Predicting Incident Heart Failure from the Microbiome: The DREAM FINRISK challenge

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Motivation and Aim

- Heart failure (HF) is a clinical syndrome with signs and symptoms caused by structural and/or functional cardiac abnormality with elevated natriuretic peptide levels and/or evidence of pulmonary or systemic congestion. It occurs when the heart cannot pump blood to meet the needs of the body normally, with a lifetime risk of ~20%.
- Heart failure diagnosis is still largely based on presenting symptoms and clinical history, therefore identifying individuals at risk early on is of great interest.

What about the microbiome association with heart failure?

Several studies have found differences in the microbiome composition of HF patients compared to controls, however, studies of the microbiome and HF are often small (<100 HF patients) and lack of temporal follow-up.

Thus, we proposed this DREAM challenge (launched in September 2022) to study the role of the microbiome in incident HF using a large population-based resource.

Read more:



https://synapse.org/finrisk

Aim: to use a combination of taxonomic profiling (n=5749 taxonomic features) and clinical data to evaluate the potential of gut microbiome composition for incident HF risk predictions over conventional risk factors in large human population study of 7231 Finnish adults

Challenge Overview

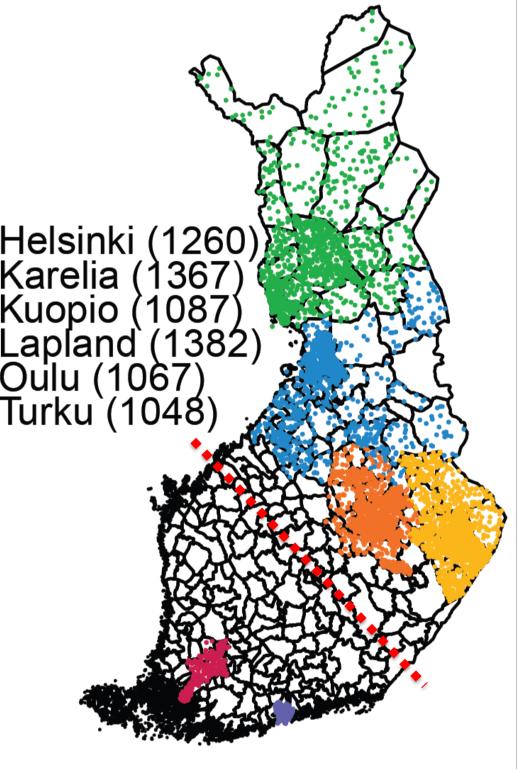
A. FINRISK 2002 cohort

13,498 invitees

8,738 participated

7,231 donated Fecal sample (54% participation rate)

DNA extractions And shallow metagenomic sequencing (~1M reads/sample)



Participants were followed through for 15+ years. There are 493 incident heart failure among 6902 participants with complete phenotype.

B. Synthetic Dataset

The synthetic relation was created as the synthetic multino many that we from inverse rank normalized data, which closely mimics the real data of FINRISK 2002, to protect the privacy of individuals. The challenge's participants will have access to the synthetic dataset, to build their model, which later will be evaluated in a real dataset. Figure 1 shows the comparison of FINRISK 2002 and the synthetic dataset.

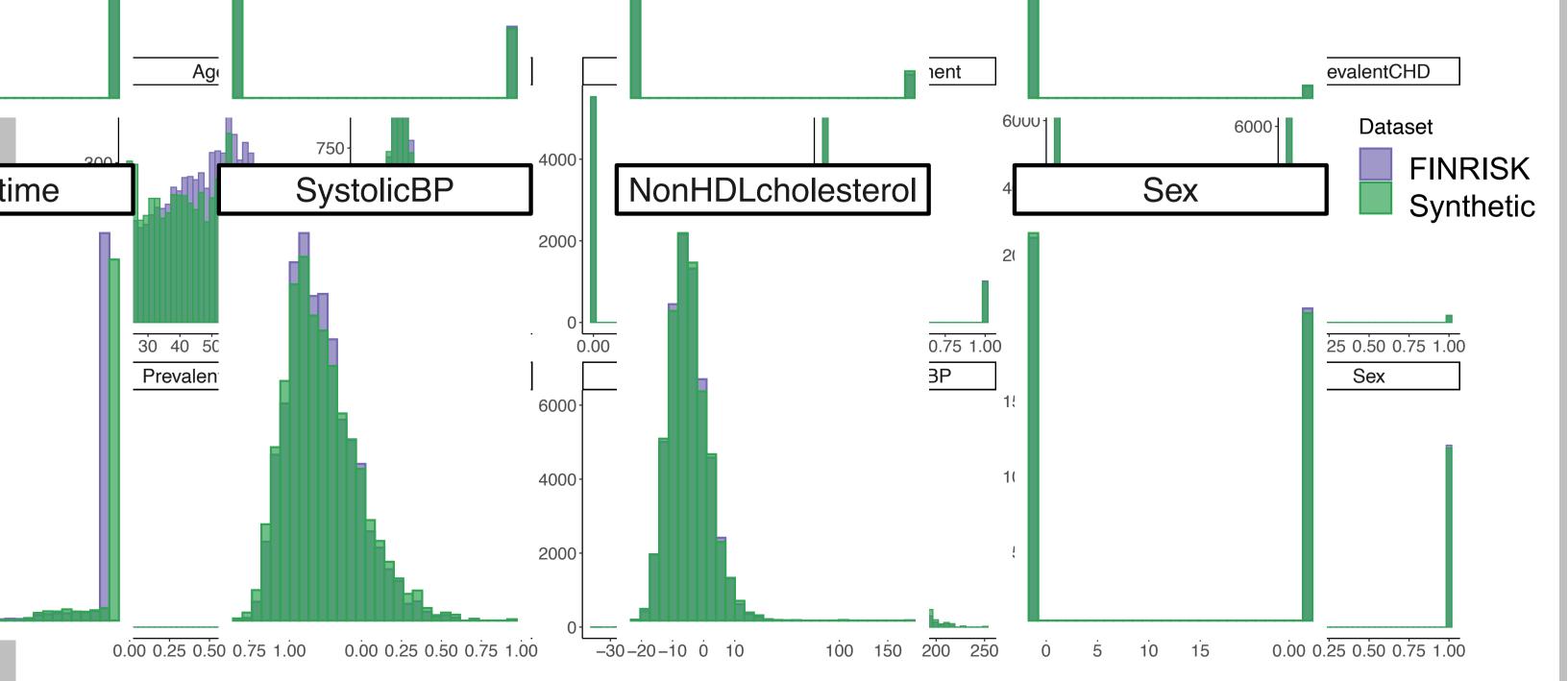


Figure 1. Comparison of FINRISK 2002 and synthetic dataset

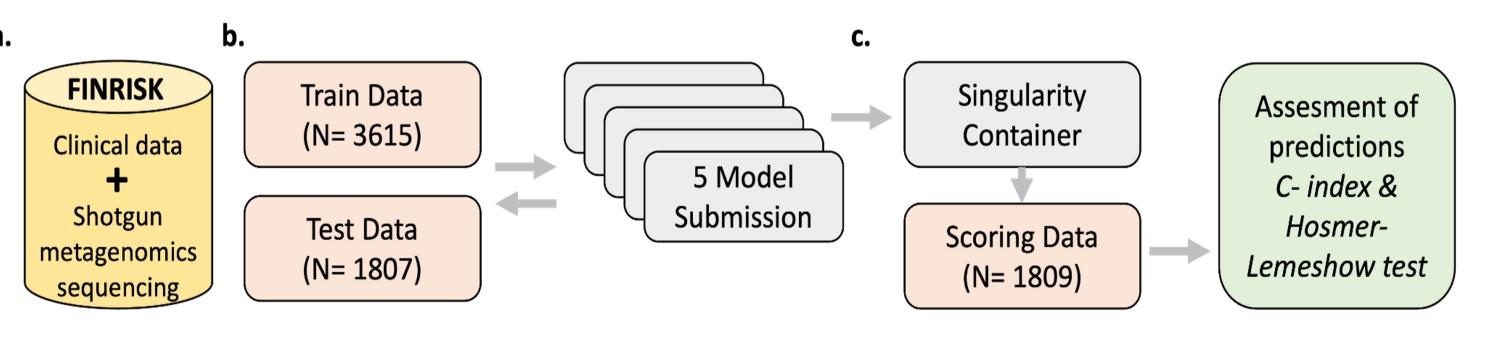
C. Benchmark Model

We provided participants with 3 benchmark Cox proportional hazard models (coxph), based on (1) age and sex, (2) all covariates, and (3) all covariates with the microbiome. In the challenge, we will evaluate the participant submission using Harell's C statistic for model accuracy and the Hosmer-Lemeshow test for model calibration. Table 1 shows the performance of our benchmark model based on two matrices.

Table 1. Benchmark Models Performance

	Real Dataset		Synthetic Dataset	
	Harrel's C	Hosmer-Lemeshow	Harrel's C	Hosmer-Lemeshow
Age+sex	0.815517316181654	0.4419724712633	0.723091773400037	9.539331163593e-99
All covariates	0.855461670628663	0.110166895232517	0.71097917920827	1.26281928124e-150
All covariates	0.823621342999035	1.718778805022e-07	0.659159003314443	1.27643033558e-259

D. Challenge workflow



Real data is hosted by Finnish institute for healh and welfare and analyzed in a secured *in-house server*. All submitted algorithms and descriptions are hosted in an open computational platform, Synapse.org, which can be accessed by all credible users.

F. Perspective

- The outcomes of the challenge could contribute to advancing our understanding on the potential of microbiome-based biomarkers to complement clinical risk factors in identifying individuals with an elevated risk of HF.
- The crowdsourced *Challenge* provides an avenue for a unique way on solving scientific problem.
- The synthetic dataset has proven beneficial for challenge participants and could become an option for data sharing while ensuring privacy protection.



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