# Abstract

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**Objective**: Although elevated serum triglyceride (TAG) is a well-described risk factor for type 2 diabetes (T2DM), few data are available regarding the role of the specific fatty acid composition within serum TAG (TAGFA) in the pathogenesis of T2DM. Our aim, therefore, was to examine longitudinal associations of TAGFA with insulin sensitivity (IS) and beta-cell function.

**Research Design and Methods**: We used longitudinal data (3 visits over 6 years) from the Prospective Metabolism and Islet Cell Evaluation (PROMISE) cohort of adults (n=477) who were at-risk for diabetes at baseline. Glucose and insulin from an OGTT were used to calculate the Matsuda index (ISI), HOMA2-%S, the Insulinogenic Index over HOMA-IR (IGI/IR), and the Insulin Secretion-Sensitivity Index-2 (ISSI-2). Gas chromatography quantified TAGFA composition. Generalized estimating equations (GEE) adjusted for confounders and partial least squares (PLS) were used for the analysis.

**Results**: The outcome variables declined by 14% to 27% over the 6-years. In the adjusted GEE models, four TAGFA (14:0, 16:0, 14:1n-7, 16:1n-7 as mol%) had strong negative associations with IS while others (e.g. 18:1n-7, 18:1n-9, 20:2n-6, 20:5n-3) had strong positive associations. Few associations were seen for beta-cell function, except for 16:0 (negative) and 18:1n-7 (positive). PLS analysis indicated that four TGFA (14:0, 14:1-7, 16:0, 16:1n-7) that are markers of de novo lipogenesis (DNL) clustered together and strongly predicted lower IS. These four TAGFA also correlated highly (r>0.4) with clinically measured TAG.

**Conclusions**: We found that higher proportions of a cluster of four DNL TAGFA strongly predicted lower IS as well as hypertriglyceridemia.