

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

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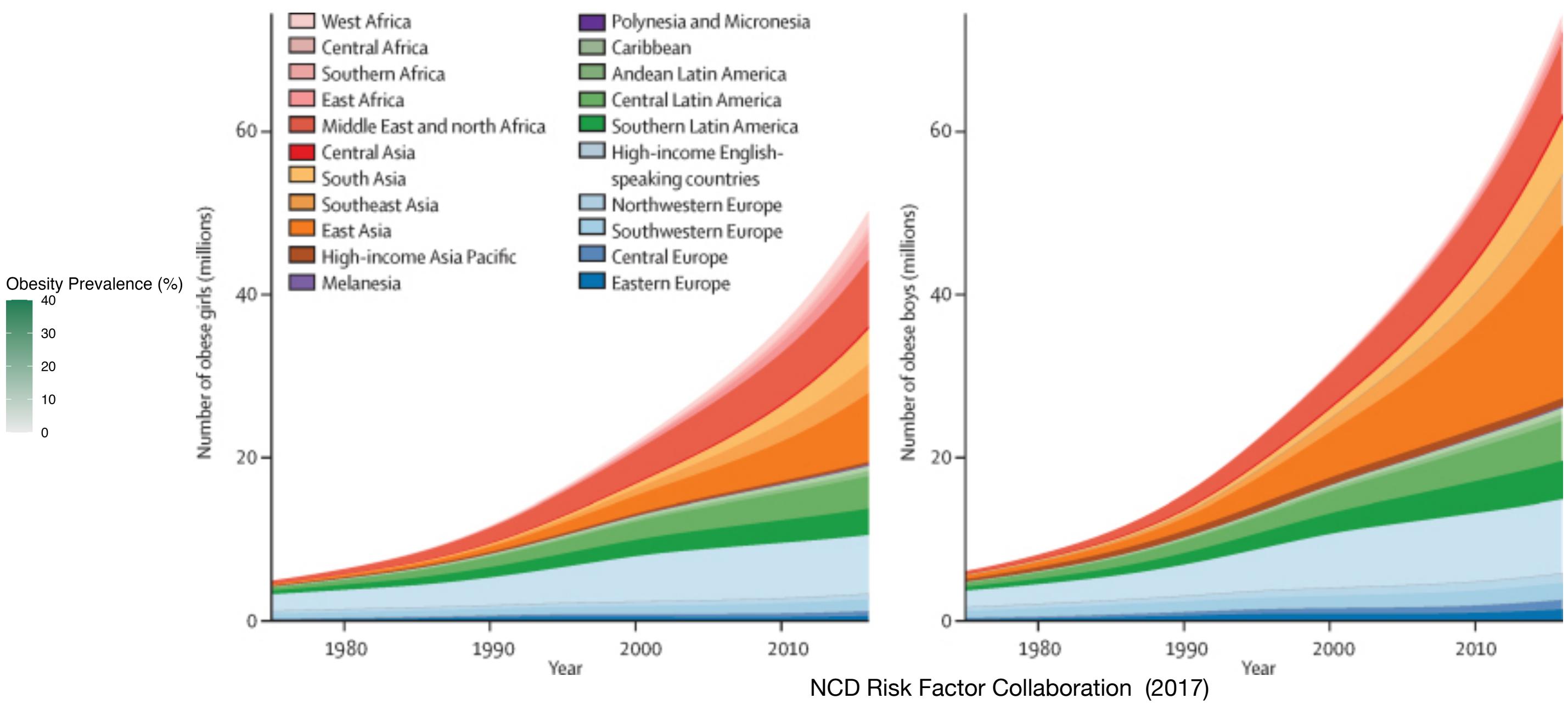
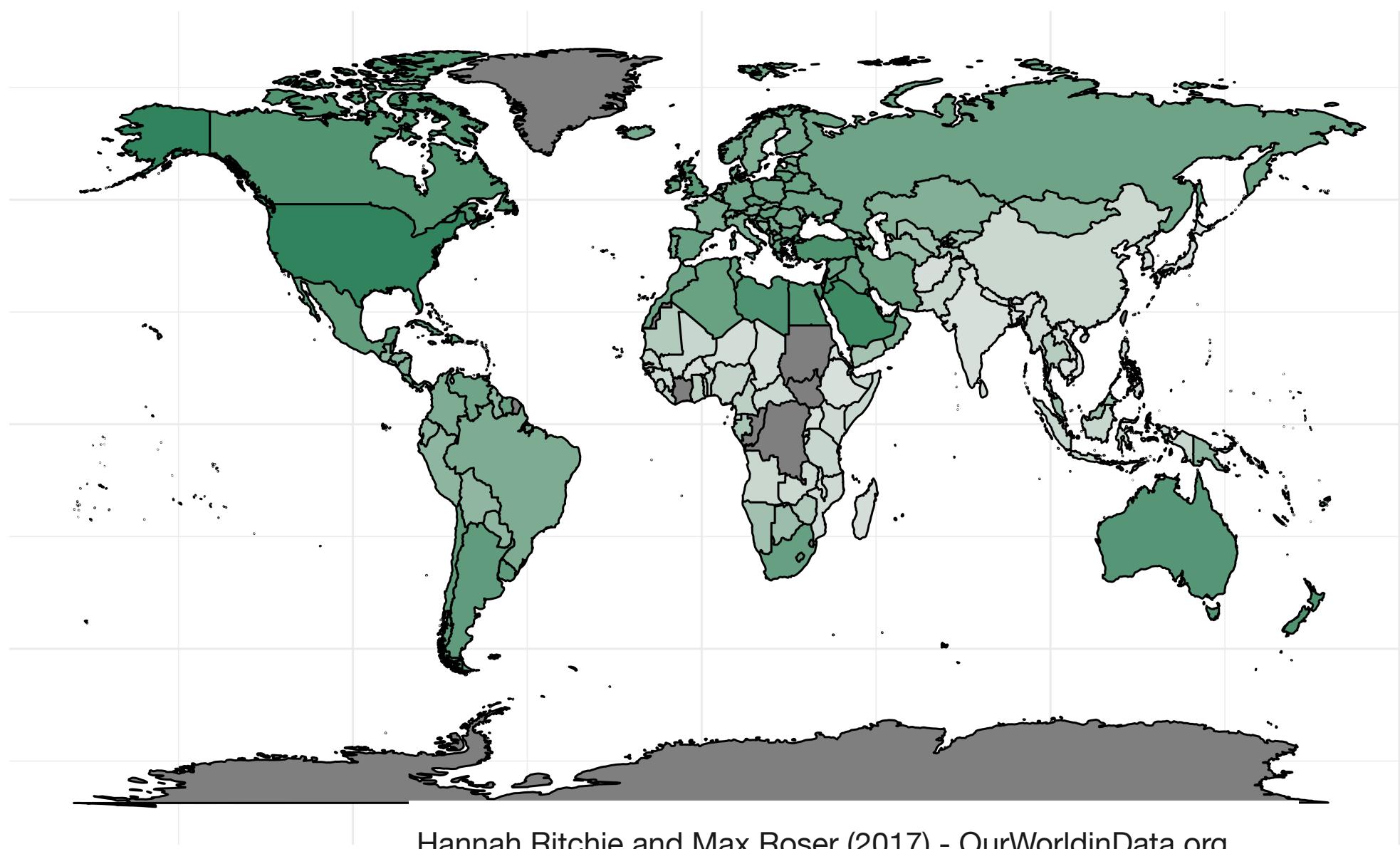
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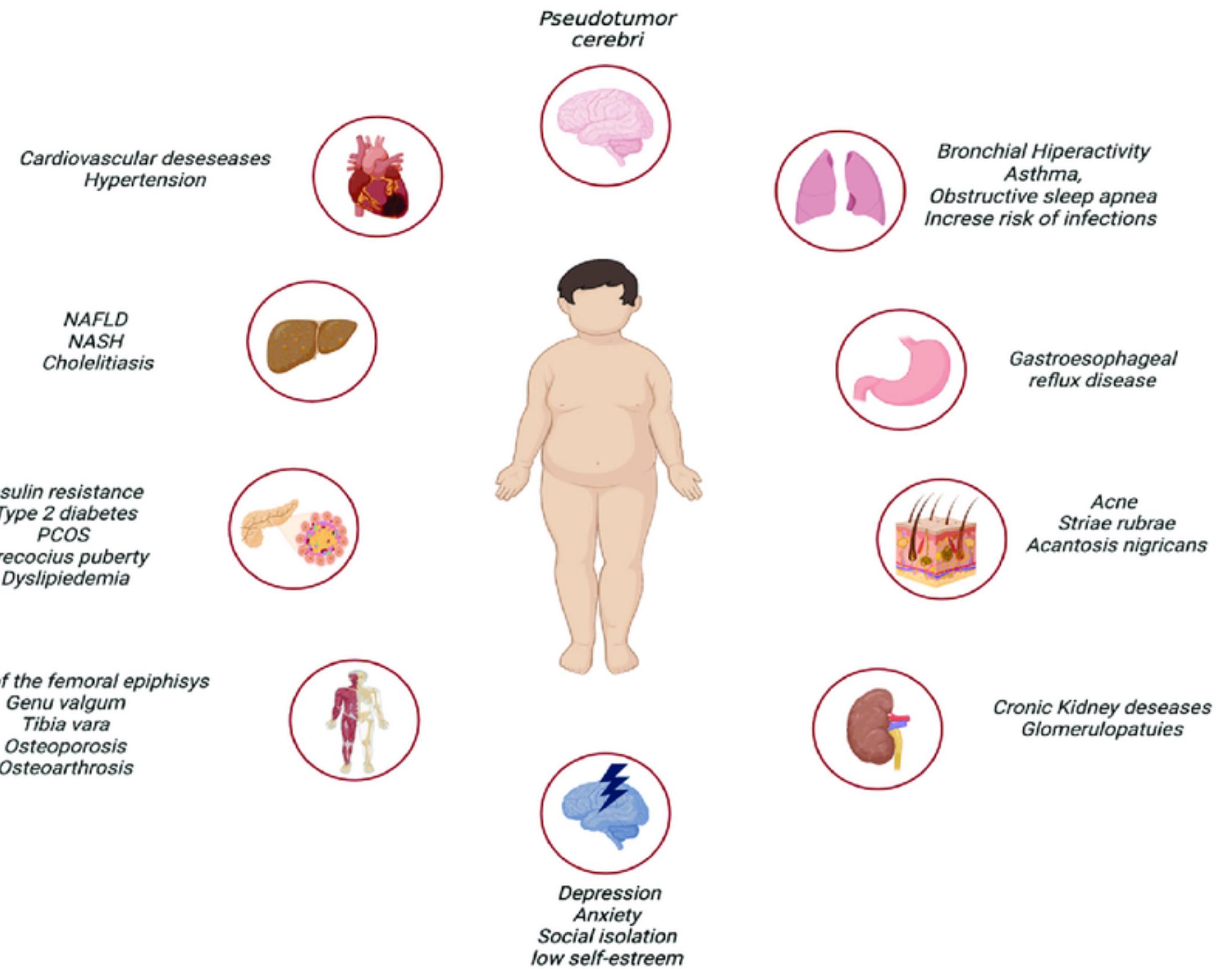
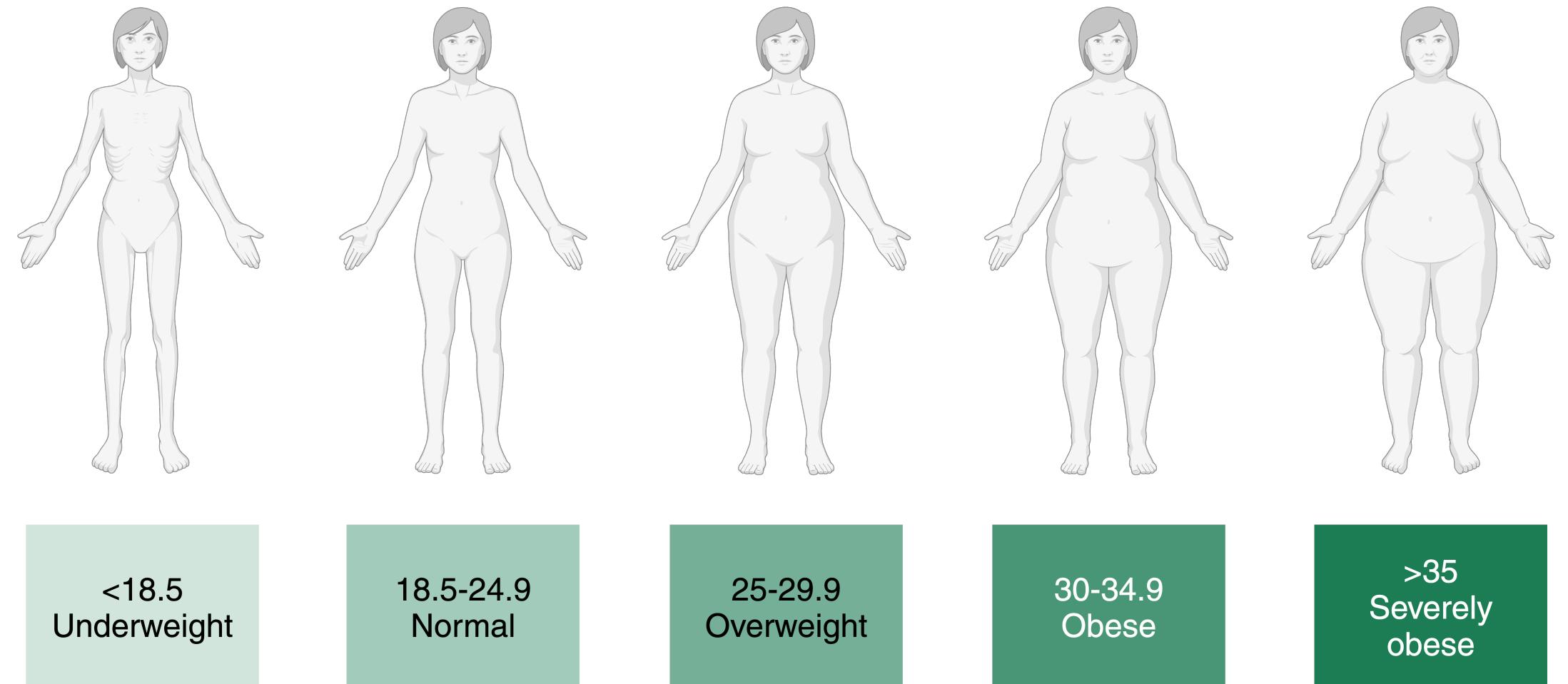
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Obesity is an epidemic

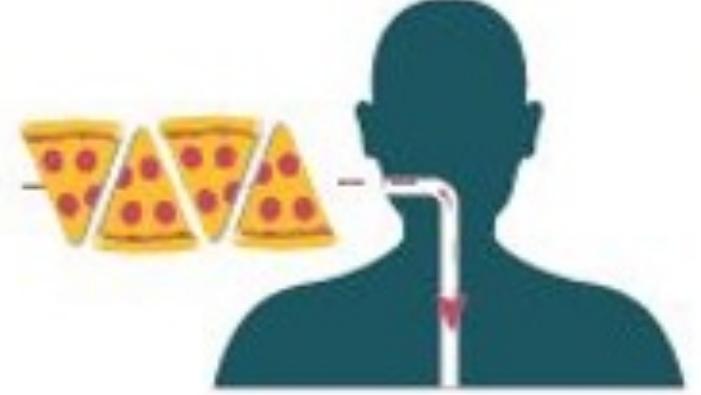
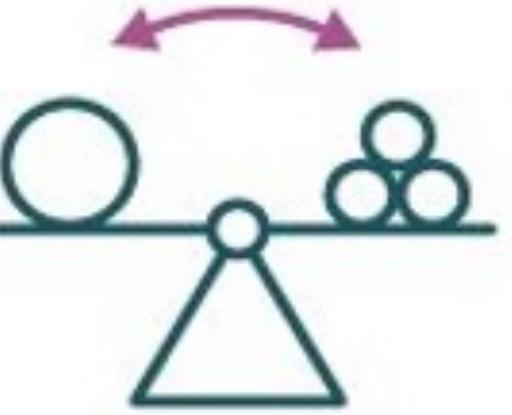
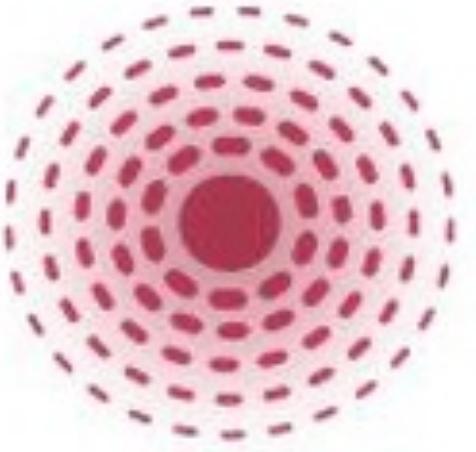
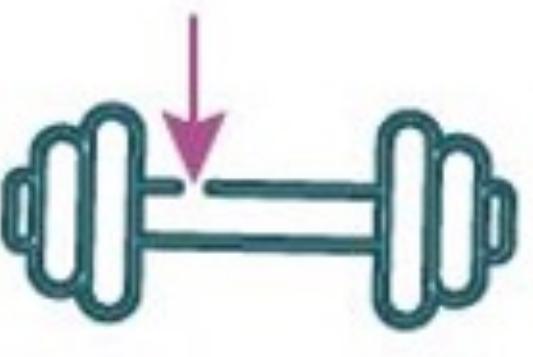


Obesity is a chronic disease



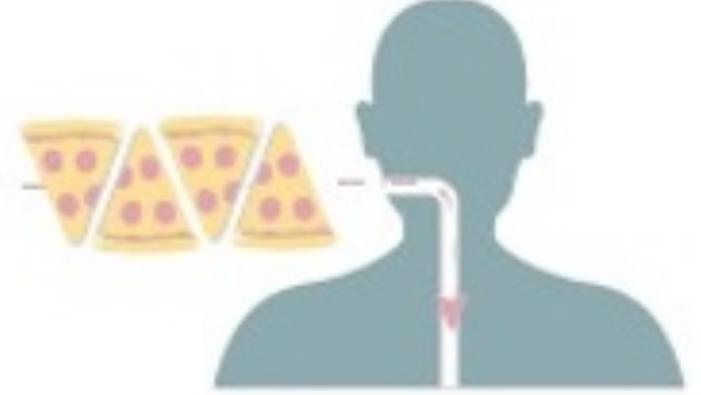
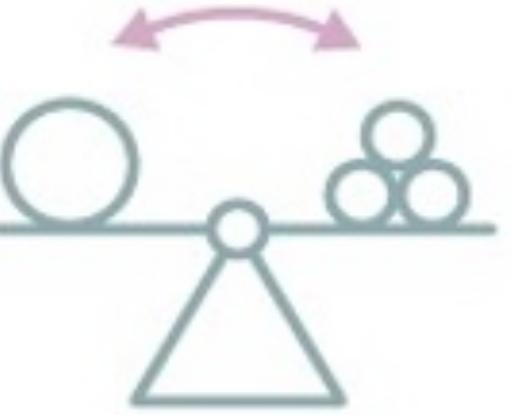
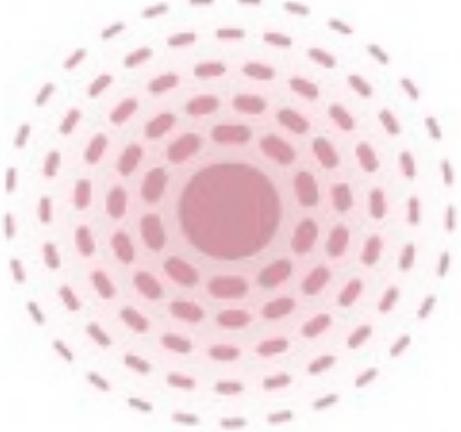
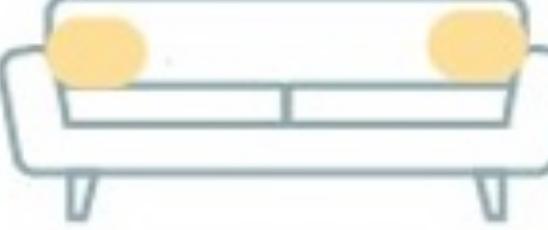
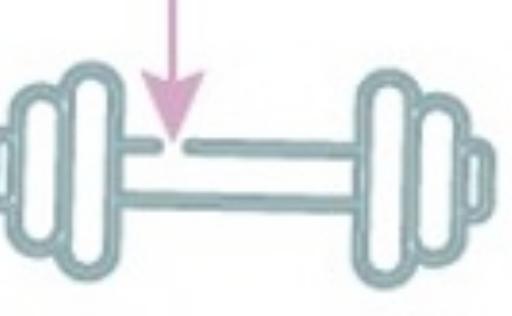
Calcaterra et al. 2023

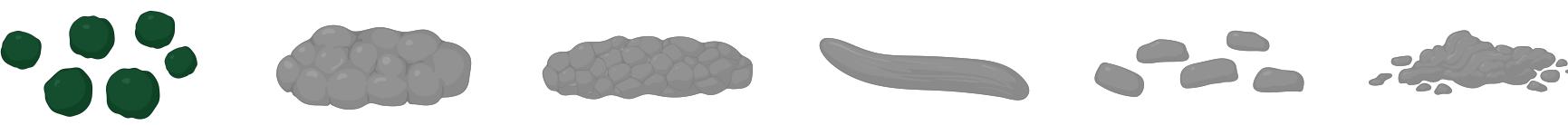
Potential Causes of Obesity

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

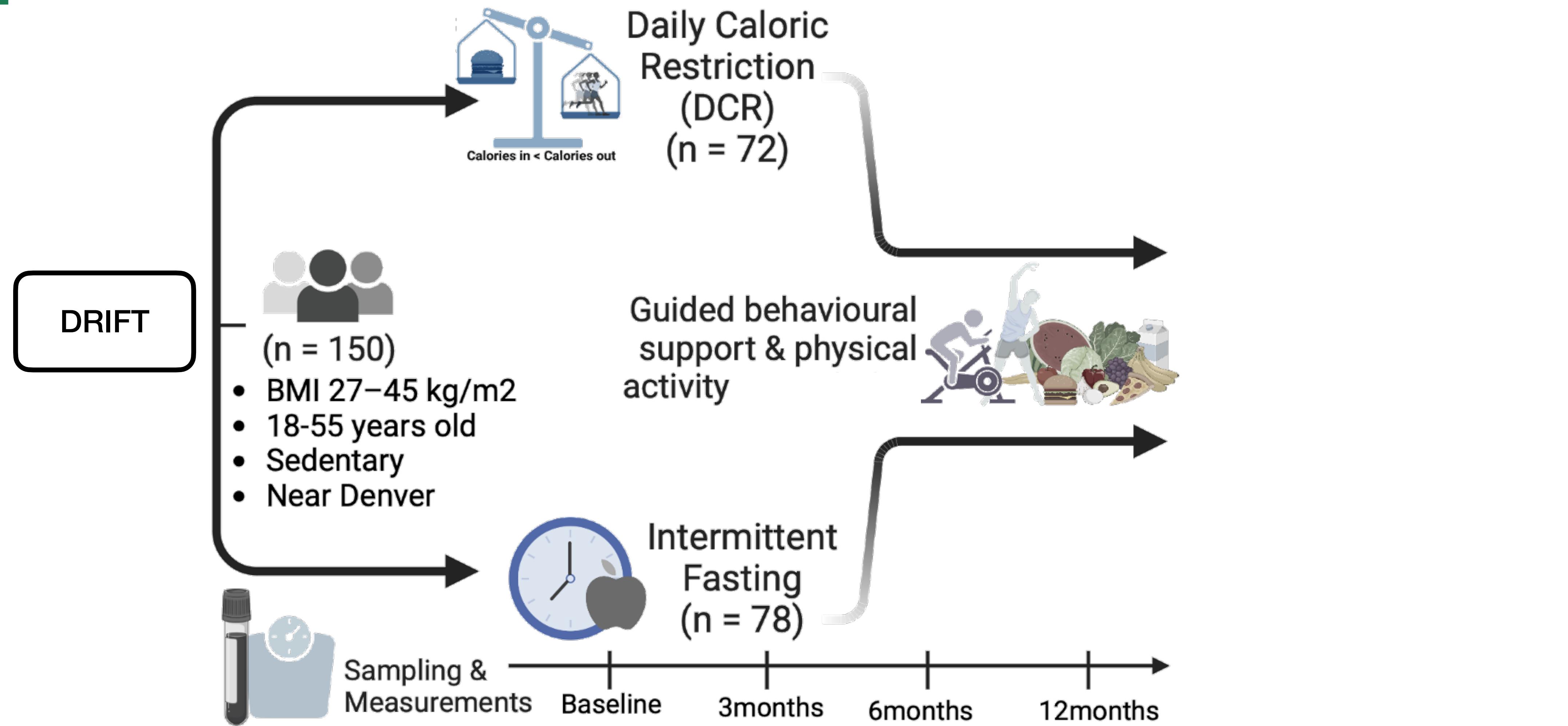


Potential Causes of Obesity

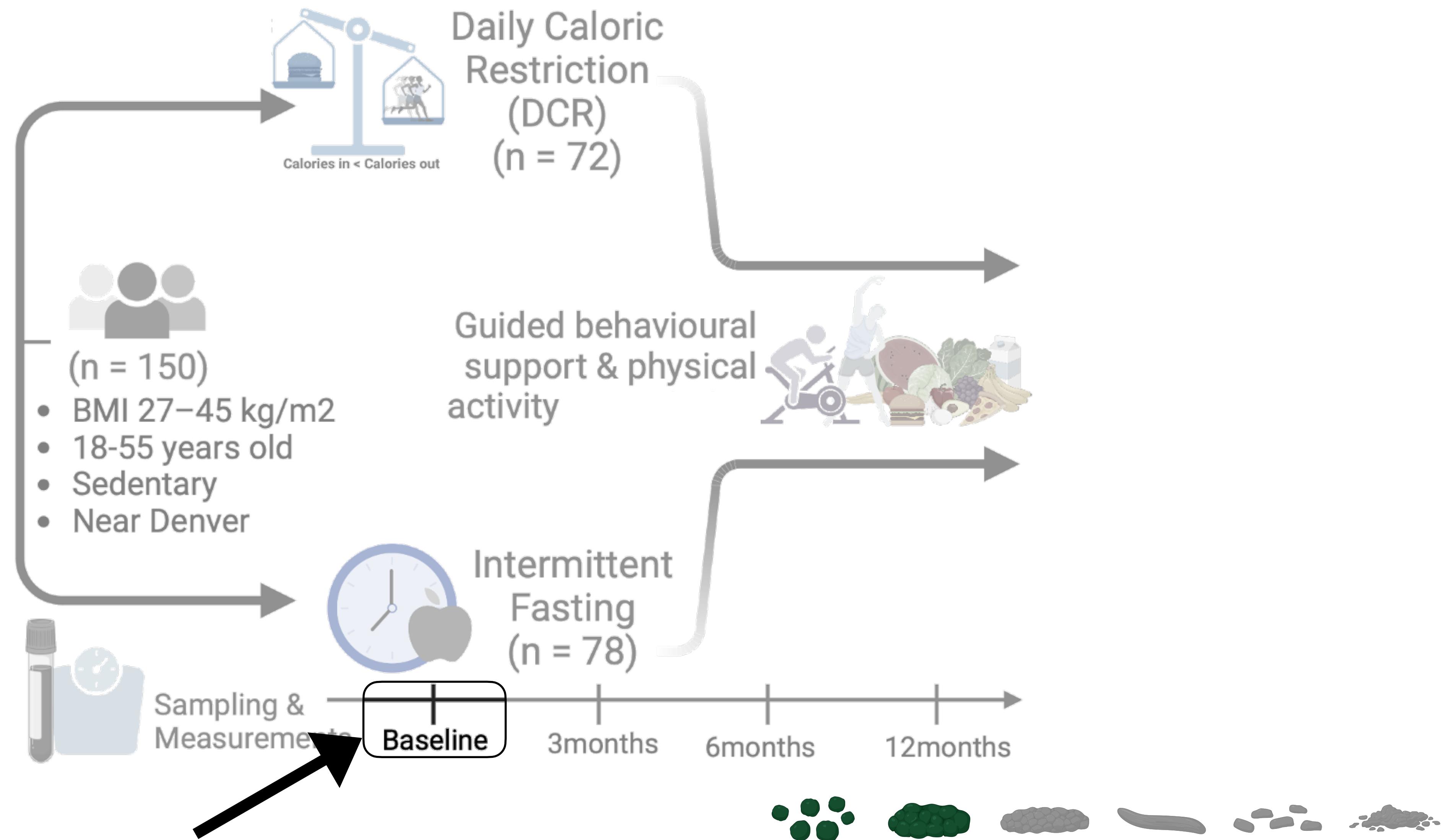
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Daily Caloric Restriction vs Intermittent Fasting Trial DRIFT



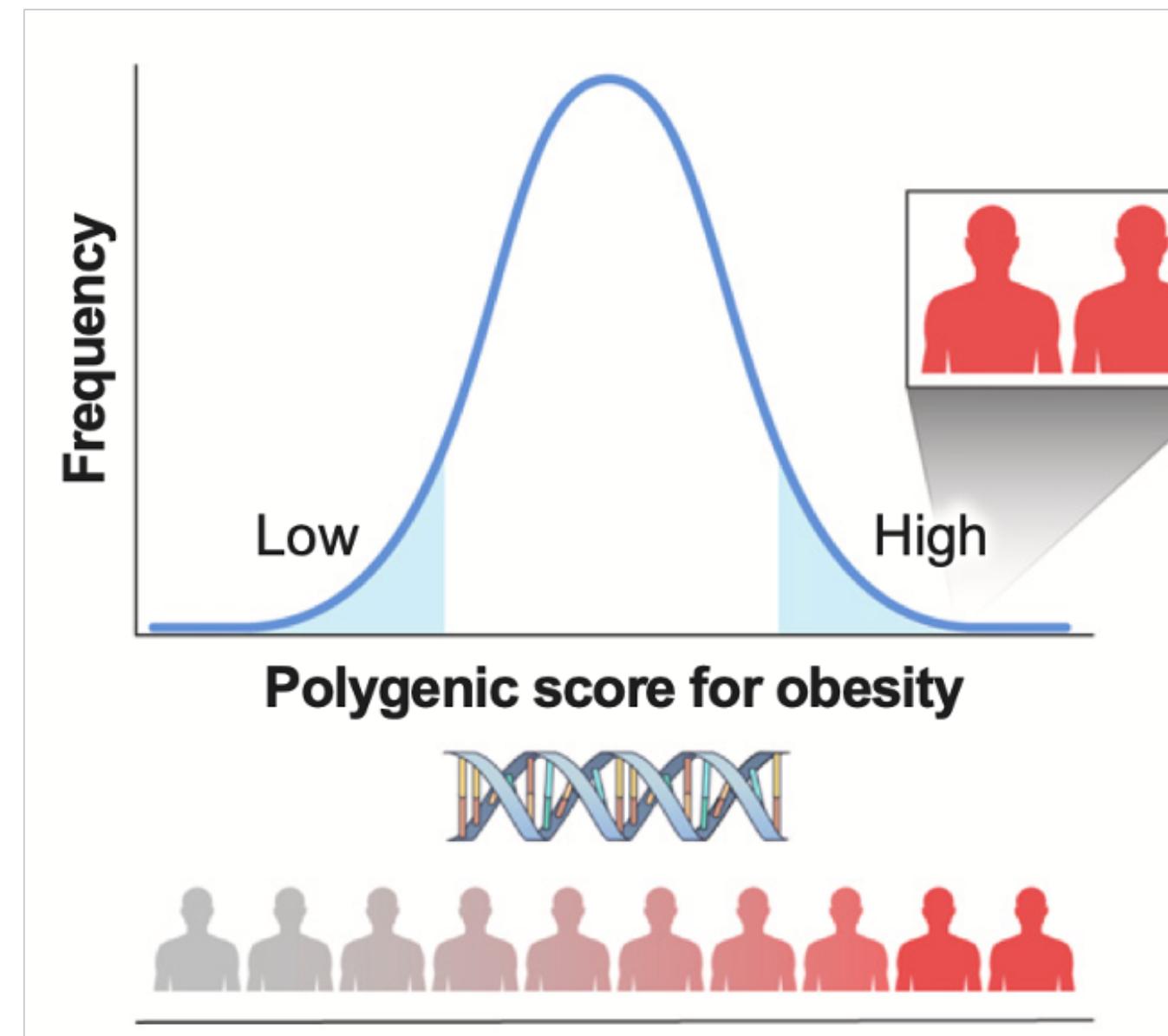
Daily Caloric Restriction vs Intermittent Fasting Trial DRIFT



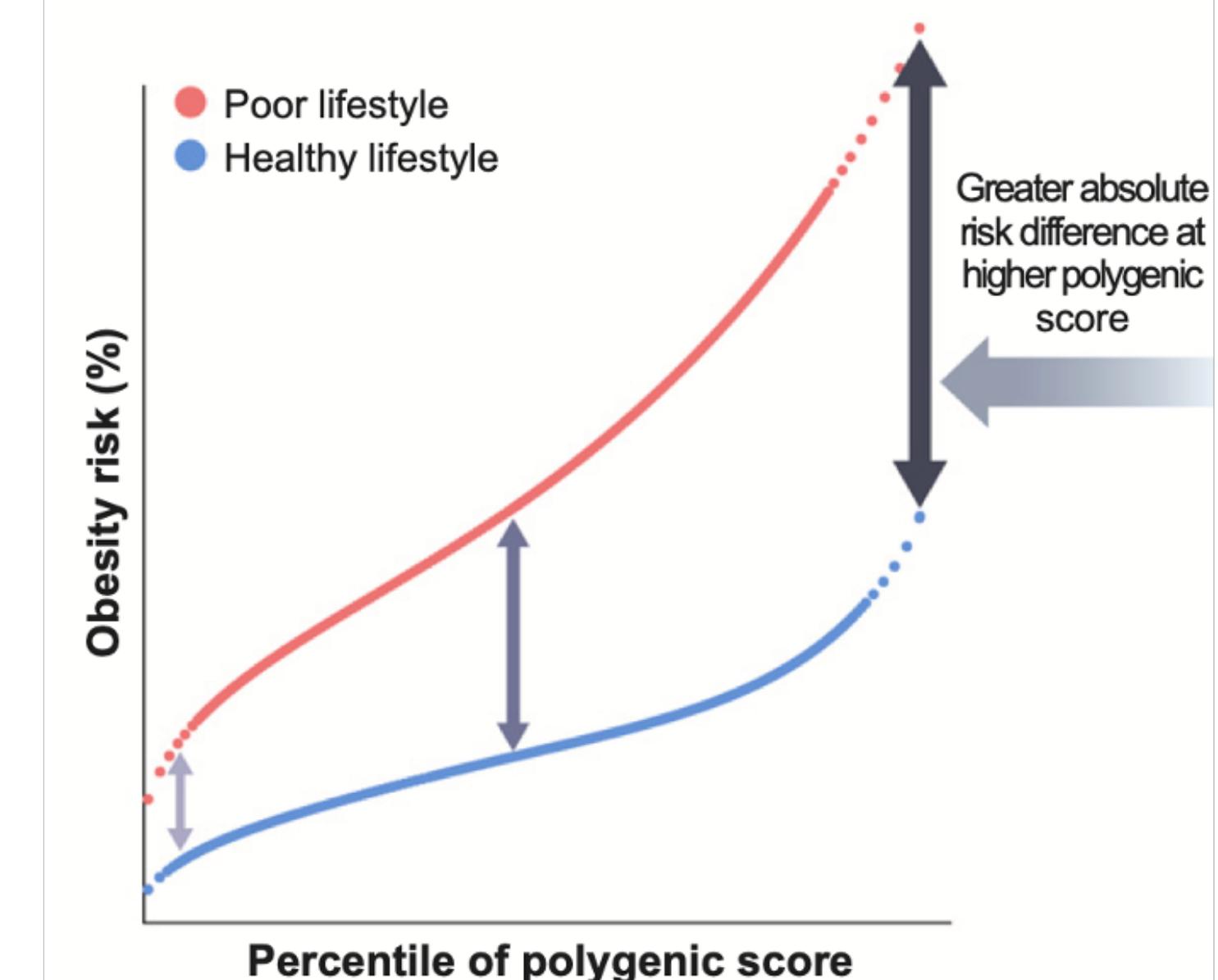
Research Questions

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

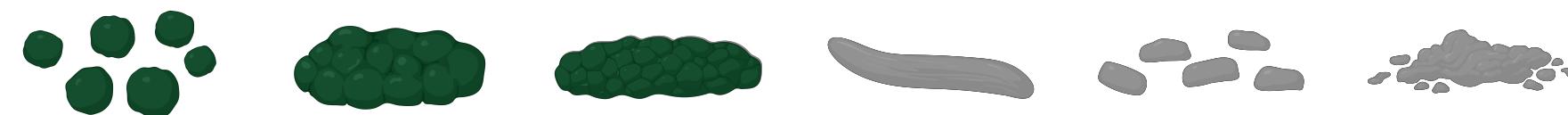


Kim et al., 2024, Cell Metabolism 36, 1494–1503, July 2, 2024

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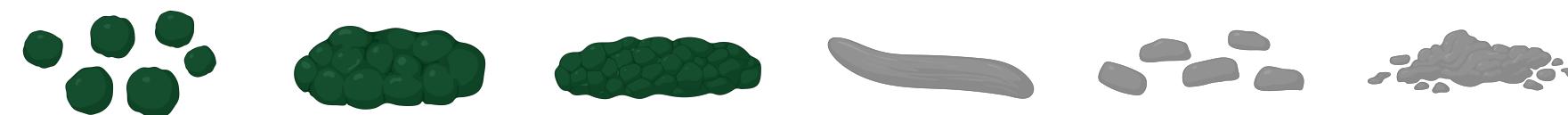
Are there gut microbial attributes that can be used to identify the difference in participant's actual BMI vs genetic risk?



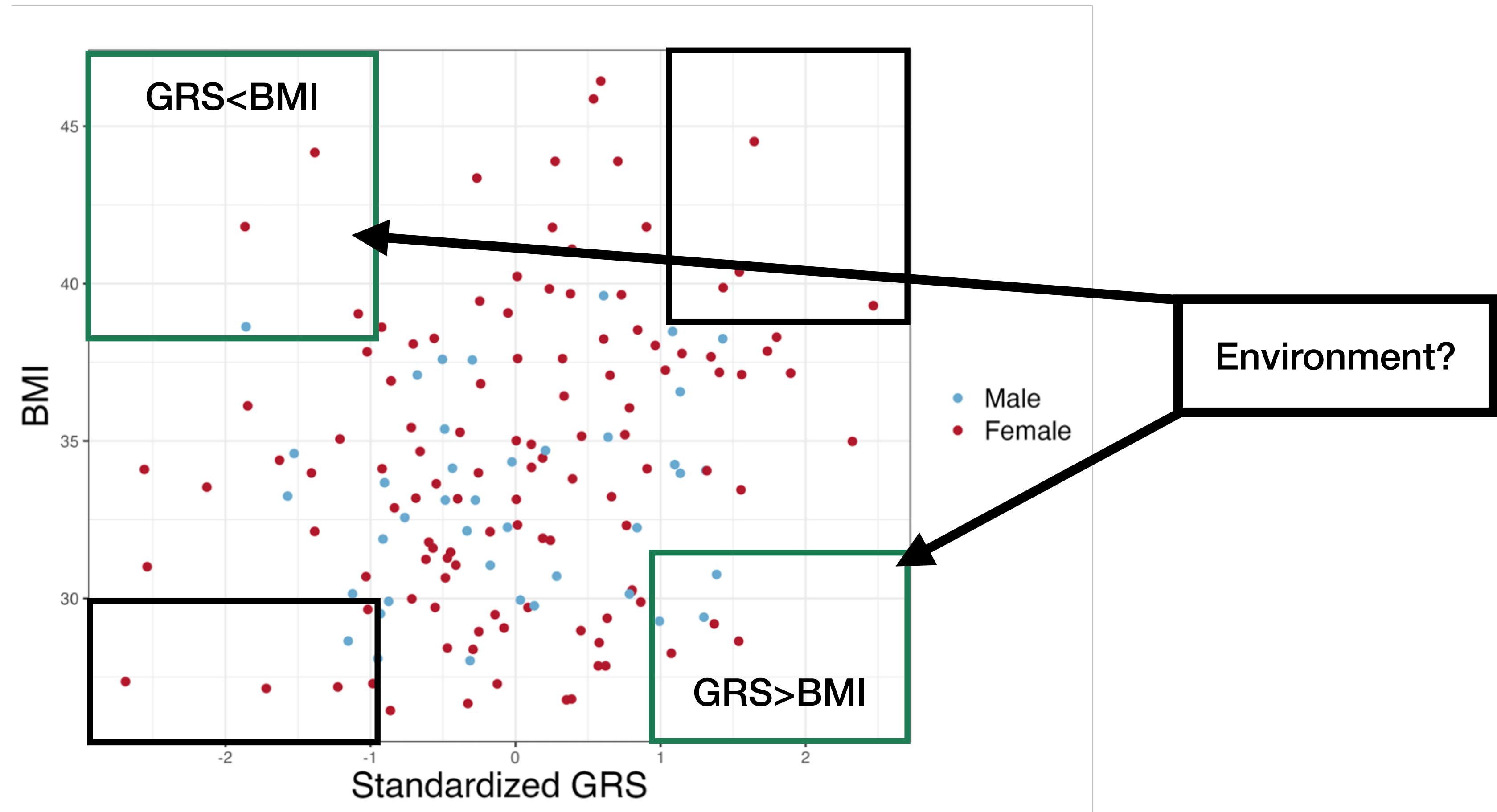
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(Emily Yeo & Ashley Scadden)

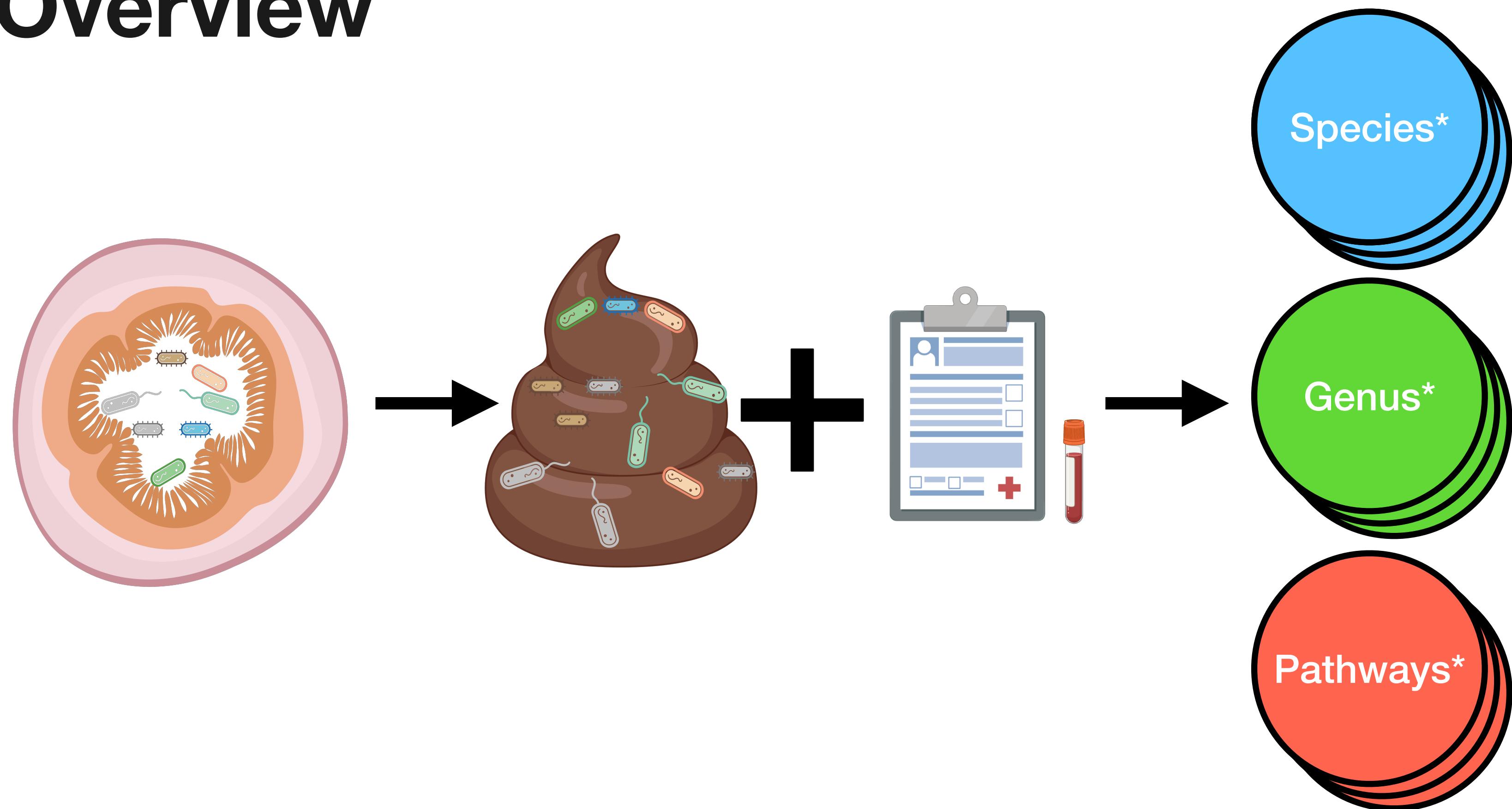
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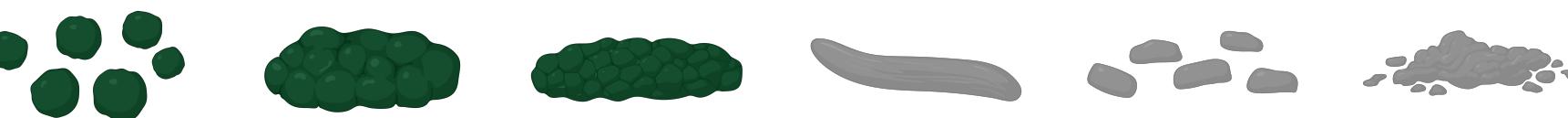
BMI verses genetically expected BMI – Genetic Risk Score (GRS)



Dataset Overview

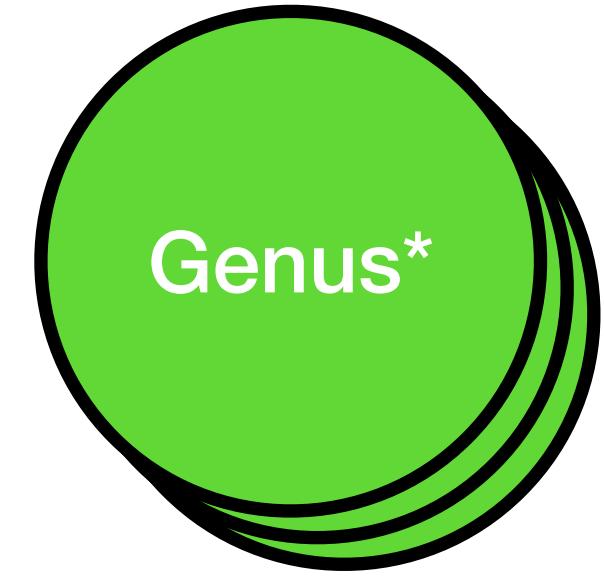


*Taxa, w/, w/o clinical information &
minus redundant features



Dataset, Models, and Metrics Overview

Datasets



Models

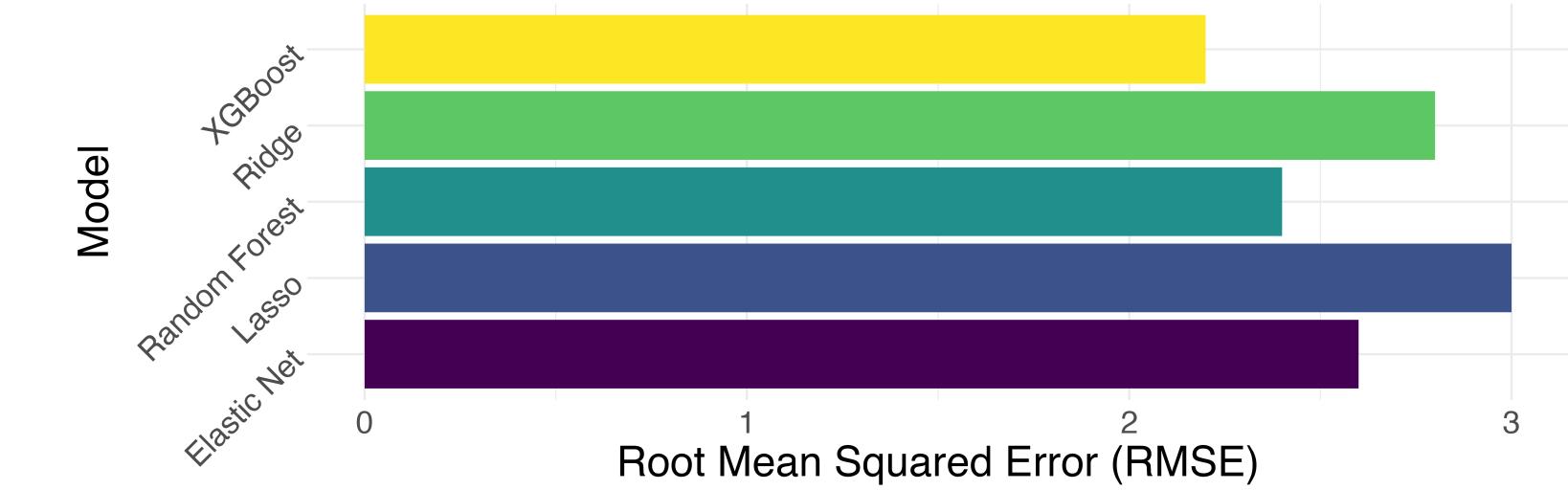
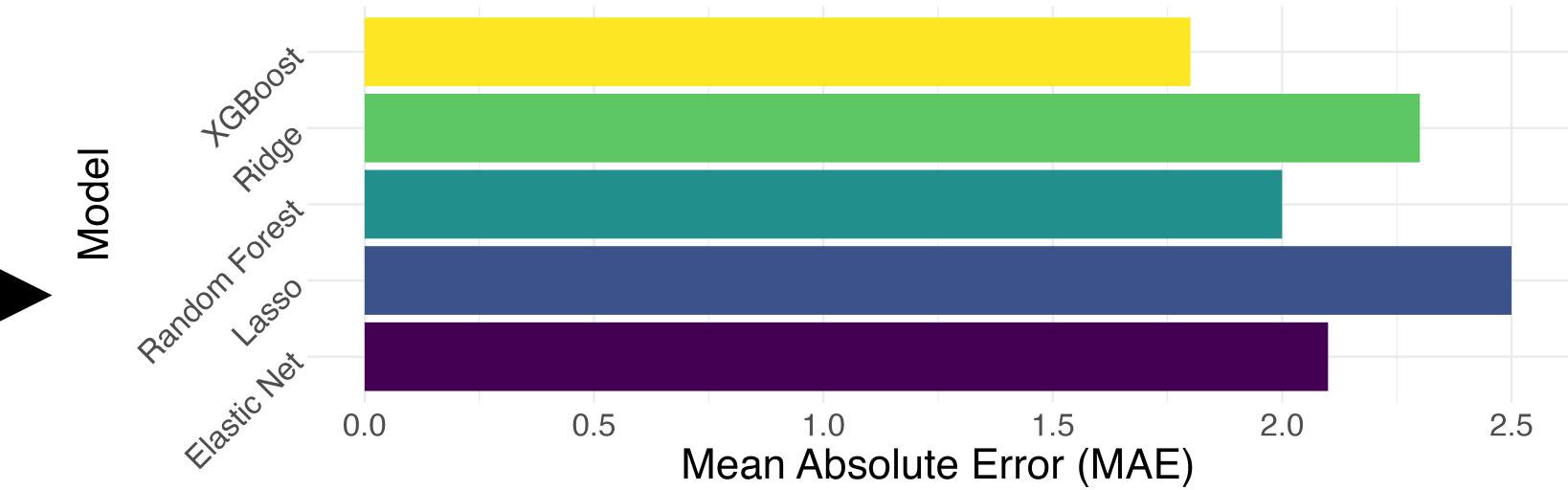
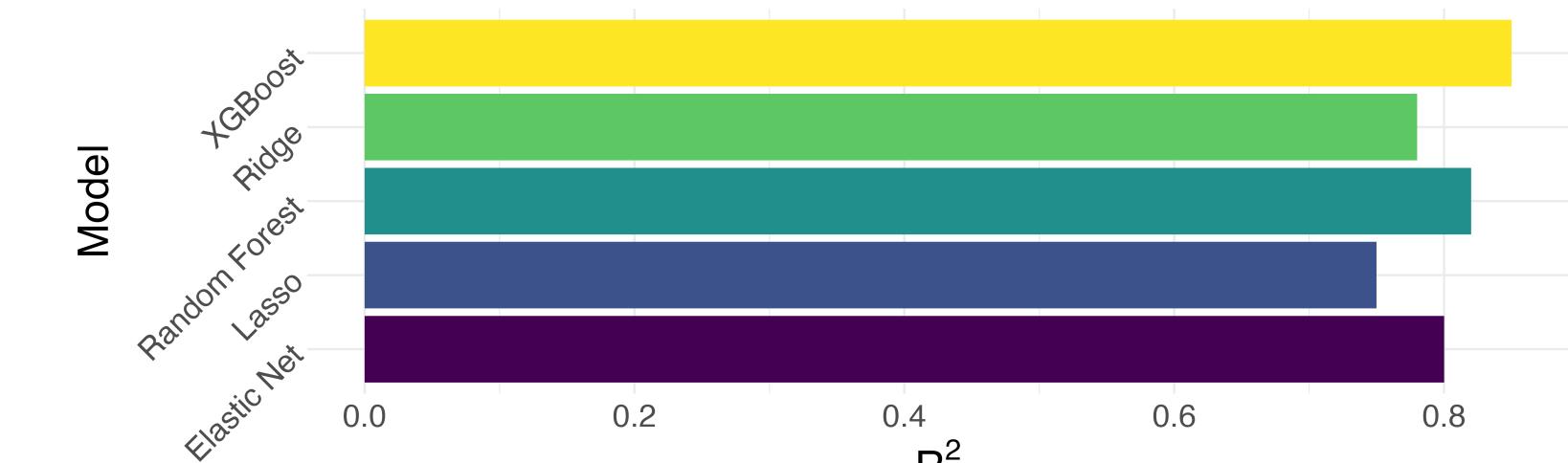
Penalized Regression Models

Elastic Net
Lasso
Ridge

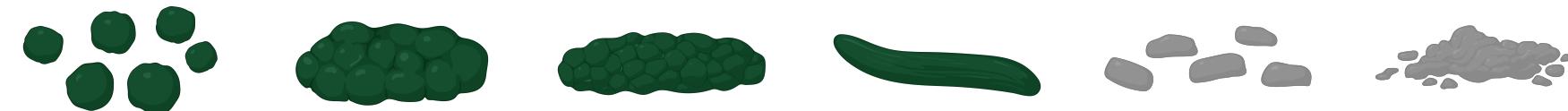
Ensemble Learning Methods

Random Forest
XGBoost

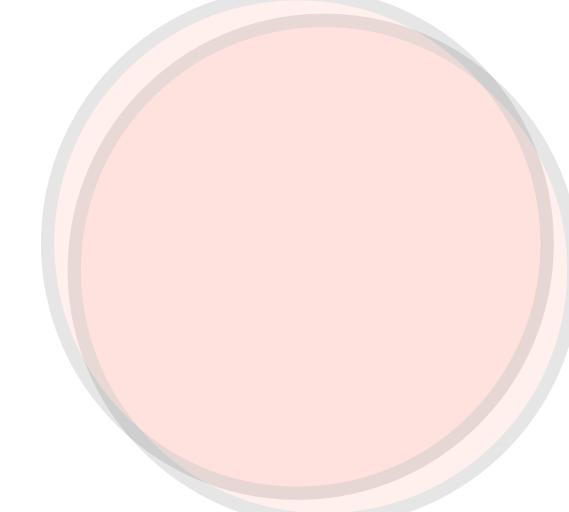
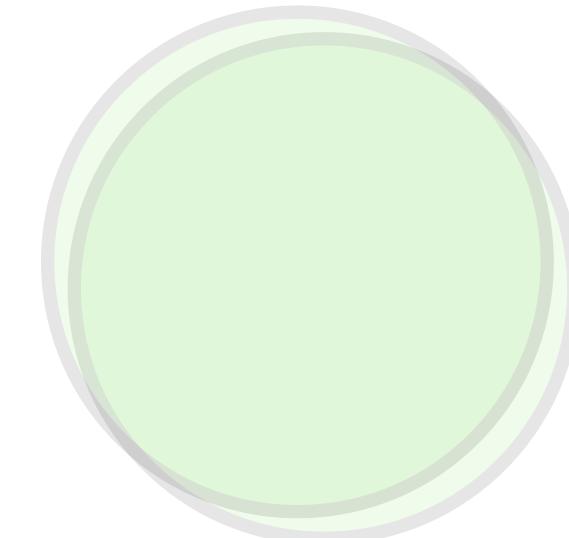
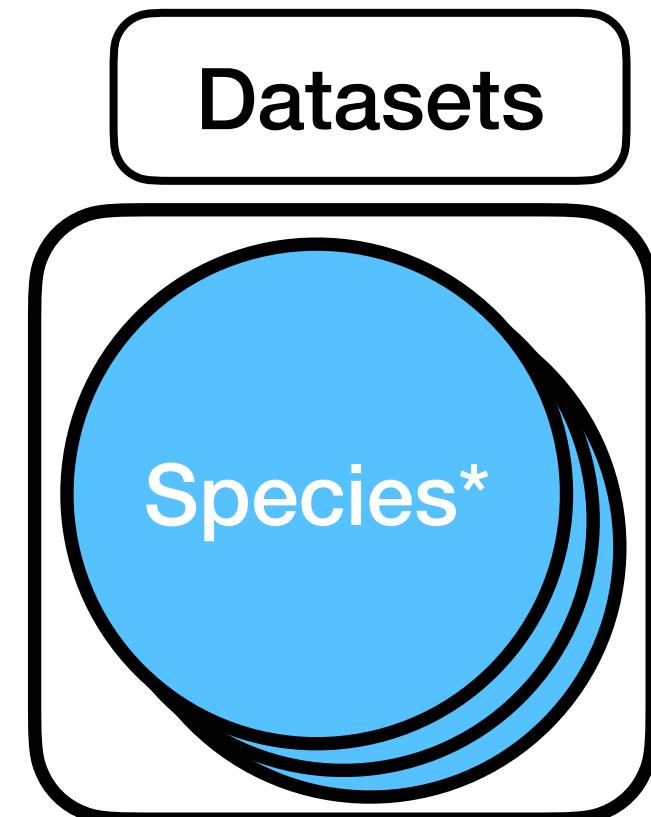
Metrics



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



Dataset, Models, and Metrics Overview



*Taxa, w/, w/o
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Models

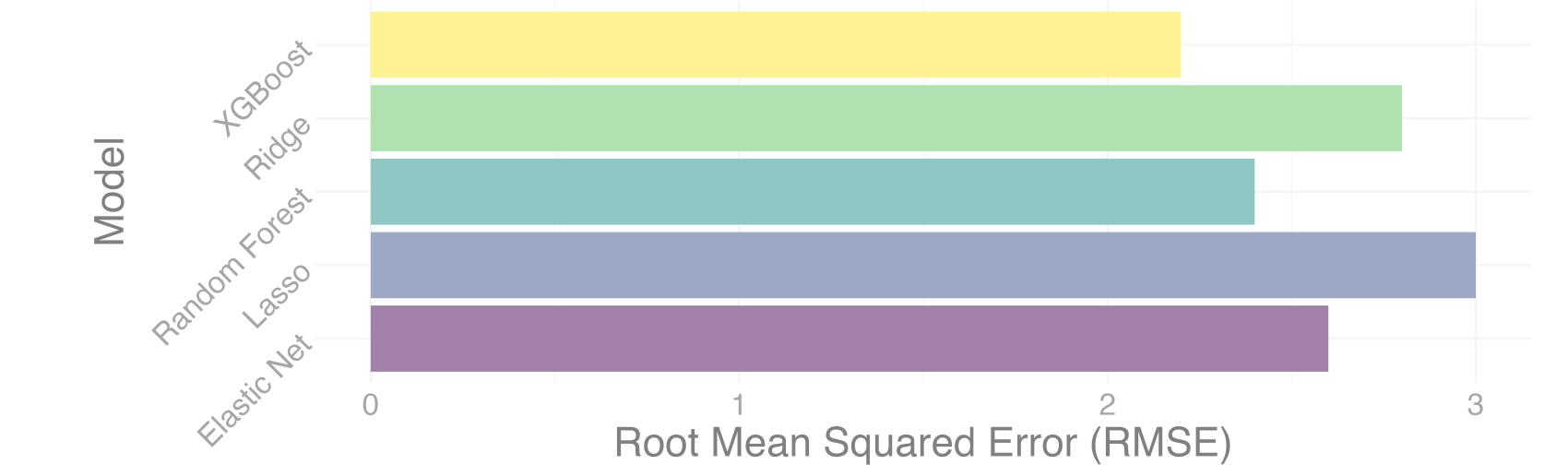
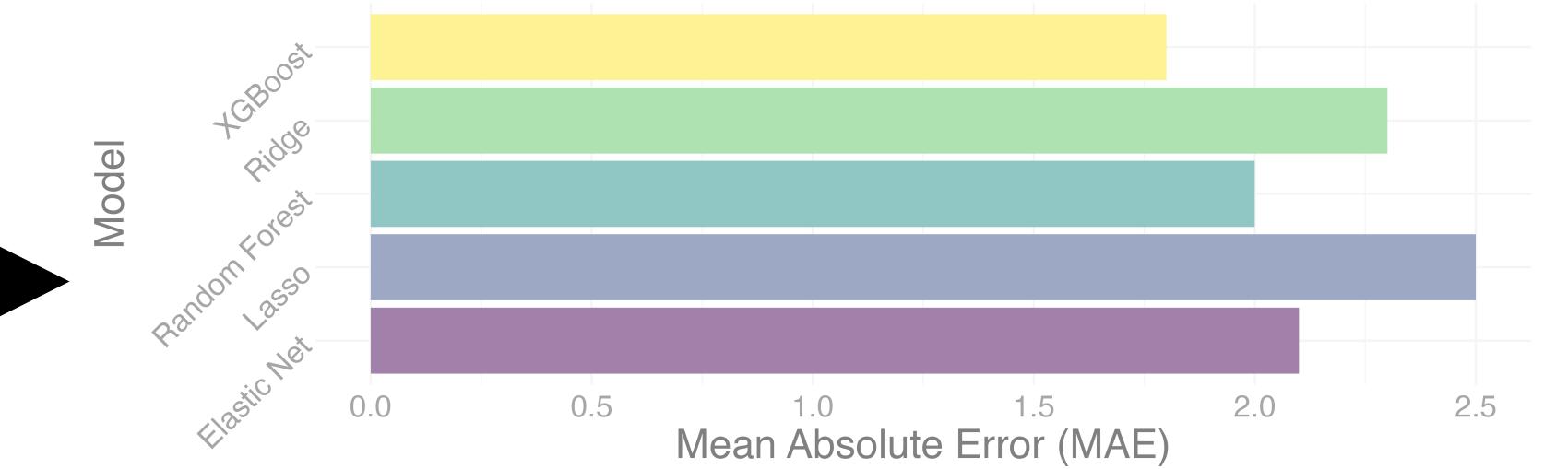
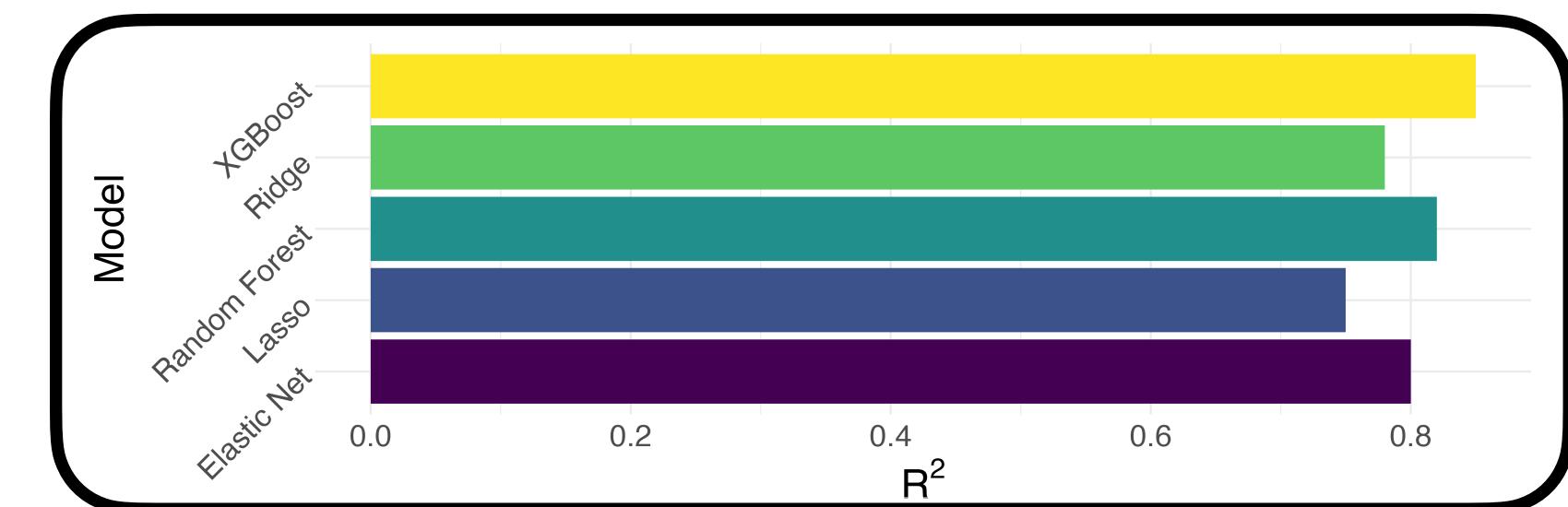
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Ensemble Learning Methods

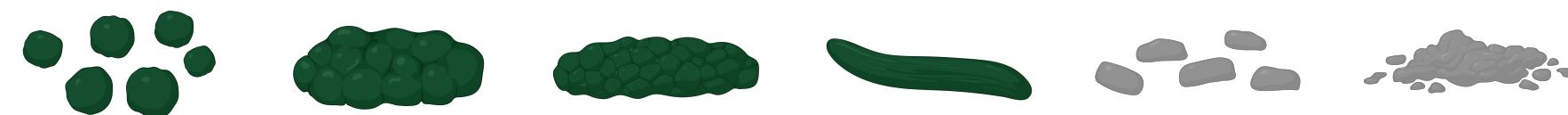
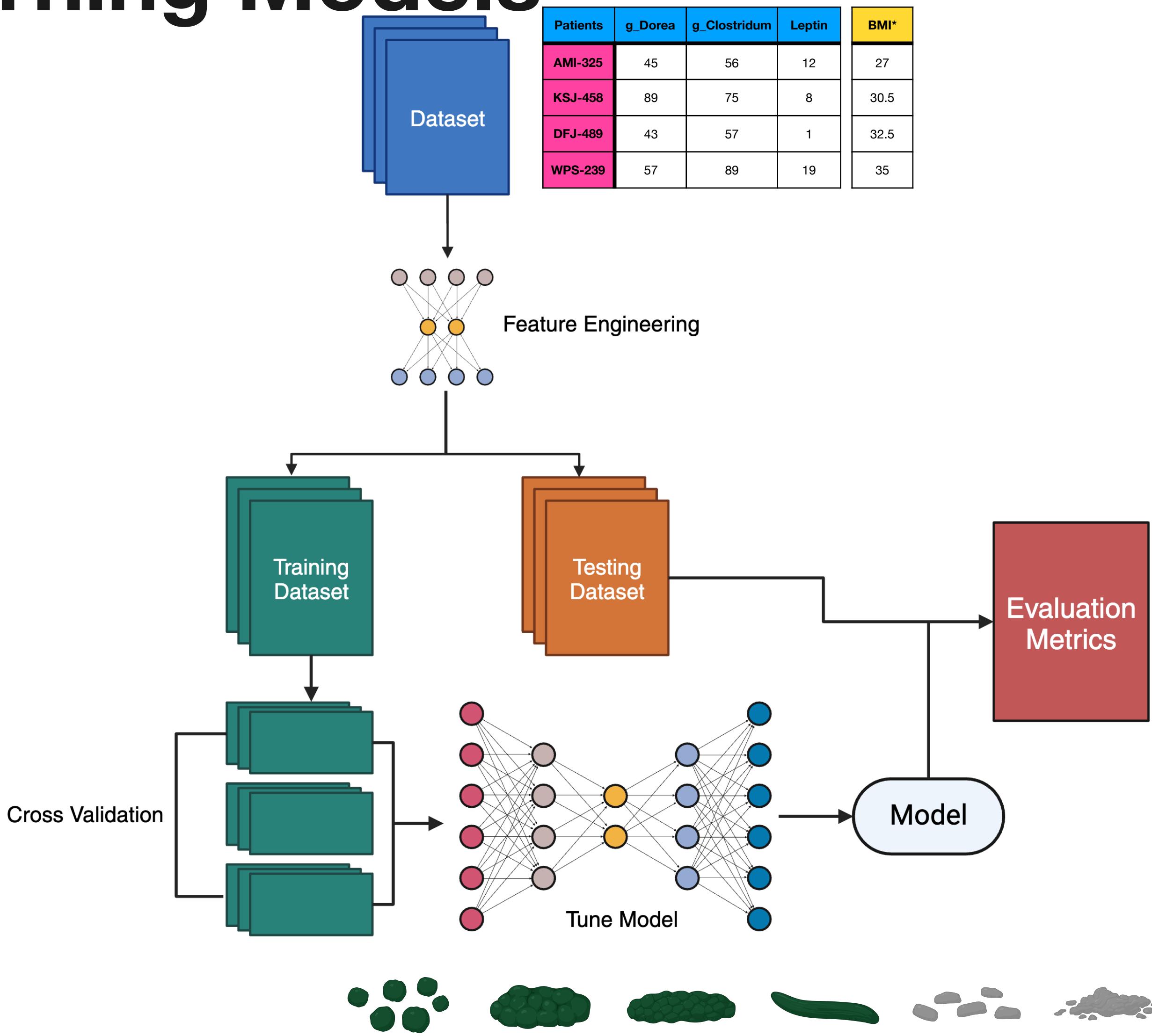
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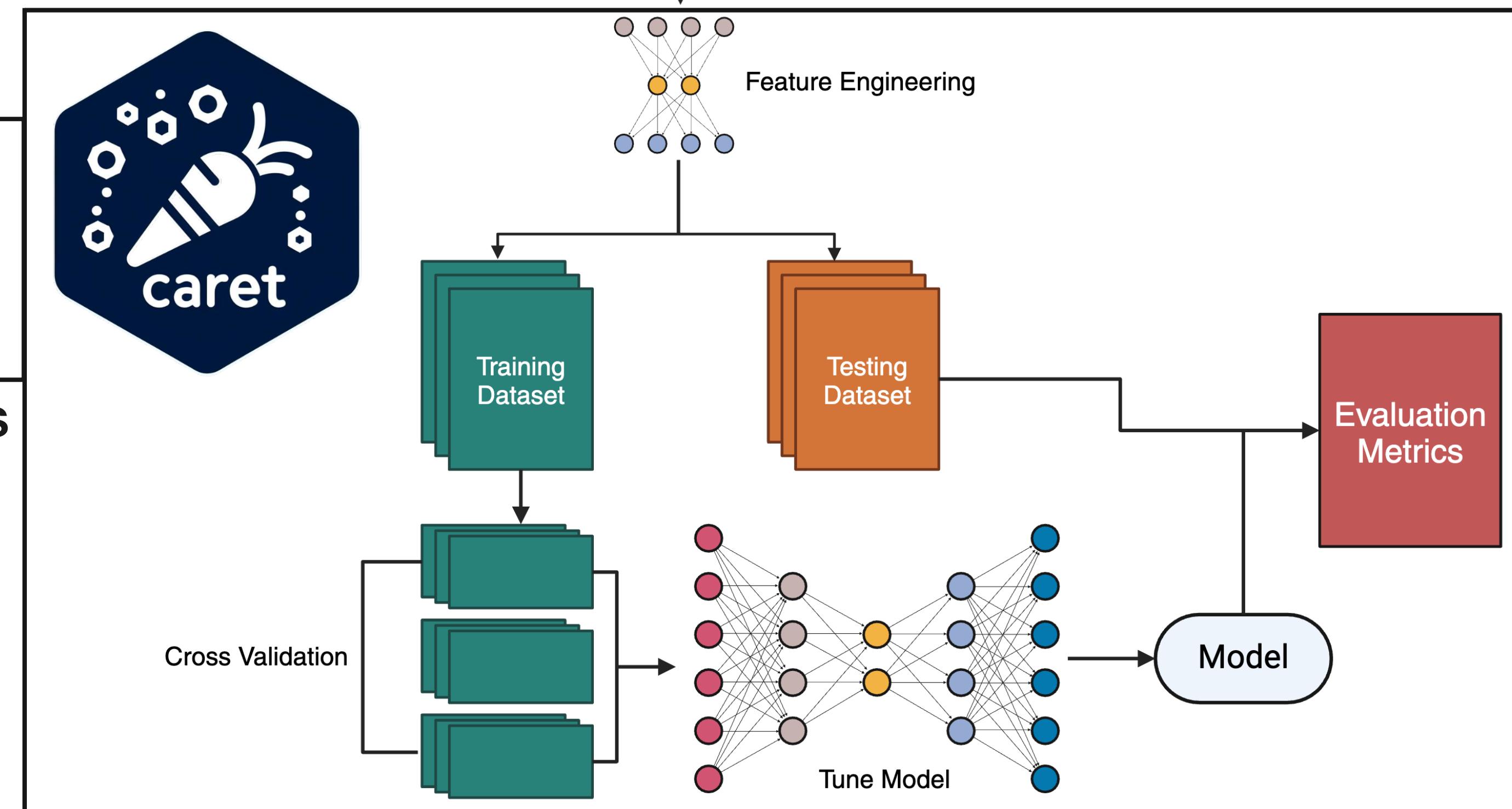
Overview of Machine Learning Models

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

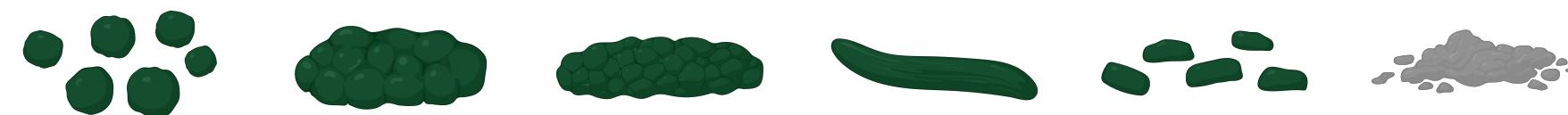
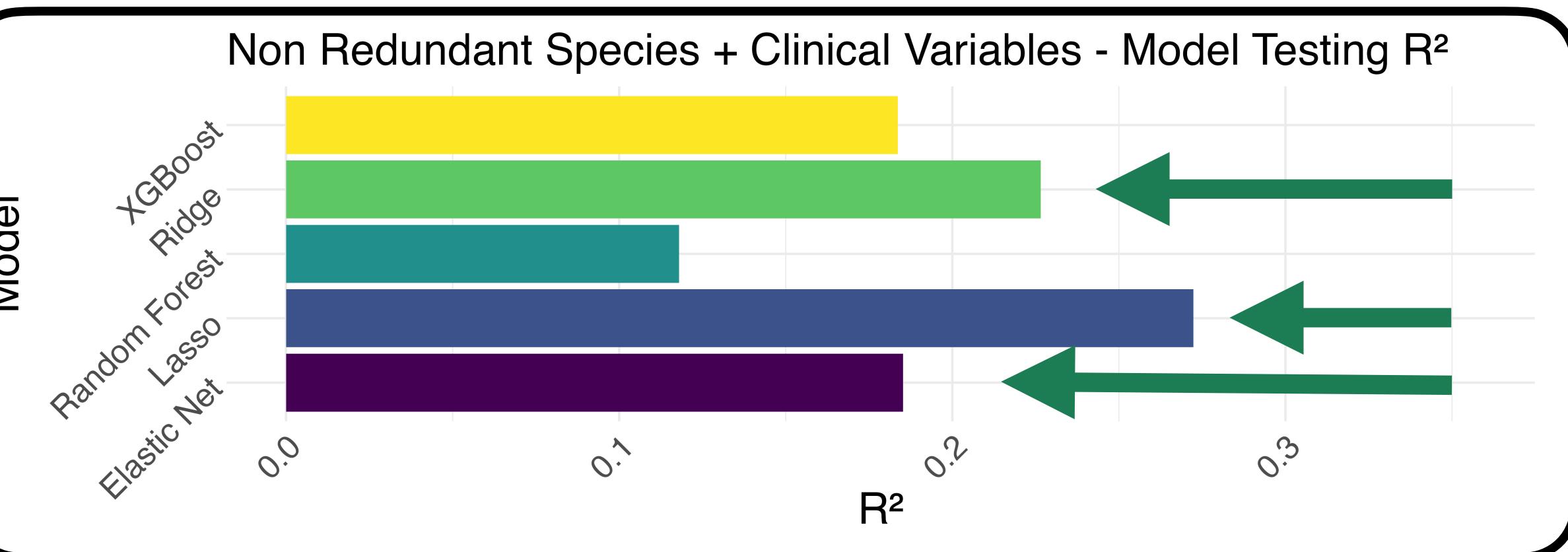
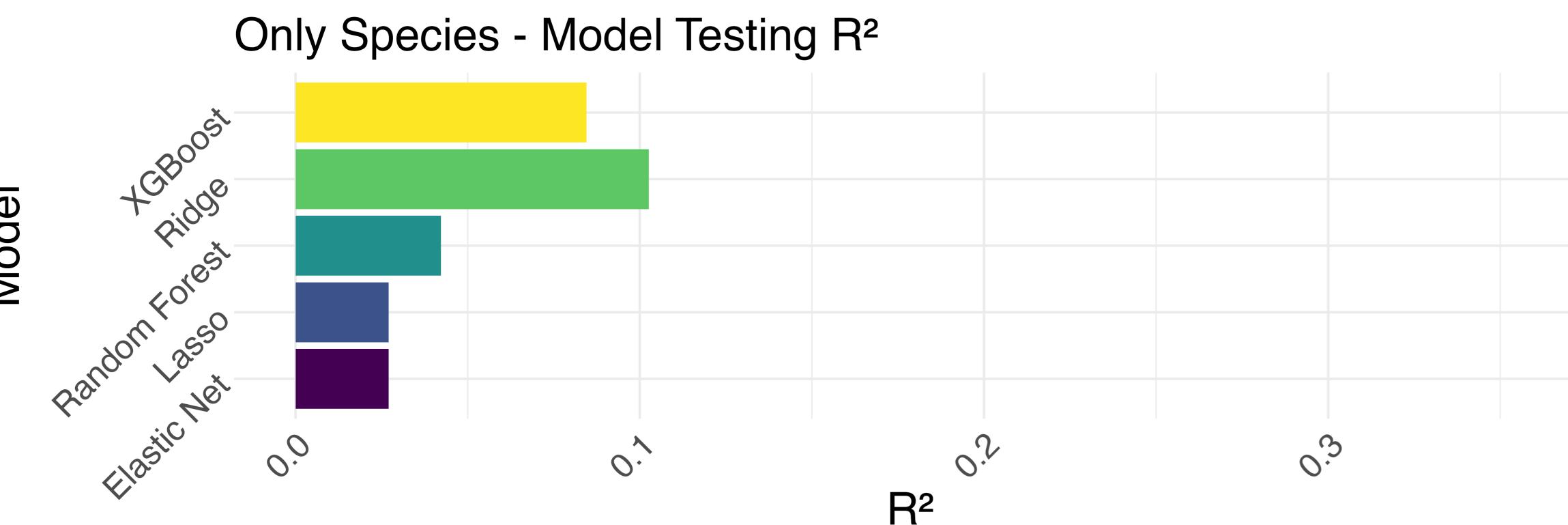
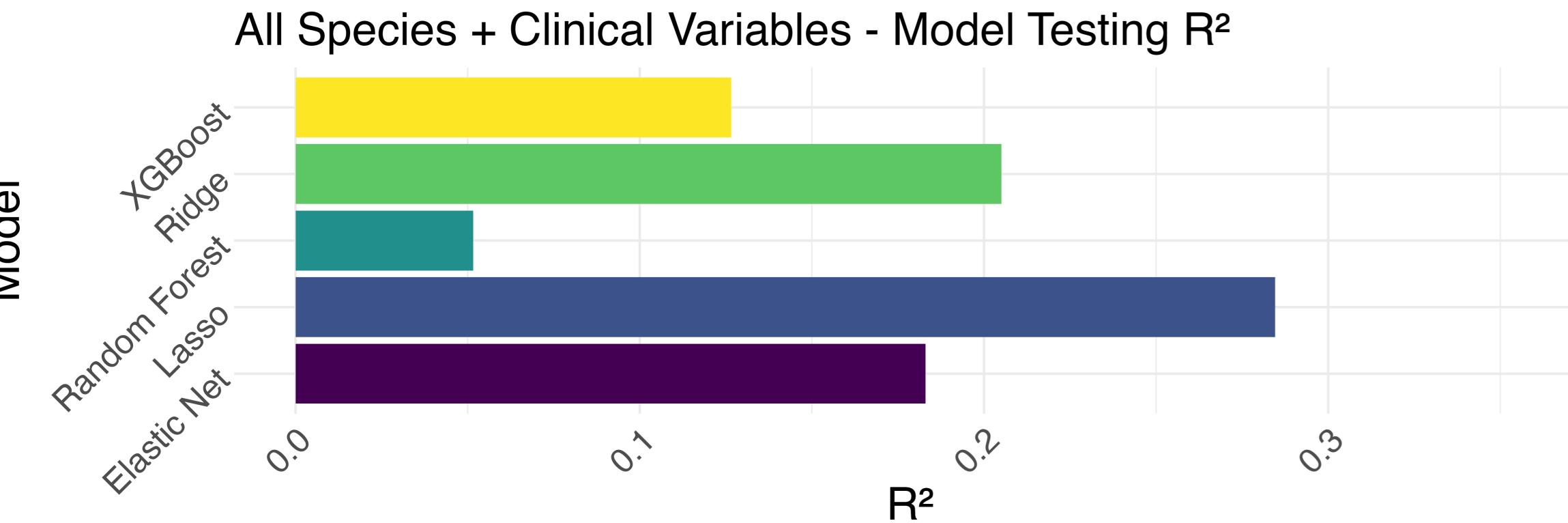
1. Understand and Prepare Data
2. Feature Engineering
3. Split the Dataset
4. Train the Model*
5. Test and Evaluate the Model
6. Interpret and Communicate the Results
7. Iterate and Improve



*Train:Test Split & Cross Validation



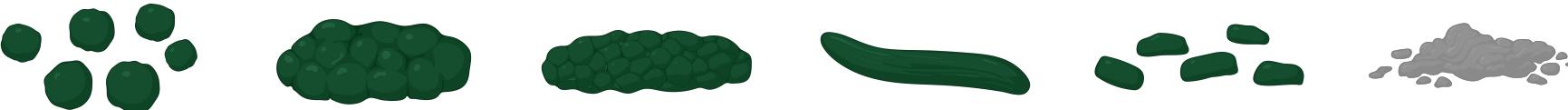
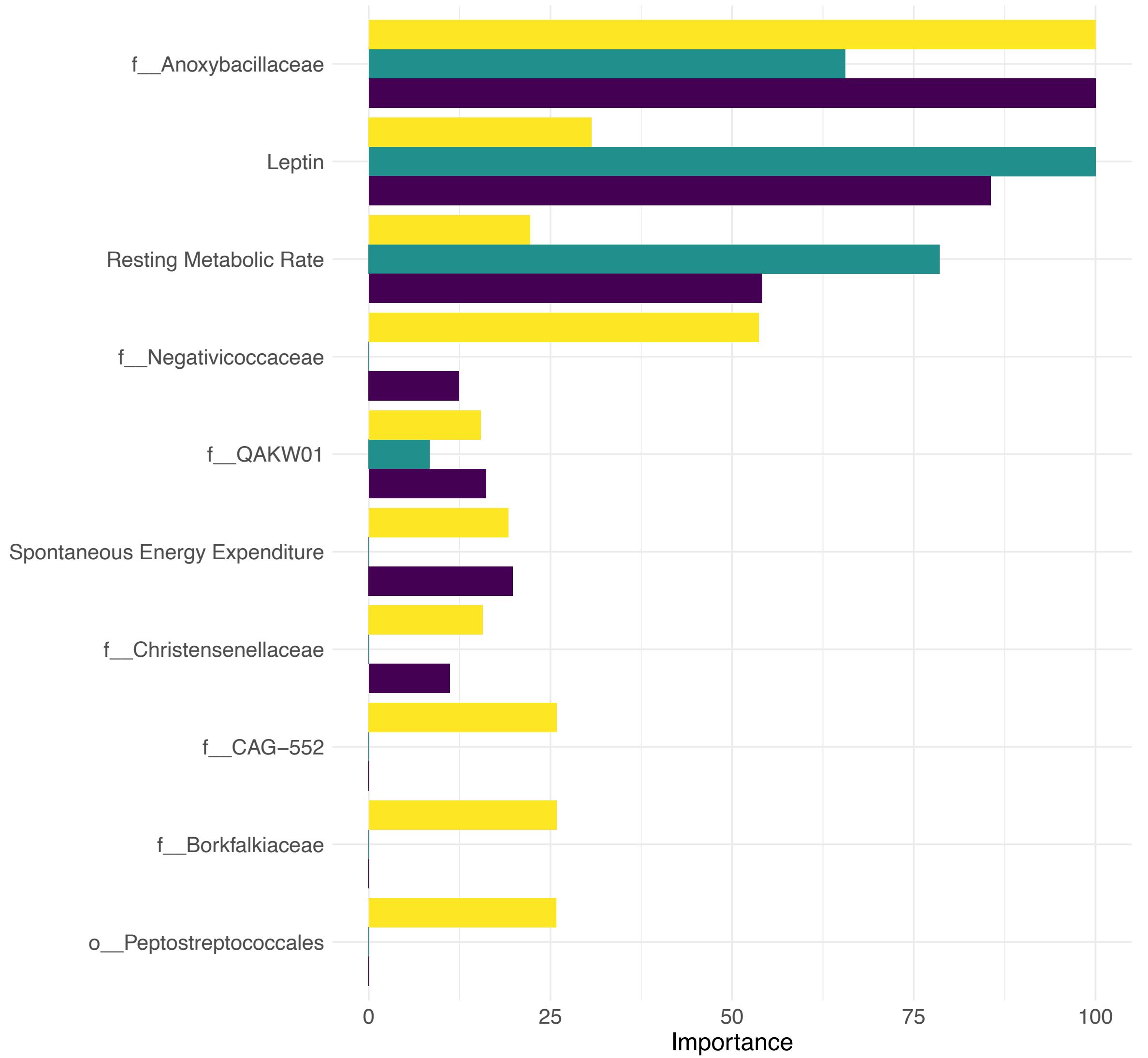
Test R^2 Metrics



Comparing Top 10 Features Across Models

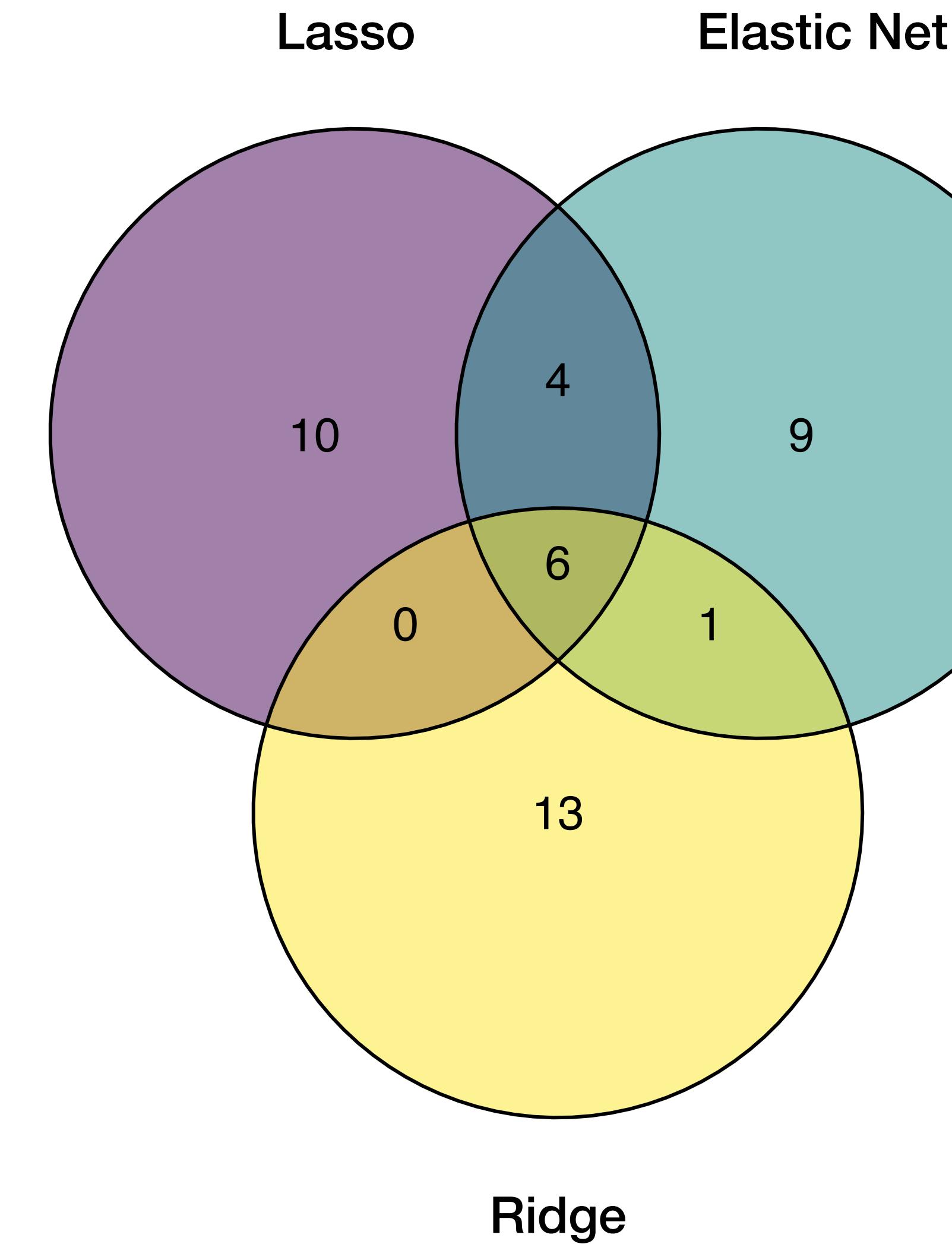
Top 10 Features – Non Redundant Genus + Clinical Variables

Model Elastic Net Lasso Ridge



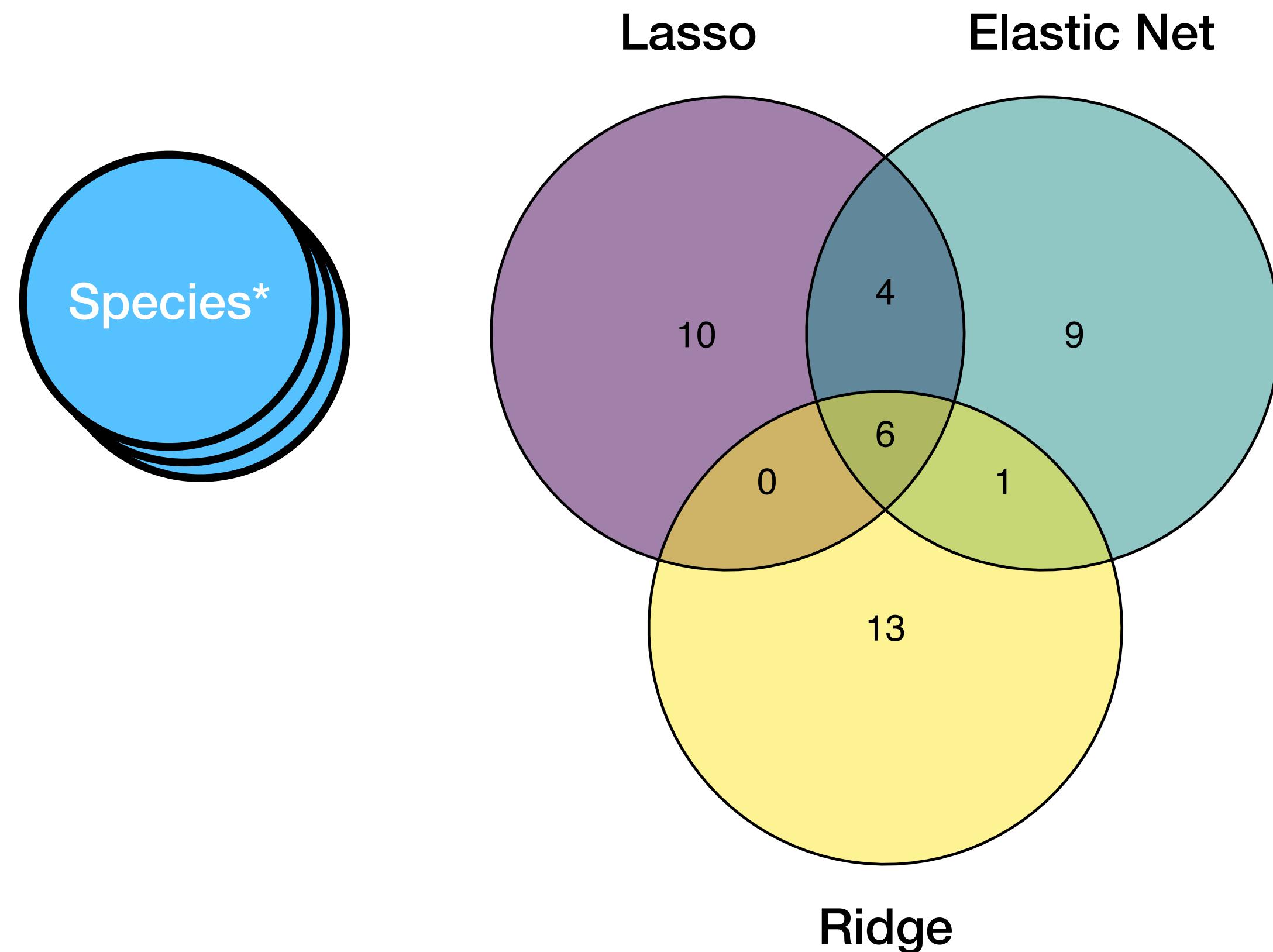
Non Redundant Species + Clinical Variables Top 20 Features Venn diagram

Feature Comparison

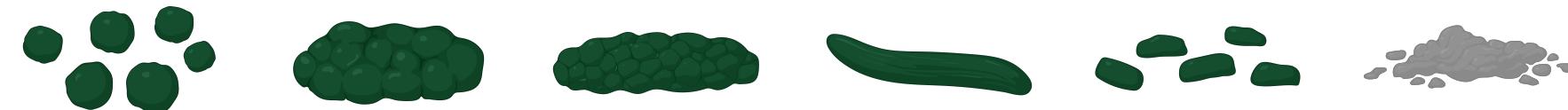
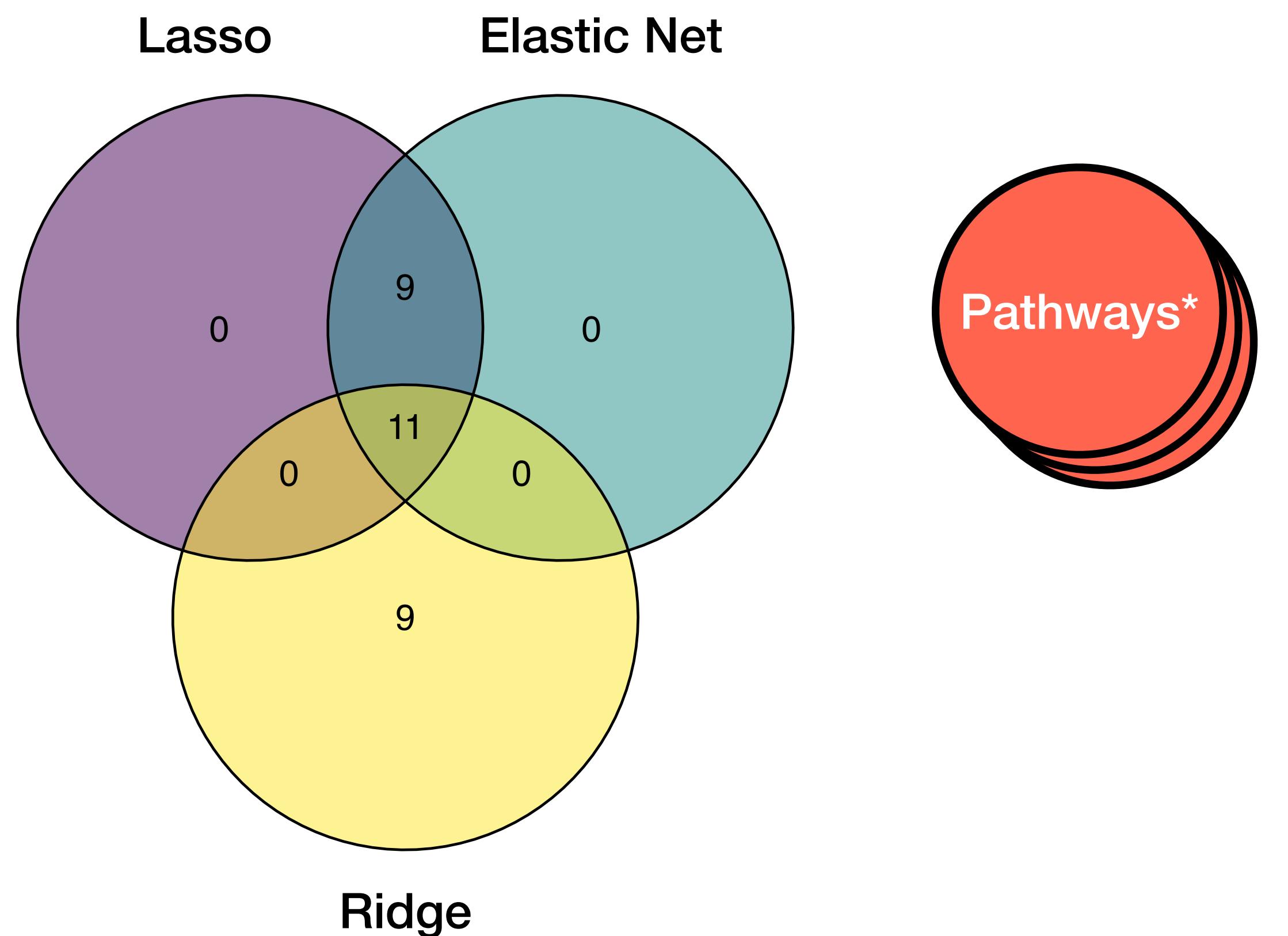


Species and Pathways Feature Comparison

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

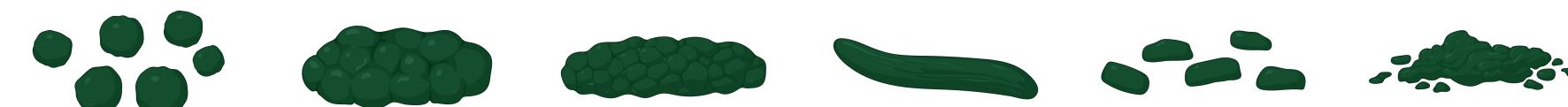
- Microbial species, genera, and pathways significantly associated with differences between actual and genetically predicted BMI
- Key clinical features
 - Leptin
 - Total Daily Energy Expenditure
 - Resting Metabolic Rate
 - Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)

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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Jennifer Fouquier
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Paul MacLean
Edward Melanson
Daniel Bessesen
Victoria Catenacci
Sarah Borengasser



Department of Biomedical Informatics
SCHOOL OF MEDICINE
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**



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Questions?