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**Aim:** To investigate the independent effects of 6-months of energy restriction or exercise training on whole-body and hepatic fat oxidation of patients with NAFLD.

**Methods:** Participants were randomised into either circuit exercise training (EX; $n = 13$; 3 h/week without changes in dietary habits), or dietary energy restriction without changes in structured physical activity (ER; $n = 8$). Respiratory quotient (RQ) and whole-body fat oxidation rates ($Fat_{ox}$) were determined by indirect calorimetry under basal, insulin-stimulated and exercise conditions. Severity of disease and steatosis was determined by liver histology; hepatic $Fat_{ox}$ was estimated from plasma b-hydroxybutyrate concentrations; cardiorespiratory fitness (CRF) was expressed as VO2peak. Complete-case analysis was performed (EX: $n = 10$; ER: $n = 6$).

**Results:** Hepatic steatosis and NAFLD activity score decreased with ER but not with EX. β-Hydroxybutyrate concentrations increased significantly in response to ER ($0.08 \pm 0.02$ vs. $0.12 \pm 0.04$, $P = 0.03$) but remained unchanged in response to EX ($0.10 \pm 0.03$ vs. $0.11 \pm 0.07$, $P = 0.39$). Basal RQ decreased ($P = 0.05$) in response to EX, while this change was not significant after ER ($P = 0.38$). VO2peak ($P < 0.001$) and maximal $Fat_{ox}$ during aerobic exercise ($P = 0.03$) improved with EX but not with ER ($P > 0.05$). The increase in β-hydroxybutyrate concentrations was correlated with the reduction in hepatic steatosis ($r = -0.56$, $P = 0.04$).

**Conclusions:** ER and EX lead to specific benefits on fat metabolism of patients with NAFLD. Increased hepatic $Fat_{ox}$ in response to ER could be one mechanism through which the ER group achieved reduction in steatosis.

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## Consumption of sugar sweetened beverages and type 2 diabetes incidence in Thai adults: Results from an eight year prospective study

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**Introduction:** The global prevalence of type 2 diabetes mellitus (T2DM) is high and increasing in countries undergoing rapid socio-economic development, such as Thailand. Sugar sweetened beverage (SSB) intake may contribute to the risk of developing T2DM. However, this has not been assessed in Thai adults. We aimed to assess the association between SSB intake and T2DM risk and whether this association was mediated by obesity in a prospective study of Thai adults.

**Methods:** Data were from Thai Cohort Study participants surveyed in 2005, 2009 and 2013. The sample included participants who were free of diabetes in 2005 and who were followed up in 2009 ($n = 59{,}314$) and/or in 2013 ($n = 39{,}175$). We used multivariable logistic regression to assess associations between SSB intake and four and eight year T2DM incidence. We used a counterfactual mediation analysis to explore potential mediation of the SSB intake and T2DM risk relationship.

**Results:** Frequent consumption of SSBs was associated with increased risk of T2DM in women, but not in men at both the four (SSB intake 1—6 times per week OR = 1.7, 95% confidence intervals (CI) 1.3—2.4 and >1 per day-OR = 2.5, 95%CI 1.5—4.1) and eight year follow-ups (SSB intake 1—6 times per week OR = 1.7, 95%CI 1.2—2.3 and >1 per day OR = 3.1, 95%CI 2.0—5.0). The addition of both weight gain and body mass index (BMI) to the full regression model only slightly attenuated these effects. Having a BMI of 25 $kg/m^2$ or over in 2009 was a significant mediator of the total effect of SSB intake in 2005 on T2DM risk in 2013 (natural indirect effect 1.10, 95%CI (1.07, 1.13) and mediated 15.9% of the total relationship.

**Conclusion:** The consumption of SSBs increased the risk of T2DM incidence in women but not in males. Obesity mediated a proportion of this relationship but most of the effect appeared to act through other mechanisms.

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## Invited talk: Lipid metabolism and the complications of diabetes

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Diabetes is a disorder of lipid as well as glucose metabolism. The lack of insulin signalling, caused by either insulin deficiency in type 1 diabetes or insulin resistance in type 2 diabetes, disrupts lipid metabolism in part through effects on the process of de novo lipogenesis. This process requires the activity of fatty acid synthase (FAS), a multifunctional enzyme that synthesises the saturated fatty acid palmitate from malonyl-CoA, acetyl-CoA, and NAPDH. Studies over the past decade have demonstrated that FAS has complex tissue-specific effects that are relevant to the complications of diabetes. In liver, FAS participates in the generation of an endogenous phospholipid ligand for PPARalpha, a transcription factor that promotes fatty acid oxidation and is the target of fibrate drugs used in clinical practice. In the hypothalamus, FAS controls feeding behaviours. At the vascular endothelium and at the intestinal epithelium, FAS is required for normal homeostasis by promoting the palmitoylation of endothelial nitric oxide synthase (eNOS) and mucin 2, respectively. In cardiac muscle and skeletal muscle, FAS alters calcium metabolism through effects on the membrane environment. In macrophages, FAS promotes inflammation and atherosclerosis. In adipose tissue, FAS regulates the conversion of beige adipocytes in part by generating ether lipid ligands for PPARgamma, a transcription factor required for adipogenesis. Pharmacological inhibitors of FAS have been demonstrated to treat diabetes in animal models. However, potentially detrimental effects of FAS inhibition in certain tissues limit this approach. Available evidence suggests that FAS channels lipids to specific intracellular sites, raising that possibility that modulating this process could treat diabetes complications such as retinopathy, vascular disease, and other disorders related to chronic inflammation.

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## Invited talk: Protein kinase Ce in adipose tissue — Not merely an effector but a regulator of lipid intermediates?

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Obesity and lipid oversupply have been linked with defective insulin action in liver and muscle for some time. As lipid-activated kinases, isoforms of the protein kinase C (PKC) family are strong candidates for mediating the inhibitory effects of lipid intermediates. More specifically, PKC$\varepsilon$ is widely believed to play a direct role in liver insulin resistance through inhibition of proximal insulin signalling. Our laboratory has extensively investigated the effects of global and tissue-specific PKC$\varepsilon$ ablation on in mice. This has revealed previously unsuspected roles for the kinase in the regulation of lipid metabolism and glucose homeostasis.

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## Invited talk: Ectopic lipids and defective glucose metabolism: Cause or association?

Clinton Bruce

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Accumulation of lipids in non-adipose tissues, particularly liver and skeletal muscle, is associated with the development of insulin resistance.