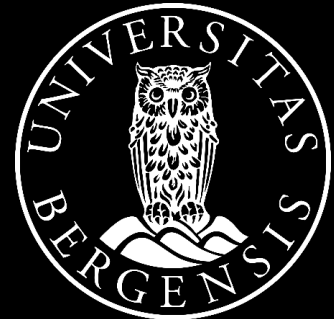


Biomarkers of one-carbon metabolism and B-vitamin status

Targeted metabolomics in rats and humans
exploring the effects of PPAR α -activation and
dietary composition



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PhD defence, 04.10.2019
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Many thanks to

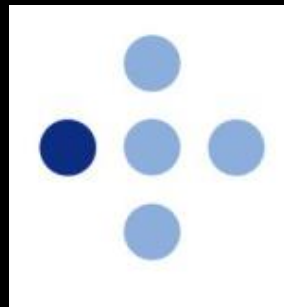
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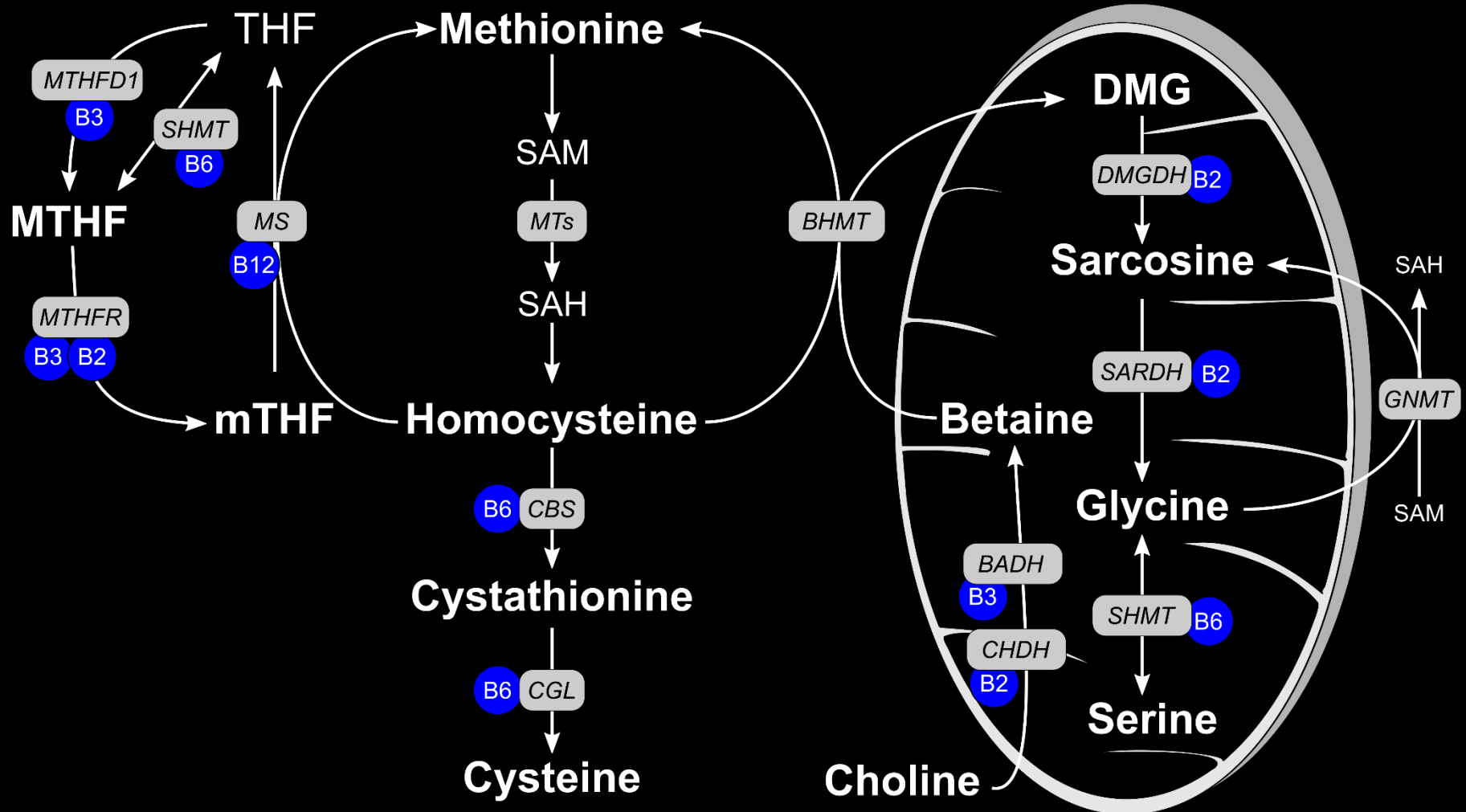
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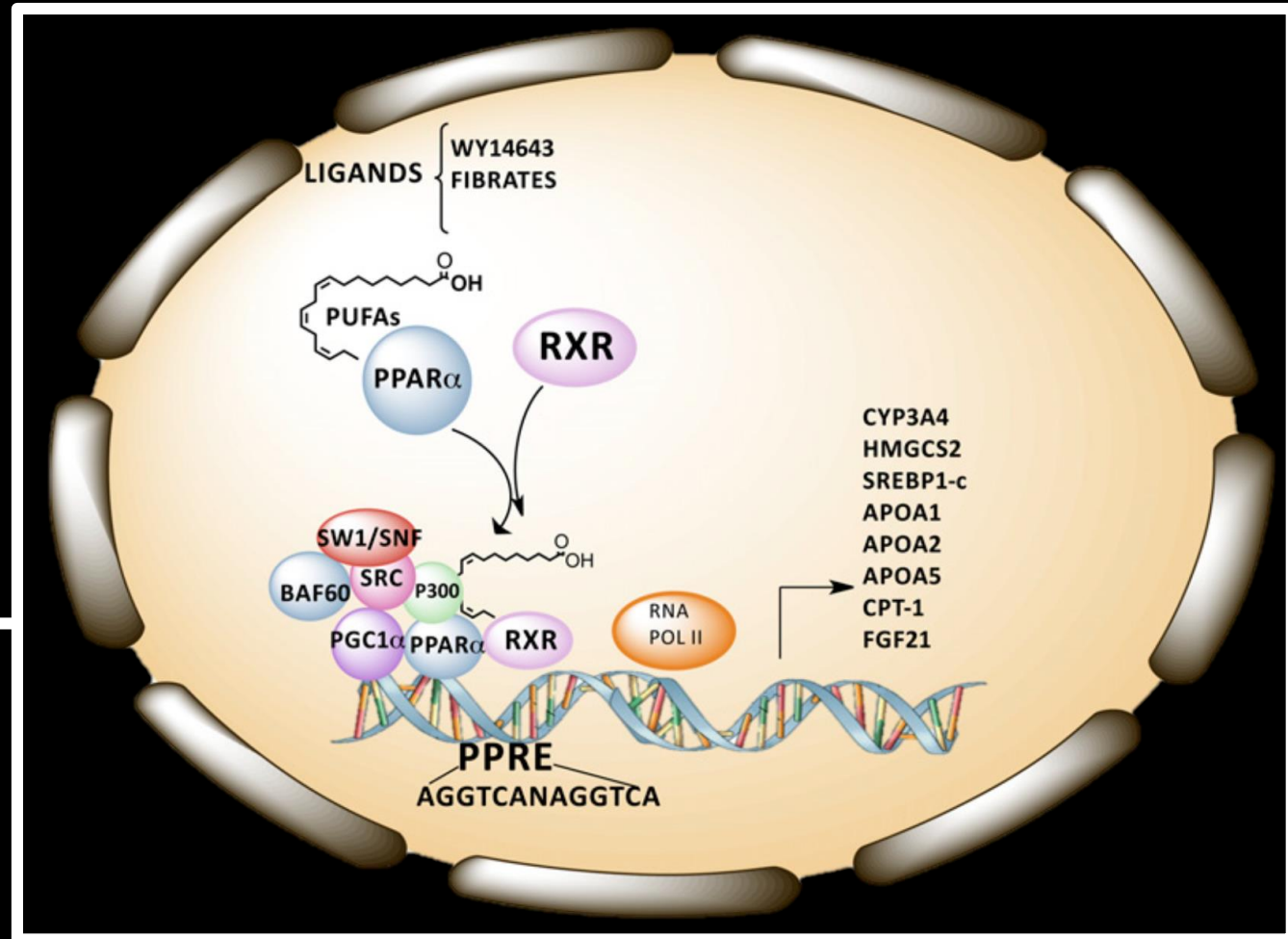
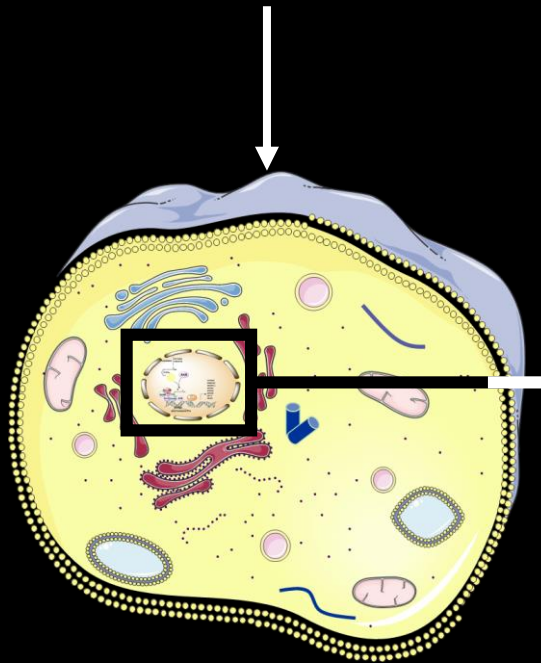
One-carbon metabolism



PPAR α

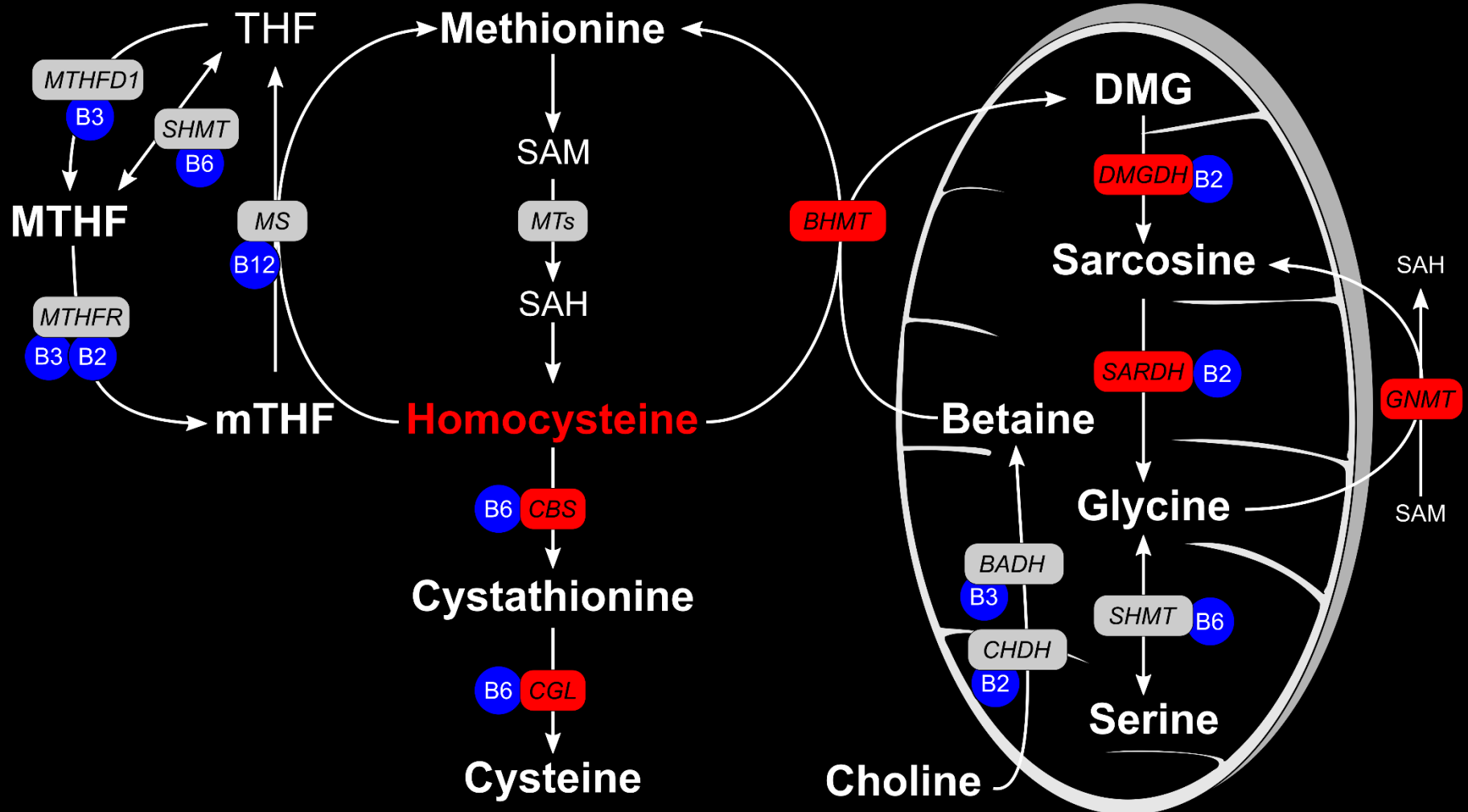
Fibrates

Fatty acids
(PUFA > MUFA > SFA)



Adapted from Contreras (2013)

PPAR α and one-carbon metabolism



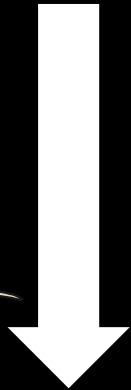
Aim of thesis

Paper I
Paper II

PPAR α -
activation

Dietary
composition

Paper III



??



One-carbon metabolites and B-vitamins

Papers

- I. Peroxisome Proliferator-Activated Receptor Activation is Associated with Altered Plasma One-Carbon Metabolites and B-Vitamin Status in Rats. Nutrients. 2016;8(1)**
- II. PPAR α activation influences plasma one-carbon metabolites and B-vitamin status in rats. Manuscript submitted to Plos One**
- III. Dietary macronutrient composition and plasma concentration of one-carbon metabolites and markers of B-vitamin status. A cross-sectional study. Manuscript submitted to J Nutr**



Animal studies

Paper I

20 male Wistar rats

Control
(n = 10)

TTA
(n = 10)

50 weeks

High fat

Non-fasting

Independent t-test

SMD (95% CI)

Duration

Diet

Sacrifice

Statistics

Results

Paper II

20 male Wistar rats

Control
(n = 8)

PPAR α
(n = 6)

PPAR γ
(n = 6)

12 days

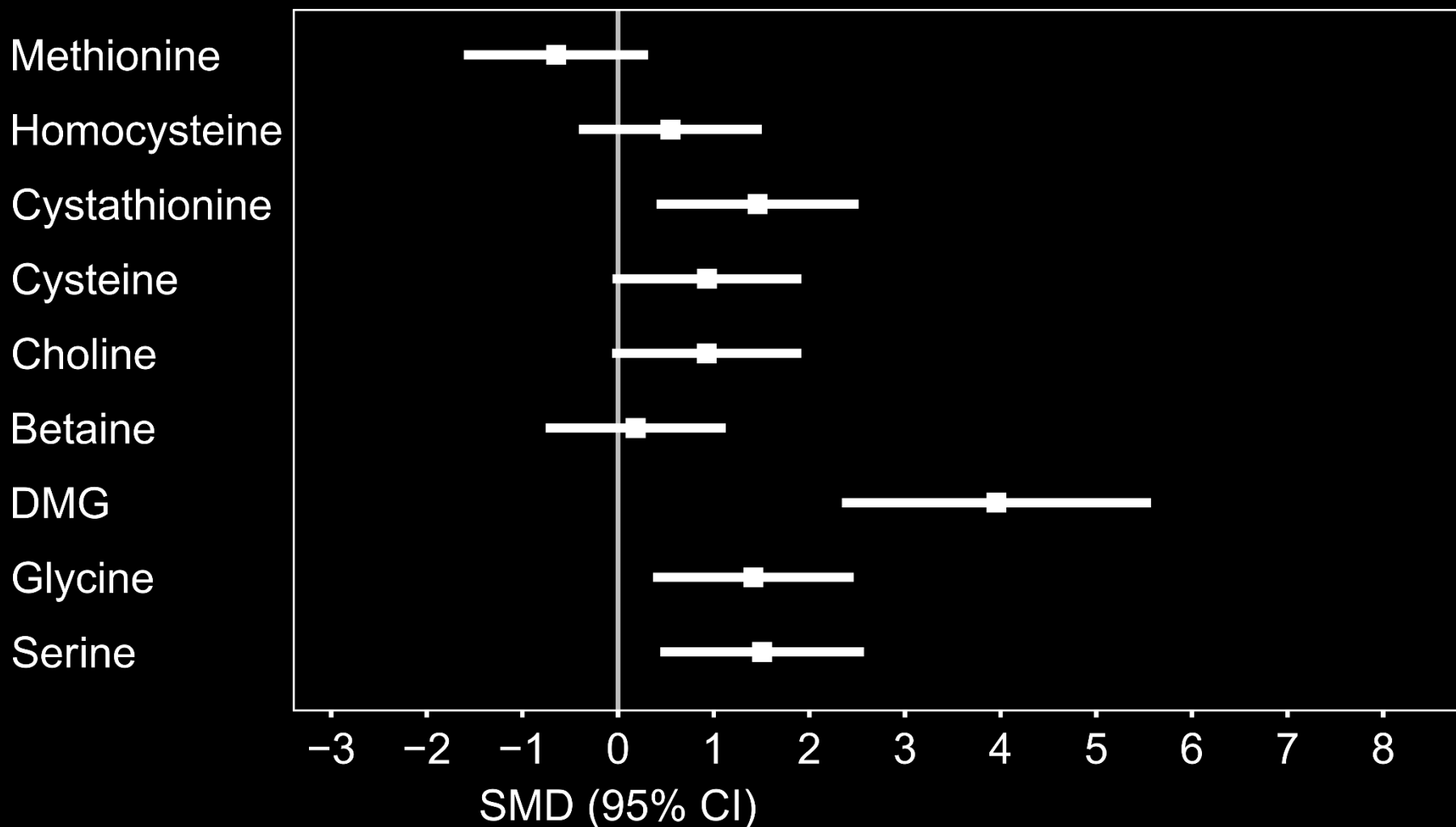
Low fat

Fasting

One-way ANOVA and planned
contrasts towards control

SMD (95% CI)

TTA and one-carbon metabolites



TTA and B-vitamins

Riboflavin

FMN

NAM

mNAM

PL

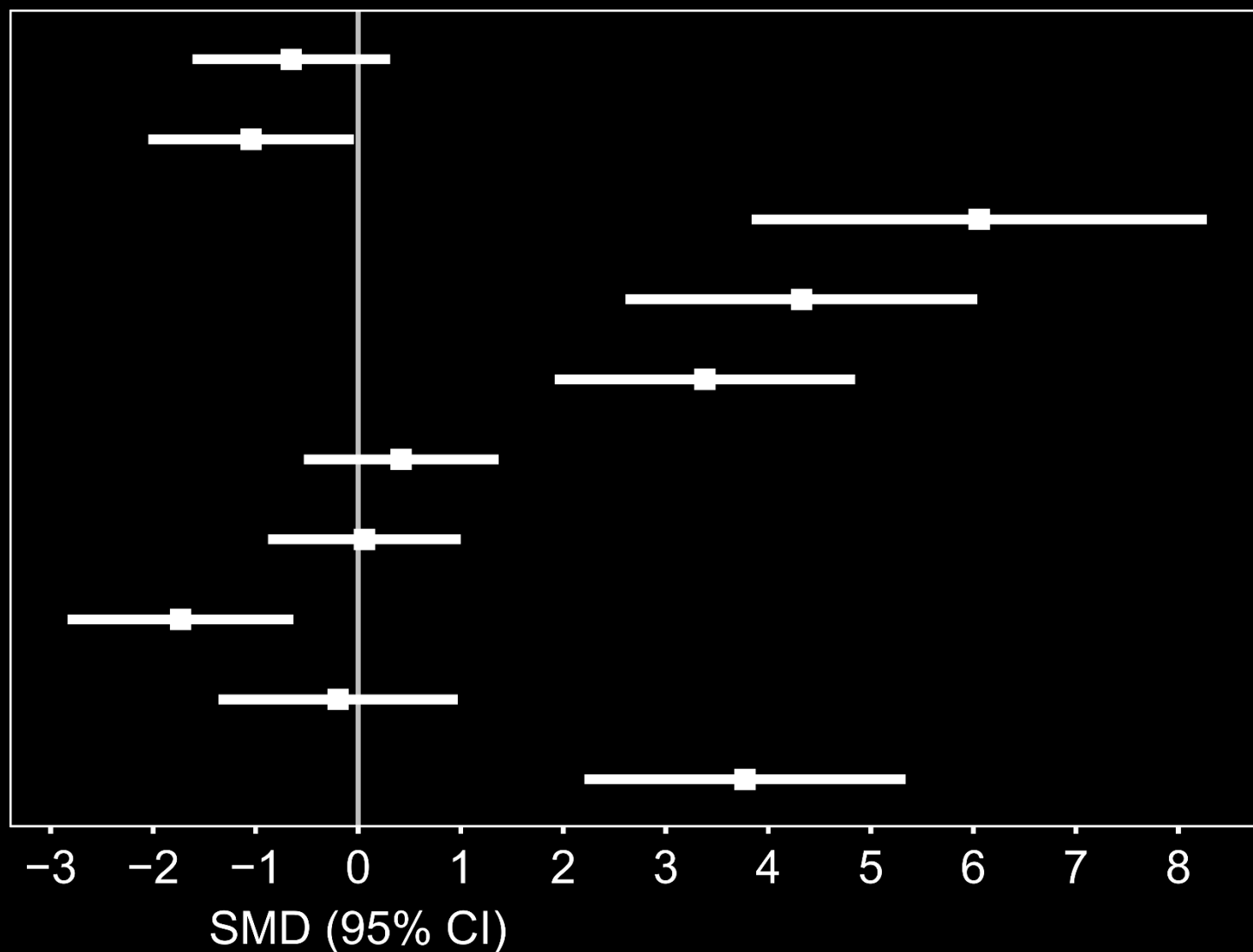
PLP

PA

Folate

Cobalamin

MMA



Summary so far

Strongest effects of TTA-treatment:

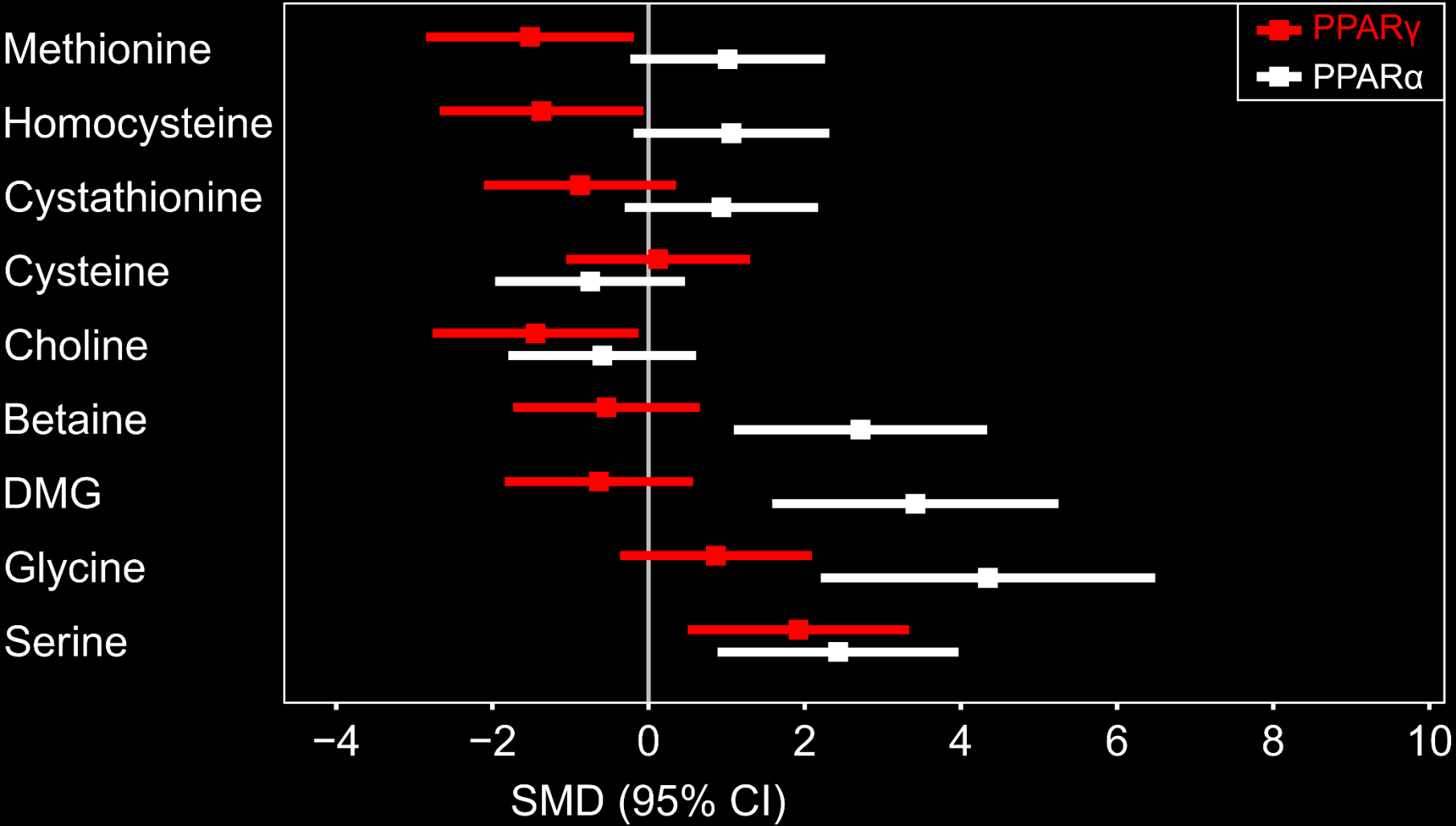
↑ NAM, mNAM, PL, MMA and DMG

↓ FMN and folate

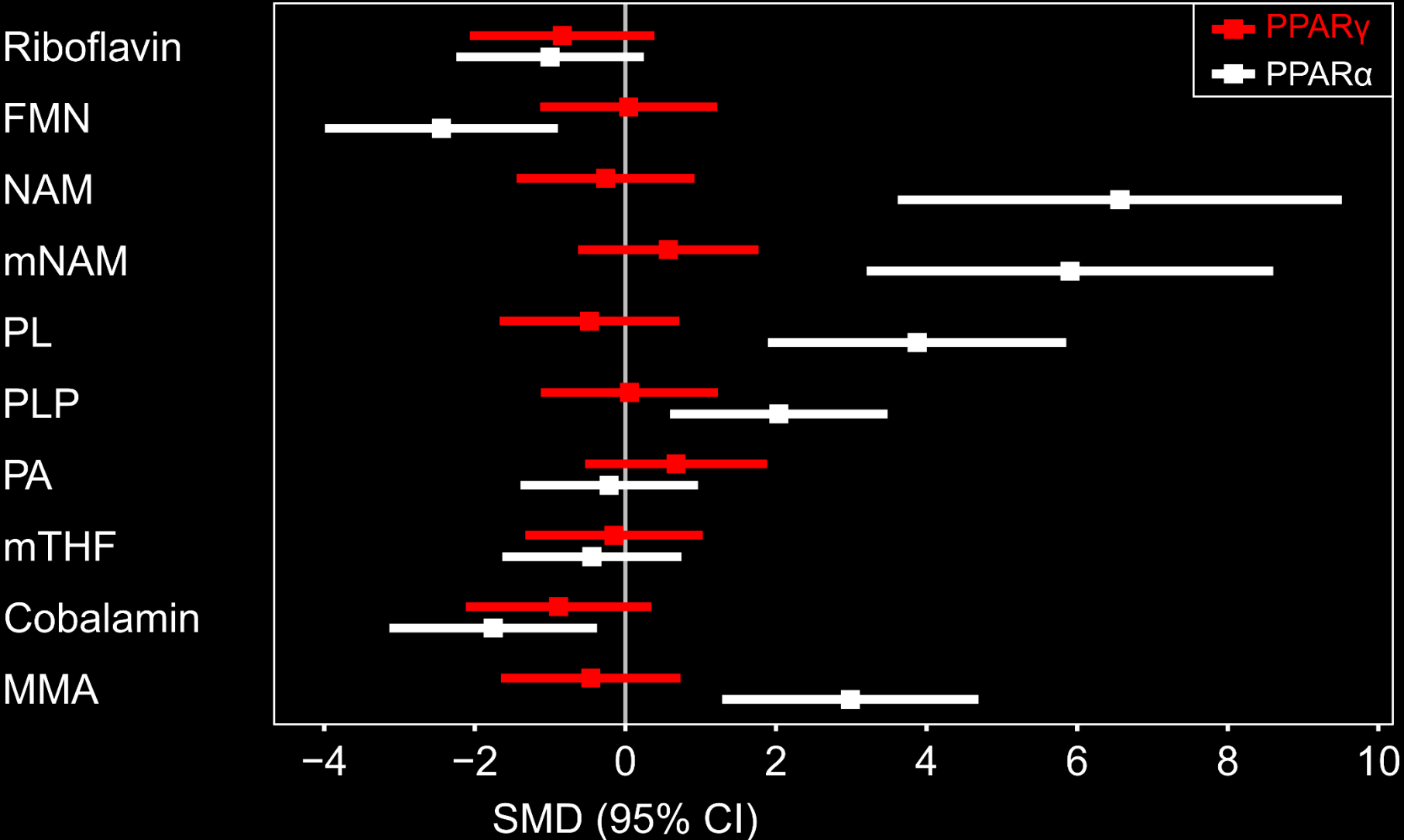
Open questions

- Is this reflecting PPAR α -activation?
- Are other PPARs involved?
- Are there PPAR-independent effects of TTA?

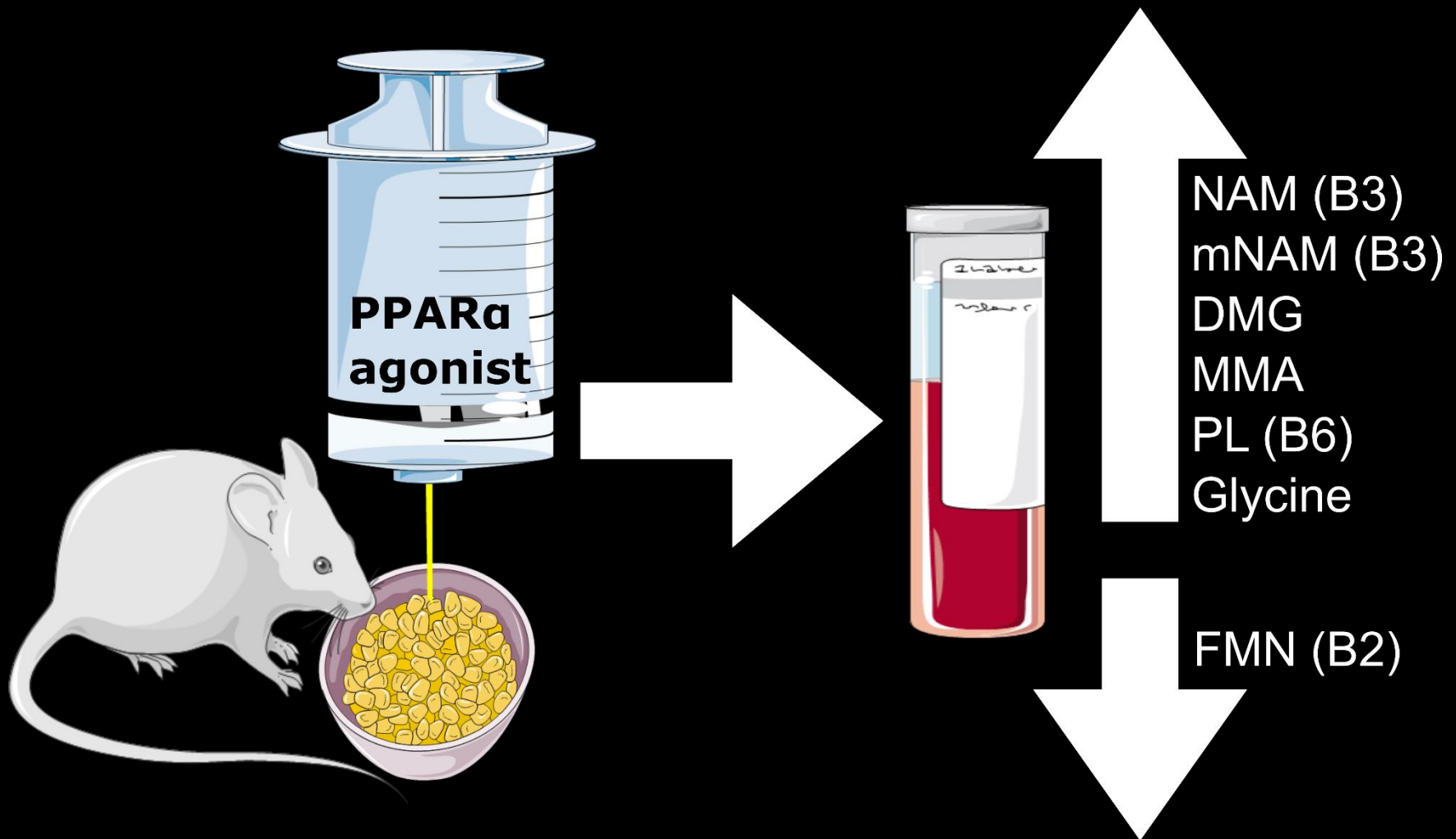
PPARs and one-carbon metabolites



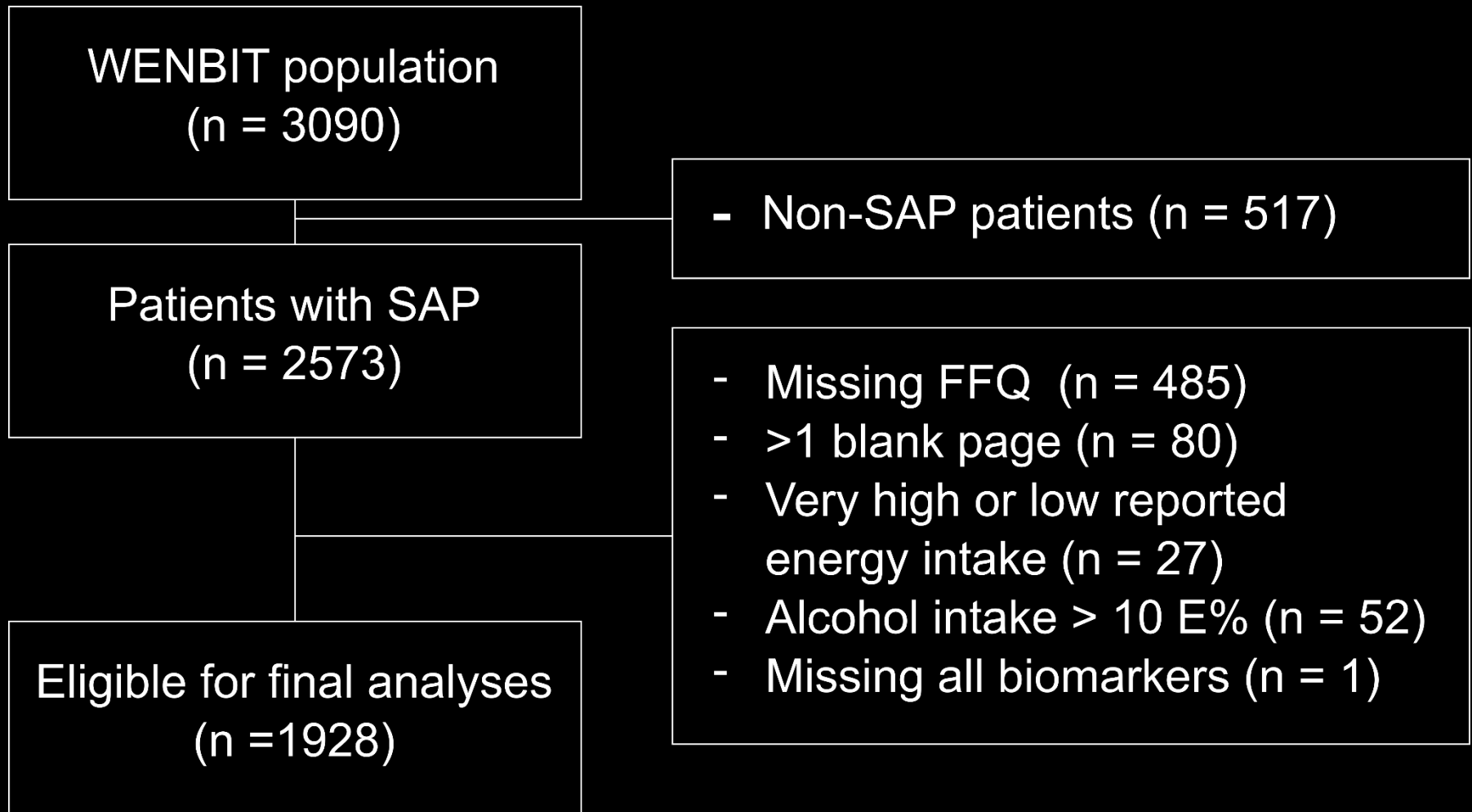
PPARs and B-vitamins



Findings from animal studies



Human study

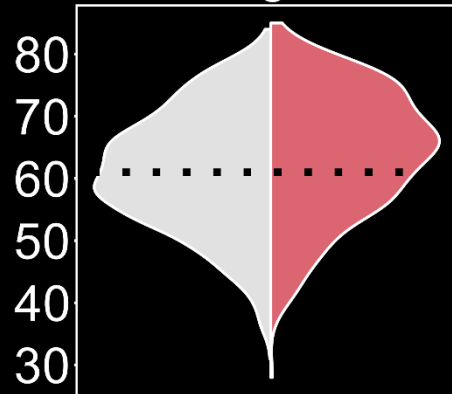


Cohort characteristics

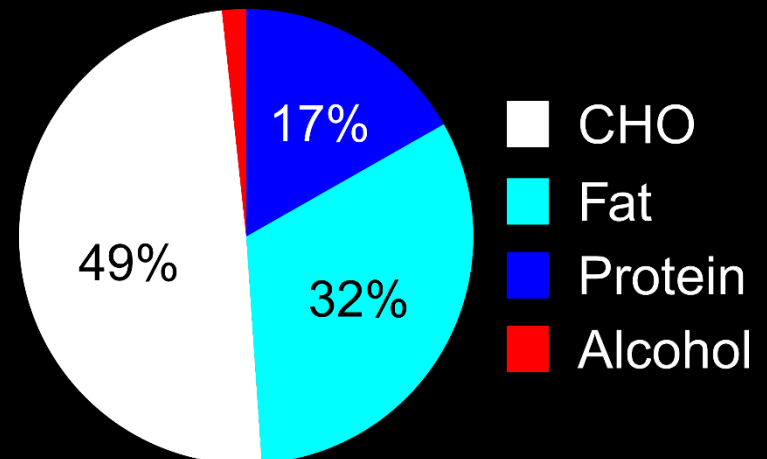
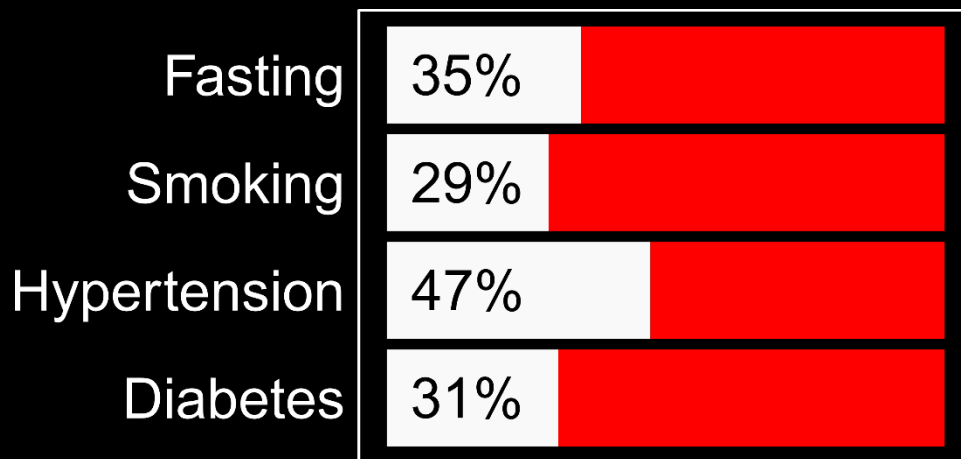
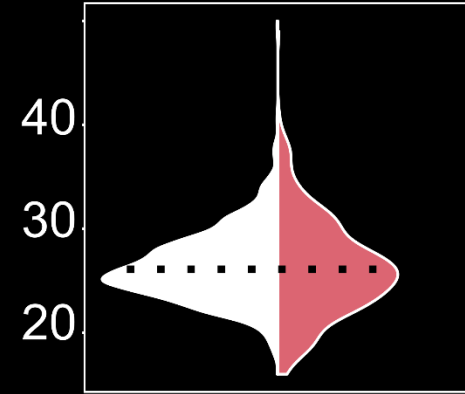
N = 1928



Age



BMI



Aims

Macronutrient intake

- Carbohydrate
- Fat
- Protein

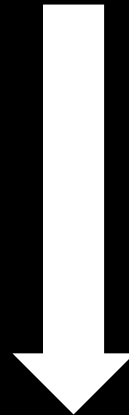


?

Dietary substitutions

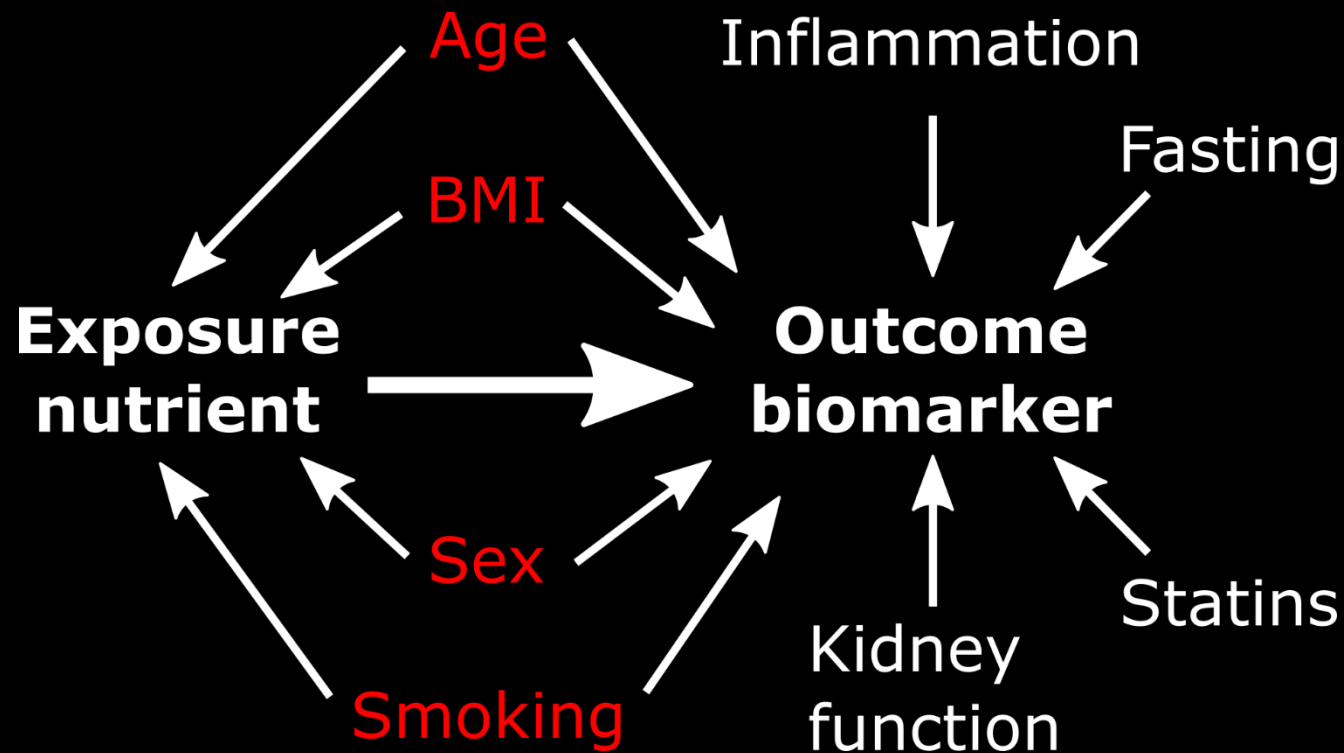
Between:

- Macronutrients
- Fatty acid classes



One-carbon metabolites and B-vitamins

Linear regression models



Final model also adjusted for reported **total energy** and **alcohol** intake.

Main findings

Protein, but not carbohydrate or fat, intake was associated with several biomarkers

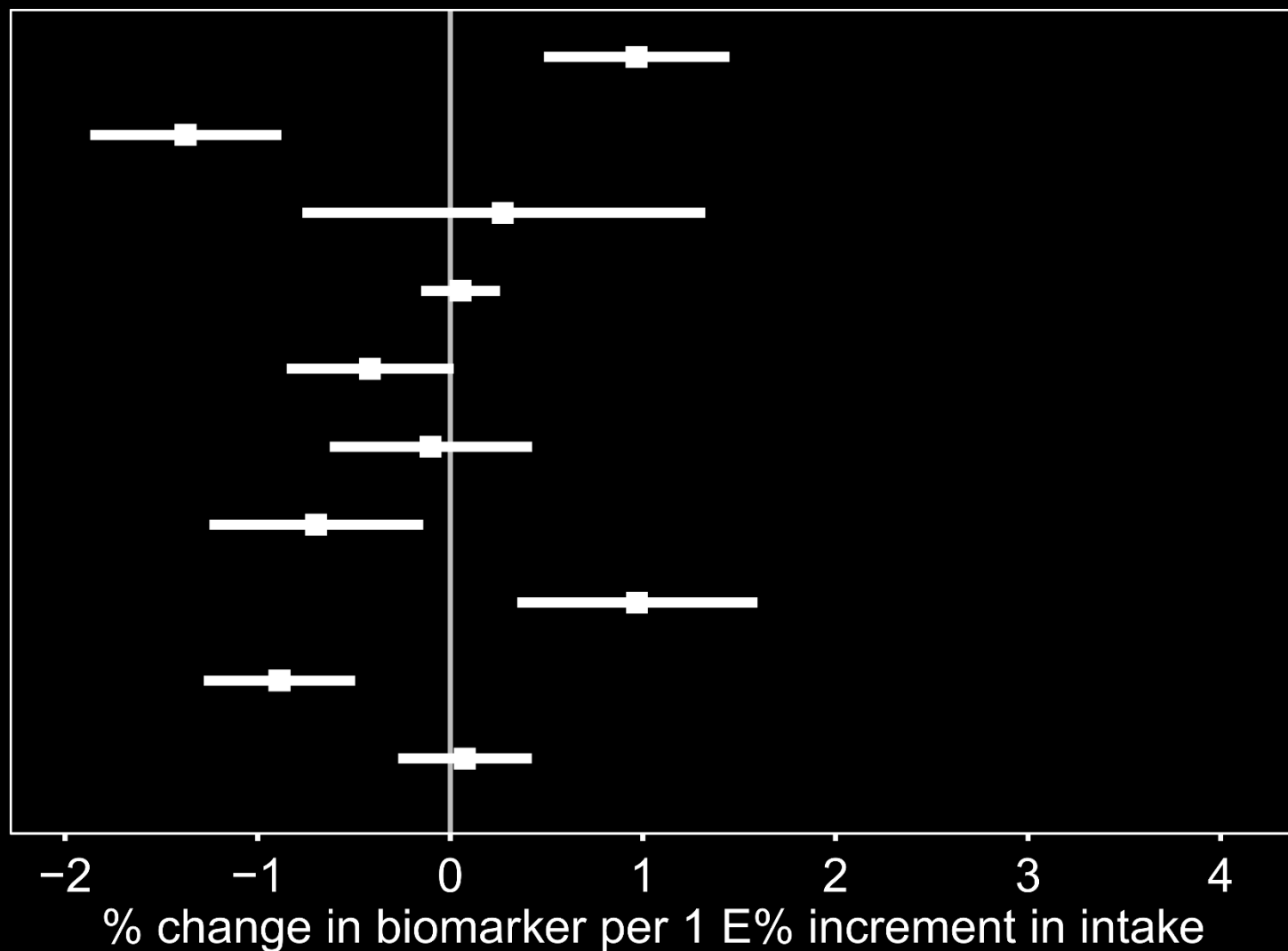
The same patterns were seen whether protein replaced carbohydrate or fat

Dietary fat composition appeared to influence several biomarkers

- PUFA replacing SFA

Protein and one-carbon metabolites

Methionine
Homocysteine
Cystathionine
Cysteine
Choline
Betaine
DMG
Sarcosine
Glycine
Serine



Protein and B-vitamins

Riboflavin

NAM

mNAM

PL

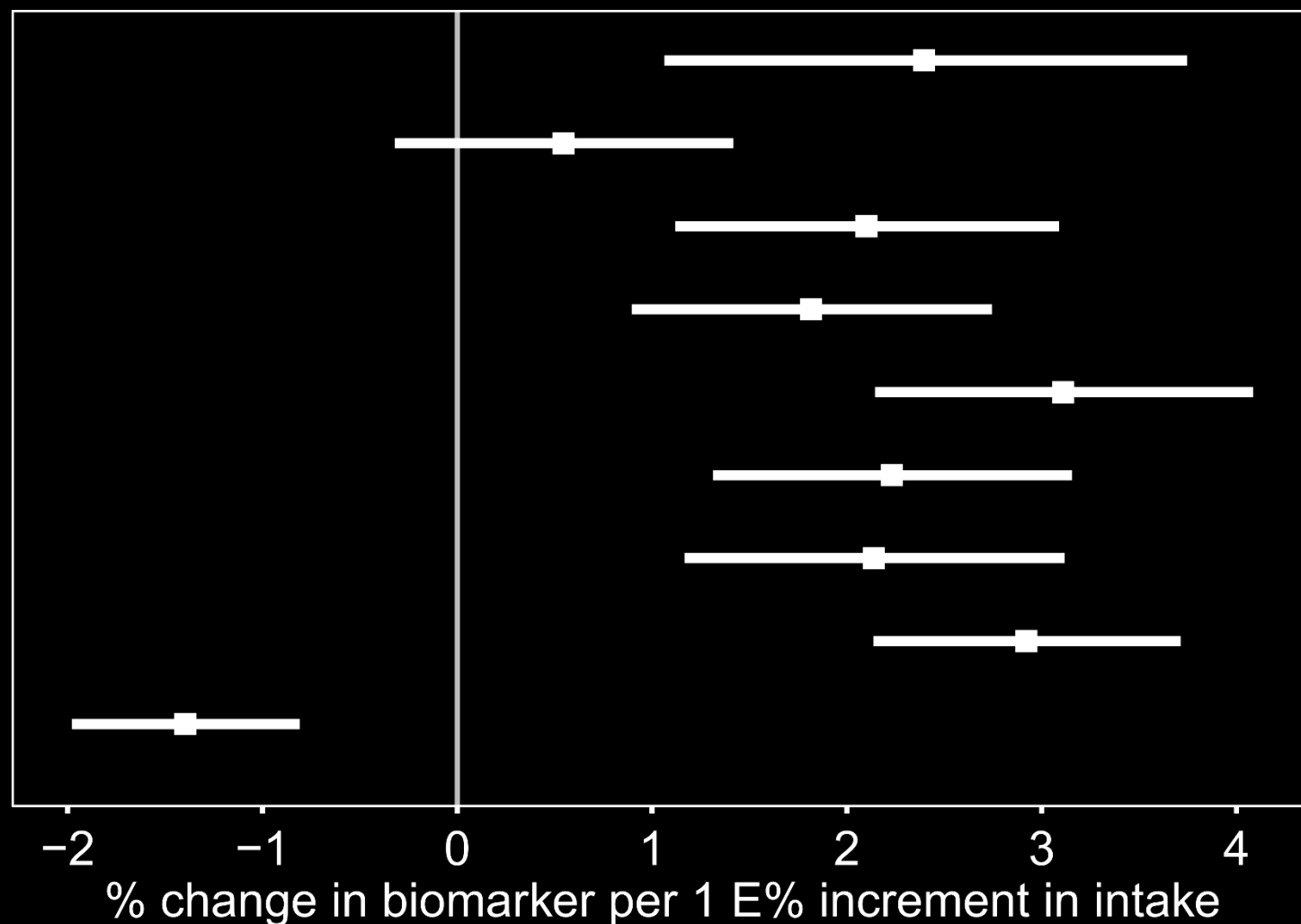
PLP

PA

Folate

Cobalamin

MMA

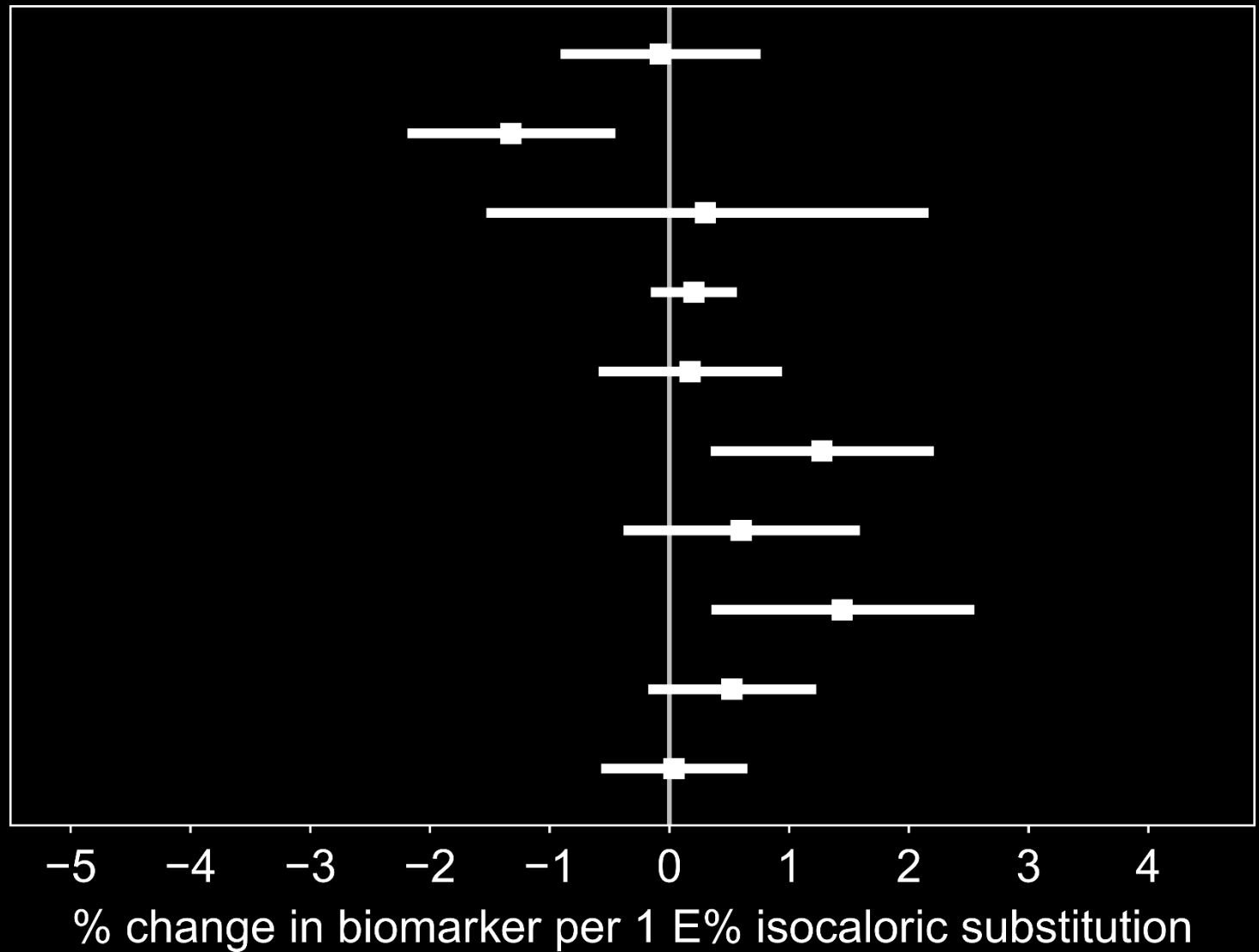


Protein and food profile



PUFA ↑ SFA ↓

Methionine
Homocysteine
Cystathionine
Cysteine
Choline
Betaine
DMG
Sarcosine
Glycine
Serine



PUFA ↑ SFA ↓

Riboflavin

NAM

mNAM

PL

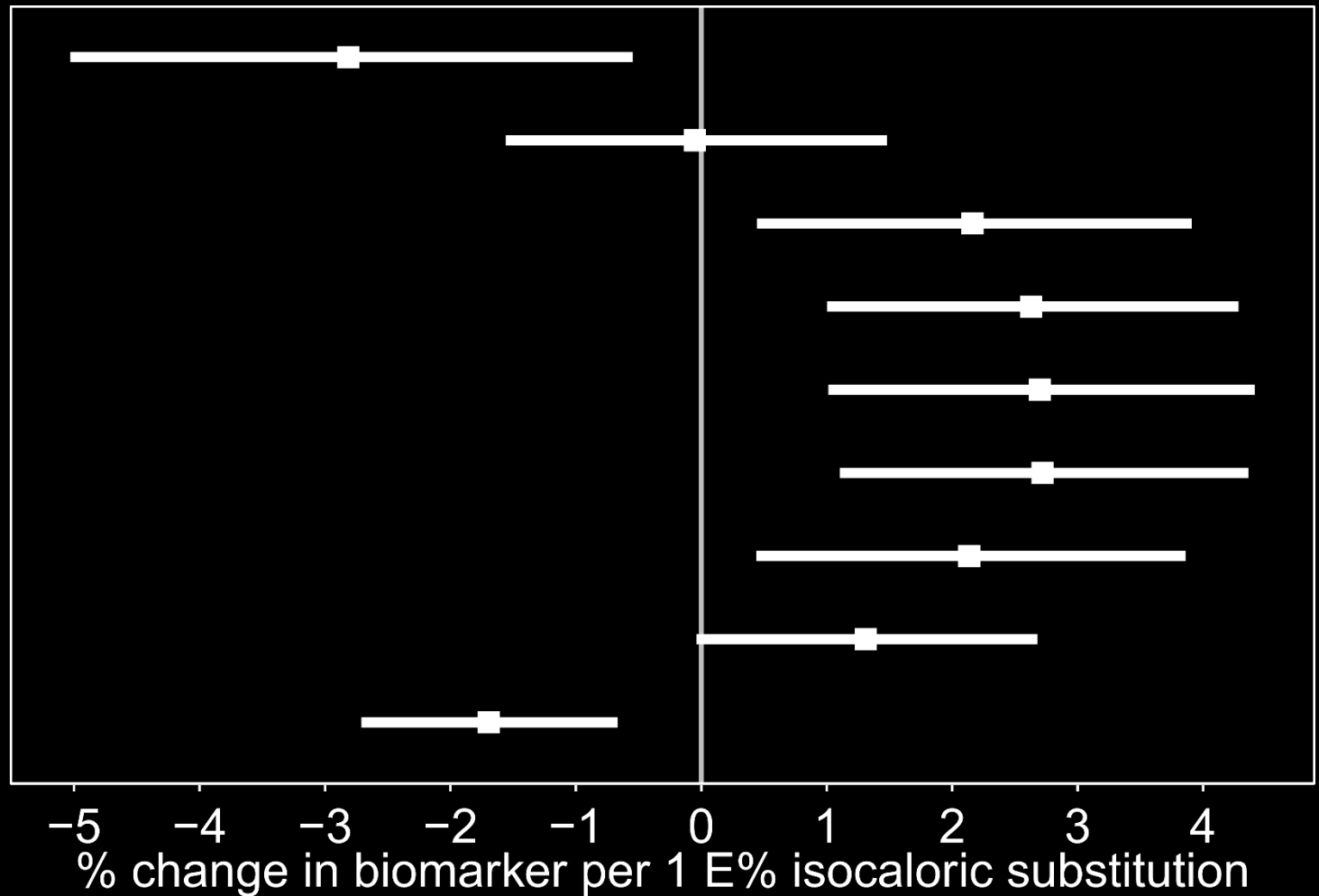
PLP


PA

Folate

Cobalamin

MMA





PPAR α -activation and dietary composition influences the one-carbon metabolome

PPAR α -activation \Rightarrow Consistent and strong effect on many biomarkers

- Potential biomarkers of PPAR α -activity

Protein \Rightarrow Most B-vitamins higher

Substituting PUFA for SFA \Rightarrow Similar metabolic profile to PPAR α -activation