

# Genomic & Gut Microbial Attributes of Body Mass Index (BMI)

**Zachary Caterer**

**University of Colorado Boulder**

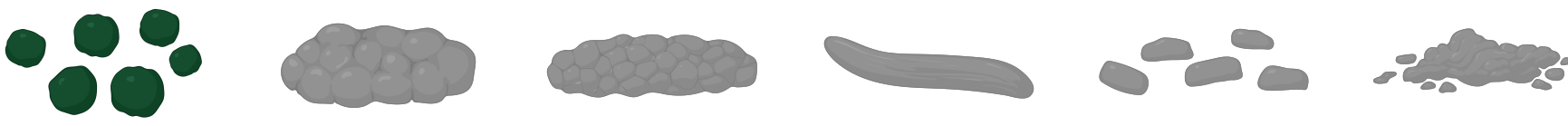
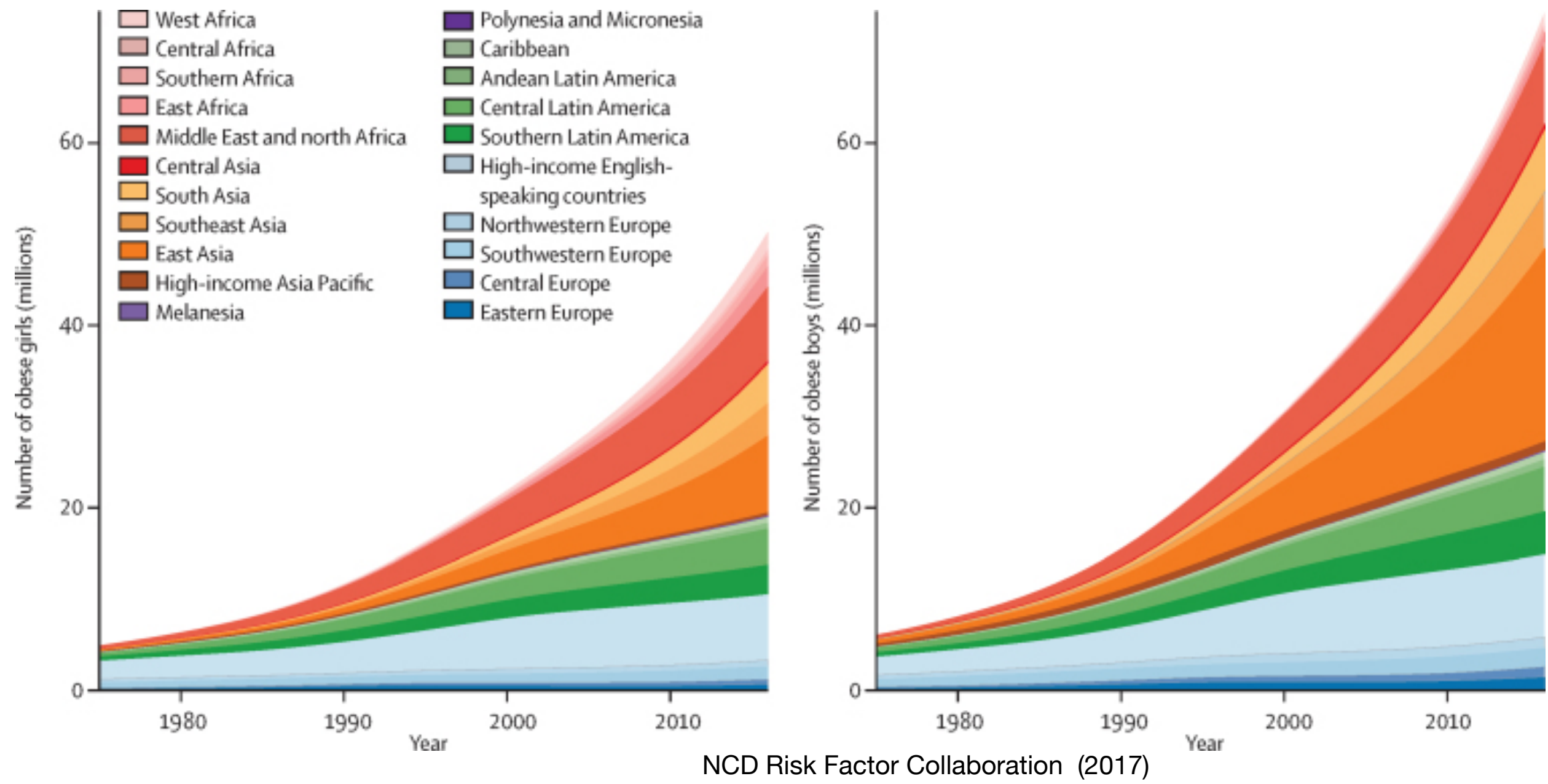
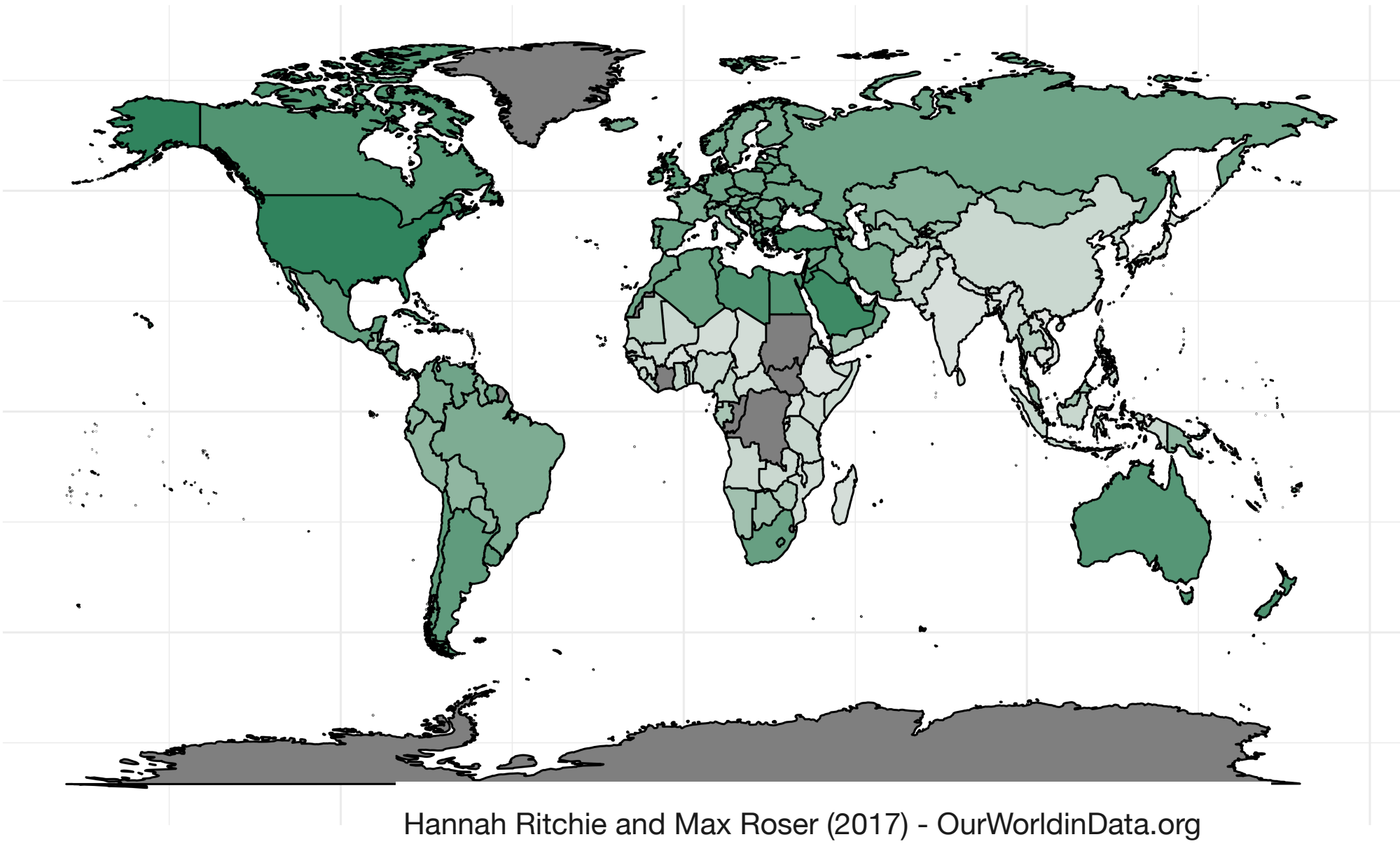
Department of Chemical and Biological Engineering + IQ Biology

**Dr. Maggie Stanislawski**

**University of Colorado Anschutz**

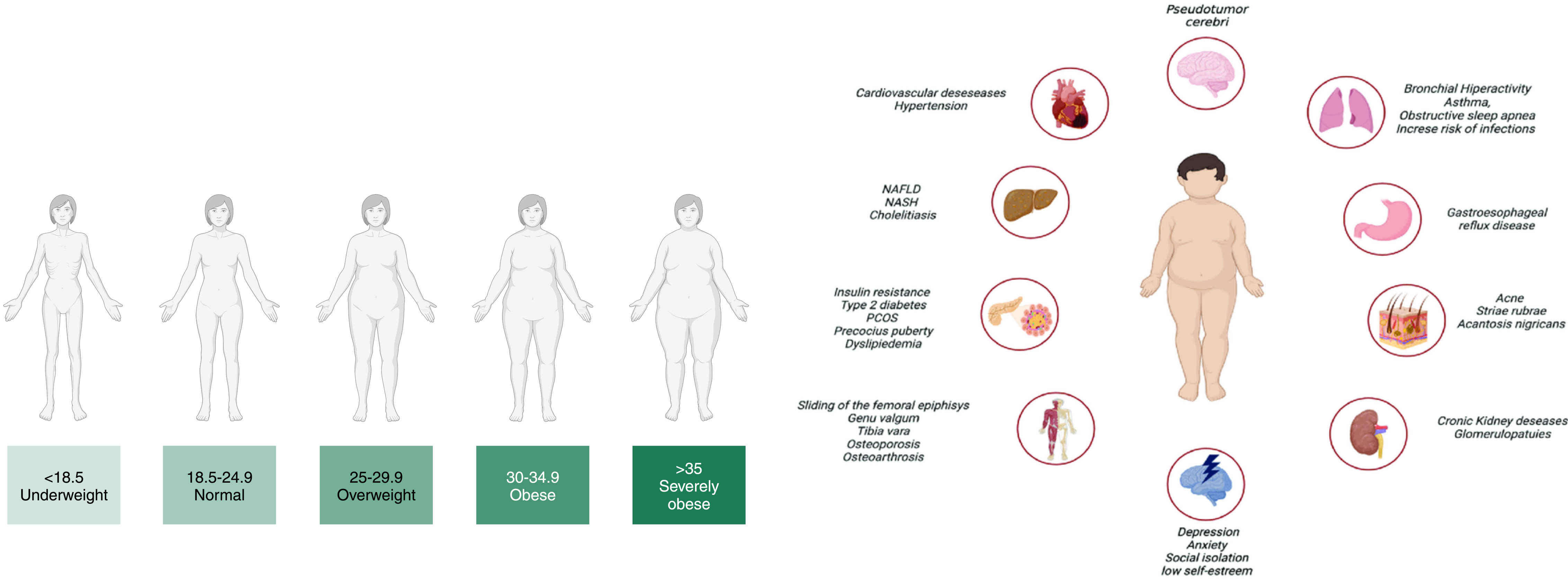
Department of Biomedical Informatics + Biofrontiers Institute

# Obesity is an epidemic

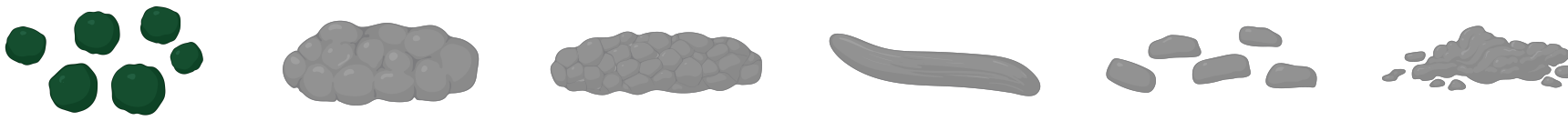




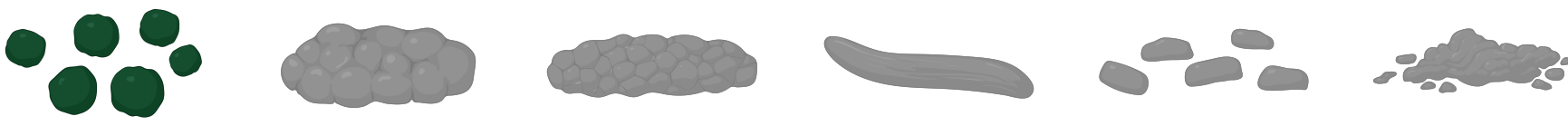
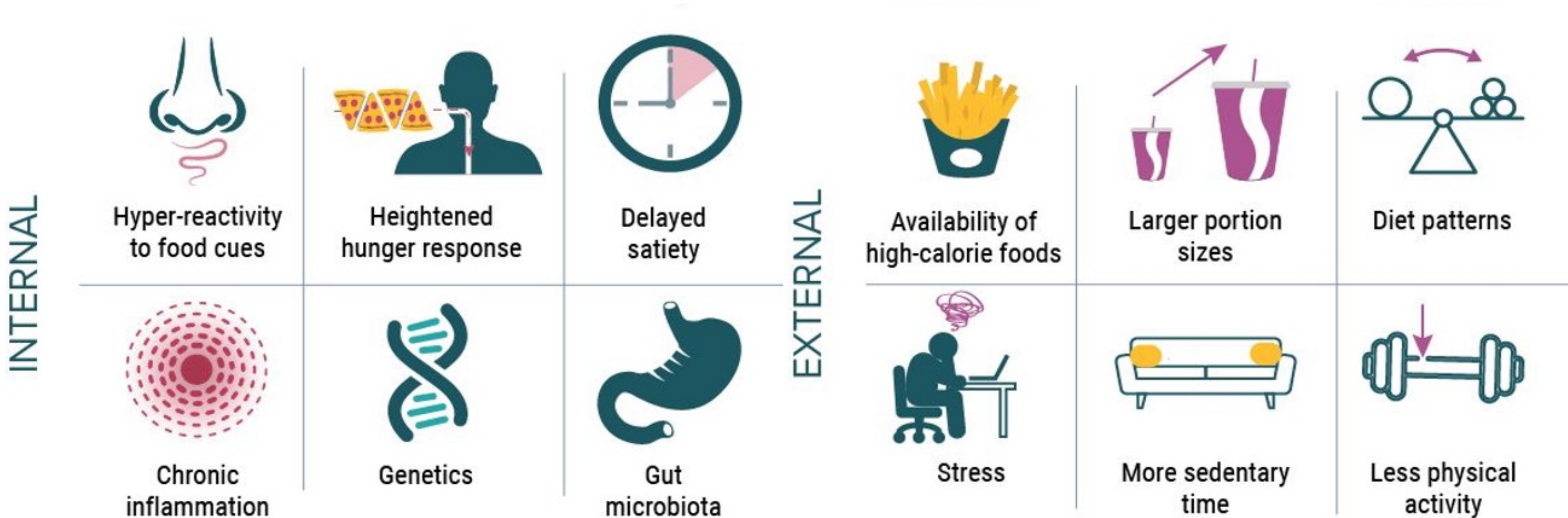
# Obesity is a chronic disease



Calcaterra et al. 2023

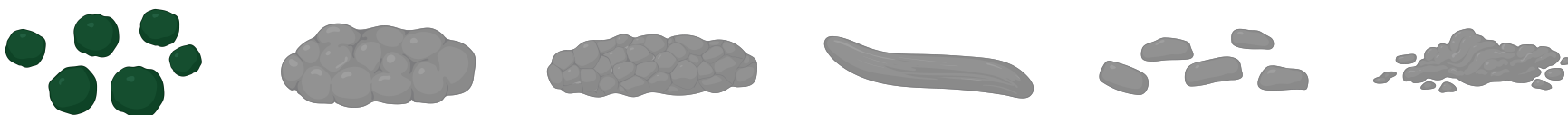
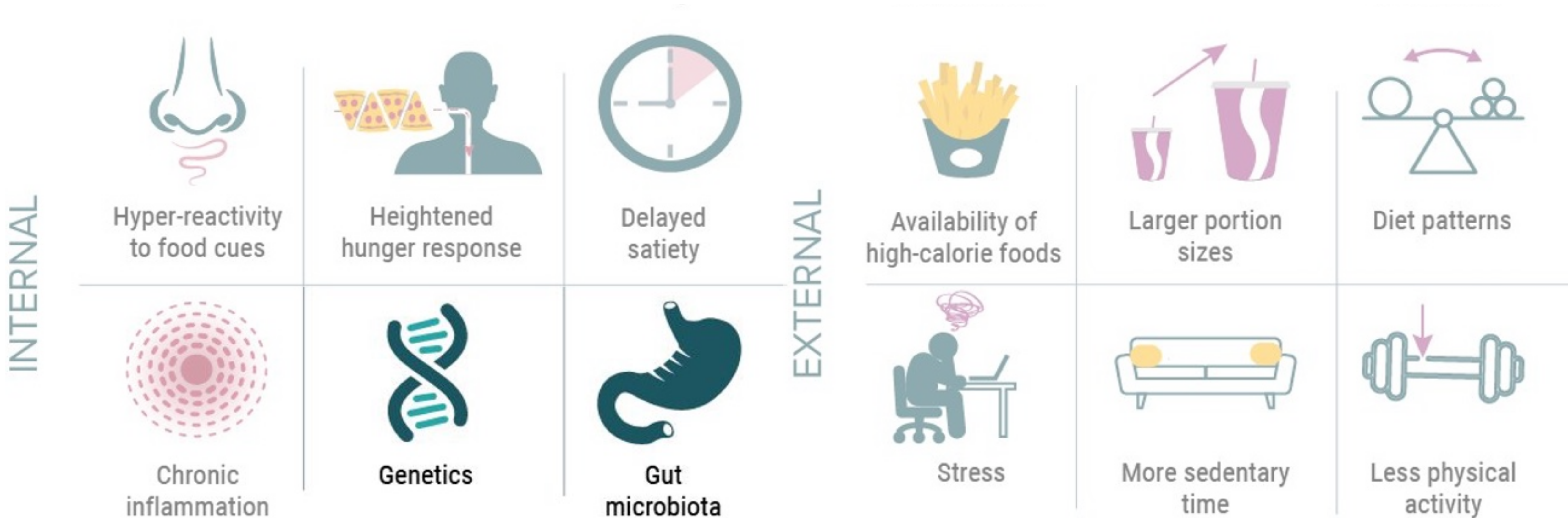


# Potential Causes of Obesity

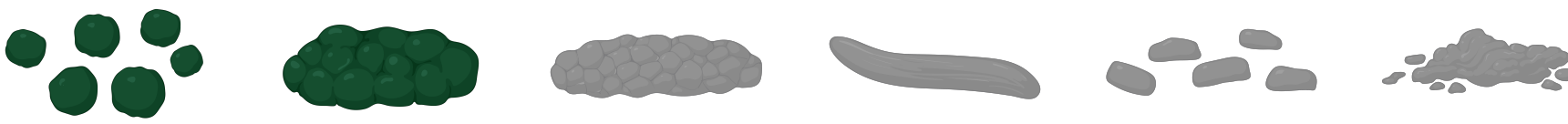
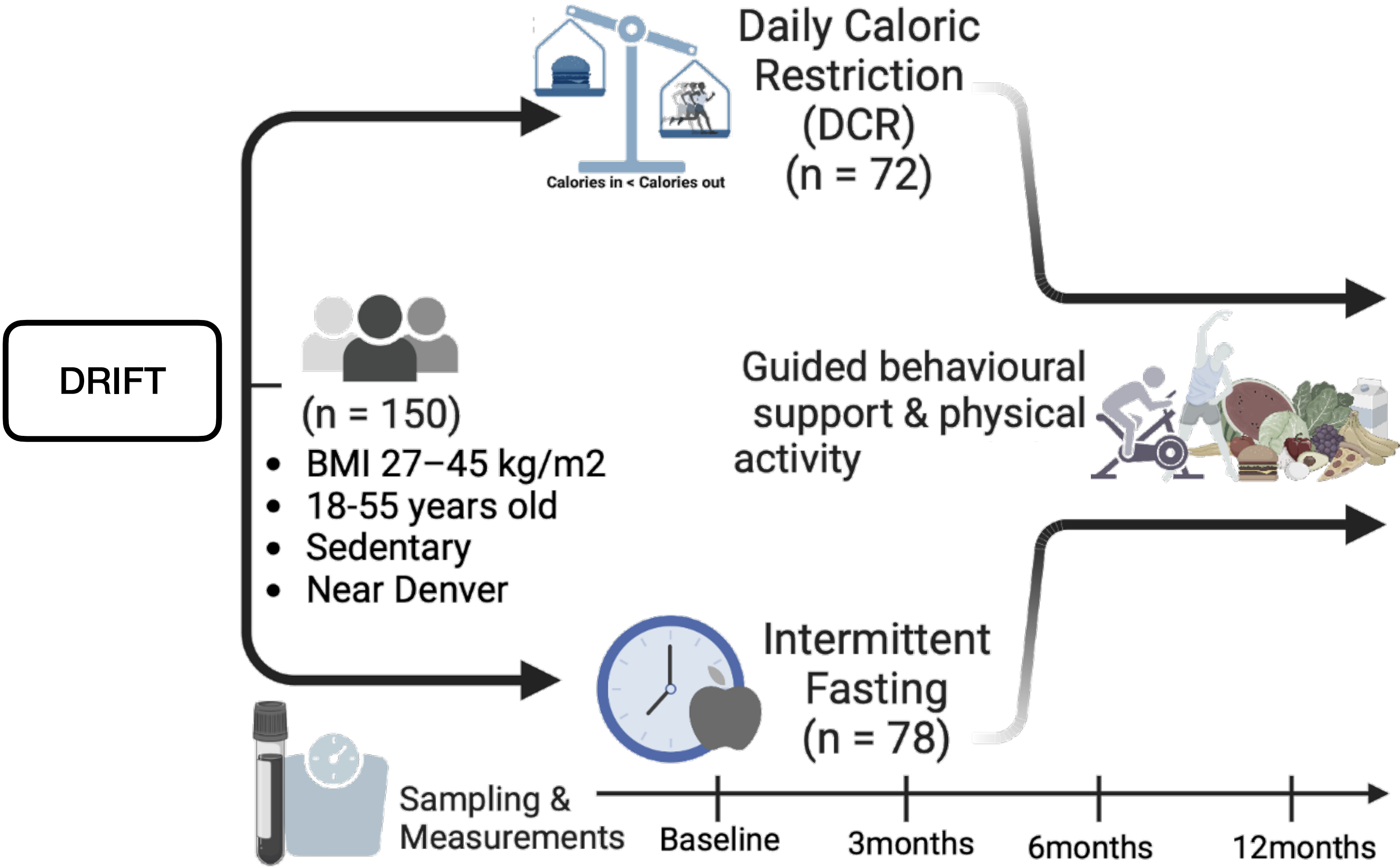




# Potential Causes of Obesity

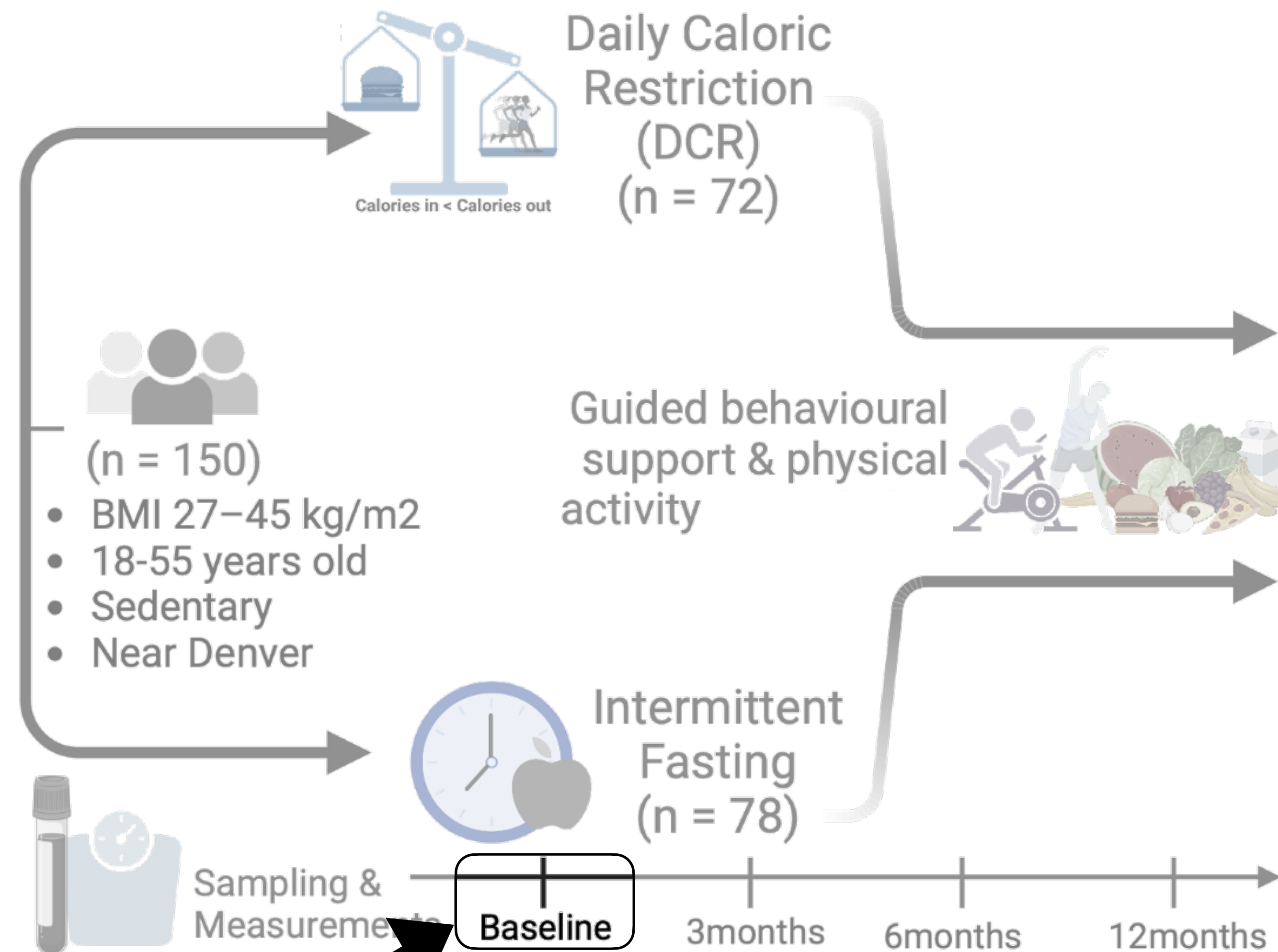


# Daily Caloric Restriction vs Intermittent Fasting TRIAL





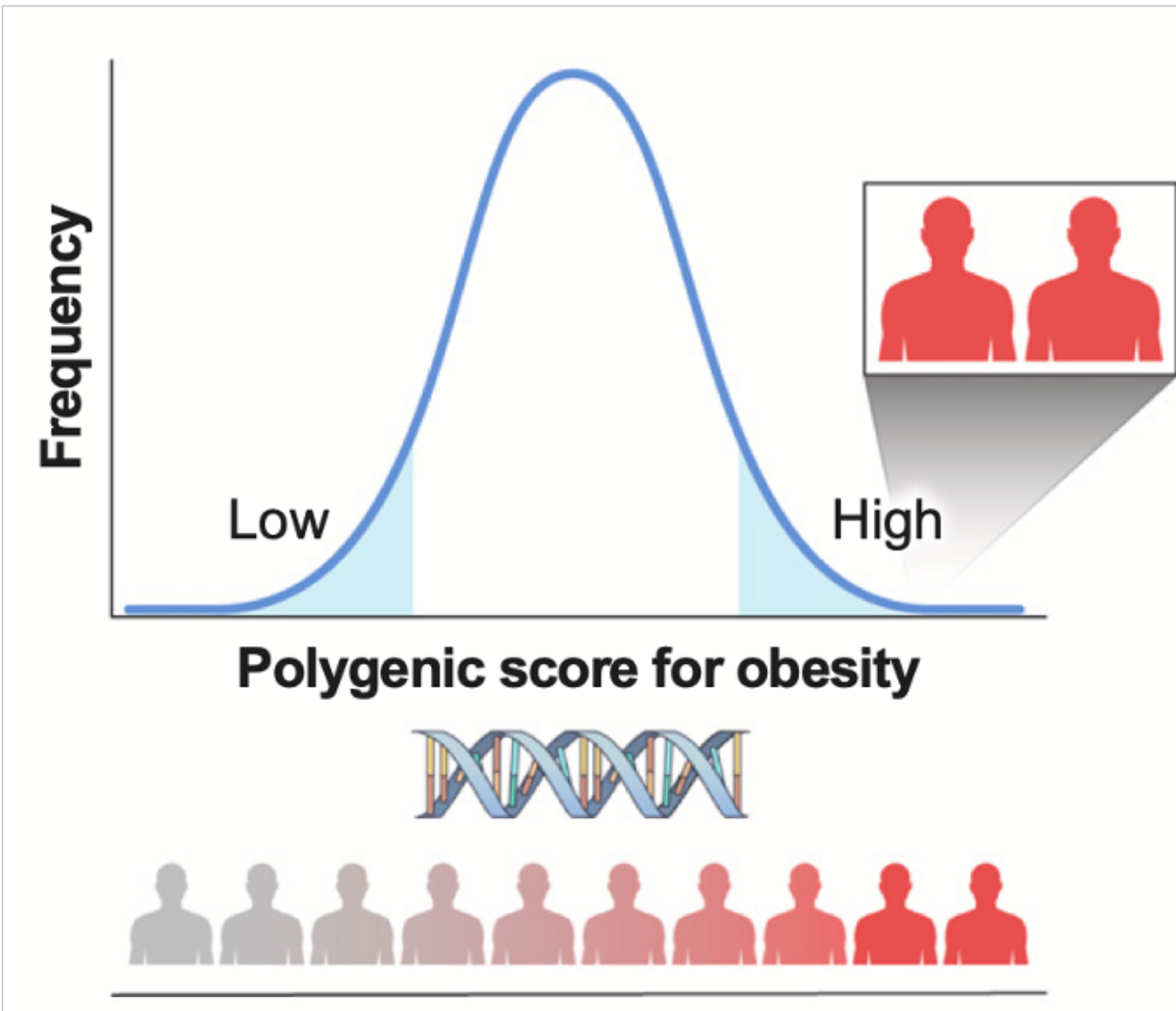
# Daily Caloric Restriction vs Intermittent Fasting TRIAL



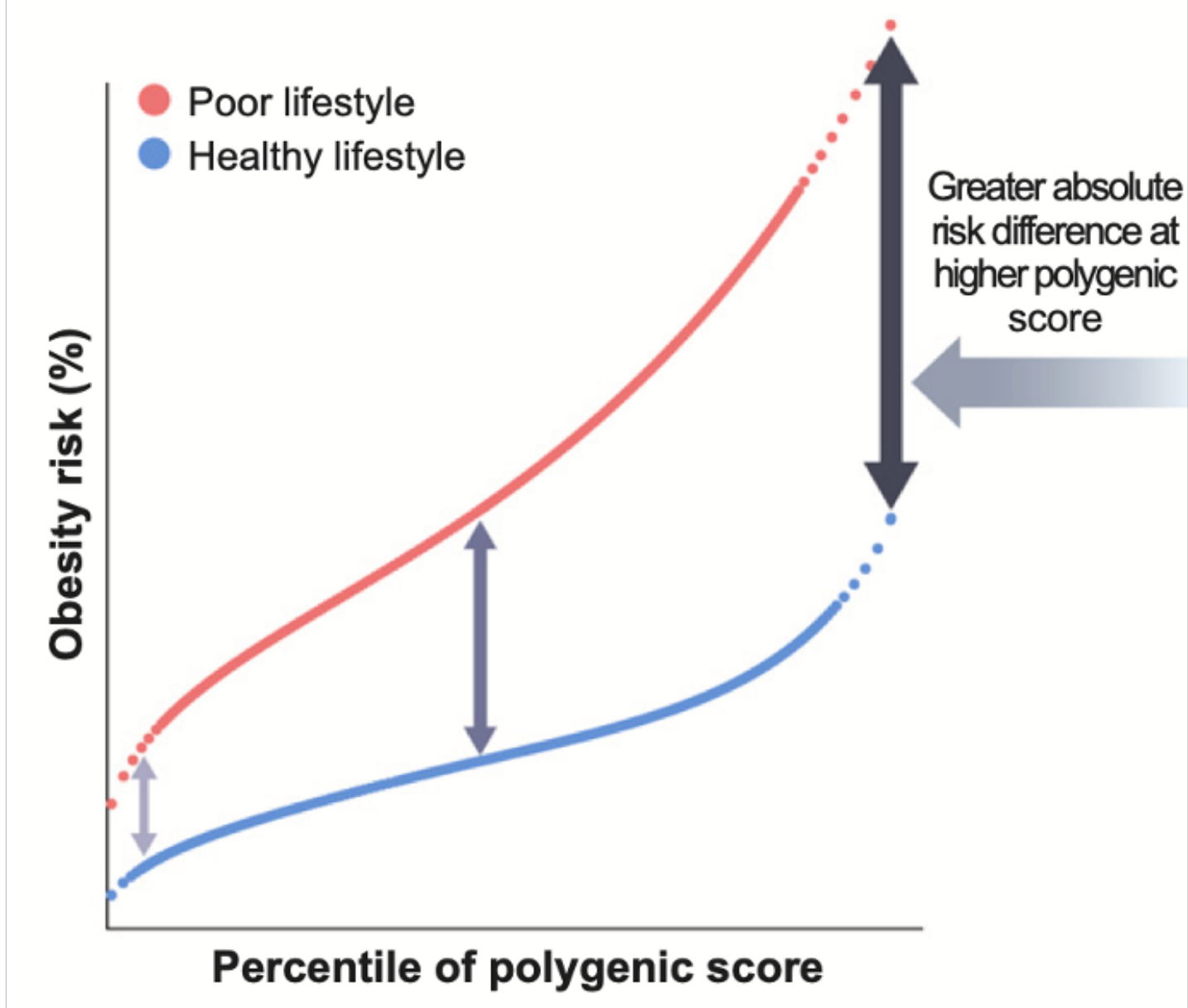
# Research Questions

Are there associations between participant BMI genetic risk scores and weight loss?

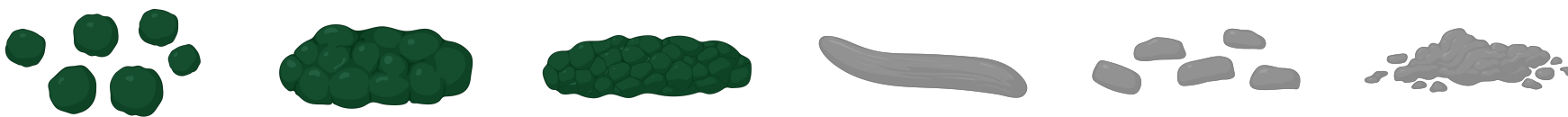
Increased risk of obesity and obesity related morbidities in high genetic risk group



Healthy lifestyle can prevent multi-morbidities even for individual at high genetic risk



Kim et al., 2024, Cell Metabolism 36, 1494–1503, July 2, 2024



# Research Questions

Are there associations between participant BMI genetic risk scores and weight loss?

Are there gut microbial attributes that can be used to identify the difference in participant's actual BMI vs genetic risk?



# Research Questions

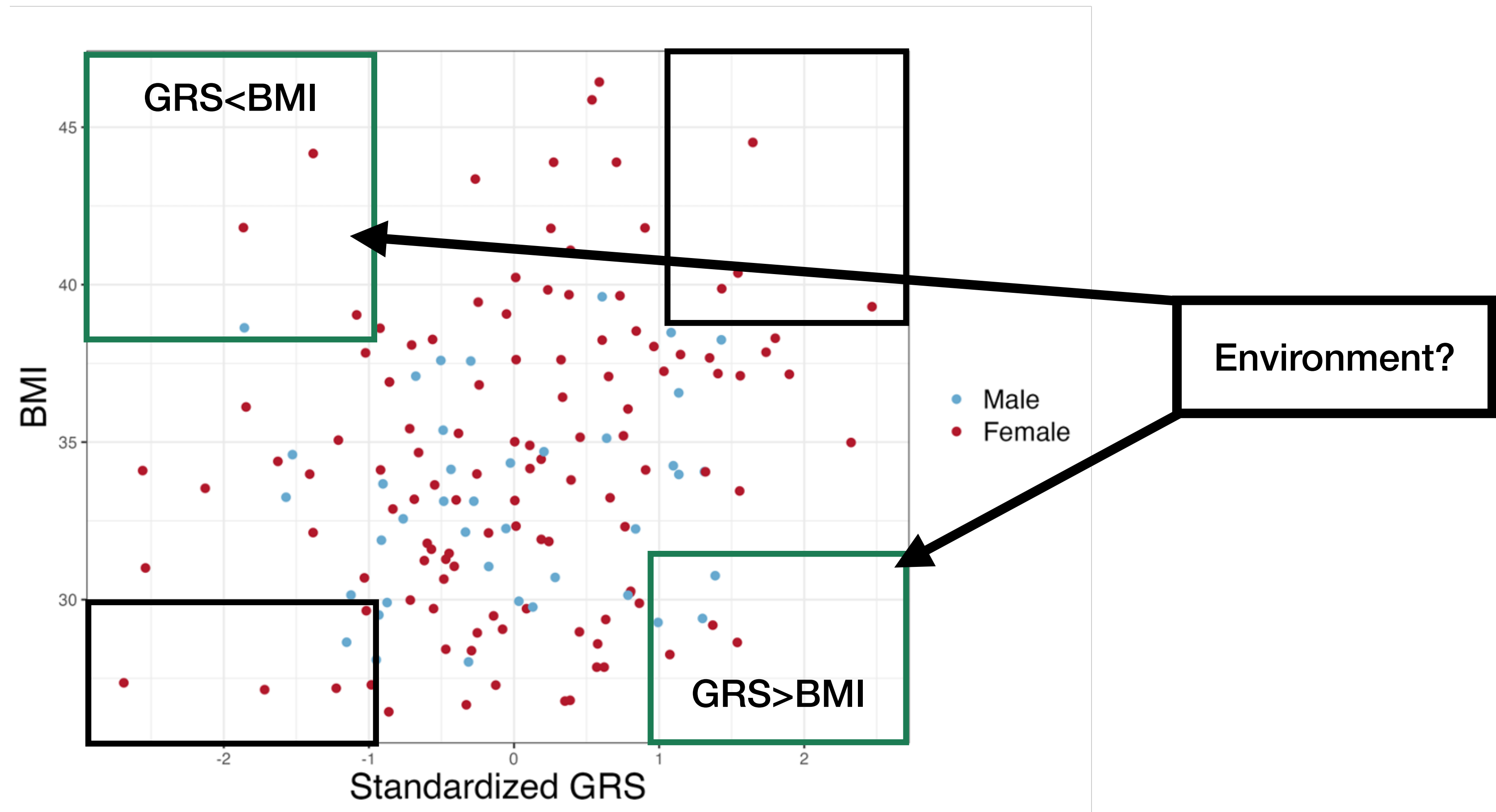
Are there associations between participant BMI genetic risk scores and weight loss?  
(Emily Yeo & Ashley Scadden)

Are there gut microbial attributes that can be used to identify the difference in participant's actual BMI vs genetic risk?

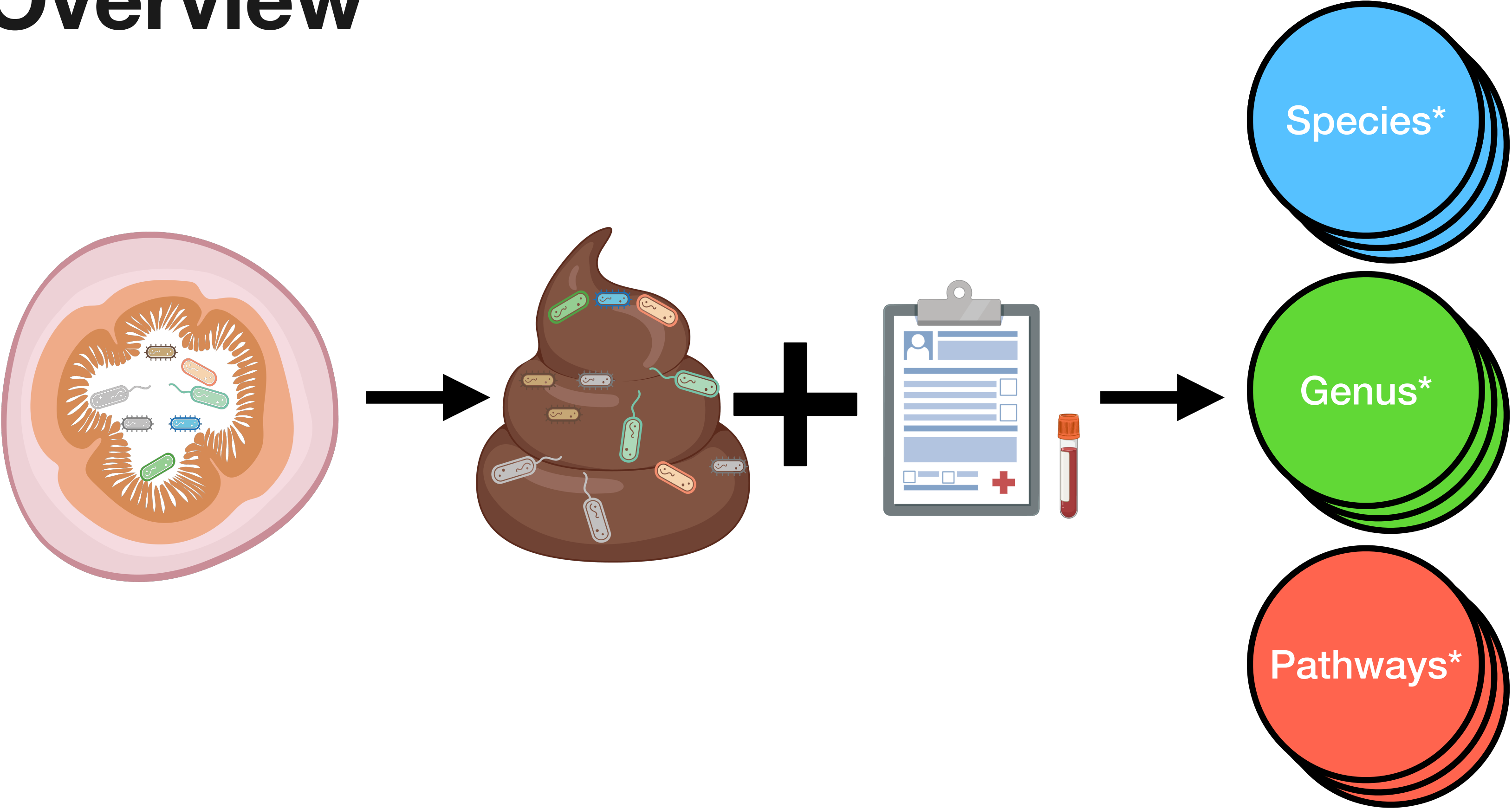




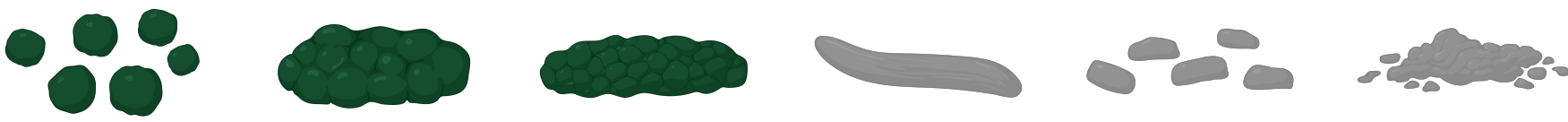
# BMI verses genetically expected BMI – Genetic Risk Score (GRS)



# Dataset Overview

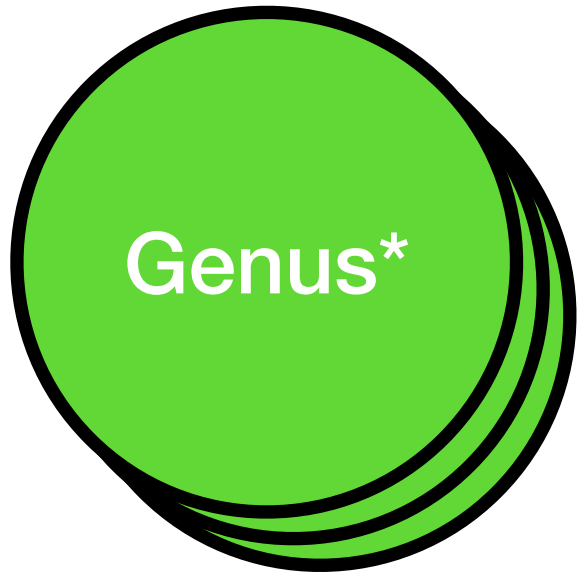


\*Taxa, w/, w/o clinical information & minus redundant features



# Dataset, Models, and Metrics Overview

## Datasets



\*Taxa, w/, w/o  
clinical information  
& minus redundant  
features

## Models

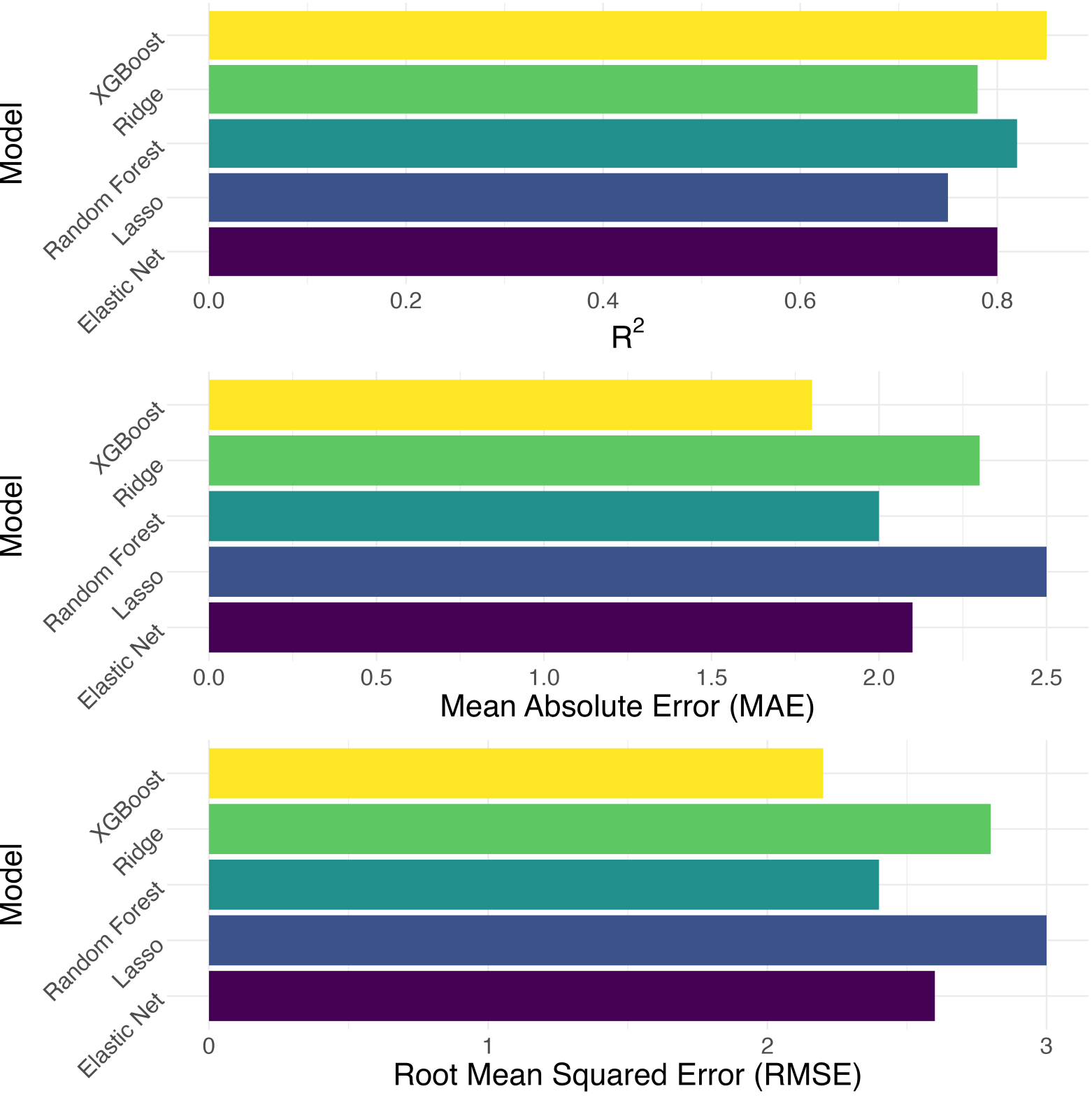
### Penalized Regression Models

Elastic Net  
Lasso  
Ridge

### Ensemble Learning Methods

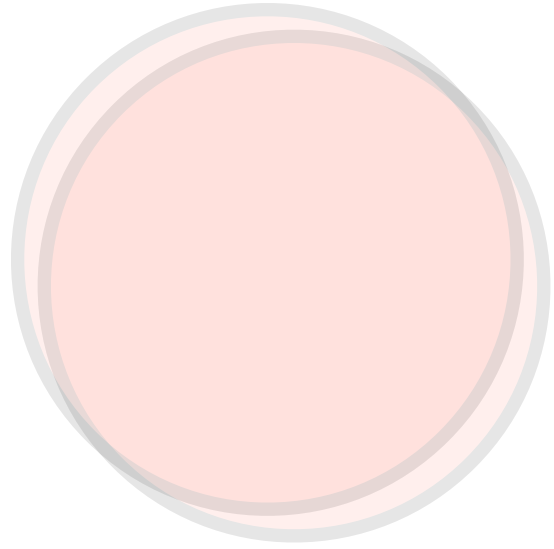
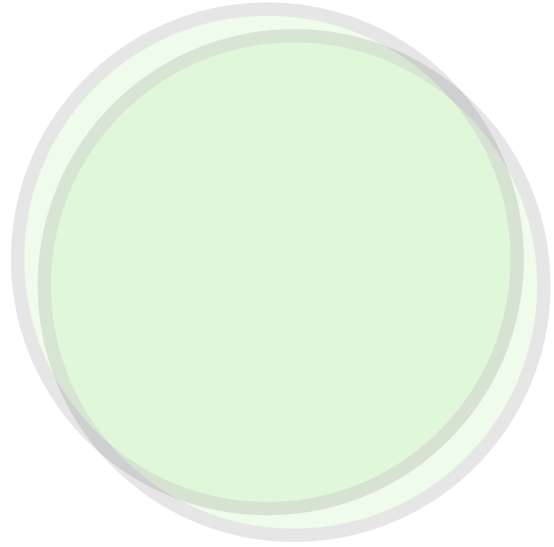
Random Forest  
XGBoost

## Metrics



# Dataset, Models, and Metrics Overview

Datasets



\*Taxa, w/, w/o  
clinical information  
& minus redundant  
features

Models

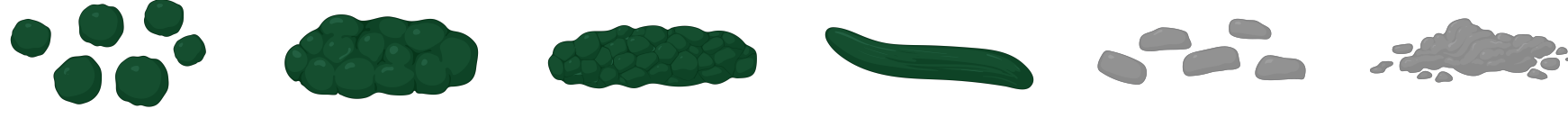
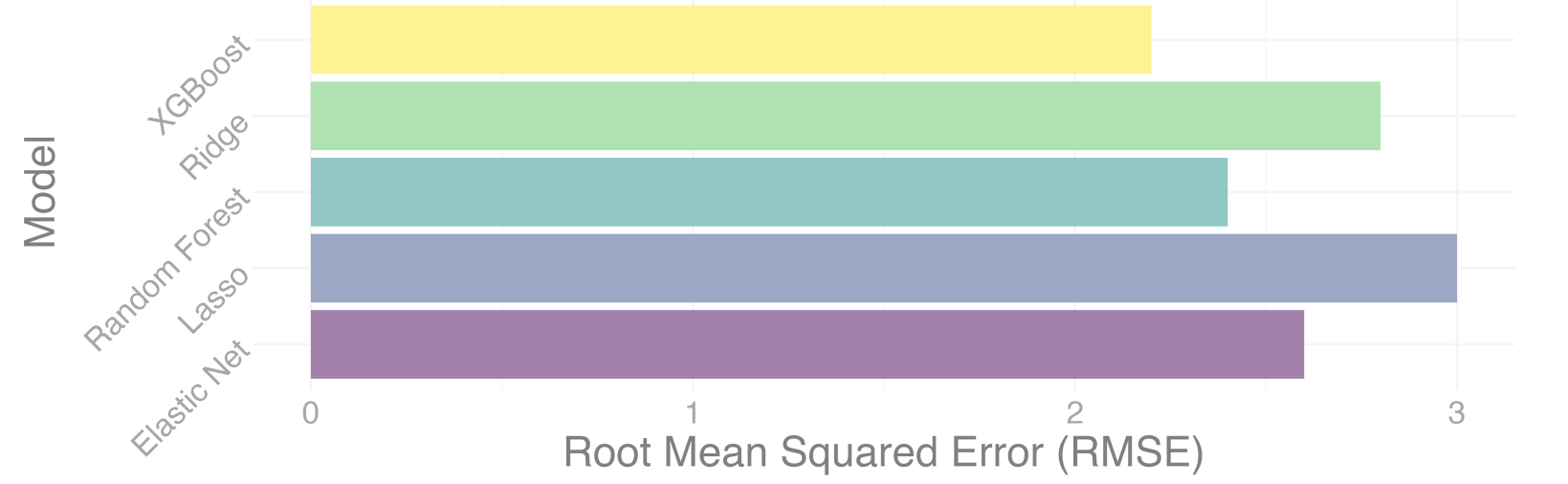
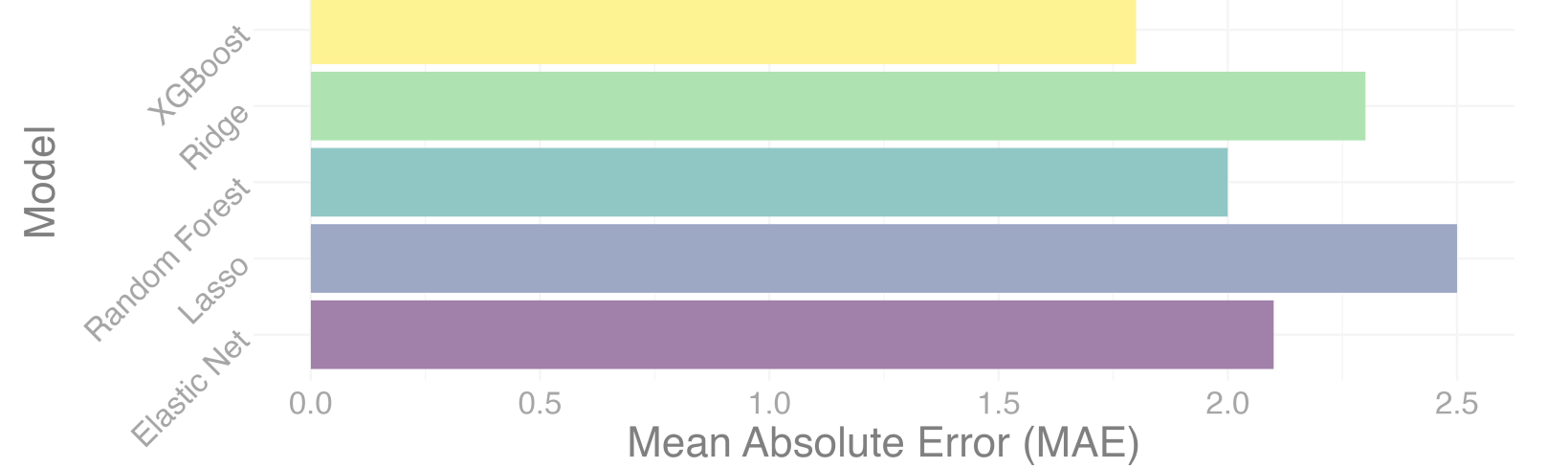
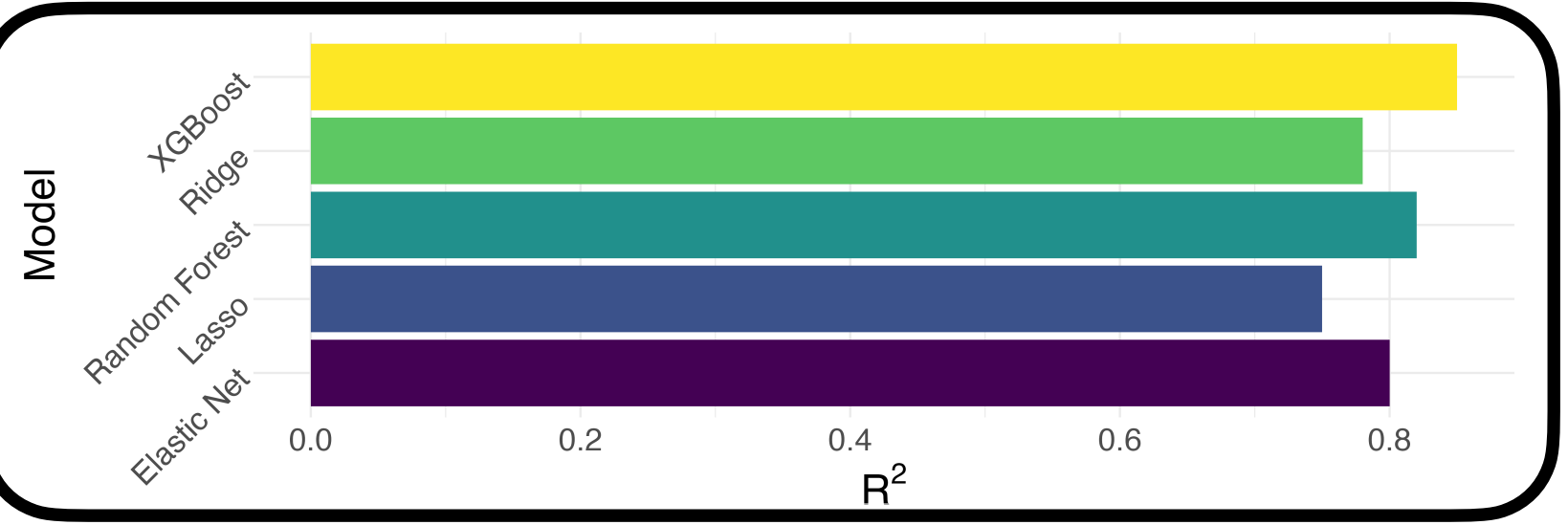
Penalized  
Regression Models

Elastic Net  
Lasso  
Ridge

Ensemble  
Learning Methods

Random Forest  
XGBoost

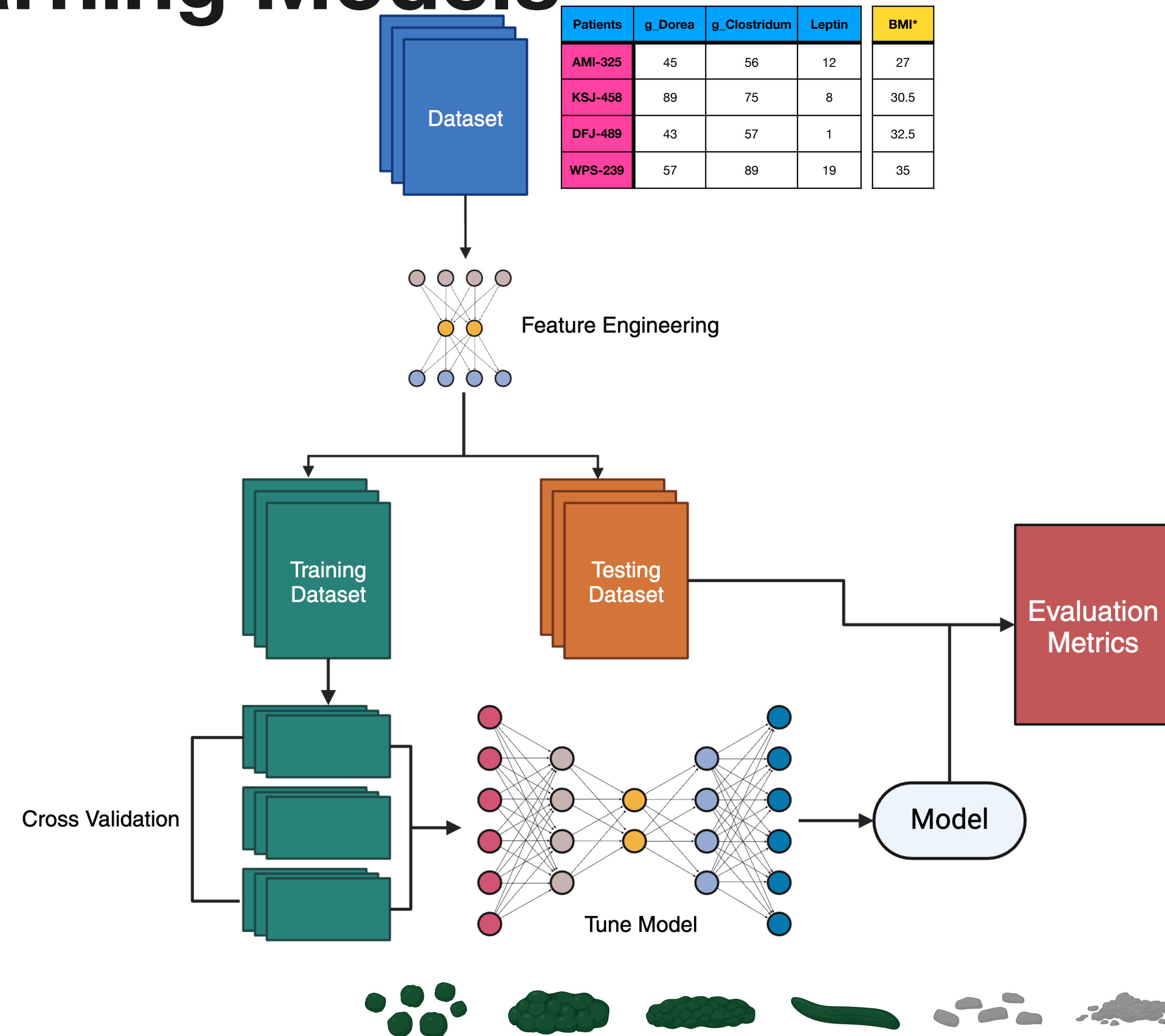
Metrics





# Overview of Machine Learning Models

1. Understand and Prepare Data
2. Feature Engineering
3. Split the Dataset
4. Train the Model
5. Test and Evaluate the Model
6. Interpret and Communicate the Results
7. Iterate and Improve

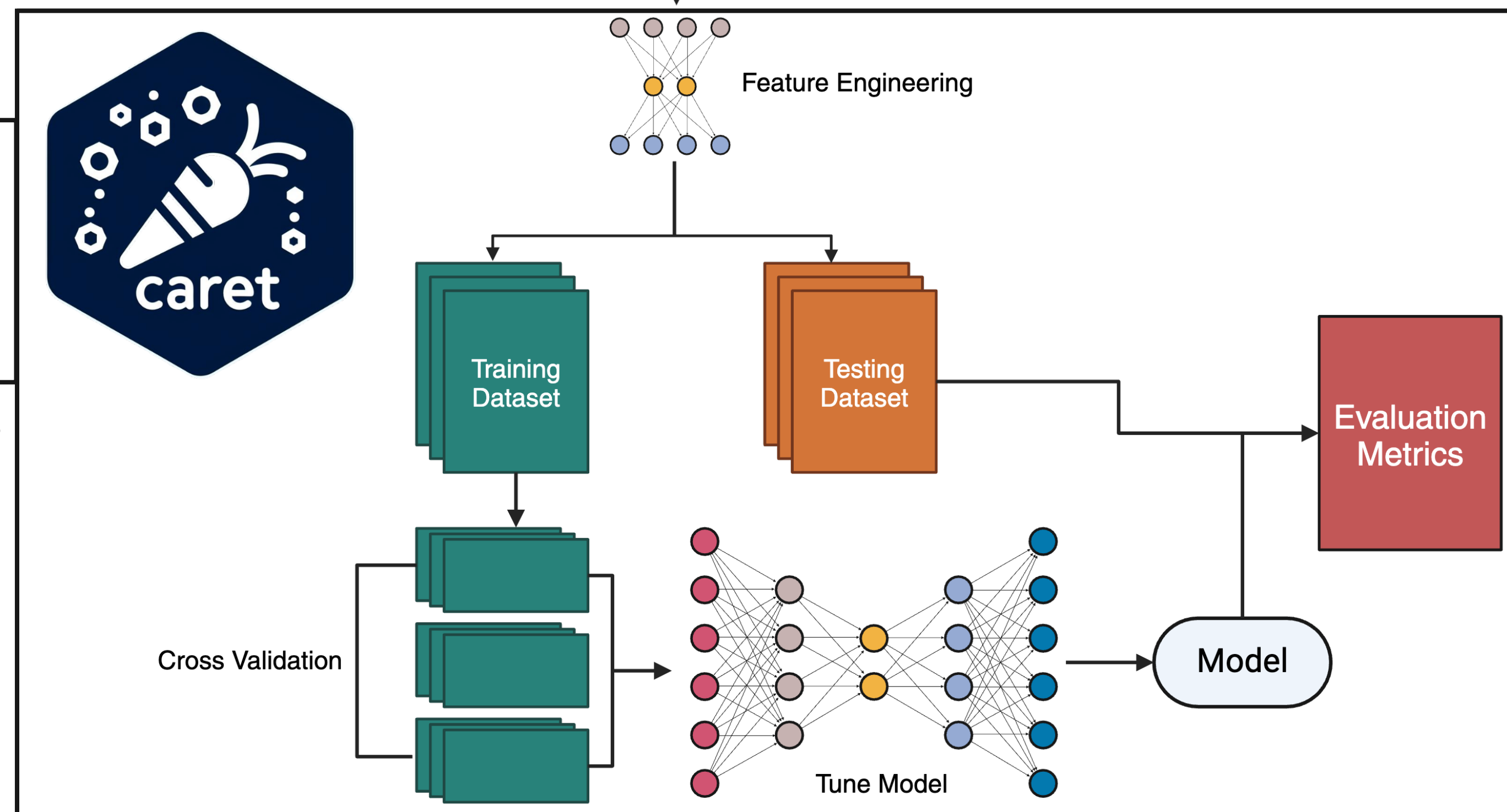


# Overview of Machine Learning Models

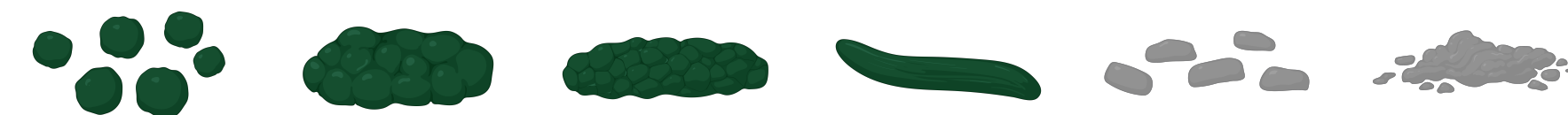


Patients	g_Dorea	g_Clostridium	Leptin	BMI*
AMI-325	45	56	12	27
KSJ-458	89	75	8	30.5
DFJ-489	43	57	1	32.5
WPS-239	57	89	19	35

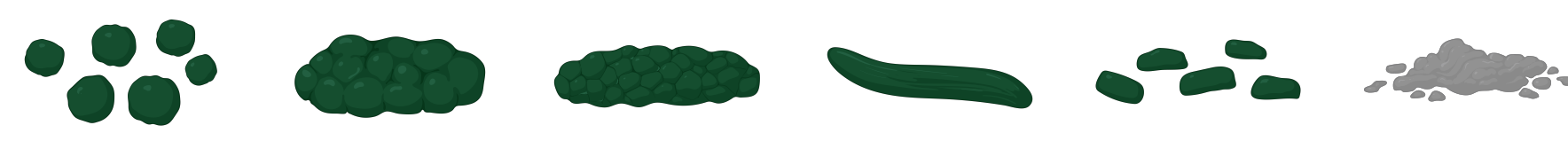
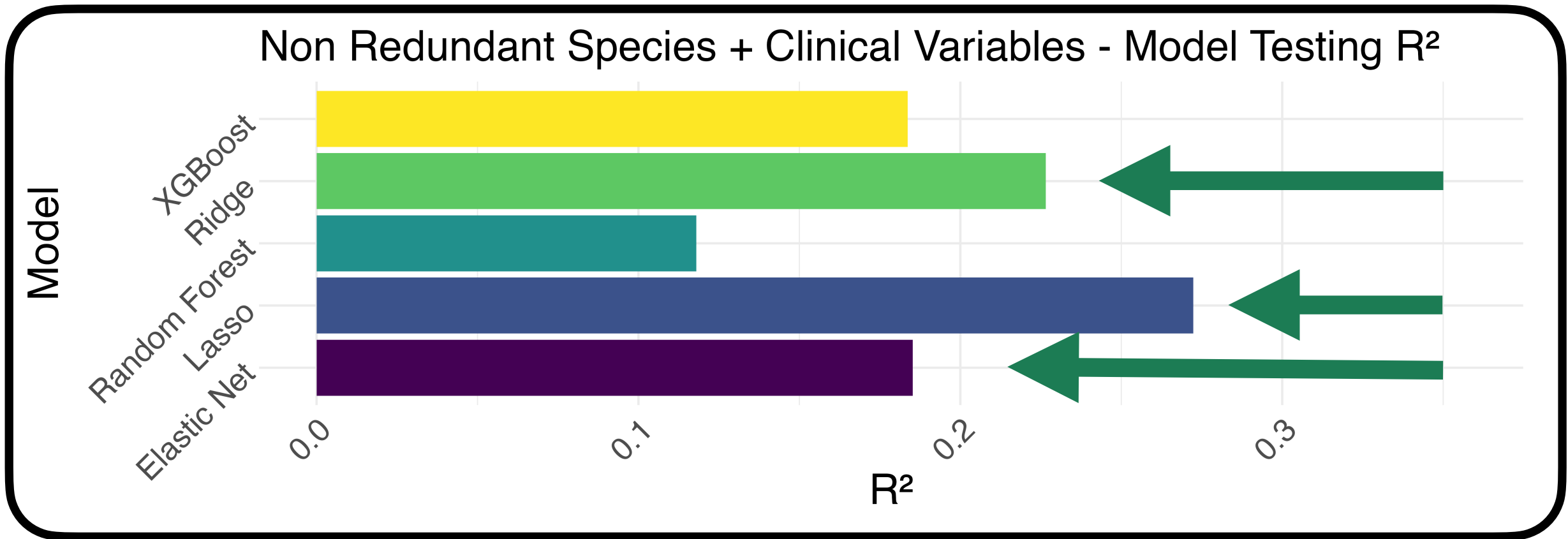
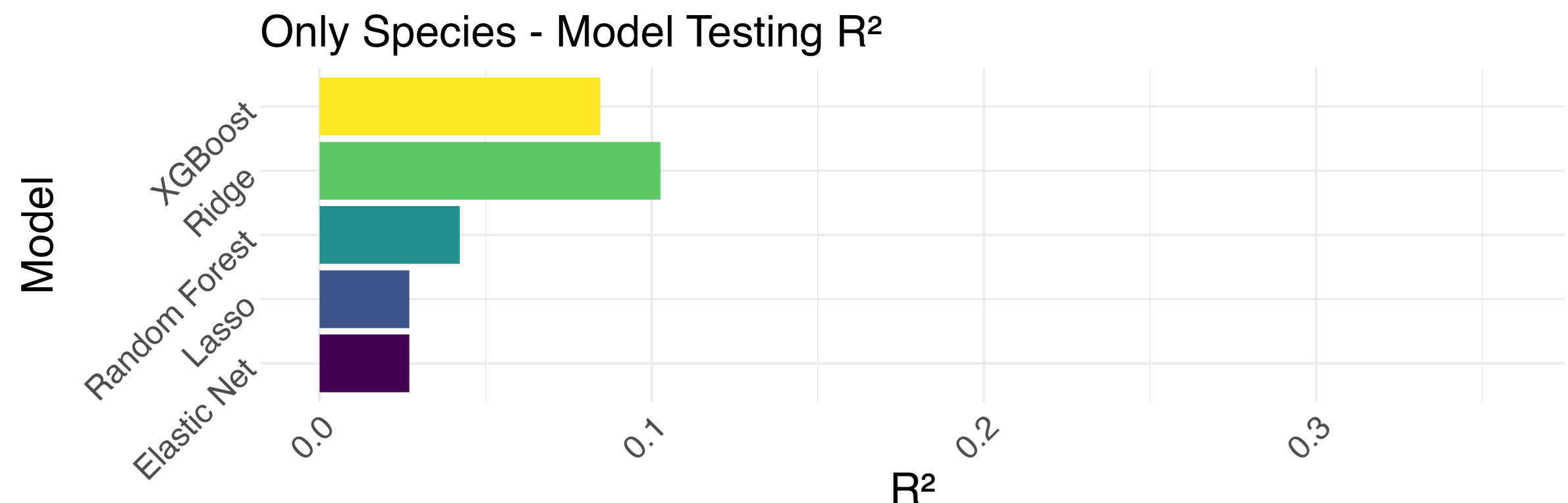
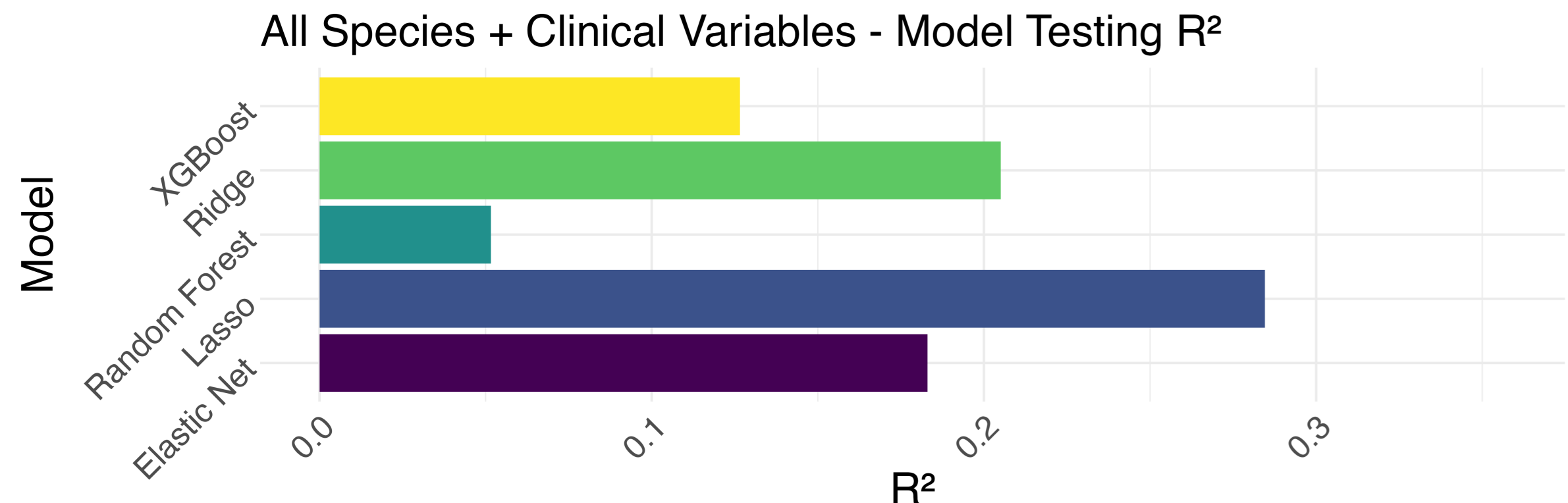
1. Understand and Prepare Data
2. Feature Engineering
3. Split the Dataset
4. Train the Model\*
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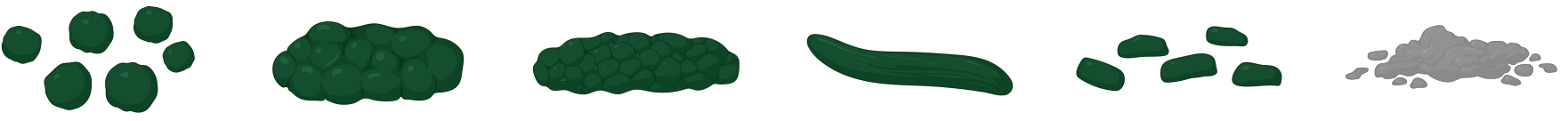
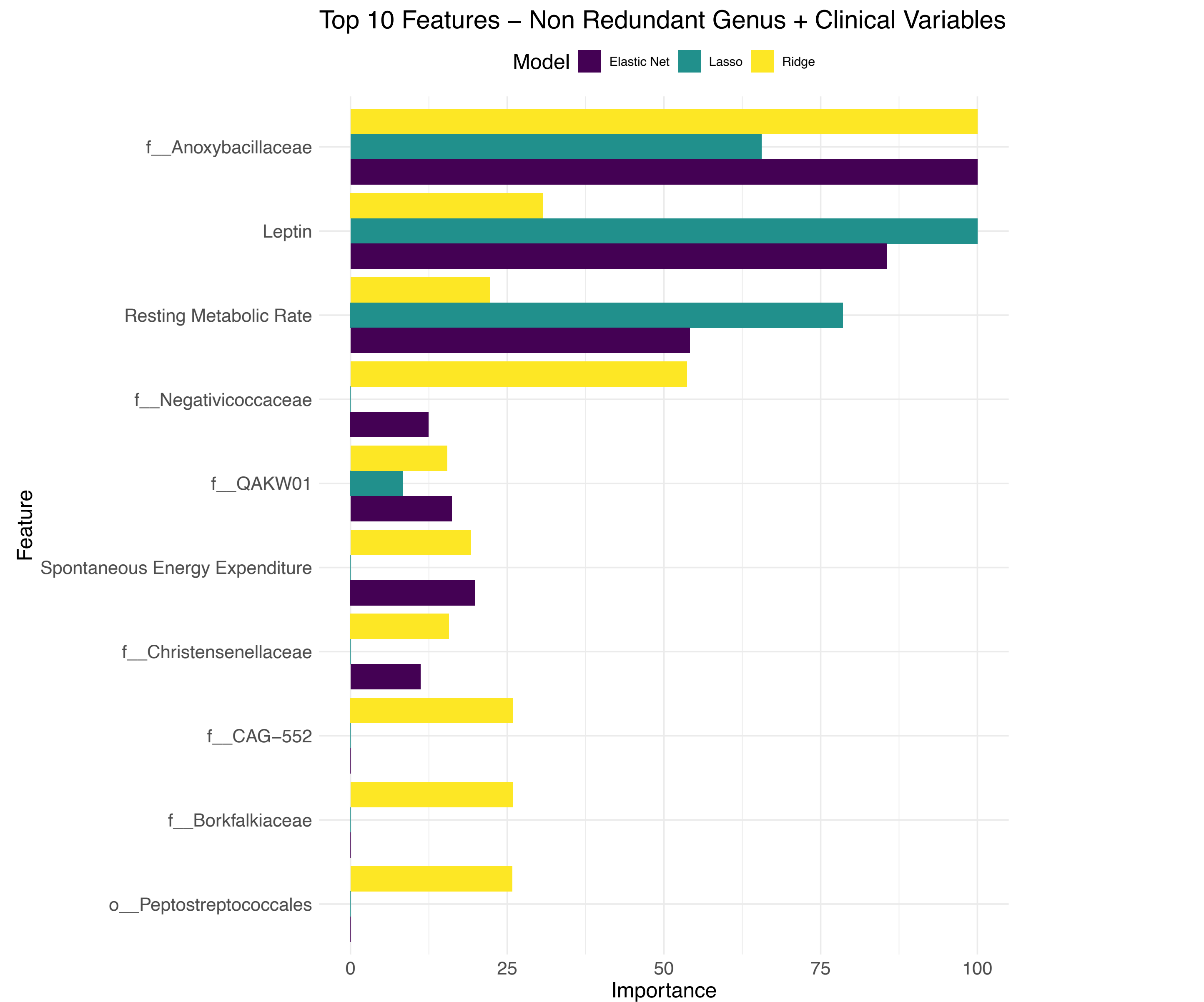
\*Train:Test Split & Cross Validation



# Test $R^2$ Metrics



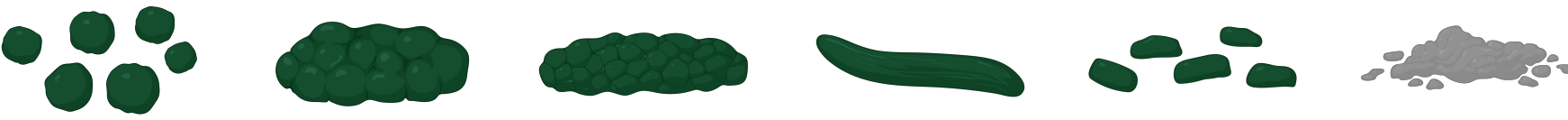
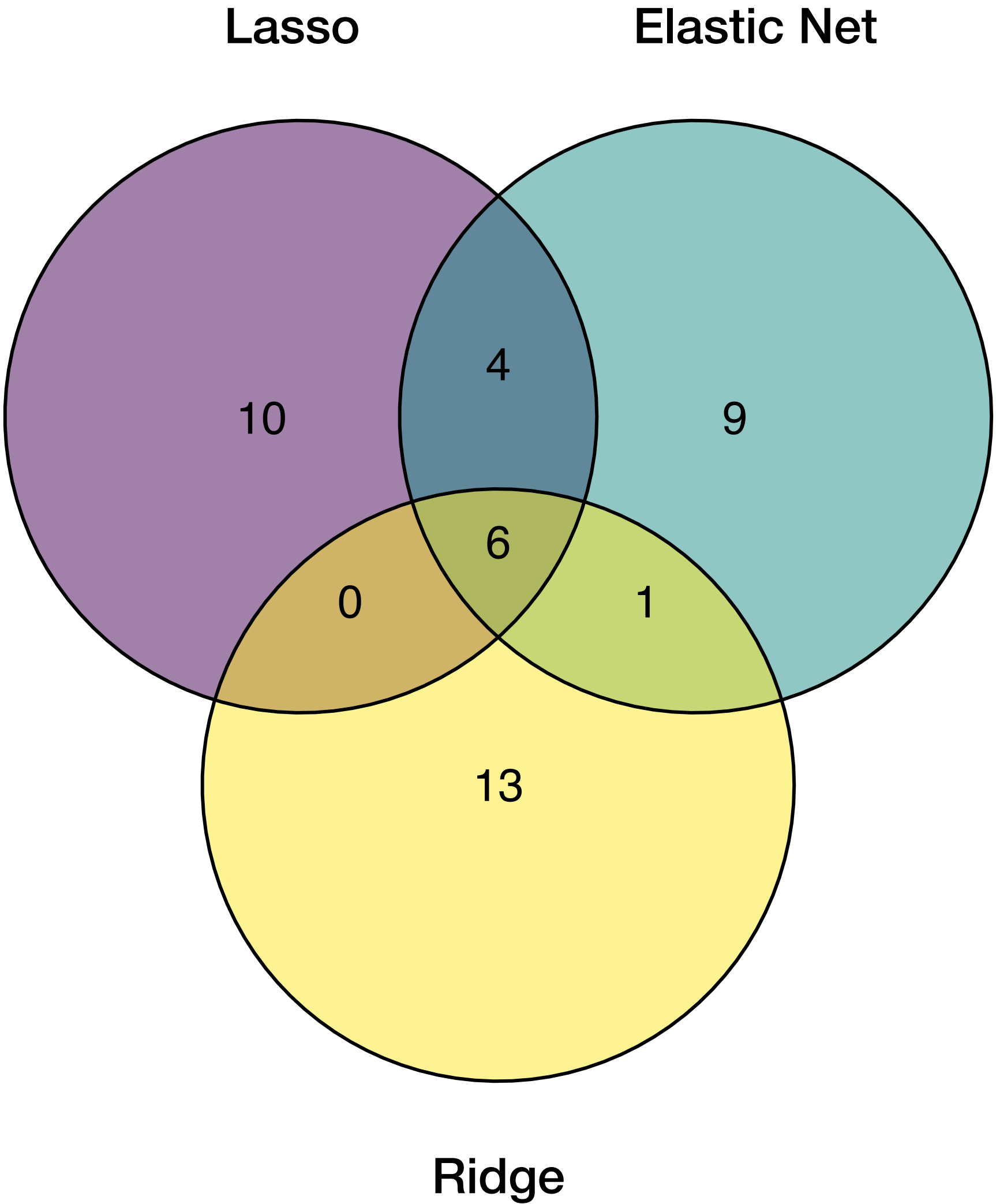
# Comparing Top 10 Features Across Models





Non Redundant Species + Clinical Variables Top 20  
Features Venn diagram

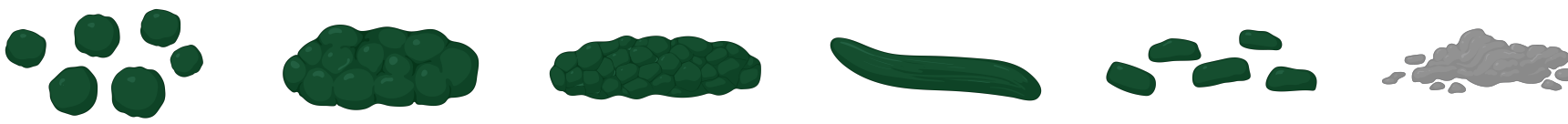
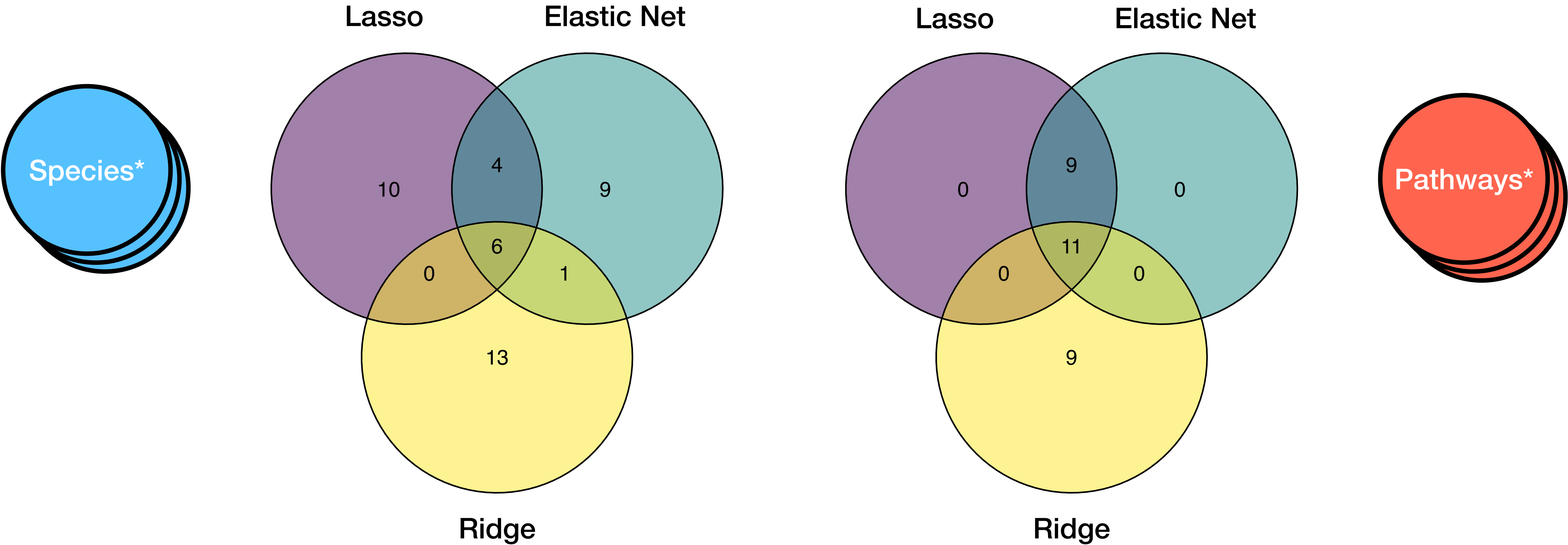
# Feature Comparison



# Species and Pathways Feature Comparison

Non Redundant Species + Clinical  
Variables Top 20 Features Venn diagram

All Pathways + Clinical Variables  
Top 20 Features Venn diagram



# Conclusions and Discussions

## 1. Gut Microbiota and Clinical Variables Influence BMI Discrepancies

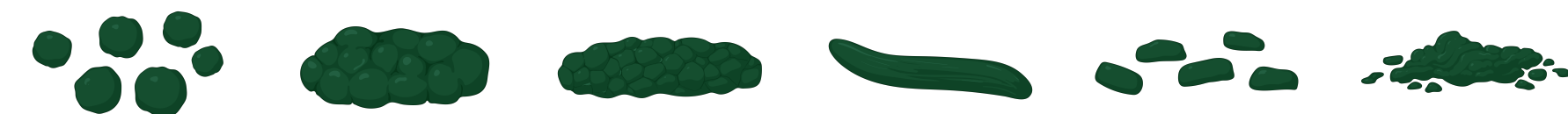
- Microbial species, genera, and pathways significantly associated with differences between actual and genetically predicted BMI
- Key clinical features
  - Leptin
  - Total Daily Energy Expenditure
  - Resting Metabolic Rate
  - Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)

## 2. Elastic Net, Lasso, and Ridge Performed Best

- Testing  $R^2$ 
  - Elastic Net: 0.35
  - Lasso: 0.27
  - Ridge: 0.26

## 3. Implications for Personalized Obesity Interventions

- Identified features provide potential targets for tailored weight management strategies
- Incorporating gut microbiota composition can refine obesity treatment approaches





# Thank you



Dr. Maggie Stanislawski



Ashley Scadden



Emily Yeo

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Jennifer Fouquier  
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Questions?