Modelling the Interplay between Lifestyle Factors and Genetic Predisposition on Markers of Type 2 Diabetes Mellitus Risk.

The risk of developing type 2 diabetes mellitus (T2DM) is determined by a complex interplay involving lifestyle factors and genetic predisposition. Despite this, many studies do not consider the relative contributions of this complex array of factors to identify relationships which are important in progression or prevention of complex diseases. We aimed to describe the integrated effect of a number of lifestyle changes (weight, diet and physical activity) in the context of genetic susceptibility, on changes in glycaemic traits in overweight or obese participants following 12-months of a weight management programme. A sample of 353 participants from a behavioural weight management intervention were included in this study. A graphical Markov model was used to describe the impact of the intervention, by dividing the effects into various pathways comprising changes in proportion of dietary saturated fat, physical activity and weight loss, and a genetic predisposition score (T2DM-GPS), on changes in insulin sensitivity (HOMA-IR), insulin secretion (HOMA-B) and short and long term glycaemia (glucose and HbA1c). We demonstrated the use of graphical Markov modelling to identify the importance and interrelationships of a number of possible variables changed as a result of a lifestyle
intervention, whilst considering fixed factors such as genetic predisposition, on changes in traits. Paths which led to weight loss and change in dietary saturated fat were important factors in the change of all glycaemic traits, whereas the T2DM-GPS only made a significant direct contribution to changes in HOMA-IR and plasma glucose after considering the effects of lifestyle factors. This analysis shows that modifiable factors relating to body weight, diet, and physical activity are more likely to impact on glycaemic traits than genetic predisposition during a behavioural intervention.