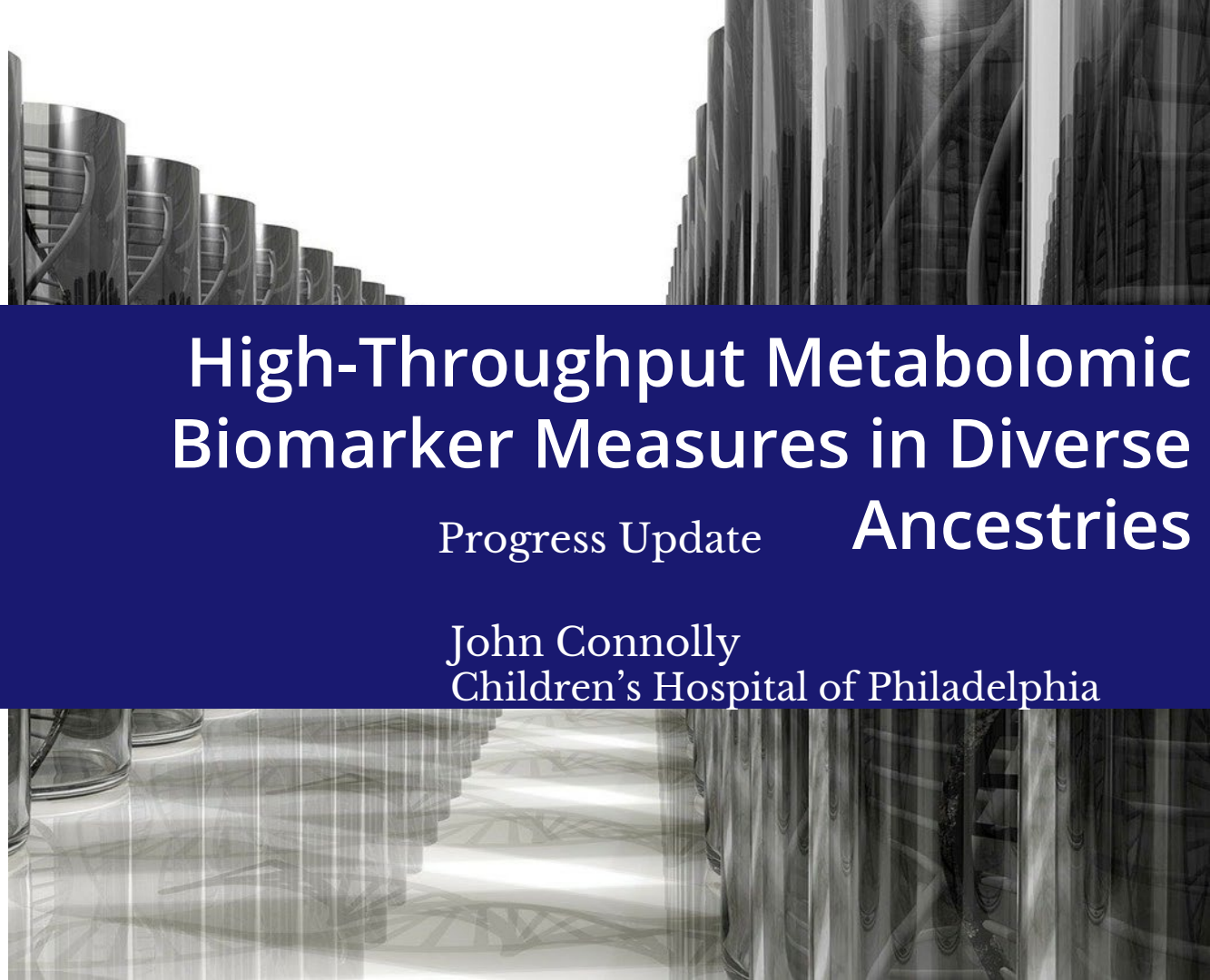
3rd Nov 2021



High-Throughput Metabolomic Biomarker Measures in Diverse Ancestries

Progress Update

John Connolly
Children's Hospital of Philadelphia

Outline

- Project Overview
- Preliminary Data & Lessons Learned
- Timeline & Next Steps

High-Throughput Metabolomic Biomarker Measures in Diverse Ancestries

Principal Investigators

- Adam Butterworth, University of Cambridge & **South Asian Cohorts**
- Andre Brunoni, Universidade de São Paulo & **ELSA-Brasil**
- Arash Etemadi, National Cancer Institute, NIH & **Golestan Cohort Study**
- Hakon Hakonarson, **Children's Hospital of Philadelphia**

Team Members

- John Connolly, Patrick Sleiman (CHOP)
- Praveen Surendran (South Asian Cohorts)
- Alexandre Pereira (ELSA)

Background

- Chronic diseases impose a high burden on the health system.
- Health outcomes can be significantly improved through early diagnosis and intervention.
- Early diagnosis often unavailable particularly for individuals in low and middle income countries and minority populations in high income countries.
- Metabolic profiling represents a highly-scalable model for risk prediction and prevention.
  - Because of its relatively low cost, it offers a route to individualized medicine for these populations.

Aims

- Generate Metabolic Profiles on 5,000 Individuals with Genetic and/or Health Outcome Data.
- Analyses of associations with phenotypes of interest
- Analyses of association between metabolic metabolite levels (such as lipid profiles) and genetic data

Participating Cohorts

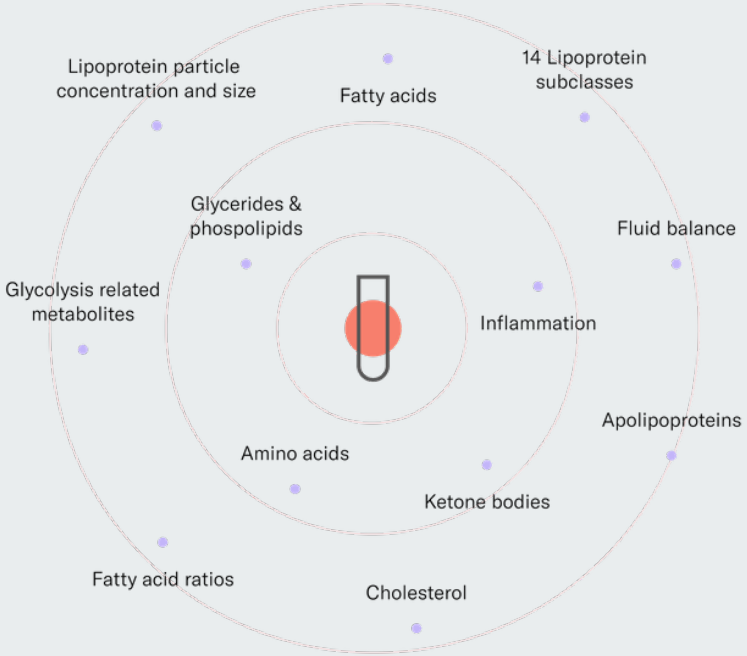
Cohort Name	Study samples	Principal Investigator/Lead(s)
South Asian Cohorts (BELIEVE)	1,500 samples of South Asian ancestry from Dhaka, Bangladesh	Adam Butterworth
ELSA-Brasil	1,000 samples from Brazilian civil servants	Andre Brunoni
Golestan Cohort Study	1,000 samples from Northeast Iranian general population	Arash Etemadi
Children's Hospital of Philadelphia (CHOP)	1,500 samples of African American children	Hakon Hakonarson

Target Phenotypes

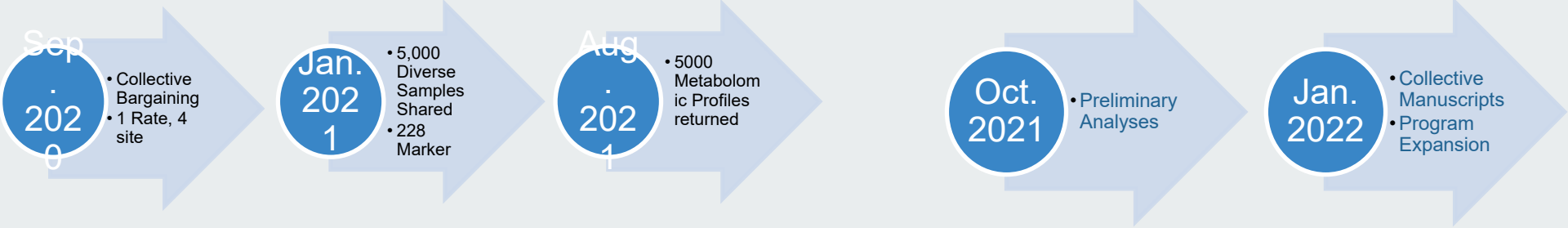
Cohort Name	Study samples	Phenotypes
South Asian Cohorts (BELIEVE)	1,500 samples of South Asian ancestry from Dhaka, Bangladesh	Diabetes
ELSA-Brasil	1,000 samples from Brazilian civil servants	Broad-based
Golestan Cohort Study	1,000 samples from Northeast Iranian general population	Ischemic heart disease
Children's Hospital of Philadelphia (CHOP)	1,500 samples of African American children	22q11.2 deletion Autoimmune and autoinflammatory

Nightingale Platform

- NMR-based (Nuclear Magnetic Resonance spectroscopy) platform
- 228 biomarkers
- 100µl of plasma or serum



Progress & Timeline Overview

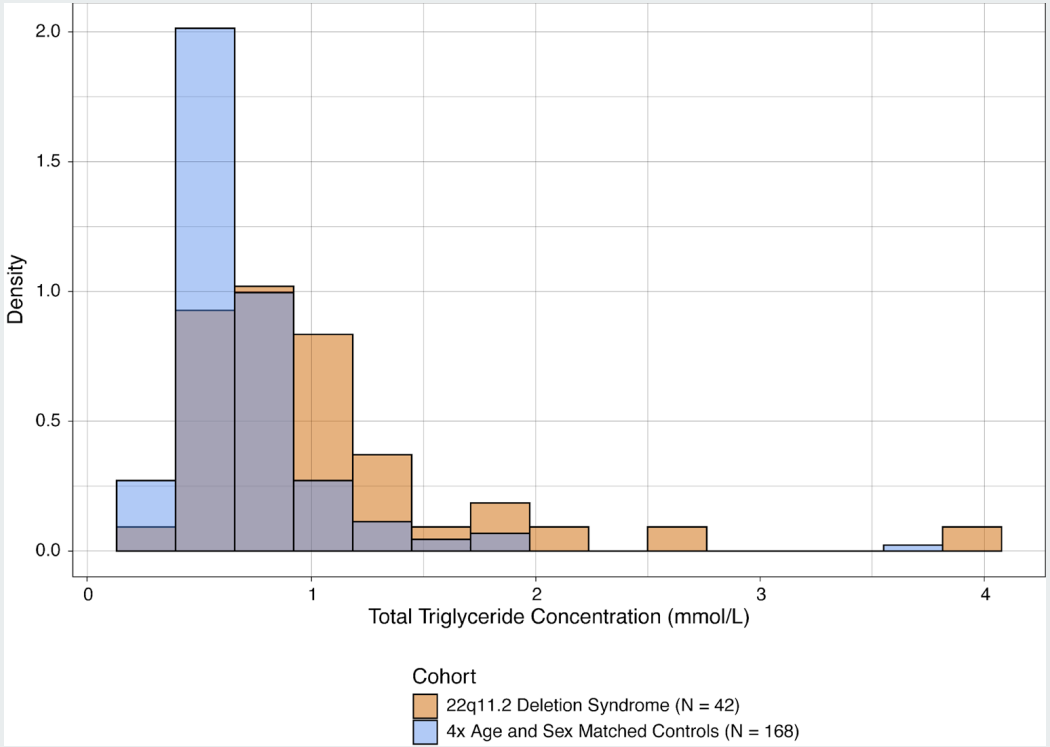


Preliminary Data

- Significant signals for
  - Obesity
  - Asthma
  - Sickle cell disease
  - Type 1 diabetes
  - 22q11.2 deletion syndrome
- Hypothesis driven in analytical approach

Preliminary Data

Metabolomics Recovers Known Elevations in Triglyceride Concentrations Among Individuals with 22q11.2 Deletion Syndrome



Lessons Learned

- Collective bargaining works
- Nightingale platform is efficient with little requirement in terms of overheads
- IHCC publication policy works
- Template for expansion

Next Steps

- Publication
  - IHCC Guidance and policy
- Data-Sharing
  - IHCC Data Atlas
  - Metabolights - EMBL-EBI
- Study Expansion
  - Several cohort members with existing data
  - Prospectively expand to more sites

Thank You

Funding & Support

Wellcome Trust
National Institutes of Health
IHCC

Principal Investigators

Adam Butterworth: **South Asian Cohorts**
Andre Brunoni: **ELSA-Brasil**
Arash Etemadi: **Golestan Cohort Study**
Hakon Hakonarson, **Children's Hospital of Philadelphia**

Study Team

Ian Campbell (CHOP)
Patrick Sleiman (CHOP)
Praveen Surendran (South Asian Cohorts)
Alexandre Pereira (ELSA)
Huiqi Qu (CHOP)

Questions/Comments ...