

Gut microbe associations with host genotype vary across ethnicities and potentially influence cardiometabolic traits



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Supervisor: Max Nieuwdorp



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Gut microbiome associations with host genotype vary across ethnicities and potentially influence cardiometabolic traits

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Poster # 2

Longitudinal study on the variation of the human gut microbiome composition in a multi-ethnic cohort and its predictive relationship with metabolic health



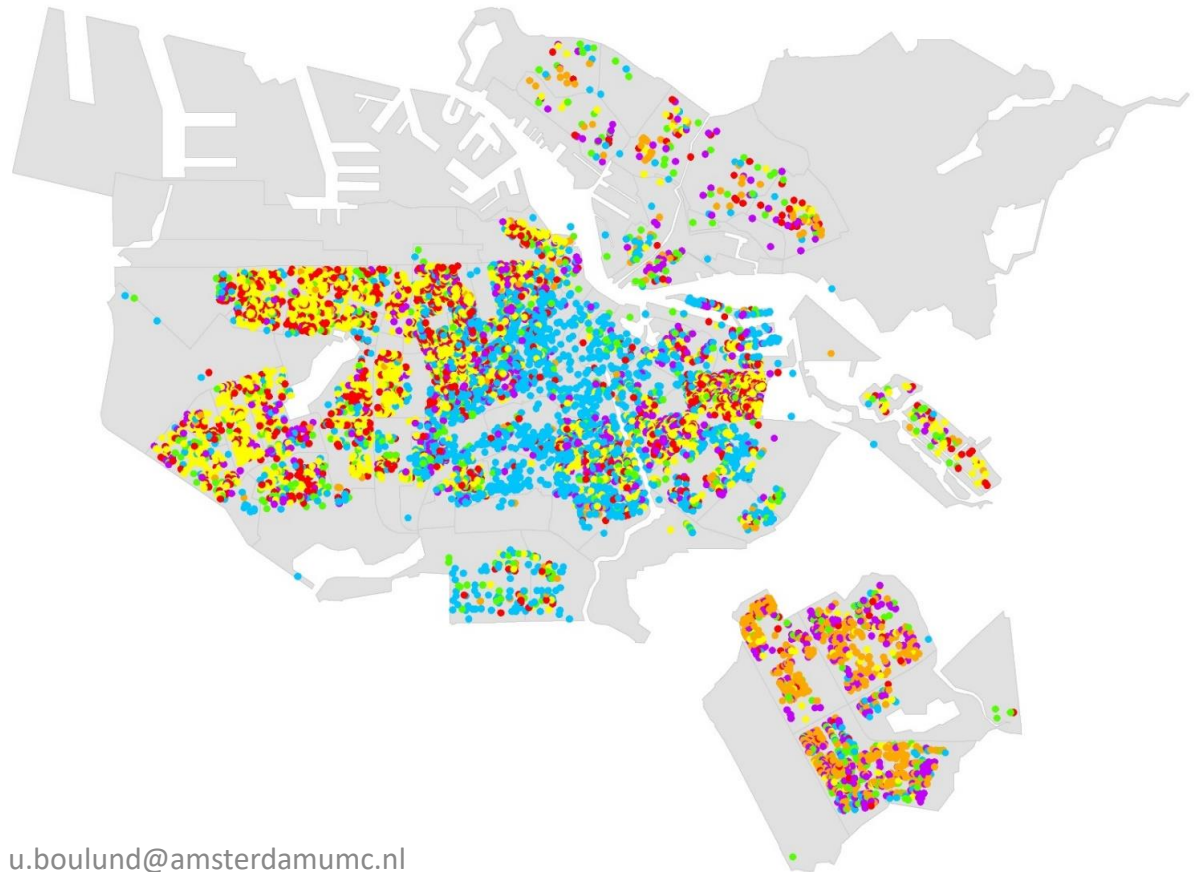
Healthy Life in an urban setting

First data collection: 2011-2015

25.000 participants

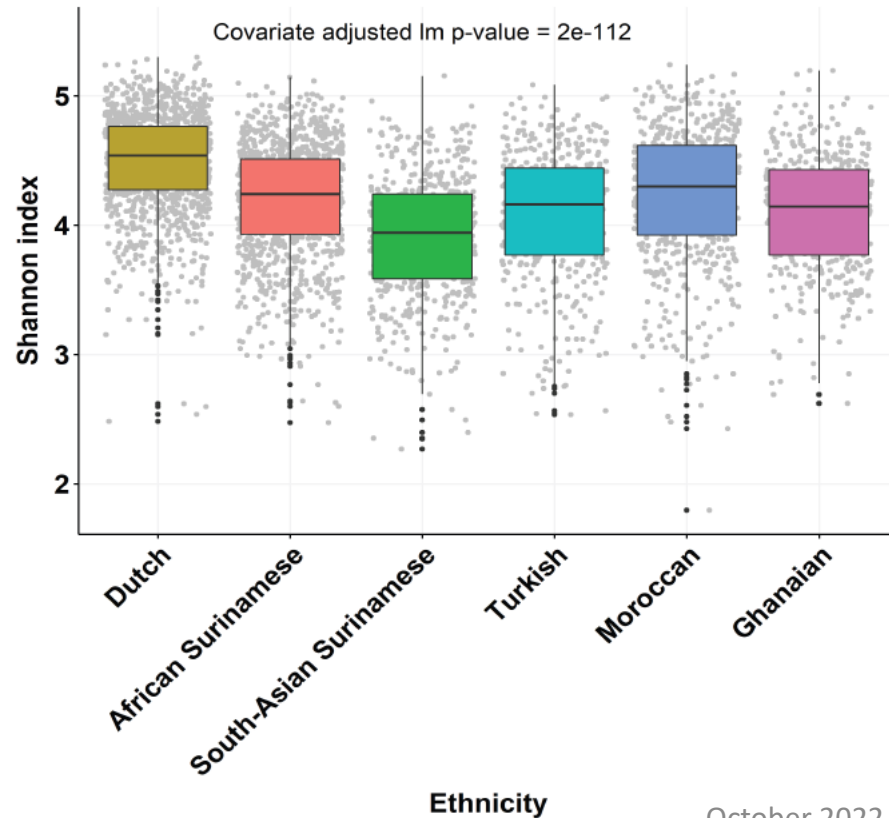
6 different ethnicities

Age 18-70 years

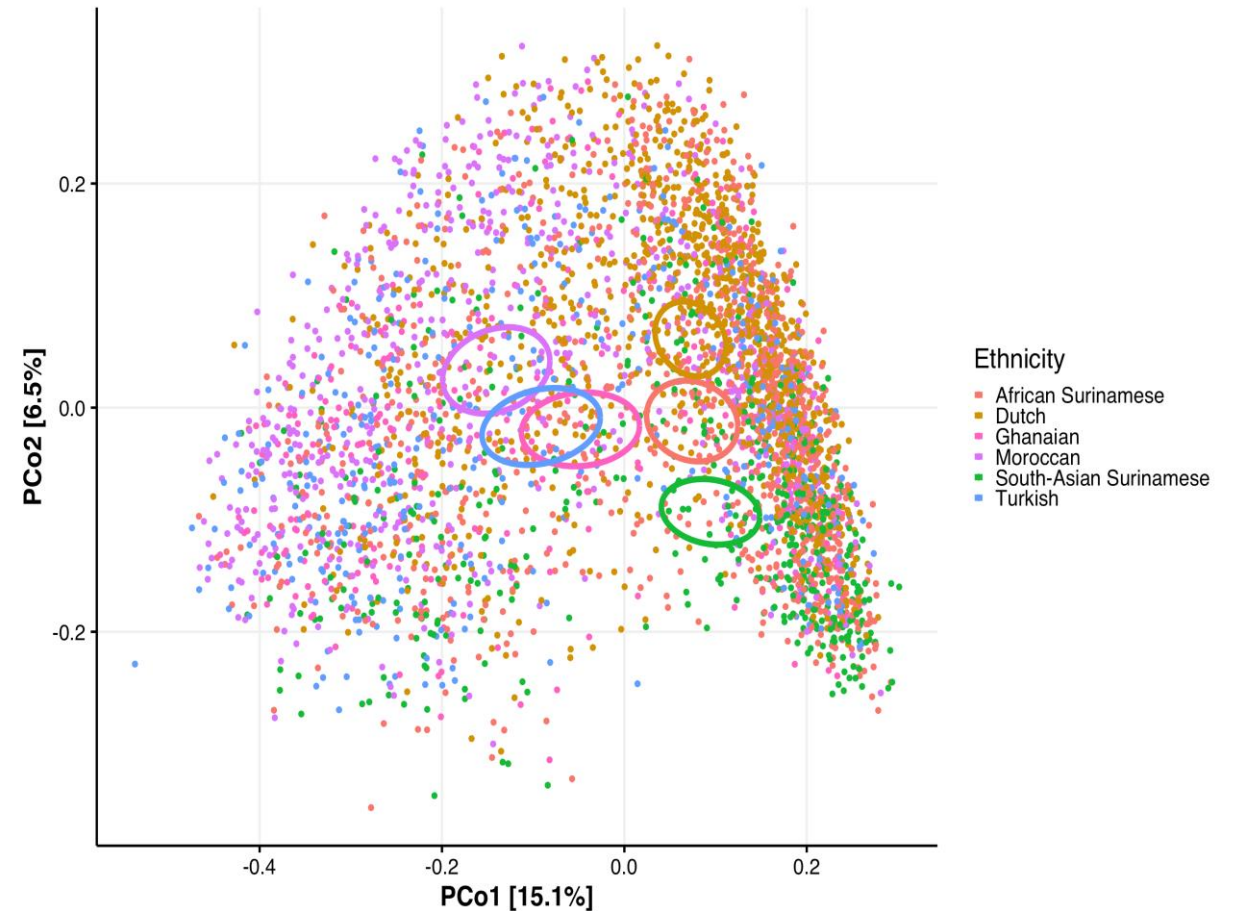
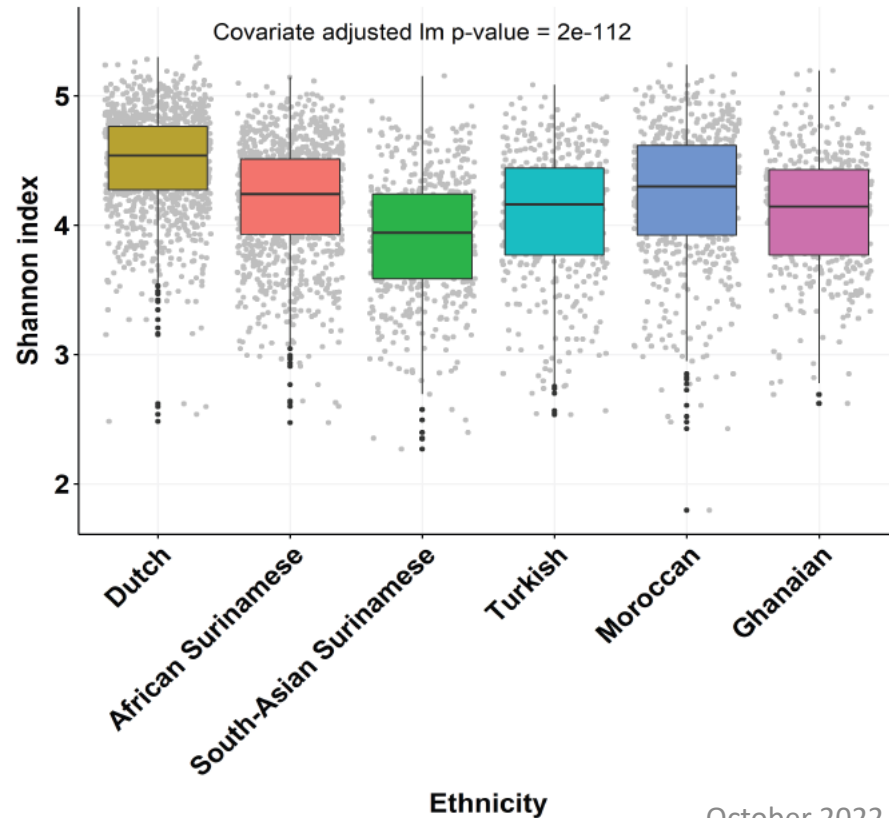


The gut microbiome composition differs between ethnicities

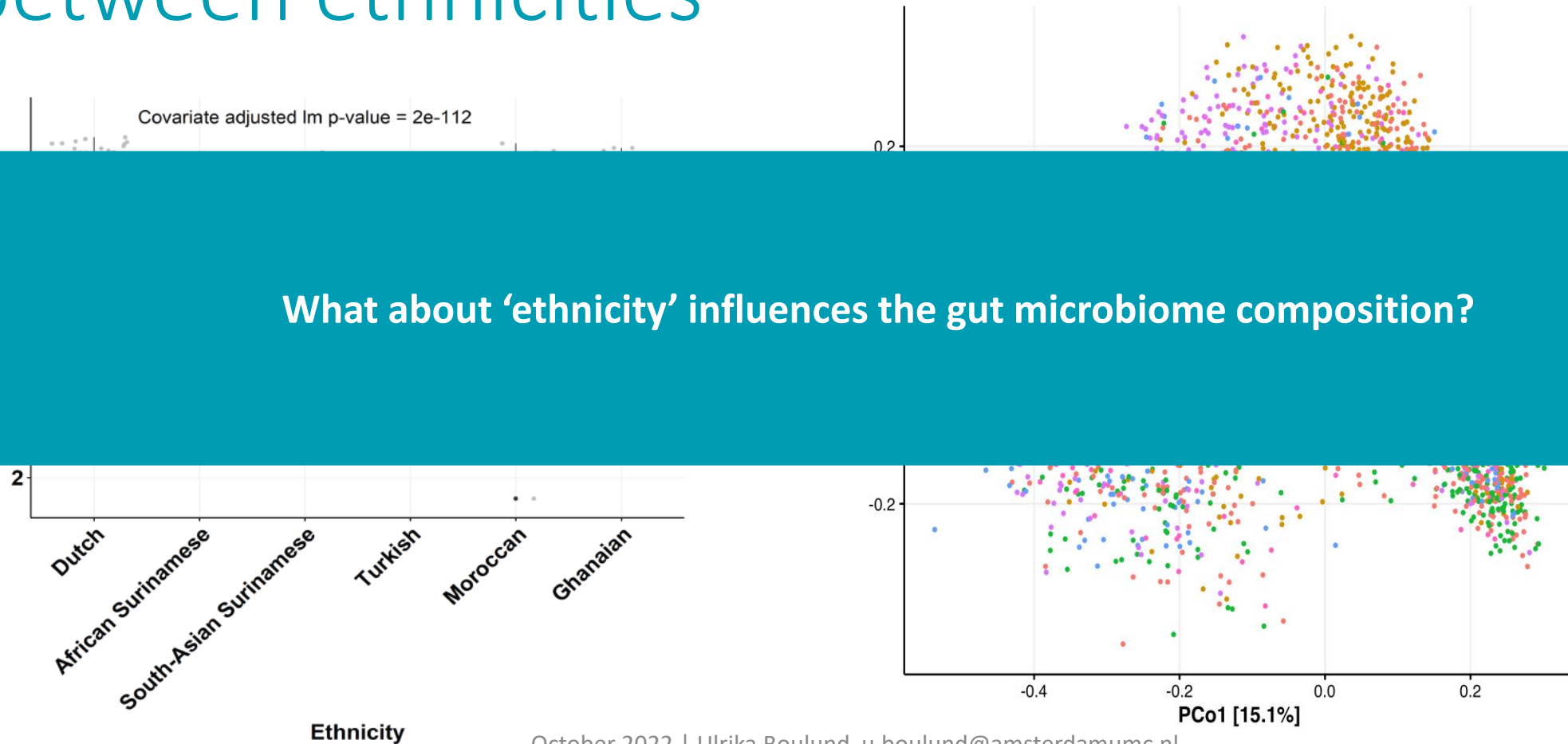
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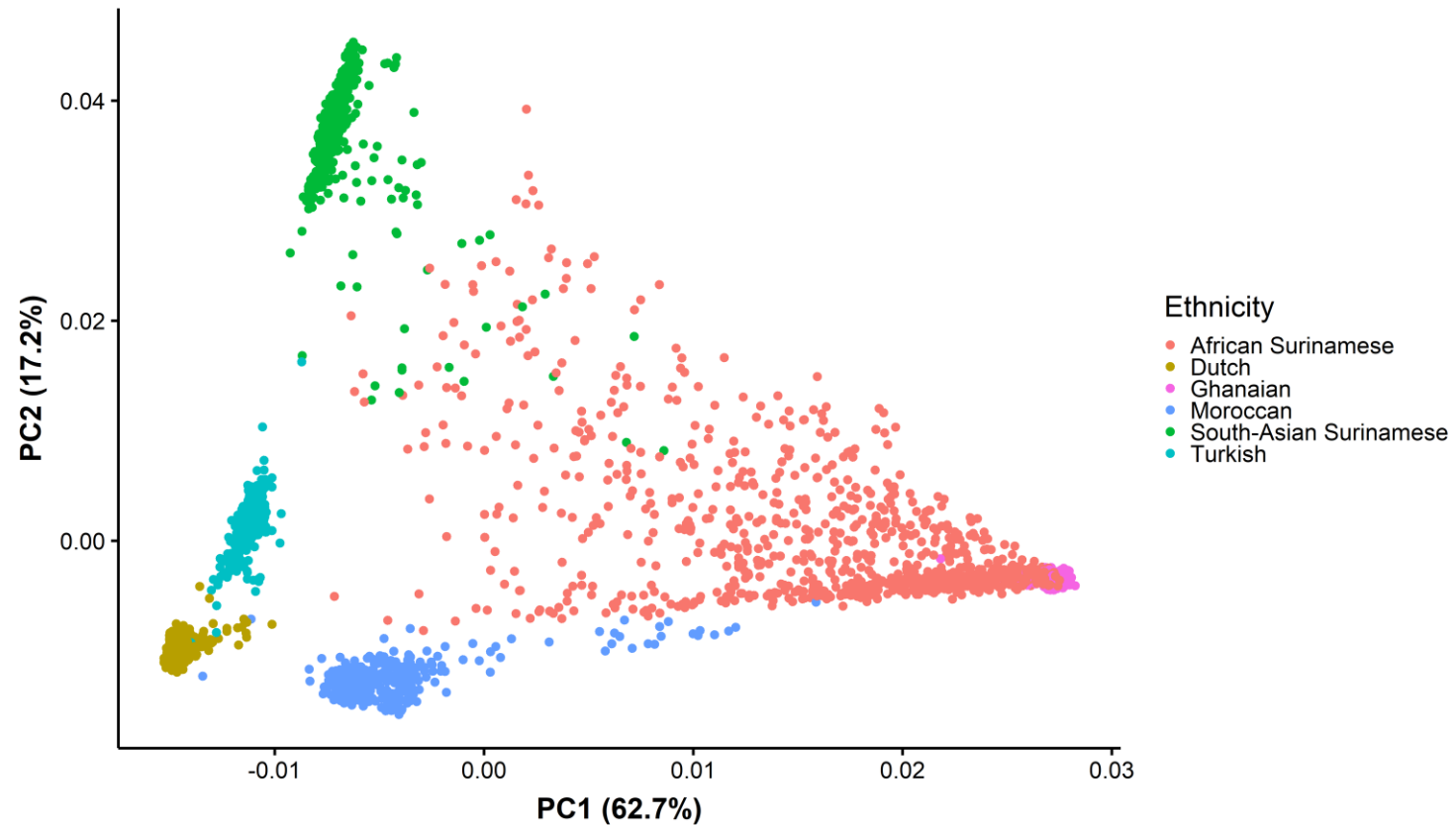


The gut microbiome composition differs between ethnicities



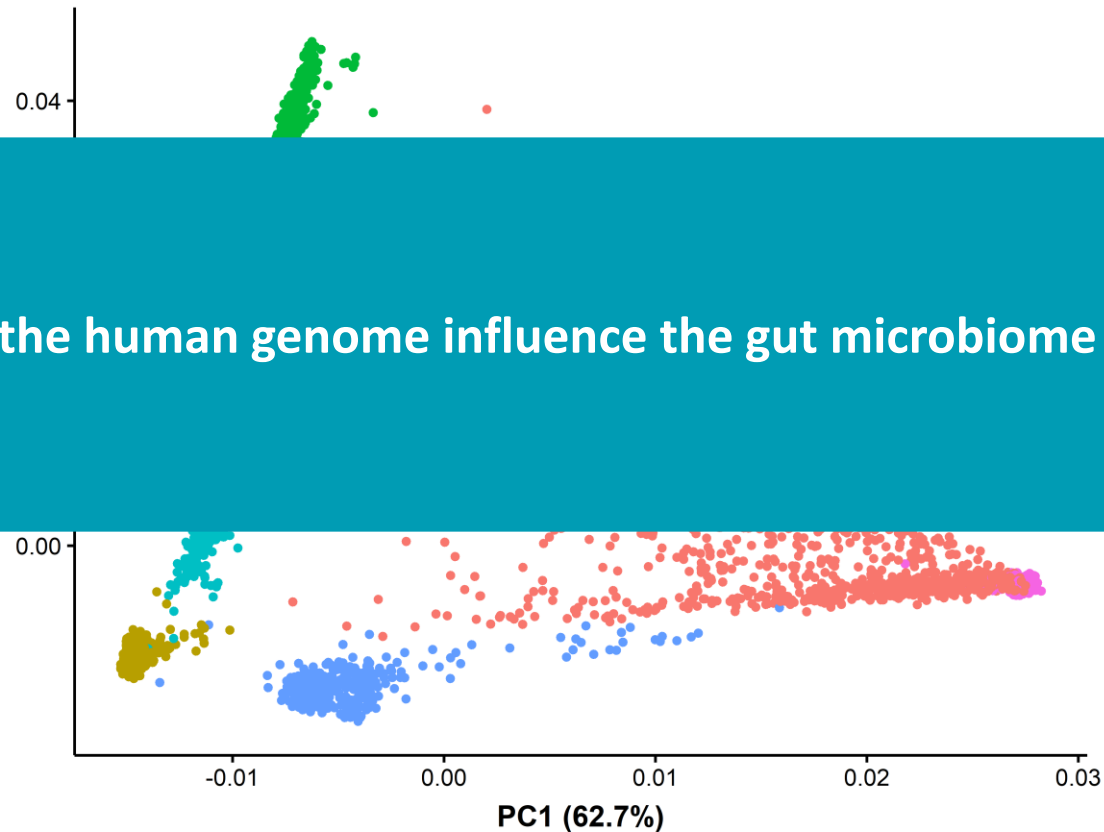
What about 'ethnicity' influences the gut microbiome composition?

Ethnicity is many things, including genotype



Ethnicity is many things, including genotype

Does the human genome influence the gut microbiome composition?



Gut microbiome composition is associated with genome



Gut microbiome composition is associated with genome

Microbe-associated loci are related to:

- Immune system
- ABO/FUT2 gene
- Vitamin D receptor
- Mucus genes



Gut microbiome composition is associated with genome

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 - Mucus genes
-
- Small, mainly European cohorts



Gut microbiome composition is associated with genome

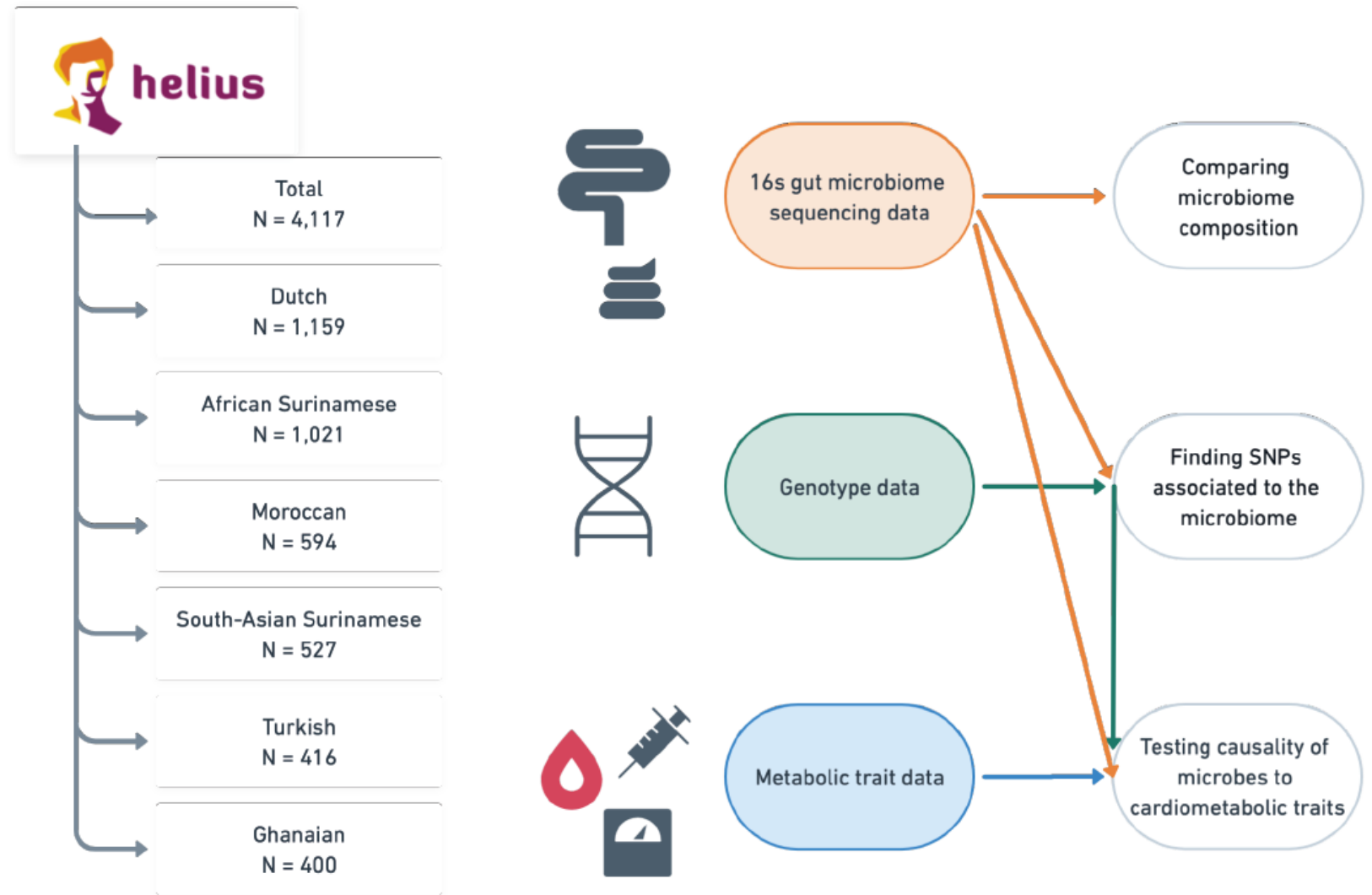
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What associations are seen in other ethnicities?



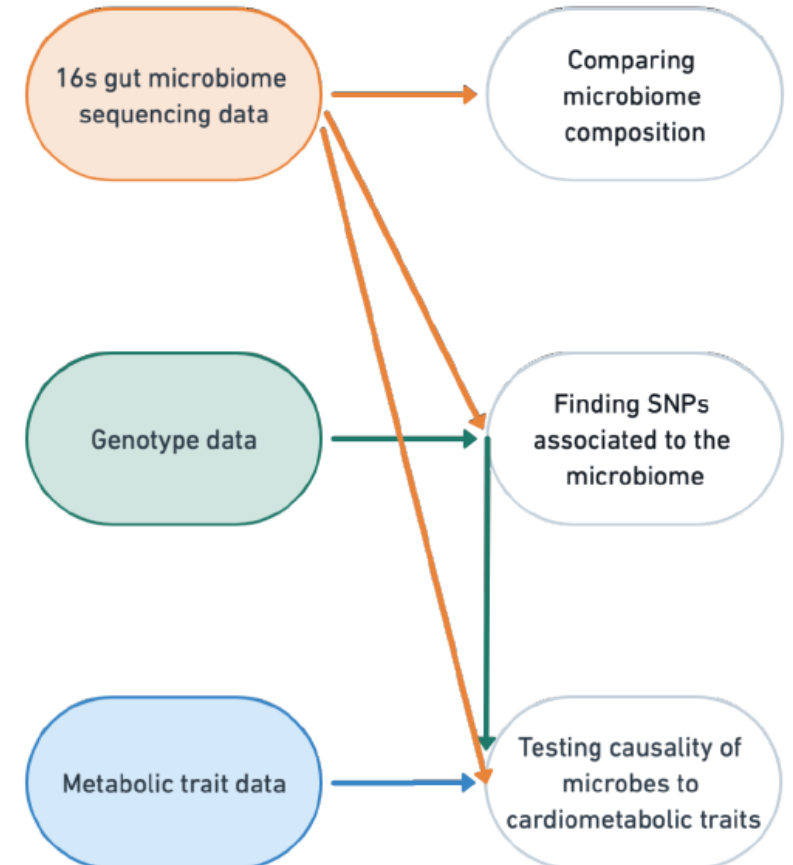
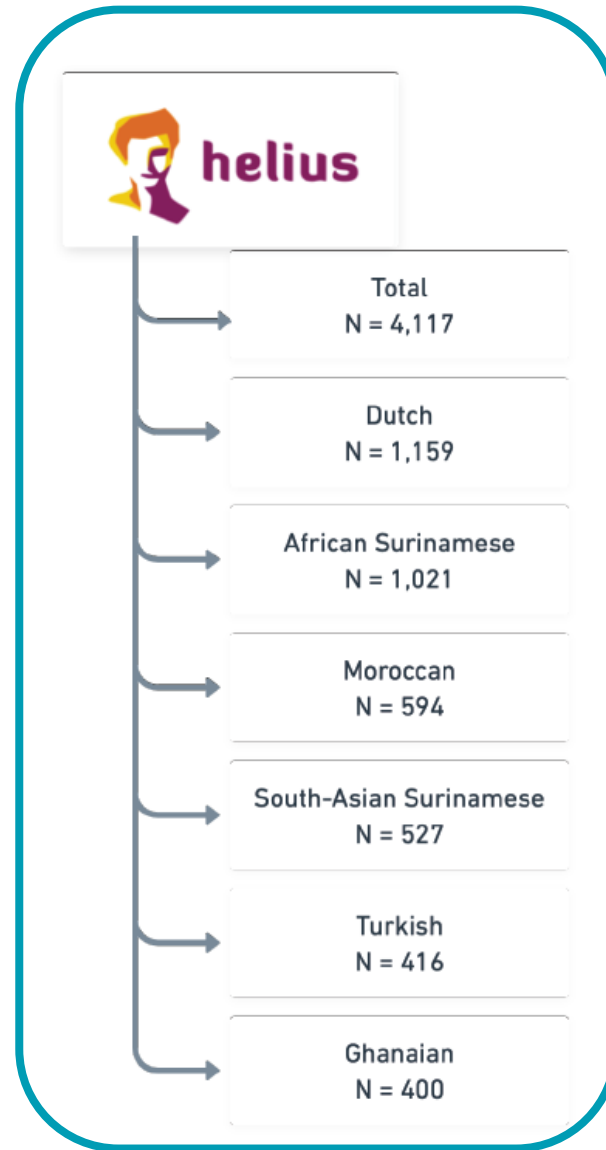
Study design



Study design

Largest single-cohort
study: N = 8,000

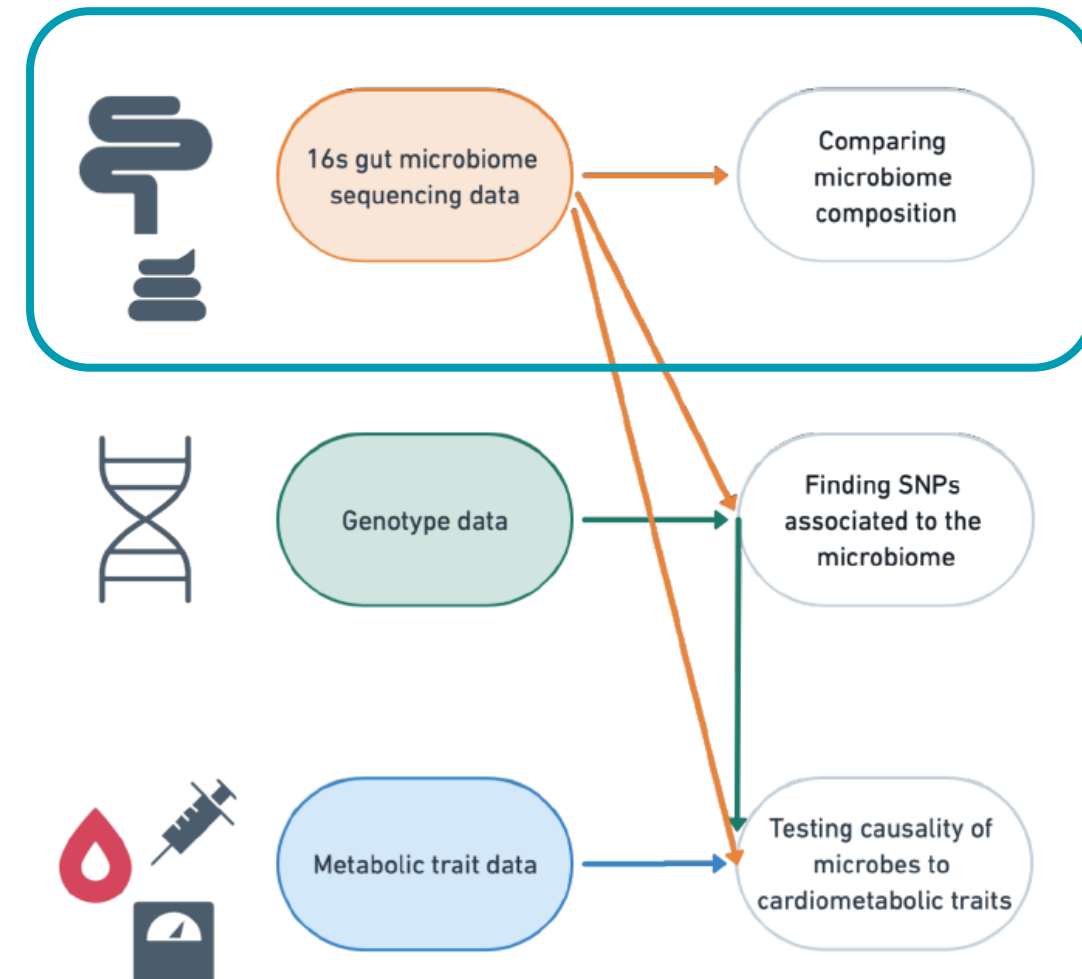
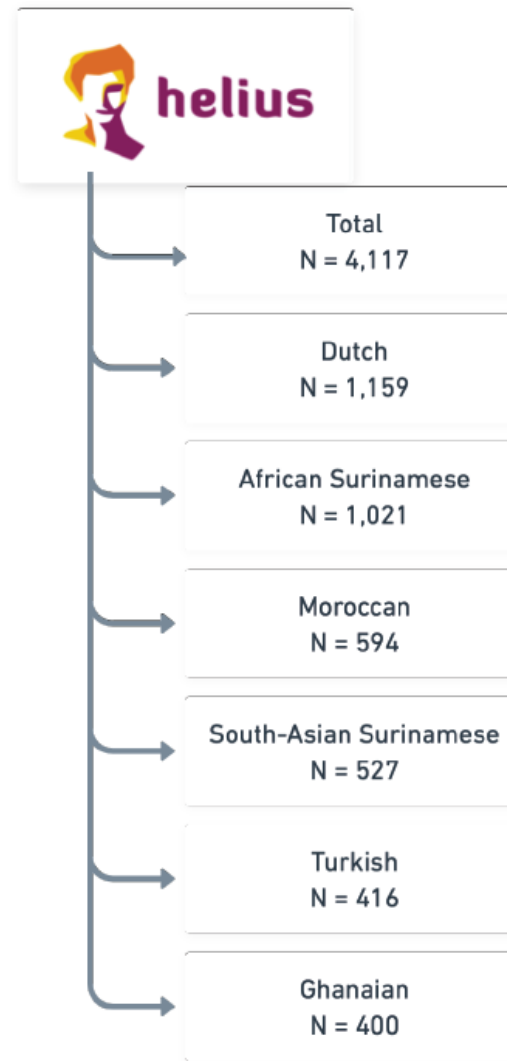
Largest multi-ethnic
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Study design

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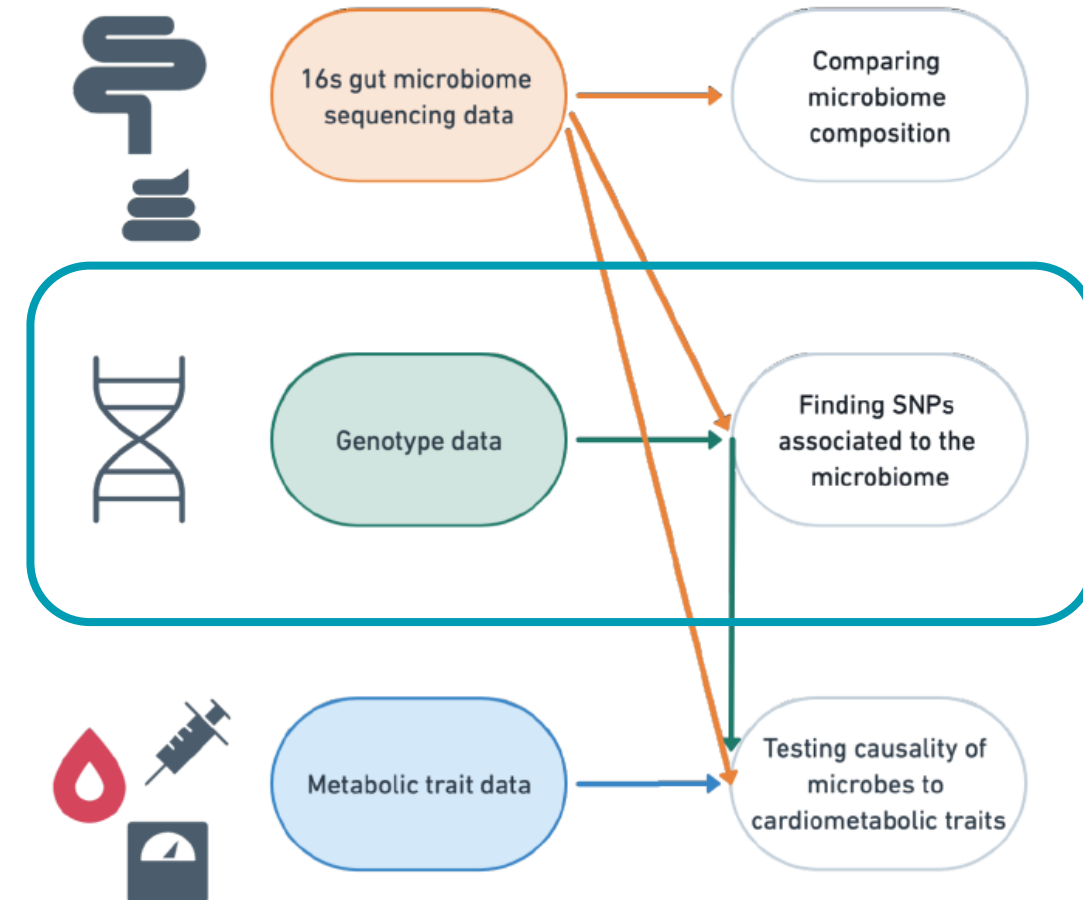
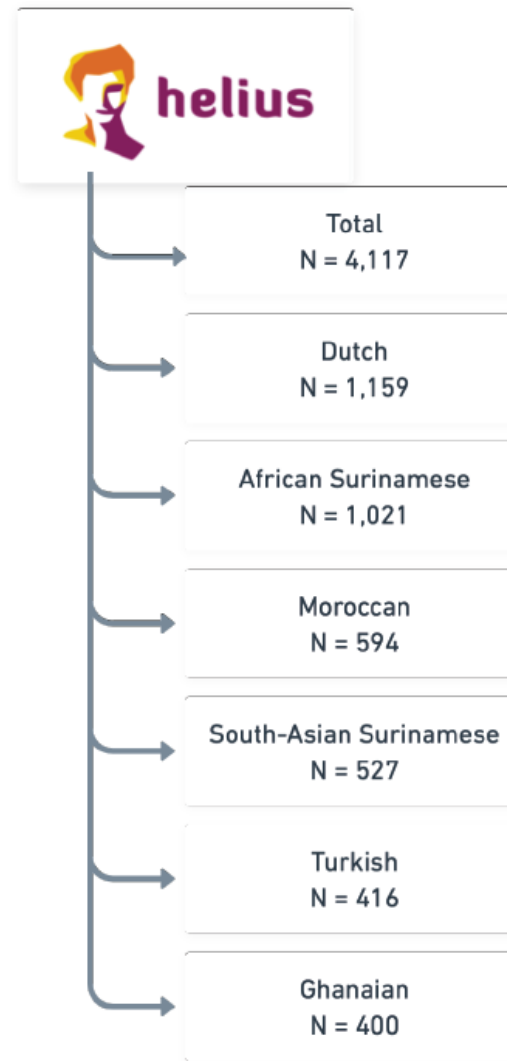
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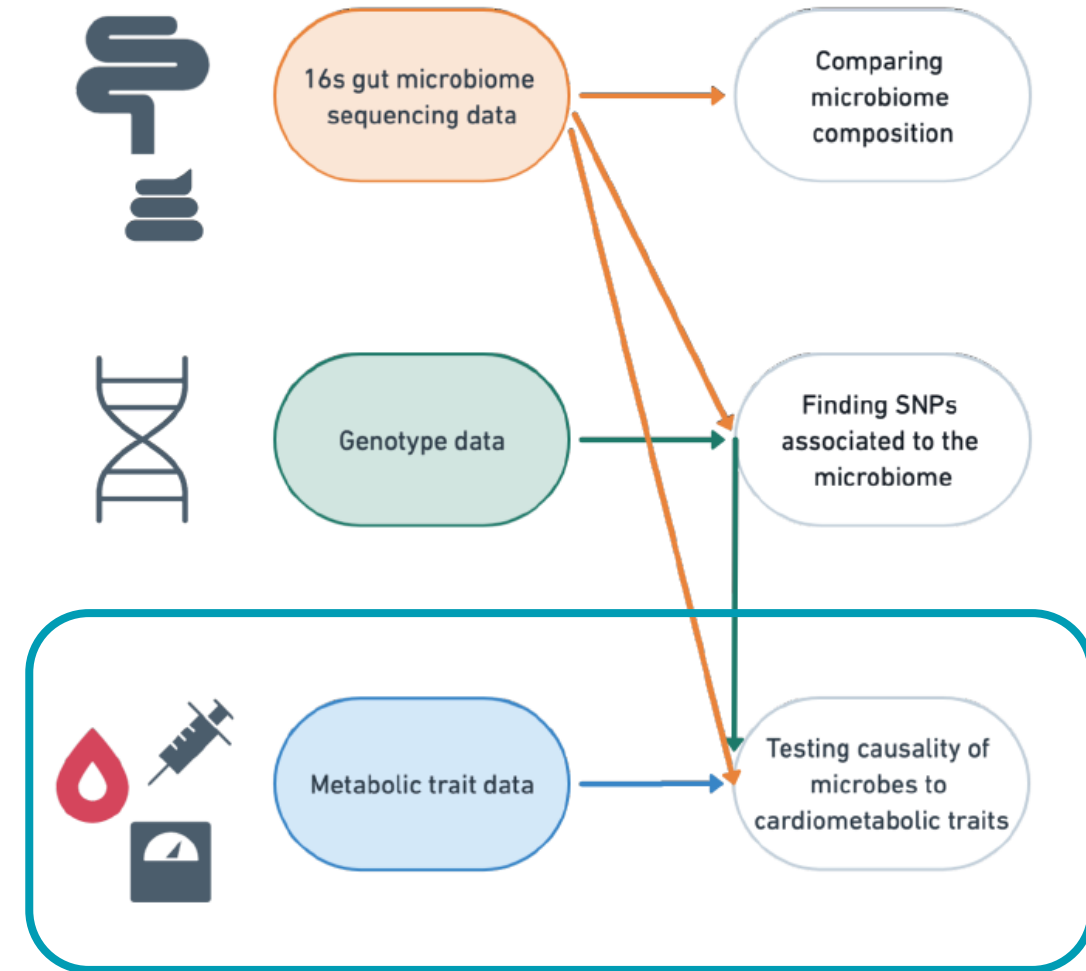
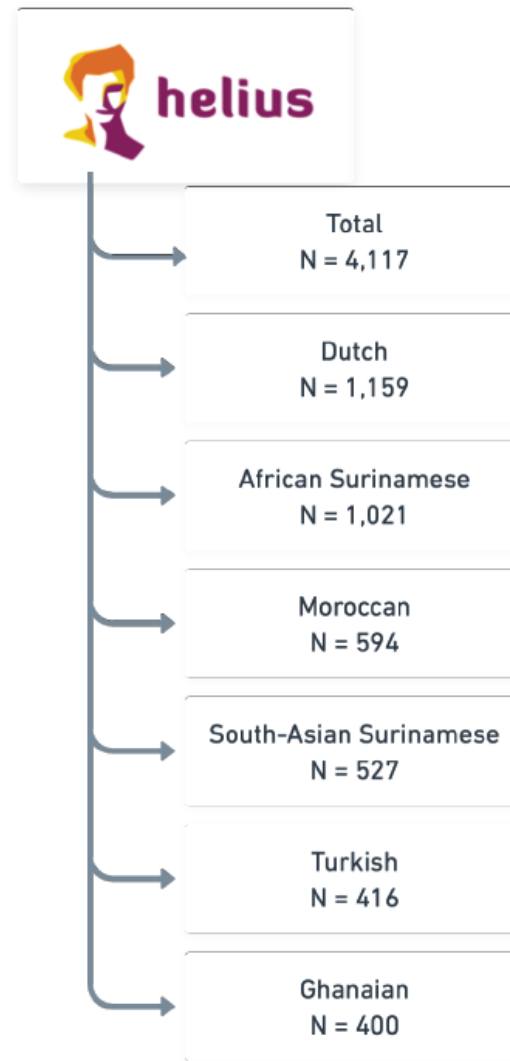
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Research questions

Which microbes are influenced by the human genome?

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How can the genome influence the human gut microbiome?

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How can the genome influence the human gut microbiome?

Which gut microbes are potentially causal in cardiometabolic phenotypes?

Research questions

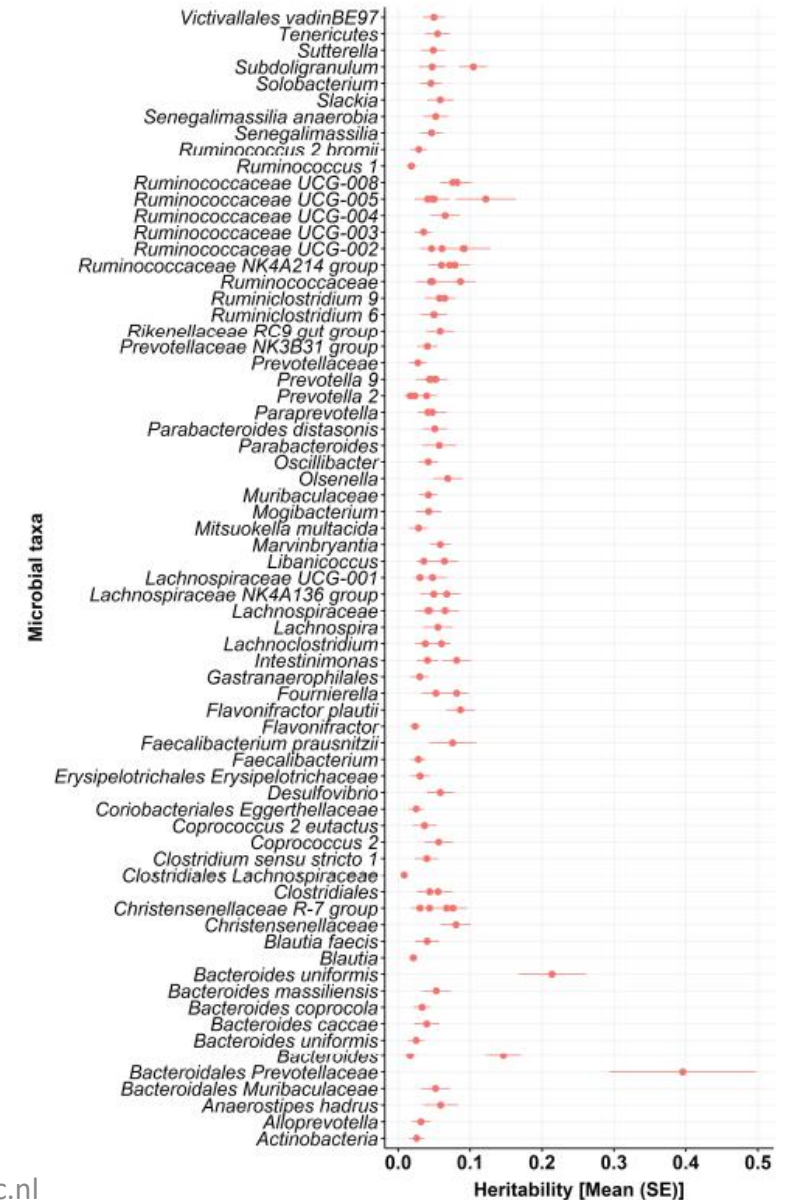
Which microbes are influenced by the human genome?

How can the genome influence the human gut microbiome?

Which gut microbes are potentially causal in cardiometabolic phenotypes?

Are these effects ethnicity specific?

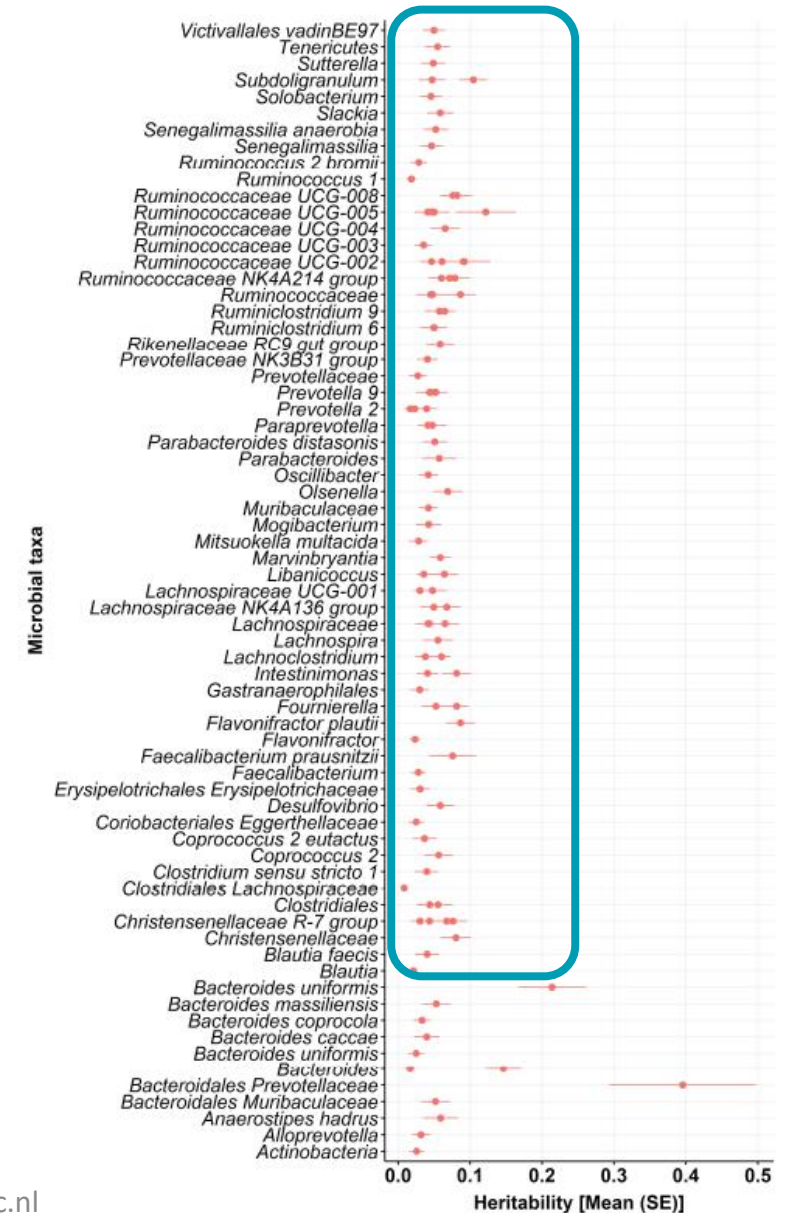
Gut microbes exhibit varying heritability



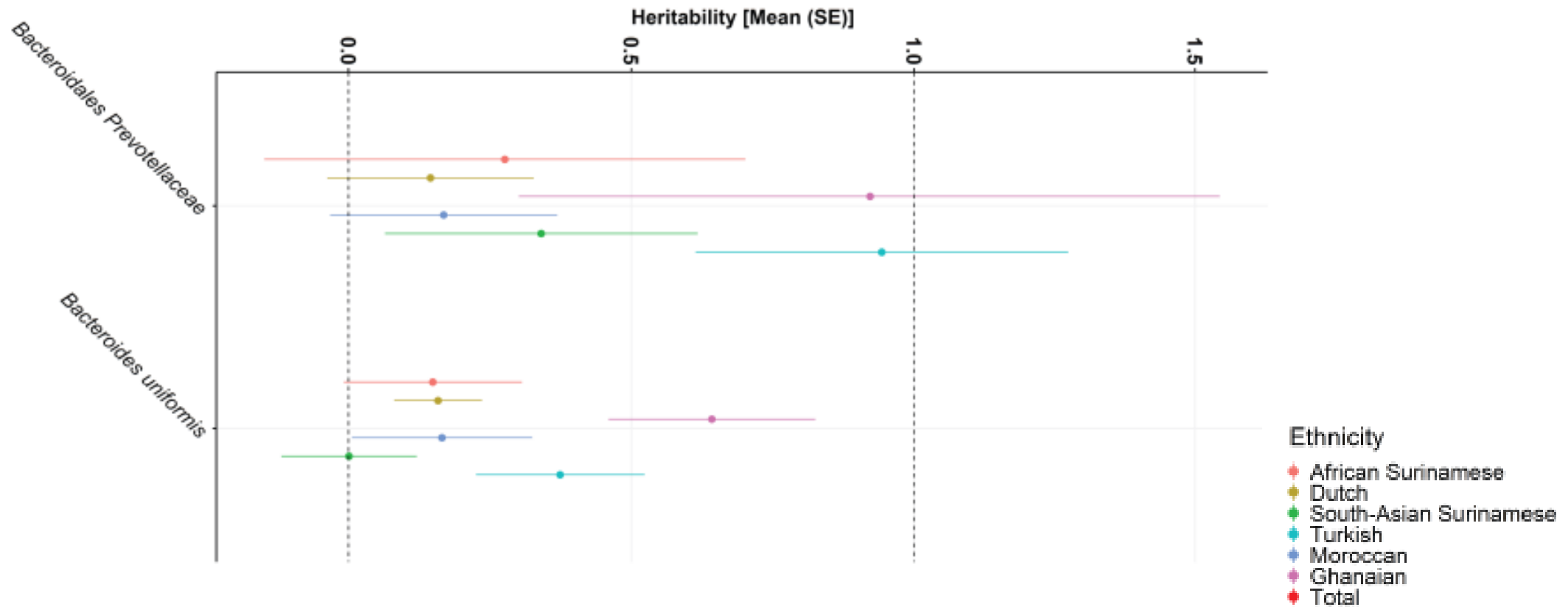
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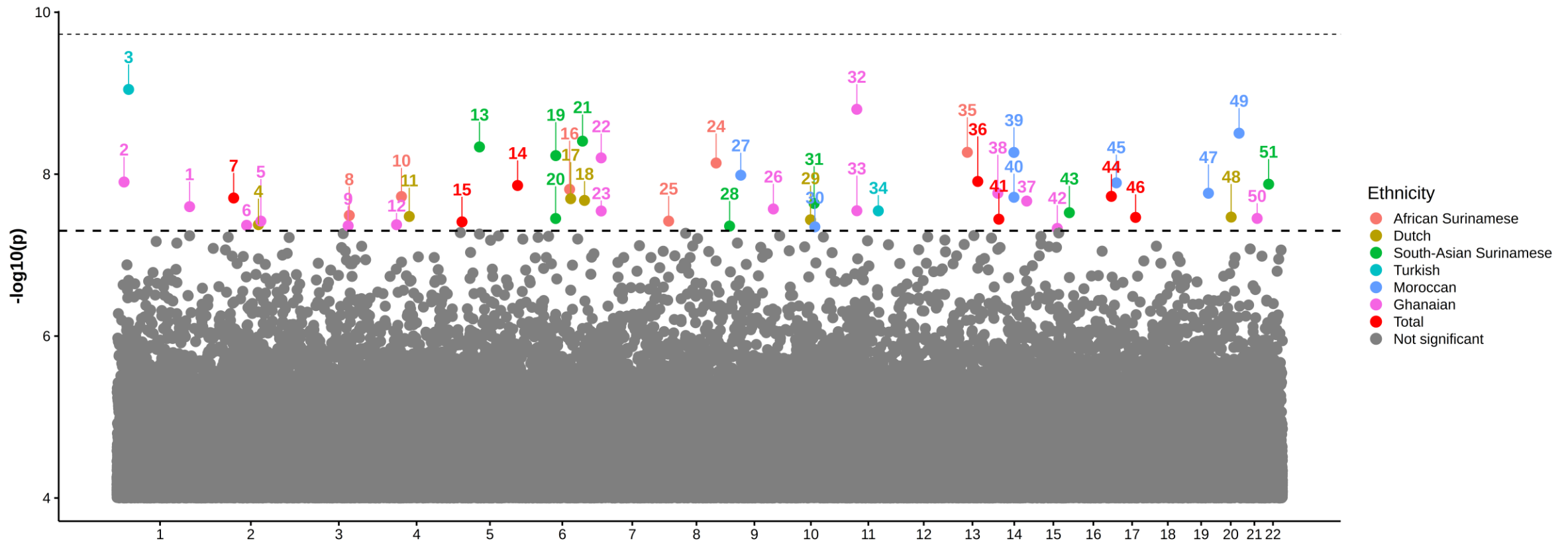
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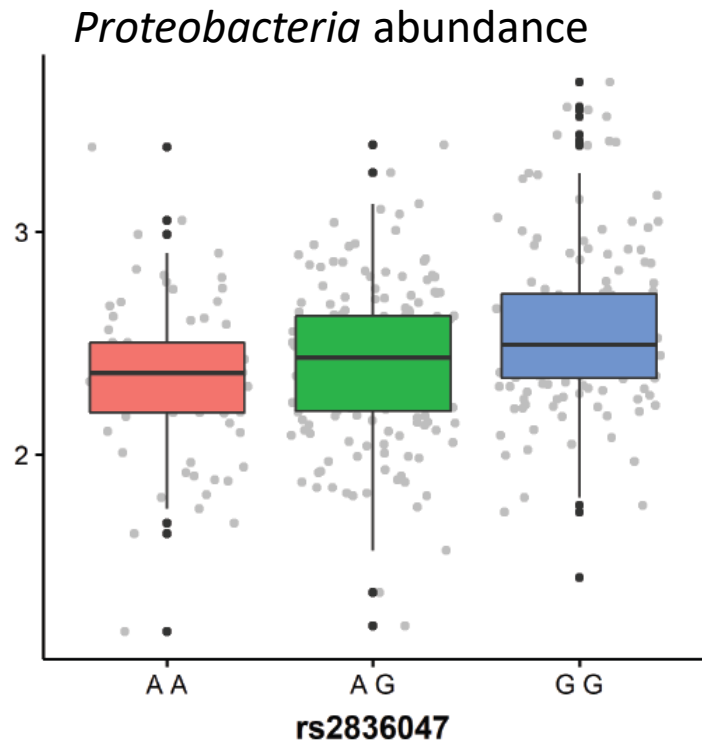
Gut microbe heritability differs between ethnicities



Human genetic loci associated with various gut microbes across ethnic groups

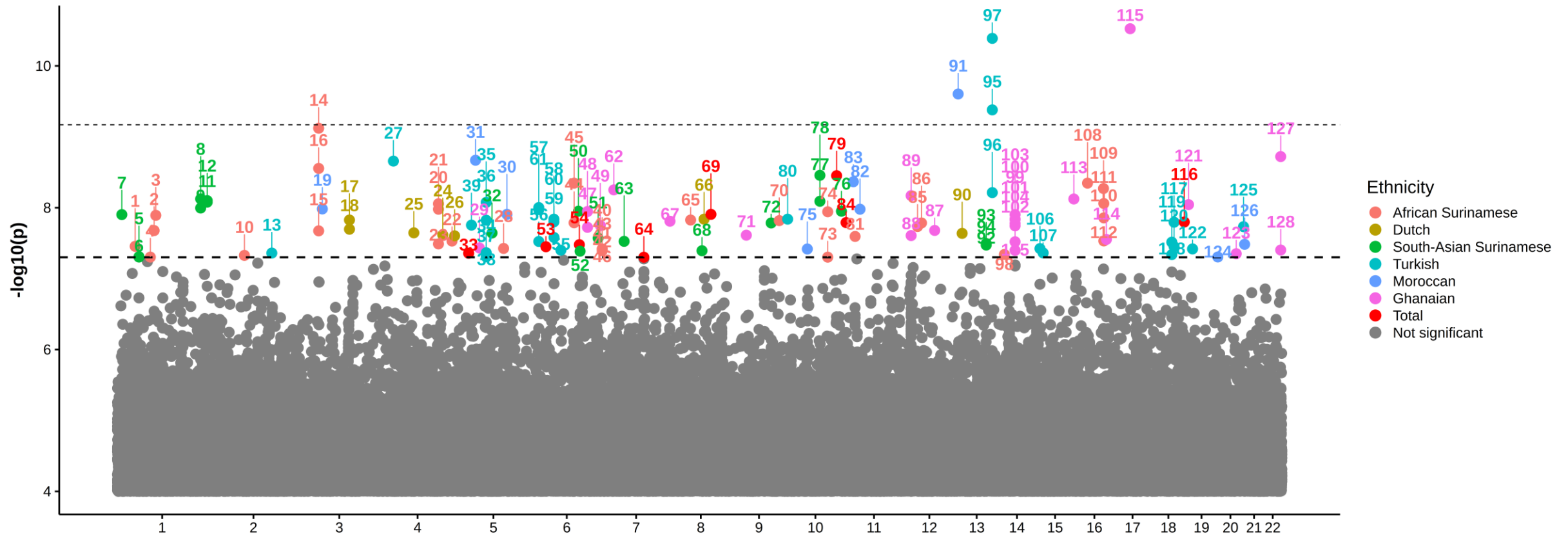


Loci associated with gut microbes are expressed in the pancreas and gut



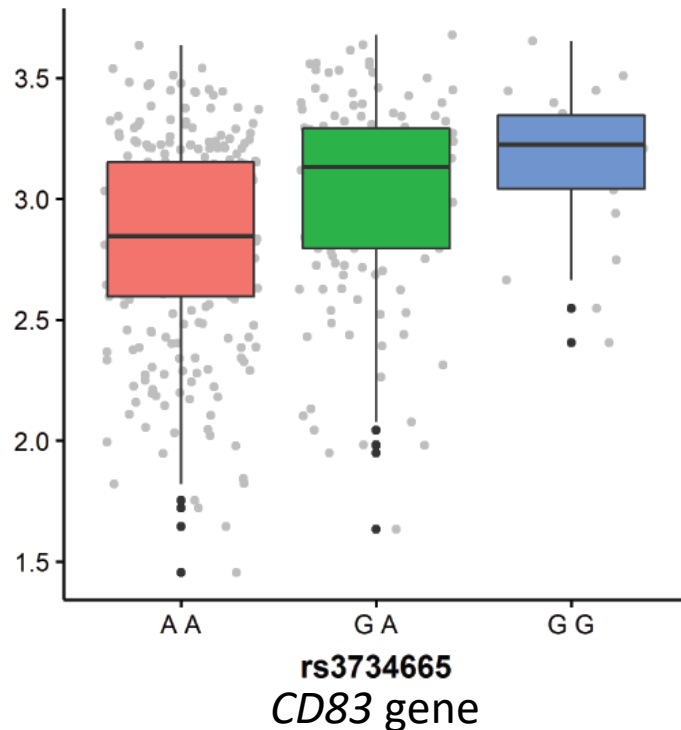
The *KCNJ6* gene encodes a potassium channel
Expressed in the pancreas
Regulates insulin secretion

Human genetic loci associated with various gut microbial pathways across ethnic groups

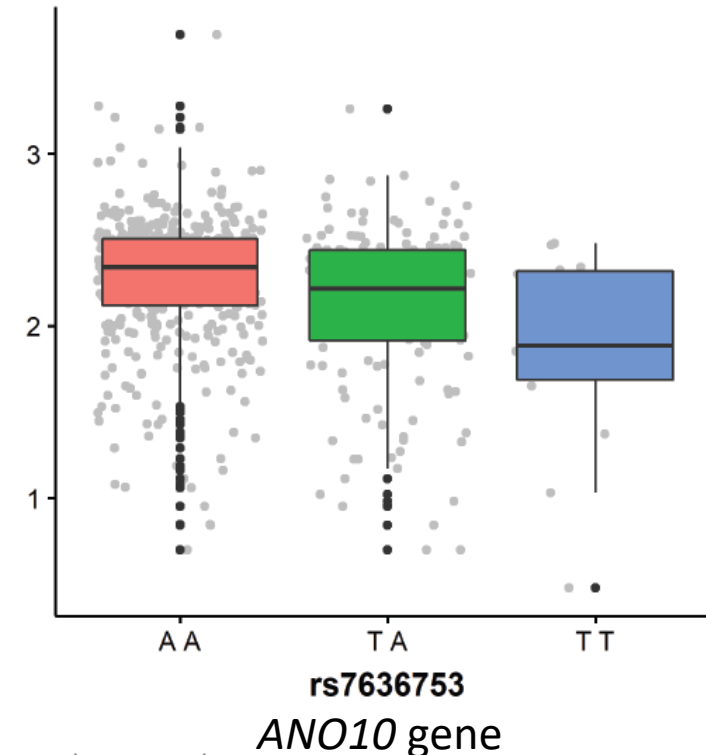


Loci associated with microbial pathways are involved in the immune system and expressed in the gut

Superpathway of pyridoxal 5'-phosphate biosynthesis and salvage



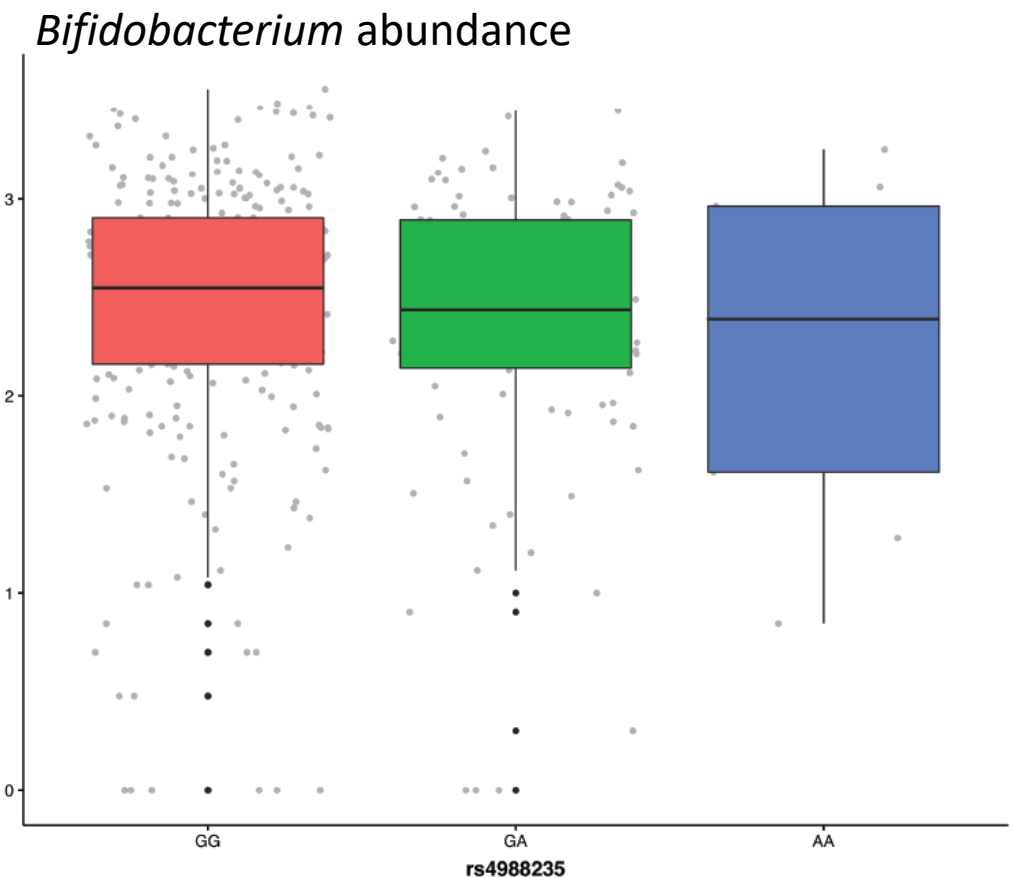
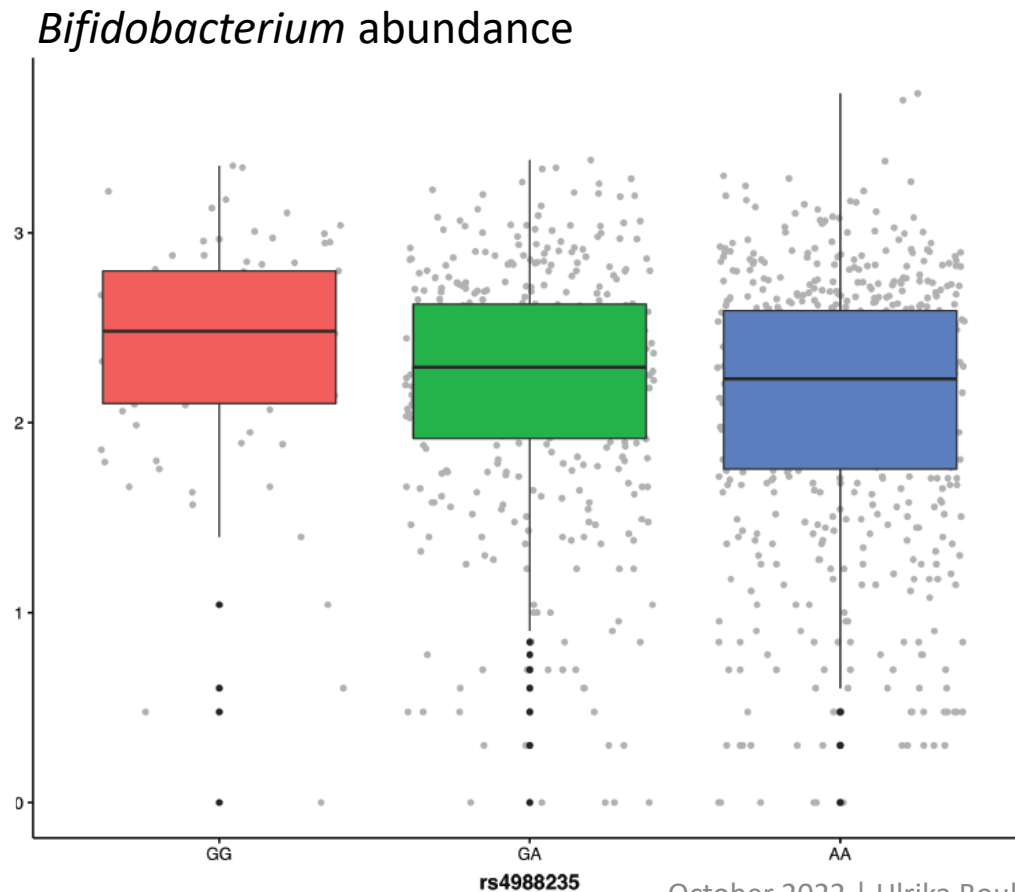
Lactose and galactose degradation



Bifidobacterium is associated with the LCT locus, but this may be ethnicity specific

European Dutch, p-value = 8.42×10^{-4}

Ghanaian, p-value = 0.59



Immune system

Hematopoietic progenitors

Immune tolerance

B and T cell development and activation

Lysosomal activation

Basophil histamine release

Cytokine and chemokine signaling

Toll-like receptor activation

Inflammasome assembly



Signaling and transport

Satiety

Food preferences

Glutamate receptor signaling

Vitamin A receptor signaling

Transmembrane transport



Secretions and metabolism

Intestinal motility

Vitamin A metabolism

Bile acid secretion

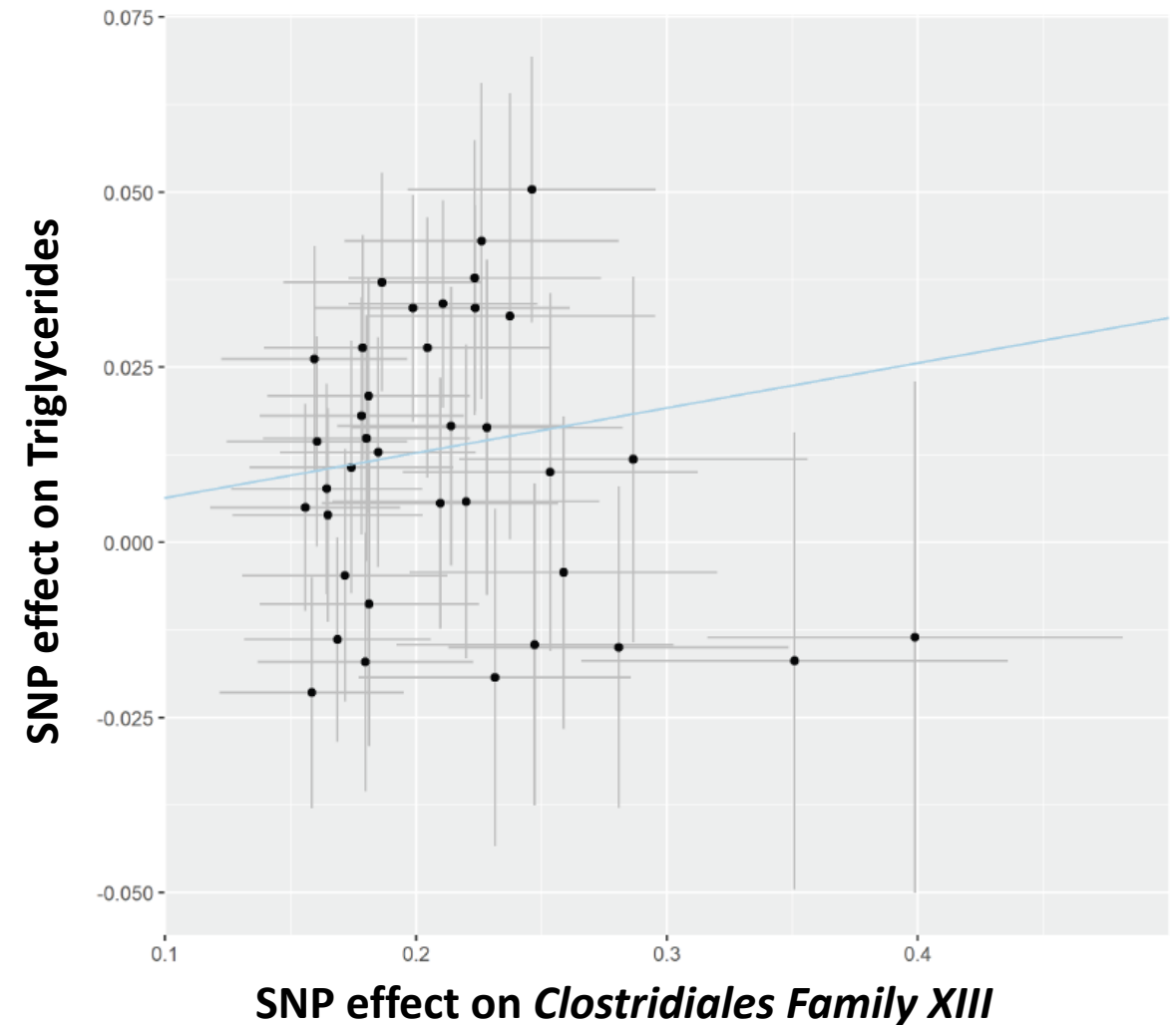
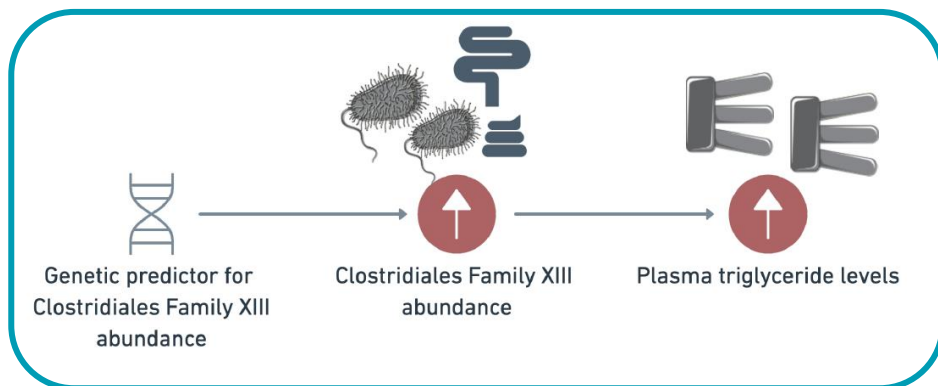
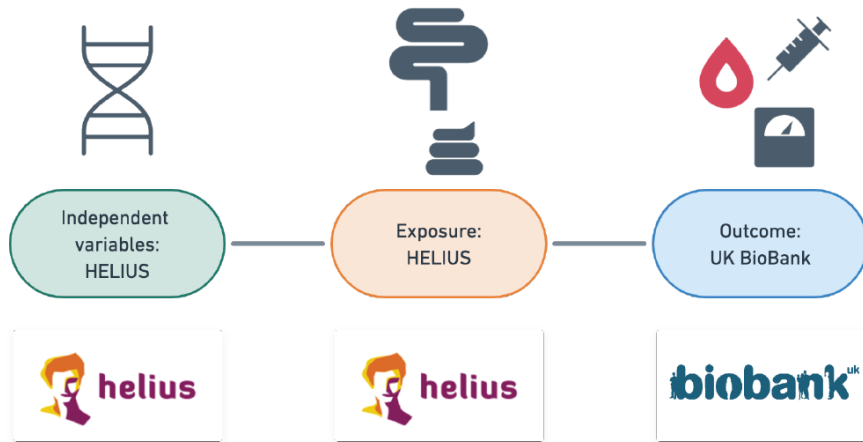
Gastric acid secretion

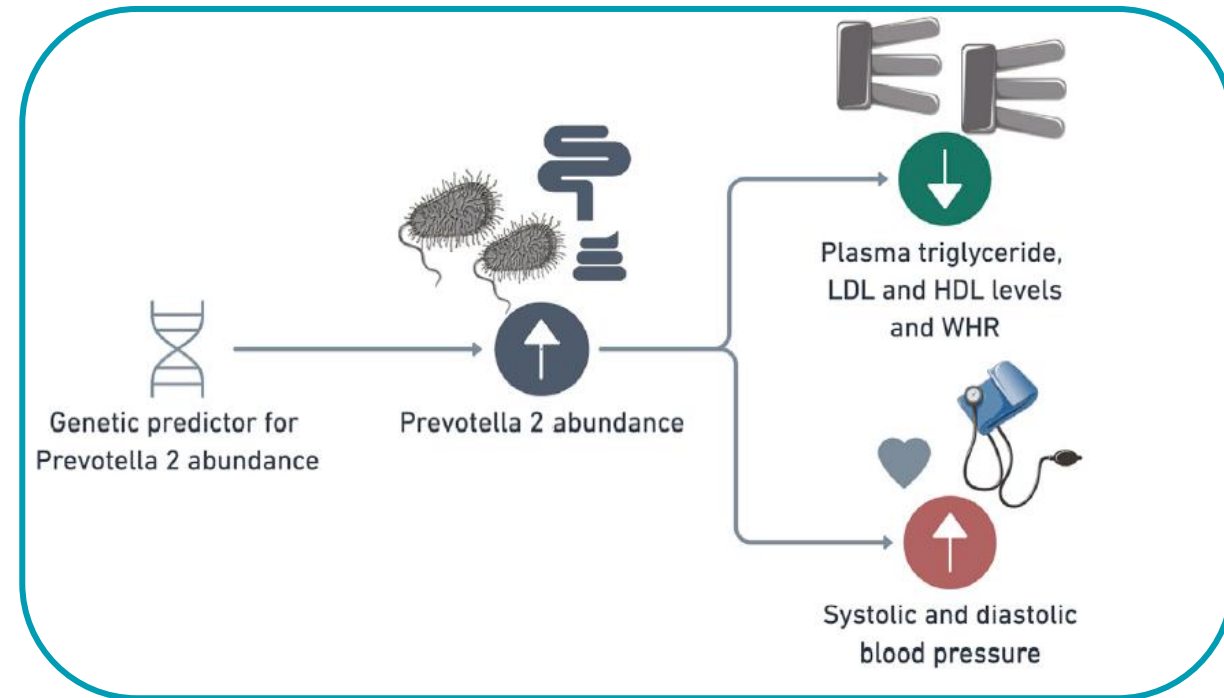
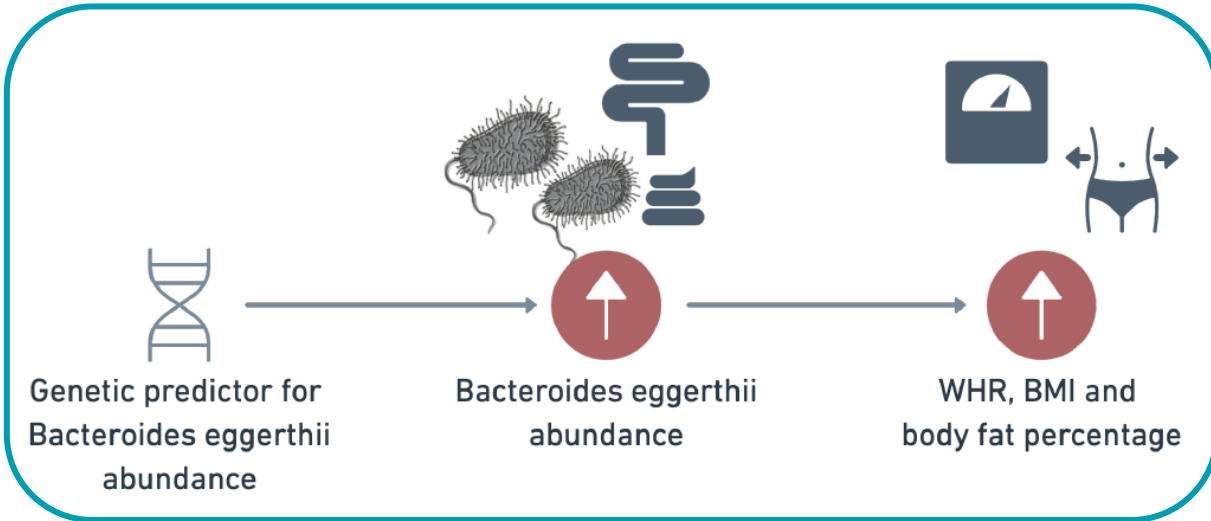
Insulin secretion

Mucus production



Clostridiales Family XIII potentially increases triglycerides





Conclusion

Ethnicities exhibit different gut-microbe-to-genotype associations

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Microbe-associated loci are involved in immune functions or intestinal secretions

Microbe-associated loci are located in genes expressed in the gut and pancreas

Gut microbes may influence cardiometabolic health factors

Future prospects

Expanding cohorts in size and diversity

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Characterize genome associated microbes

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Mechanistic studies of potentially causal microbes

Acknowledgements

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