

Fatty Acids Produced by De Novo Lipogenesis (DNL) of Refined Carbohydrates are Associated with Worsening of Metabolic Syndrome (MetS) Components: The Prospective Metabolism and Islet Cell Evaluation (PROMISE) Cohort

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Background

Hypertriglyceridemia is a known risk factor for metabolic dysfunction and is a component of the metabolic syndrome (MetS) (1,2); however, the role of the specific fatty acid (FA) composition of the serum triacylglycerol (TAG) fraction on MetS has not been well studied.

Objectives: To investigate the contribution of individual TAGFA on the components of MetS and to identify potential clusters of TAGFA underlying MetS.

Methods

Cohort: Adults (n=477) at-risk for diabetes were recruited from Toronto and London, ON and followed every 3-yrs.

Predictors: Fasting TAGFA were quantified as mol% (proportion of total) by thin layer chromatography and gas chromatography from the baseline.

Outcomes: The MetS components fasting glucose (FG), waist circumference (WC), HDL, clinically measured triglyceride (Tg), and mean arterial pressure (MAP; used in the analyses as systolic and diastolic blood pressure are highly correlated) were measured using standard laboratory procedures.

Statistics: Done using R version 3.4.0 (2017-04-21) and statistical methods are described within each figure. The code is available at doi.org/10.6084/m9.figshare.5077663.

Key findings

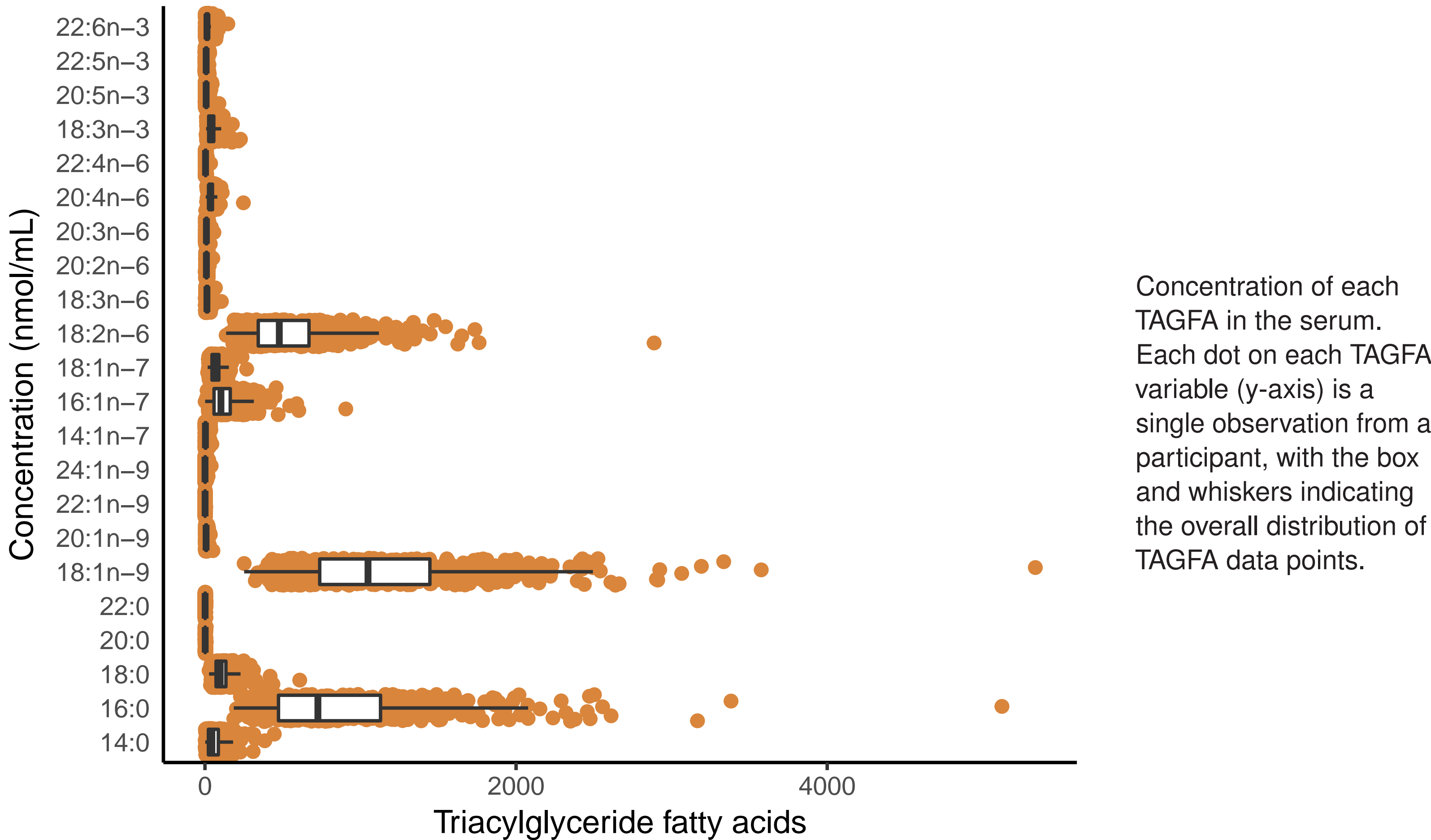
We found that a higher proportion of four TAGFA strongly predicted worsening of MetS components. These four TAGFA are products of DNL from refined carbohydrates (3,4). Our results provide further evidence to support the harmful impact of refined/simple carbohydrates on metabolic health.

Results: Descriptive summary of basic characteristics of participants in the PROMISE cohort for 3 clinic visits over 6 years

Values are presented as either mean (standard deviation) or count (percent of total).

Measure	Baseline	3-yr	6-yr
Tg (mmol/L)	1.5 (0.8)	1.4 (0.8)	1.4 (0.7)
Chol (mmol/L)	5.2 (0.9)	5.1 (1.0)	5.1 (0.9)
HDL (mmol/L)	1.4 (0.4)	1.3 (0.4)	1.4 (0.4)
MAP (mmHg)	95.3 (11.4)	95.4 (11.0)	94.6 (10.6)
Age (yrs)	50.1 (9.8)	53.2 (9.7)	56.5 (9.6)
BMI (kg/m ²)	31.1 (6.4)	31.4 (6.5)	31.1 (6.6)
WC (cm)	98.5 (15.5)	99.3 (15.7)	100.4 (15.7)
Ethnicity			
- European	336 (70%)		
- Latino/a	58 (12%)		
- Other	51 (11%)		
- South Asian	32 (7%)		
Sex			
- Female	349 (73%)		
- Male	128 (27%)		

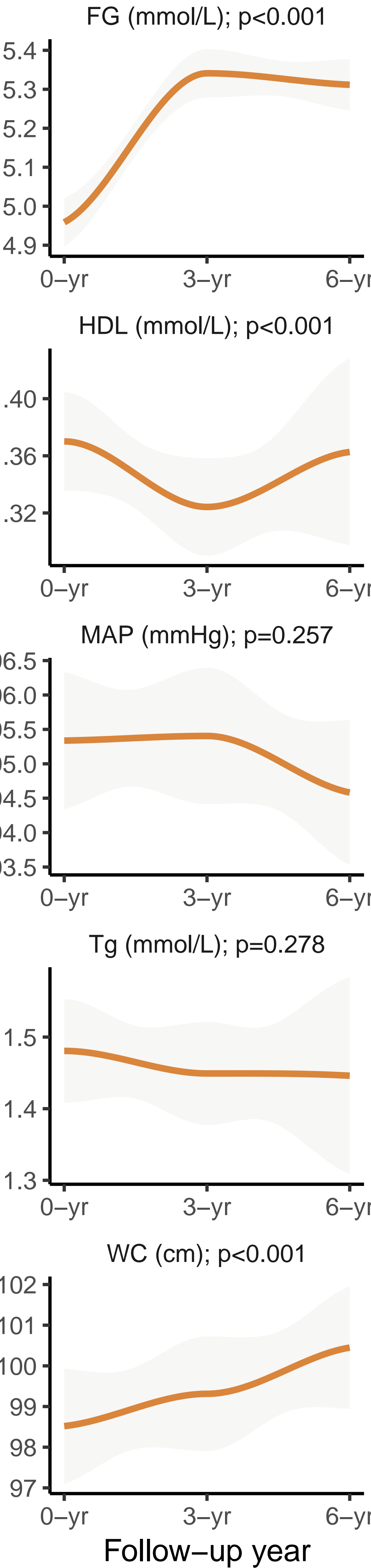
Results: Distribution of individual TAGFA as a concentration in the serum of PROMISE participants.



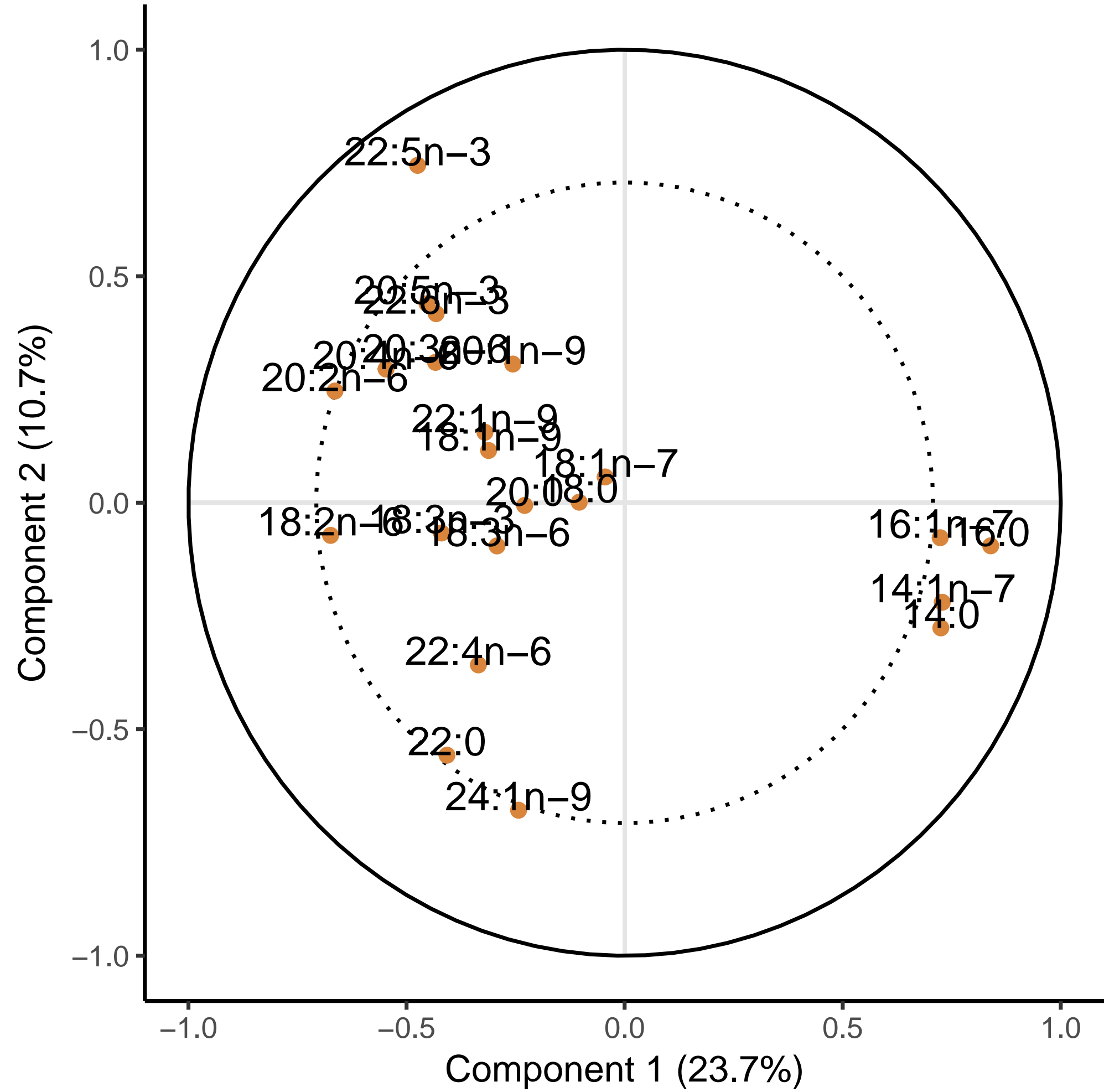
Results: Correlation heatmap of individual TAGFA with each MetS component



Results: MetS components' change over 6 years of followup

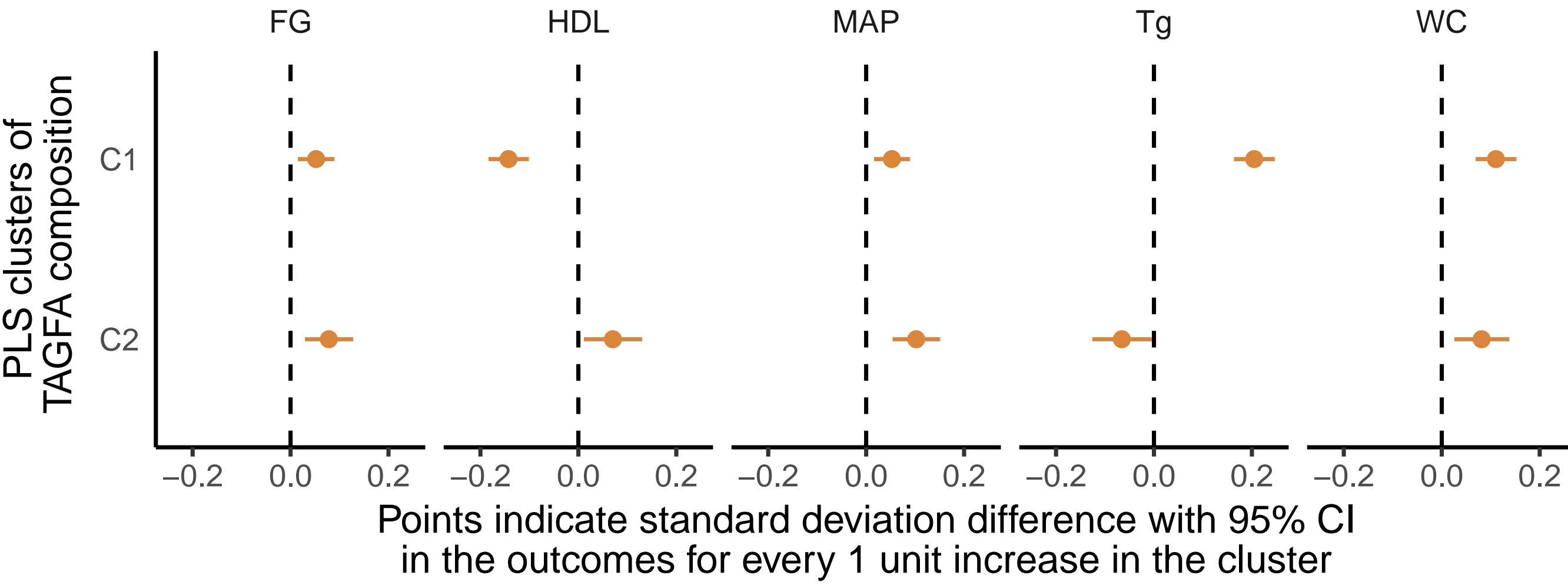


Results: Partial least squares (PLS) clustering of TAGFA composition underlying the MetS components.



To analyze the high-dimensional, multivariate nature of the TAGFA (as mol%) composition with the MetS components, we used partial least squares analysis (PLS). The TAGFA variables are included as the predictors (x) and the five MetS components (FG, HDL, MAP, Tg, WC) as the outcomes (y) within a single model. This technique is used to identify underlying structures or clusters of variables (TAGFA) contained within the outcome (MetS). Each axis is the extracted score or PLS component, with the explained variance shown on the axes. TAGFA between the two circles (solid and dotted) contribute substantially to the explained variance of the MetS components. Two clusters are identified: four TAGFA (14:0, 16:0, 14:1n-7, 16:1n-7) and every other TAGFA.

Results: Longitudinal associations of the partial least squares clustering of TAGFA composition on each MetS component



PLS scores were extracted from the PLS model with the TAGFA clusters and used as predictors in generalized estimating equation (GEE) modeling (adjusting for time, baseline age, ethnicity, and sex) to analyze the data for longitudinal associations with the MetS components as outcomes.

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- ▶ Comments or questions? Please contact: luke.johnston@mail.utoronto.ca

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