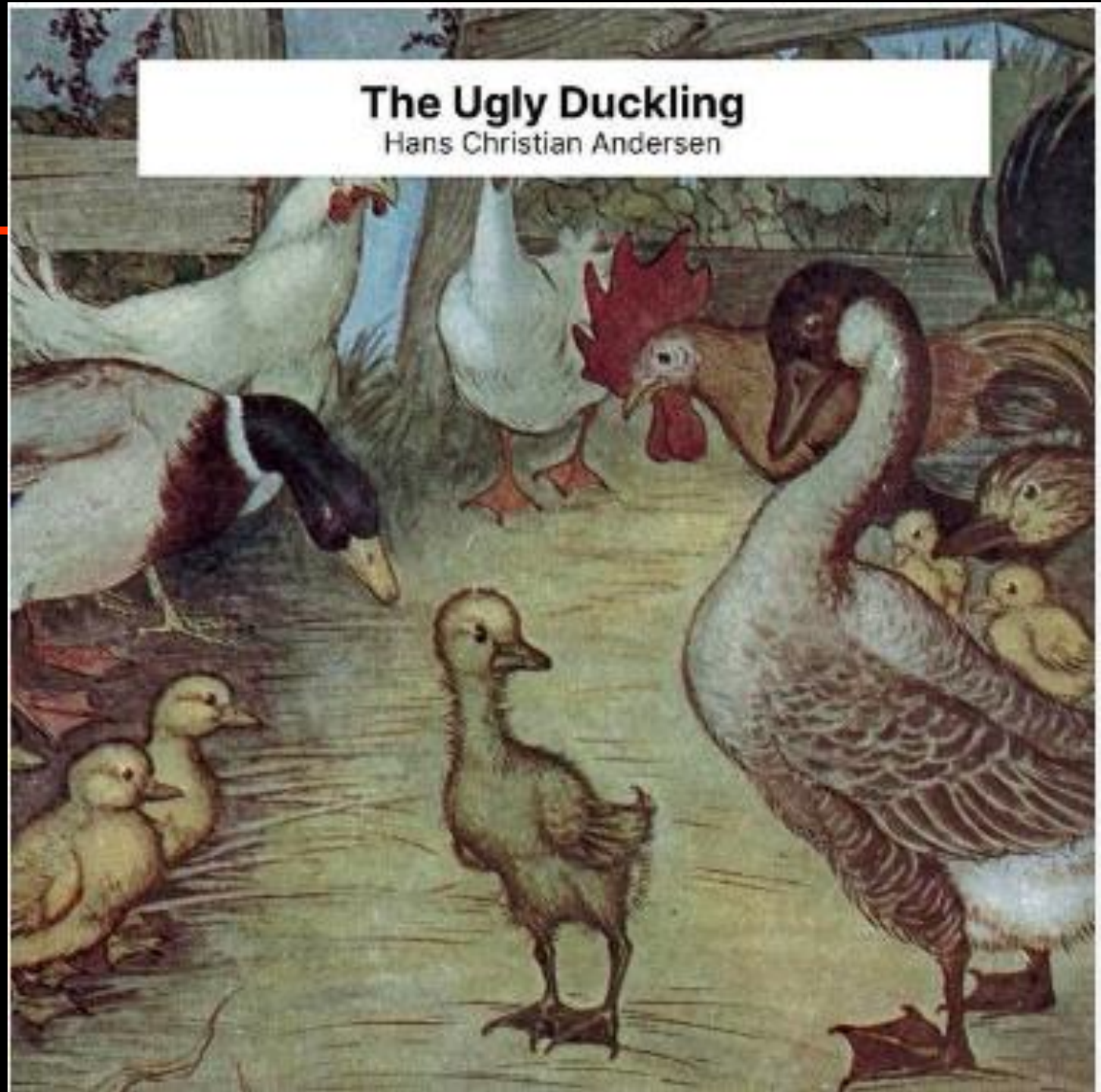
Role of predicting weight loss, what have we learnt from SOPHIA?

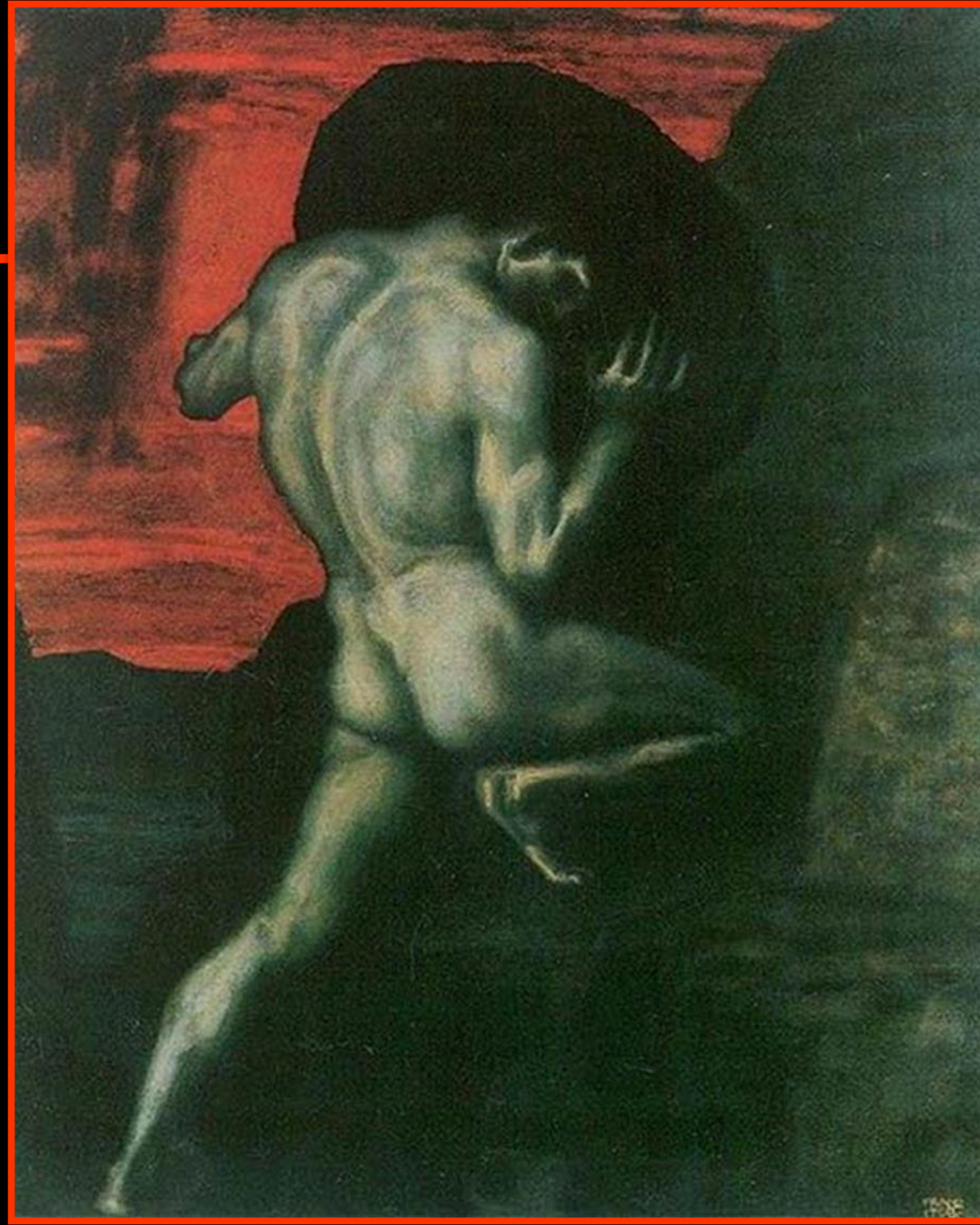
Carel le Roux

University College Dublin
Ulster University
University of Pretoria

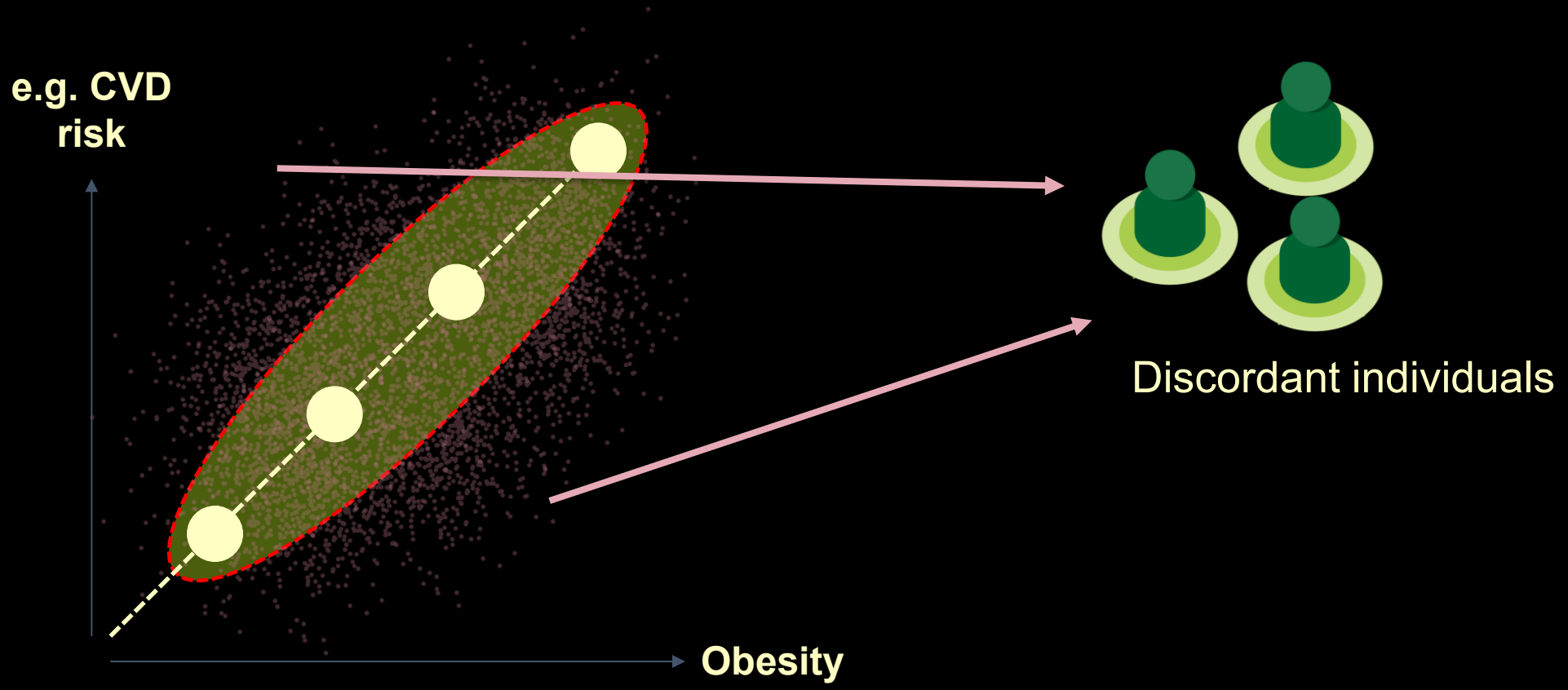


Conflicts of interest

- Consilient Health
- Novo Nordisk
- Herbalife
- Johnson & Johnson
- Covidien
- Fractyl
- GI Dynamics
- Lilly
- Boehringer Ingelheim
- Keyron
- Astra Zeneca
- Roche
- Arrowhead
- Amgen



What we know: Risk doesn't always follow BMI



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BC: Baseline Concordant profile

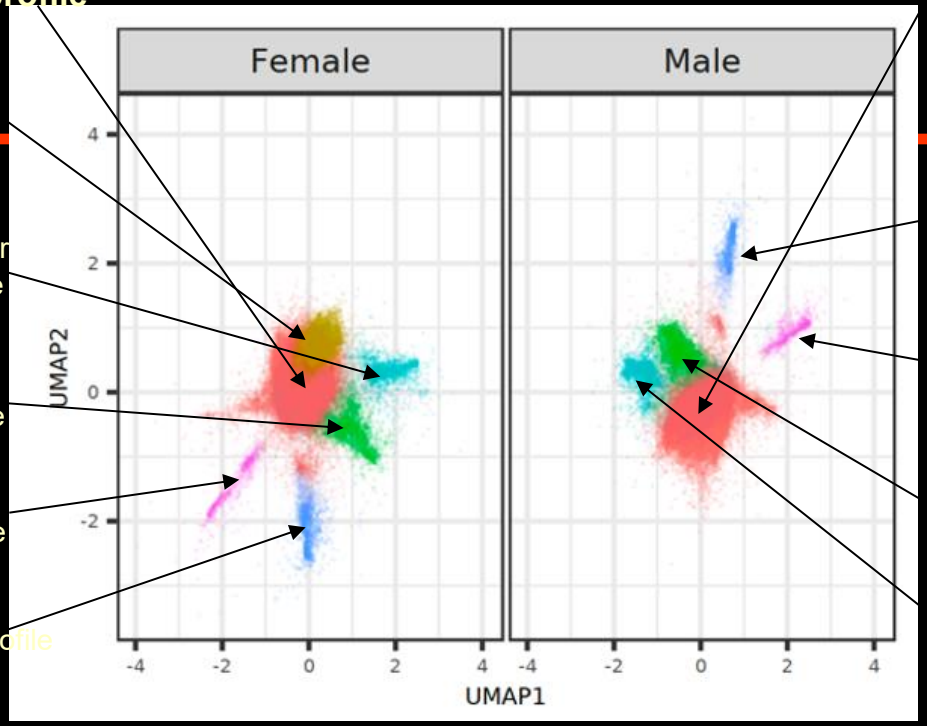
DHT: Discordant Hypertensive profile

DLT: Discordant Liver Transaminases profile

DAL: Discordant Adverse Lipid profile

DHG: Discordant Hyperglycaemic profile

DIS: Discordant Inflammatory State profile



BC: Baseline Concordant profile

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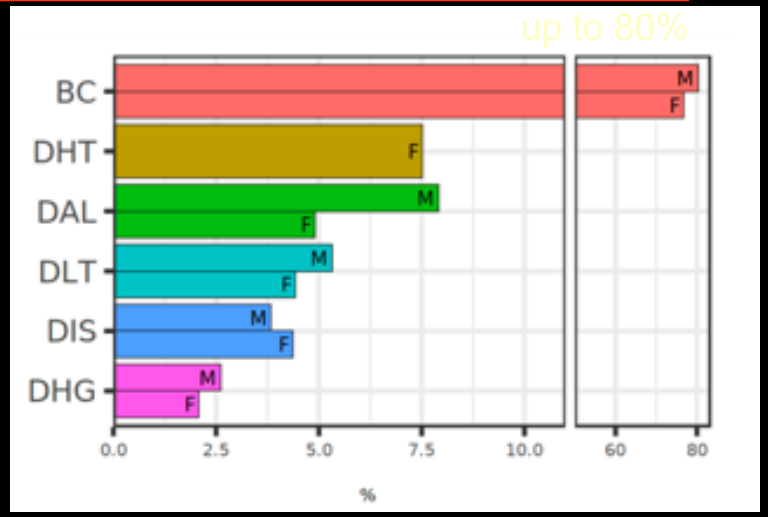
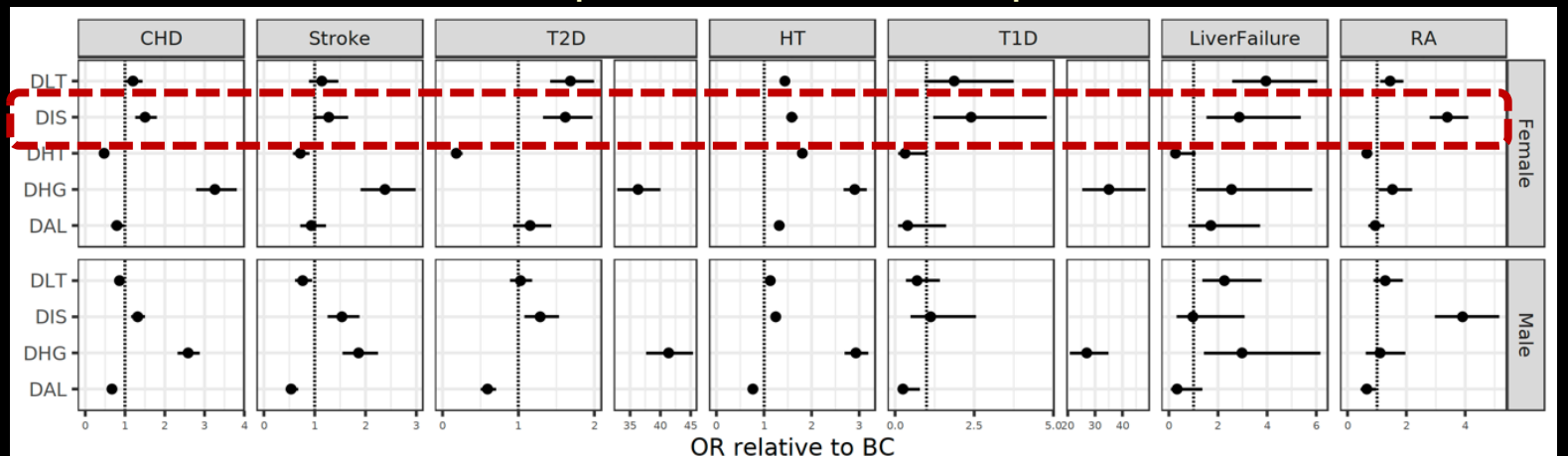


Discordant profiles and disease prevalence



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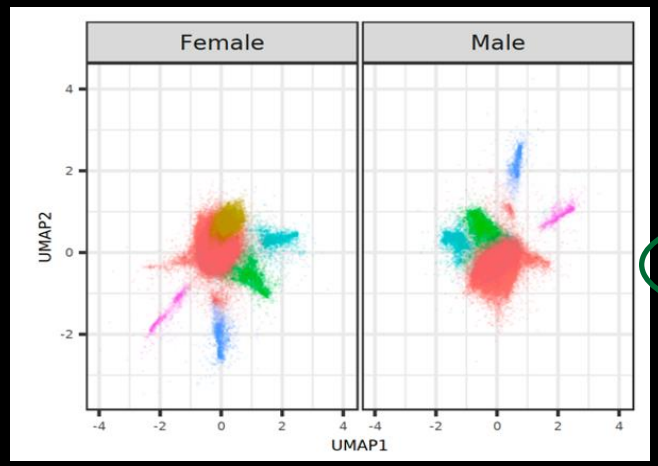
Mapping onto SOS (University of Gothenburg)

Effect of surgery intervention vs. usual care (diet/exercise) after 2 years

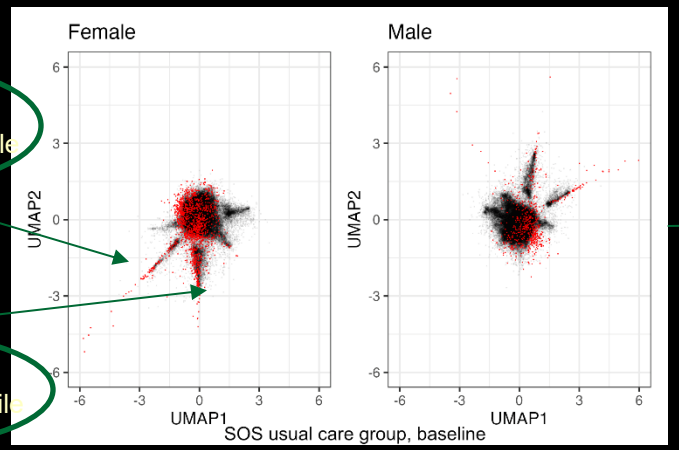
SOPHIA UMAP

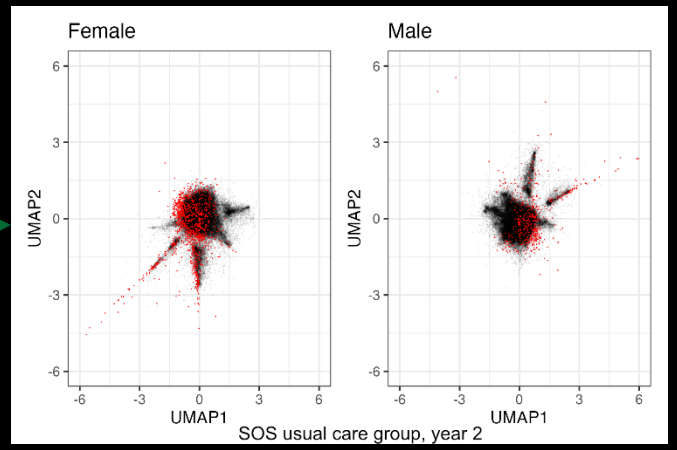


DHG: Discordant Hyperglycaemic profile

DIS: Discordant Inflammatory State profile

SOS usual care

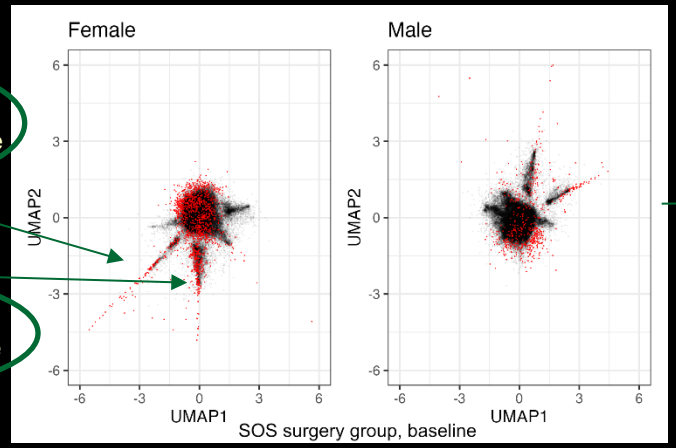


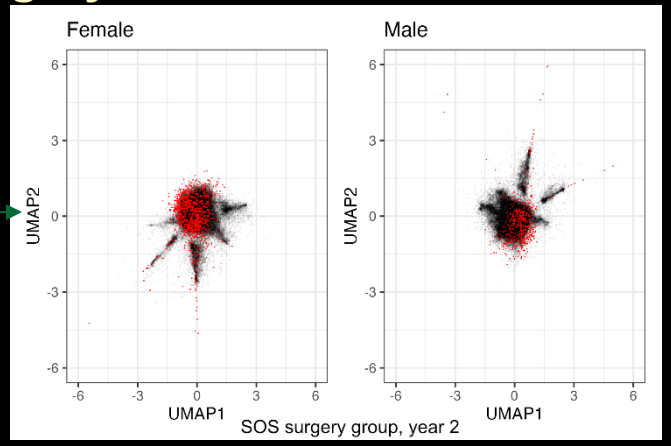


DHG: Discordant Hyperglycaemic profile

DIS: Discordant Inflammatory State profile

SOS surgery





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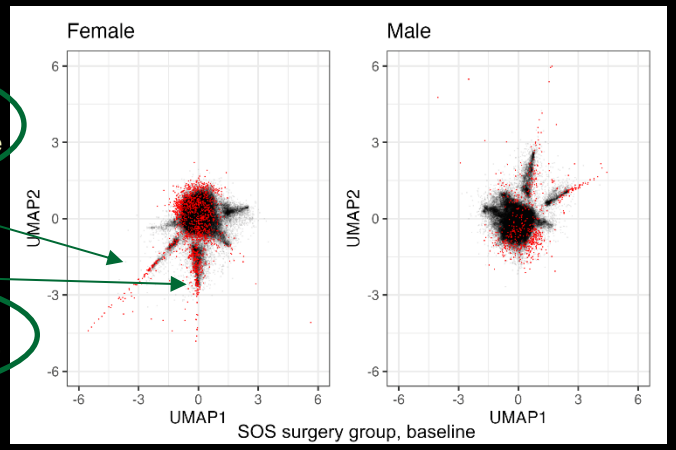
Those with specific obesity subtypes seem to benefit more from treatment

- Women in the Discordant Inflammatory State cluster benefit more from a bypass than woman in the concordant (baseline) cluster
- Men and women in the Discordant Hyperglycaemic cluster do not benefit as much from a bypass than in the concordant (baseline) cluster

Term	Estimate	Pval
IntArm2 * cluster		2.63e-5
• probDHT:IntArm2	-0.0247	NS
• probDAL:IntArm2	0.08366	NS
• probDLT:IntArm2	-0.0610	NS
• probDIS:IntArm2	-0.1126	0.0281
• probDHG:IntArm2	0.178036	3.921e-4

DHG: Discordant Hyperglycaemic profile

DIS: Discordant Inflammatory State profile



DHG: Discordant Hyperglycaemic profile

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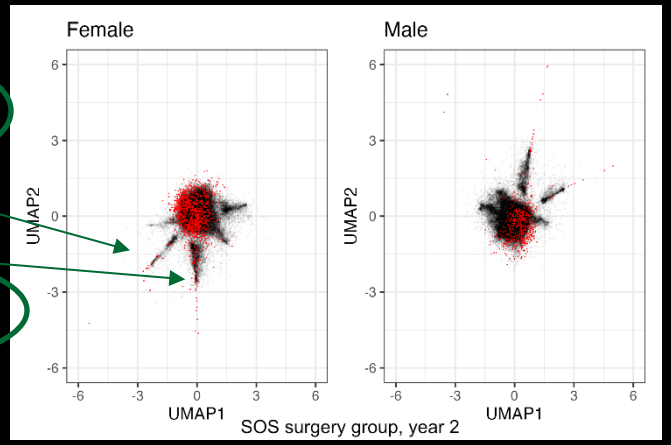

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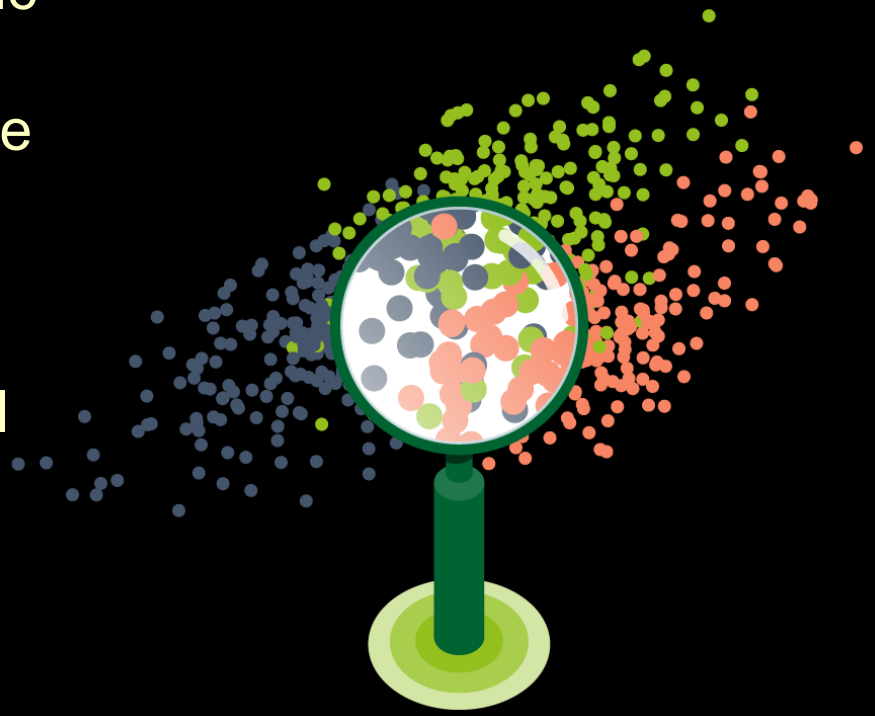
Changing how we understand obesity

- We uncovered 5 phenotypic profiles defined by specific patterns of biomarker discordance with BMI that were robustly replicated across four independent large-scale population-based cohorts
- These discordant profiles, around 20% of the general population, exhibit different relationships between BMI and risk biomarkers
- Demonstrates substantial heterogeneity in the link between BMI and risk
- Conceptualizing these as different subtypes of obesity requires further validation (future work)



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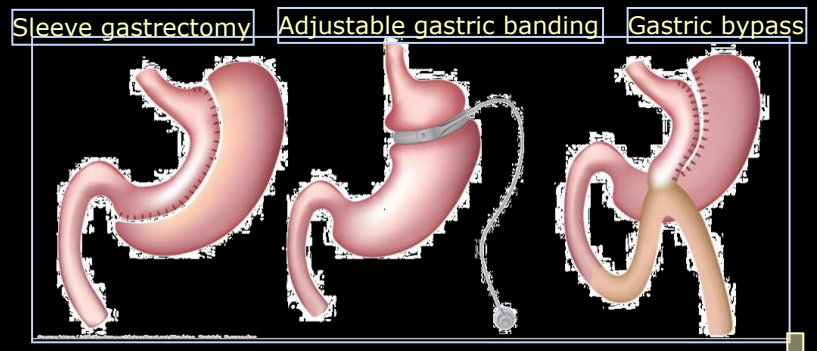
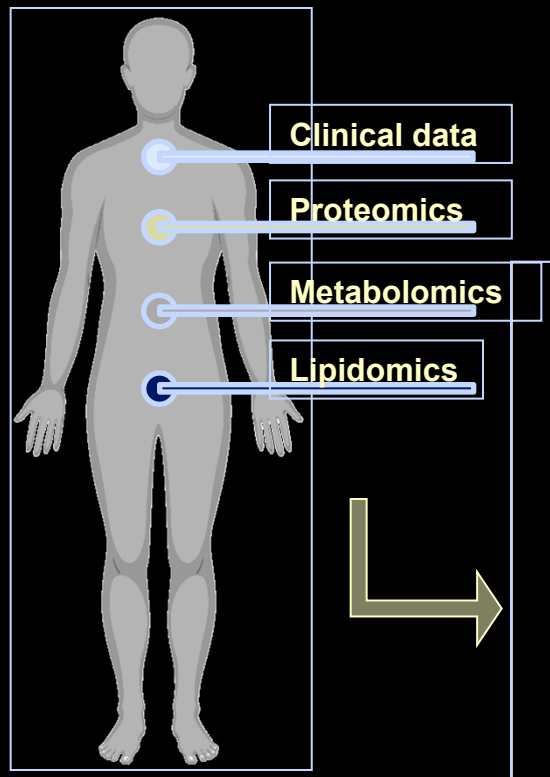
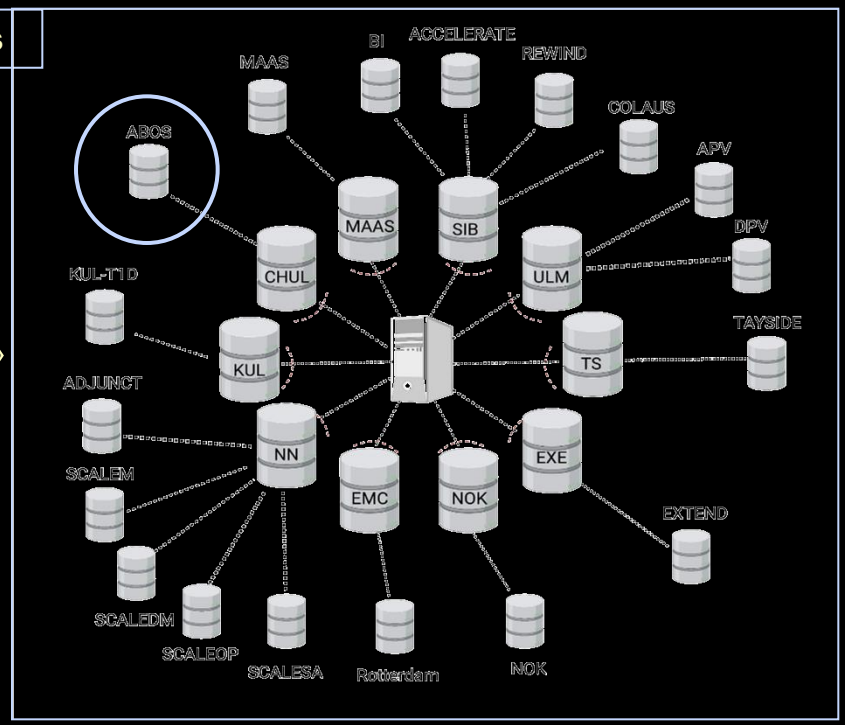
ABOS omics data in the federated database system







Omics analyses through the federated database system

Challenges

- Cannot see data
- Long runtime
- Few analysts working in FDB

ABOS
(N = 1602)

Filtering: prior history of gastric surgery, omics data for follow-up available

Final dataset
(N ~ 250)

Summary level data of all proteins, lipids, and metabolites

+

Linear model in federated database

Δanalyte ~ procedure + ΔBMI + BMI_{t0}

SOPHIA
Stratification of Obese Phenotypes to Optimize Future Obesity Therapy

ABOS OMICS EXPLORER

Carl Delfin

ABOS Omics Explorer app

SOPHIA Stratification of Obese Phenotypes to Optimize Future Obesity Therapy — ABOS OMICS EXPLORER

Trajectory plot | Volcano plot | Forest plot | Estimates table | About

Omics type
Metabolomics

Analyte
carotene diol (1)

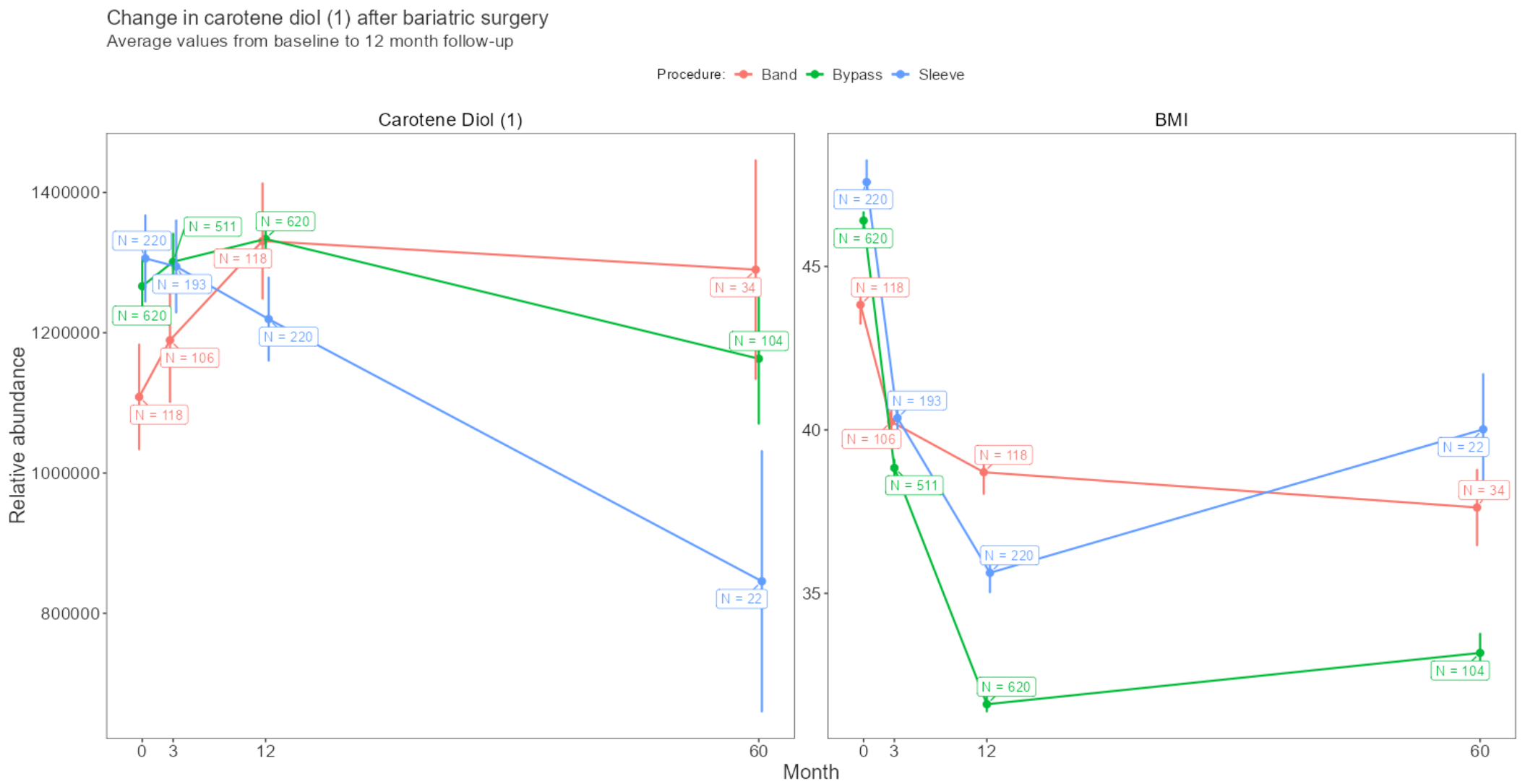
Type of average
Mean

Error bars
Standard error

Show sample size
Yes

Include BMI trajectory
Yes

Download data (CSV)



ABOS Omics Explorer app

SOPHIA ABOS OMICS EXPLORER
Stratification of Obese Phenotypes to Optimize Future Obesity Therapy

Trajectory plot | Volcano plot | Forest plot | Estimates table | About

Omics type
Metabolomics

Timepoint
12 months

Covariates
delta_bmi + baseline_bmi

Show estimate for
Procedures

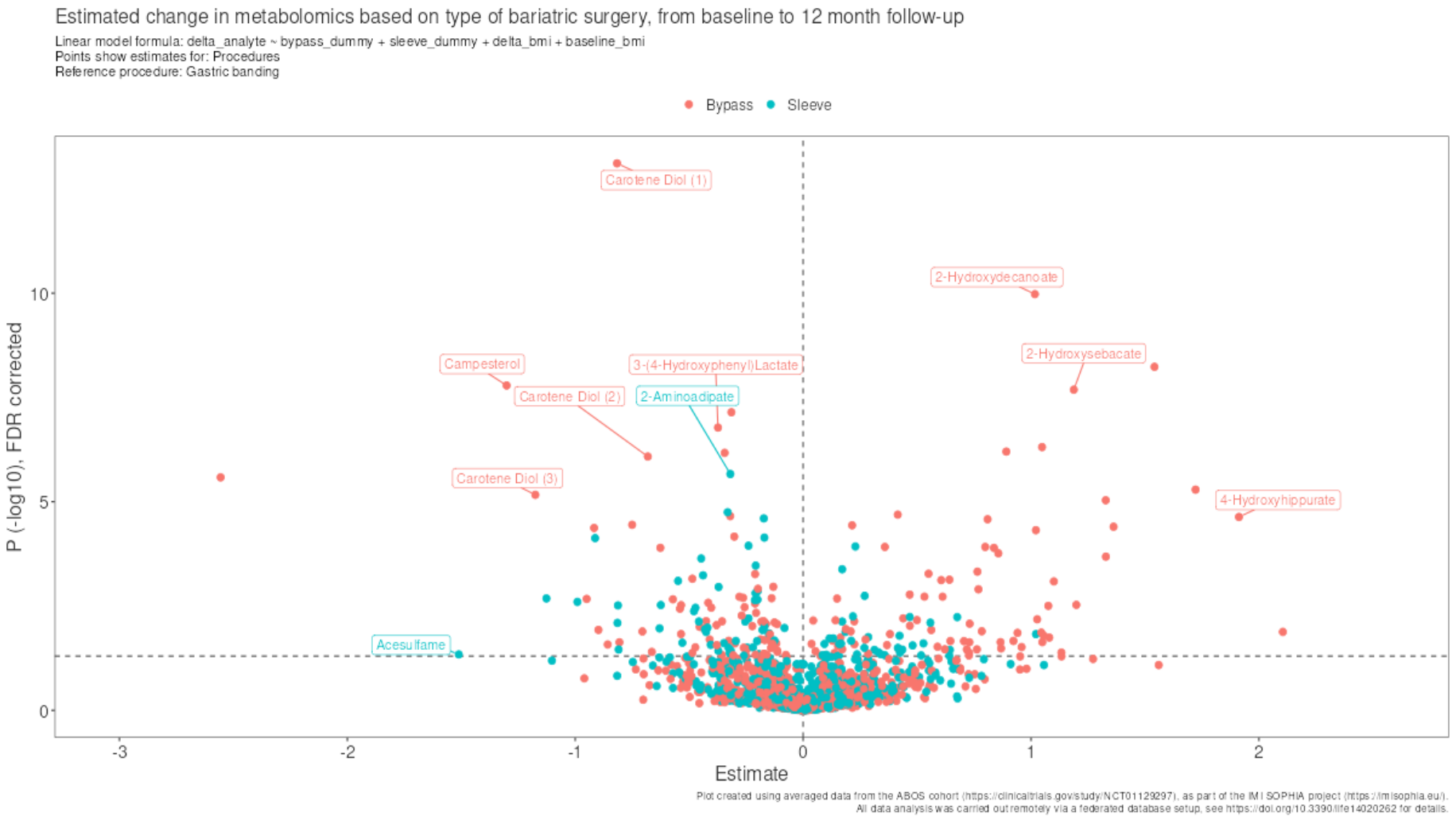
Select label
Name

P-value adjustment
FDR

P-value cutoff (-log10)
0 — 3

Estimate cutoff (absolute)
0 — 5

Download data (CSV)



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SOPHIA ABOS OMICS EXPLORER
Stratification of Obese Phenotypes to Optimize Future Obesity Therapy

Trajectory plot | Volcano plot | Forest plot | Estimates table | About

Omics type
Lipidomics

Timepoint
12 months

Covariates
delta_bmi + baseline_bmi

Show estimate for
BMI delta

Select color
Group

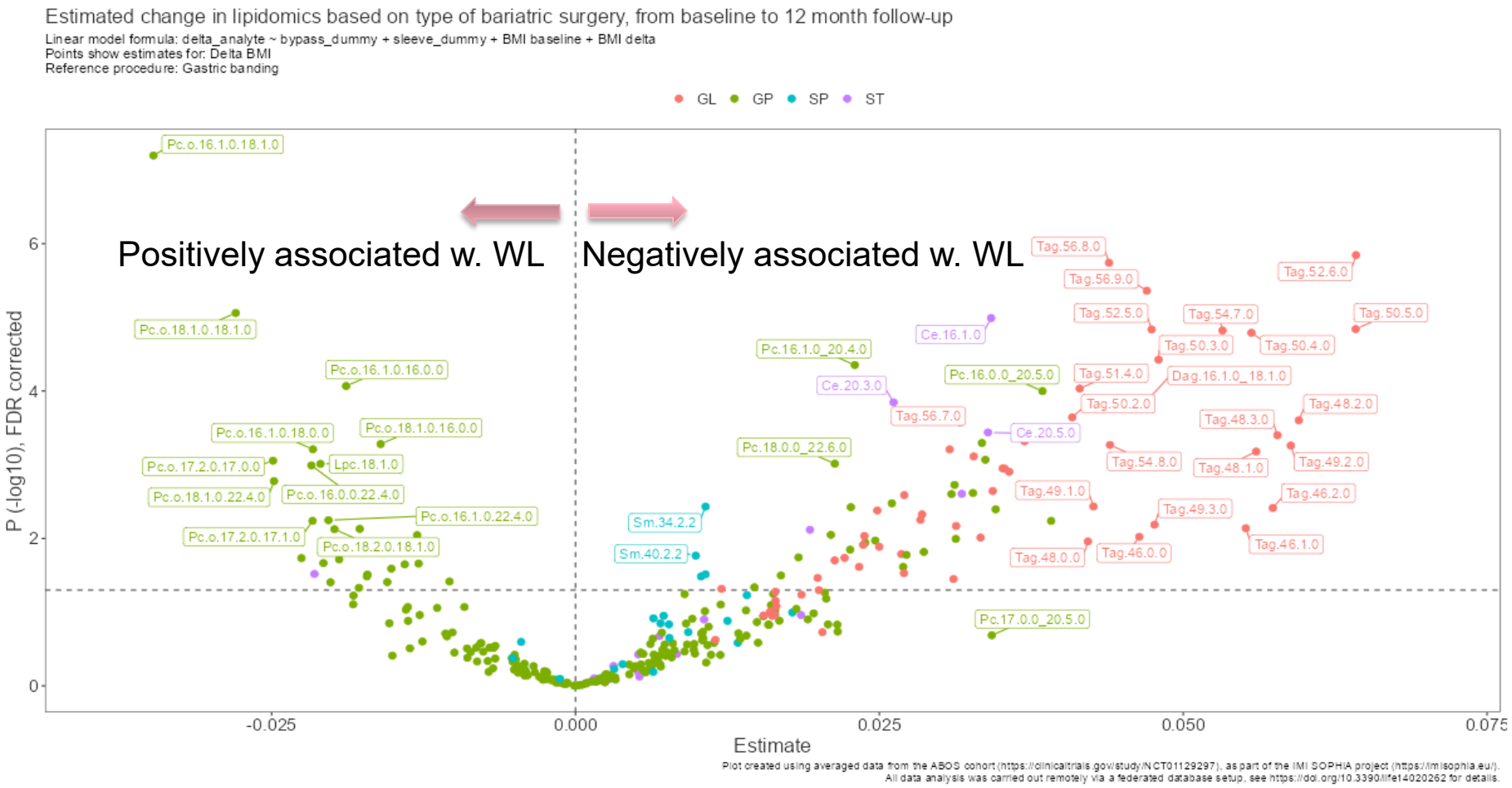
Select label
Name

P-value adjustment
FDR

P-value cutoff (-log10)
0 — 3

Estimate cutoff (absolute)
0 — 5

Download data (CSV)



ABOS Omics Explorer app

SOPHIA Stratification of Obese Phenotypes to Optimize Future Obesity Therapy — ABOS OMICS EXPLORER

Trajectory plot | Volcano plot | Forest plot | Estimates table | About

Omics type
Metabolomics

Timepoint
12 months

Covariates
delta_bmi + baseline_bmi

Show estimate for
Procedures

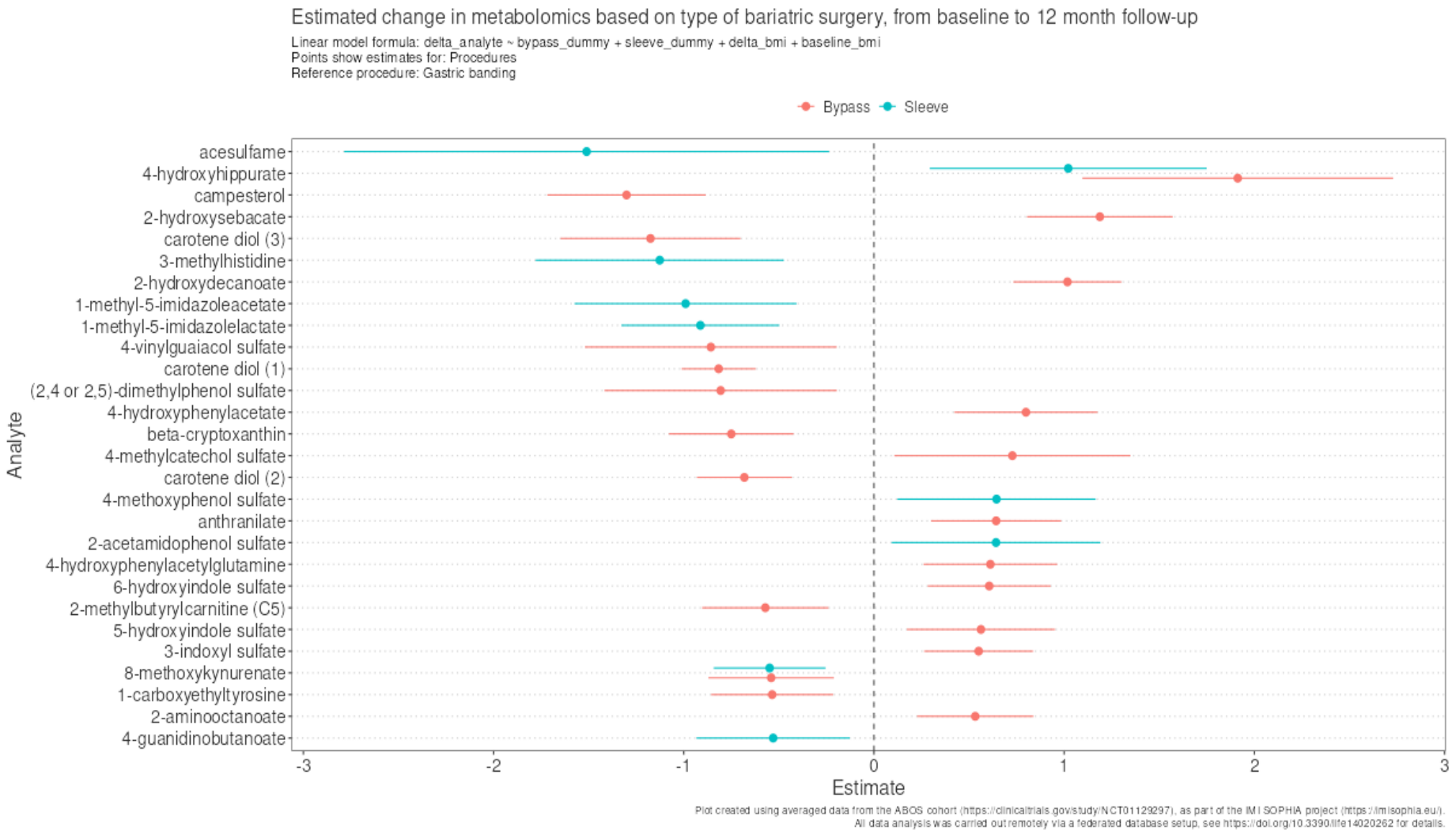
P-value adjustment
FDR

P-value cutoff (-log10)
0 — 1.3 — 3

Estimate cutoff (absolute)
0 — 0.5 — 5

Limit top hits
0 — 30 — 50

Download data (CSV)



Weight

120 kg

Height

170 cm

Age

65 years

Non-smoker **Smoker**

Type 2 diabetes

Diabetes

Diabetes duration

10 years

Surgery

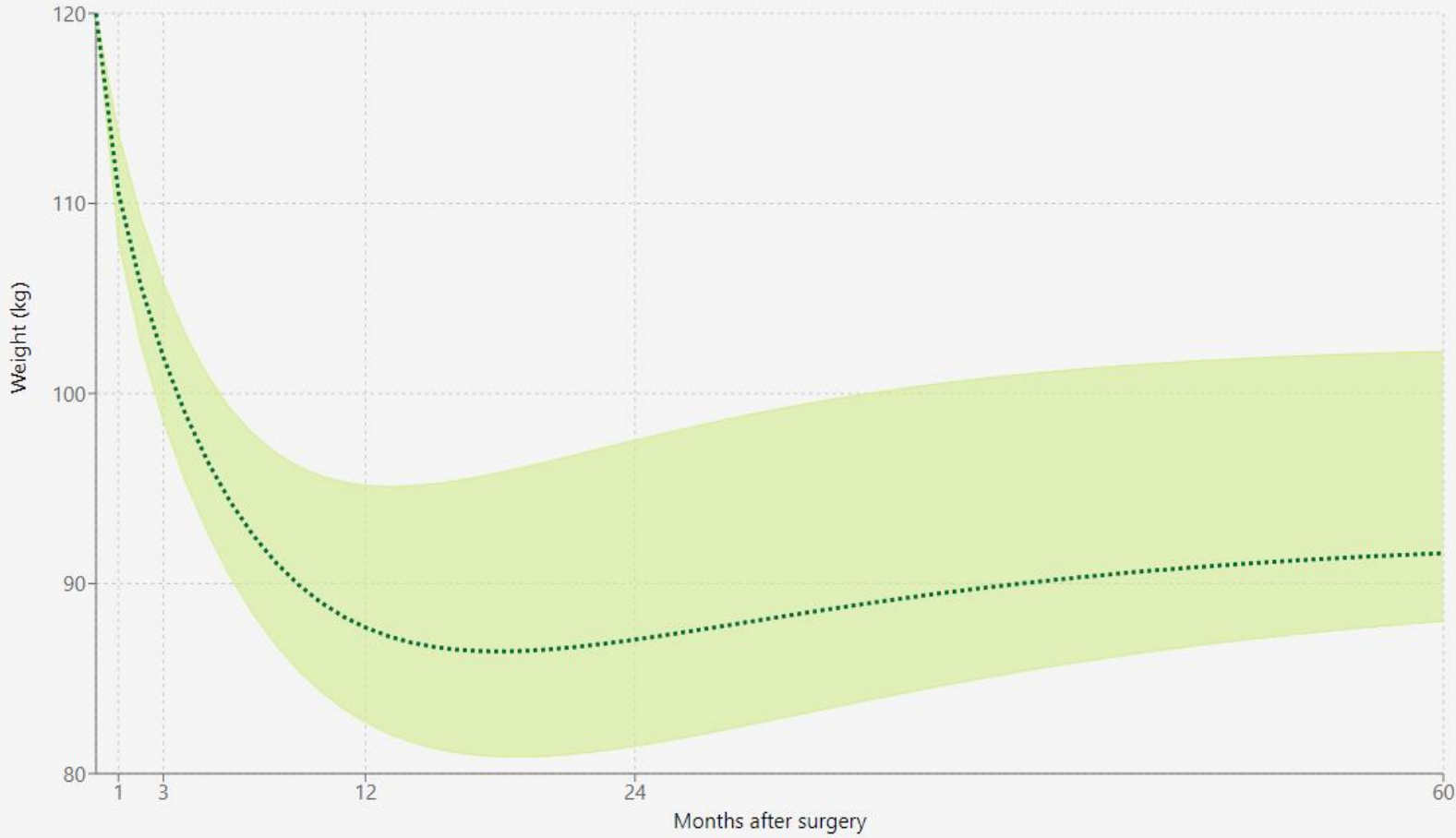
Type of intervention

Gastric Bypass

Predict trajectory

	Weight (kg)	Height (cm)	Age (years)	Smoker	Type 2 diabetes	Diabetes duration (years)	Type of intervention
Current prediction	120	170	65	Yes	Diabetes	10	Gastric Bypass

Weight



Prediction of weight trajectory after surgery

Conclusions

- The future of obesity care will include
  - Chronic treatment aimed at health gain not weight loss
  - Recognising the biological basis for the disease
  - Needing more and different treatments for the subtypes of the disease
  - Not blaming our patients for their disease or if they don’t respond


METABOLIC
MEDICINE
HEROES