

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

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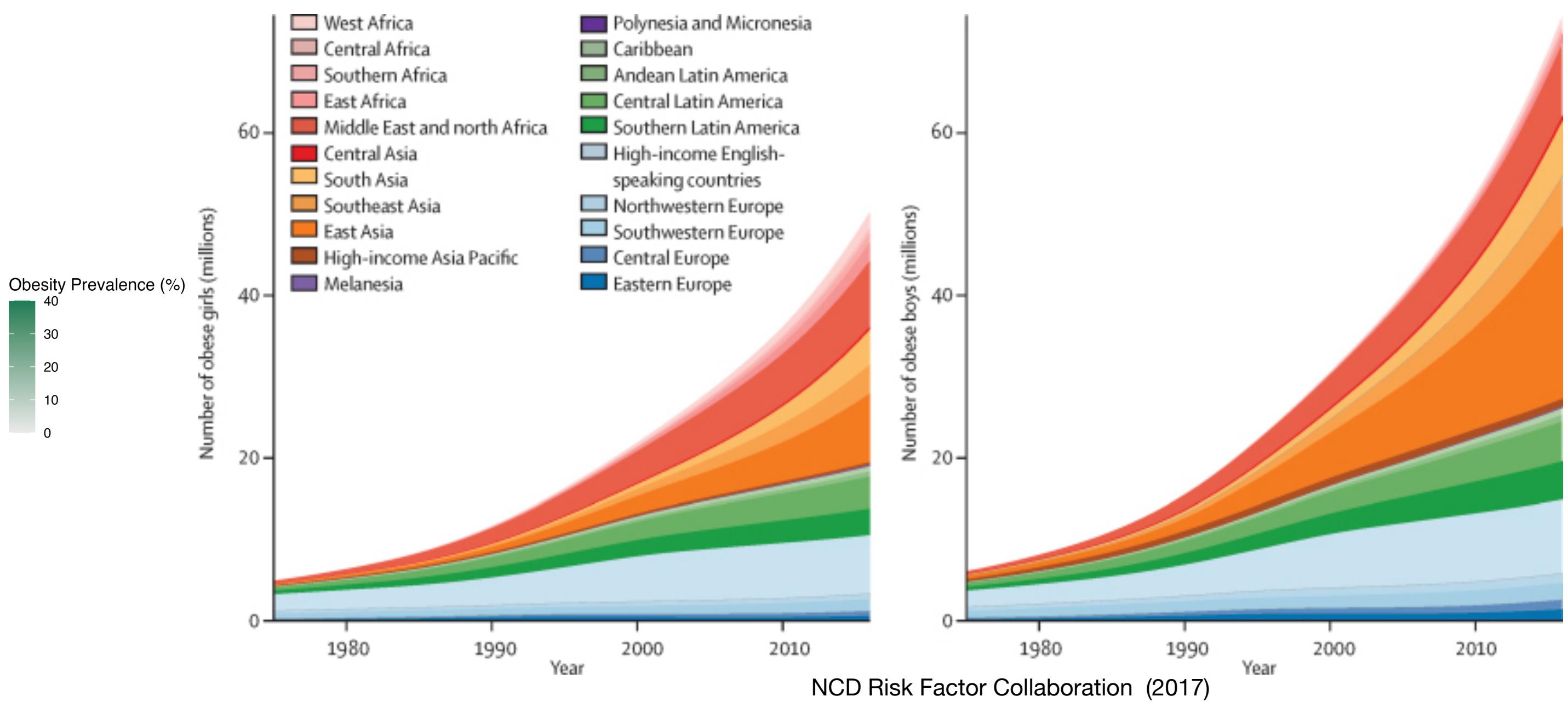
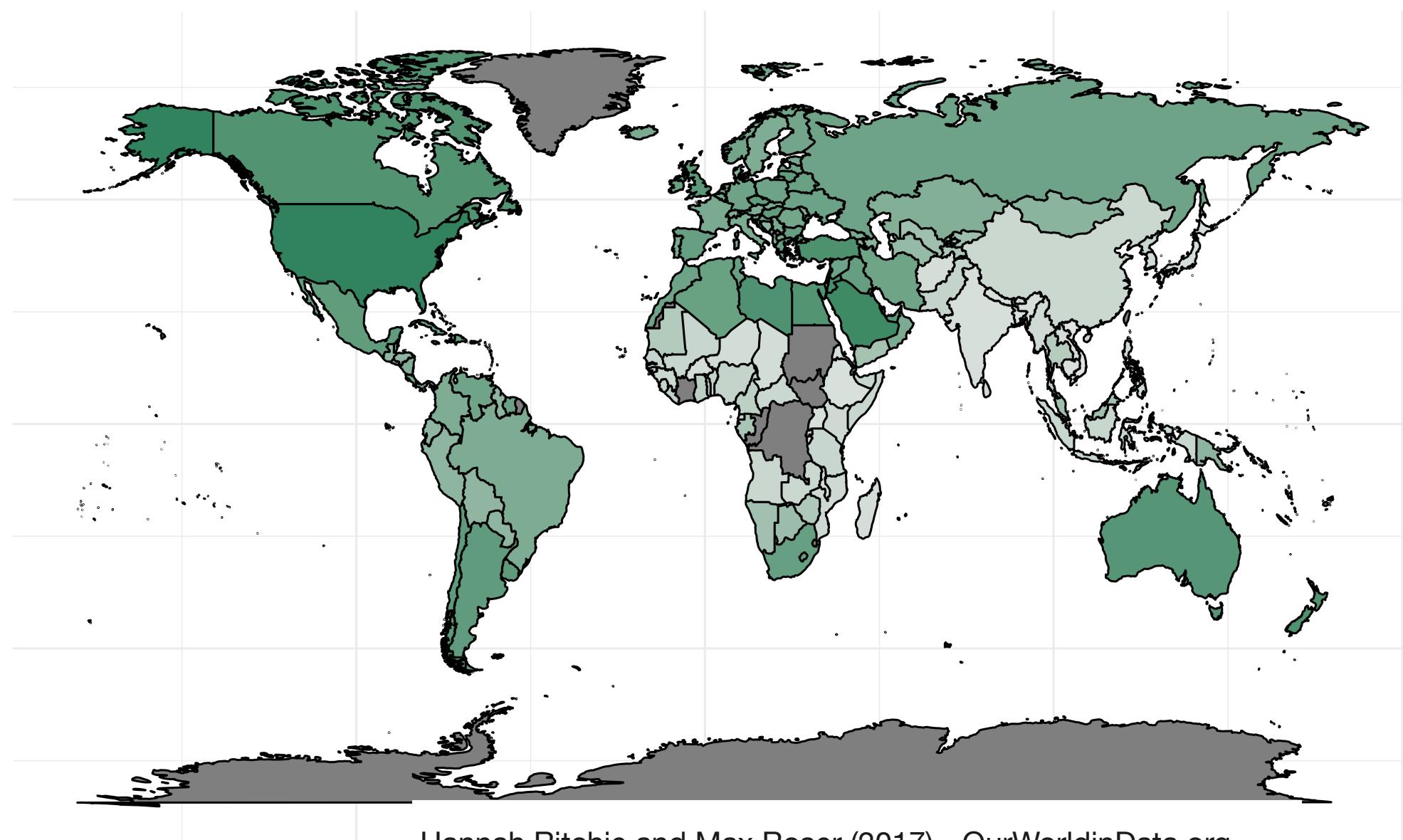
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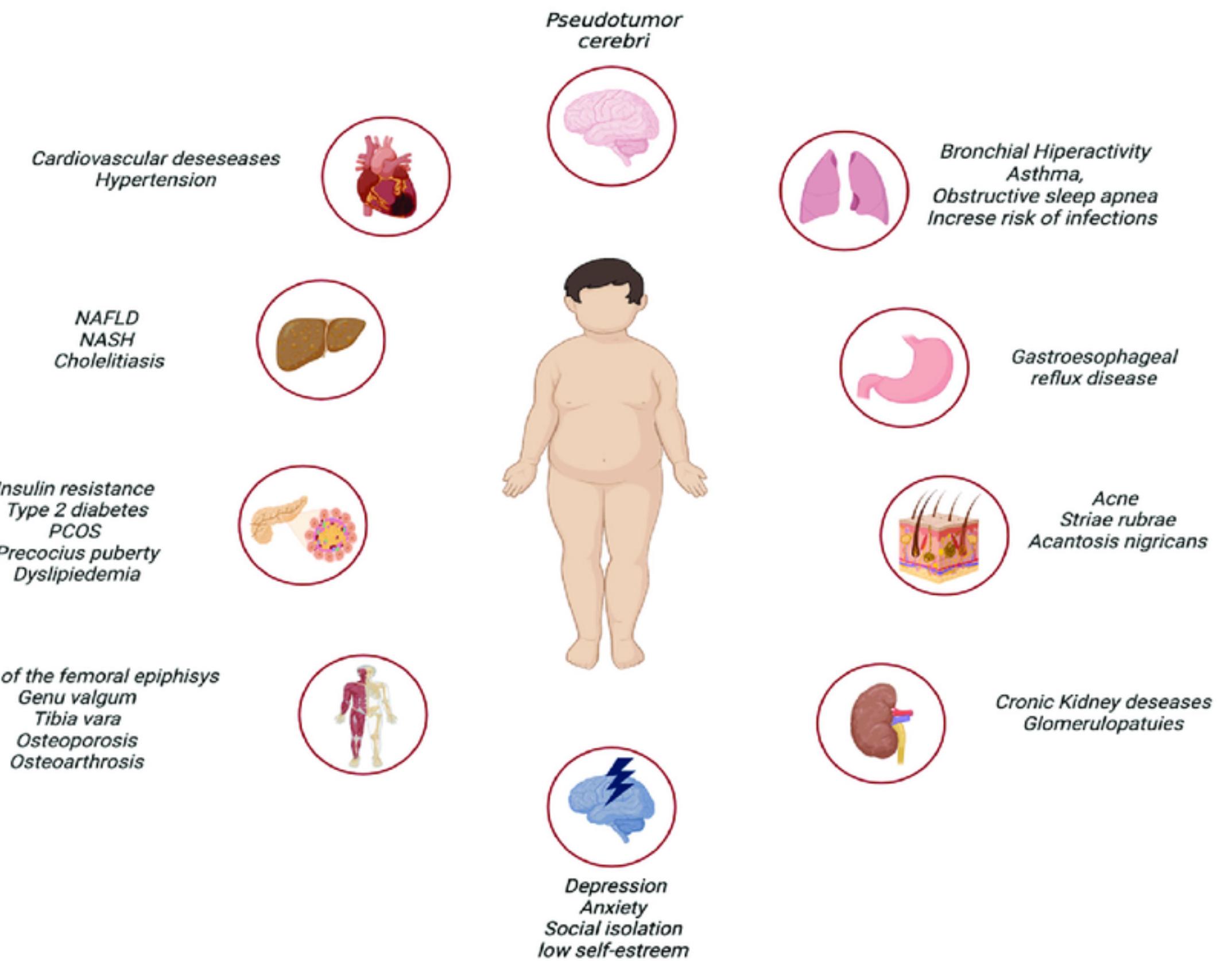
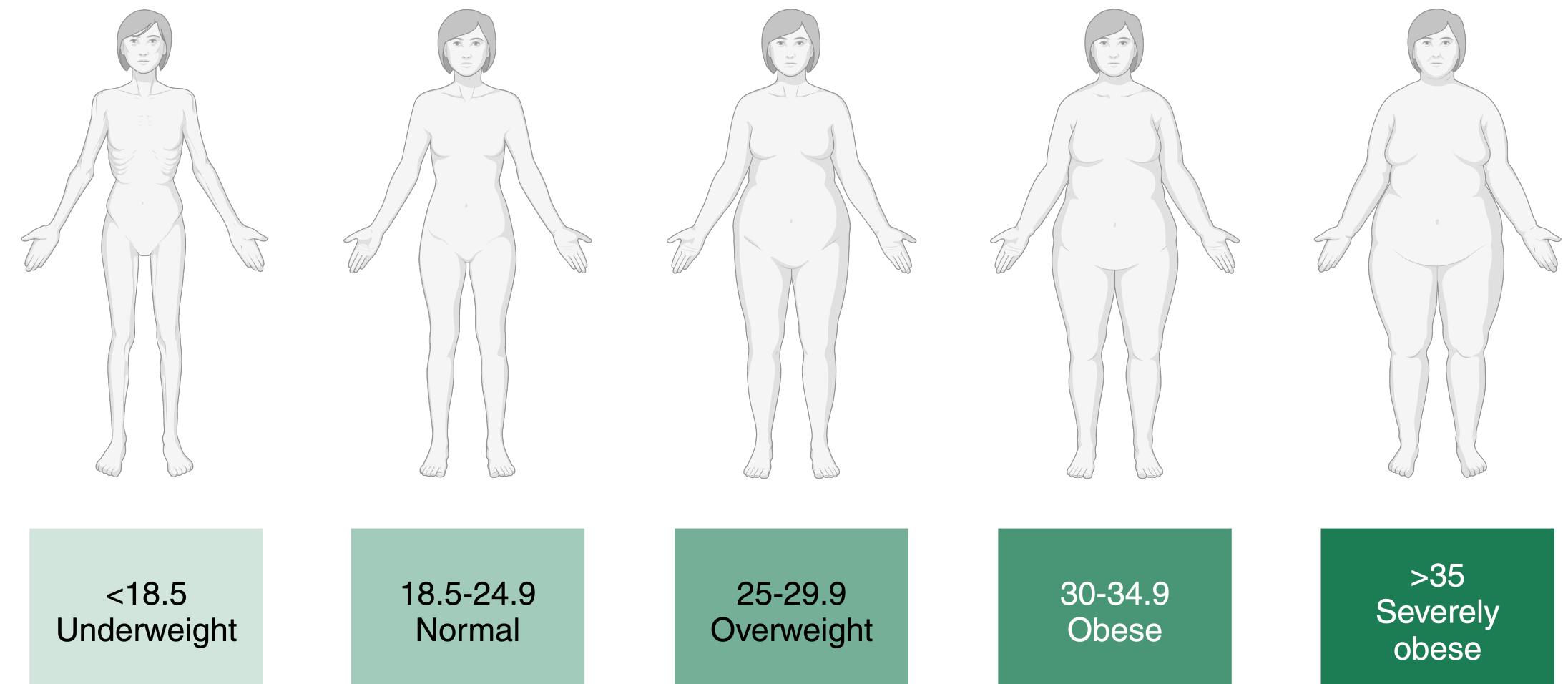
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Obesity is an epidemic

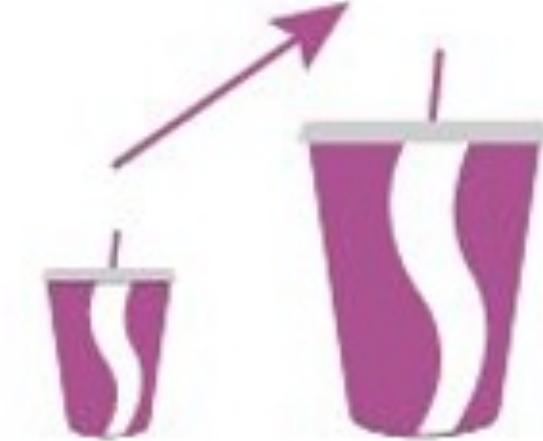
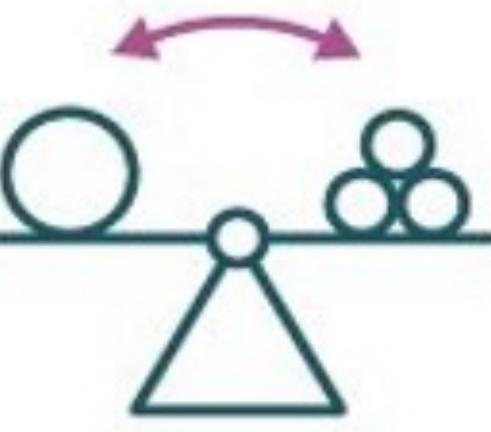
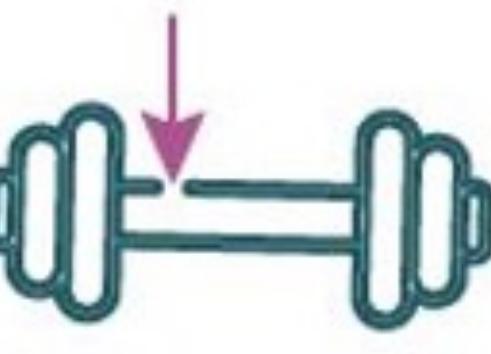


Obesity is a chronic disease

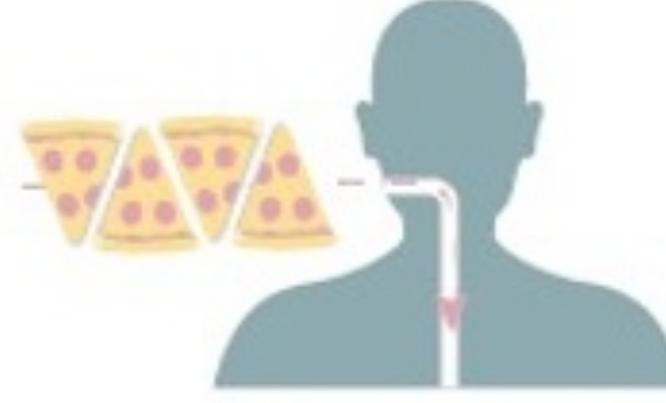
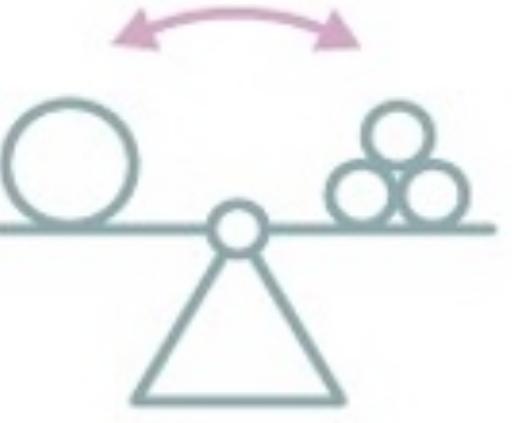
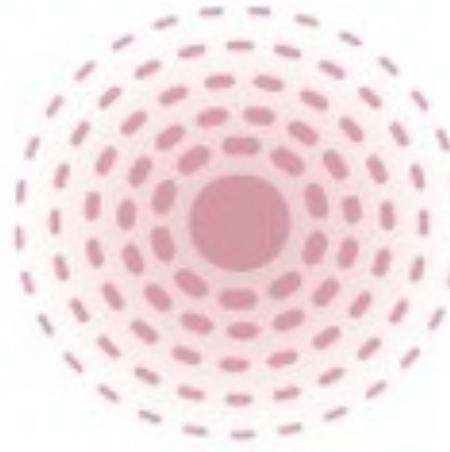
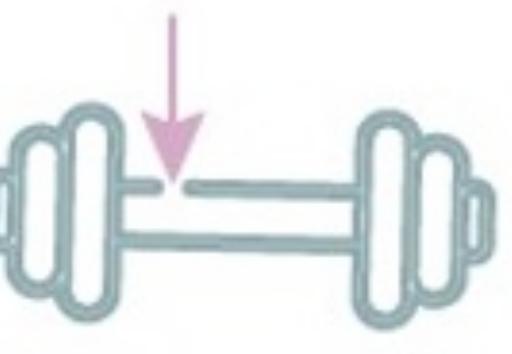


Calcaterra et al. 2023

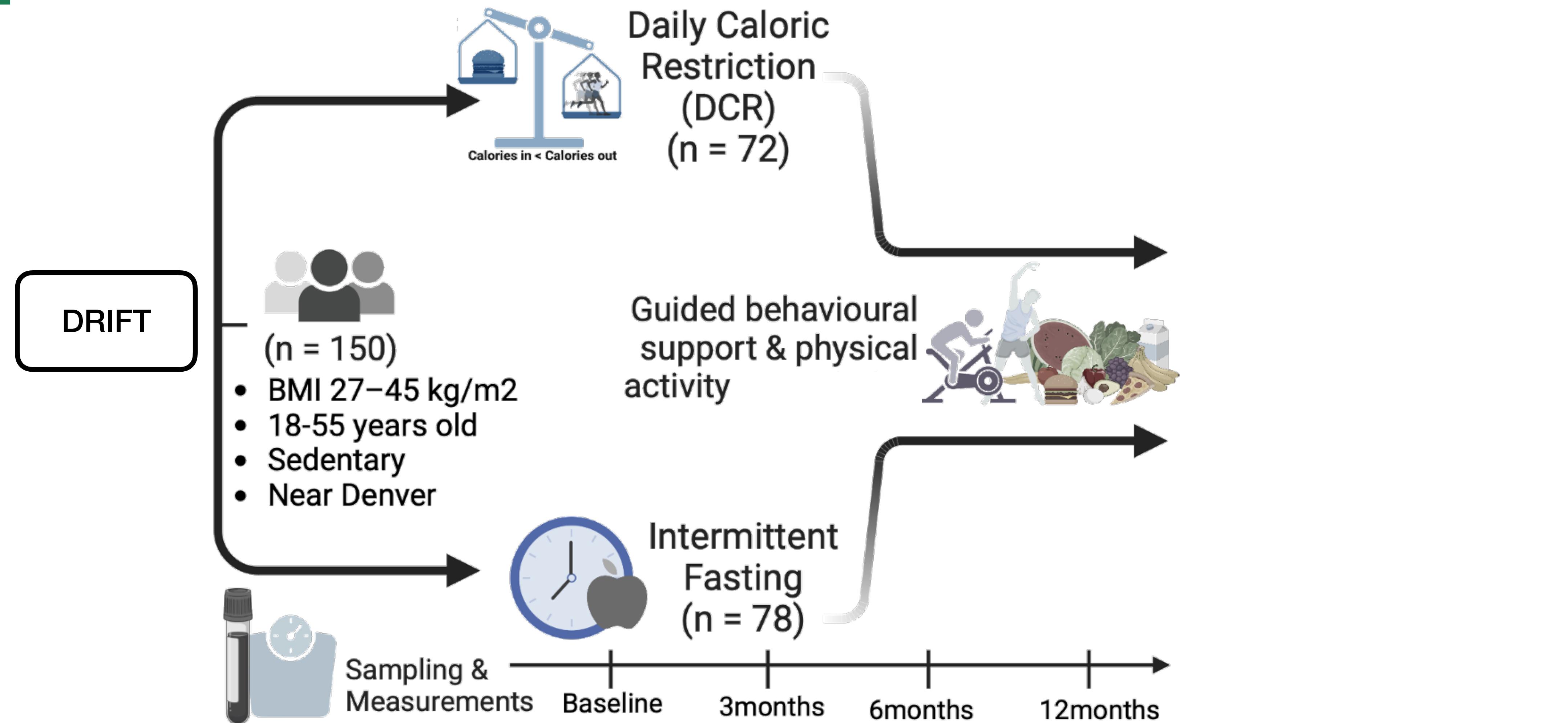
Potential Causes of Obesity

INTERNAL			EXTERNAL		
					
Hyper-reactivity to food cues	Heightened hunger response	Delayed satiety	Availability of high-calorie foods	Larger portion sizes	Diet patterns
					
Chronic inflammation	Genetics	Gut microbiota	Stress	More sedentary time	Less physical activity

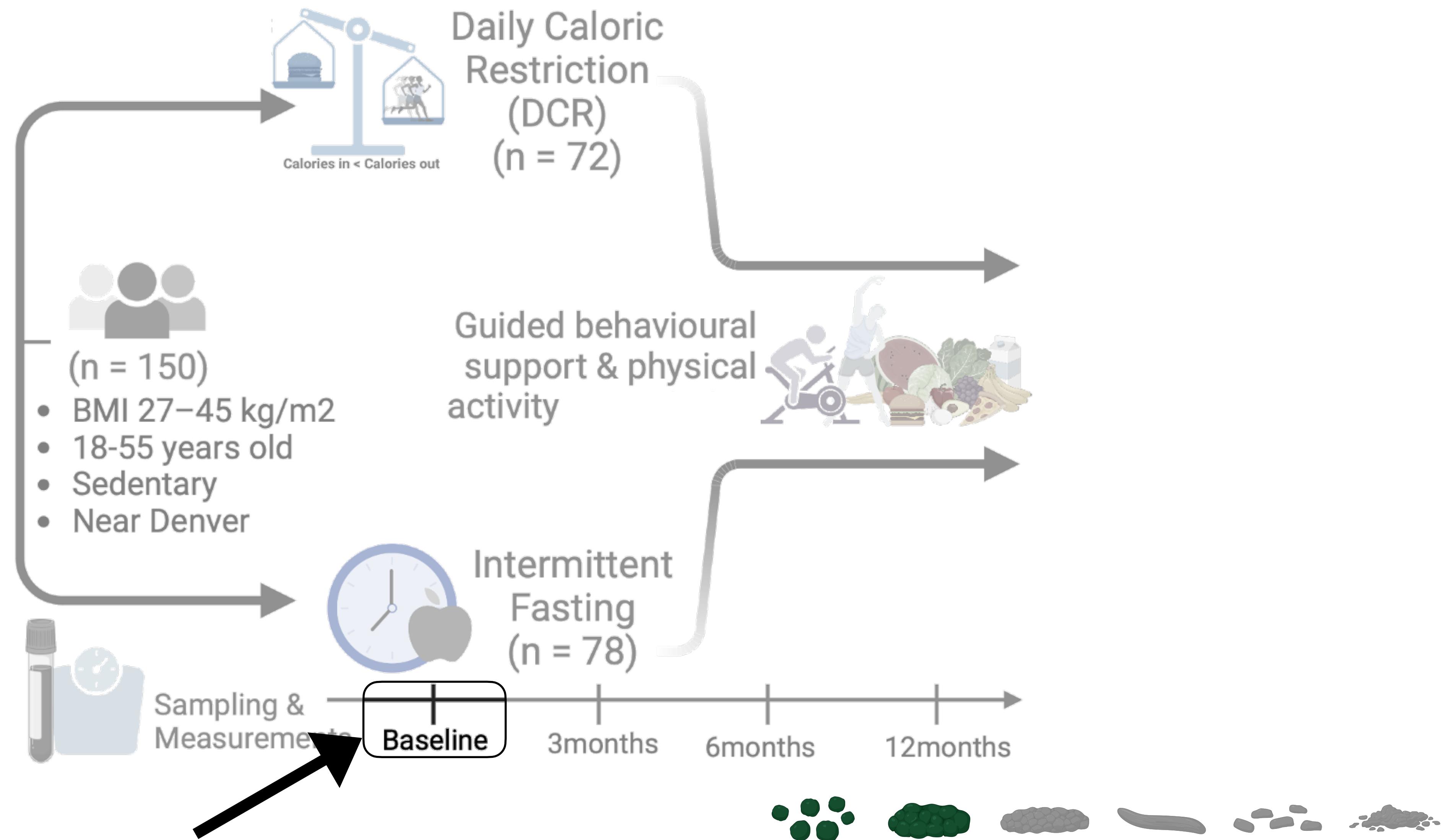
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Daily Caloric Restriction vs Intermittent Fasting Trial DRIFT



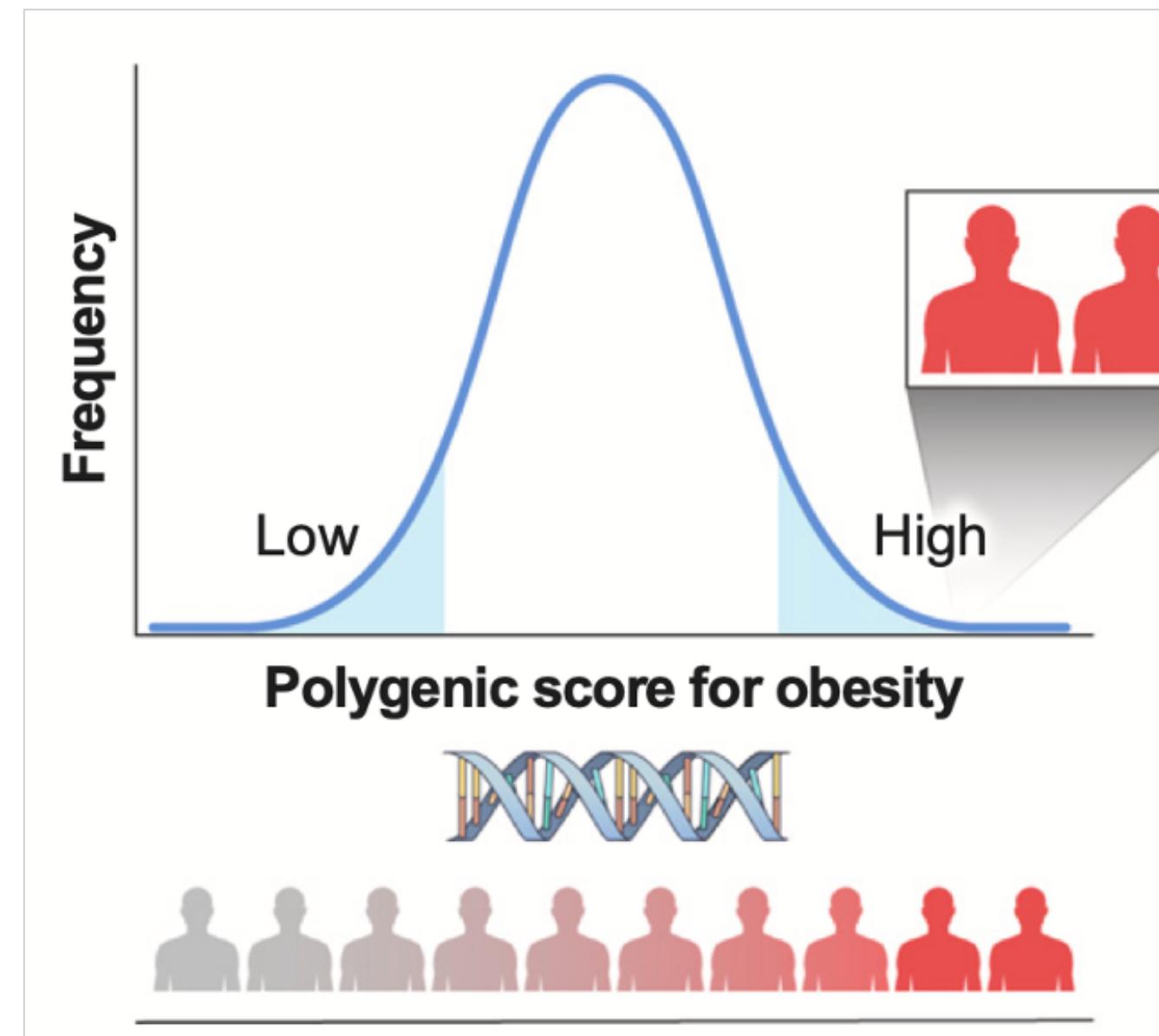
Daily Caloric Restriction vs Intermittent Fasting Trial DRIFT



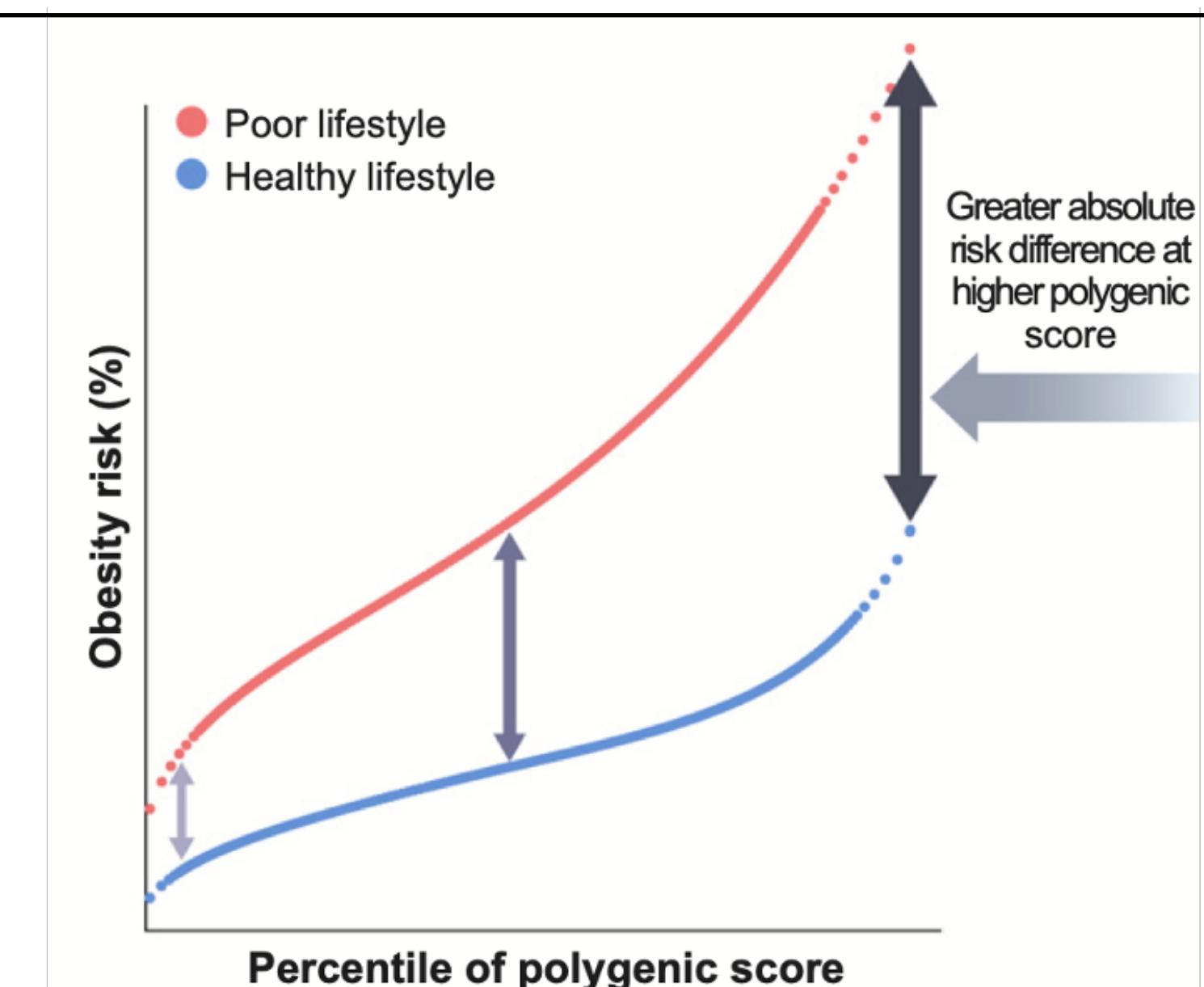
Research Questions

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?

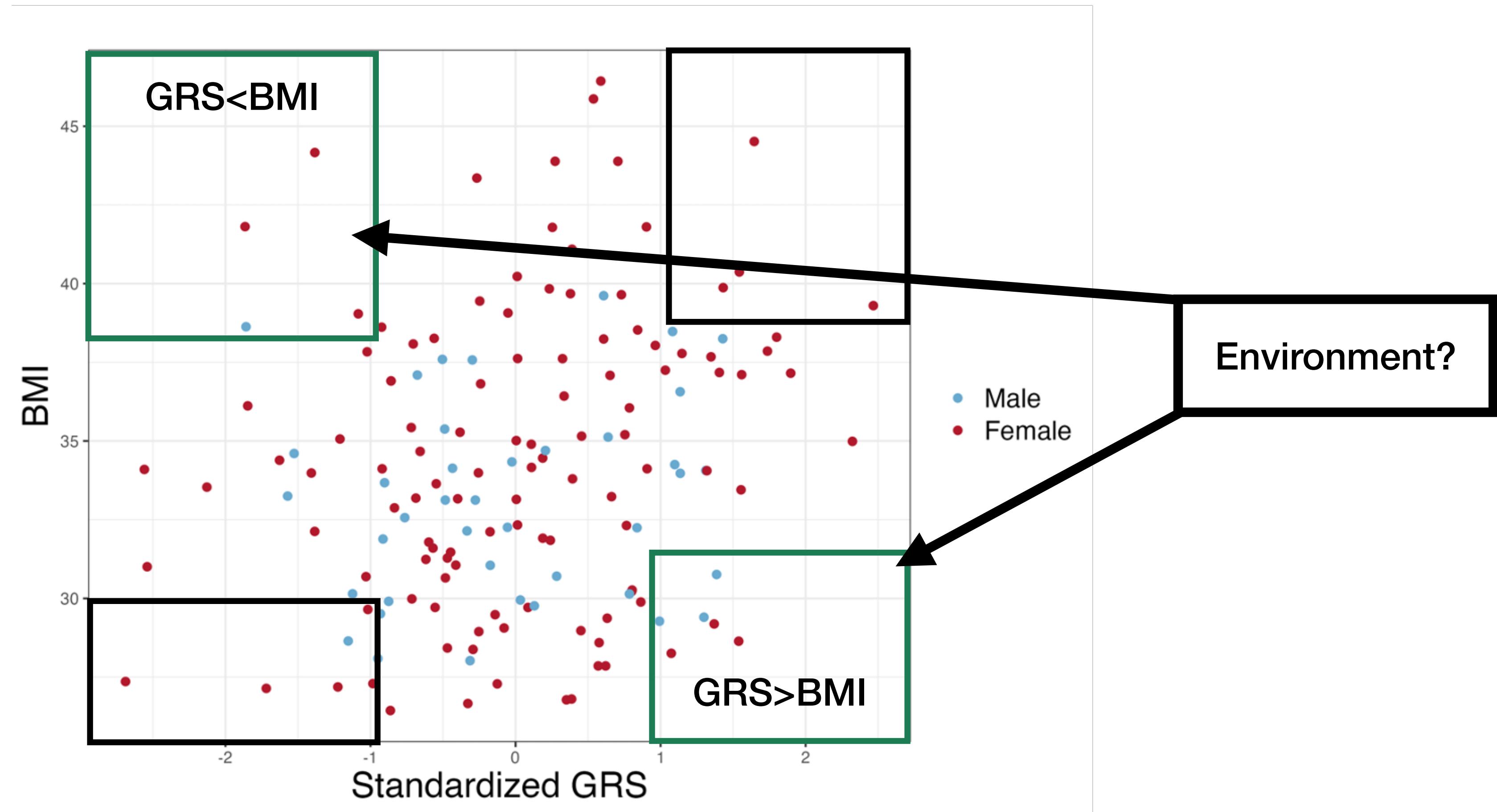


Research Questions

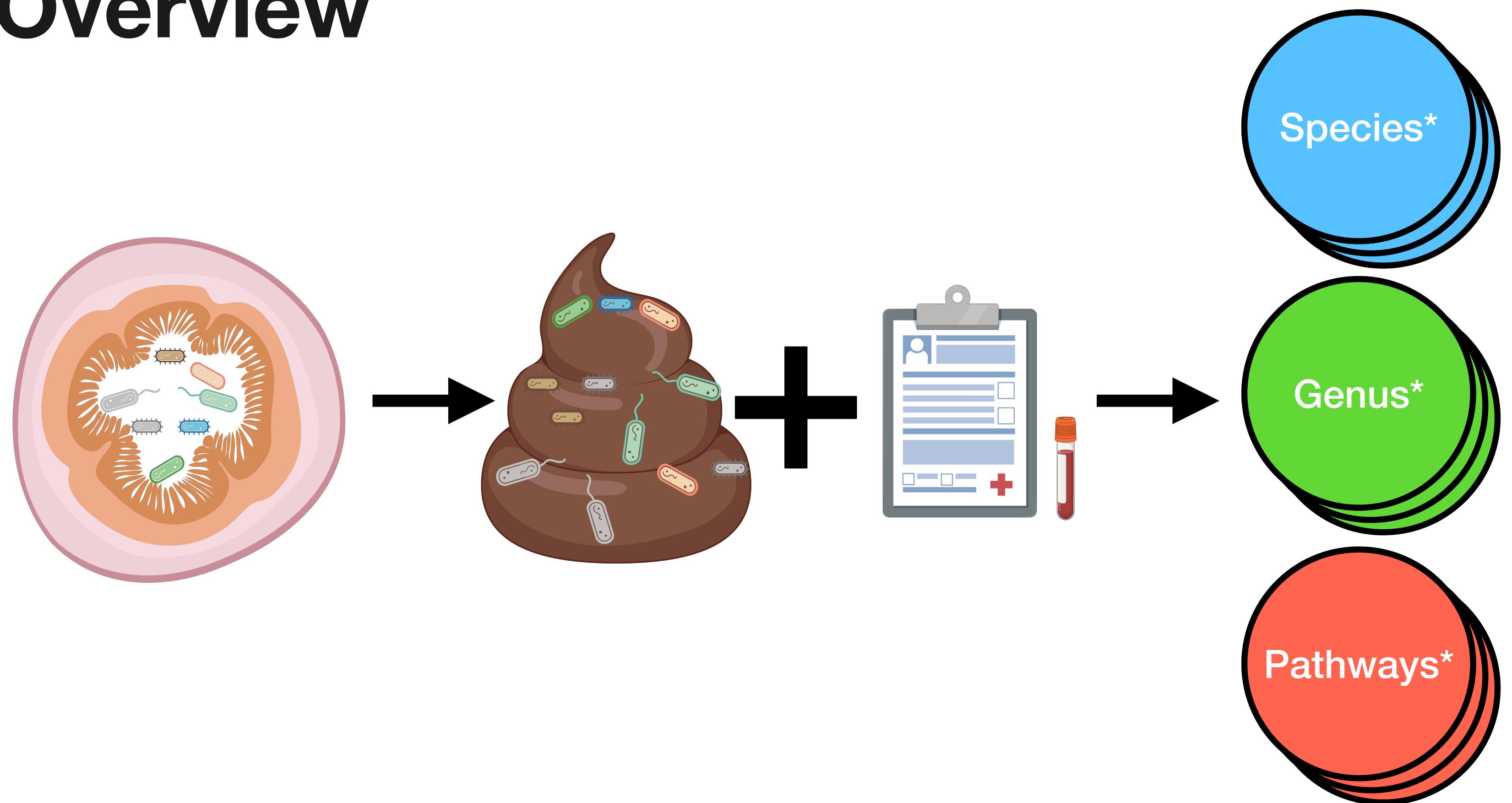
Are there associations between participant BMI genetic risk scores and weight loss?
(Emily Yeo & Ashley Scadden)

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



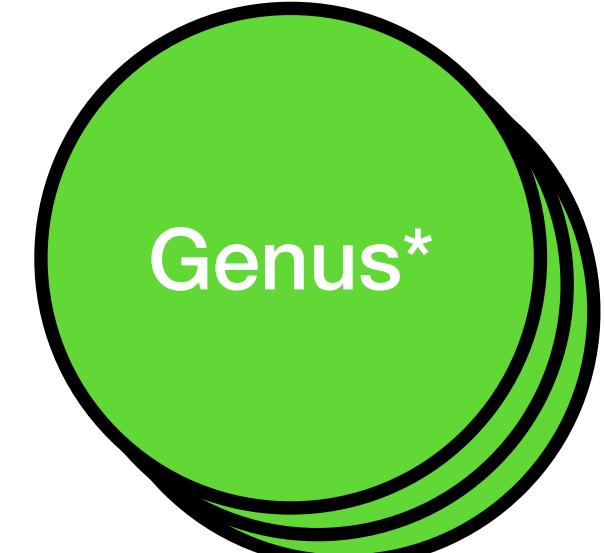
*Taxa, w/, w/o clinical information &
minus redundant features

Dataset, Models, and Metrics Overview

Datasets



Species*



Genus*



Pathways*

Models

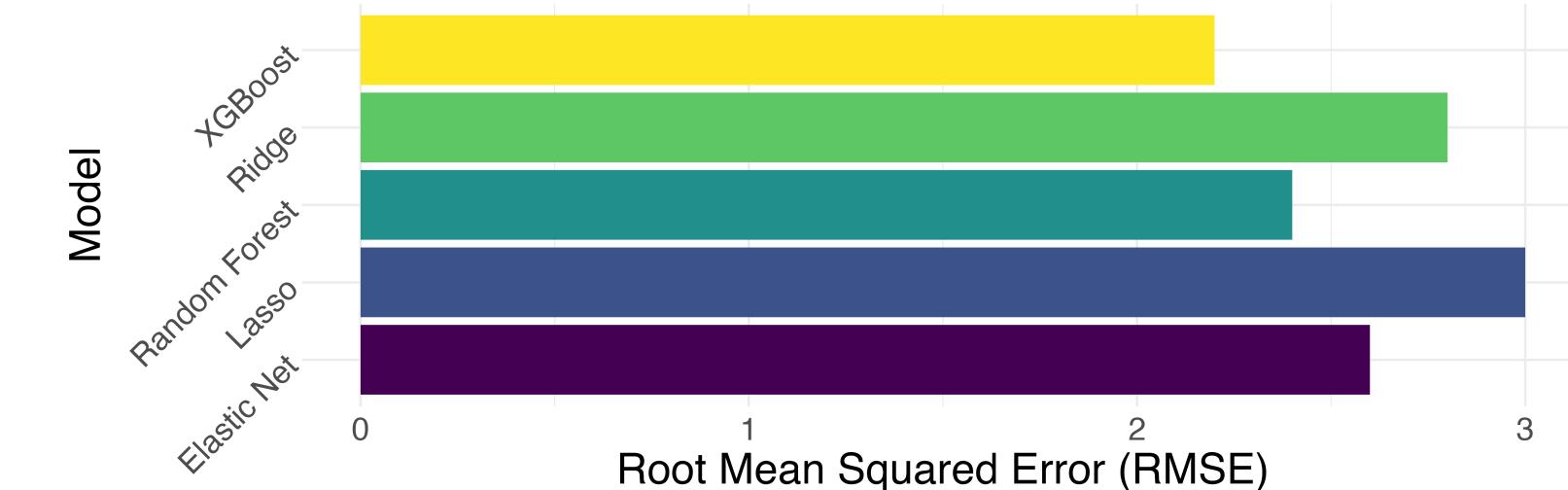
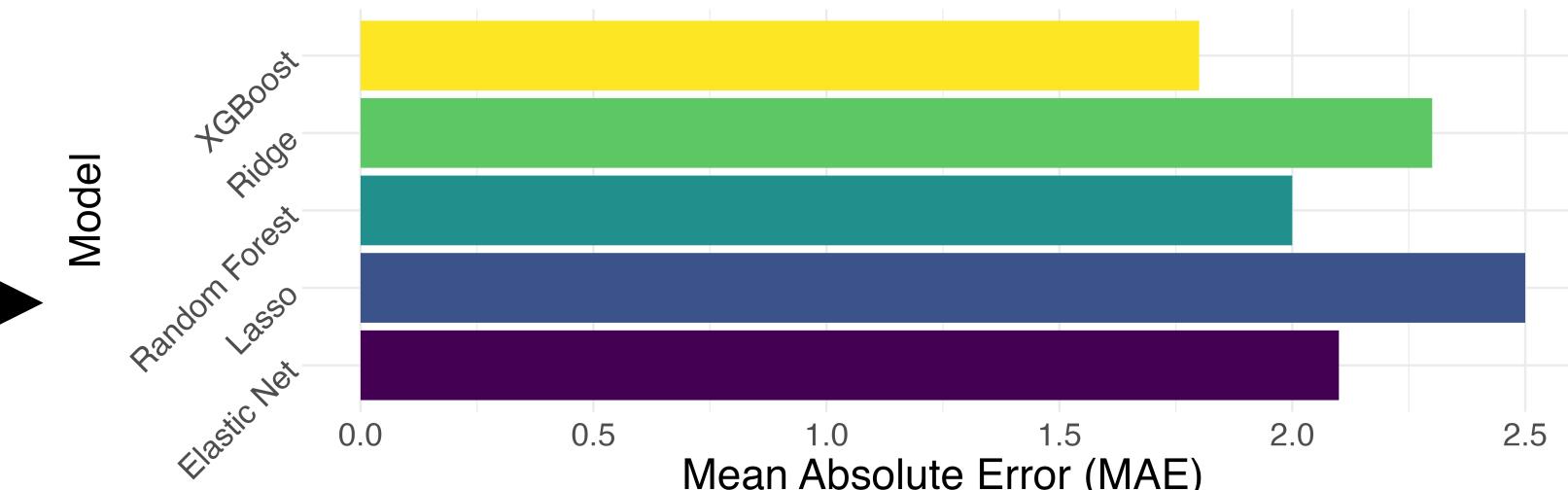
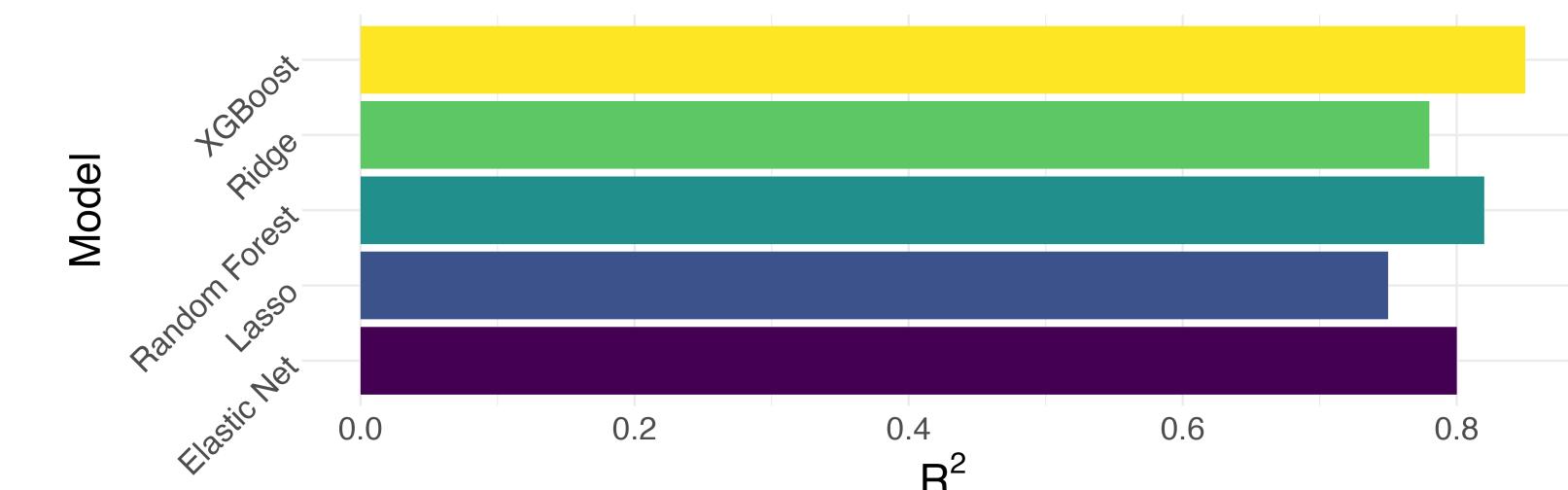
Penalized Regression Models

Elastic Net
Lasso
Ridge

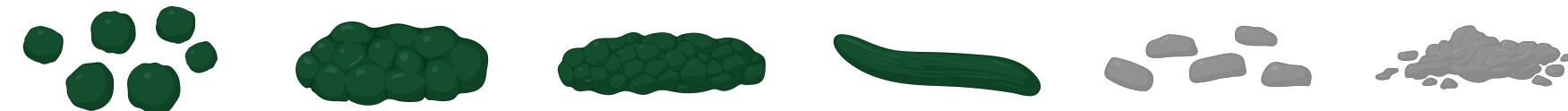
Ensemble Learning Methods

Random Forest
XGBoost

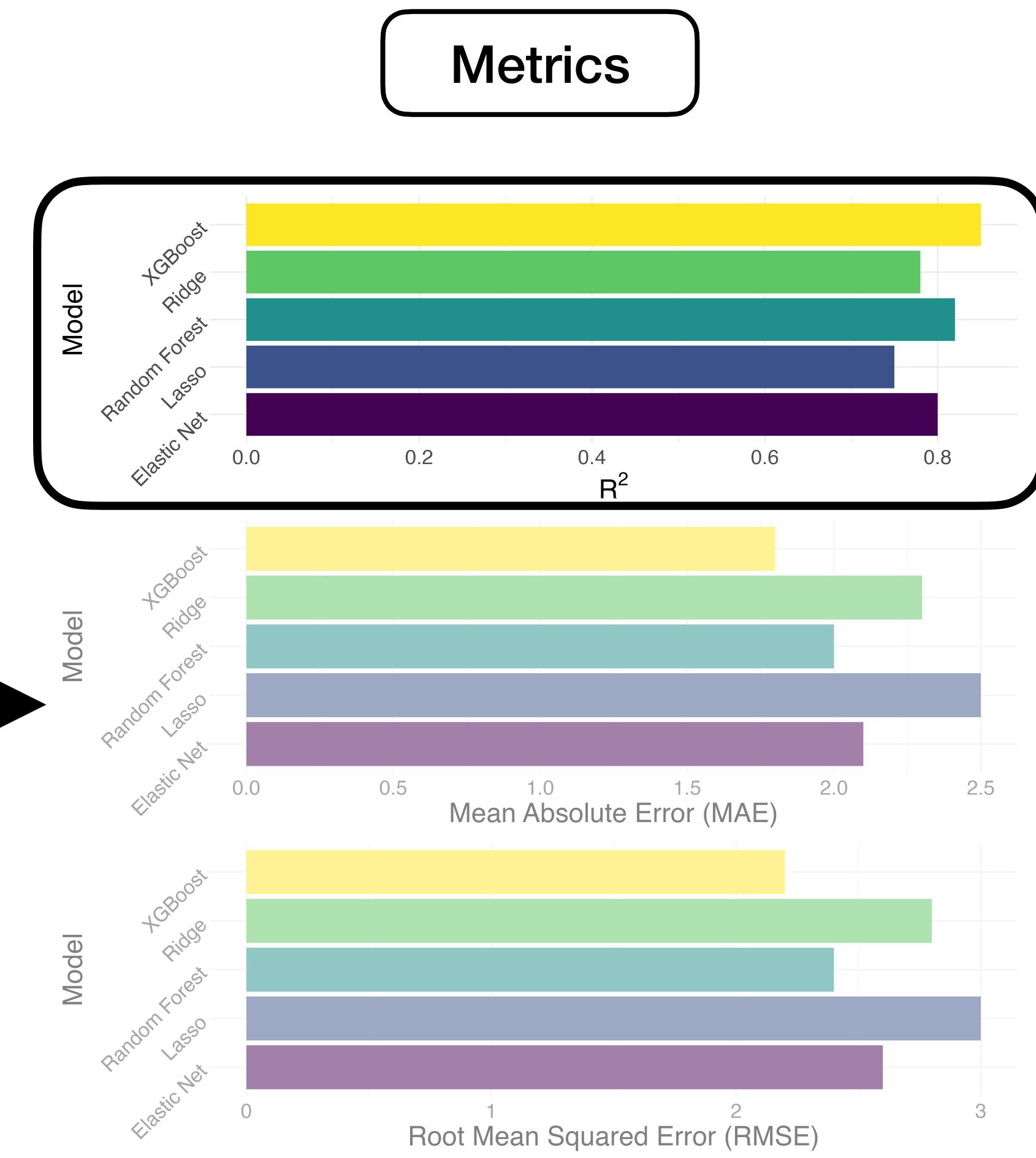
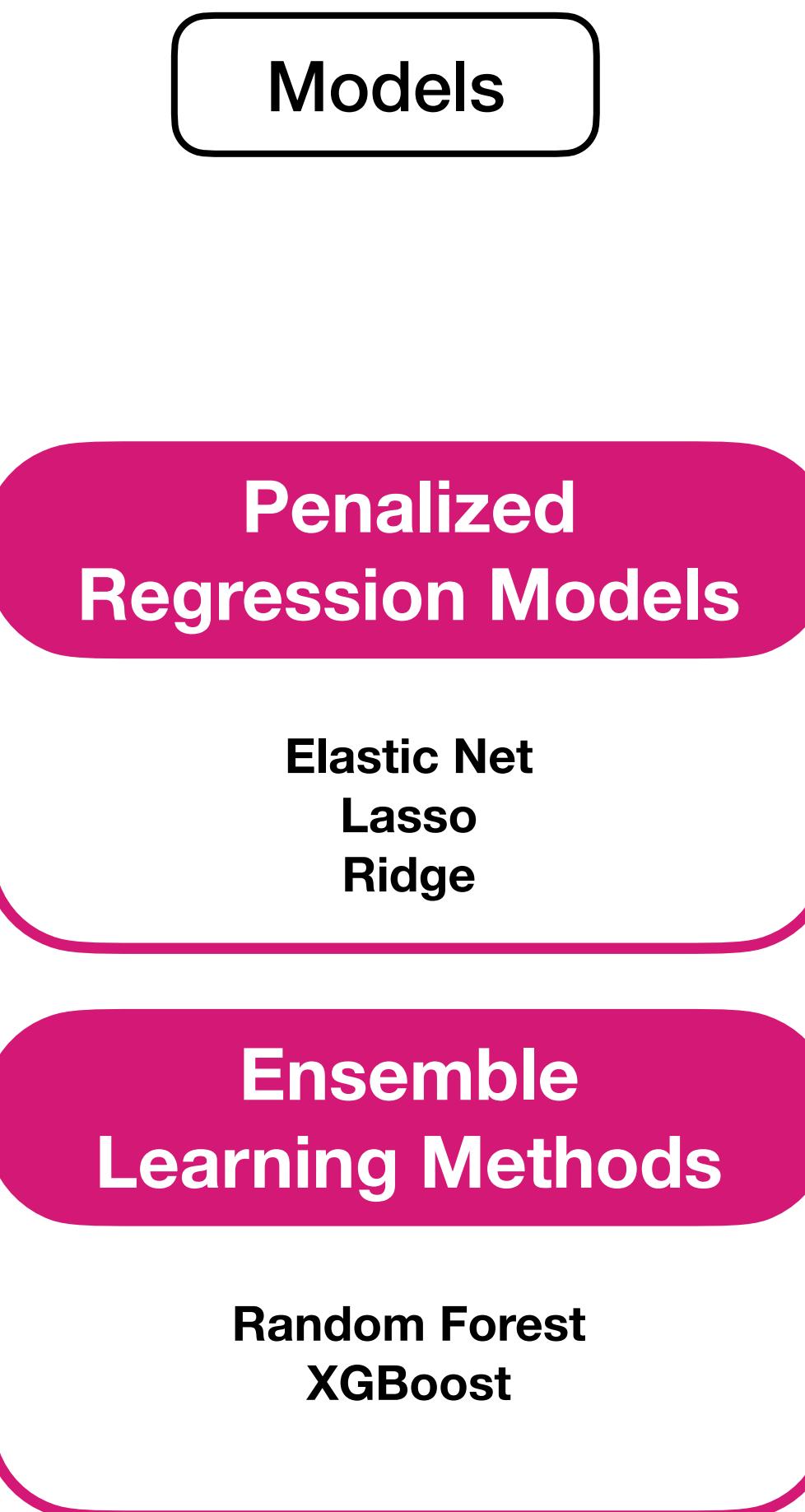
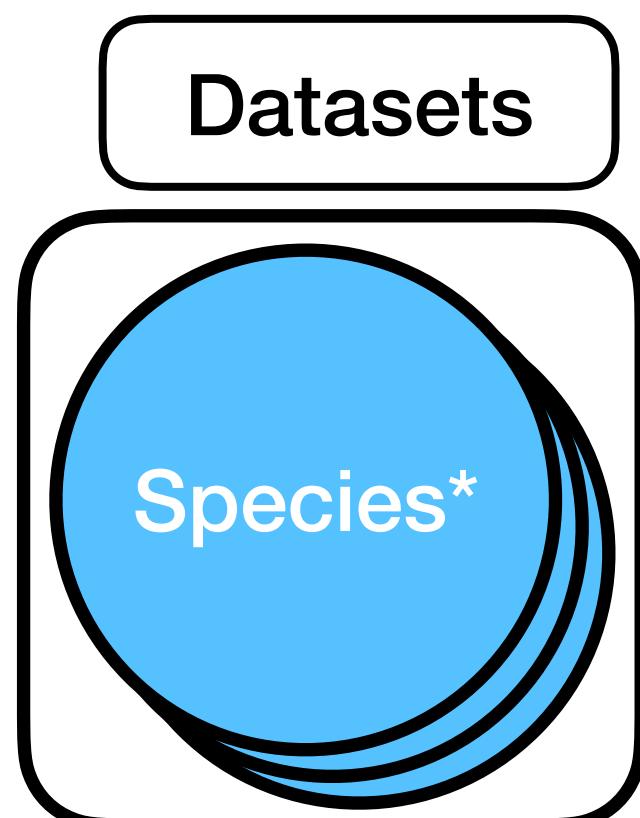
Metrics



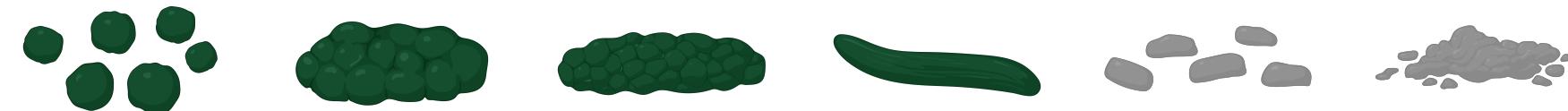
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Dataset, Models, and Metrics Overview

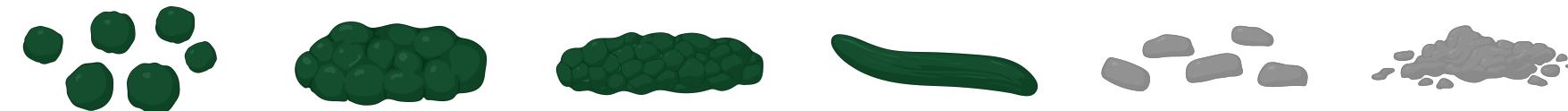
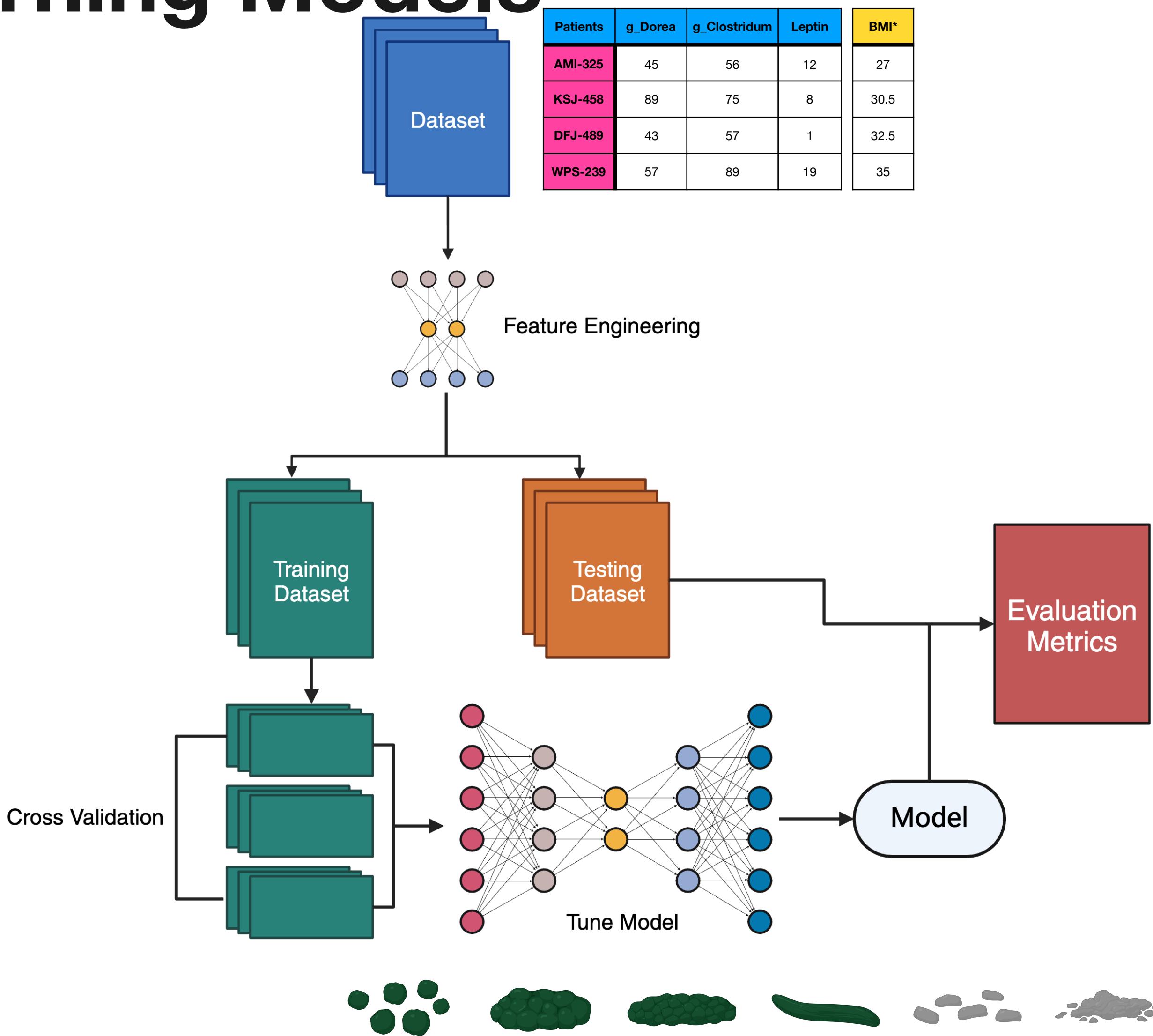


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Overview of Machine Learning Models

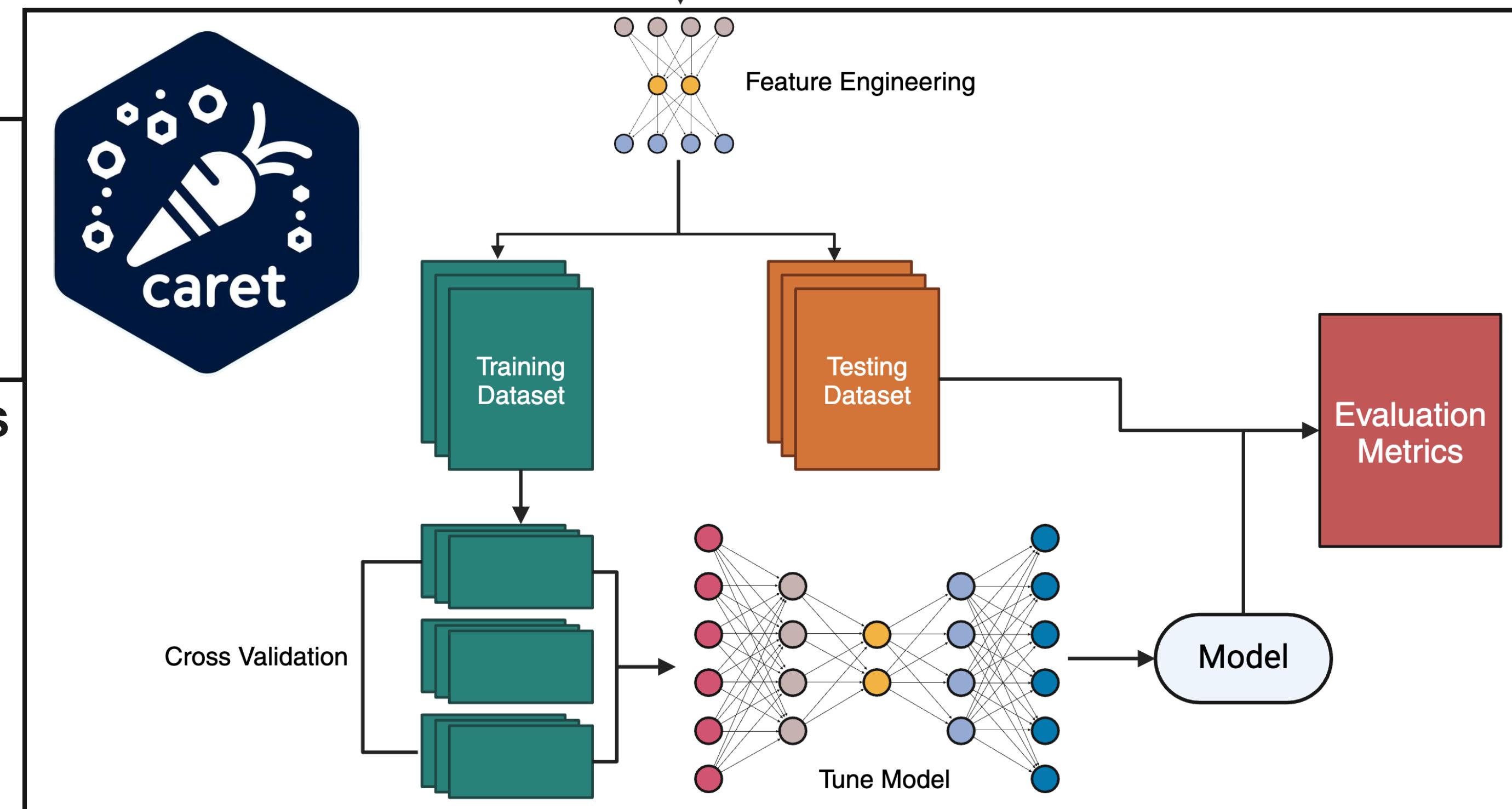
1. Understand and Prepare Data
2. Feature Engineering
3. Split the Dataset
4. Train the Model
5. Test and Evaluate the Model
6. Interpret and Communicate the Results
7. Iterate and Improve



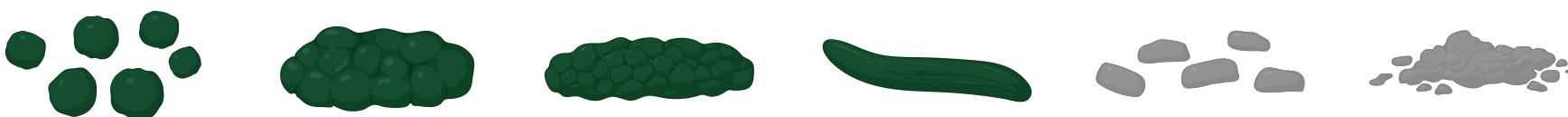
Overview of Machine Learning Models

Patients	g_Dorea	g_Clostridum	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

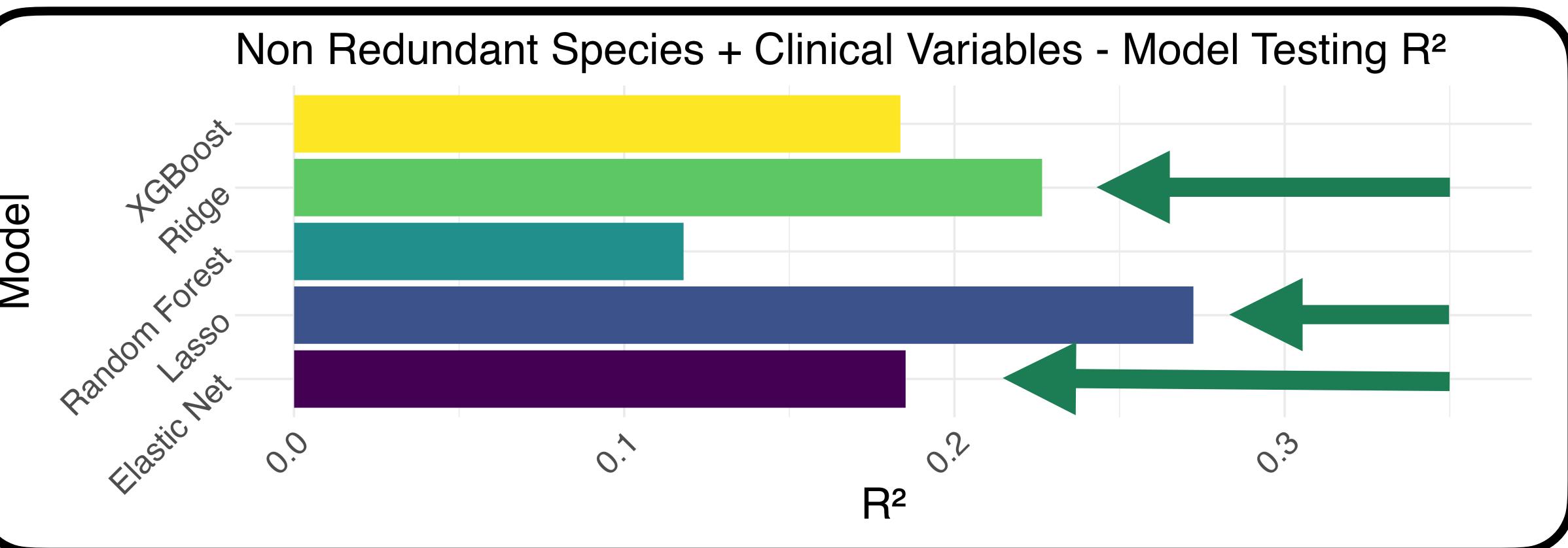
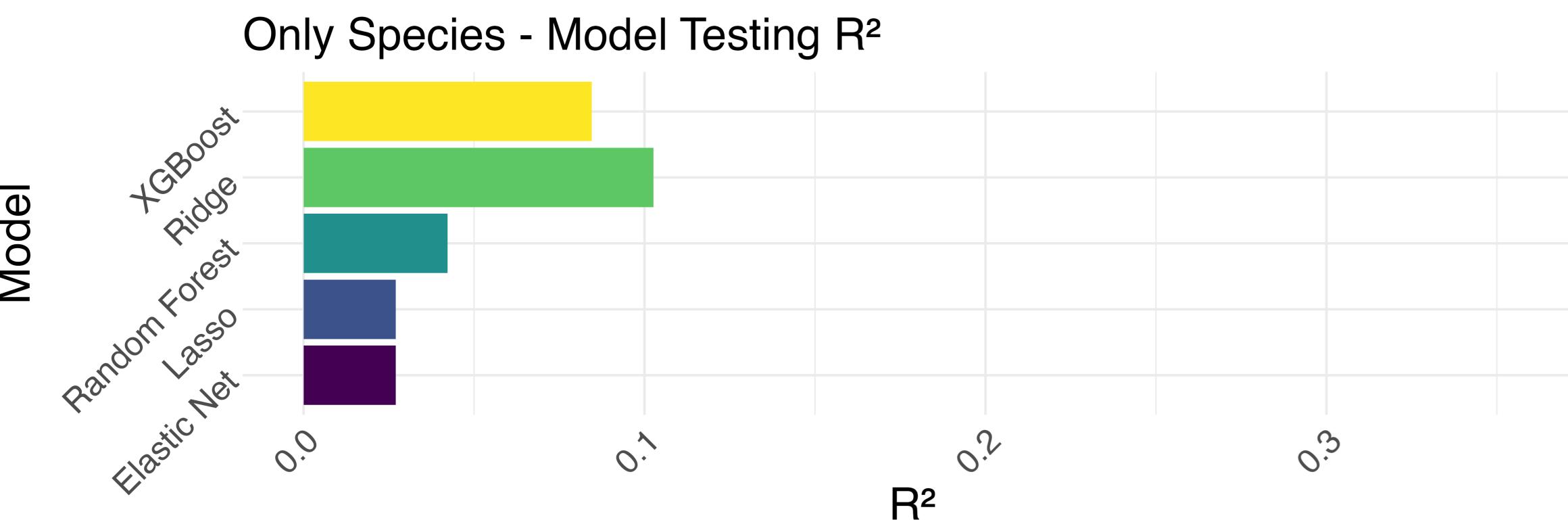
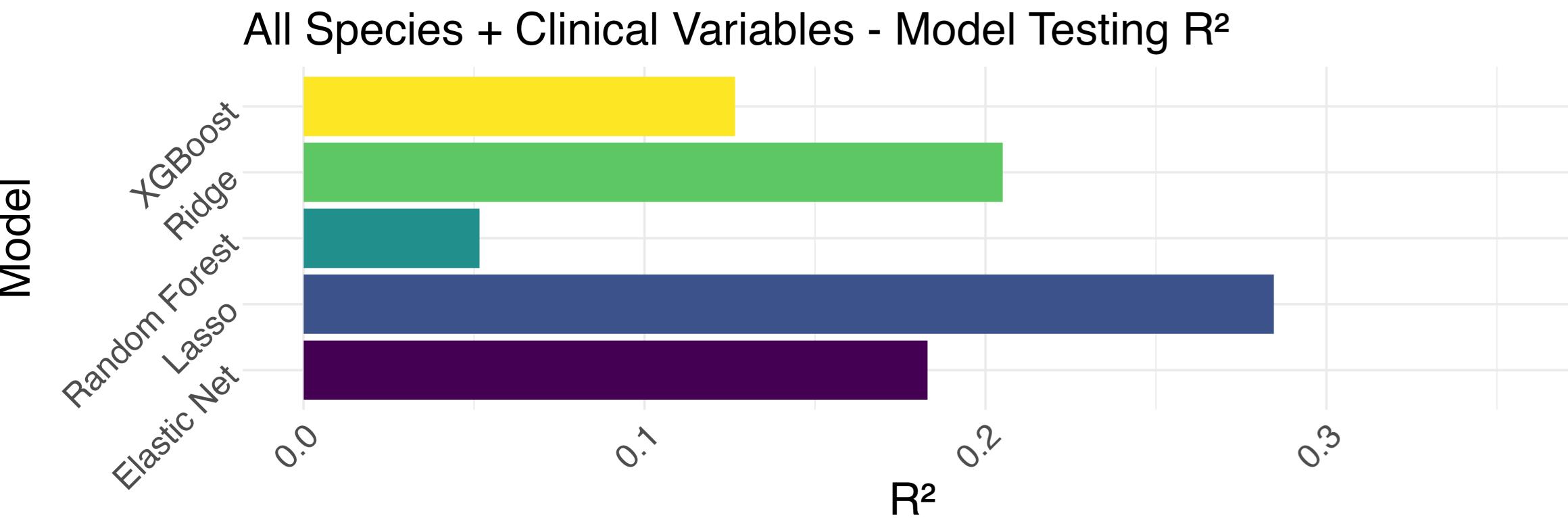
1. Understand and Prepare Data
2. Feature Engineering
3. Split the Dataset
4. Train the Model*
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*Train:Test Split & Cross Validation



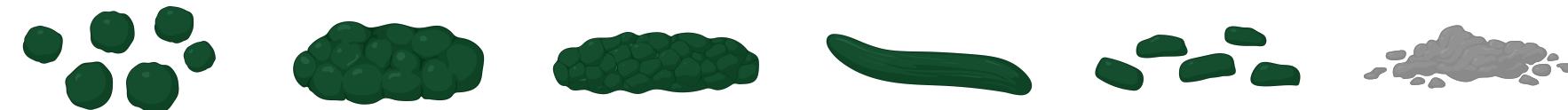
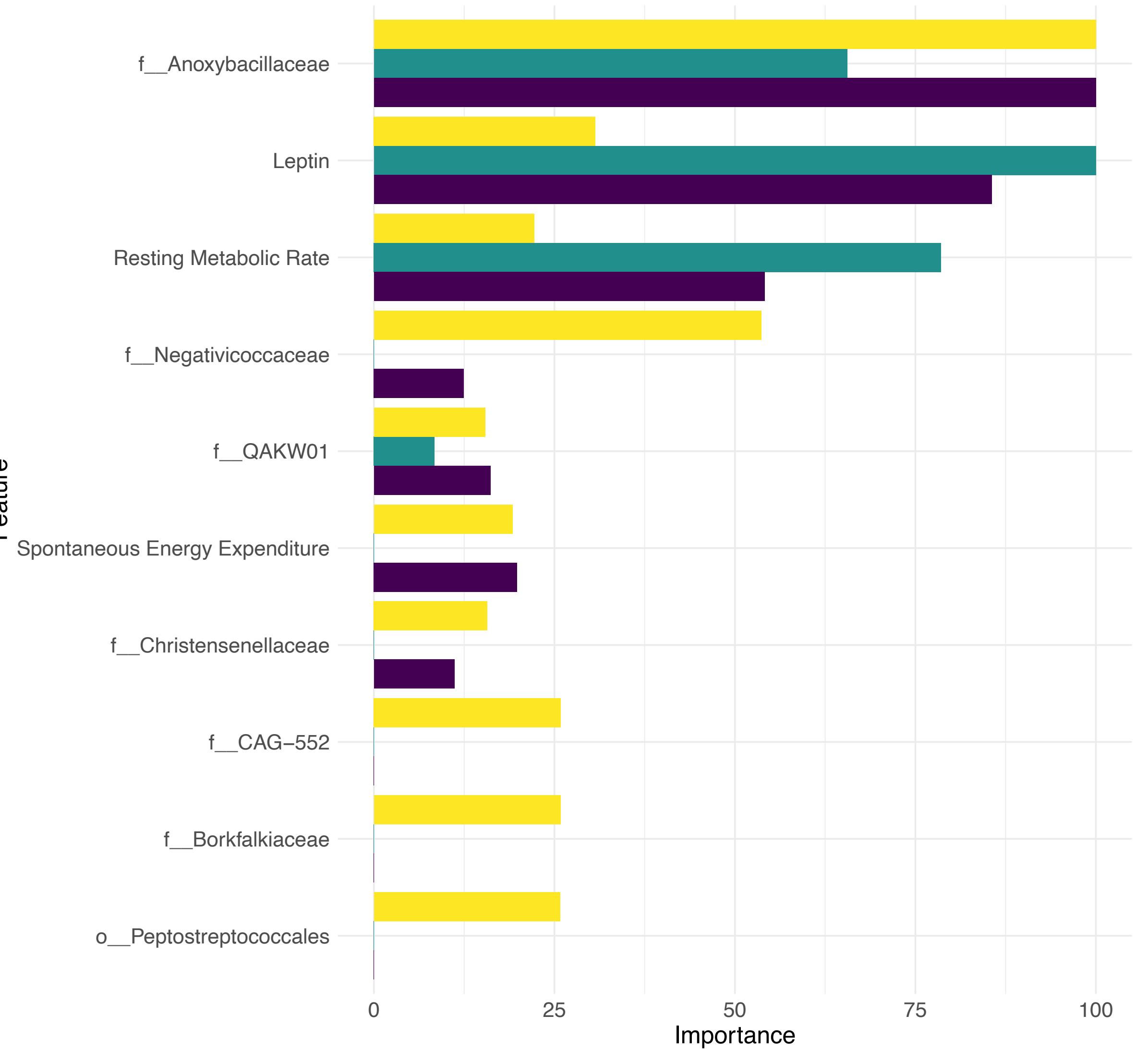
Test R^2 Metrics



Comparing Top 10 Features Across Models

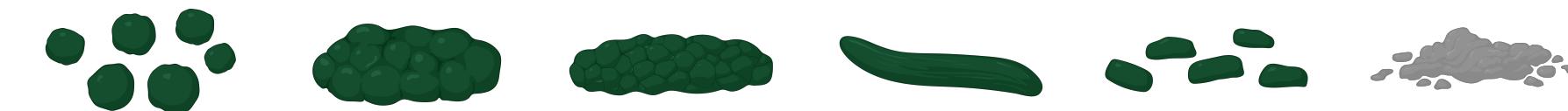
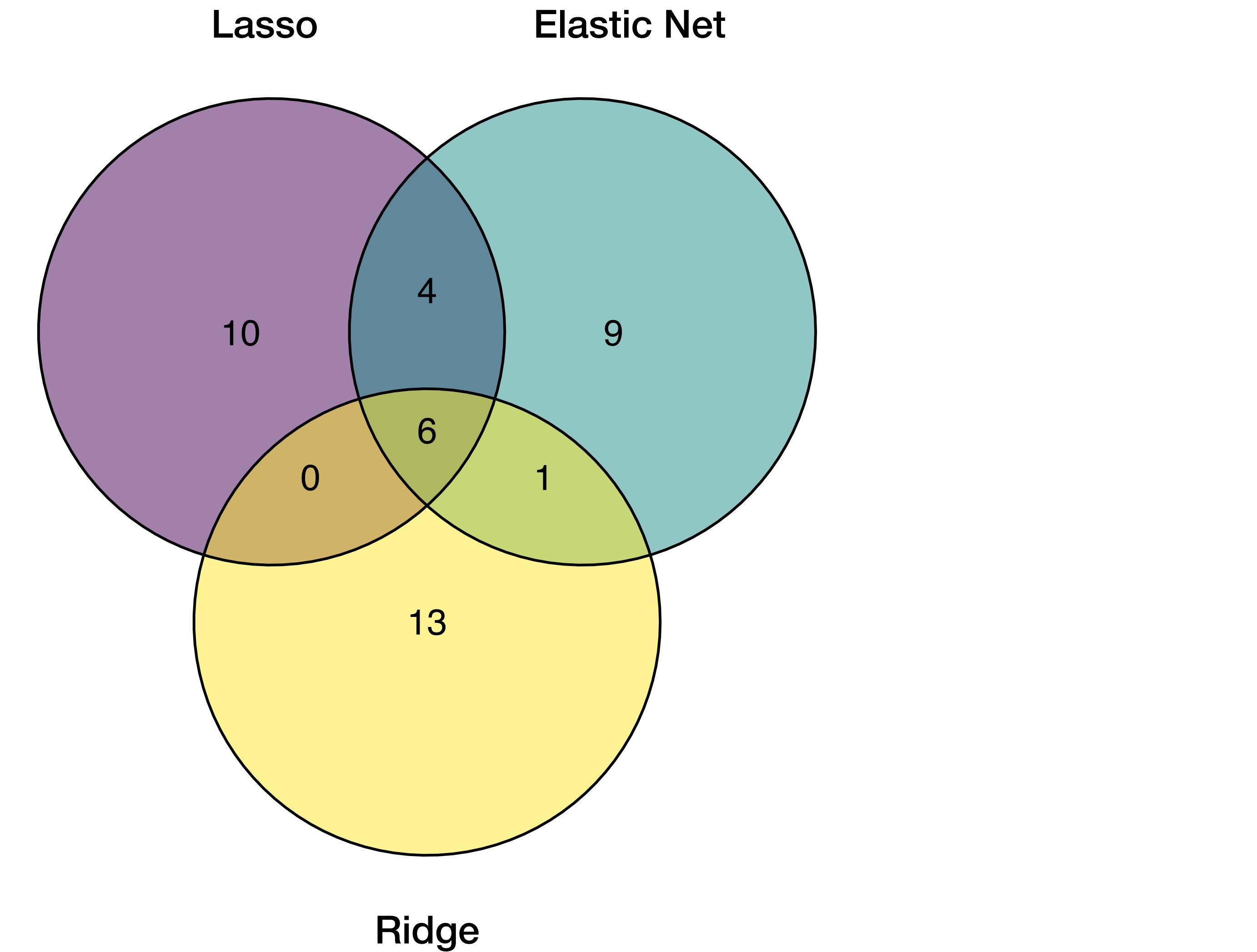
Top 10 Features – Non Redundant Genus + Clinical Variables

Model █ Elastic Net █ Lasso █ Ridge



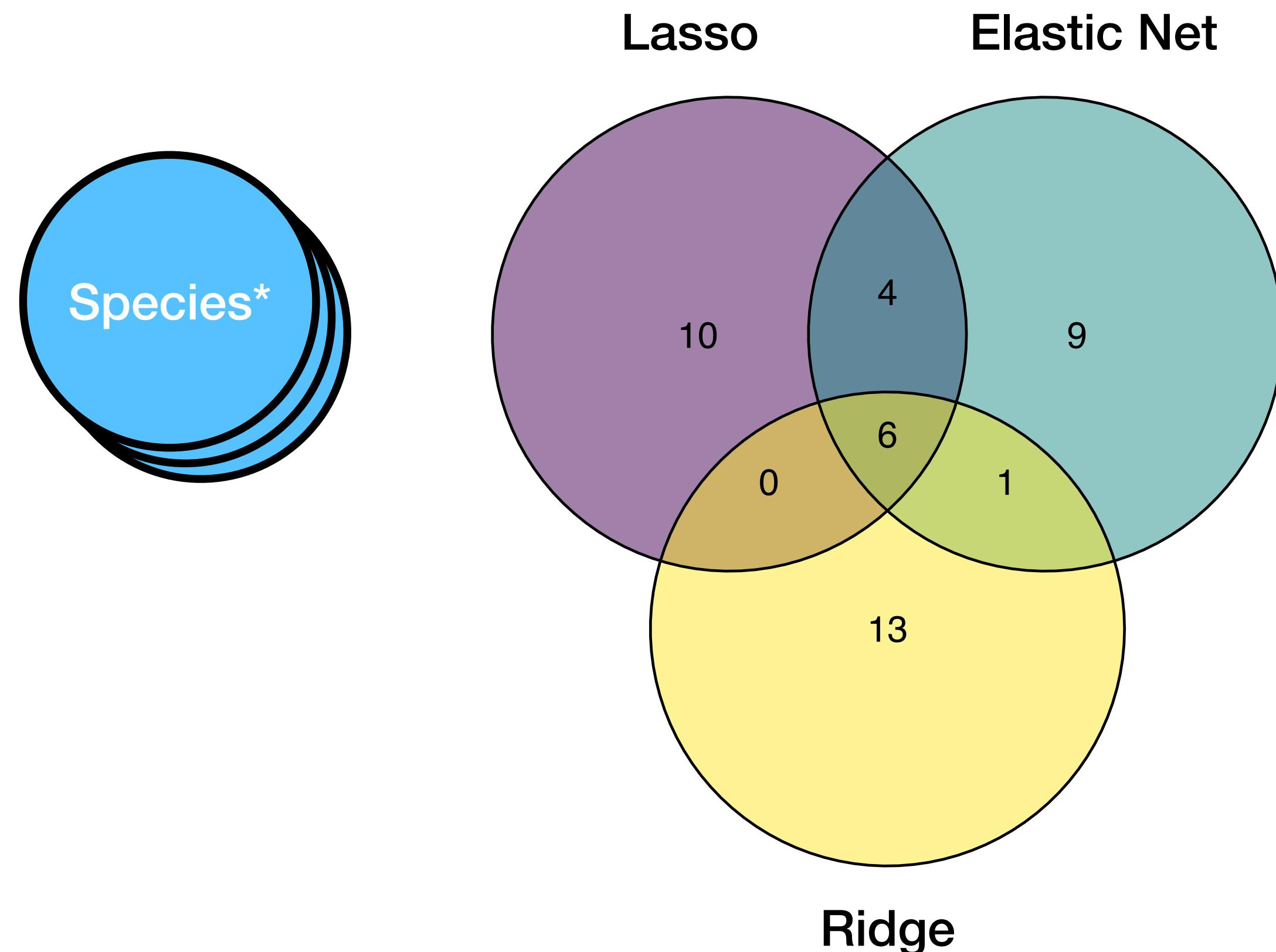
Non Redundant Species + Clinical Variables Top 20 Features Venn diagram

Feature Comparison

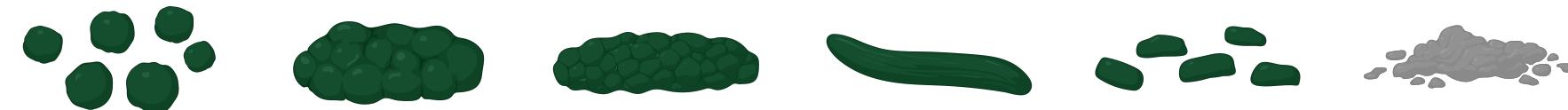
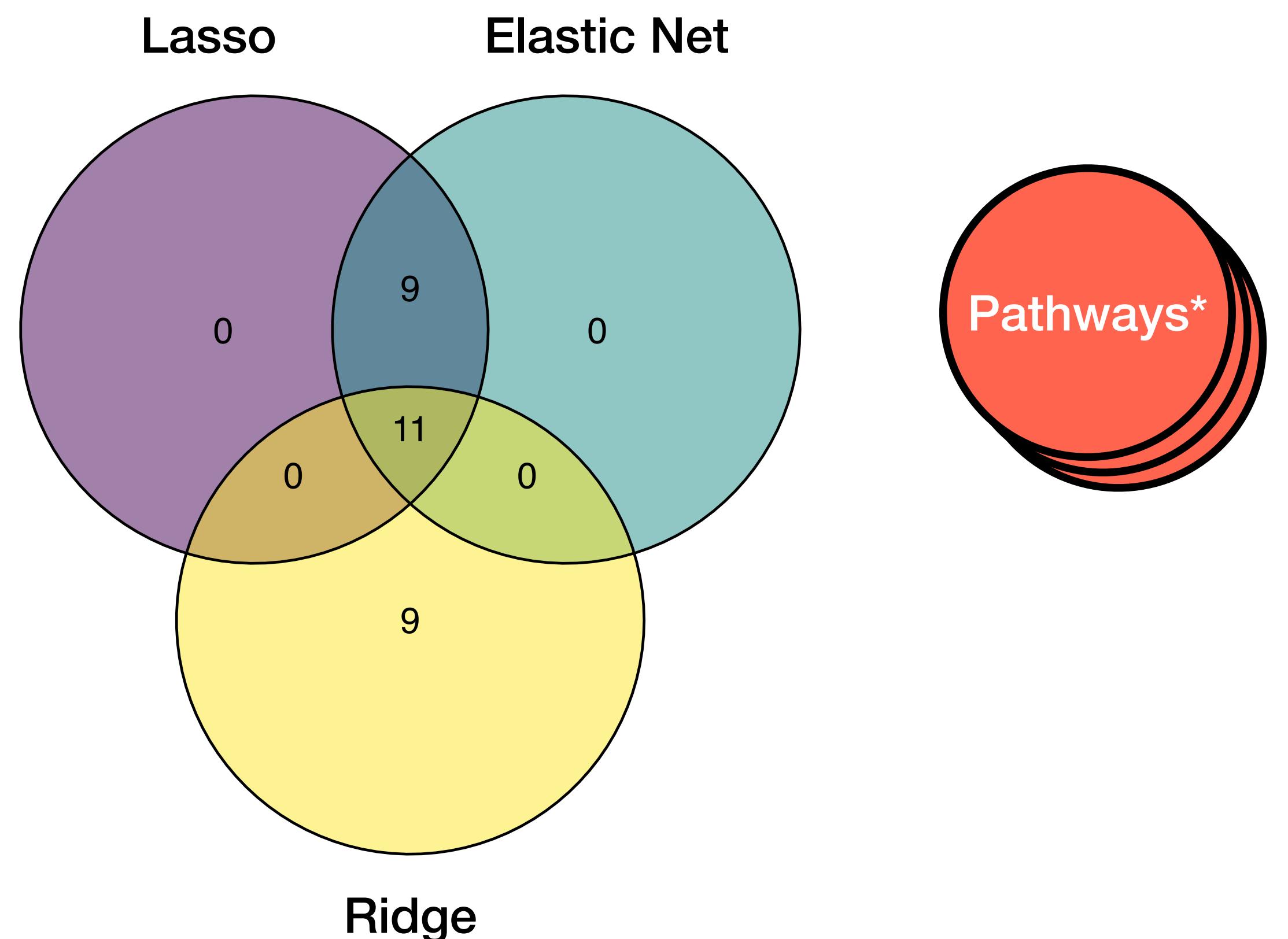


Species and Pathways Feature Comparison

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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Edward Melanson
Daniel Bessesen
Victoria Catenacci
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SCHOOL OF MEDICINE
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**



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Questions?