# Abstract

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**Objective**: There are limited data on the role of the specific triacylglyceride fatty acid (TAGFA) composition on diabetes pathogenesis. Our aim was to examine the longitudinal association of TAGFA on 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) at-risk for diabetes. 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. Most TAGFA modeled as a concentration had strong negative associations with IS in adjusted GEE models; when as a mol%, four TAGFA (14:0, 16:0, 14:1n-7, 16:1n-7) had strong negative associations while most 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). The PLS analysis identified that the four 'harmful' TAGFA (14 and 16 carbon TAGFA) clustered together and strongly predicted lower IS.

**Conclusions**: We found that a higher proportions of a cluster of four TAGFA (14:0, 14:1-7, 16:0, 16:1n-7) strongly predicted lower IS. Previous research suggests these four FA are heavily derived from the de novo lipogenesis (DNL) of higher intakes of simple or refined carbohydrates, especially 16:1n-7. Our results suggest that greater simple or refined carbohydrate intake may impact risk for diabetes through greater DNL and higher FA associated with lipotoxicity (e.g. 16:0), leading to hypertriglyceridemia and lower IS.