Genetic predisposition to an adverse lipid profile limits the improvement in total cholesterol in response to weight loss.

Overweight and obesity are associated with a dyslipidaemia which can be improved by weight loss. Whether genetic predisposition to an adverse lipid profile modifies such beneficial effects of weight loss on lipid levels in overweight and obese individuals was examined. White European participants (n = 374) who completed a 12-month weight loss trial were genotyped for 36 lipid-associated single nucleotide polymorphisms (SNPs), previously identified in genome-wide association studies (GWAS). Genetic predisposition scores (GPSs) were calculated for four lipid traits by summing the number of risk alleles (RA) for each participant. The associations of each GPS with four lipid traits were assessed at baseline, and with lipid changes in response to weight change after 12 months. At baseline, the trait-specific GPSs were associated with 0.11 ± 0.04 mM higher total cholesterol/RA (P = 0.004), 0.05 ± 0.02 mM higher low density lipoprotein cholesterol/RA (P = 0.005), 0.03 ± 0.007 mM lower high density lipoprotein cholesterol/RA (P = 0.00002) and 0.04 ± 0.01 mM higher triglyceride/RA (P = 0.00002). After the intervention, weight loss was associated with improvements in all lipids (P< 0.01). GPS attenuated the weight loss-associated reduction in TC so those with a higher GPS had less...
improvement (interaction = 0.01 ± 0.005 mM/GPS/kg weight loss, P = 0.003). A similar pattern was observed for LDLC (interaction = 0.004 ± 0.002 mM/GPS/kg weight loss, P = 0.07). There was no evidence of a GPS-modifying effect for change in HDLC or TG. Genetic predisposition is an important determinant of lipid levels and appears to limit the improvement in TC and to some extent LDLC levels, but not in other plasma lipids, in response to weight loss. © 2013 American Institute of Chemical Engineers AIChE J, 2013.