# Aetiology of type 2 diabetes: twin-cycle hypothesis



Why me ?

Positive calorie balance

++

Pre-existing insulin resistance

Why me ?

↑ liver fat

**Liver cycle**

Resistance to insulin suppression of

Why me ?

↑ VLDL triglyceride

↑ basal insulin secretion

↑ plasma glucose

**Pancreas cycle**

↑ islet triglyceride

↓ acute insulin response

Why me ?
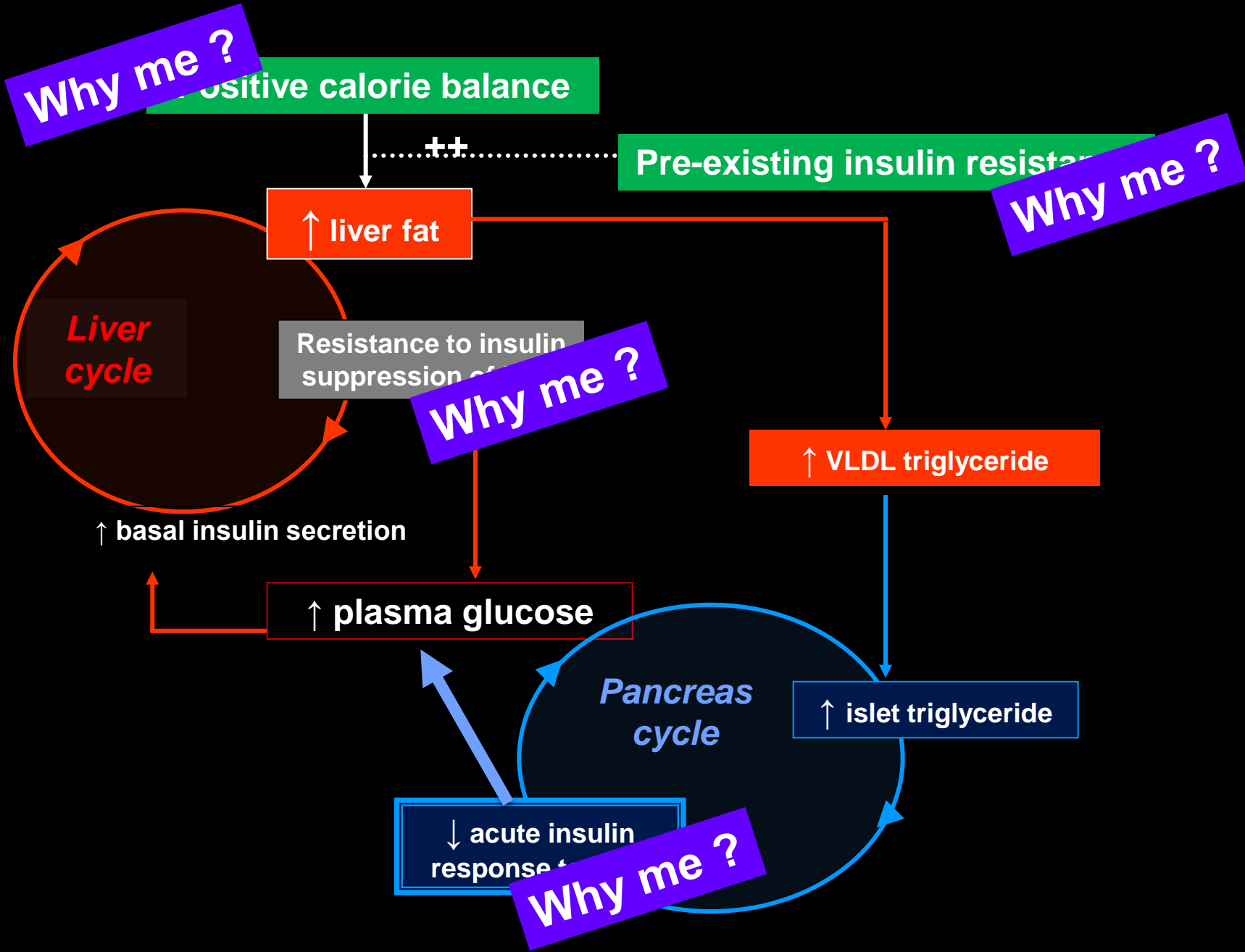
# BMI distribution of participants –
# Start of UK Prospective Diabetes Study
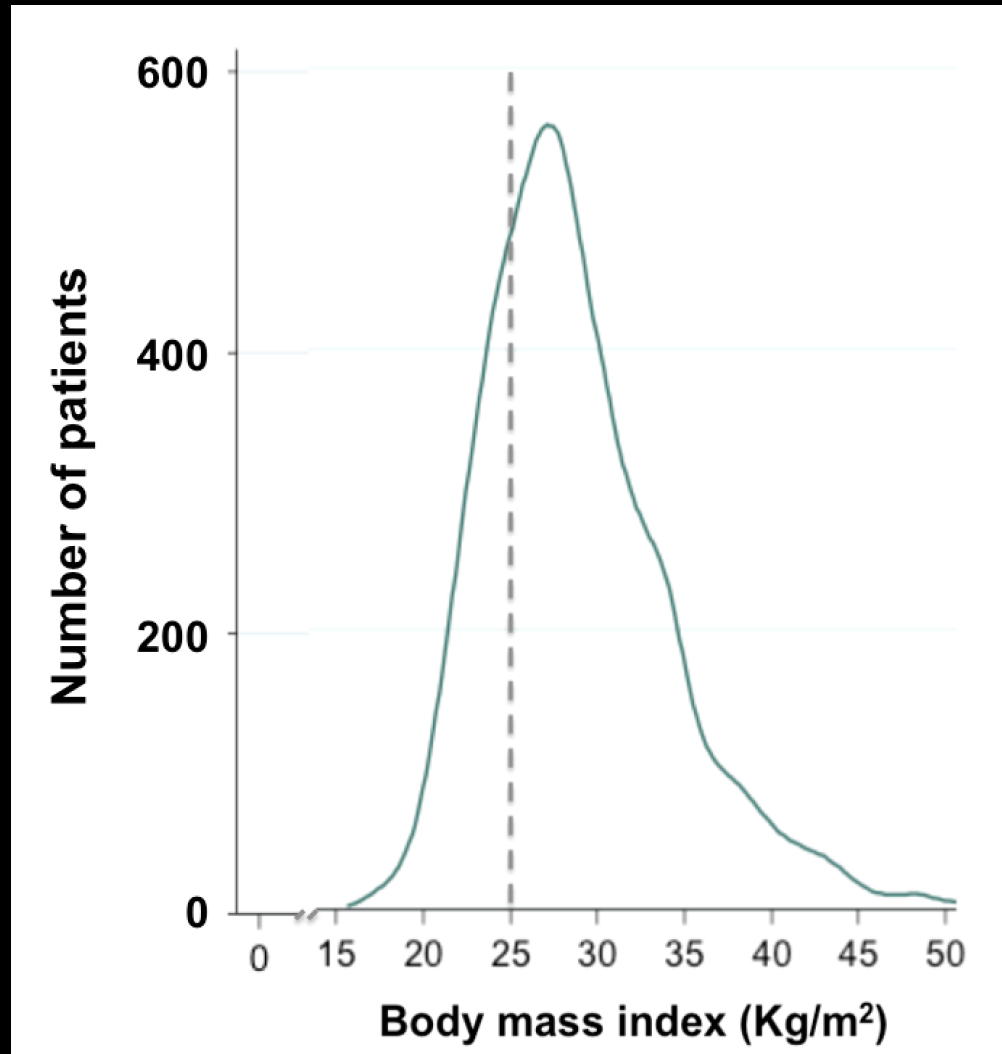
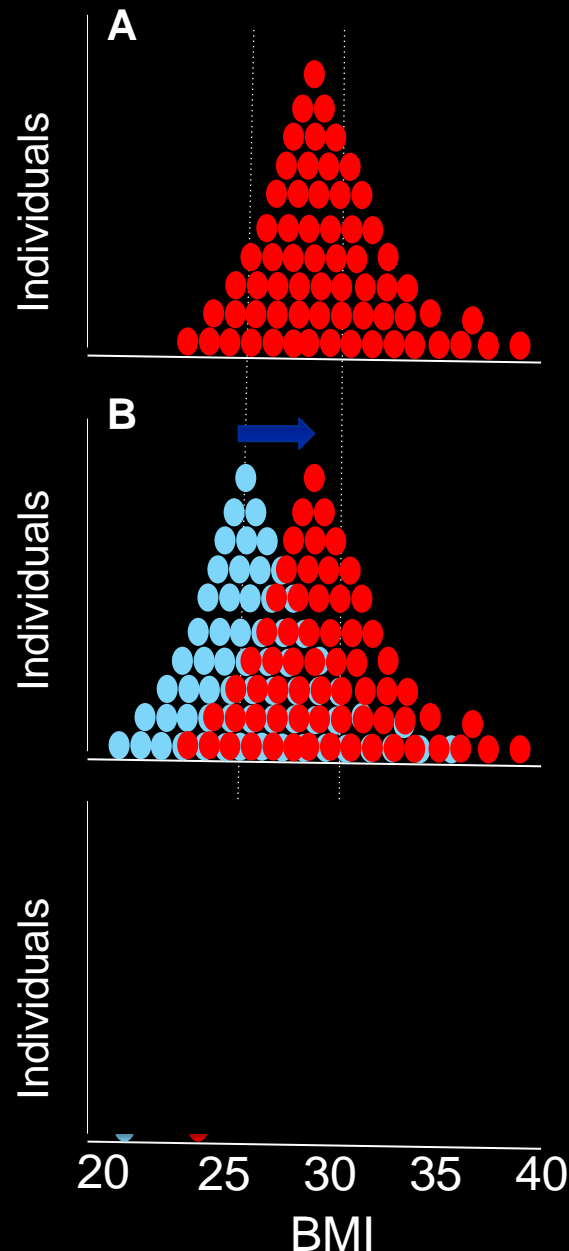# BMI distribution of individuals with type 2 diabetes
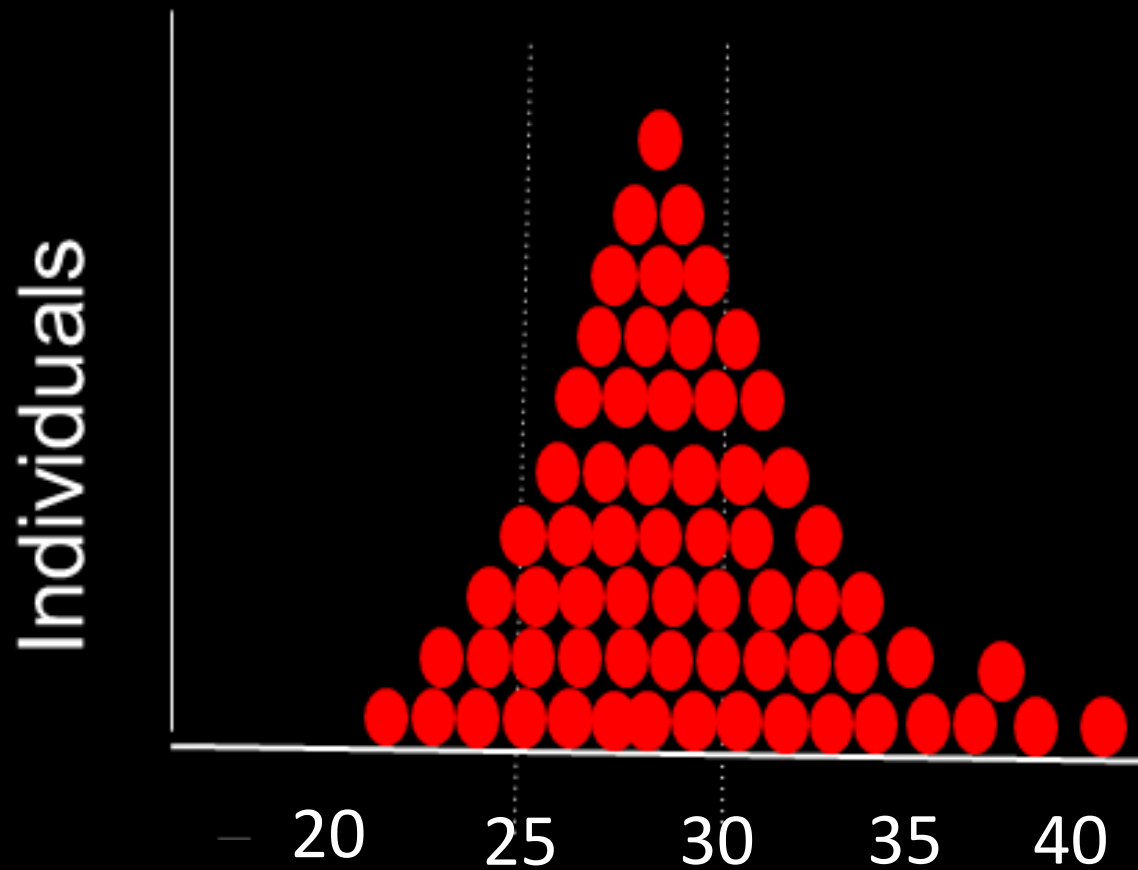
# Personal vs population

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).
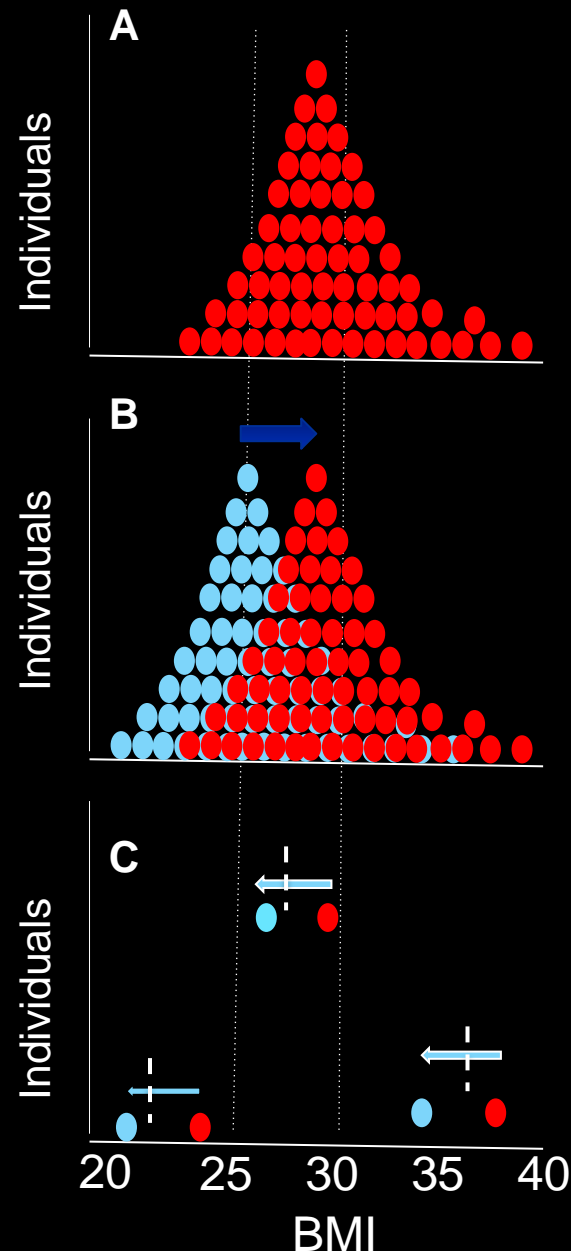
OR –

If those people with T2DM lose 15kg, they lose their type 2 diabetes

# Personal vs population

Take 3 individuals for example.
Each lost 15kg and reversed their diabetes. But by BMI criteria they remain obese, overweight and normal respectively.
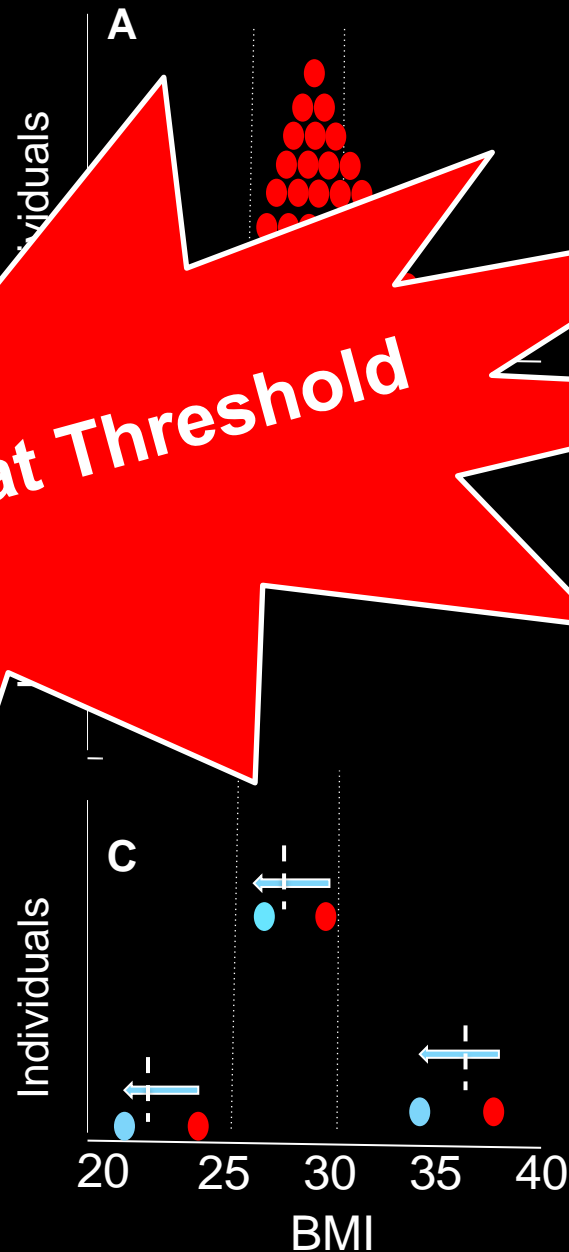
Each individual must have crossed a threshold of fat mass, personal to them.



*Taylor & Holman, Clin Sci* 128: 405-410 *2015*

# Personal vs population



**The Personal Fat Threshold**

explains the "Why me" factor – indivduals have personal capacity to store fat safely. If the PFT is exceeded, T2DM slowly develops.

*Taylor & Holman, Clin Sci* **128**: 405-410 *2015*

# Amount of weight lost and effect on reversal of diabetes – 92 people after bariatric surgery