# Gut microbiome composition is predictive of incident type 2 diabetes in a population cohort of 5572 Finnish adults

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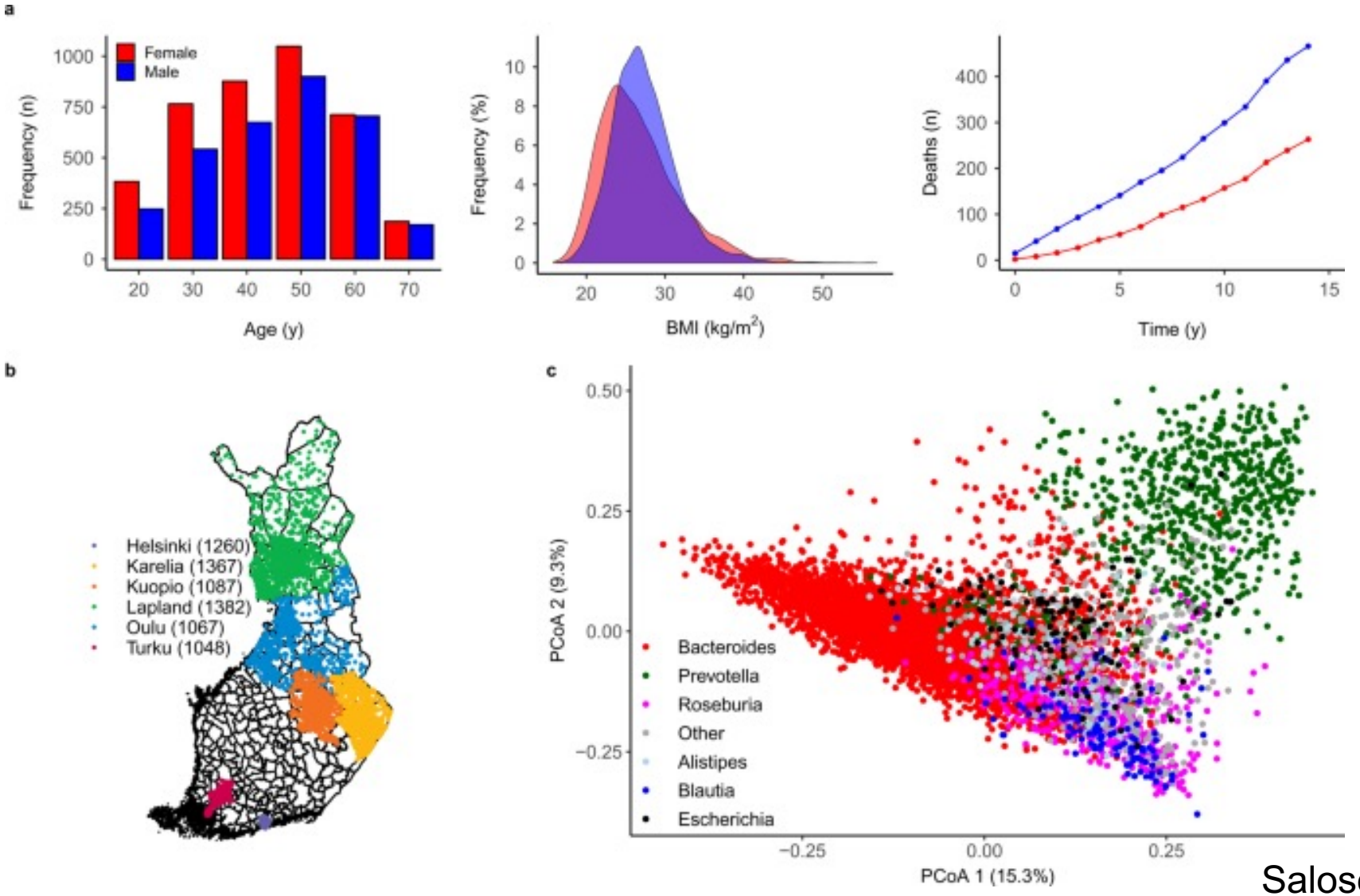
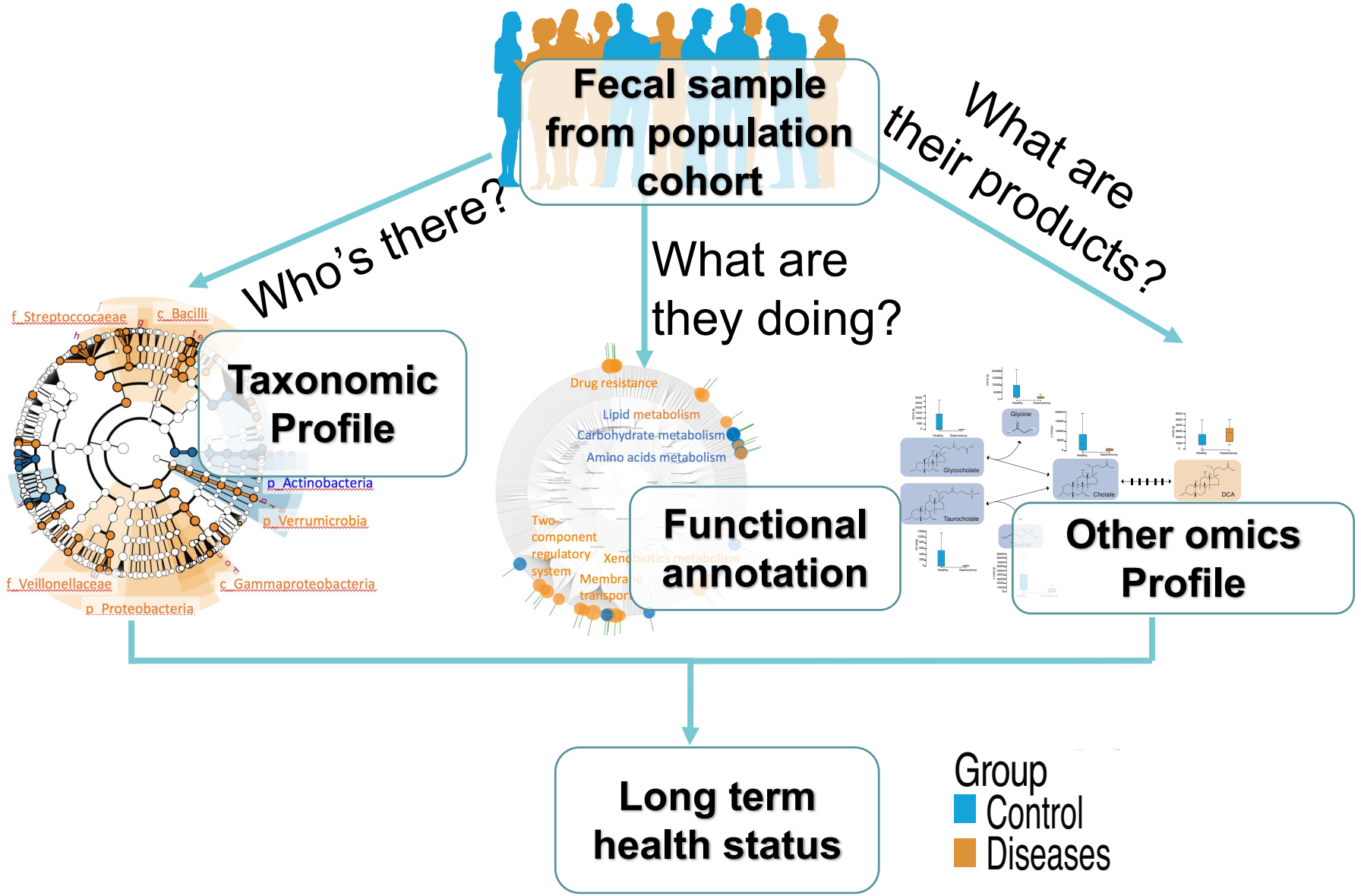
# FINRISK 2002




Salosensaari et al., 2021

# Central questions we can answer with FINRISK 2002 microbiome data

Potential of clinical applicability of baseline gut microbiome as non-invasive biomarker for early detections of future health status



# Highlight of recent findings from FINRISK02 microbiome studies

- Combination of conventional risk factors with gut microbiota may have potential clinical utility in early risk stratifications of liver diseases (Liu et al., 2022)
- Integration of gut microbiome and conventional risk factors can improve the predictions capacities of incident chronic obstructive pulmonary diseases (Liu et al, 2022, *Preprint*)
- Identifications and characterizations of combined effects of host genetics and diet on human gut microbiota and incident diseases (Qin et al., 2022)
- **Gut microbiomes signatures is predictive of incident type 2 diabetes**

**Aim**

To examine the previously unknown long-term association between gut microbiome composition and incident type 2 diabetes in a representative population cohort.

## Research outcome

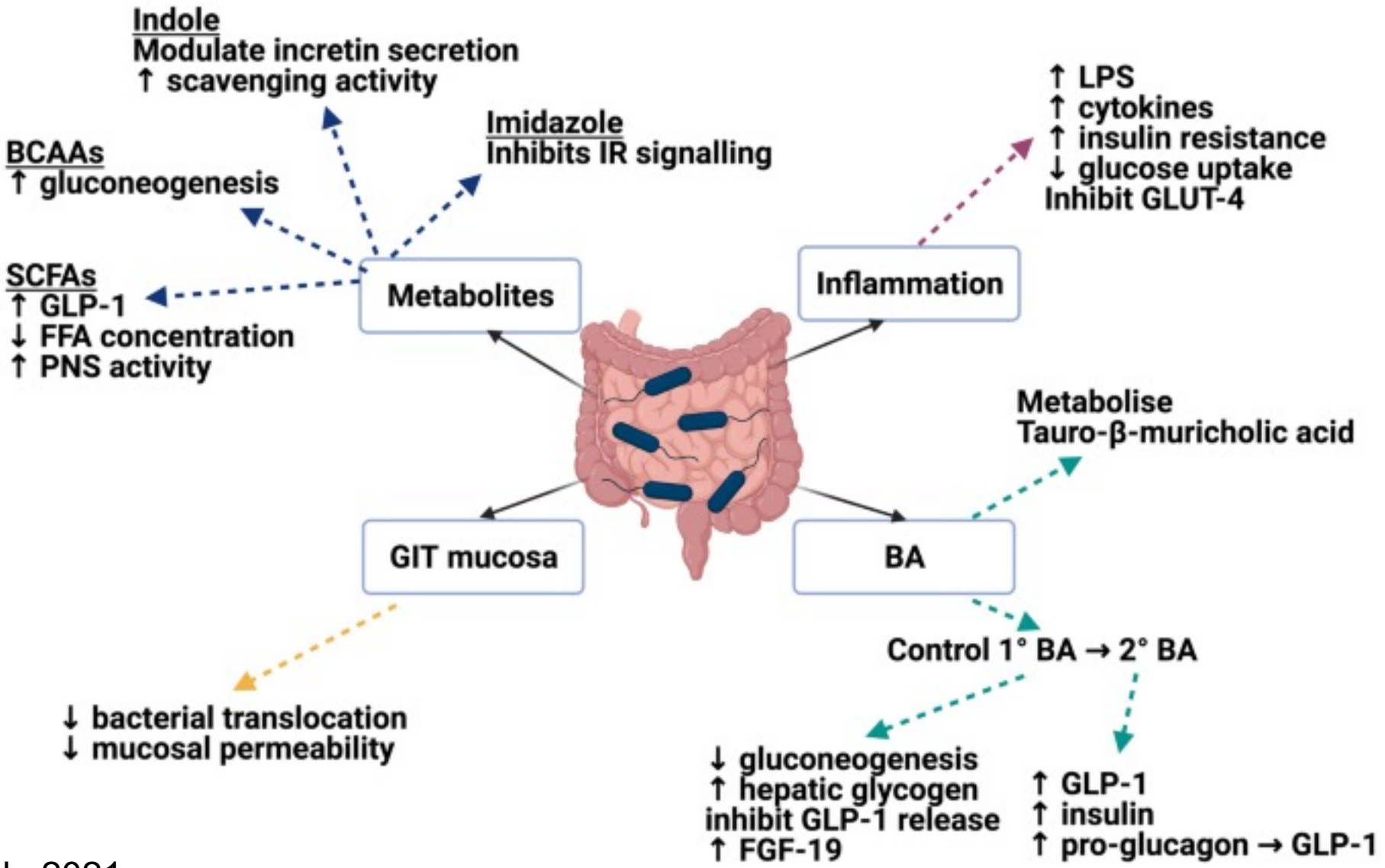
- The gut microbiome could potentially be used to improve risk prediction for type 2 diabetes.

# Potential mechanisms of microbiota effects on metabolism in the type 2 diabetes patient

- Modulation of inflammations
- Increased intestinal permeability
- Glucose homeostasis
- Fatty acid oxidation, synthesis and energy expenditure
- Combined effects of inter-microbial interactions

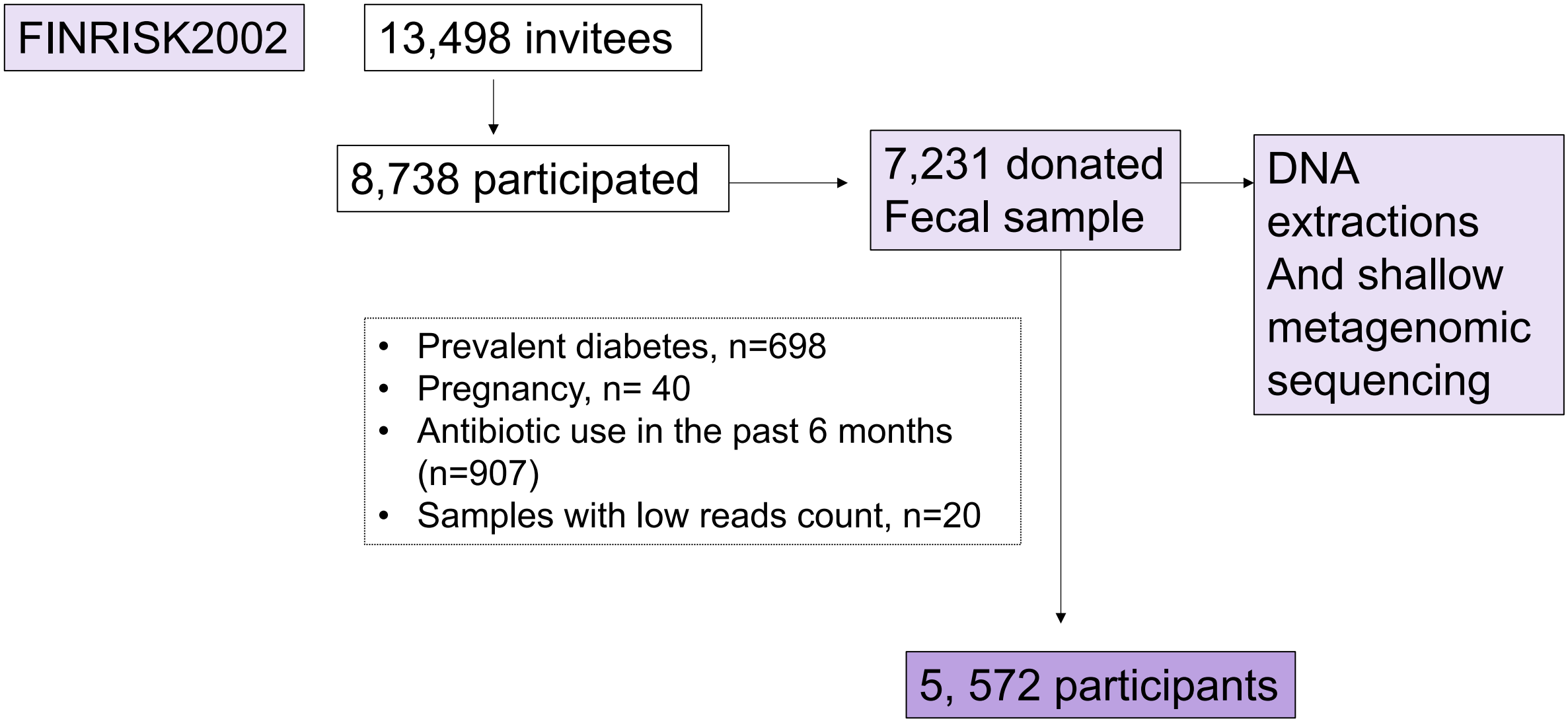
Gurung et al., 2020

# Microbiota influence in glucose homeostasis




Cunningham et al., 2021

# Research Methods



# Research Methods

Type 2 diabetes diagnosis:
- ICD-10 codes E10–E14, ICD-9 code 250, or ICD-8 code 250

Prevalent diabetes also was determined based on three or more drug purchases with Anatomical Therapeutic Chemical drug code A10 → **Our results were also not confounded by antidiabetic drugs, including metformin which were widely reported to largely influence gut microbiome**

Information available at baseline:
- Physical examination (e.g BMI)
- Blood sampling for metabolomic
- Demographic data
- Dietary habbit
- Lifestyle
- Diseases

The participant were followed through 31 December 2017 (for this study) on national health registers of Finland

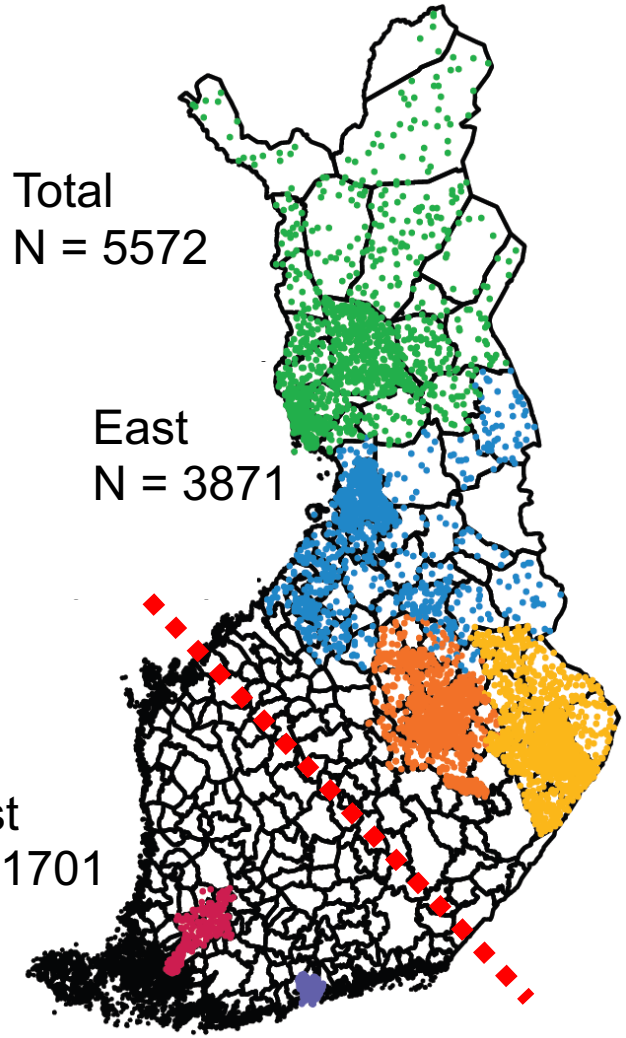
Altogether, 432 cases of incident diabetes occurred over the median follow-up of 15.8 years.

# Research Methods

Taxonomic profile:
- Filtering to core taxa:
detection > 0.01% and prevalence > 1% (N = 119)'
- Alpha and beta diversity metrics

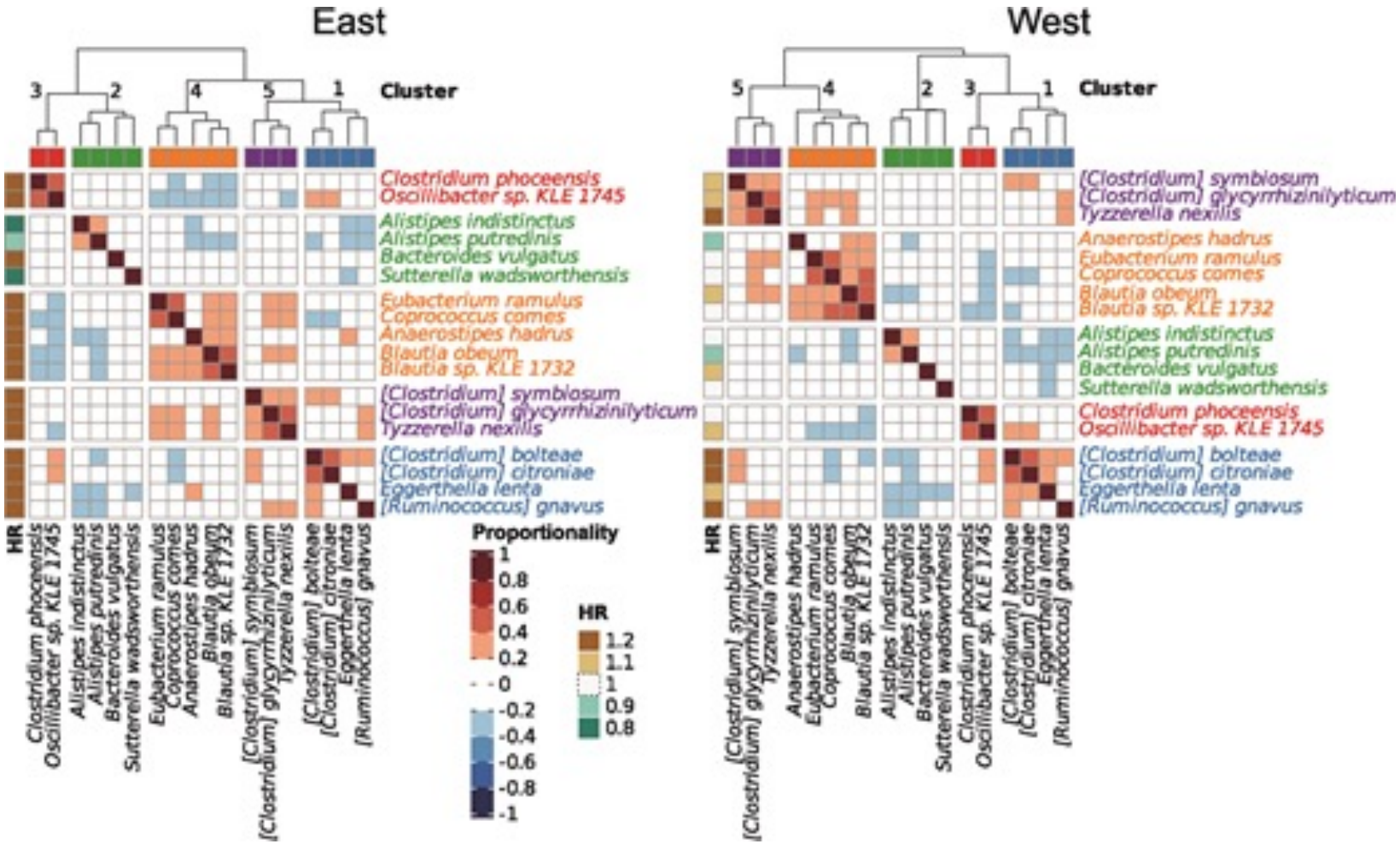
Features selections in eastern subpopulation
- Cox proportional hazard model adjusted by covariates*
- Clustering of proportionally abundant taxa (5 resulting clusters) and tested the same model

Applied the same model with selected features in eastern sub-population to western sub-population



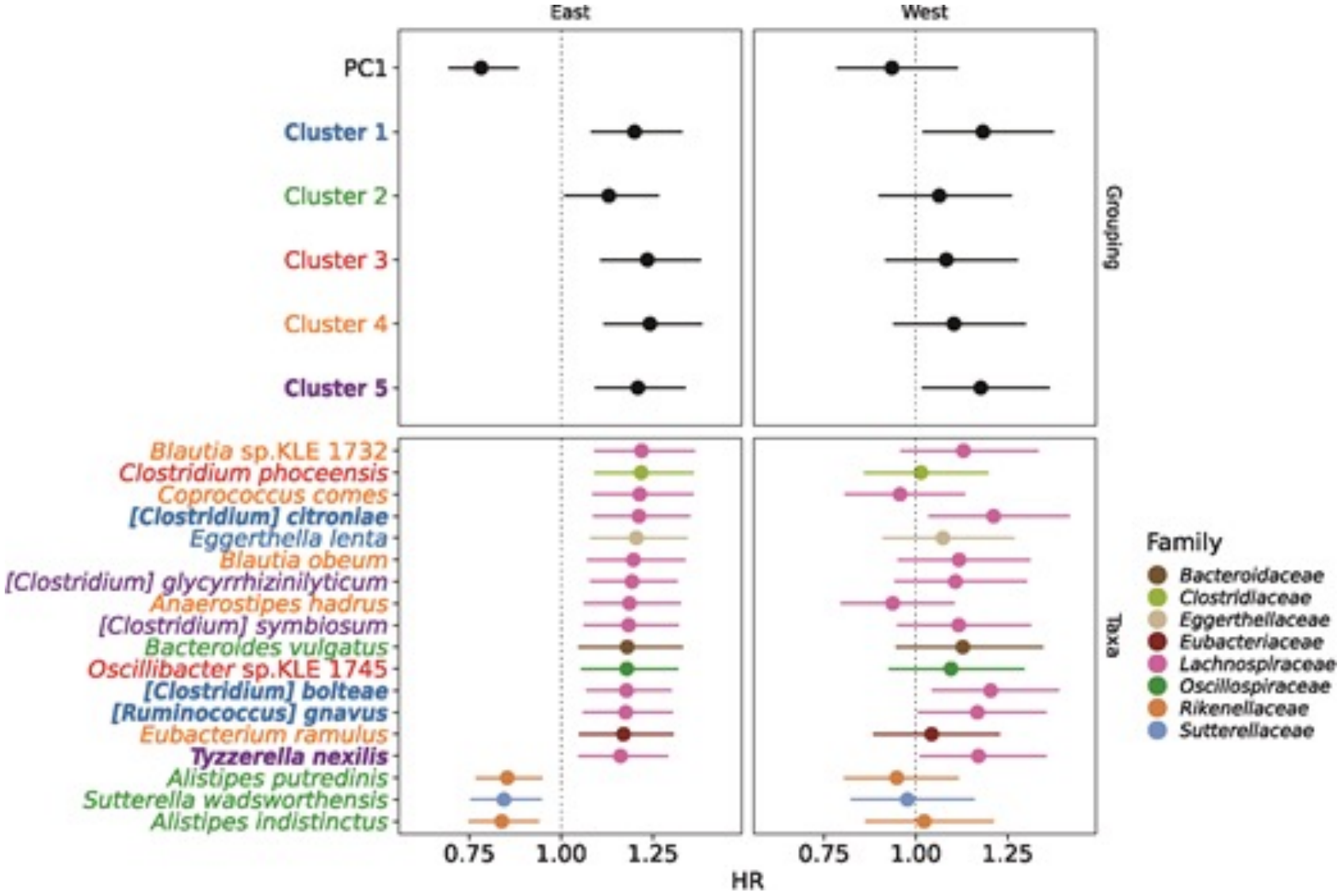

*covariates: baseline age, BMI, sex, systolic blood pressure, non-HDL cholesterol, triglycerides, and current smoking status of the participants.

# Cluster of 18 Species that were significantly associated with incident type 2 diabetes (adjusted P < 0.05 from East data)




Ruuskanen M, Erawijantari PP, et al., 2022

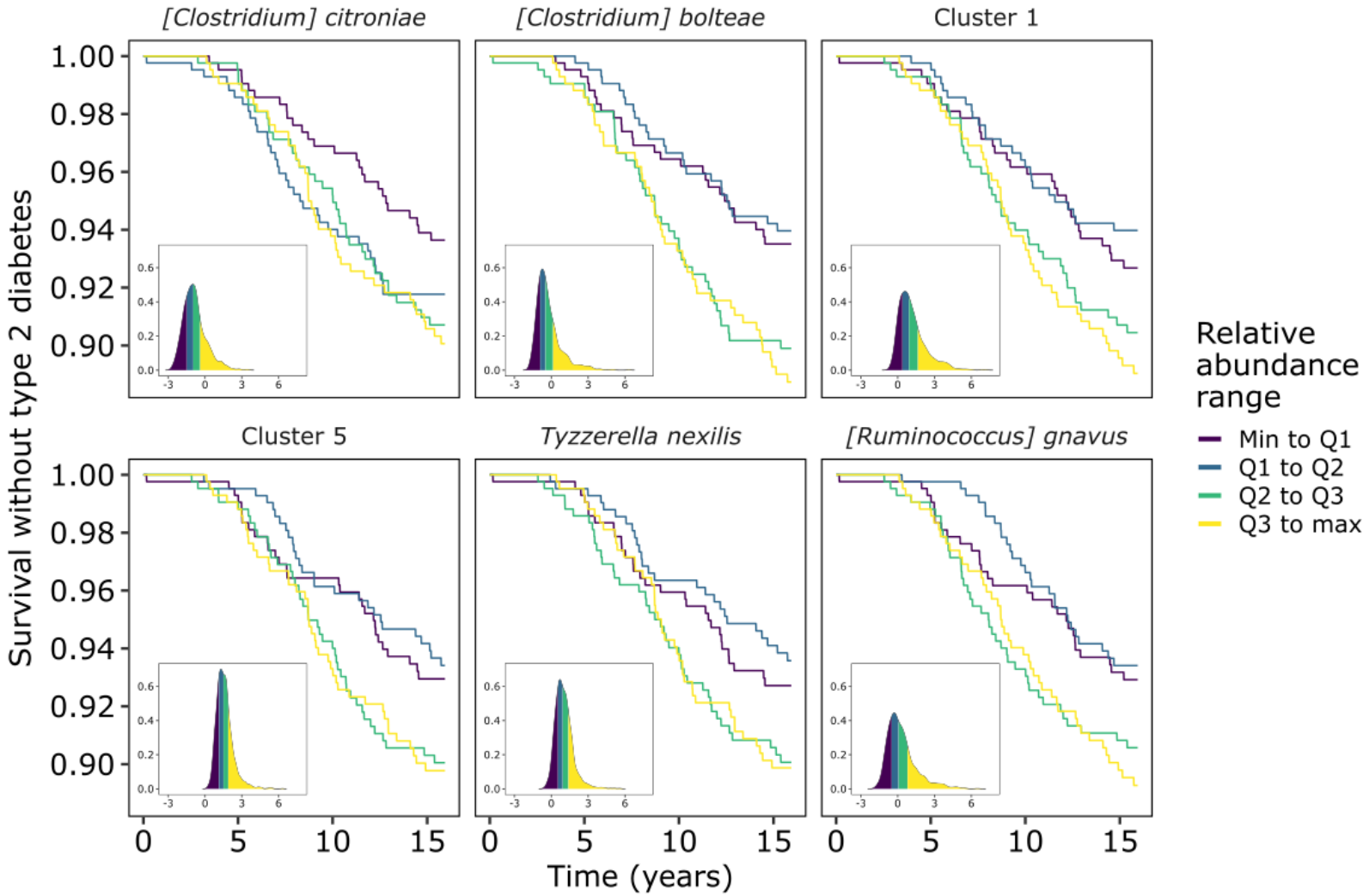
# 4 taxa and 2 clusters were positively associated with incident type 2 diabetes in both population




- *C. citroniae* has been positively associated with production of trimethylamine N-oxide (TMAO) production, likely connected with intake of red meat, which has been known as type 2 diabetes risk factor[1]
- *C. bolteae* has been reported to be enriched in type 2 diabetes patients in previous cross-sectional study along with other opportunistic pathogens[2] and negatively associated with acabose consumption[3]
- *T. nexilis* has been observed to decrease drastically in response to feeding participants a soluble fibre, polydextrose[4]
- The abundance *R.gnavus* is potentially related with glucose metabolism regulation and linked to increases in inflammatory cytokines, both of which are related to type 2 diabetes pathophysiology[5]

Ruuskanen M, Erawijantari PP, et al., 2022

# The difference in type 2 diabetes incidence between relative abundance quartiles begins to show only after around 5 years of follow-up




Ruuskanen M, Erawijantari PP, et al., 2022

The species were robustly associated with incident type 2 diabetes only in the groups with 0-10 and 0-15 years of follow-up time

**Table 1. 0-5 years follow-up time (n of incident= 43)**

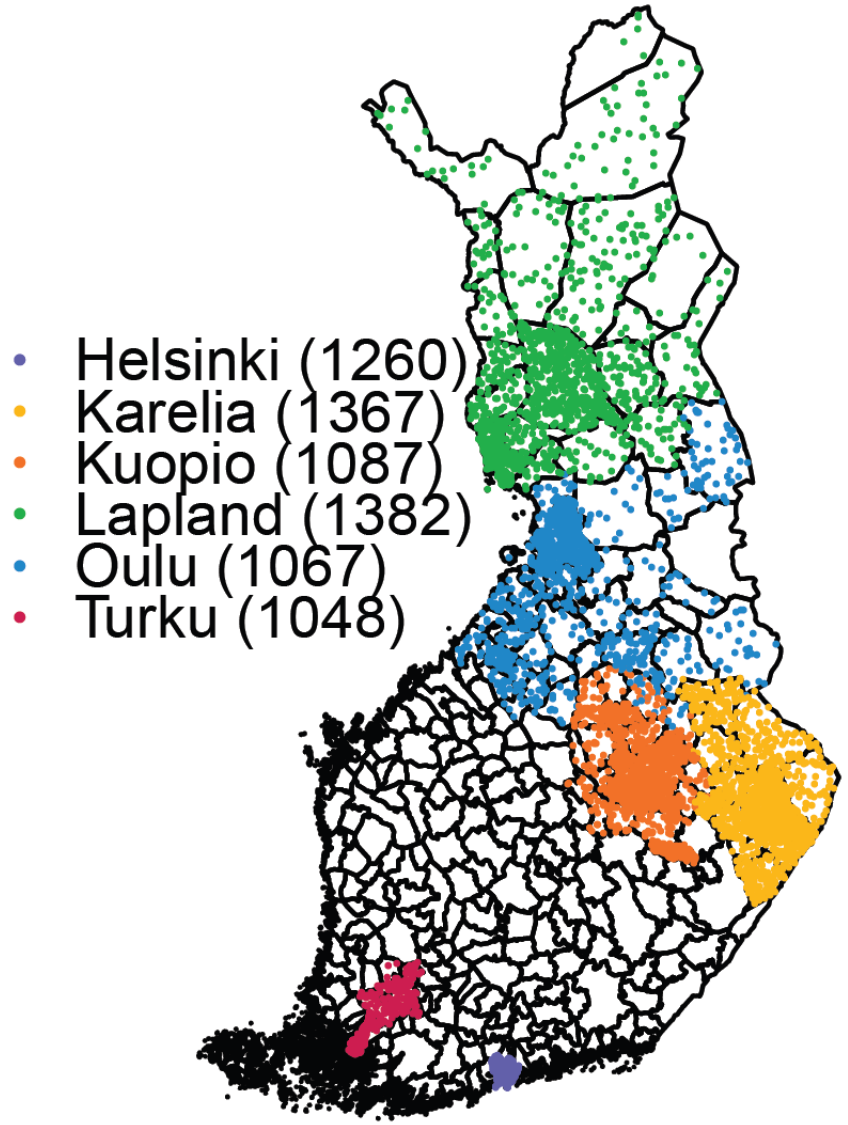
| Predictor | Coefficient | HR | P.value |
|---|---|---|---|
| Cluster 1 | 0.321 | 1.378 (95% CI, 1.066-1.782) | 0.0145135889568437 |
| Cluster 5 | 0.275 | 1.317 (95% CI, 1.021-1.698) | 0.0337993465813785 |
| *[Clostridium] citroniae* | 0.237 | 1.267 (95% CI, 0.958-1.676) | 0.0972084481416306 |
| *[Clostridium] bolteae* | 0.258 | 1.295 (95% CI, 1.022-1.641) | 0.032235957877583 |
| *Tyzzerella nexilis* | 0.173 | 1.189 (95% CI, 0.91-1.553) | 0.203862710208228 |
| *[Ruminococcus] gnavus* | 0.162 | 1.176 (95% CI, 0.901-1.534) | 0.232735865242045 |

**Table 2. 0-10 years follow-up time (n of incident = 235)**

| Predictor | Coefficient | HR | P.value |
|---|---|---|---|
| Cluster 1 | 0.237 | 1.267 (95% CI, 1.128-1.423) | 6.23365780011579e-05 |
| Cluster 5 | 0.202 | 1.224 (95% CI, 1.091-1.373) | 0.000577547047524432 |
| *[Clostridium] citroniae* | 0.243 | 1.275 (95% CI, 1.132-1.437) | 6.69719882893286e-05 |
| *[Clostridium] bolteae* | 0.175 | 1.191 (95% CI, 1.068-1.329) | 0.00173541180356872 |
| *[Ruminococcus] gnavus* | 0.156 | 1.169 (95% CI, 1.042-1.311) | 0.0075894612035767 |
| *Tyzzerella nexilis* | 0.139 | 1.149 (95% CI, 1.022-1.292) | 0.020194545301951 |

**Table 3. 0-15 years follow-up time (n of incident = 404)**

| Predictor | Coefficient | HR | P.value |
|---|---|---|---|
| Cluster 1 | 0.201 | 1.223 (95% CI, 1.118-1.338) | 1.15537978015434e-05 |
| Cluster 5 | 0.184 | 1.202 (95% CI, 1.1-1.314) | 4.78164969970047e-05 |
| *[Clostridium] citroniae* | 0.191 | 1.211 (95% CI, 1.103-1.329) | 5.84181218846101e-05 |
| *[Clostridium] bolteae* | 0.156 | 1.169 (95% CI, 1.075-1.272) | 0.000286154330023966 |
| *[Ruminococcus] gnavus* | 0.143 | 1.153 (95% CI, 1.056-1.26) | 0.0015874734461806 |
| *Tyzzerella nexilis* | 0.15 | 1.162 (95% CI, 1.063-1.27) | 0.000916898009056105 |




# SUMMARY AND FUTURE DIRECTIONS

- **Our results agree with previous finding and robust across geographical differences**

**What next?**

- Comparing the predictive capability of taxonomic signatures with conventional risk factors
- Confirming the findings with a similar cohort setting (meta-analysis)
- Explore the underlying mechanism of actions:
  - The comprehensive analysis supported by life habit (diet) and other supporting data

# Coming soon…..


Heart Failure Prediction: Microbiome
FINRISK DREAM Challenge
Finnish institute for health and welfare
UNIVERSITY OF TURKU
Baker
UNIVERSITY OF CAMBRIDGE
HEIDELBERG FACULTY OF MEDICINE
Informatics for Life
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