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## Postprandial lipemia and CVD; does the magnitude, peak concentration or duration impact intermediary cardiometabolic risk factors differentially? PREDICT I Study.

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### Abstract

Postprandial lipemia is an independent risk factor for CVD, due to effects on lipoprotein remodelling, oxidative stress, inflammation, haemostasis and endothelial dysfunction. However, it is unknown whether the total, peak or duration of the lipemic response determines risk. The PREDICT I study is the largest study to date to measure postprandial lipemic responses and intermediary acutely changing cardiometabolic risk factors at multiple time points using a standardized test meal model.

A multi-center postprandial study of 1,000 individuals from the UK (unrelated, identical and non-identical twins) and 100 unrelated individuals from the US, assessed postprandial (hourly 0–6h) metabolic responses to sequential mixed-nutrient dietary challenges (50 g fat, 85 g carbohydrate at 0 h; 22 g fat, 71 g carbohydrate at 4h) in a clinic setting. We investigated the relationship of different postprandial triacylglycerol (TG) measures (4 and 6 h TG iAUC, 4 and 6 h TG concentration, 4 and 6 h TG increase from fasting) with lipoprotein remodelling (XXL-VLDL (including chylomicron remnants and VLDL particles) and XL-VLDL particle concentrations (average diameters > 75, 64 nm respectively), HDL-C) and levels of glycosylated acute phase proteins (GlycA; marker of cardiovascular inflammation), all of which have been implicated as independent predictors of CVD risk.

Following adjustment (for use of medication, demographic characteristics, fasting TG, insulin and glucose levels), all six postprandial TG measures (4 and 6 h TG iAUC, 4 and 6 h TG concentration, 4 and 6 h TG increase from fasting) were strongly correlated with markers of atherogenic lipoprotein remodelling and the marker of cardiovascular inflammation (GlycA). The strongest correlation (interim analysis) was observed for the 6 h TG increase from fasting (all  $P < 0.001$ , Pearson's coefficient  $r = 0.94$  [95%CI's; 0.93, 0.95] for XXL-VLDL-P;  $r = 0.95$  [95%CI's; 0.95, 0.96] for XL-VLDL-P;  $r = 0.89$  [95%CI's; 0.88, 0.91] for GlycA;  $r = -0.61$  [95%CI's; -0.66, -0.55] for HDL-C). Inter-individual variability in postprandial lipemic responses was high in the tightly controlled clinic setting (interim analysis,  $n = 656$ ); IQR (median) was; iAUC (0–6h) 2.39 (2.31) mmol/L.h; Cmax 1.32 (2.06) mmol/L; Tmax 30.0 (300) min; and increase above fasting at 6 h 0.78 (0.62) mmol/L.

This is the most detailed postprandial study performed to date and suggests that identifying predictors of the postprandial 6 h TG rise will have the highest CVD relevance. Ongoing exploration in PREDICT I of the determinants of postprandial lipemic responses considering environmental, genetic and microbiome variables will significantly advance our ability to predict an individual's postprandial response and its links to cardiovascular risk.

### Conflict of Interest

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