

1.52±5.34). 121 participants (60%) were assessed at 24 months ($n=53$ control, $n=68$ intervention). The reduction in BMI SDS at 12 months from baseline was lost in both groups at 24 months ($\hat{\alpha}\sim 0.03$ control [95% CI: $\hat{\alpha}\sim 0.14$ to 0.09] and $\hat{\alpha}\sim 0.02$ intervention [$\hat{\alpha}\sim 0.12$ to 0.08]). However, participants who attended $\geq 70\%$ of intense intervention sessions had a reduction in BMI SDS of $\hat{\alpha}\sim 0.22$ compared to a return to baseline levels for those attending $< 70\%$ ($p=0.002$). Intervention participants were faster on the 550m walk/run test ($\hat{\alpha}\sim 0.57$ mins, $p<0.0001$), and both groups reported improvements in quality of life ($p<0.05$), and reduction in sweet drink intake ($p<0.001$).

Conclusion: High adherence to the intense intervention resulted in sustained reductions in BMI SDS at two years. Further, even with home-based assessments only, improvements in quality of life and reduction in sweet drink intake were achieved. Obesity programmes incorporating assessments and an intense intervention can result in improvements, with attendance being key to long-term outcome.

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Improved vascular structure and function following intermittent energy restriction in adolescents with obesity



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Background: In adults, intermittent energy restriction (IER), popularised as the 5:2 diet, is as effective for weight loss and improved cardiovascular risk as continuous energy restriction. We investigated the impact of IER on vascular structure and function in adolescents with obesity.

Methods: During weeks 1–12, participants followed an IER plan consisting of a Very Low Energy Diet (VLED) 3 days/week (500–600 kcal/day) and a standard healthy diet 4 days/week. For weeks 13–26, participants were given a choice to continue with 1–3 days of VLED/week or follow a standard healthy diet. Outcomes measured at 0, 12 and 26 weeks were BMI expressed as a percentage of the 95th percentile (BMI%95th), blood pressure, fasting lipids, pulse wave velocity (PWV), carotid intima-media thickness (CIMT), and flow mediated dilation (FMD).

Results: 30 participants, aged 12–17 years (median 15.2 years, female $n=25$) with a median BMI 34.9 kg/m² (range: 27.7–52.4), were recruited. Compared with baseline, BMI%95th was significantly reduced at 12 weeks (mean difference [SD], $n=23$, -5.4 [2.2],

$p<0.0001$) and 26 weeks ($n=21$, -5.0 [9.3], $p=0.02$). Triglycerides and brachial systolic blood pressure were also reduced at 26 weeks compared with baseline ($n=21$, -0.22 mmol/L [0.31], $p=0.008$ and $n=13$, -5.6 mmHg [8.9], $p=0.042$, respectively). CIMT ($n=16$, -0.06 μ m [0.05], $p=0.001$) and FMD ($n=15$, absolute increase of 0.51% [0.5], $p=0.001$) improved between baseline and 12 weeks. The improvement was maintained at 26 weeks. Reduced BMI%95th was associated with improved PWV ($\rho=0.63$, $p=0.022$) and FMD ($r^2=0.80$, $p<0.0001$) at 26 weeks.

Conclusion: IER is an effective dietary intervention in adolescents with obesity, resulting in reduced BMI%95th and cardiovascular risk in the short term. Findings demonstrate a potential benefit to cardiovascular health if maintained. A 12-month RCT is underway comparing IER with continuous energy restriction.

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Systems genetics as a tool to probe hepatic lipid and energy metabolism



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Dysregulation of lipid homeostasis is a precipitating event in the pathogenesis and progression of hepatosteatosis and metabolic syndrome. However, defining the molecular mechanisms that underpin lipid dysregulation in humans has proven challenging due to complex gene and environment interactions. Nevertheless, genome-wide association studies (GWAS) have indicated there to be an approximately 30% heritability for hepatosteatosis, however only $\sim 10\%$ has been directly attributable to genetic variants. This highlights a discrepancy that likely exists because most linear GWAS models do not account for features such as structural variation, rare variants and complex epistatic or gene-by-environment interactions. More recently, systems biology approaches utilizing genetic reference panels (GRPs) in model organisms have increased our ability in this regard, because they allow for integration of multiple layers of biological information (trans-omics), and for the control of environmental influence. Accordingly, we undertook a systems genetics analysis of mammalian lipid metabolism. Here we quantify 311 individual lipid species in the liver and plasma of replicate animals from 107 strains of an inbred mouse GRP (>300 individual mice), and integrated these data with matched hepatic proteomics performed on the same set of mice. Subsequent analysis of correlation networks and QTL mapping incorporating strain-specific phenotype and genotype data facilitated the generation of a powerful resource that expands our understanding of mammalian lipid metabolism, identifies *bona fide* effectors of lipid abundance, and provides several targets of interest for disease intervention.

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Metabolomic analysis of insulin resistance across different mouse strains and diets



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Insulin resistance is a major risk factor for many diseases. However, its underlying mechanism remains unclear in part because