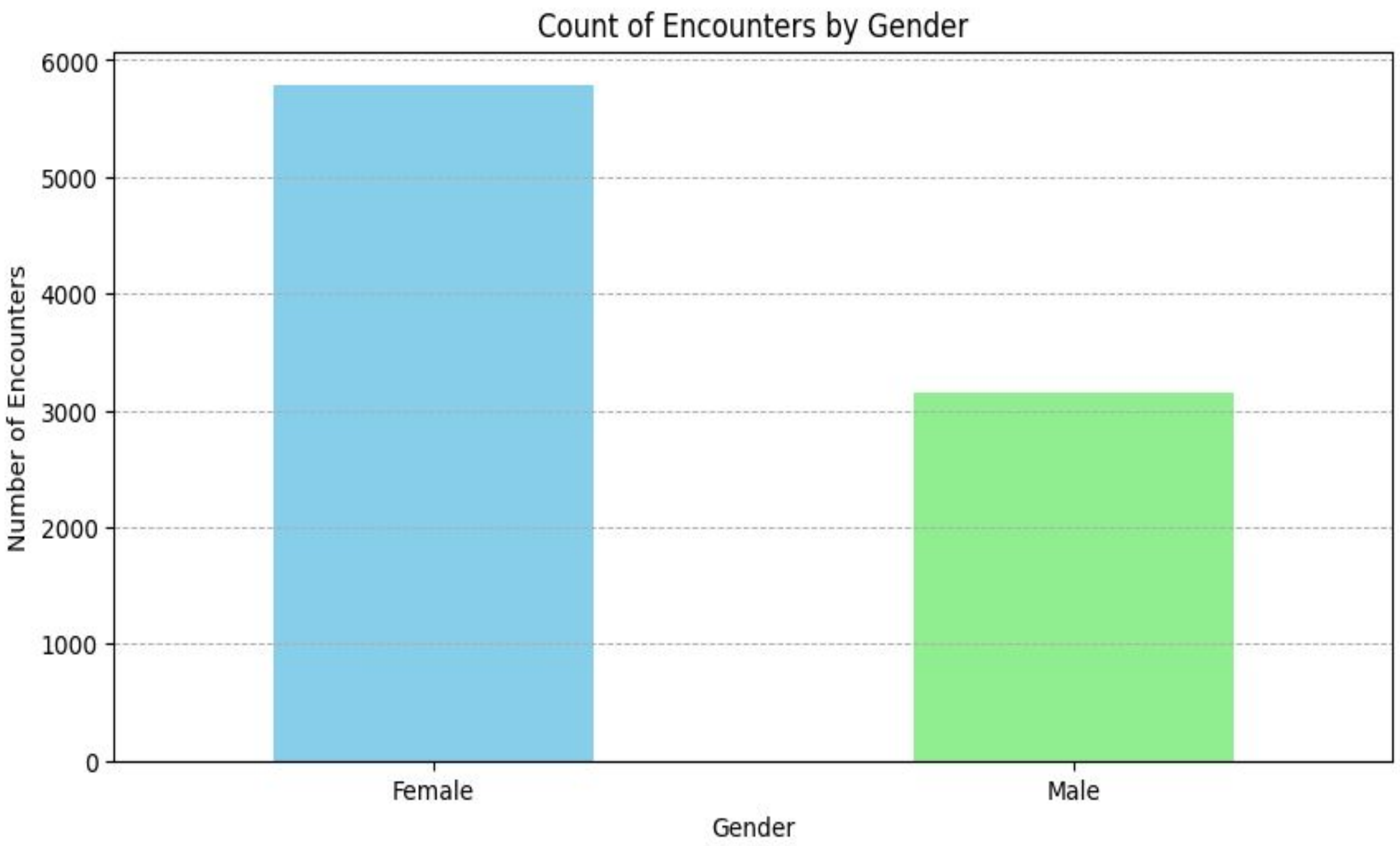
Group 2: Data Analysis – Count of Encounters by Gender



- Females have more encounters with the clinical stuff than males
-

	encounter_count	average_age
gender		
Female	5786	74.185620
Male	3158	61.428119

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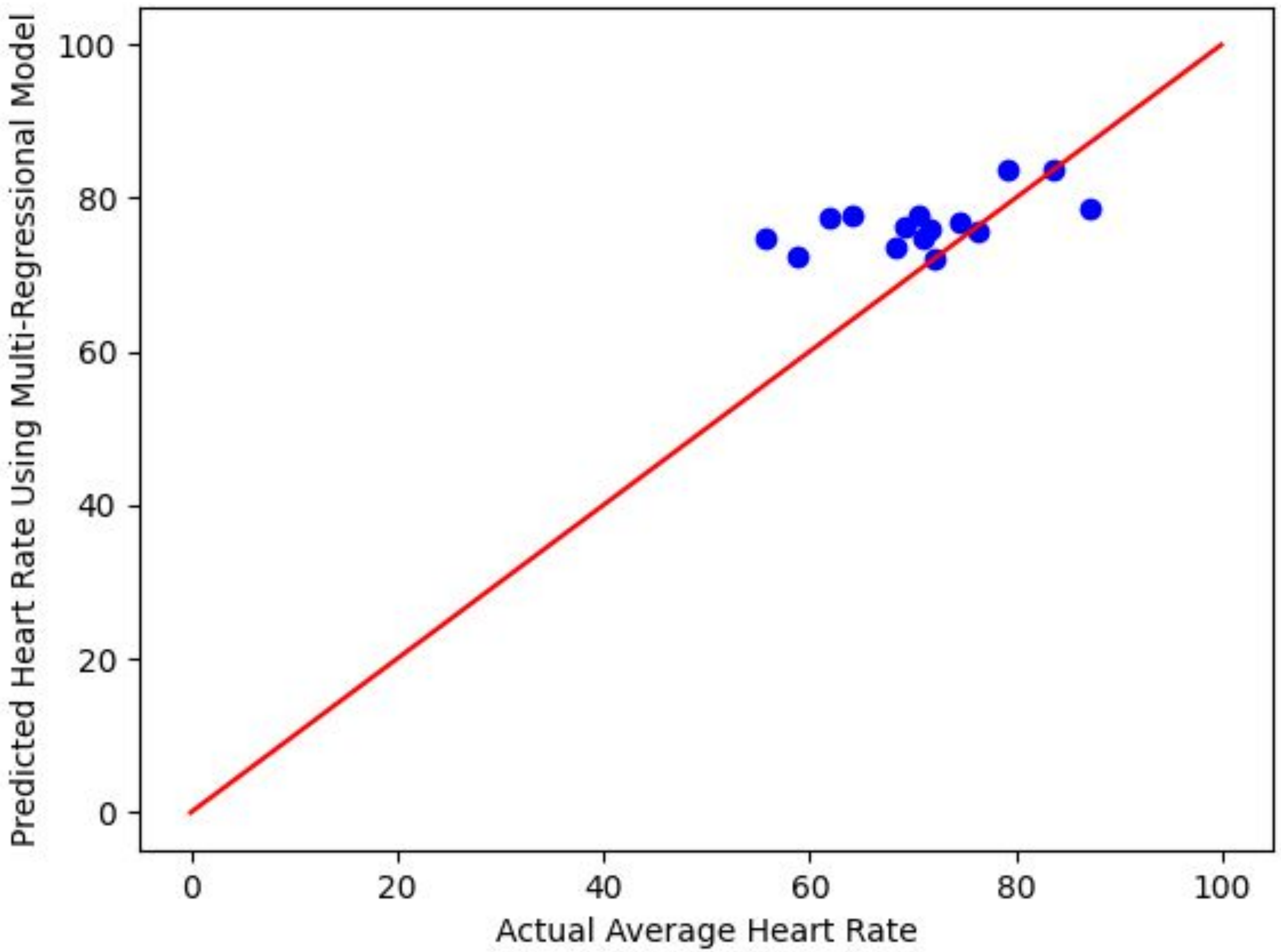
Group 2: Data Analysis – Multi Regression Model Using Supervised Machine Learning



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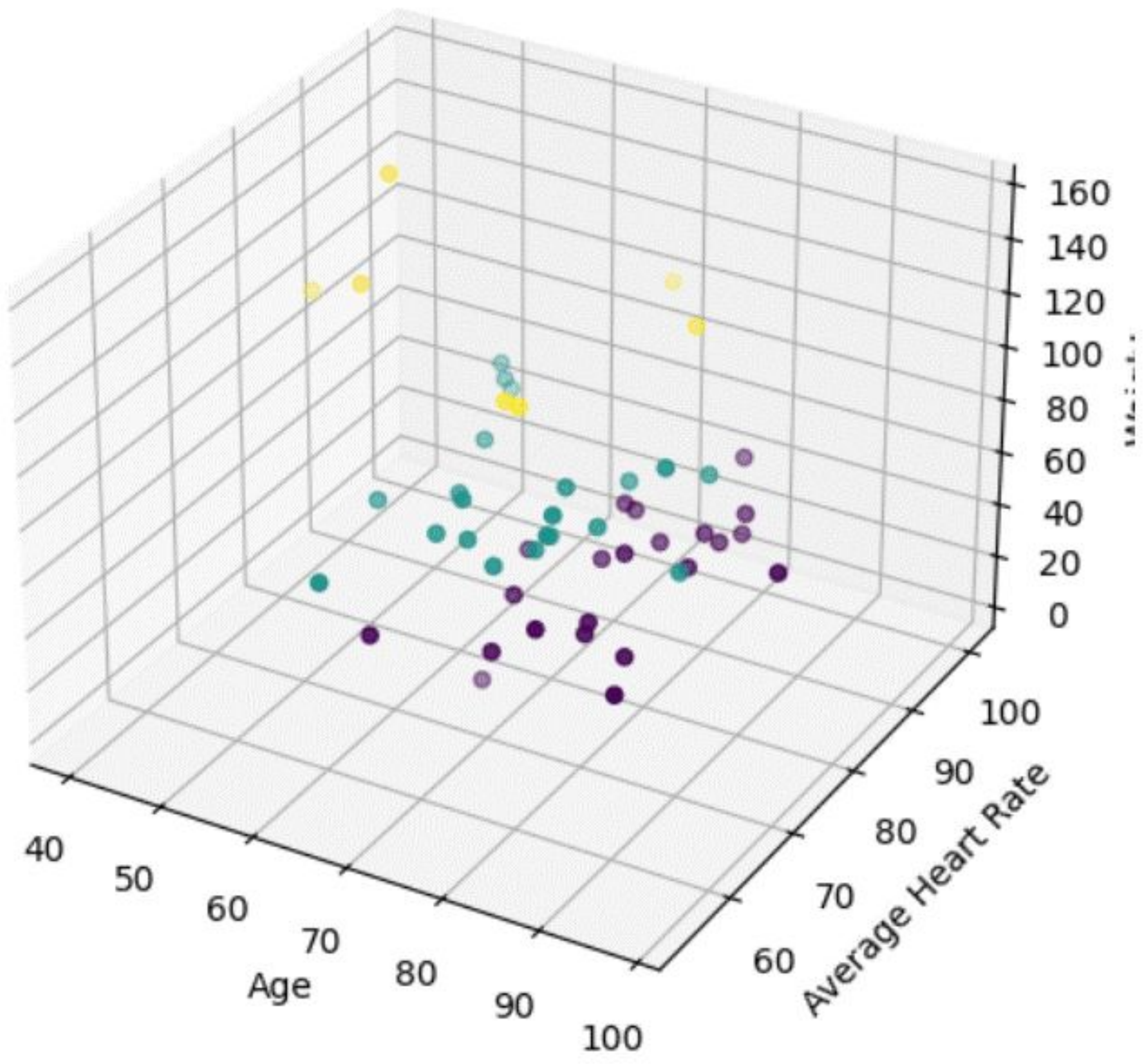
Group 2: Data Analysis – Clustering Algorithm (K-Means Clustering)



- Unsupervised machine learning K-means clustering algorithm
- Age, Avg. Heart Rate and Weight.
- Overweight and high average heart rate (Yellow): be monitored frequently
- High heart rate (Green): be monitored moderately increased frequency
- Older with medium to high average heart rate (Purple): be monitored with moderately increased frequency

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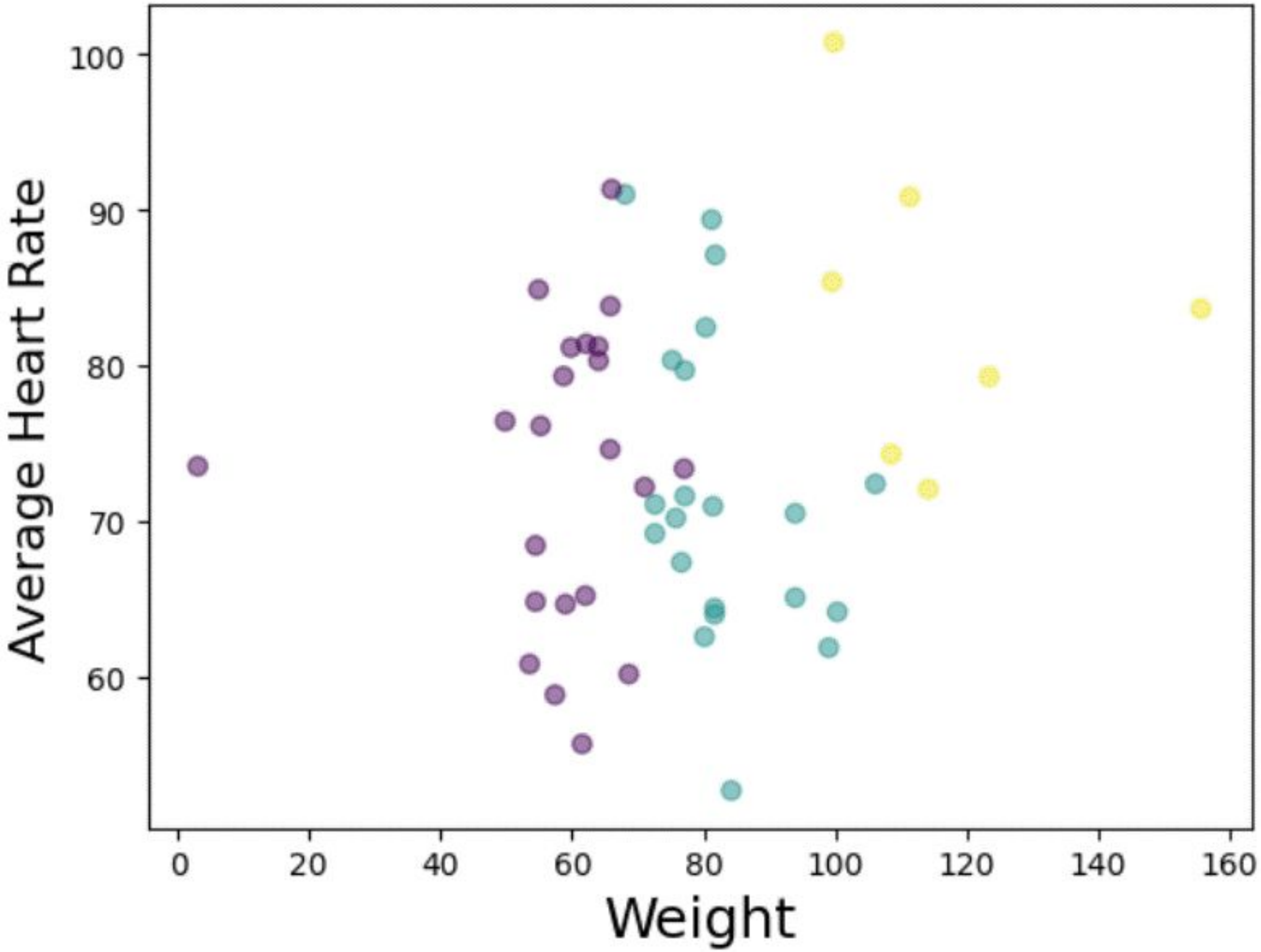
Group 2: Data Analysis – Clustering Algorithm (K-Means Clustering)



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Modeling Degradation of Kidney Function

- Data:
  - Chronic Kidney Disease Research of Outcomes in Treatment and Epidemiology (CKD-ROUTE)
  - The dataset consists of **1,138 patients** with **51 variables**

- Goal:
  - Predict patient's kidney function
  - Alert patient and clinicians if patient will rapidly deteriorate
  - Done by predicting **eGFR**: a measure of kidney filtration rate

- A variety of modelling approaches taken:
  - Gaussian process regression
  - Deep neural network
  - Minimal decay model
  - Multistage decay model

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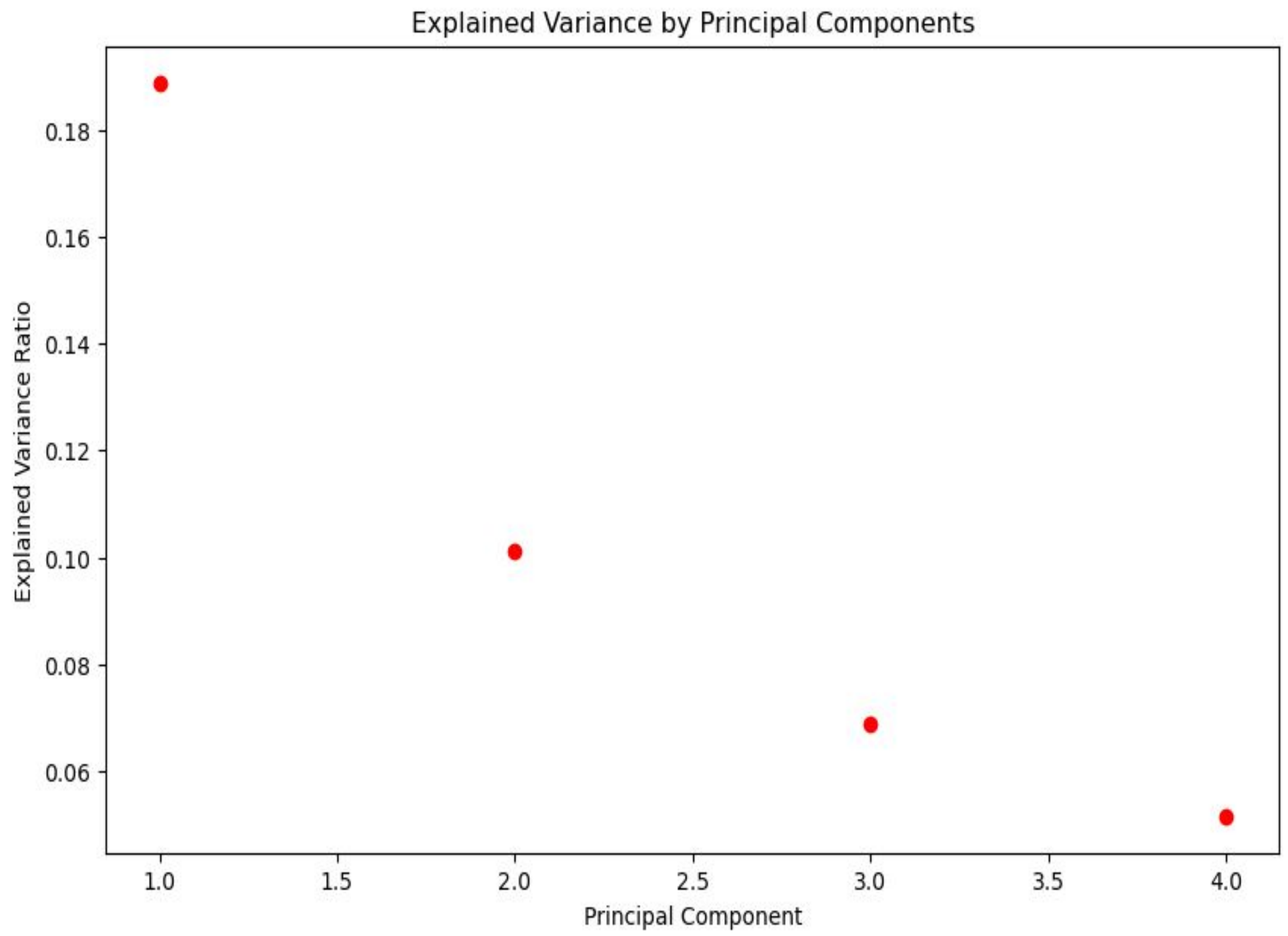
Principal Component Analysis

	PC1	PC2	PC3	PC4
age	-0.059105	-0.158466	-0.057784	0.014922
SBP	-0.021517	0.090176	-0.090455	-0.013455
BMI	-0.046206	0.025776	-0.164993	0.021794
Hb	0.142398	0.063381	-0.137592	-0.085289
Alb	0.081716	-0.161591	0.045123	-0.169917
Cr	-0.225580	-0.059740	0.169716	-0.077296
UPCR	-0.074825	0.236259	-0.051573	0.203696
eGFR(0M)	0.262532	0.129977	-0.087609	0.040105
eGFR(6M)	0.269172	0.106740	-0.092514	0.014963
eGFR(12M)	0.270752	0.097607	-0.083450	-0.011930
eGFR(18M)	0.271166	0.080181	-0.077024	0.011196
eGFR(24M)	0.272832	0.075660	-0.080702	-0.000095
eGFR(30M)	0.272994	0.061074	-0.072926	-0.008348
eGFR(36M)	0.270799	0.054922	-0.067294	0.007997
gender_1	-0.014376	-0.032961	-0.131780	-0.197872
gender_2	0.014376	0.032961	0.131780	0.197872
etiology of CKD_1	-0.111784	0.084156	-0.092029	0.243663
etiology of CKD_2	-0.010691	-0.205368	-0.125948	-0.149742
etiology of CKD_3	0.066982	0.209339	0.056768	-0.101371
etiology of CKD_4	0.057285	-0.039521	0.203549	0.059884



- The explained variance by each principal component is visualized in the scree plot

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Gaussian Process Regression

- A non-parametric, supervised, probabilistic model
  - Non-parametric: Allows for modeling arbitrary nonlinear functions
  - Supervised: Model is trained on inputs and expected outputs
  - Probabilistic: Model gives a confidence interval

- Two different measures for future kidney function were used:
  - eGFR 6 months from now
  - Deterioration rate over the next 36 months

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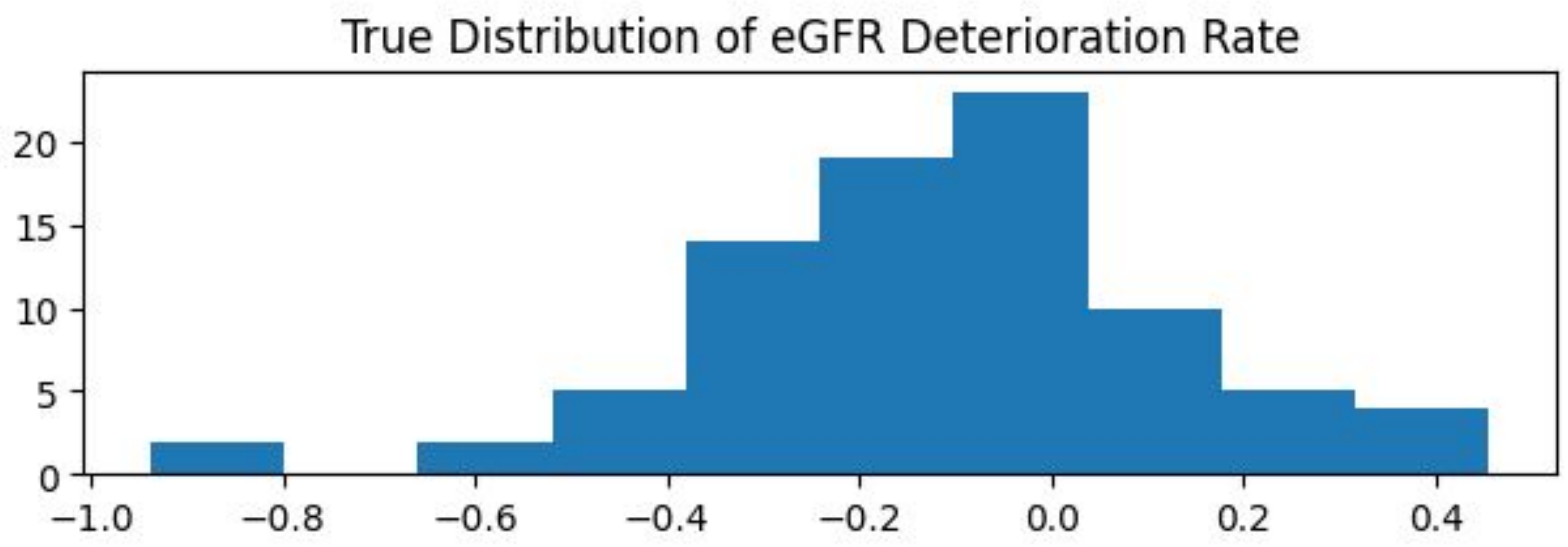
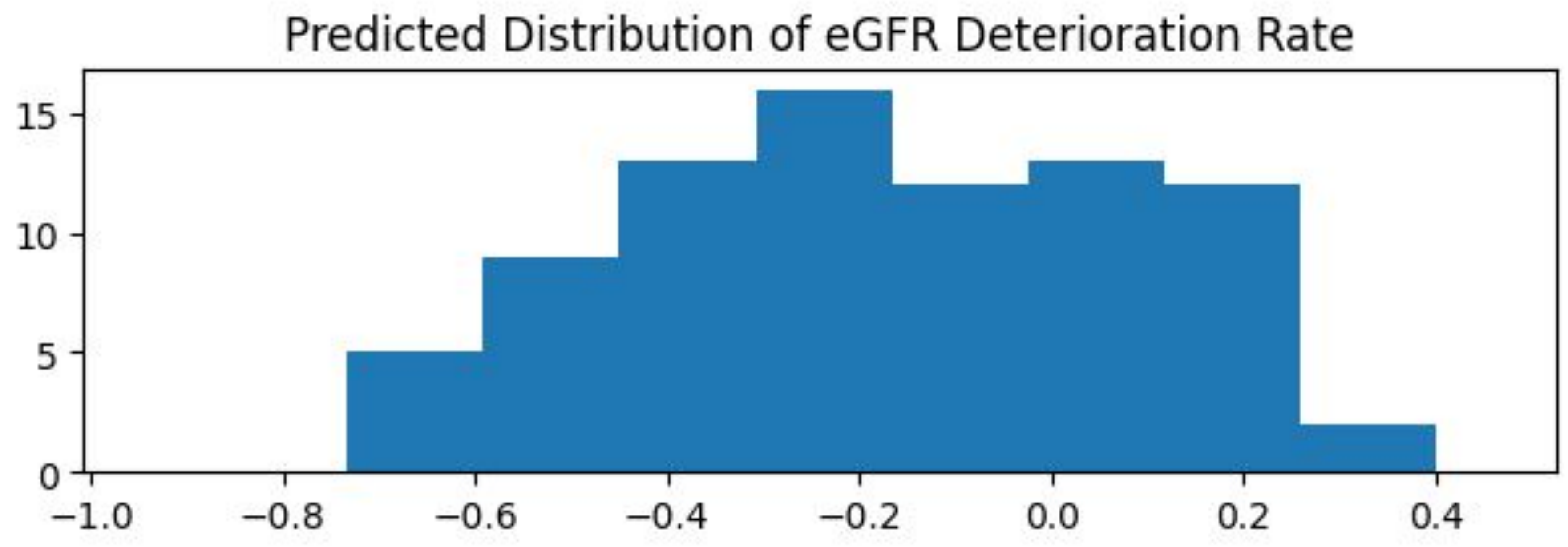
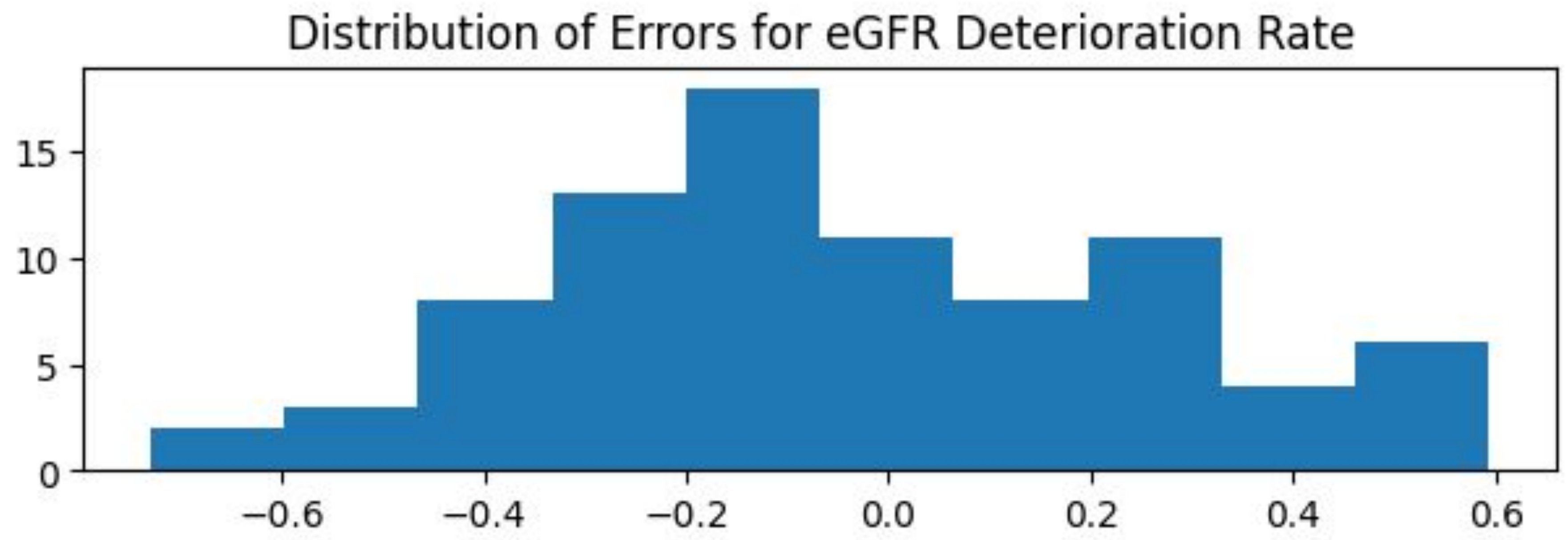
Gaussian Process Regression: Deterioration Rate







- Approximates the distribution of deteriorations fairly well
- Tends to lack sensitivity as a predictive tool
- Currently, it is fairly inaccurate

- Mean Squared Error: 0.247
- Average deterioration rate: -0.1 eGFR/Month
- Standard deviation: 0.34 eGFR/Month

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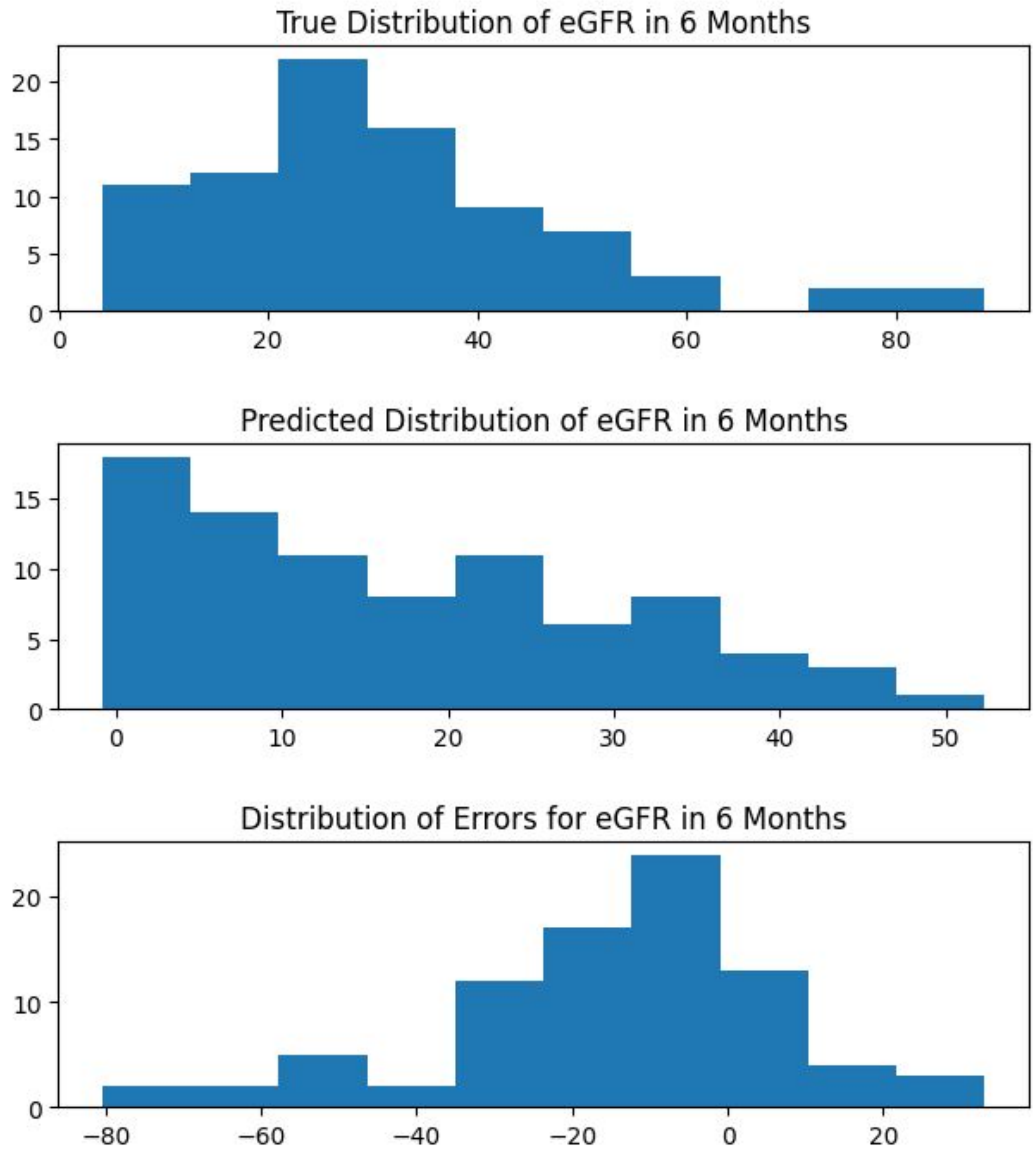
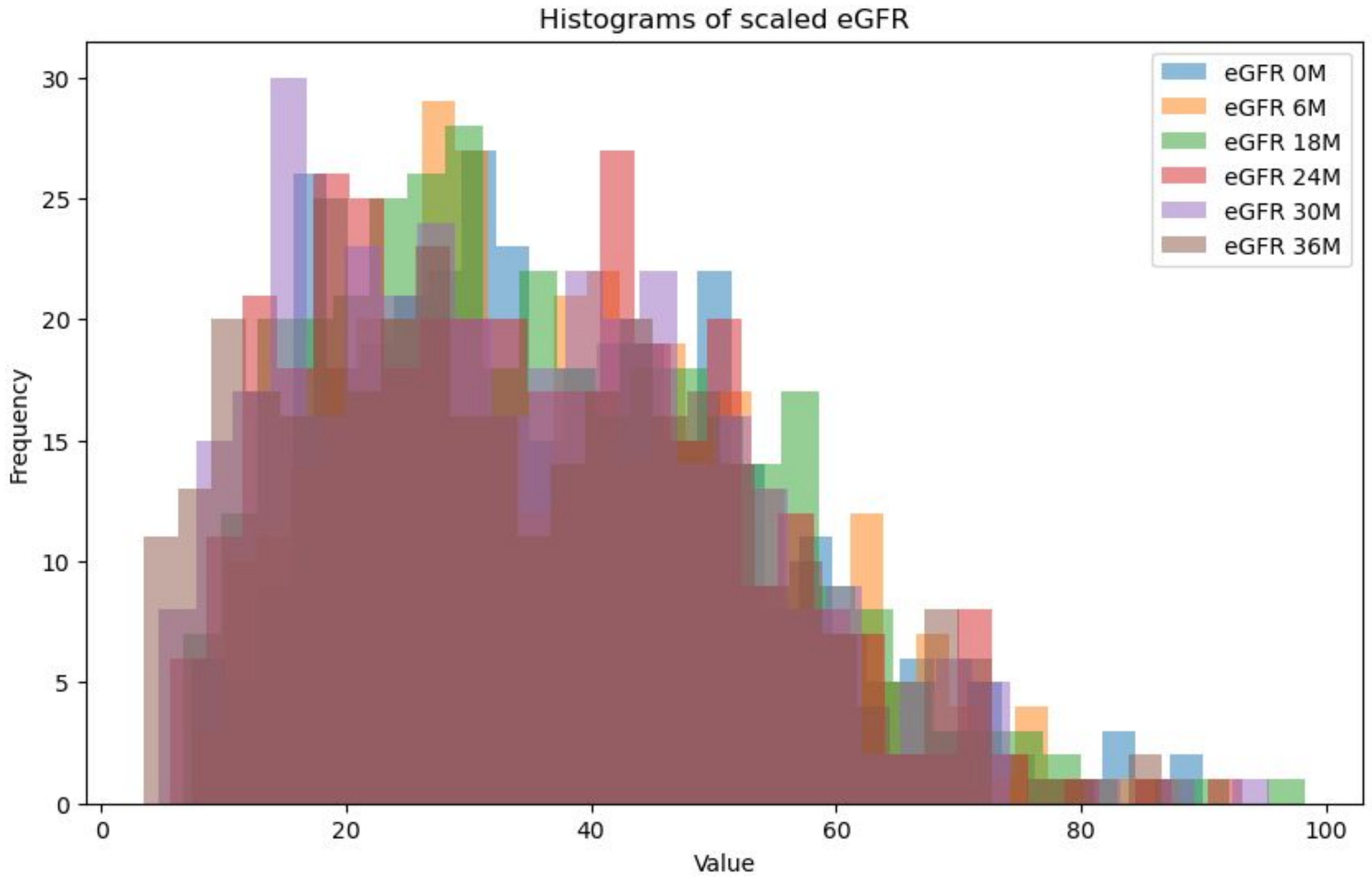
Gaussian Process Regression: eGFR in 6 Months



- Another fair approximation of the distribution
- Tends to lack specificity as a predictive tool
- Fairly inaccurate

- GPR gives fairly inaccurate results overall, but could be a decent result in the future

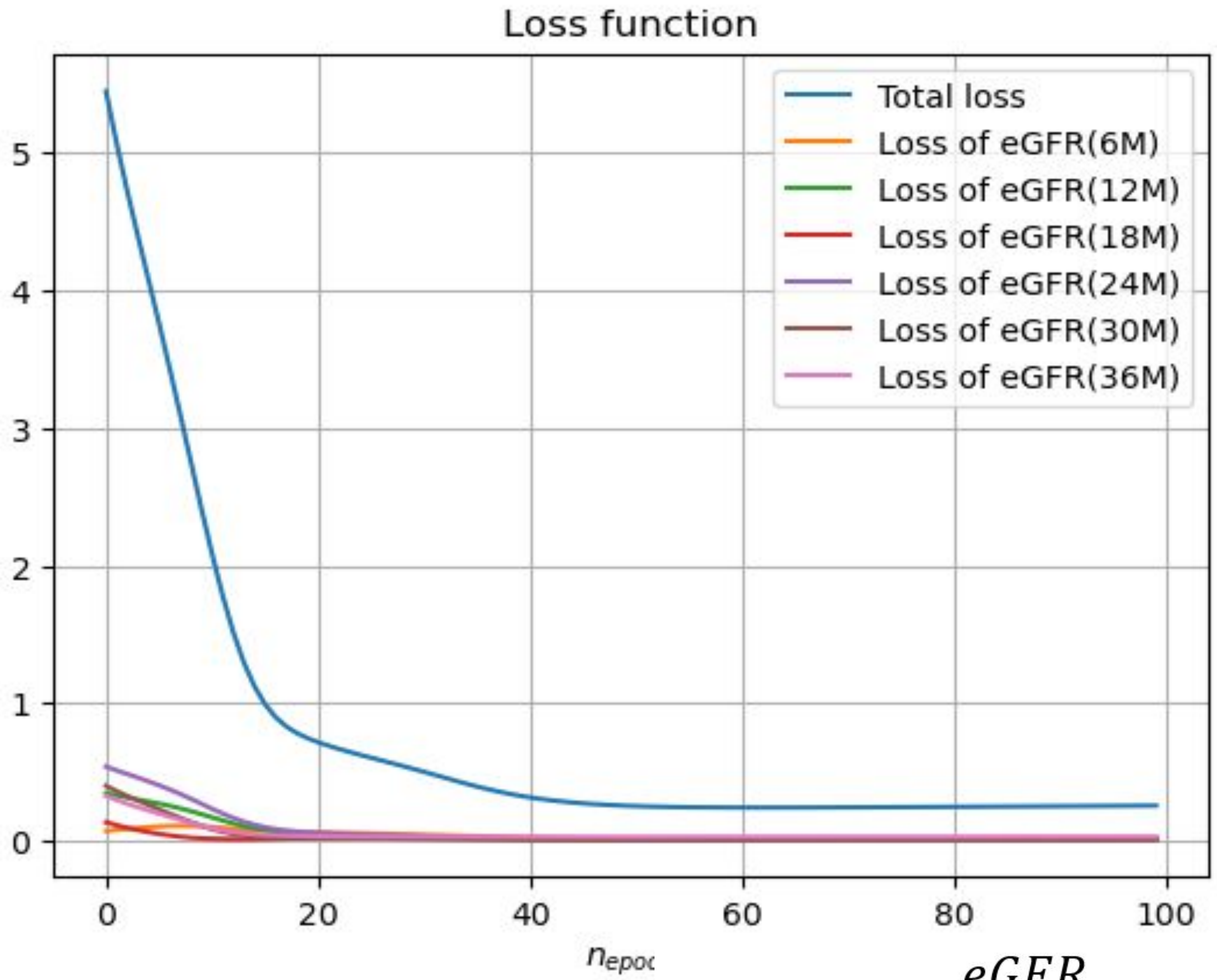
Deep Neural Network



Input: Age, Gender, SBP, BMI, proteinuria, eGFR(0M).

Output: eGFR(6M), eGFR(12M), eGFR(18M), eGFR(24M), eGFR(30M), eGFR(36M).

Network Architecture: fully connected, 3 layers (10 - 20 - 10 neurons), tanh activation function.



Use standardized eGFR: $\widehat{eGFR} = \dfrac{eGFR}{\text{mean}(eGFR)} - 1$

Data: 441 follow-up observations;
80% in train set, 20% in test set.

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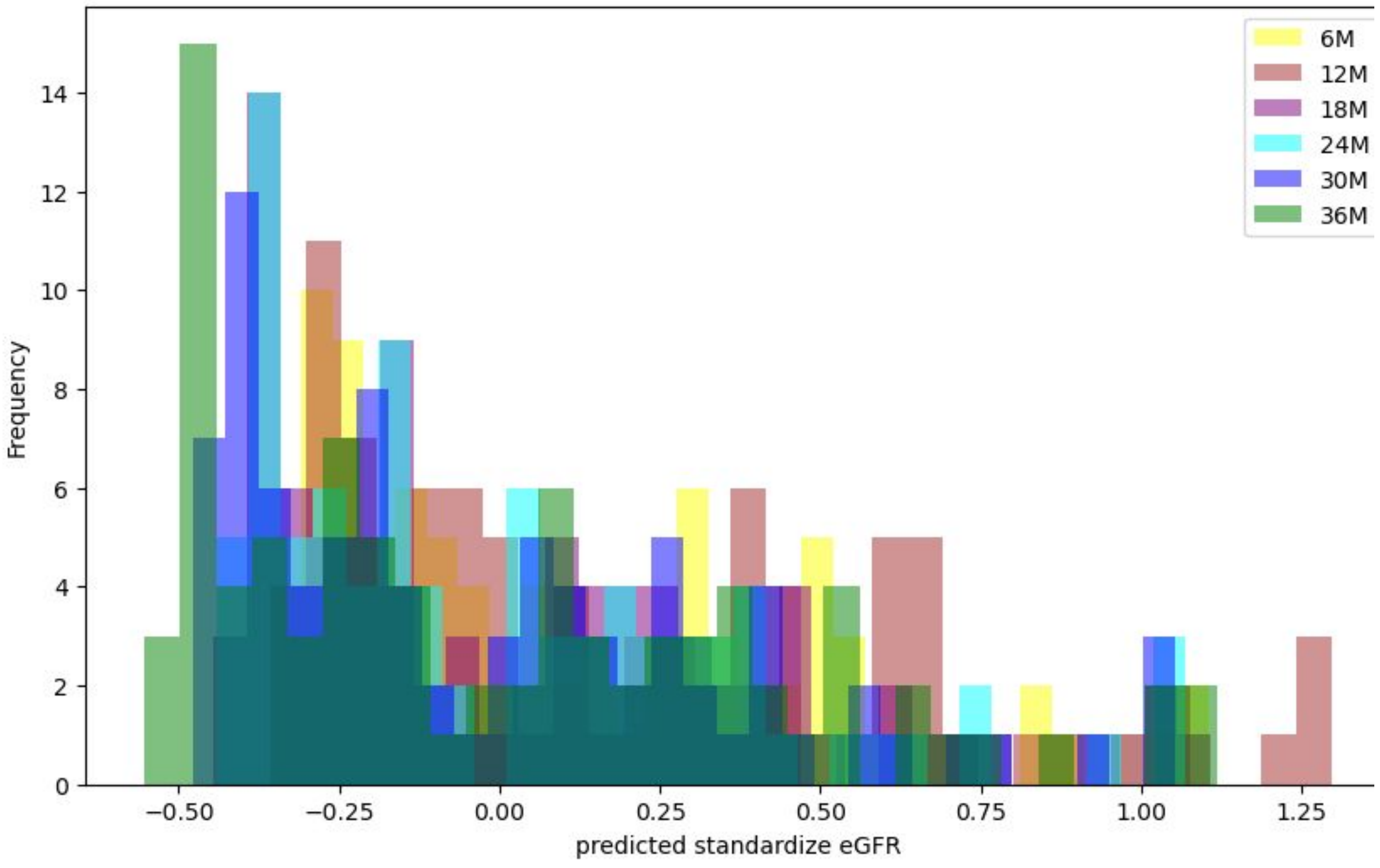
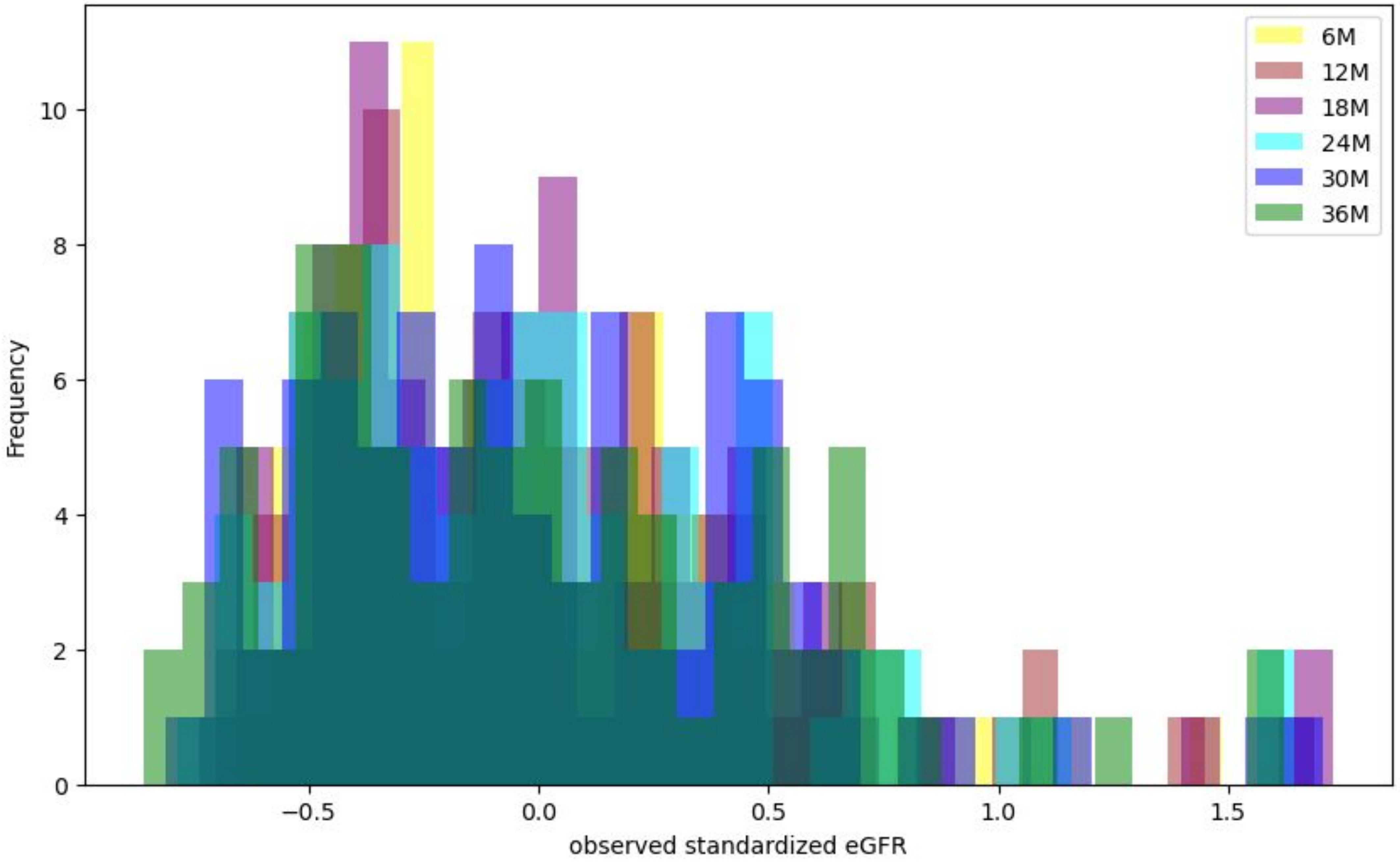
Deep Neural Network





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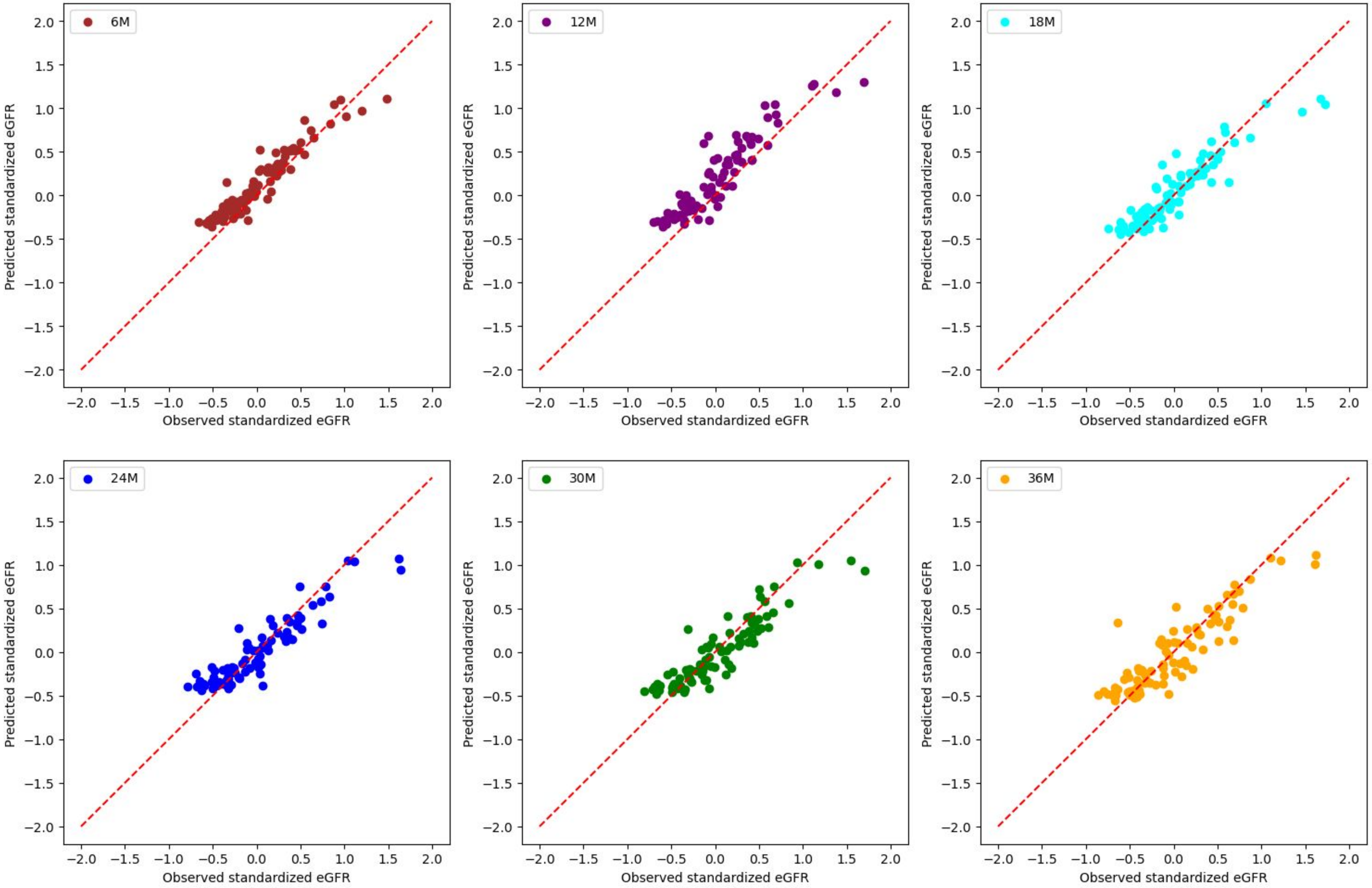
Deep Neural Network



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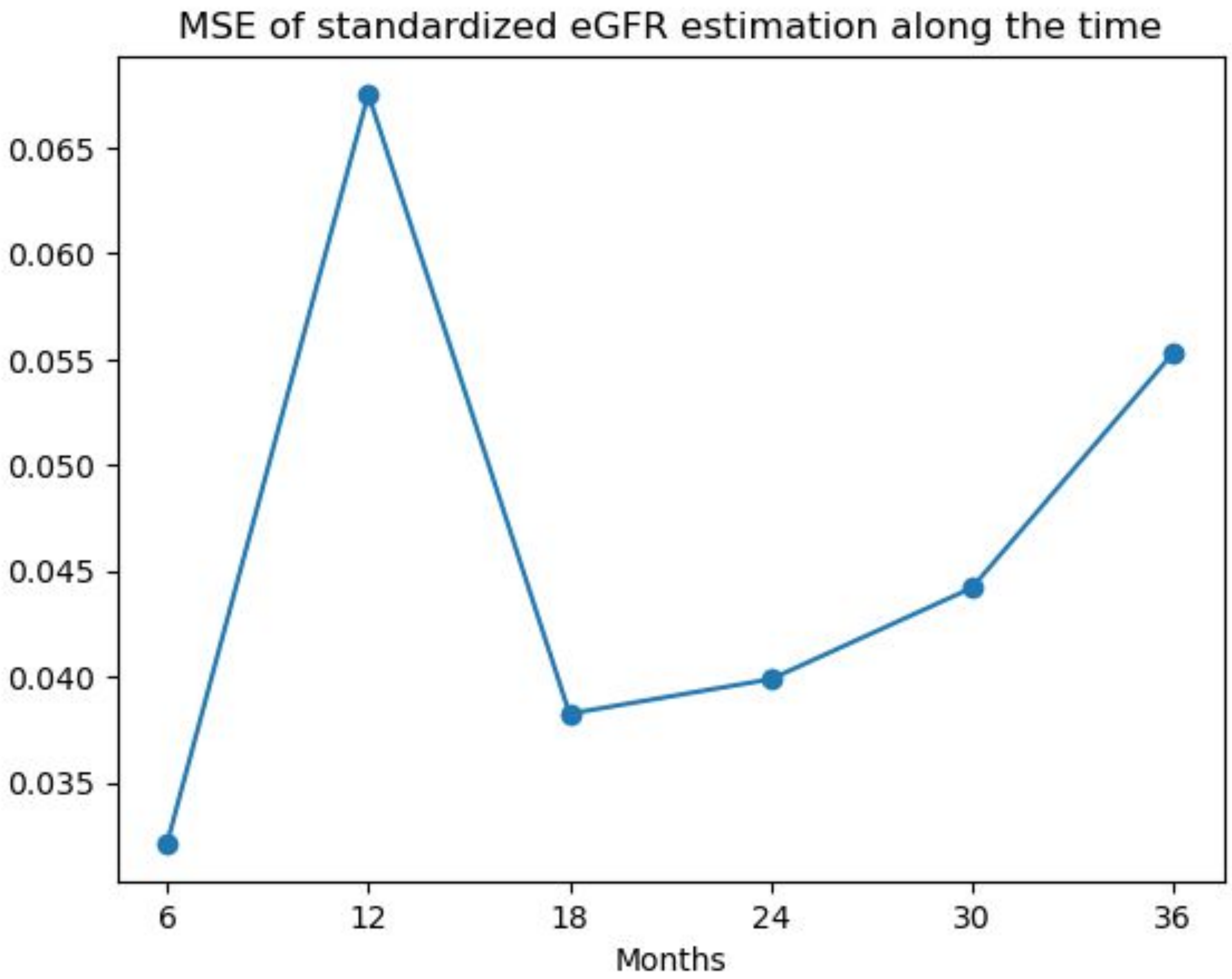
Deep Neural Network



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Minimal Decay Model

- Venturing into an agent based frame: “Filter” as agent
- Filtration rate per agent is fixed and filter population decays
- Decay rate is an inner product of features and their weights

$$X(t) = X_0 \exp\{-w^T f\}t$$

Features used:
Age, Systolic blood pressure, Body mass index, Hemoglobin level, albumin level, creatinine level.

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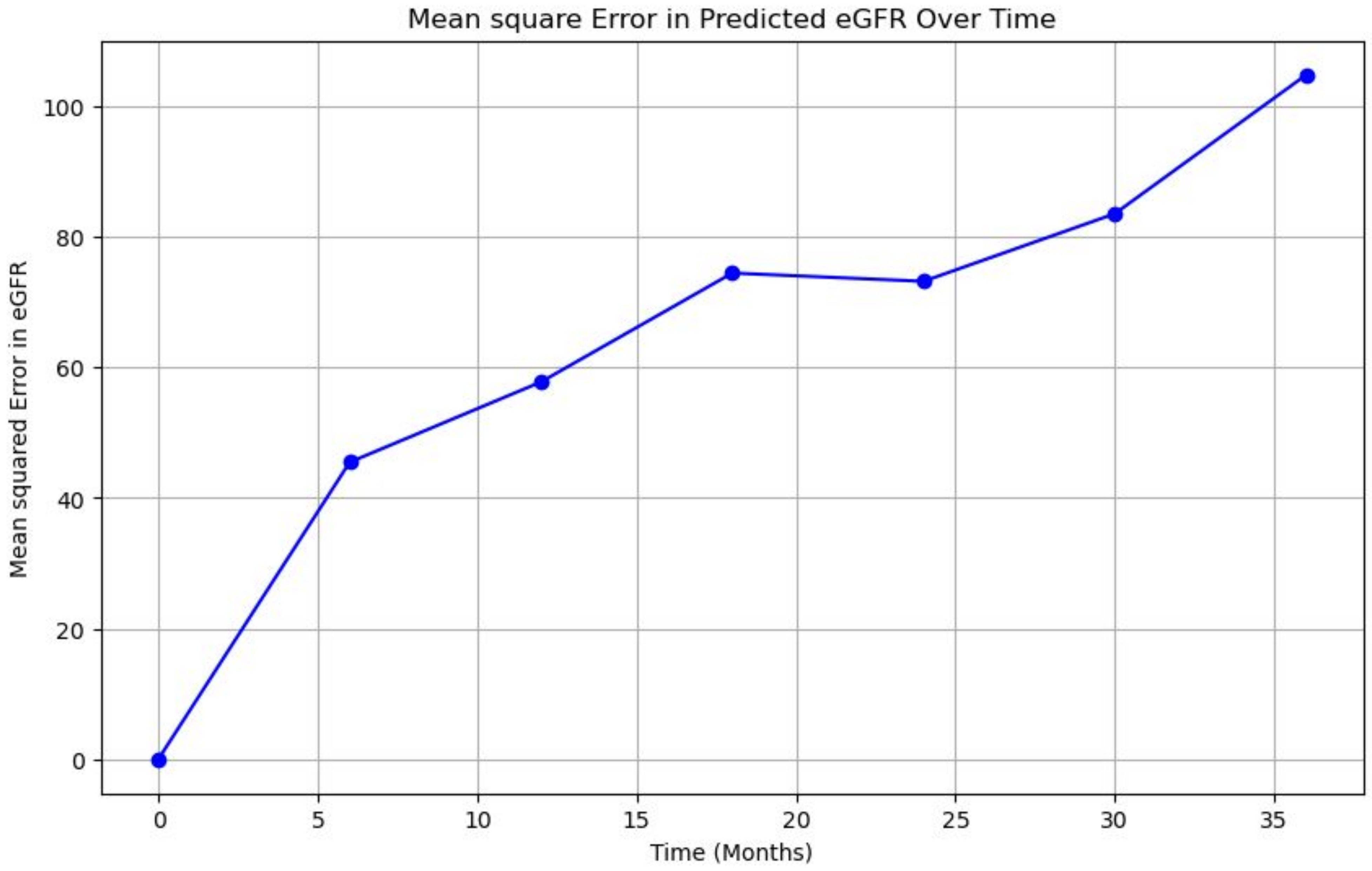
Minimal Decay Model



	Time	Actual	Predicted
0	0	34.146986	34.146986
1	6	26.454698	33.903286
2	12	24.331582	33.661325
3	18	24.682189	33.421090
4	24	21.614854	33.182570
5	30	20.420524	32.945753
6	36	18.495328	32.710625
7	0	73.570568	73.570568
8	6	78.287758	72.720524
9	12	71.343858	71.880302
10	18	72.845992	71.049787
11	24	71.908942	70.228869
12	30	71.562914	69.417435
13	36	67.225032	68.615377

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Chain Decay Model

- We extend the first decay model by incorporating two factors: multistage decay and potential recovery
- Features have different r/ships to decline at different stages

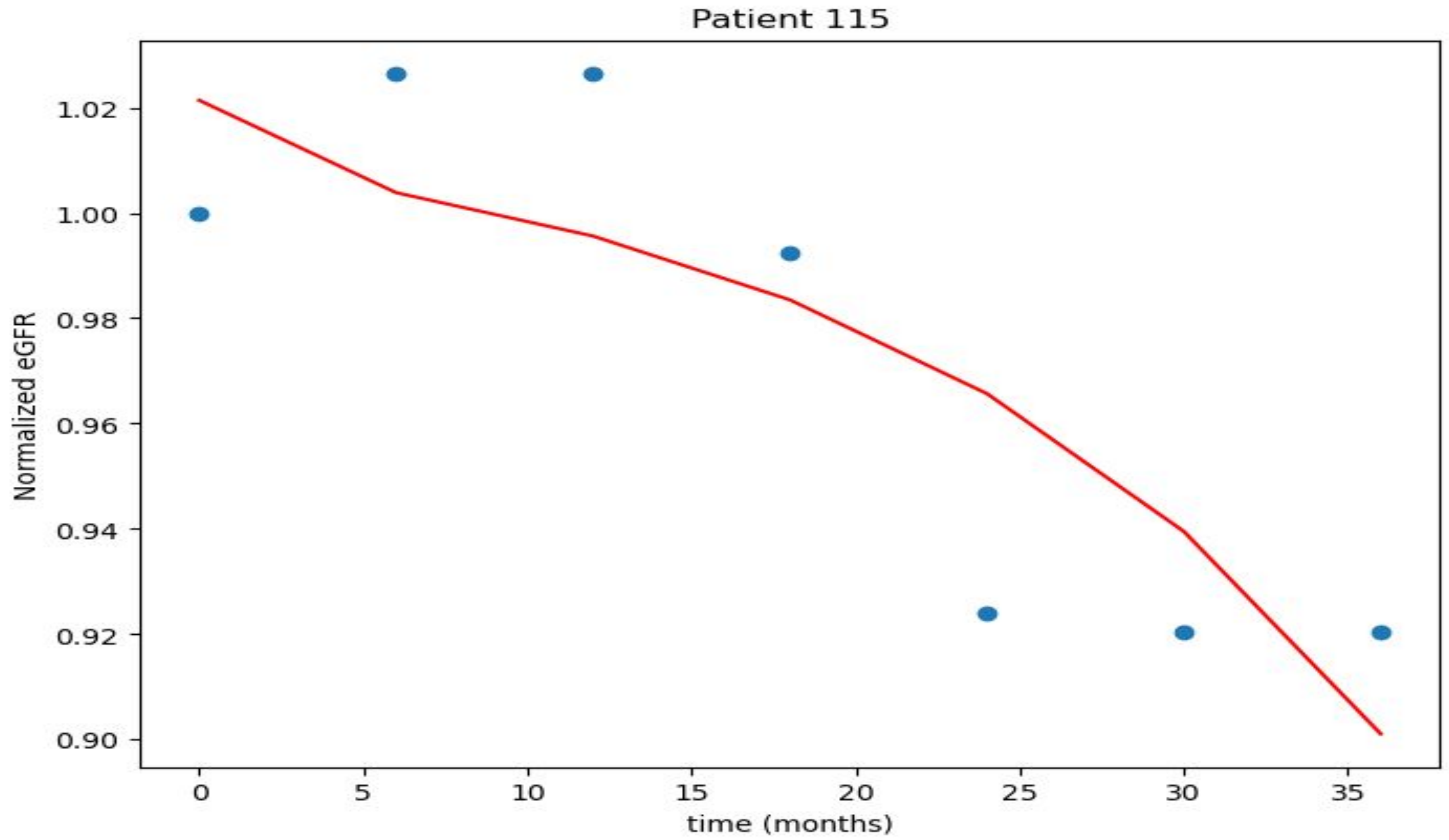
$$x_1 \rightarrow x_2 \rightarrow x_3 \rightarrow x_4 \rightarrow x_5$$

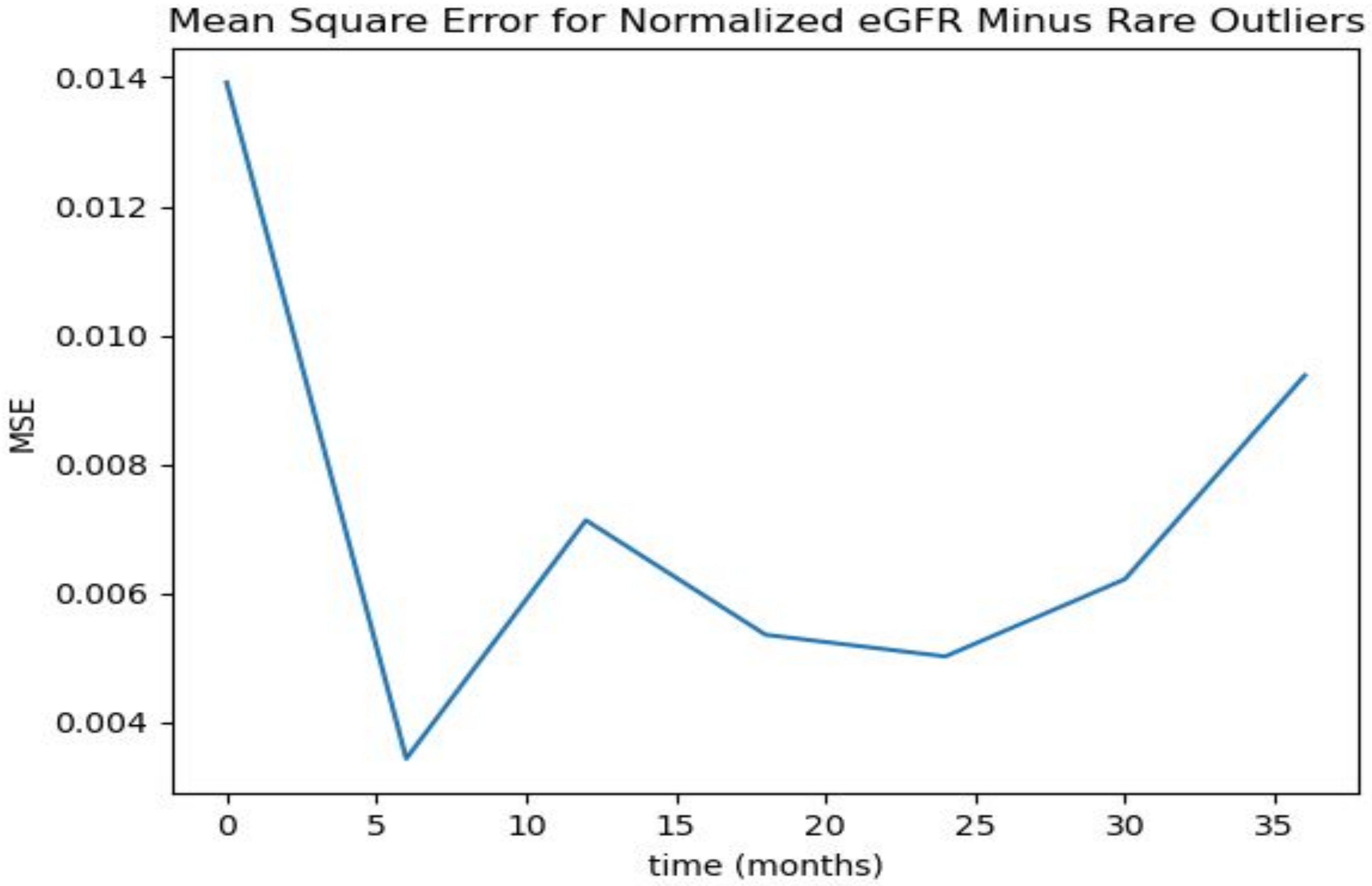
$$\frac{dF}{dt} = \sum_{j=1}^{n} \sum_{i=1}^{j-1} x_1(0) \lambda_i c_i e^{-\lambda_i t} v_j$$

$$\boldsymbol{c_i} = \prod_{j=1, i \neq j}^{D} \frac{\boldsymbol{\lambda_j}}{\boldsymbol{\lambda_j} - \boldsymbol{\lambda_i}}$$

Trends from Chain Decay Model

- Two stage, one feature version
- Patients randomly selected
- Feature: BMI (increasing initial weights)
- Estimated mean variance for the optimal weights is below 1 for 85 percent of the patients





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Future Works

- **eGFR** is already an **e**stimation for the metric **GFR**
  - A <u>very</u> noisy metric as is
  - Is affected by: lifestyle changes, treatment changes, and progression of the disease
- Feature changes lead to time dependent coefficients for our ODE models
- Using noise to factor in variables that are hard to account for

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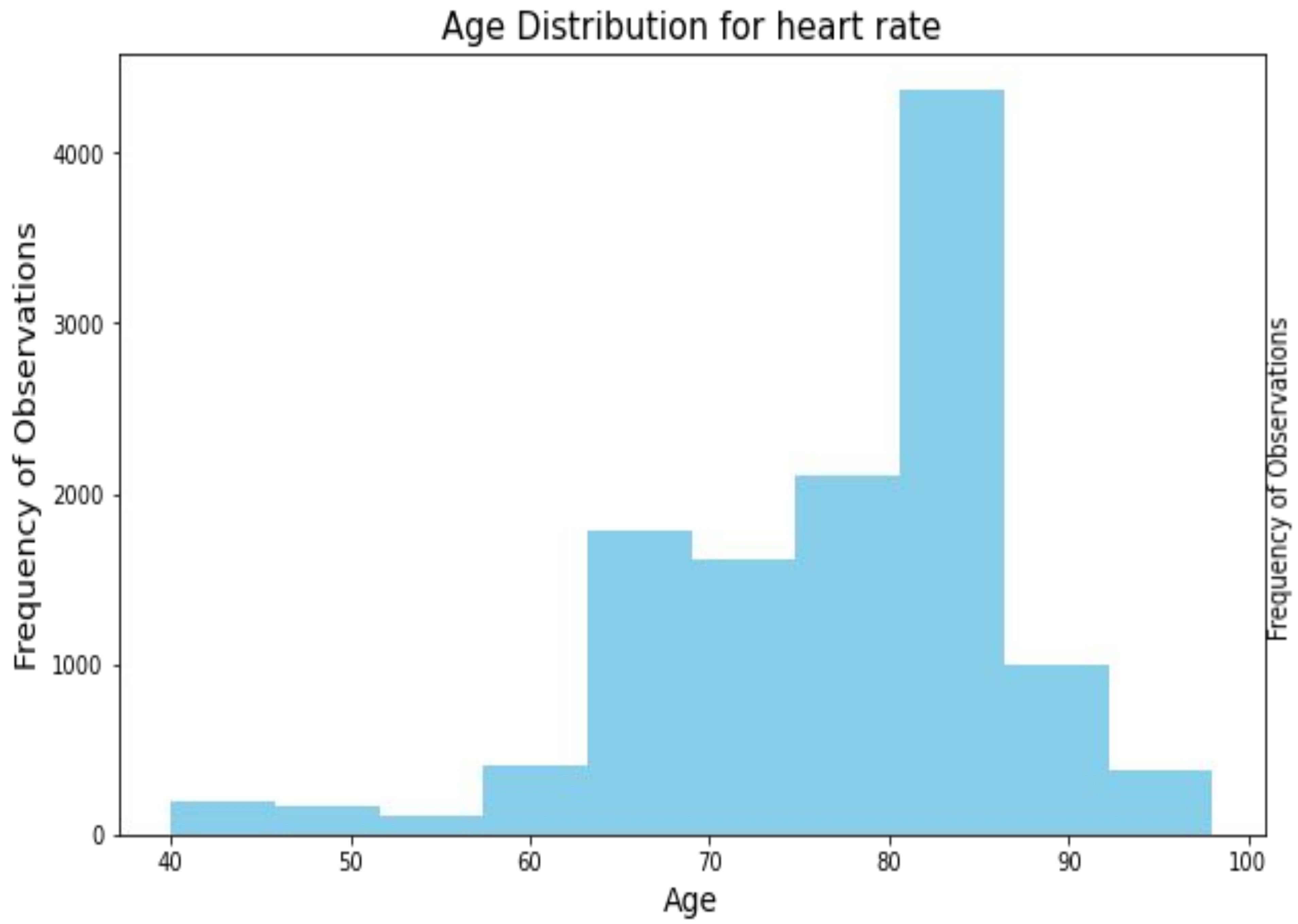
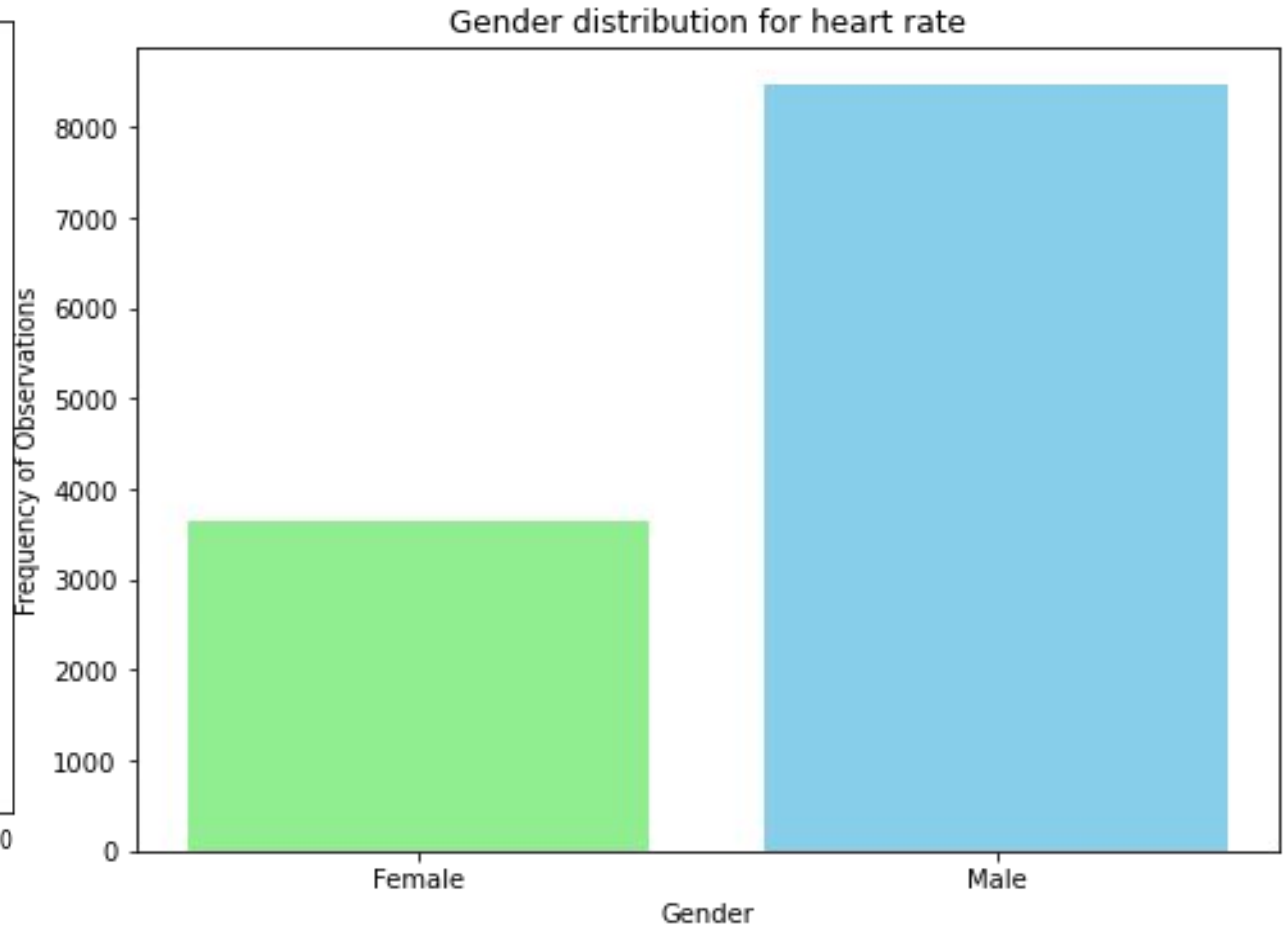
Group 2: Backup Slide





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Group 2: Backup Slide

f(avg_heart_rate) = 1.81*smoking_habit -0.092*age +1.80*gender+ 0.036*height + 0.054*weight

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