

## **Breakout Session 2: Track A**

# **COnsortium of METabolomics Studies**

Dr. Kelly Crotty  
*Program Director, NCI*

Ms. Kailing Chen  
*Cloud Architect, CBIIT*

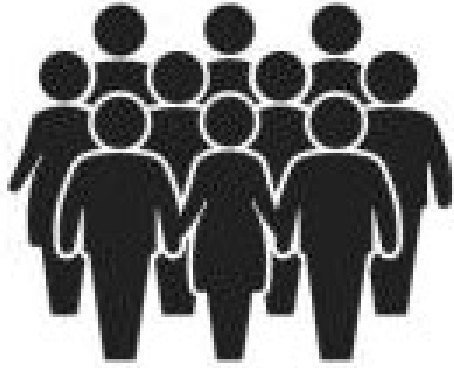
# COnsortium of METabolomics Studies



*Kelly Crotty and Kai-Ling Chen*

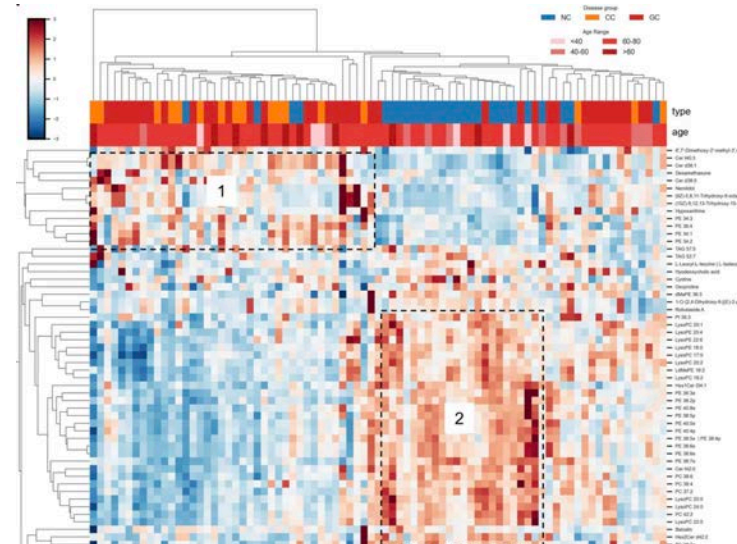
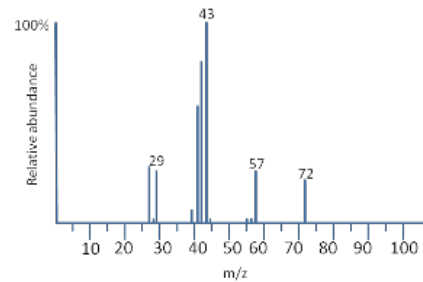
*National Cancer Institute*

# Prospective Cohort Studies

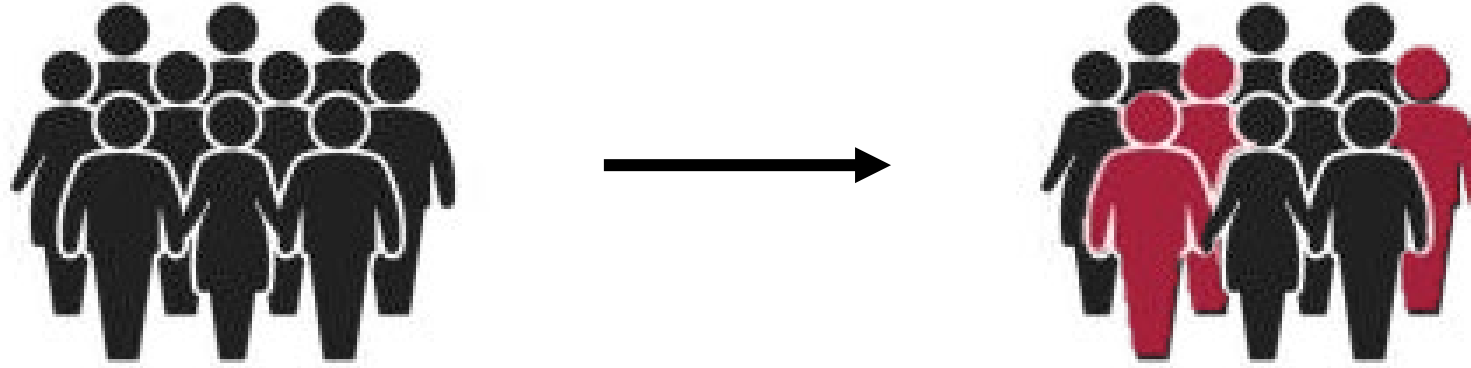


Collect demographic information and samples for baseline measurements

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



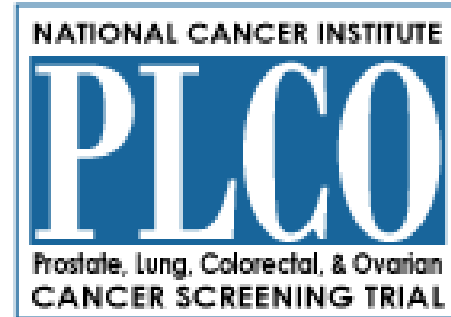


# CONsortium of METabolomics Studies

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



Mano-A-Mano Mexican American Cohort



## 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

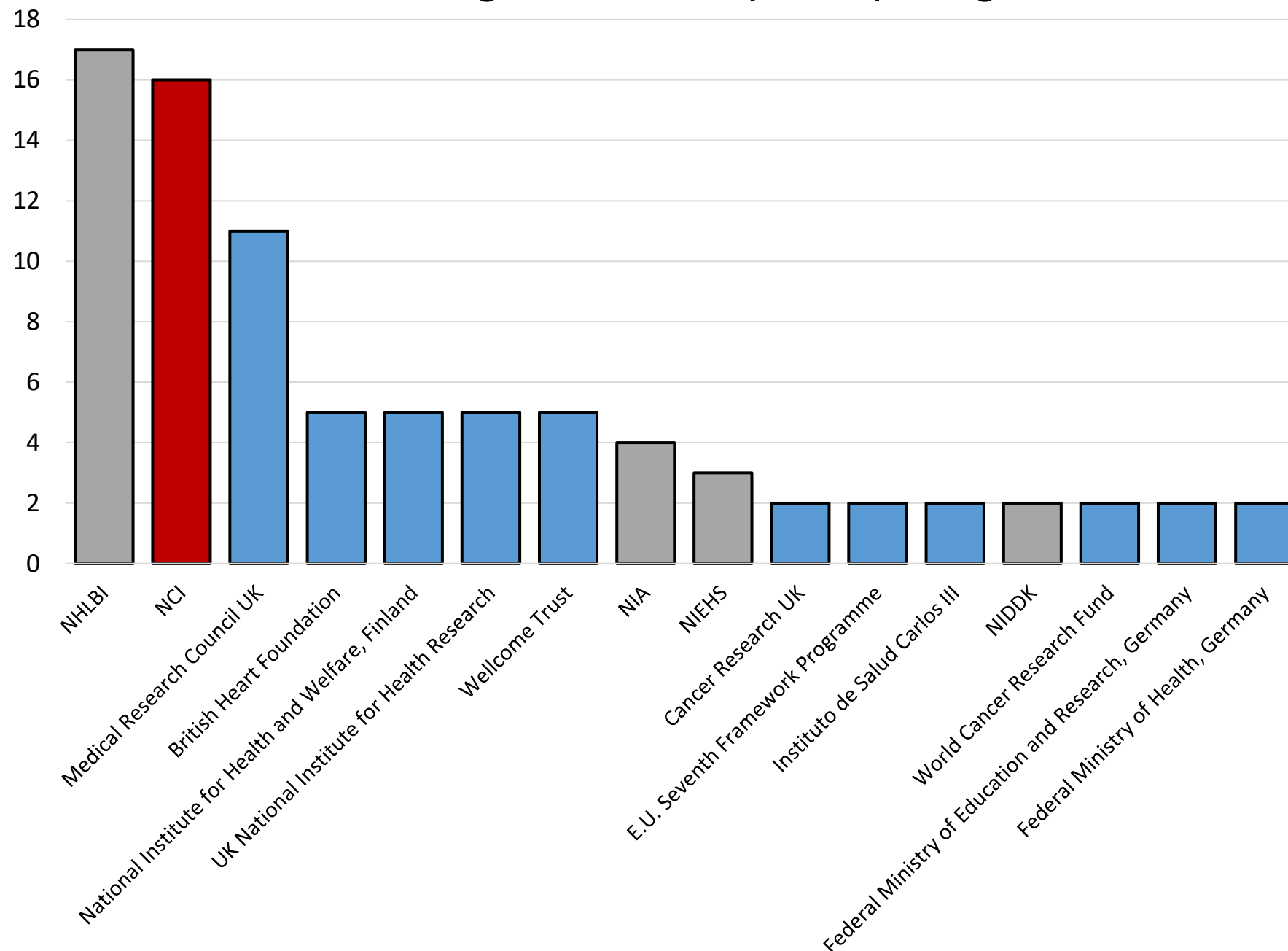
CORSA  
COPSAC 2000, 2010  
Estonia OE  
ATBC  
DIPP  
Finrisk 1997, 2002,  
2007, 2012  
Health 2000  
HELIX  
ESTHER  
KORA  
EHS  
RS  
GDM  
NEFRONA  
AMD Biomarker  
NSHDS  
SIMPLER  
ORCADES  
AIRWAVE  
ALSPAC  
BiB  
BWHHS  
CaPS  
ET2DS  
EPIC, EPIC-Norfolk  
NSHD  
POPS  
SABRE  
Fenland  
Twins 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



Security

Many institutes/studies cannot transfer data



Expertise

Working with raw data requires extensive expertise

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



# 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 conditional logistic models

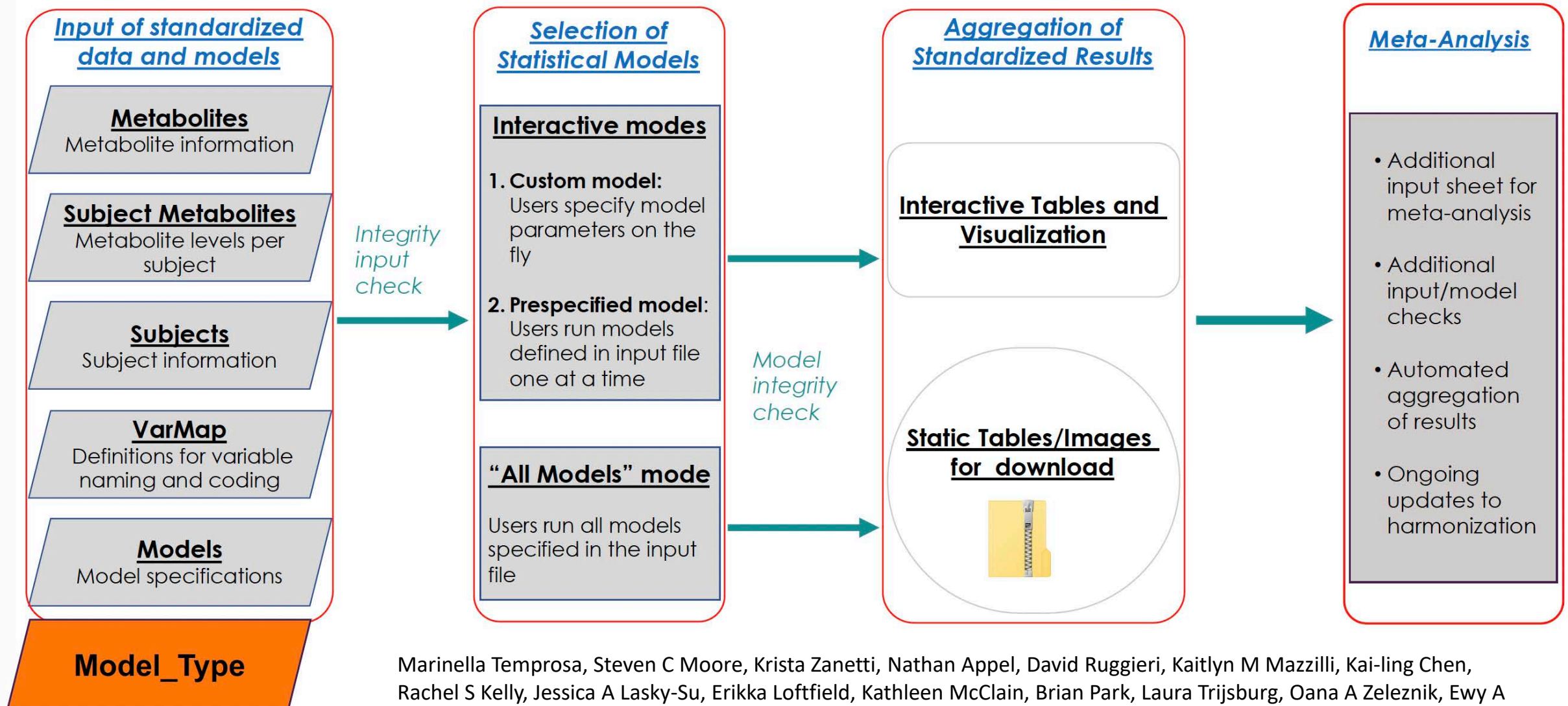
Check out the R Package NEWS for more information.



# 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

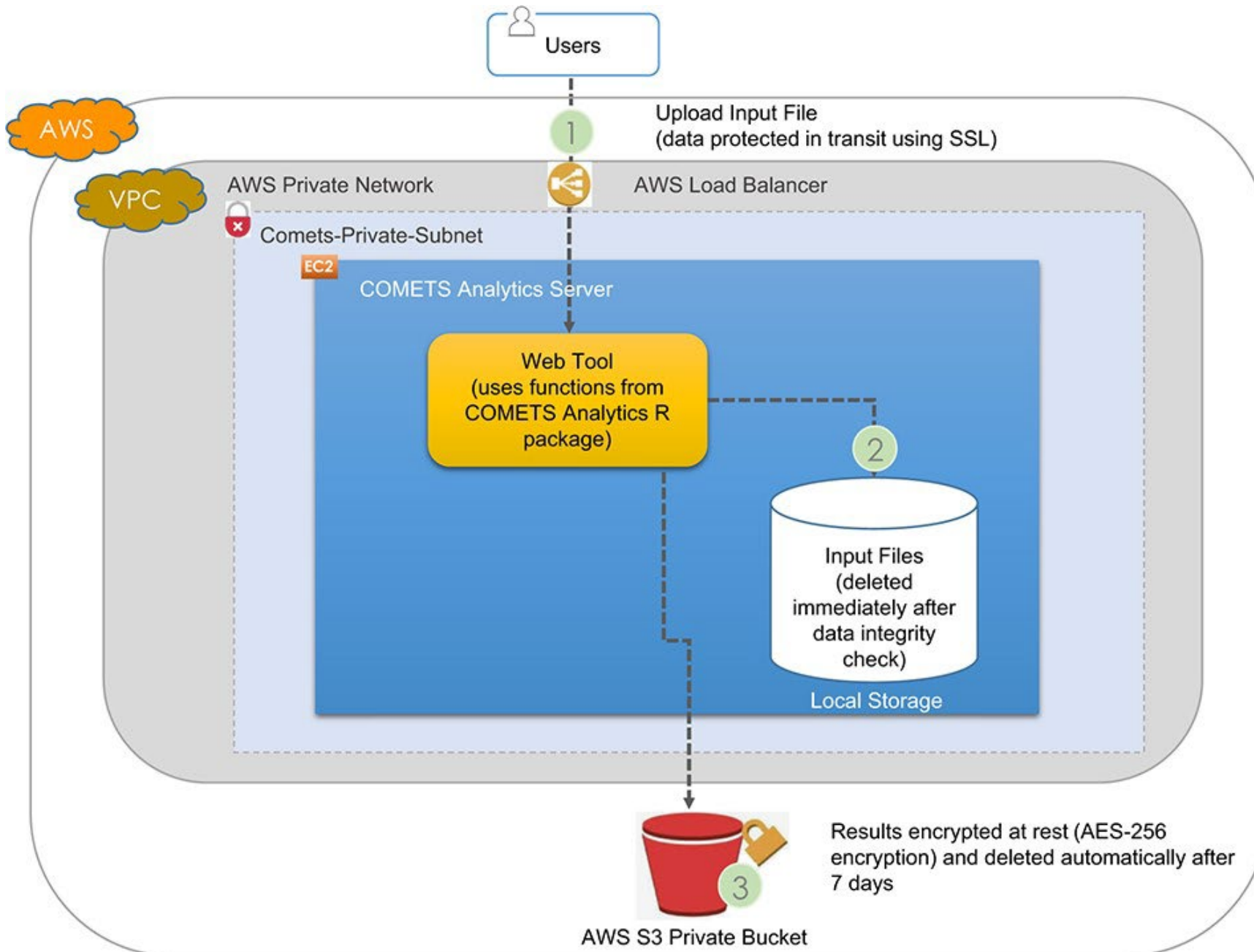


[Comets-analytics.org](https://comets-analytics.org)

User-friendly, requires no coding  
Operates on secure cloud-based servers that delete data after analyses

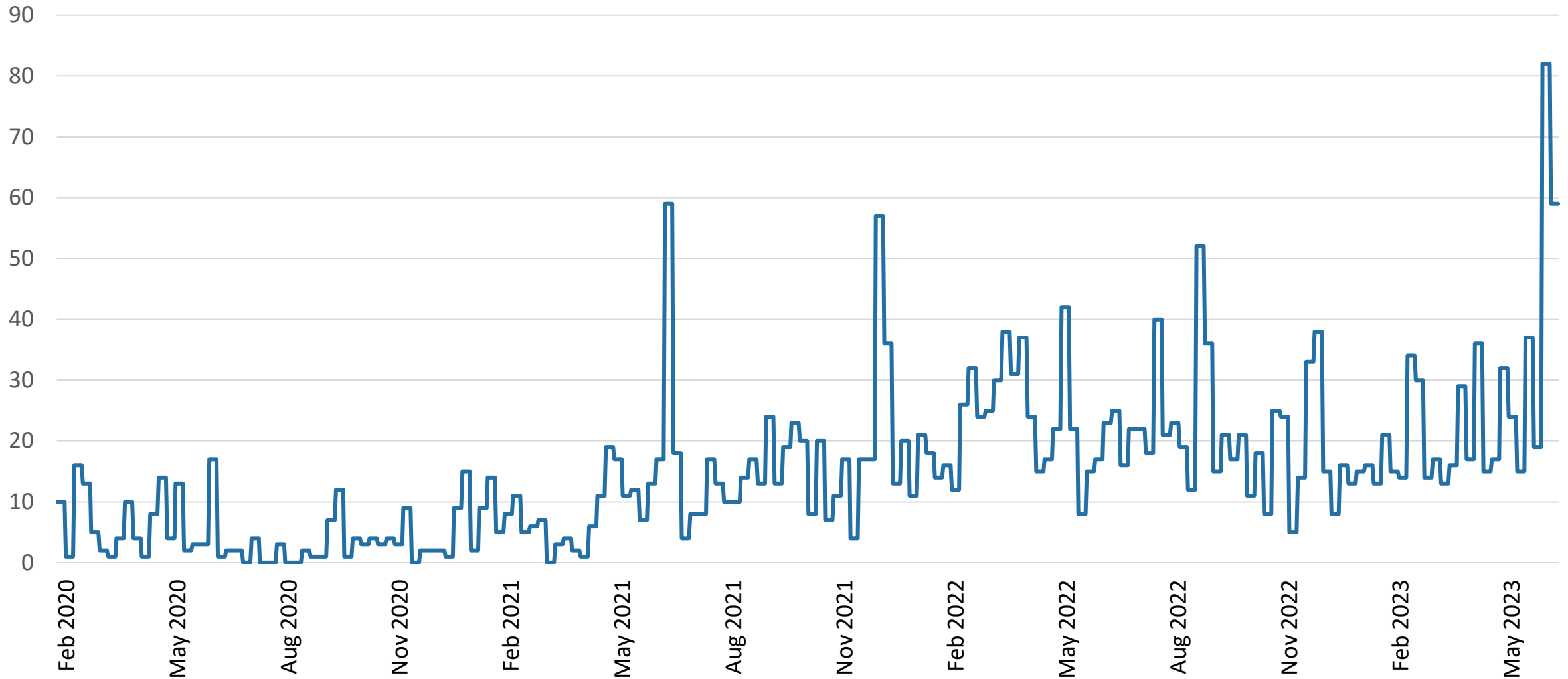
**Cloud costs supported by  
STRIDES award in FY2020**

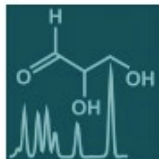






# Weekly Visits to COMETS Analytics Site





*metabolites*

Article

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

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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 ...

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*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

COMETS Analytics - A Platform for Consortium-based Metabolomics Analyses

Conduct cohort-specific correlation analyses

Specify Cohort \*  
PLCO

Choose Input Data File \*  
Choose File: cometsinput (B1).xlsx  
Upload of "cometsinput (B1).xlsx" Complete

Specify Method Of Analyses  
Batch as specified in the input file  
Interactive user input

Choose Model \*  
All models

E-Mail Address \*

Help  
Download Sample Input  
Download Master Metabolite List

Integrity Check Results  
Passed all integrity checks, analyses can proceed. If you are part of COMETS, please download metabolite list below and submit to the COMETS harmonization group.

Download Results

Input Data Summary

Metabolites sheet	Subject data sheet	Subject metabolites sheet
611 metabolites	1000 subjects with 17 covariates	1000 subjects with 611 metabolites

Harmonization Summary

N Metabolites	N Harmonized	N not Harmonized	N with zero variance	N with > 25% at min
611	611	0	0	80

Variance in transformed metabolite abundances

Distribution of Variance

Distribution of the Number/Missing Values

25:17 / 1:06:25

Scroll for details



## 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