Aetiology of type 2 diabetes: twin-cycle hypothesis

- Positive calorie balance
  - ↑ liver fat
  - ↑ basal insulin secretion
- Pre-existing insulin resistance
- Resistance to insulin suppression of HGP
  - ↑ VLDL triglyceride
- ↑ plasma glucose
- ↓ acute insulin response to food

Liver cycle
- ↑ basal insulin secretion
- Resistance to insulin suppression of HGP
- ↑ plasma glucose

Pancreas cycle
- ↑ islet triglyceride
- ↓ acute insulin response to food
BMI distribution of participants – Start of UK Prospective Diabetes Study

Taylor & Holman, Clin Sci 128: 405-410 2015
BMI distribution of individuals with type 2 diabetes

Taylor & Holman, Clin Sci 128: 405-410 2015
The top panel shows the BMI distribution of individuals at diagnosis of type 2 diabetes.

However, a generation ago, the alter egos of those people would have been ~15 mg lighter and would not have had diabetes (blue dots).

OR –

If those people with T2DM lose 15kg, they lose their type 2 diabetes
Take 3 individuals for example. Each lost 15kg and reversed their diabetes. But by BMI criteria they remain obese, overweight and normal respectively.

Each individual must have crossed a threshold of fat mass, personal to them.
explains the “Why me” factor – individuals have personal capacity to store fat safely. If the PFT is exceeded, T2DM slowly develops.
Amount of weight lost and effect on reversal of diabetes – 92 people after bariatric surgery

Steven, Carey, Small & Taylor; Diabetic Med 2014