

# Biomarkers of one-carbon metabolism and B-vitamin status

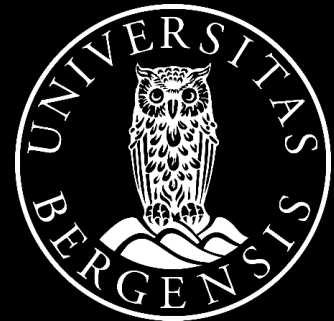
Targeted metabolomics in rats and humans  
exploring the effects of PPAR $\alpha$ -activation and  
dietary composition



Vegard Lysne

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vegard.lysne@uib.no



# Many thanks to

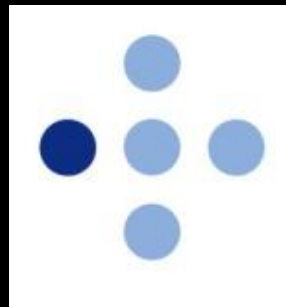
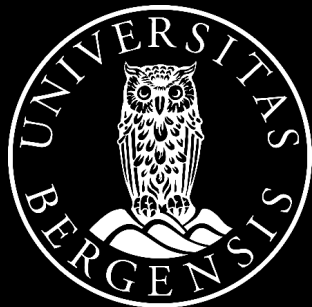
## Supervisors

Ottar Nygård  
Per M Ueland  
Jutta Dierkes  
Elin Strand

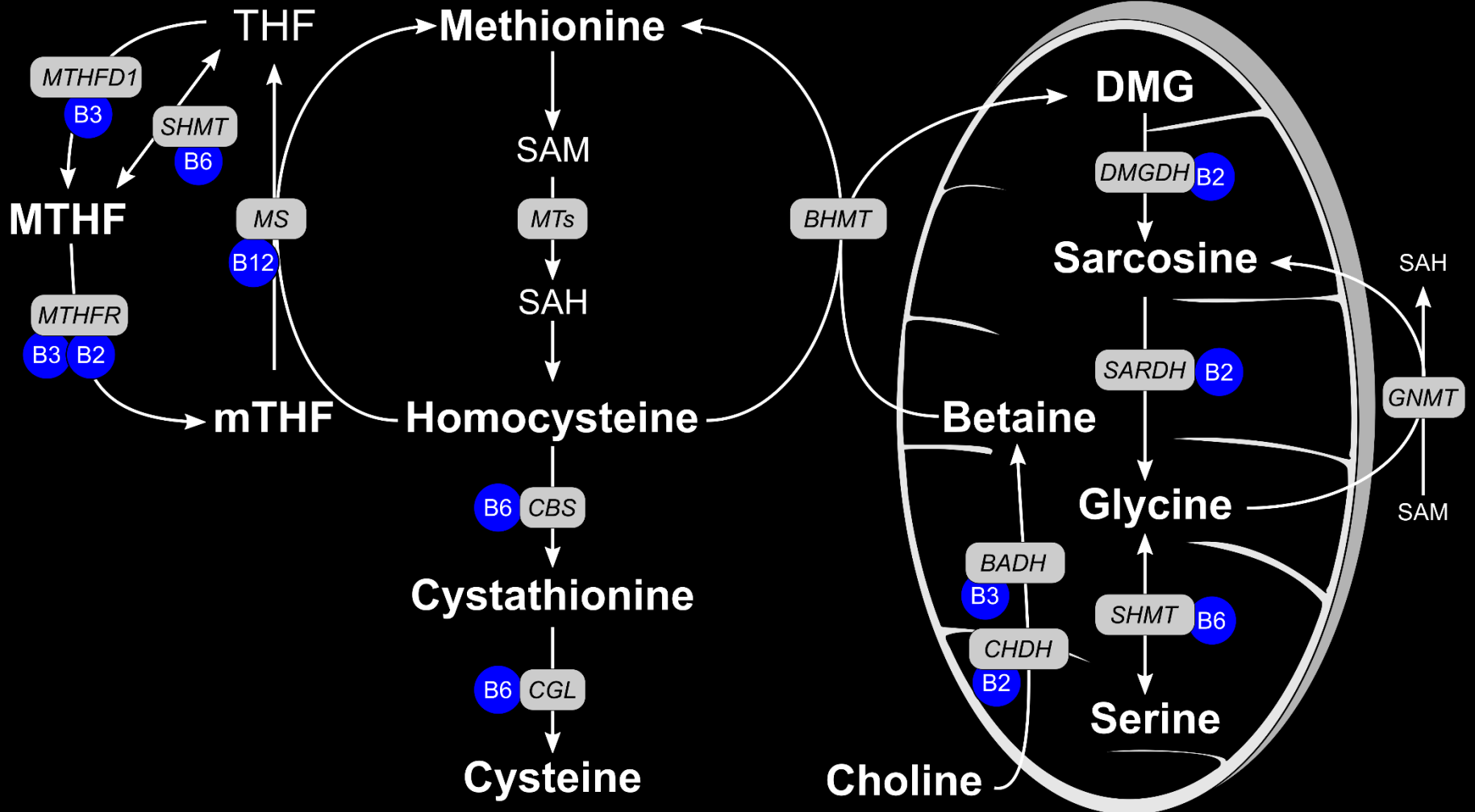
## Coauthors

Anthea Van Parys  
Thomas Olsen  
Gard FT Svingen  
Bodil Bjørndal  
Mari L Grinna  
Ingvild Marienborg  
Johnny Laupsa-Borge

Teresa Haugsgjerd  
Adrian McCann  
Eva R Pedersen  
Øivind Midttun  
Rolf K Berge  
Ellisif Nygaard



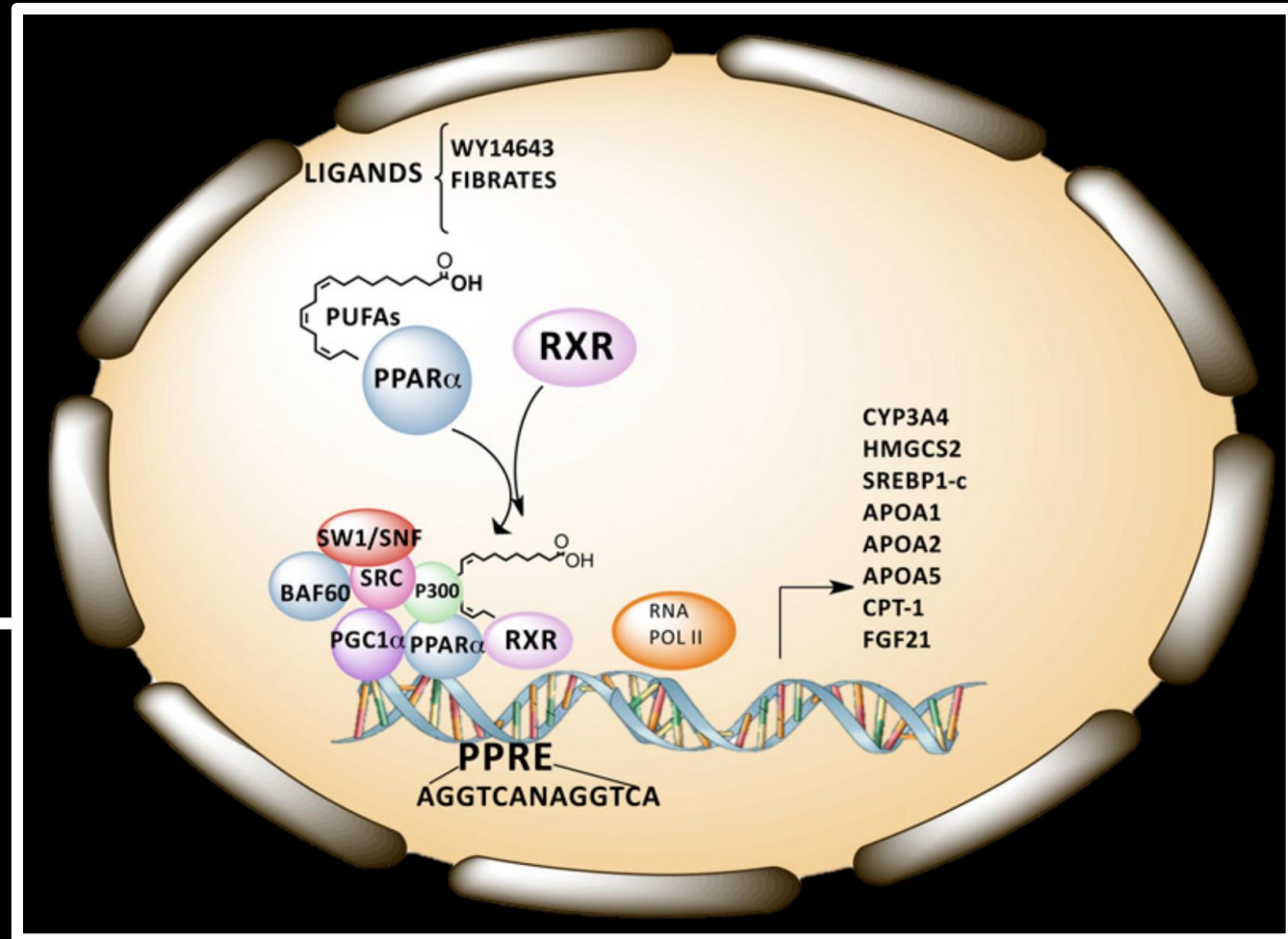
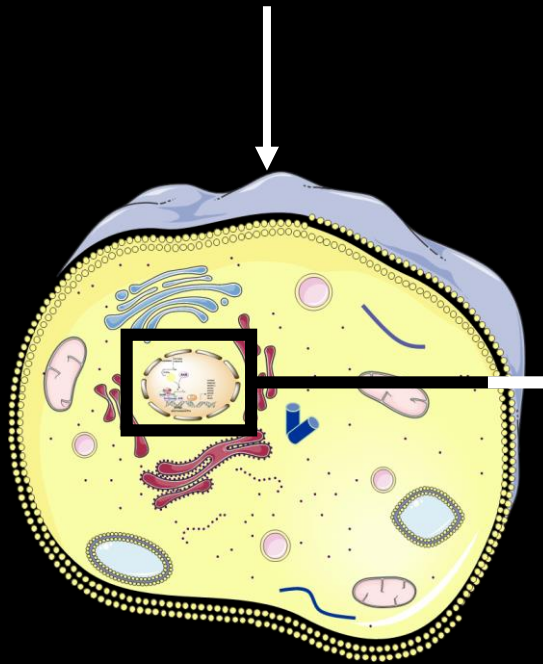
# One-carbon metabolism



# PPAR $\alpha$

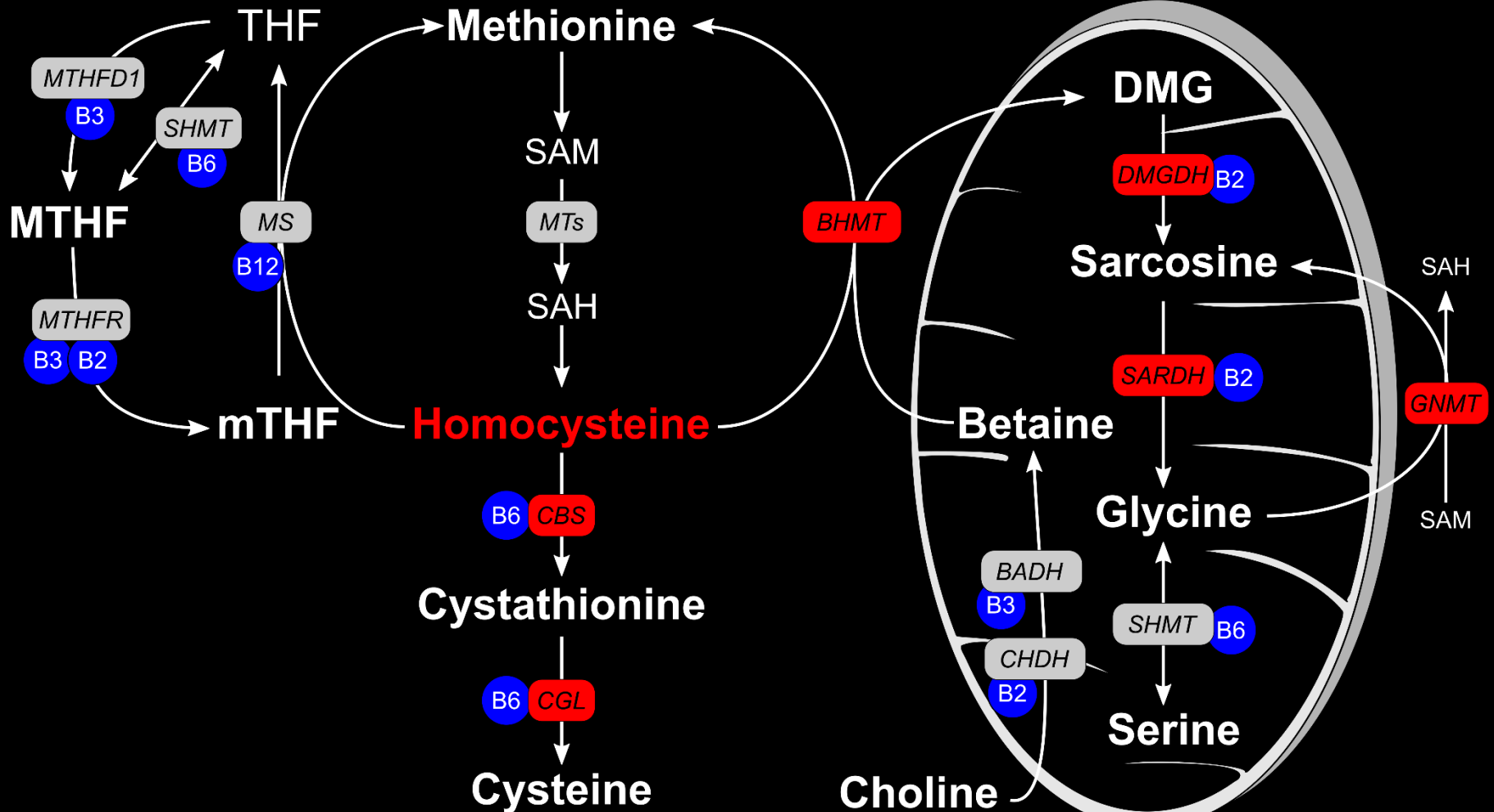
Fibrates

Fatty acids  
(PUFA > MUFA > SFA)



Adapted from Contreras (2013)

# PPAR $\alpha$ and one-carbon metabolism



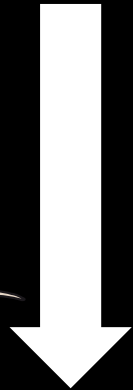
# Aim of thesis

Paper I  
Paper II

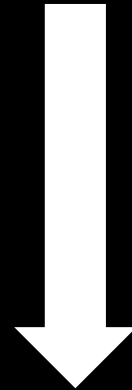
PPAR $\alpha$  -  
activation

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 $\alpha$  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)

## Paper II

20 male Wistar rats

**Control**  
(n = 8)

**PPAR $\alpha$**   
(n = 6)

**PPAR $\gamma$**   
(n = 6)

12 days

Low fat

Fasting

**Duration**

**Diet**

**Sacrifice**

**Statistics**

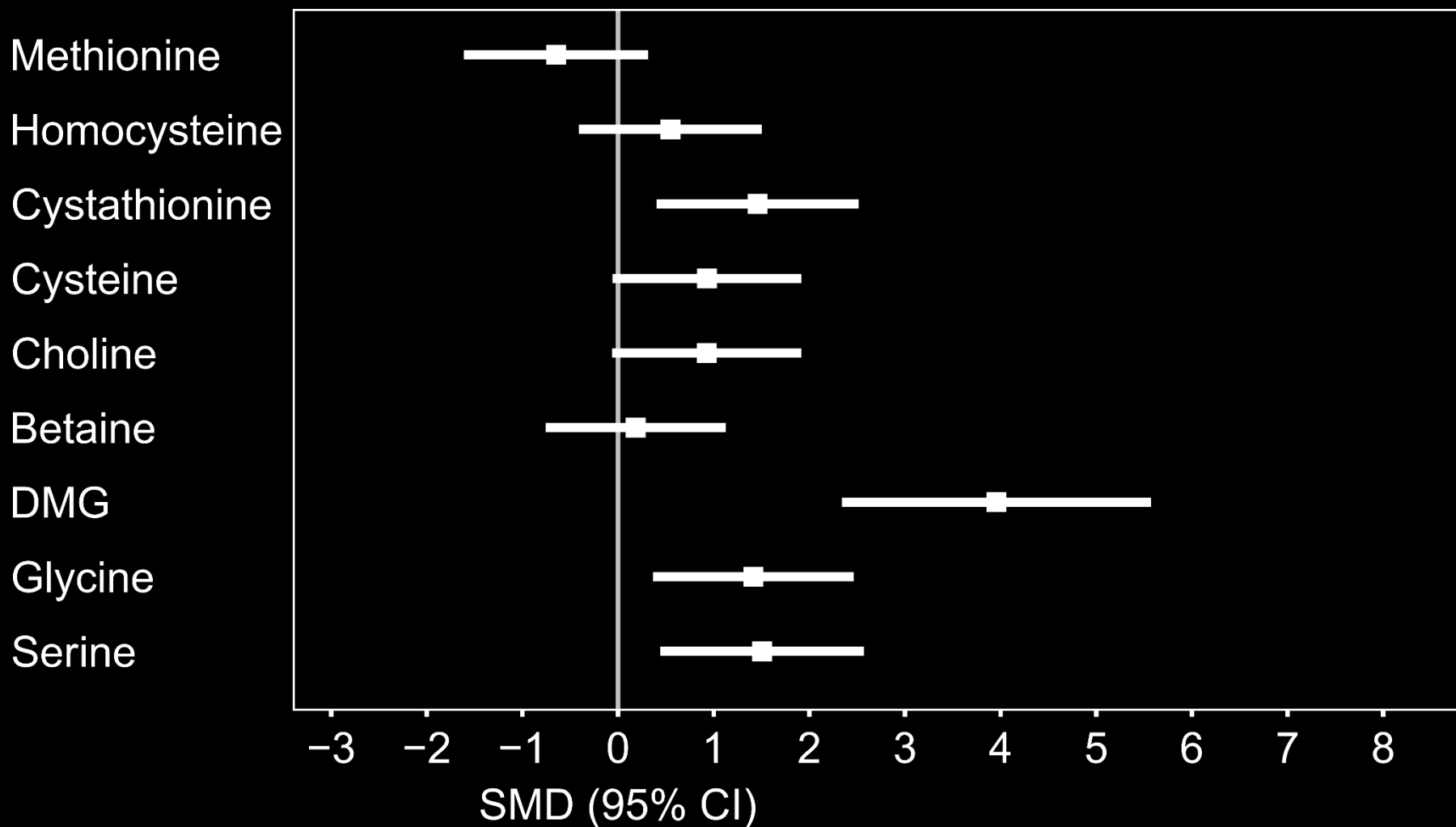
**Results**

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

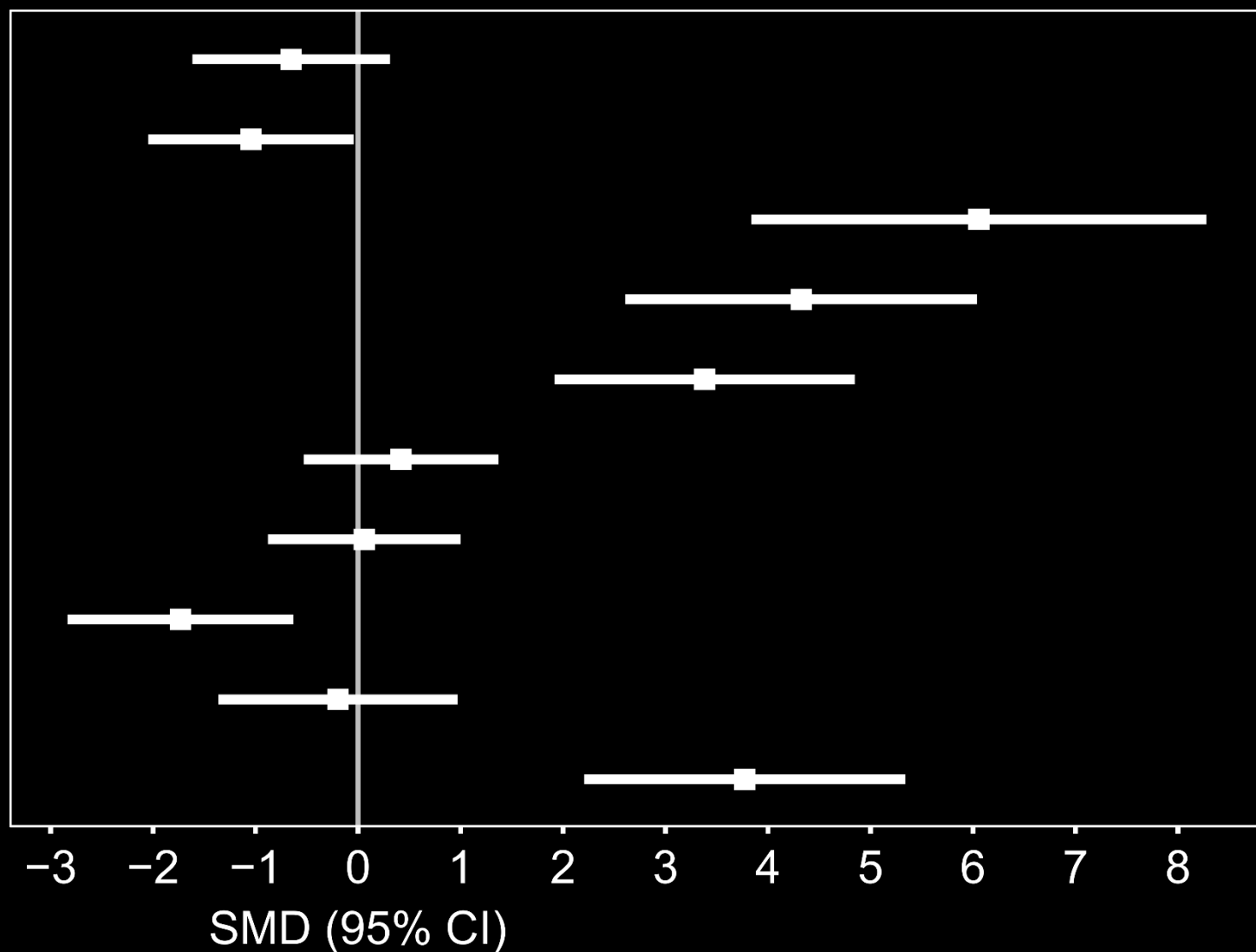
PLP

PA

Folate

Cobalamin

MMA



# Summary so far

Strongest effects of TTA-treatment:

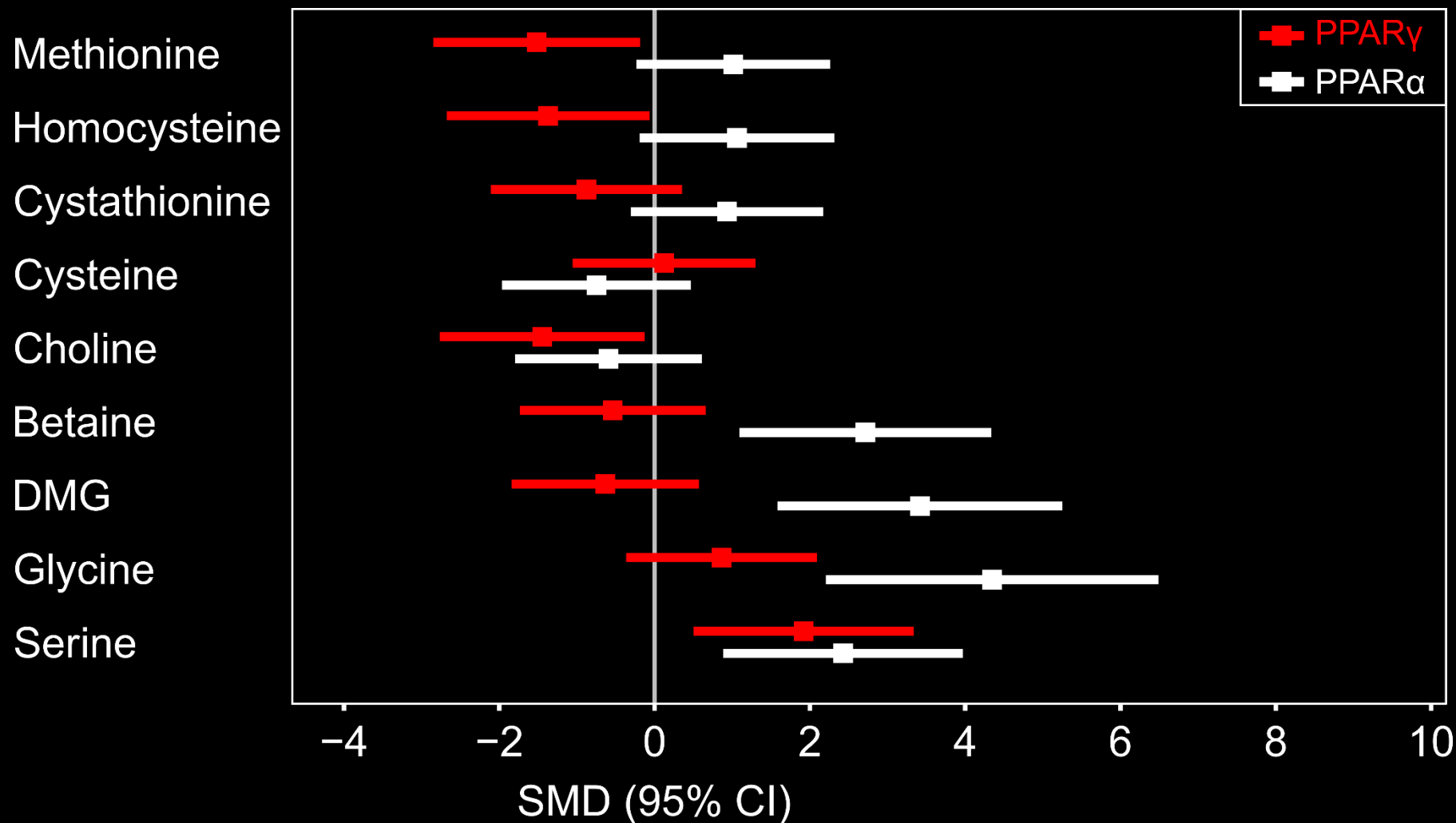
↑ NAM, mNAM, PL, MMA and DMG

↓ FMN and folate

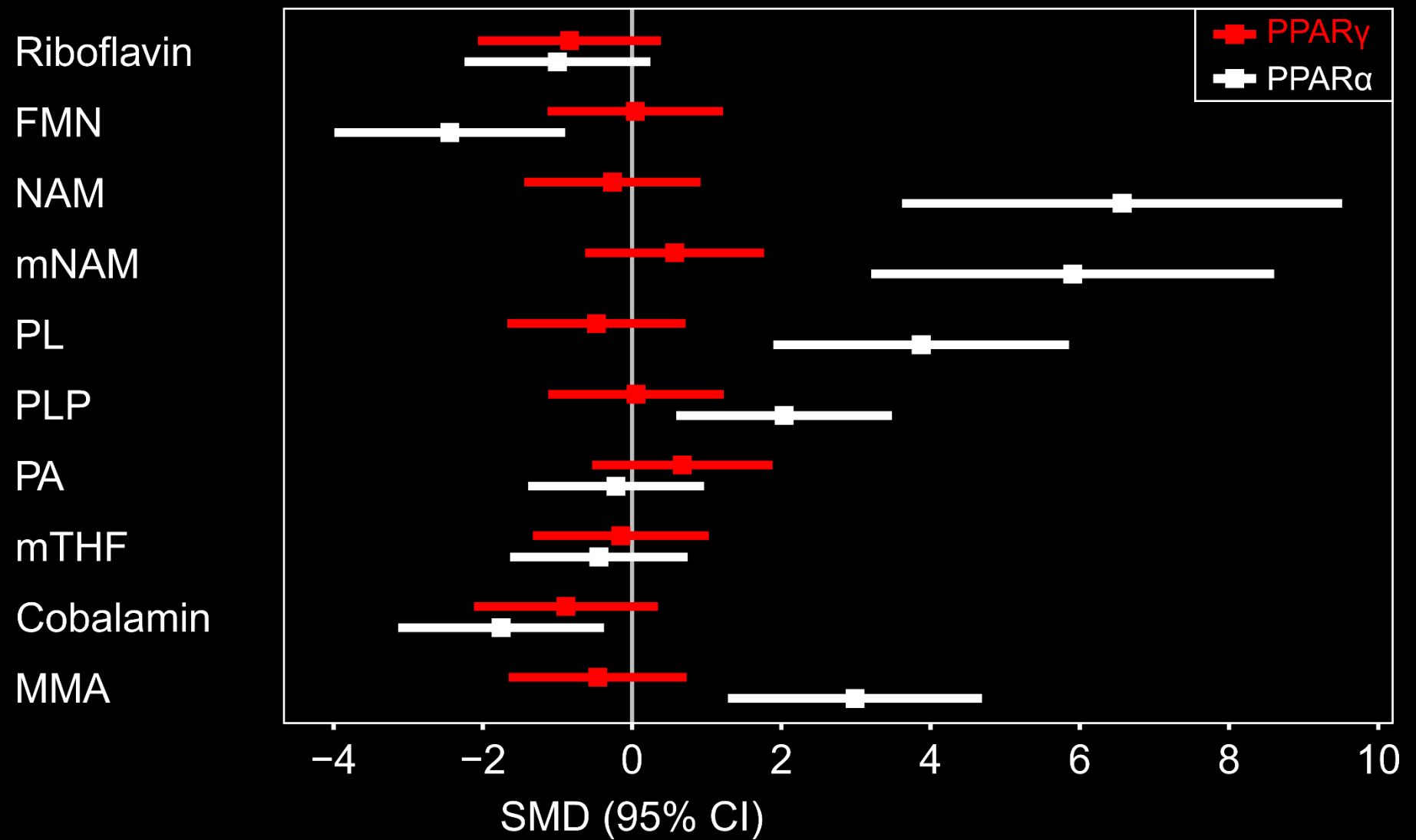
## Open questions

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

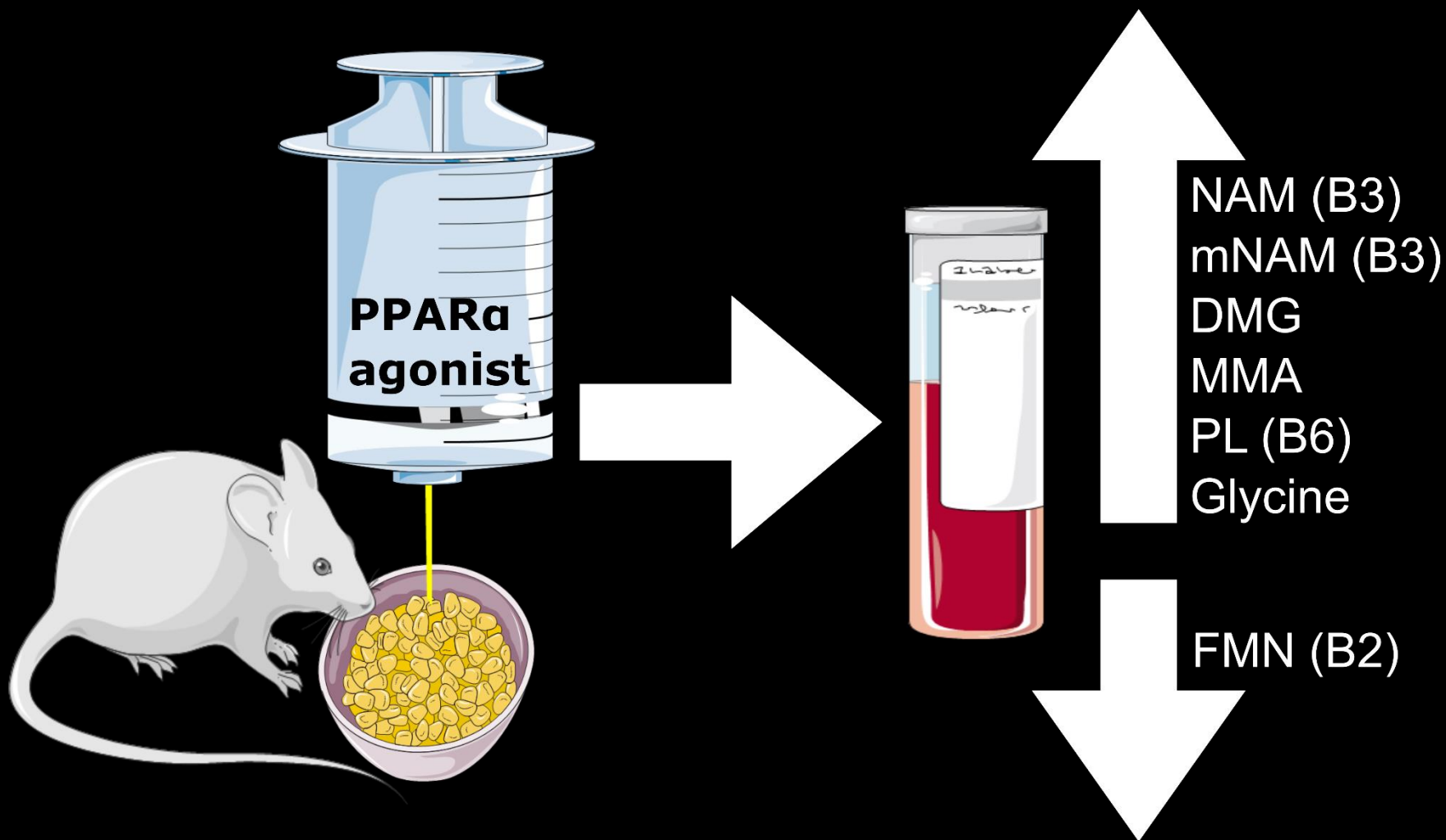
# PPARs and one-carbon metabolites



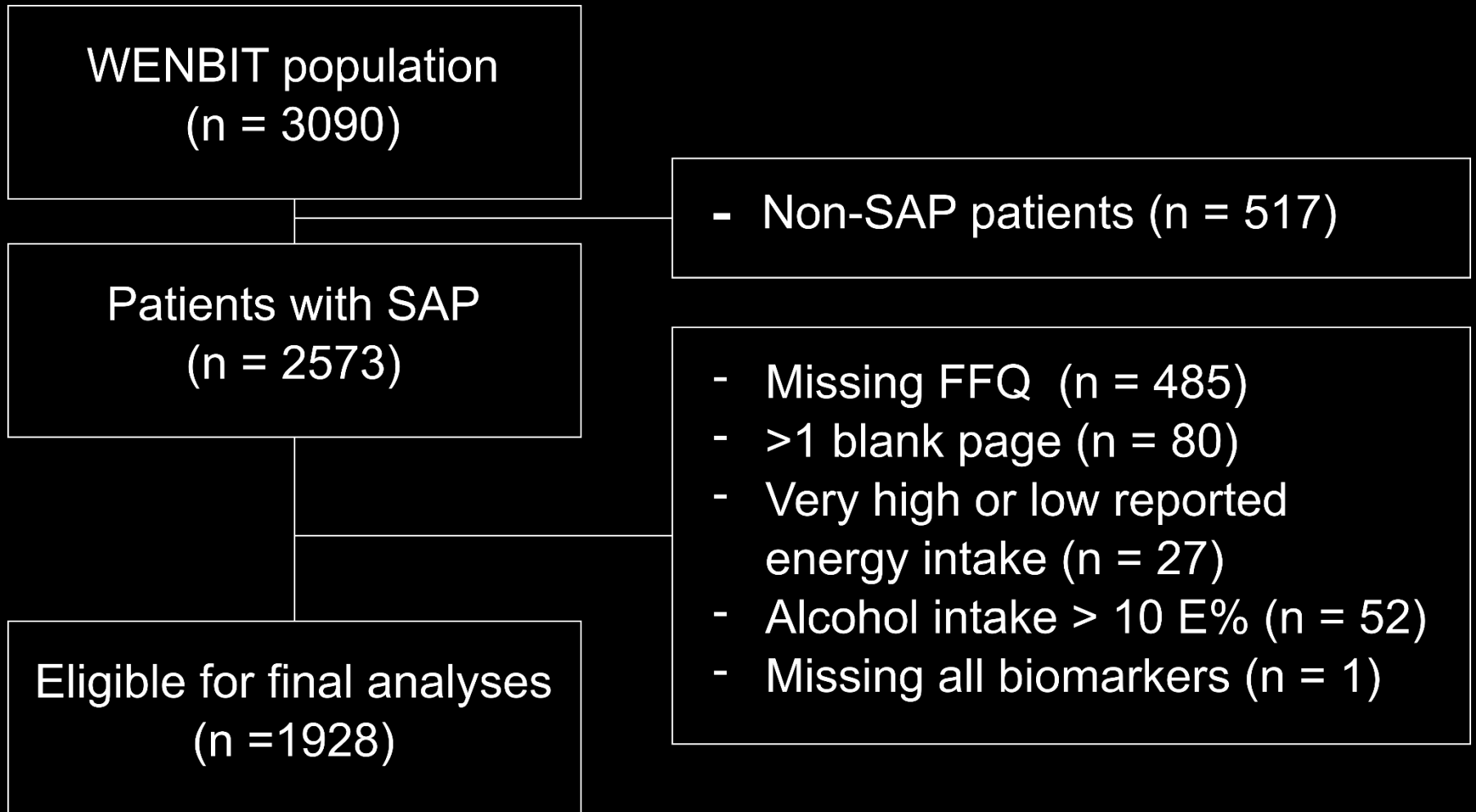
# PPARs and B-vitamins



# Findings from animal studies



# Human study

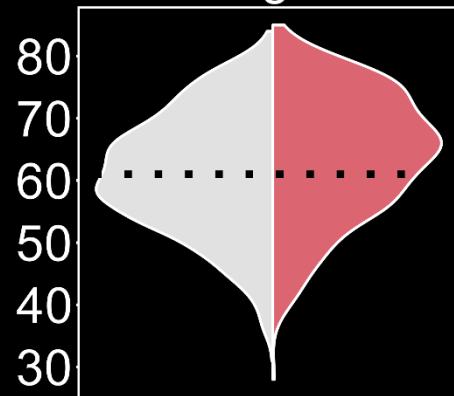


# Cohort characteristics

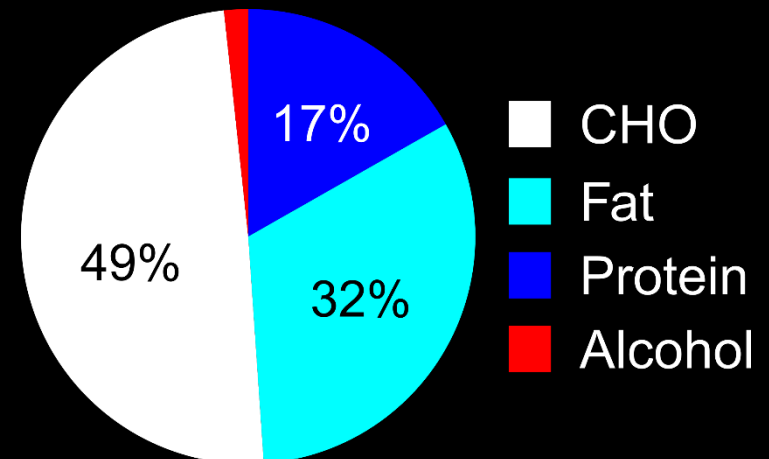
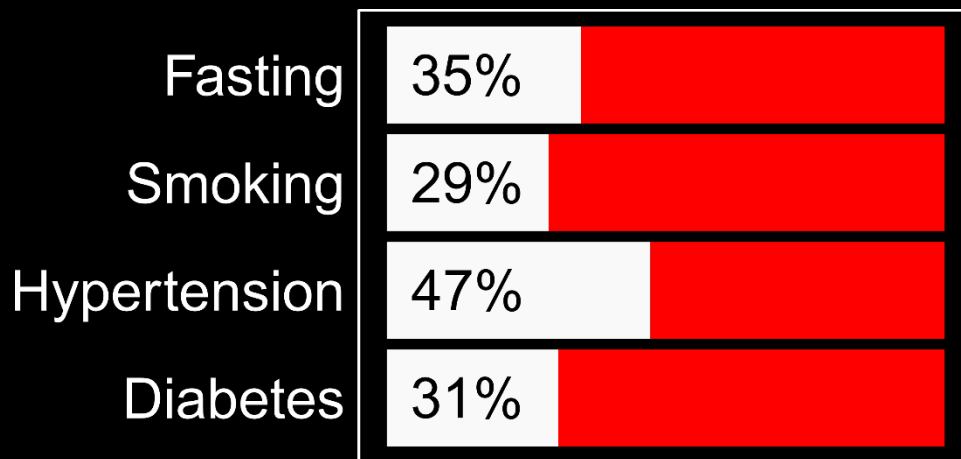
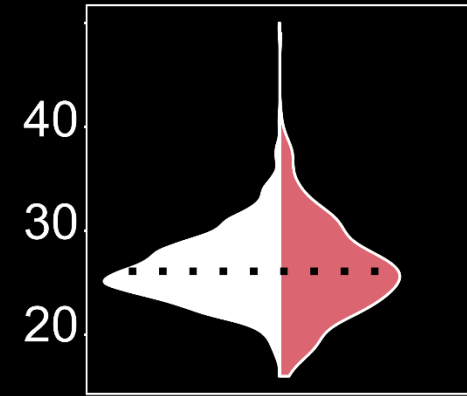
N = 1928



Age



BMI





# Aims

## Macronutrient intake

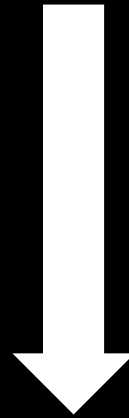
- Carbohydrate
- Fat
- Protein



## Dietary substitutions

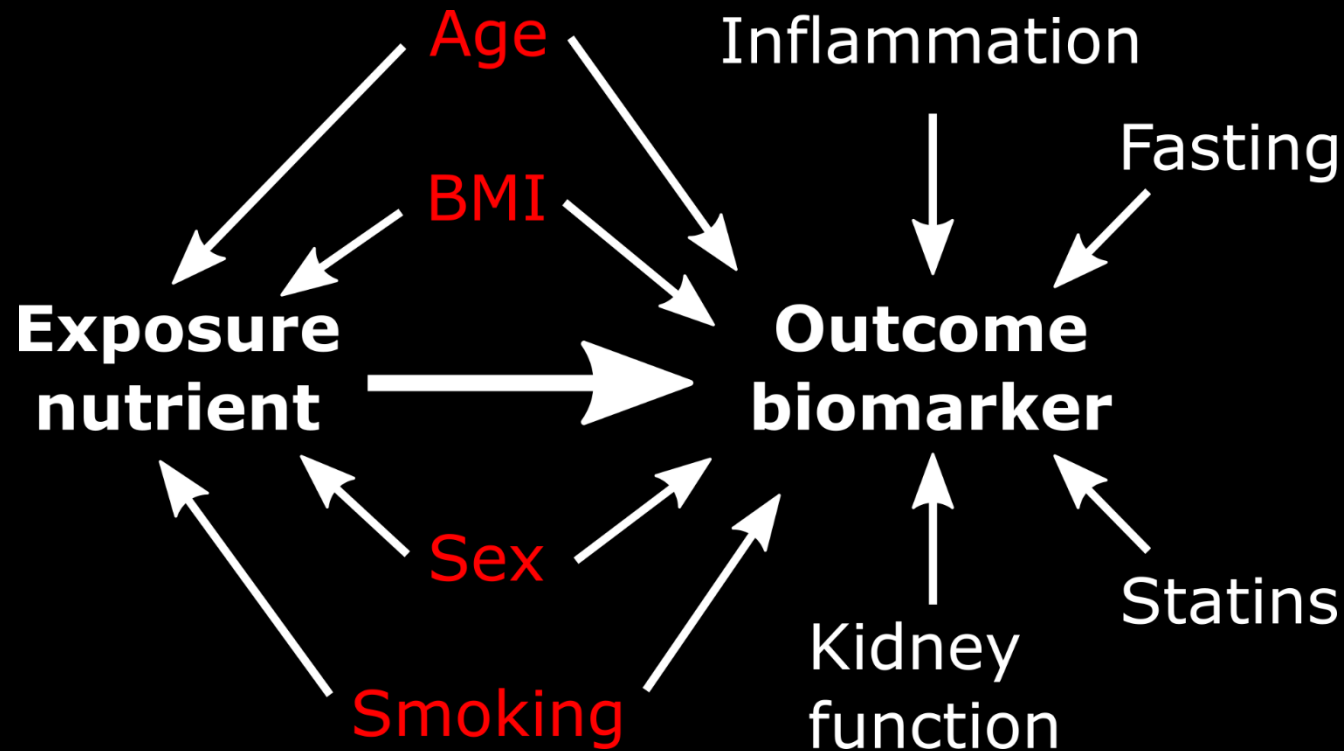
Between:

- 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

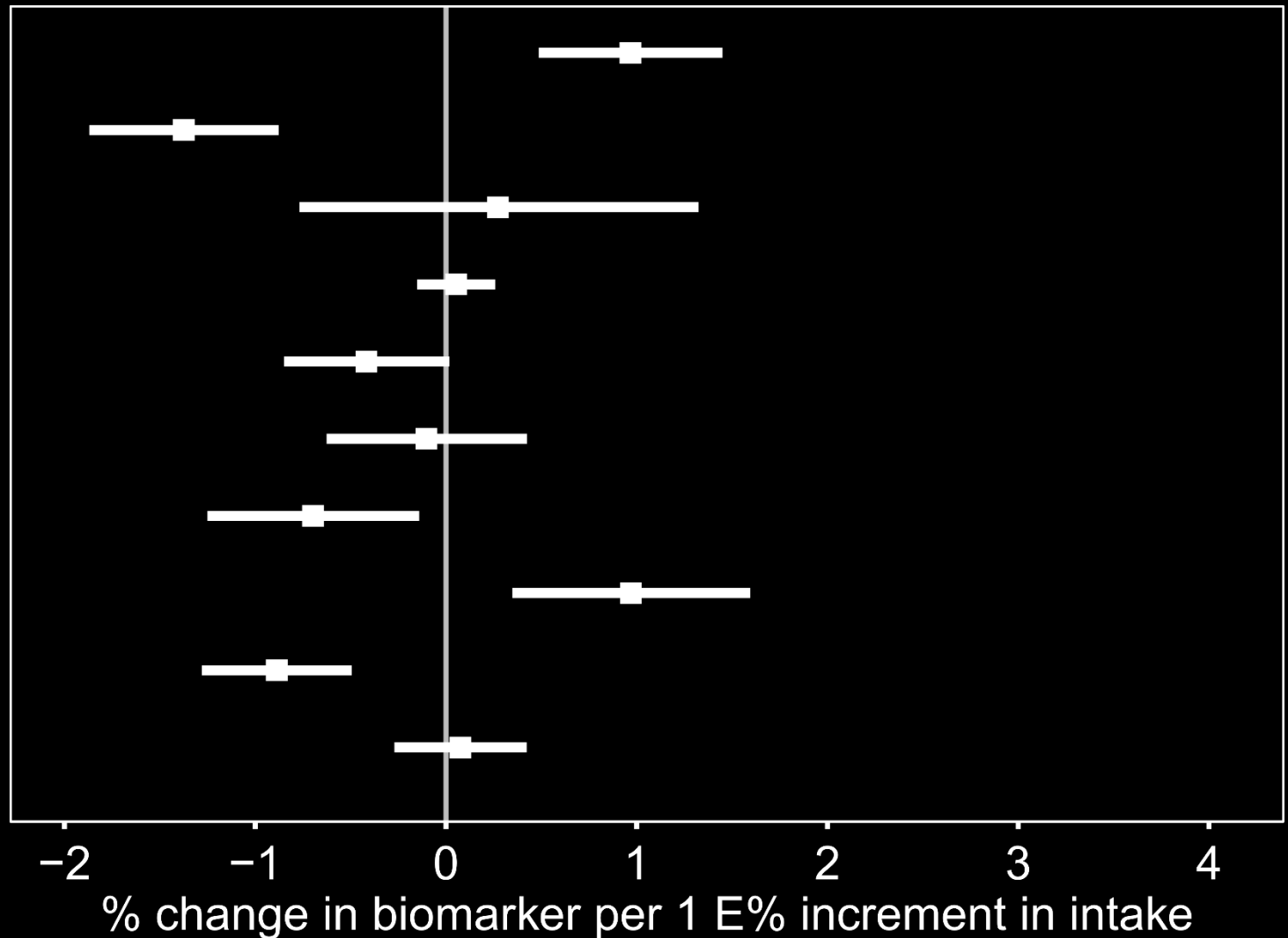
The same patterns were seen whether protein replaced carbohydrate or fat

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

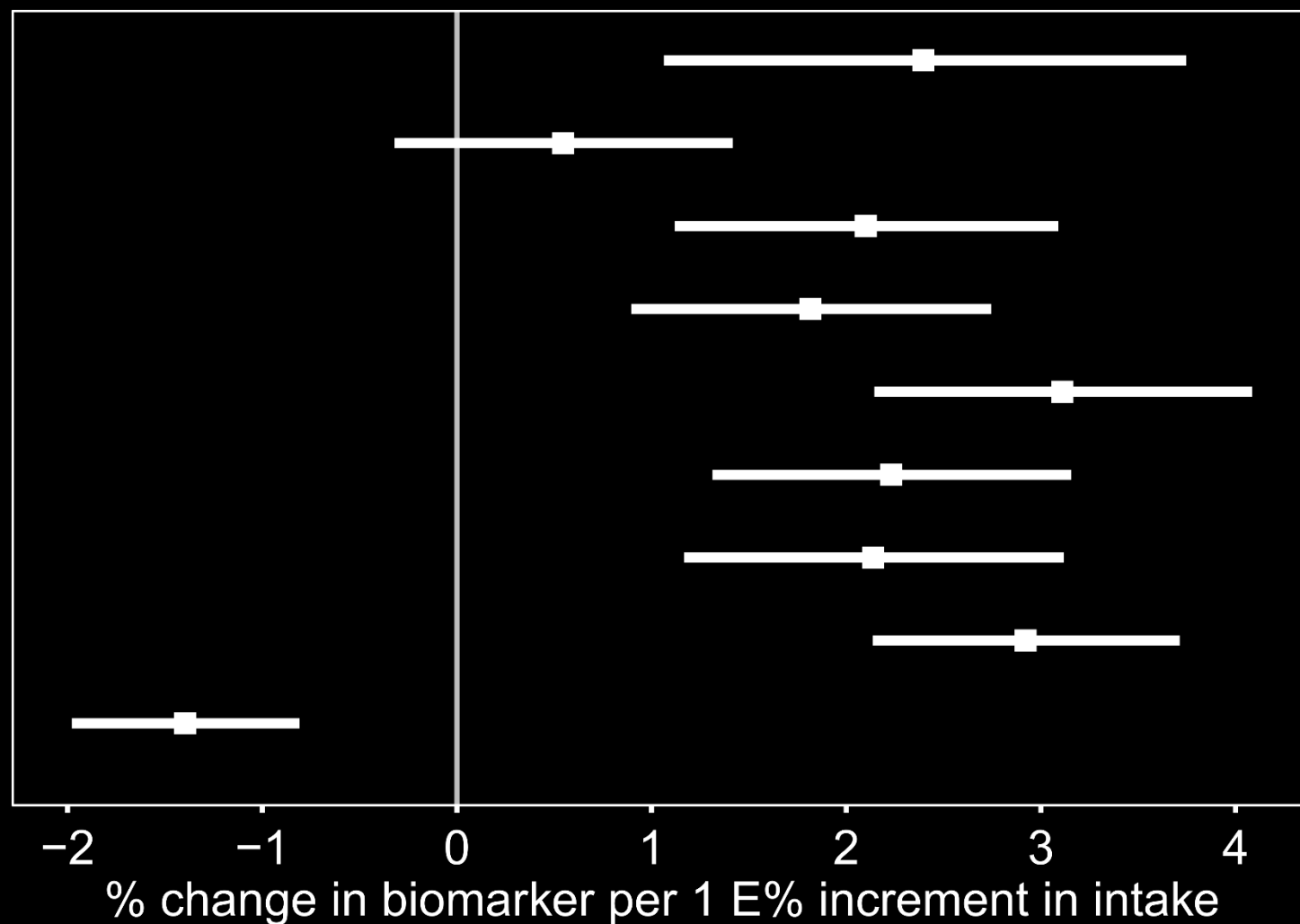
PLP

PA

Folate

Cobalamin

MMA

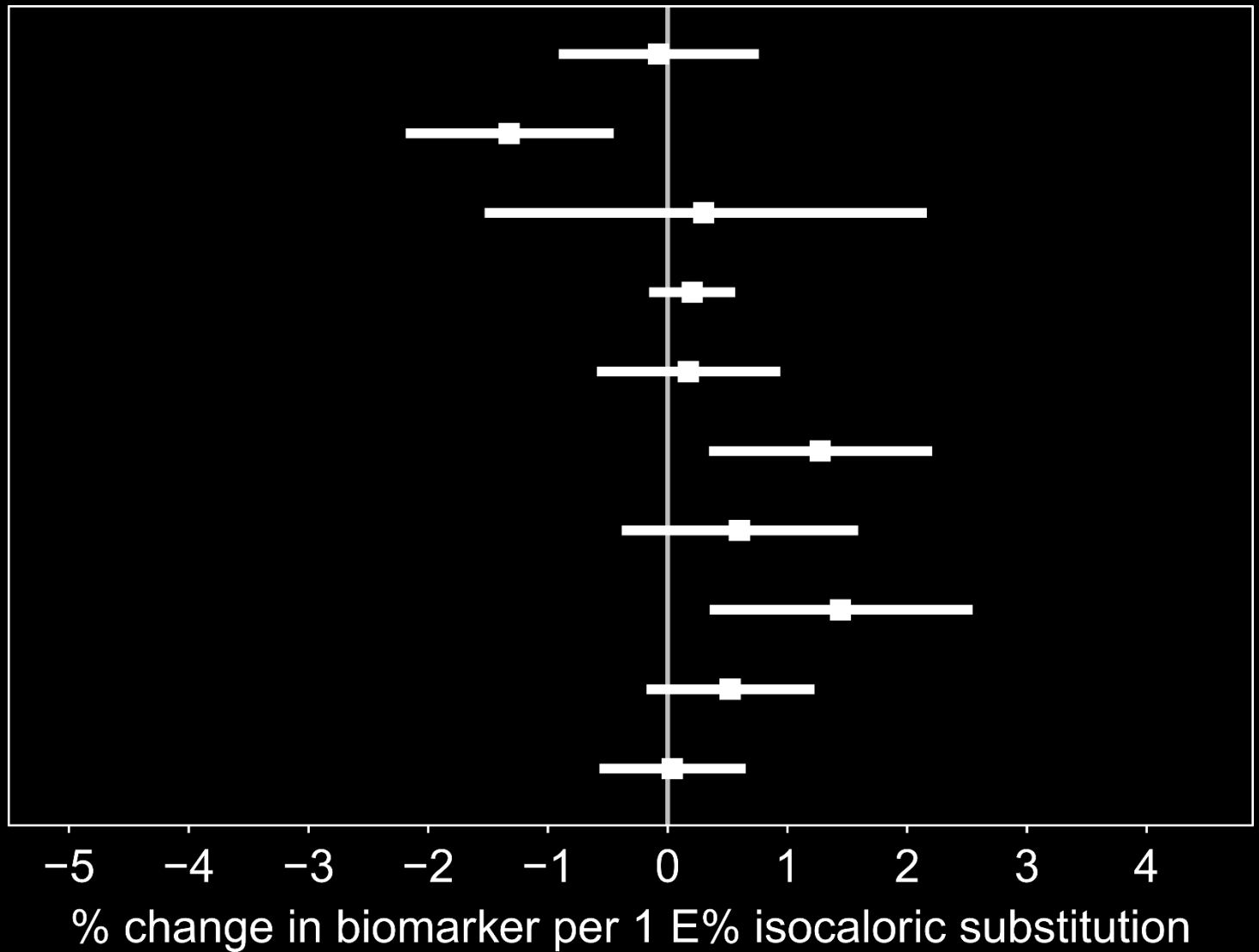


# Protein and food profile



# PUFA ↑ SFA ↓

Methionine  
 Homocysteine  
 Cystathionine  
 Cysteine  
 Choline  
 Betaine  
 DMG  
 Sarcosine  
 Glycine  
 Serine



# PUFA ↑ SFA ↓

Riboflavin

NAM

mNAM

PL

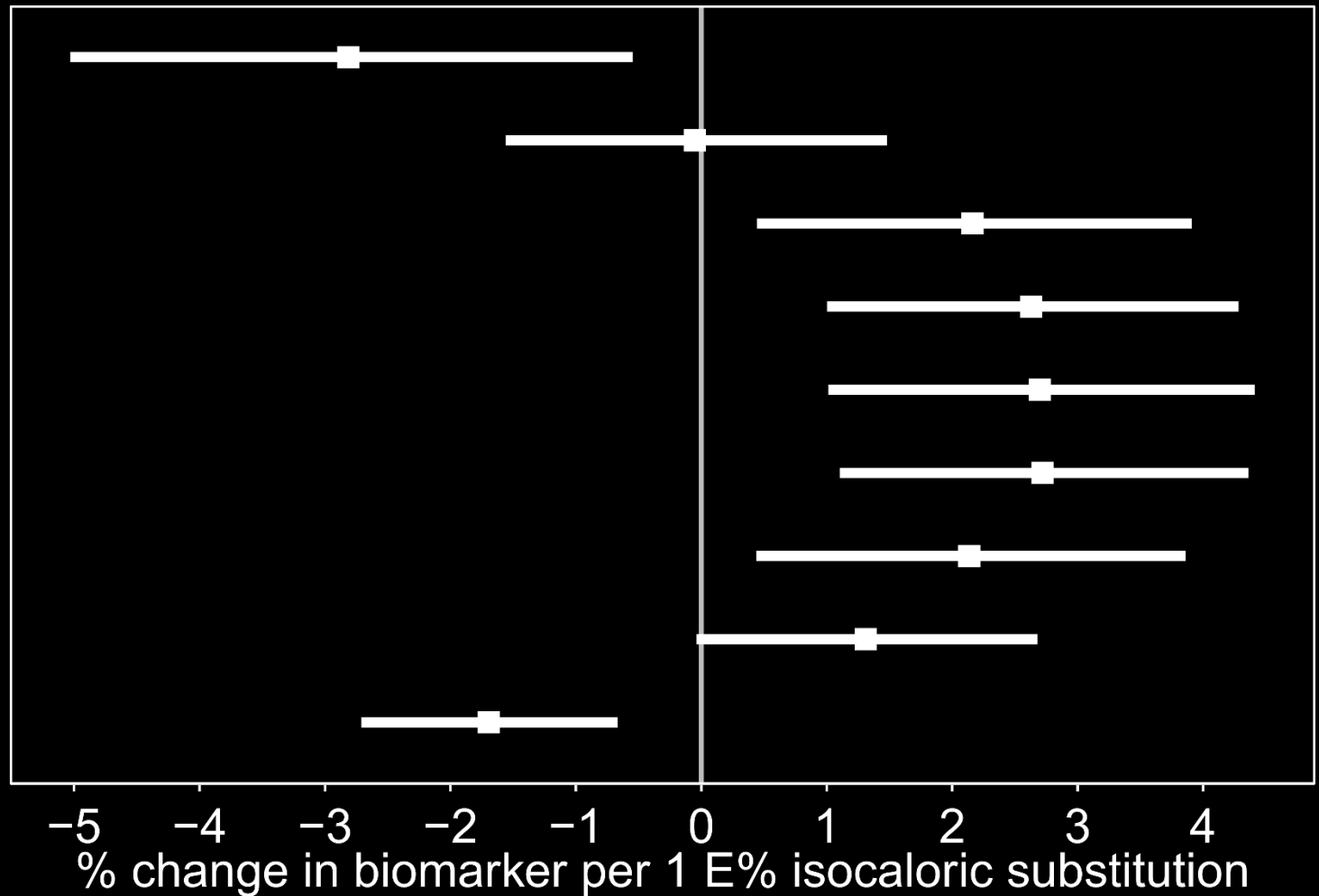
PLP

PA


Folate

Cobalamin

MMA







PPAR $\alpha$ -activation and dietary composition influences the one-carbon metabolism

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

- Potential biomarkers of PPAR $\alpha$ -activity

Protein  $\Rightarrow$  Most B-vitamins higher

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