## Breakout Session 2: Track A

# COnsortium of METabolomics Studies

Dr. Kelly Crotty
*Program Director, NCI*

Ms. Kailing Chen
*Cloud Architect, CBIIT*

# COnsortium of METabolomics Studies

*Kelly Crotty and Kai-Ling Chen*

*National Cancer Institute*

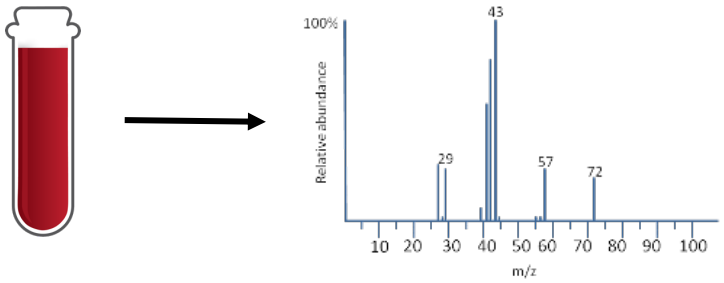
NIH NATIONAL CANCER INSTITUTE

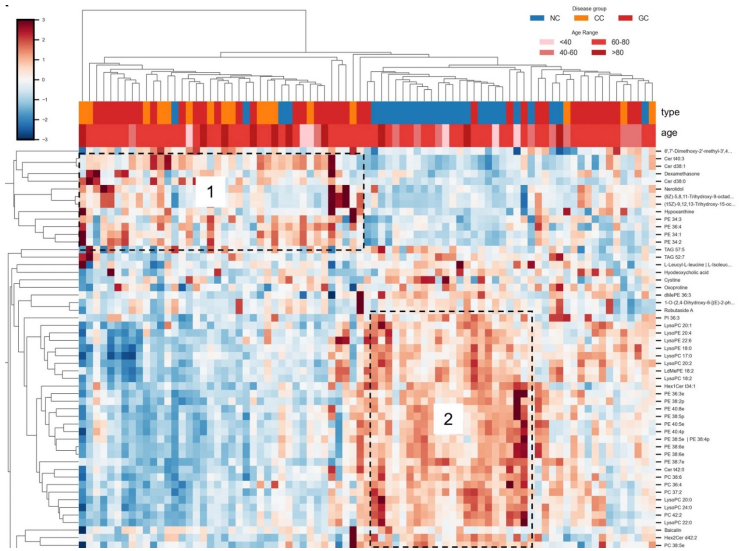
January 23, 2024

# Prospective Cohort Studies

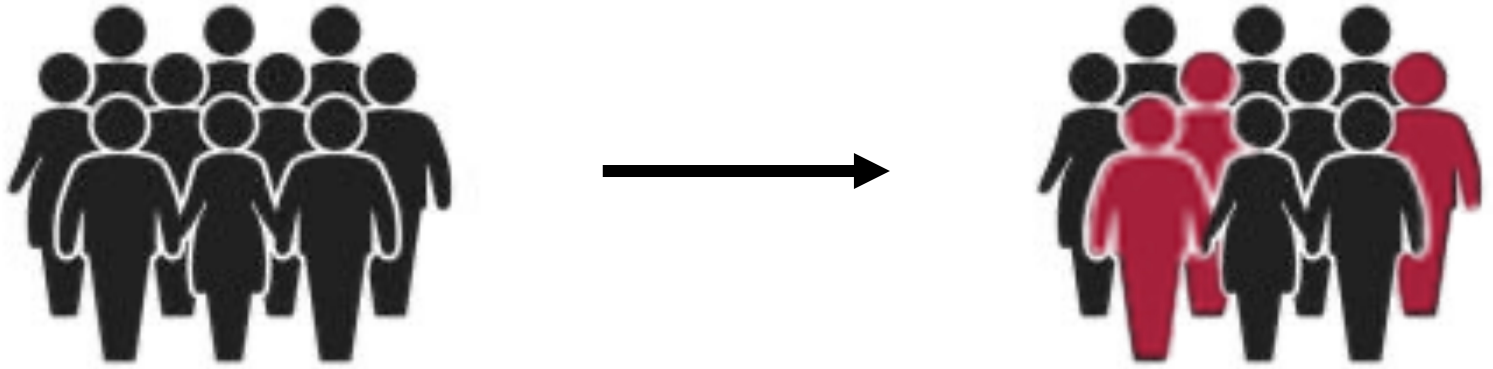
Collect demographic information and samples for baseline measurements

Follow-up: collect additional samples and information on health outcomes (i.e. cancer, diabetes, cardiovascular disease, renal disease, mortality, asthma, etc.)



# Prospective Cohort Studies



Prospective cohort studies require a considerable amount of time and resources to have sufficient statistical power and avoid selection bias.

# Collaborations among cohorts can increase statistical power of studies

# COnsortium of METabolomics Studies

COMETS provides a framework for collaborations among prospective cohort studies and creates an analytical strategy and infrastructure for meta-analysis studies

# COnsortium of METabolomics Studies

COMETS has 81 participating cohorts that include over two million study participants

sabre
Southall and Brent Revisited
Diabetes and Heart Disease Research

COPDGene®
COPD Genetic Epidemiology

HELIX
BUILDING THE EARLY-LIFE EXPOSOME

ROTTERDAM STUDY

NATIONAL CANCER INSTITUTE
PLCO
Prostate, Lung, Colorectal, & Ovarian CANCER SCREENING TRIAL

UPBEAT
Uk Pregnancies Better Eating and Activity Trial

Nurses' Health Study

DPPOS

Multiethnic COHORT STUDY

SPIROMICS

MrOS

FENLAND STUDY

pregnancy outcome prediction study

Airwave Health Monitoring Study

Mano-A-Mano Mexican American Cohort

COPSAC

BREAST CANCER FAMILY REGISTRY

HPFS

MESA

PHS PHYSICIANS' HEALTH STUDY

ARIC
Atherosclerosis Risk in Communities

WIHS Women's Interagency HIV Study

PROJECT Viva

Framingham Heart Study
Three Generations of Dedication

EPIRUS HEALTH STUDY

epic
European Prospective Investigation of Cancer

Health ABC

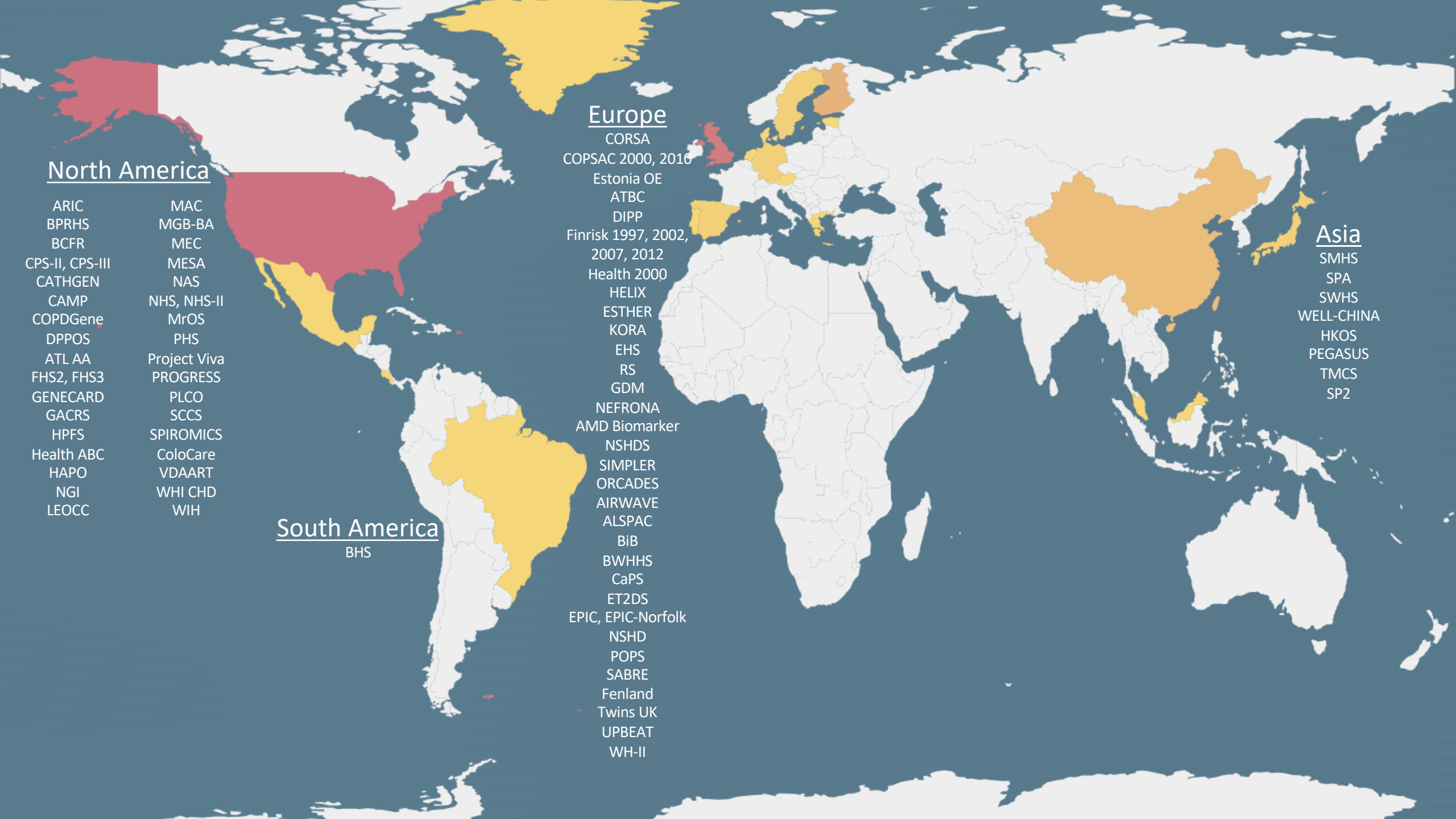
Health Professionals Follow-Up Study
VERITAS

twinsUK

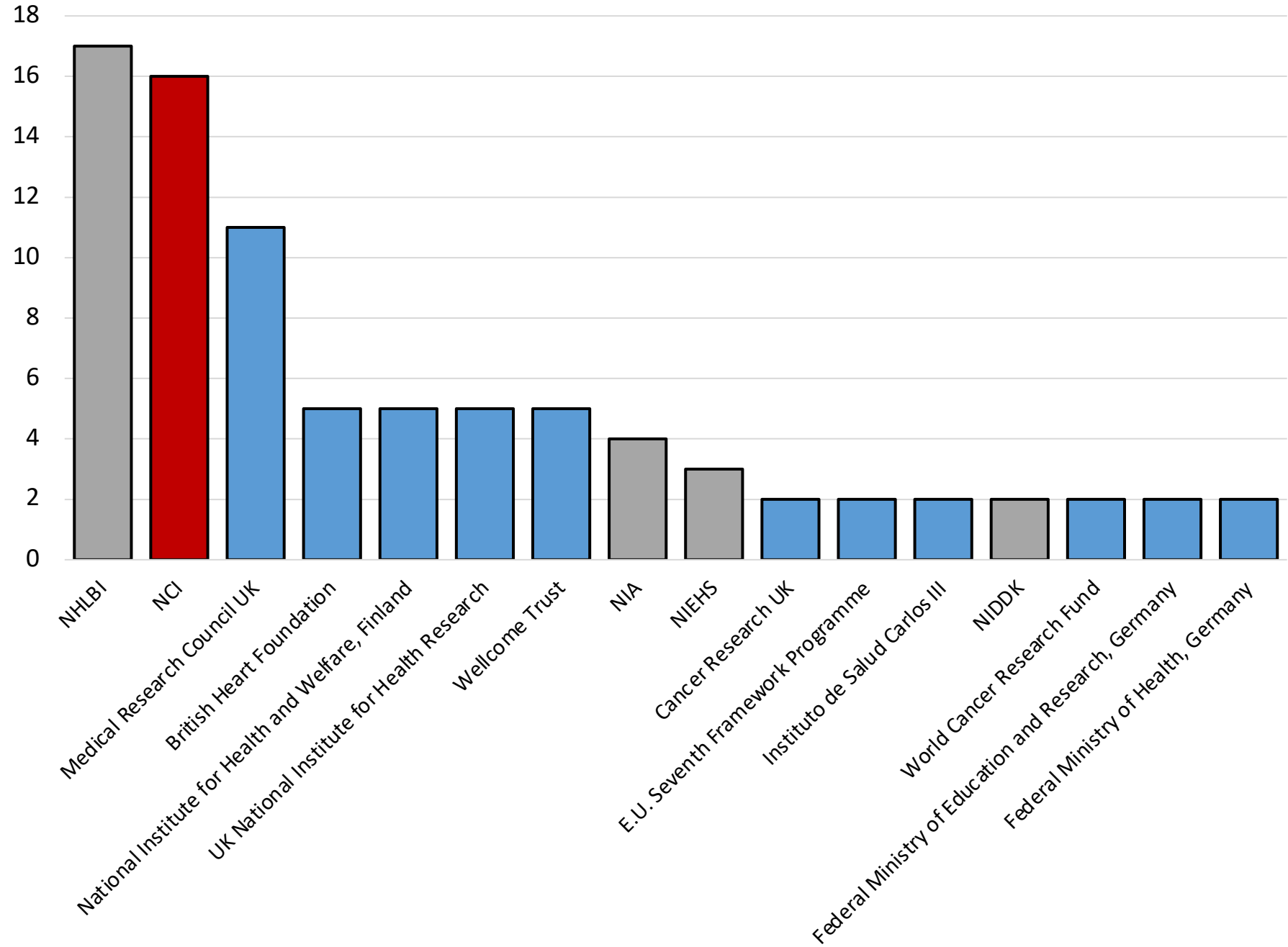
ColoCare

bib We are family BORNINBRADFORD

NIH NATIONAL CANCER INSTITUTE


North America
ARIC
BPRHS
BCFR
CPS-II, CPS-III
CATHGEN
CAMP
COPDGene
DPPOS
ATL AA
FHS2, FHS3
GENECARD
GACRS
HPFS
Health ABC
HAPO
NGI
LEOCC
MAC
MGB-BA
MEC
MESA
NAS
NHS, NHS-II
MrOS
PHS
Project Viva
PROGRESS
PLCO
SCCS
SPIROMICS
ColoCare
VDAART
WHI CHD
WIH
South America
BHS
Europe
CORSA
COPSAC 2000, 2010
Estonia OE
ATBC
DIPP
Finrisk 1997, 2002, 2007, 2012
Health 2000
HELIX
ESTHER
KORA
EHS
RS
GDM
NEFRONA
AMD Biomarker
NSHDS
SIMPLER
ORCADES
AIRWAVE
ALSPAC
BiB
BWHHS
CaPS
ET2DS
EPIC, EPIC-Norfolk
NSHD
POPS
SABRE
Fenland
Twins UK
UPBEAT
WH-II
Asia
SMHS
SPA
SWHS
WELL-CHINA
HKOS
PEGASUS
TMCS
SP2

# Funding for cohorts participating in COMETS




**Others**

ABBOTT Laboratories
Academy of Finland
Alzheimer's Society UK
American Cancer Society
Arthritis UK
Austrian Science Fund
Cambridge Biomedical Research Centre
Capital Region Research Foundation
Center for Artificial Intelligence and Robots, Hong Kong Chinese Academy of Sciences
Clinical Research Facility and Biomedical Research Centre
COPD Foundation
Danish Council for Strategic Research
Department of Epidemiology, Netherlands
Diabetes UK
Estonian Ministry of Science and Education
Eunice Kennedy Shriver NICHD
European Commission
Federal Ministry of Health
French National Cancer Institute
German Research Foundation
Hospital Samaritano
Imperial College
Joint UK Research Councils
Juvenile Diabetes Research Foundation
King's College London
National University of Singapore
National Institutes of Health: NCATS, NEI, NHGRI, NIAID, NIDCR, NIDA, NIAAA, NIDCD, Office of Research on Women's Health
NHS Digital
NHS Foundation Trust
Prefecture of Epirus Greece
Spanish Renal Research Network
Swedish Research Council
UK Economic and Social Science Research Council
UK Medical Bioinformatics Partnership
US Department of Defense

# COMETS Project Proposals

- COMETS members can submit project proposals at three due dates per year. They must define required outcome data, exposure data, covariate data, and minimum number of participants for cohorts to participate in the study
- The COMETS Steering Committee reviews the proposal and votes on approval
- The project lead reaches out to COMETS cohort representatives, who may choose to opt-in and share data or analysis results with the project lead for meta-analysis
- Progress is reported annually and reviewed by the COMETS Executive Committee

# Sample of Current COMETS Projects

- **Vicky Stevens** (Emory University) and **Steve Moore** (DCEG) – *Metabolomic analysis of breast cancer risk*
- **Burcu Darst** (Fred Hutchinson Cancer Center) – *Genetic imputation of metabolomics data*
- **Wei Jie Seow** (National University of Singapore) – *Blood metabolomics and lung cancer risk*
- **Demetrius Albanes** (DCEG) – *Blood metabolite profiling in prostate cancer risk*
- **Jennifer Ose** (Hochschule Hannover of Germany), **Marc Gunter** (Imperial College London), and **Neli Ulrich** (University of Utah) – *Metabolomic profiles of colorectal cancer: Early detection and prospective cancer risk*
- **Mary Playdon** (University of Utah) and **Steven Moore** (DCEG) – *Metabolomic profiles of dietary factors implicated in cancer etiology*
- **Fred Tabung** (The Ohio State University) – *Metabolomic profiles of inflammatory & insulinemic dietary patterns and colorectal cancer risk*
- **Demetrius Albanes** (DCEG) – *Blood metabolite profiling in malignant glioma risk*
- **Xiang Shu** (Memorial Sloan Kettering Cancer Center) – *Prospective metabolomics study of gastric cancer*
- **Rachael Z. Stolzenberg-Solomon** (DCEG) – *Metabolomic profiles and pancreatic cancer risk*
- **Hyung-Suk Yook** (Vanderbilt University Medical Center) – *Adulthood weight change, blood metabolomic profiles, and lung function*
- **Wayne R. Lawrence** (DCEG) – *Examination of vitamin D-associated and other metabolites in relation to cancer risk and mortality by race and ethnicity*

# Challenges in multi-cohort collaborations

- Metabolomics data has been generated in thousands of patients
- Important to look for consistent biomarkers or risk factors across multiple large studies

Many institutes/studies cannot transfer data

Working with raw data requires extensive expertise

***Solution:*** Federated analysis model that eliminates data transfer and pools results centrally

https://www.comets-analytics.org

# COMETS Analytics

COMETS Analytics Web Tool

HOME ANALYSIS ABOUT

# Welcome to COMETS Analytics

Perform consortium-based analyses of metabolomics data

Perform Analysis

## COMETS Analytics v2.1 New Release

New features include:

- Support for running survival and and conditional logistic models

Check out the R Package **NEWS** for more information.

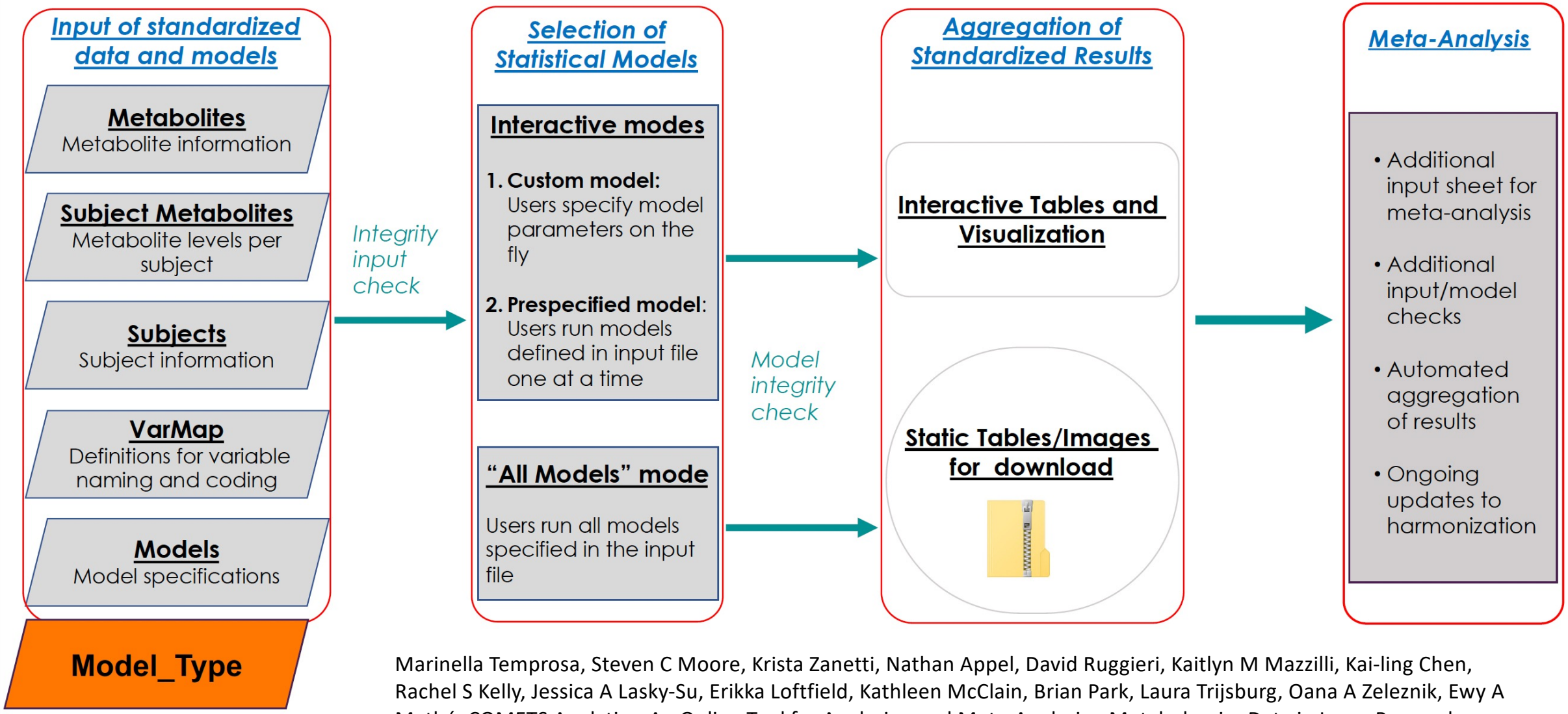
# Roles when Performing Meta-Analyses

- ***Lead Analyst(s)***
  - Coordination of entire project
  - Preparation of input sheet that defines all covariables and models
  - Input sheet sent to individual cohort analysts

- ***Cohort Analysts***
  - Running cohort-level models, using input sheet from lead analyst(s)
  - Sending results to lead analyst(s)

- ***Lead Analyst***
  - Runs meta-analysis with aggregated results

# Overview of Using COMETS Analytics




Marinella Temprosa, Steven C Moore, Krista Zanetti, Nathan Appel, David Ruggieri, Kaitlyn M Mazzilli, Kai-ling Chen, Rachel S Kelly, Jessica A Lasky-Su, Erikka Loftfield, Kathleen McClain, Brian Park, Laura Trijsburg, Oana A Zeleznik, Ewy A Mathé, COMETS Analytics: An Online Tool for Analyzing and Meta-Analyzing Metabolomics Data in Large Research Consortia, *American Journal of Epidemiology*, Volume 191, Issue 1, January 2022, Pages 147-158.

# COMETS Analytics Access

Available on github

Requires minimal knowledge of R/Rstudio to run

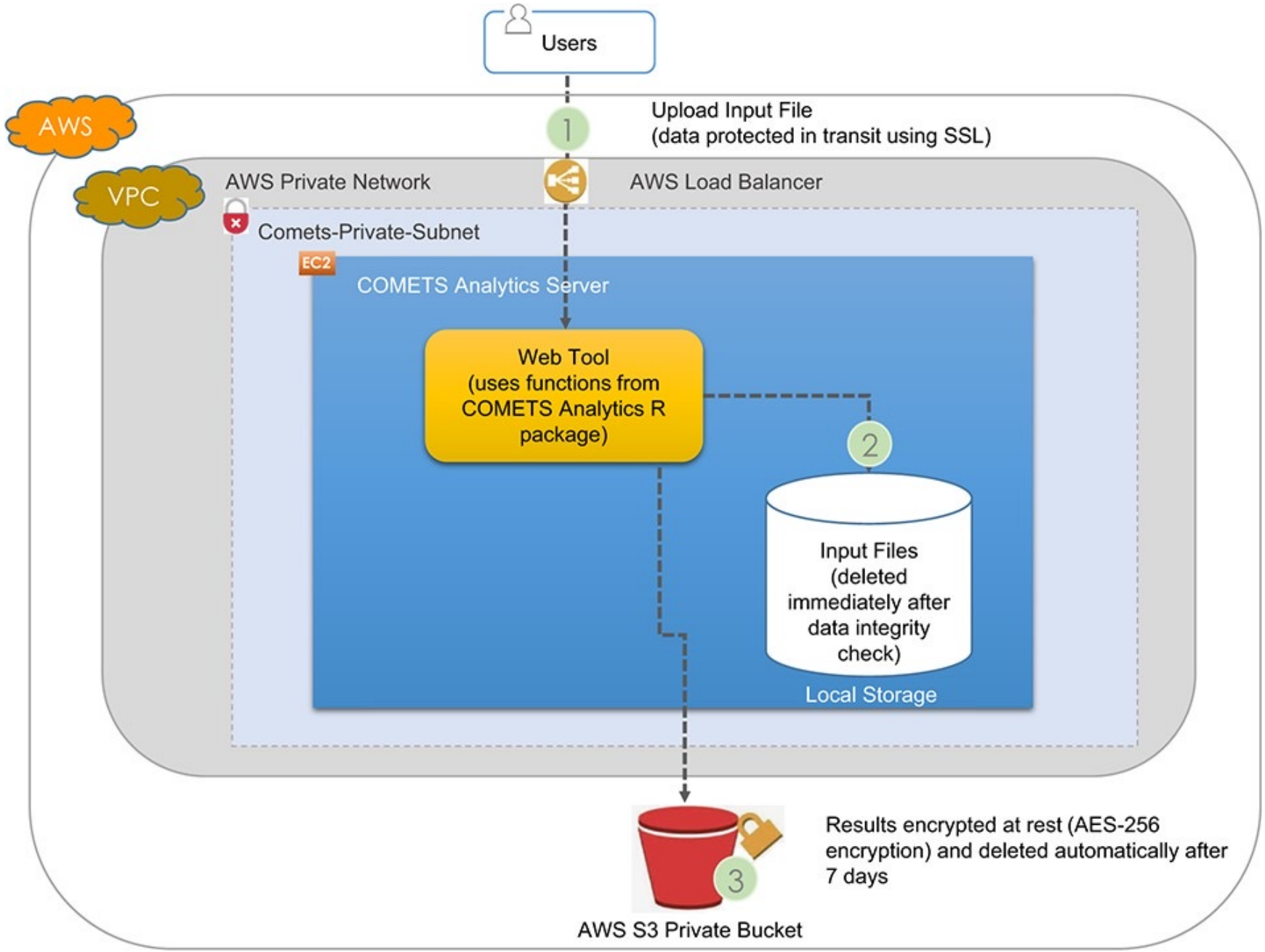
Detailed documentation on how to prepare the input and how to run through an analysis are provided

Comets-analytics.org

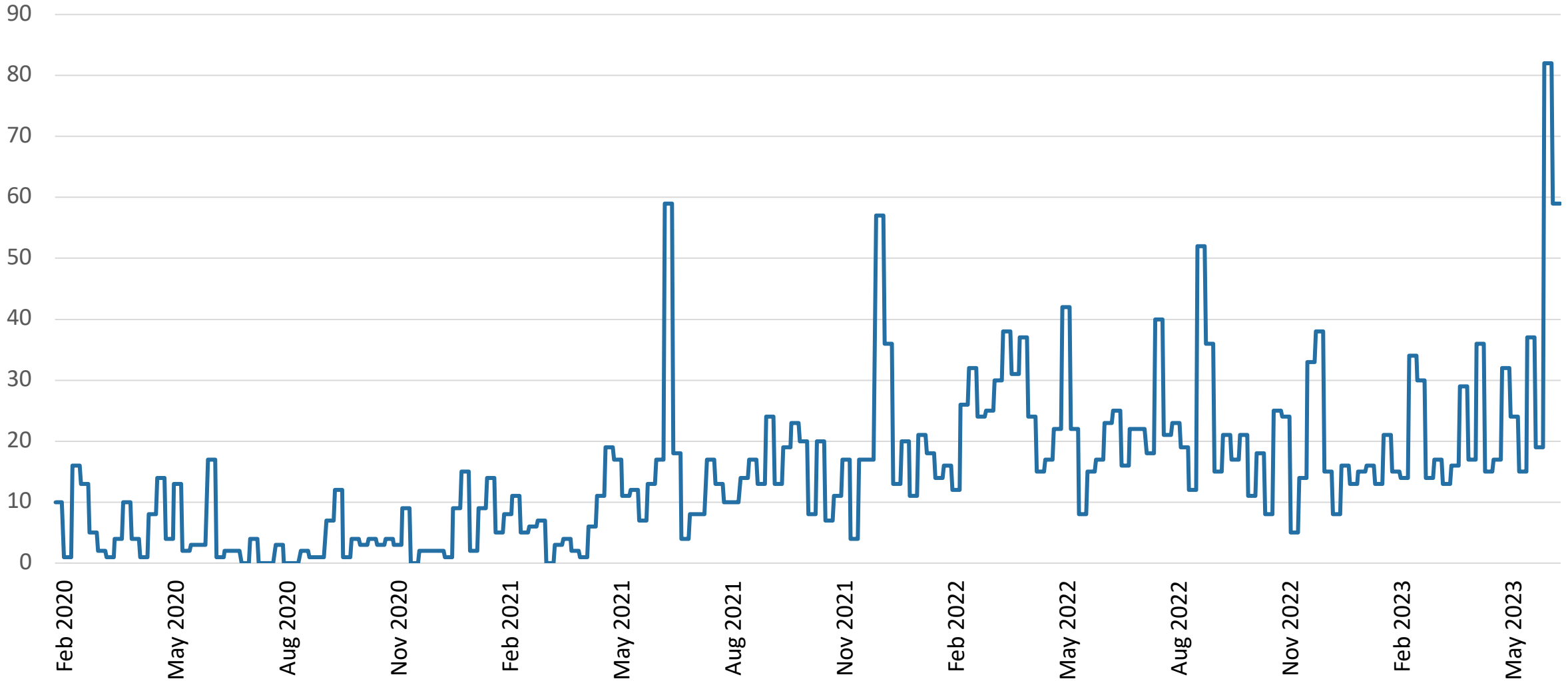
User-friendly, requires no coding

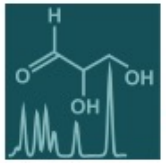
Operates on secure cloud-based servers that delete data after analyses

Cloud costs supported by STRIDES award in FY2020


Users
AWS
1
Upload Input File
(data protected in transit using SSL)
VPC
AWS Private Network
AWS Load Balancer
Comets-Private-Subnet
EC2
COMETS Analytics Server
Web Tool
(uses functions from
COMETS Analytics R
package)
2
Input Files
(deleted
immediately after
data integrity
check)
Local Storage
3
Results encrypted at rest (AES-256
encryption) and deleted automatically after
7 days
AWS S3 Private Bucket

# Weekly Visits to COMETS Analytics Site






*metabolites*

Article

# Metabolomics Analytics Workflow for Epidemiological Research: Perspectives from the Consortium of Metabolomics Studies (COMETS)

Mary C. Playdon, Amit D. Joshi, Fred K. Tabung, Susan Cheng, Mir Henglin, Andy Kim, Tengda Lin, Eline H. van Roekel, Jiaqi Huang, Jan Krumsiek et al.

Special Issue
Metabolomics in Epidemiological Studies
Edited by
Dr. Krista Zanetti

American Journal of
EPIDEMIOLOGY

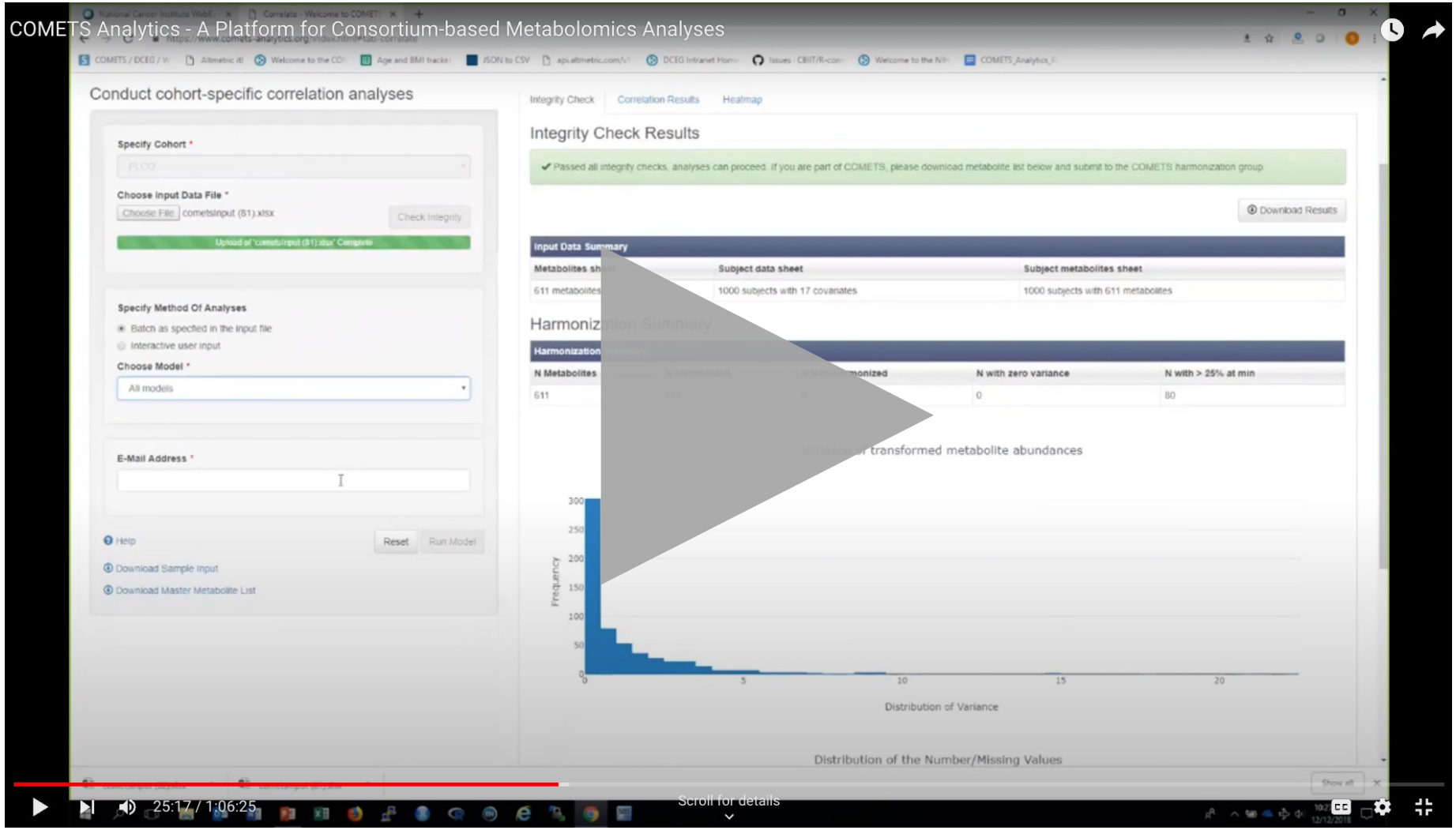
JOURNAL ARTICLE

# COMETS Analytics: An Online Tool for Analyzing and Meta-Analyzing Metabolomics Data in Large Research Consortia

Marinella Temprosa, Steven C Moore, Krista A Zanetti, Nathan Appel, David Ruggieri, Kaitlyn M Mazzilli, Kai-ling Chen, Rachel S Kelly, Jessica A Lasky-Su, Erikka Loftfield ...
Show more

*American Journal of Epidemiology*, Volume 191, Issue 1, January 2022, Pages 147–158,
https://doi.org/10.1093/aje/kwab120
**Published:** 22 April 2021 **Article history** ▾

# Demo: COMETS Analytics – A Platform for Consortium-based Metabolomics Analyses




https://www.youtube.com/watch?v=WbcbLRQZ0Jg

# Conclusions

- COMETS Analytics provides a framework with which to analyze data and aggregate results for large research consortia that has
  - Protection of data
  - Robust analytics that allow the same model to be applied to all cohorts
  - Real-time checks to ensure high-quality results
  - No requirement for specialized software, servers, or data agreements to use
- STRIDES support allowed users to run analyses through the web-based app which has a user-friendly interface, superior speed, usability, and exploratory tools and operates on secure cloud-based servers that delete data after analyses.

# COnsortium of METabolomics Studies

# Questions