Even short-term, time-restricted eating improves glycaemic control

Restricting food intake to a timed 10-hour, rather than 14-hour, daily time window (time-restricted eating; TRE) for 3 weeks in a small, European, randomised crossover trial, demonstrated improved glucose levels (fasting glucose, 24-hour glucose levels and time spent in normoglycaemia), without demonstrating any changes in insulin sensitivity or any adverse effects. The researchers, led by Professor Patrick Schrauwen, Maastricht, concluded that their findings support the use of TRE as an additional strategy for glycaemic management in those with type 2 diabetes and provide a basis for additional, longer-term studies to clarify the underlying mechanisms. Similar beneficial metabolic findings have previously been achieved with TRE in those with overweight and obesity. This TRE regimen was safe and feasible, and resulted in 0.7 kg weight loss during the 3-week intervention, despite encouragement to maintain weight.

Pam Brown
GP in Swansea

People with and without diabetes in the UK usually spread their daily food intake over at least 14 hours, leaving insufficient time for a true fasting state to be reached in most 24-hour cycles. Eating late into the evening, or irregular eating patterns as may occur with shift work, may increase risk of developing type 2 diabetes, overweight and obesity.

In this randomised, crossover study (Andriessen et al, 2022), 14 people, aged 50–75 years (average age 67.5 years) and BMI ≥25 kg/m², with type 2 diabetes (with or without glucose-lowering medication) undertook two 3-week interventions separated by a 4-week washout period. During the time-restricted eating (TRE) intervention, they ate their normal diet, but all meals were completed within a daytime 10-hour window, with eating finishing by 6 pm, whereas during the control intervention, food intake was spread over at least 14 hours. During the TRE intervention, participants would drink black tea or coffee outside the eating window, and could drink zero-calorie soft drinks in moderation during the evenings.

The effects of eating all food within a daytime 10-hour eating window were compared with spreading food intake over at least 14 hours during the control phase. Participants were able to follow their usual diet and were encouraged to eat similarly, apart from timing, during both parts of the crossover study and during the 4-week washout period.

Participants used continuous glucose monitoring, kept food and sleep diaries, and were encouraged to maintain physical activity at pre-study levels throughout. During the TRE phase, documented eating windows averaged just over 9 hours compared to 13.4 hours in the control phase. Sleep time was comparable during both phrases, around 8 hours. There was a small but significant weight loss of 0.7 kg during the TRE phase, despite participants being encouraged to maintain stable weight.

Twenty-four hour glucose levels, overnight glucose levels, morning fasting glucose and time with high glucose levels all consistently decreased during the TRE period compared with these measures in controls. There was also an increase in time in normal range from 12.2 to 15.1 hours/day. Measured fasting glucose levels were significantly lower (7.6±0.4 vs 8.6±0.4 mmol/L) during the TRE phase than during the control period, even after the same duration of fast before the blood test, which the authors suggested may demonstrate lasting changes in overnight glucose control.

The mechanism for these changes remains unclear, since no improvement in peripheral

ARTICLE

Three weeks of time-restricted eating improves glucose homeostasis in adults with type 2 diabetes but does not improve insulin sensitivity: a randomised crossover trial

Charlotte Andriessen[1] · Ciarán E. Fealy[1] · Anna Veelen[1] · Sten M. M. van Beek[1] · Kay H. M. Roumans[1] · Niels J. Connell[1,2] · Julian Mevenkamp[1,2,3] · Esther Moonen-Kornips[1] · Bas Havekes[3] · Vera B. Schrauwen-Hinderling[1,3] · Joris Hoeks[1] · Patrick Schrauwen[1]

Abstract
Aims/hypothesis Time-restricted eating (TRE) is suggested to improve metabolic health by limiting food intake to a defined time window, thereby prolonging the overnight fast. This prolonged fast is expected to lead to a more pronounced depletion of hepatic glycogen stores overnight and might improve insulin sensitivity due to an increased need to replenish nutrient storage. Previous studies showed beneficial metabolic effects of 6–8 h TRE regimens in healthy, overweight adults under controlled conditions. However, the effects of TRE on glucose homeostasis in individuals with type 2 diabetes are unclear. Here, we extensively investigated the effects of TRE on hepatic glycogen levels and insulin sensitivity in individuals with type 2 diabetes.
Methods Fourteen adults with type 2 diabetes (BMI 30.5±4.2 kg/m², HbA₁c 46.1±7.2 mmol/mol [6.4±0.7%]) participated in a 3 week TRE (daily food intake within 10 h) vs control (spreading food intake over ≥14 h) regimen in a randomised, crossover trial design. The study was performed at Maastricht University, the Netherlands. Eligibility criteria included diagnosis of type 2 diabetes, intermediate chronotype and absence of medical conditions that could interfere with the study execution and/or outcome. Randomisation was performed by a study-independent investigator, ensuring that an equal amount of participants started with TRE and CON. Due to the nature of the study, neither volunteers nor investigators were blinded to the study interventions. The quality of the data was checked without knowledge on intervention allocation. Hepatic glycogen levels were assessed with ¹³C-MRS and insulin sensitivity was assessed using a hyperinsulinaemic–euglycaemic two-step clamp. Furthermore, glucose homeostasis was assessed with 24 h continuous glucose monitoring device. Secondary outcomes included 24 h energy expenditure and substrate oxidation, hepatic lipid content and skeletal muscle mitochondrial capacity.
Results Results are depicted as mean ± SEM. Hepatic glycogen content was similar between TRE and control condition (0.15 ±0.01 vs 0.15±0.01 AU, p=0.06). AₜUC was not significantly affected by TRE (19.6±1.8 vs 17.7±1.8 μmol kg⁻¹ min⁻¹ in TRE vs control, respectively, p=0.10). Hepatic and peripheral insulin sensitivity also remained unaffected by TRE (p=0.67 and p=0.25, respectively). Yet, insulin-induced non-oxidative glucose disposal was increased with TRE (non-oxidative glucose disposal 4.3±1.1 vs 1.5±1.7 μmol kg⁻¹ min⁻¹, p=0.04). TRE increased the time spent in the normoglycaemic range (15.1±0.8 vs 12.2±1.1 h per day, p=0.01), and decreased fasting glucose (7.6±0.4 vs 8.6±0.4 mmol/l, p=0.03) and 24 h glucose levels (6.8±0.2 vs 7.6±0.3 mmol/l, p=0.01). Energy expenditure over 24 h was unaffected; nevertheless, TRE decreased 24 h glucose oxidation (260.2±7.4 vs 277.8±10.7 g/day, p=0.04). No adverse events were reported that were related to the interventions.

☐ Patrick Schrauwen
 p.schrauwen@maastrichtuniversity.nl

[1] Department of Nutrition and Movement Sciences, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, Maastricht, the Netherlands

[2] Department of Radiology and Nuclear Medicine, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, Maastricht, the Netherlands

[3] Department of Internal Medicine, Division of Endocrinology, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, Maastricht, the Netherlands

or hepatic insulin sensitivity (which was expected), nor changes in energy metabolism, or fat or glycogen content in the liver could be measured. The authors proposed that part of the improvements may result from weight loss, since there was a significant 0.7 kg difference between the TRE and control groups over the 3 weeks. However, it is thought that this small amount of weight loss would not have triggered such significant glucose changes, and similar beneficial metabolic findings have been seen with TRE without weight loss (Sutton et al, 2018).

Previous studies have demonstrated both weight loss and improved metabolic control using very short eating windows of 6–8 hours, but this 10-hour window was thought to be more achievable and sustainable in longer term studies.

The study was small, the crossover periods short (3 weeks), and some participants were on medication and some not. The authors conclude that these data highlight the potential benefits of TRE in type 2 diabetes and that follow-up, larger, longer duration studies, perhaps with different daytime eating windows, would be appropriate. TRE is safe, fast and easy to teach, does not require dietary changes, calorie counting or numeracy skills, and can be shared with people online or by leaflet, making it a useful additional option for our toolkit.

A useful recent review of human intermittent fasting studies (Varady et al, 2022), including alternate day fasting, 5:2 fasting and TRE, summarises the current state of the evidence base.

Andriessen C, Fealy CE, Veelen A et al (2022) Three weeks of time-restricted eating improves glucose homoeostasis in adults with type 2 diabetes but does not improve insulin sensitivity: a randomised crossover trial. *Diabetologia* 25 Jul [Epub ahead of print]

Sutton E, Beyl R, Early K et al (2018) Early time-restricted feeding improves insulin sensitivity, blood pressure and oxidative stress even without weight loss in men with pre-diabetes. *Cell Metab* **27**: 1212–21

Varady KA, Cienfuegos S, Ezpeleta M et al (2022) Clinical application of intermittent fasting for weight loss: progress and future directions. *Nat Rev Endocrinol* **18**: 309–21