



Fiona A. Hagenbeek<sup>1</sup>, Harmen H.M. Draisma<sup>1</sup>,  
Meike Bartels<sup>1</sup> & Dorret I. Boomsma<sup>1</sup>

<sup>1</sup>. Department of Biological Psychology, VU University, Amsterdam, The Netherlands

## ACTION

### Aggression in Children: Unraveling gene-environment interplay to inform Treatment and Intervention strategies

❖ Aggression is a complex trait characterized by "hostile, injurious, or destructive behavior" (Siever, 2008).

#### WP5: Metabolomics & Biomarkers

##### Background & aim

- ❖ Different aggression biomarkers have been investigated, including; Neurotransmitters (serotonin), hormones (testosterone), inflammatory markers (interleukin 6) and lipoproteins (LDL-C).
- ❖ The heterogeneous nature of aggression indicates different mechanisms may underlie aggression sub-types and be characterized by different biochemical disturbances.

❖ **Aim:** investigate the metabolomic profile of aggression to establish and validate biomarkers to aid the classification of sub-diagnoses.

##### Data collection (Figure 1)

- ❖ ~2000 Dutch children 7-12 years
- ❖ DNA (also parents & siblings) → epigenetics (for WP3: Genetic Epidemiology)
- ❖ Urine → enzyme immunoassays & LC-MS metabolomics
- ❖ Questionnaires → health, wellbeing, Child Behavior Check List (CBCL)

##### What's next?

- ❖ Establishment and validation of aggression biomarkers (metabolomics + enzyme immunoassays)

Figure 1. Overview data collection ACTION

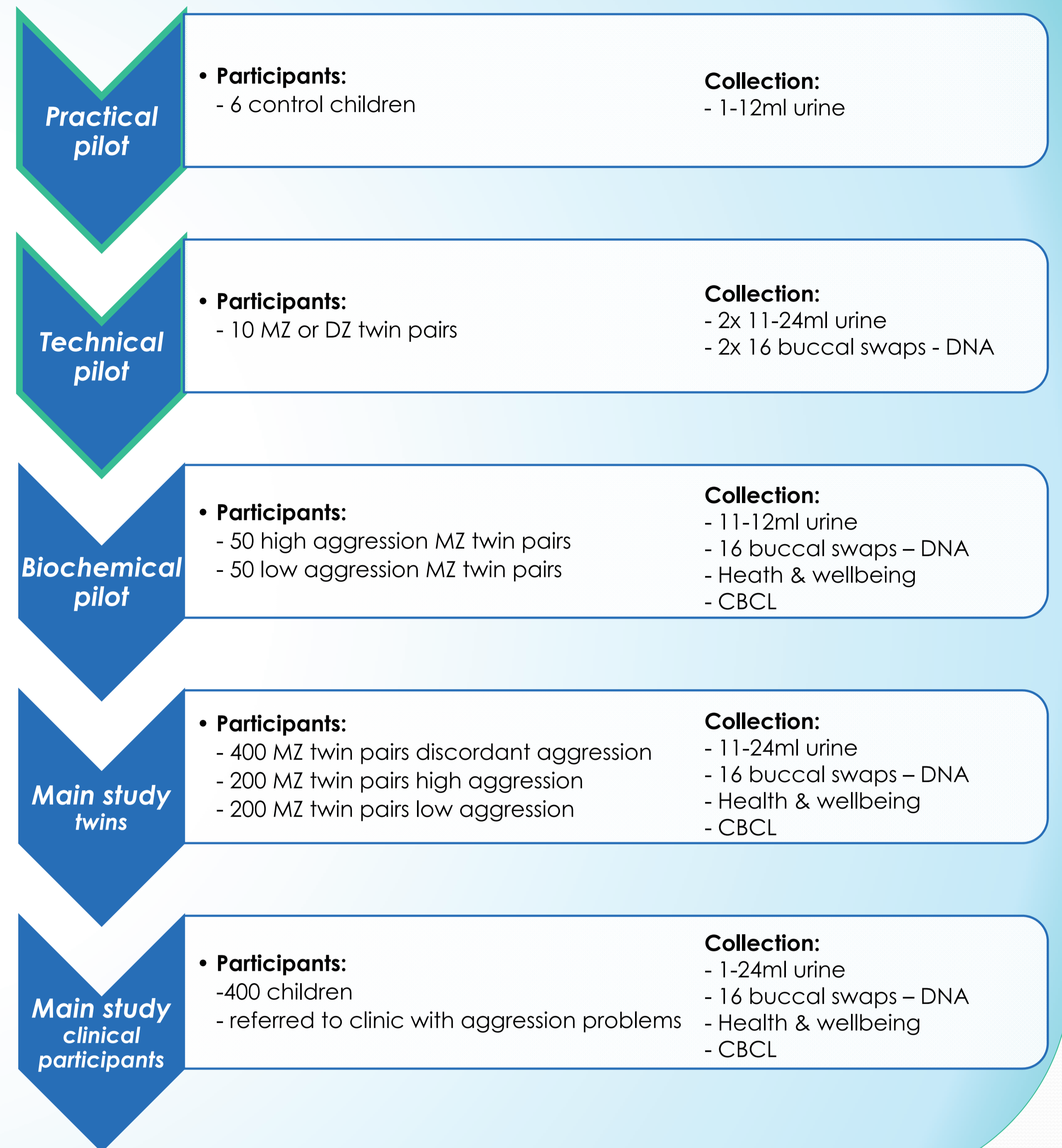
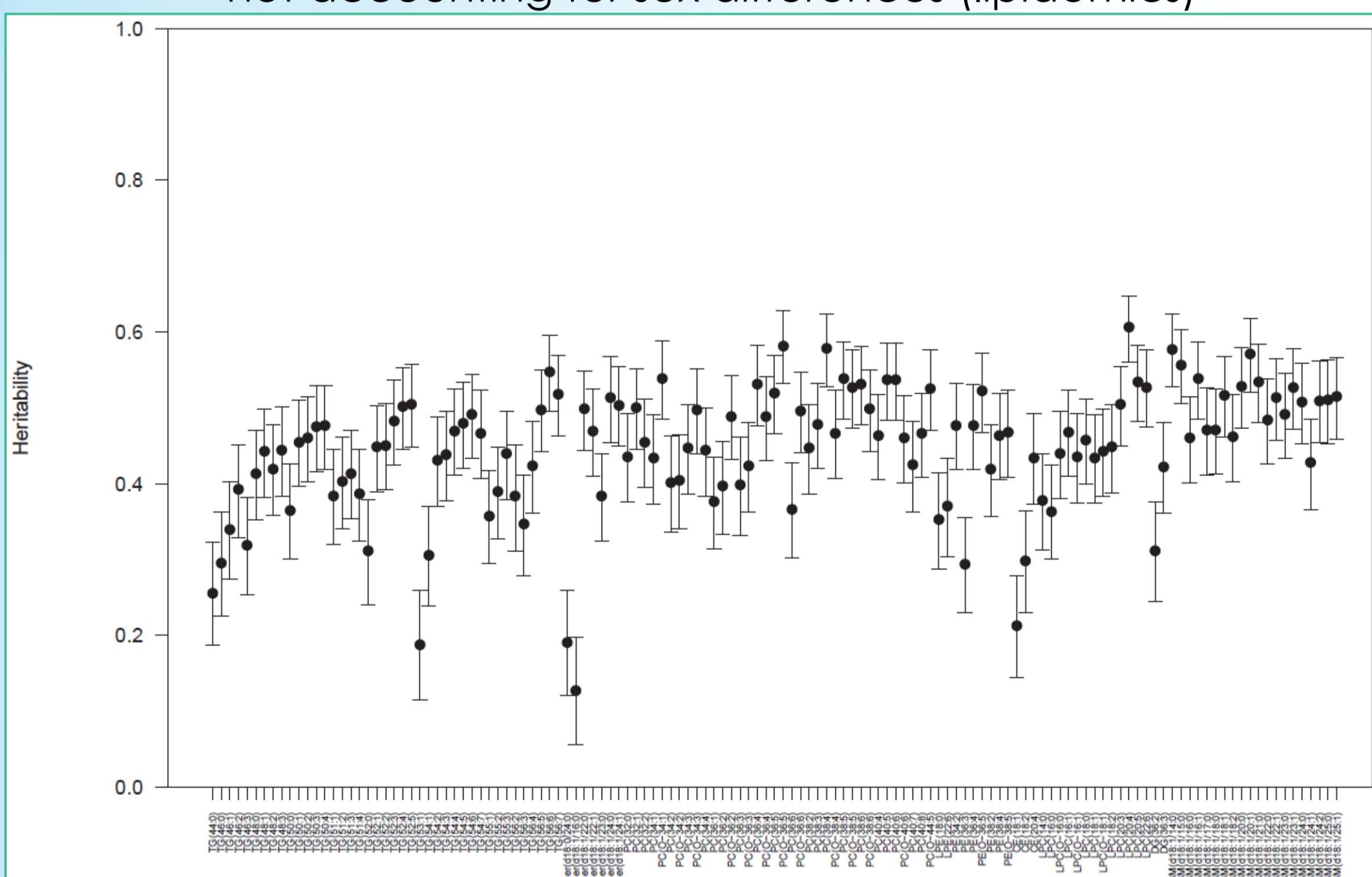


Figure 2. Heritability estimates for metabolites under AE model not accounting for sex differences (lipidomics)



The dots indicate the point estimate for the standardized A variance component, the whiskers are the maximum likelihood based 95%-confidence intervals for these point estimates. Lipids are ordered by an increasing number of carbon atoms and double bonds in their side chains for each of the lipid classes.

## Metabolomics & Heritability

- ❖ Metabolomics is the comprehensive analysis of low-molecular weight compounds in biological samples such as cells, body fluids and tissues.

### Lipidomics data

#### Methods

- ❖ **Participants:** 1387 MZ-twins & 1126 DZ-twins
- ❖ **Measurement:** 131 blood plasma lipids from 9 different classes via LC-MS.
- ❖ **Analysis:** AE genetic model (not accounting for sex differences) in Openmx (Boker et al., 2011).

#### Results

- ❖ Low to moderate (<60%) heritability estimates for blood plasma lipids (Figure 2).
  - Triglyceride heritability depends on the number of carbon atoms and double bonds in the fatty acid chains → consistent with pilot study Draisma (2011).

#### References:

- ❖ Boker, S, et al. 2011. OpenMx: an open source extended structural equation modeling framework. *Psychometrika*, 76: 306–317.
- ❖ Draisma, H. H. M. (2011). Analysis of Metabolomics Data from Twin Families. Leiden.
- ❖ Siever, L.J. 2008. Neurobiology of Aggression and Violence. *Am. J. Psychiatry* 165: 429–442.

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Contact: f.a.hagenbeek@vu.nl

#### ACTION partners:

