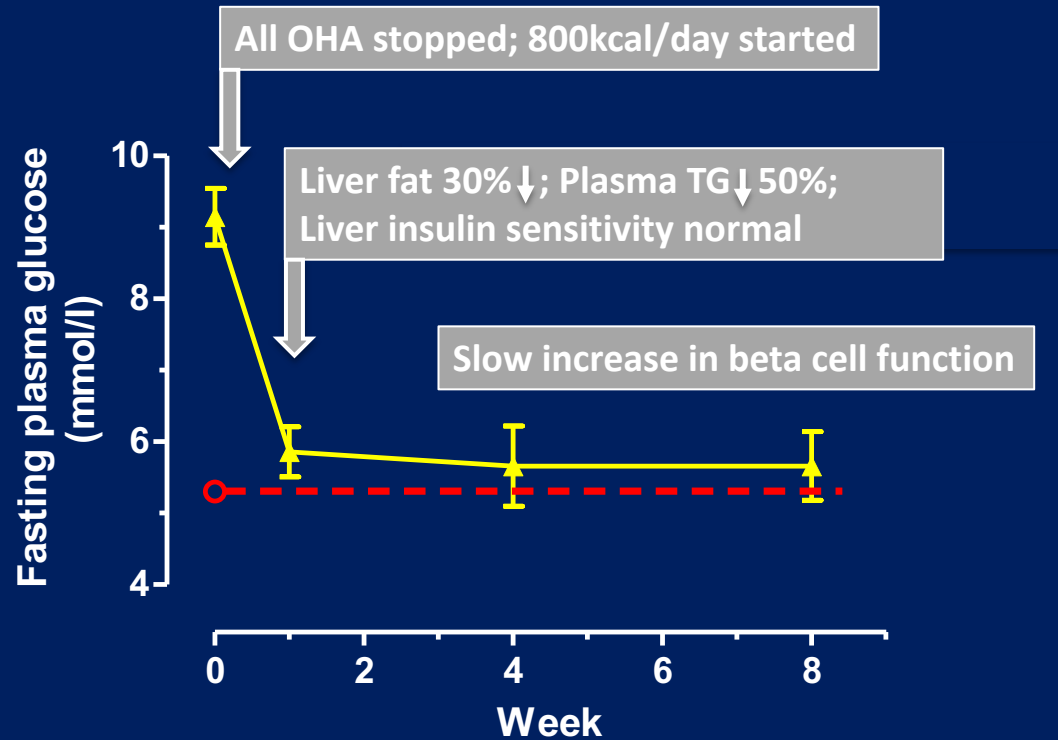


Proving the Twin Cycle Hypothesis: 2011 - The COUNTERPOINT study

Type 2 diabetes
0-4 years duration



Type 2 Diabetes

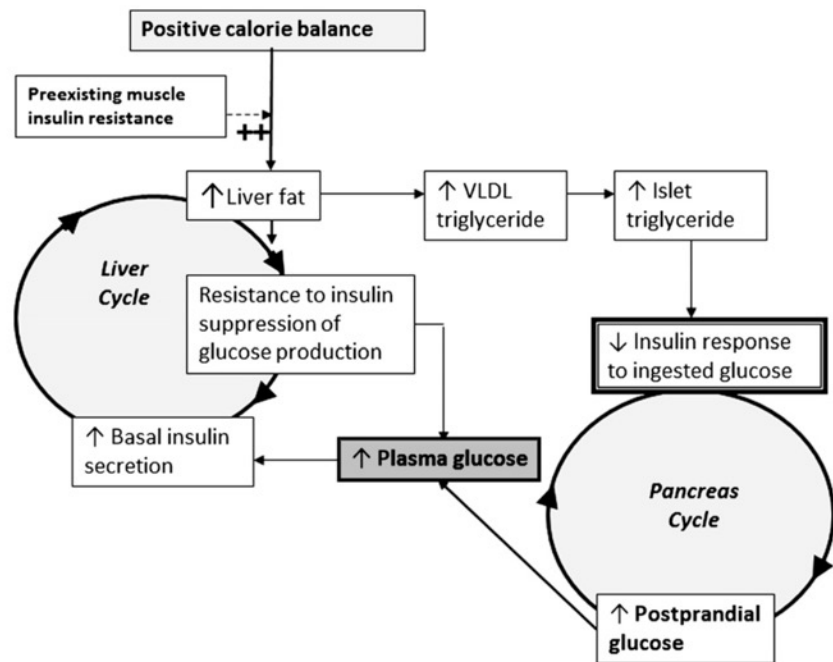
Etiology and reversibility

ROY TAYLOR, MD, FRCP

Reversal of type 2 diabetes to normal metabolic control by either bariatric surgery or hypocaloric diet allows for the time sequence of underlying pathophysiologic mechanisms to be observed.

Type 2 diabetes has to progress despite treatment, with 50% requiring insulin therapy (1). This seemingly in

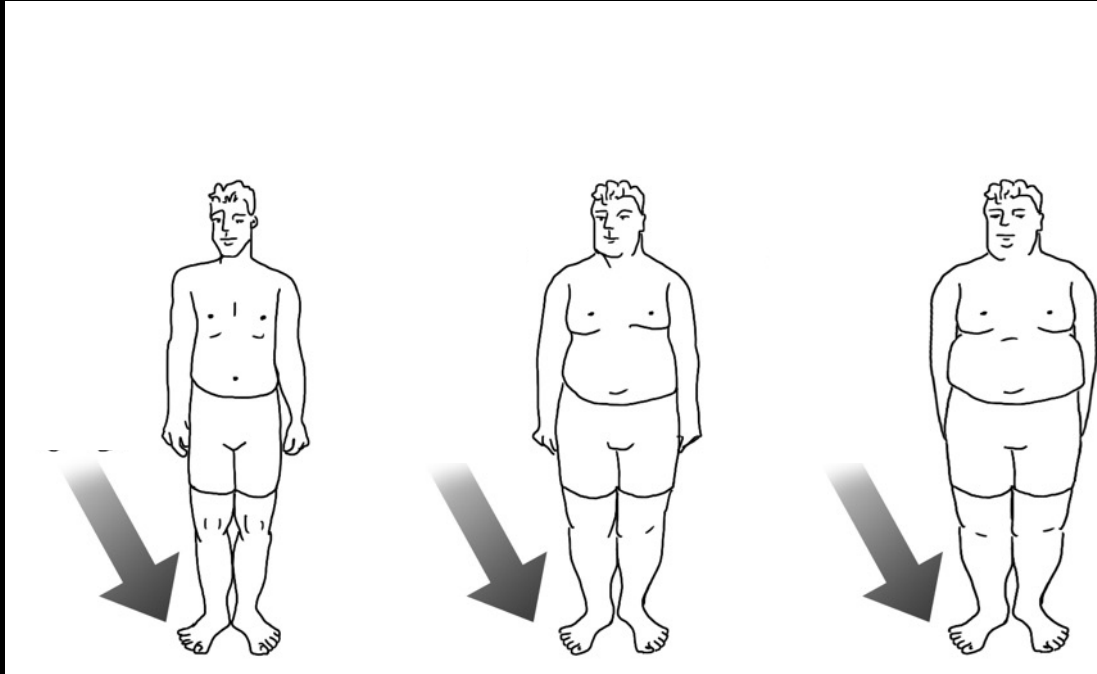
Etiology of type 2 diabetes



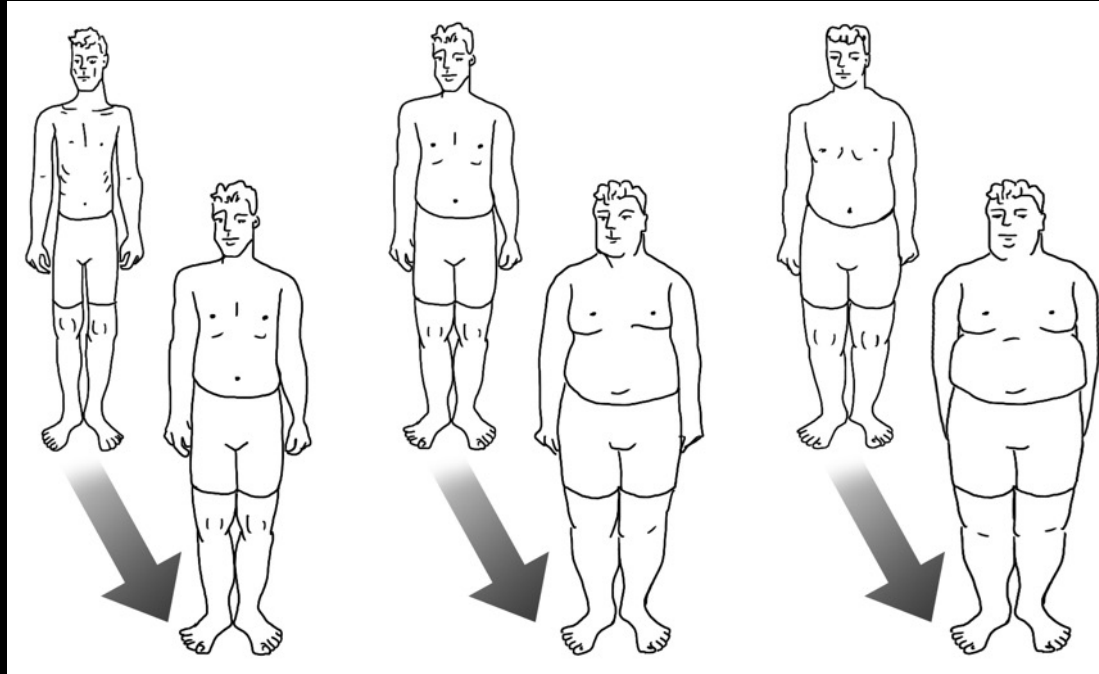
The personal fat threshold hypothesis

Individuals have differing
susceptibility to fat excess

The personal fat threshold

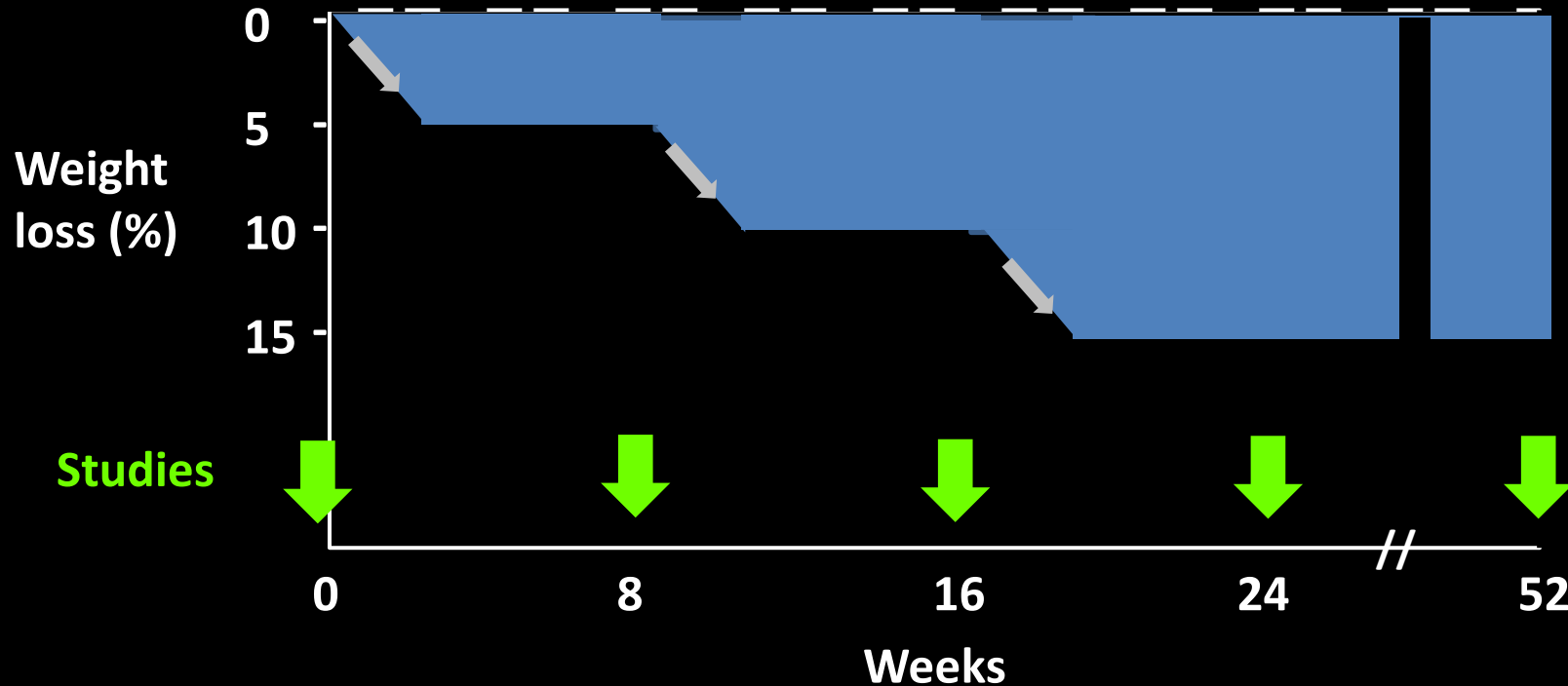


The personal fat threshold



ReTUNE protocol – Step-wise weight loss in T2DM

Baseline BMI 21-27kg/m²



Participants

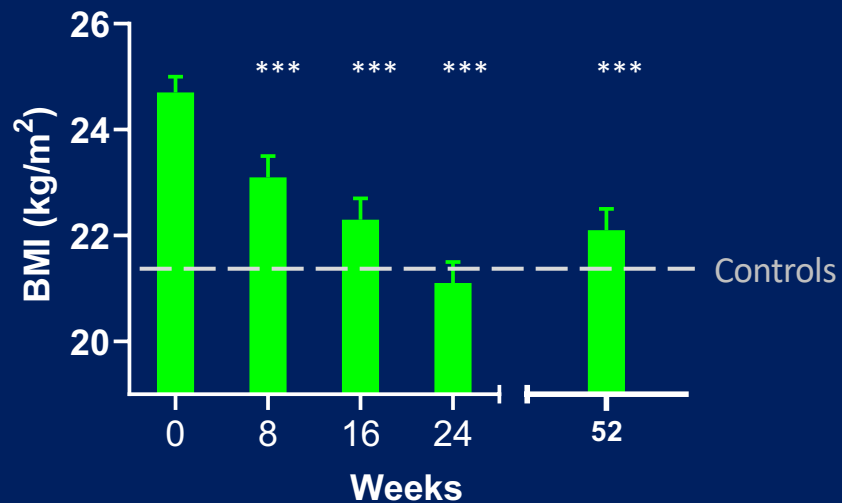
T2DM duration <6y; BMI 21-27kg/m²

	T2DM (n=20)	Controls (n=20)
Age (y)	59.0 ± 7.0	58.0 ± 10.5
BMI (kg/m ²)	24.8 ± 1.7	21.5 ± 0.5*
Weight (kg)	71.8 ± 12.6	61.5 ± 2.2*
Sex (F/M)	13/7	13/7
Duration of diabetes (y)	2.8 ± 1.9	-
HbA1c (mmol/mol)	54 ± 6	37 ± 3

*Post-weight
loss matching

N=24: 4 found not to be T2DM - 2 monogenic DM + 2 type 1 DM

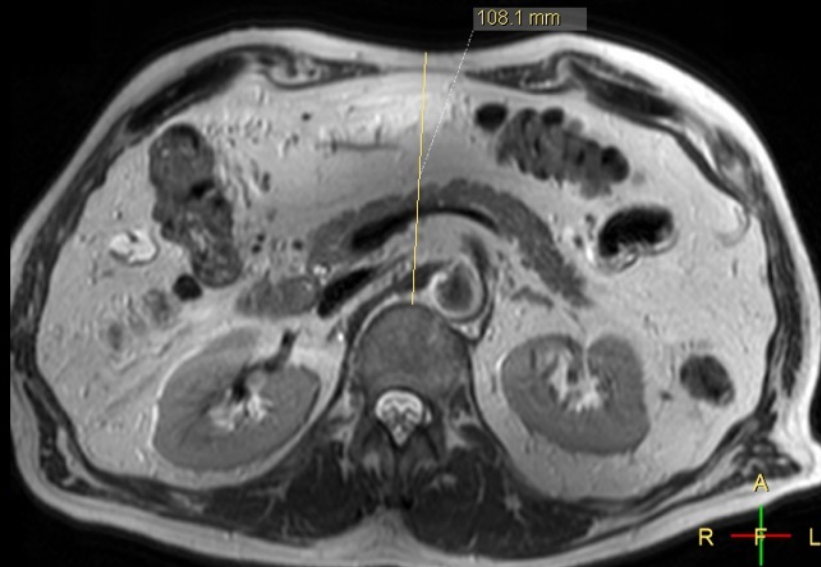
Weight loss



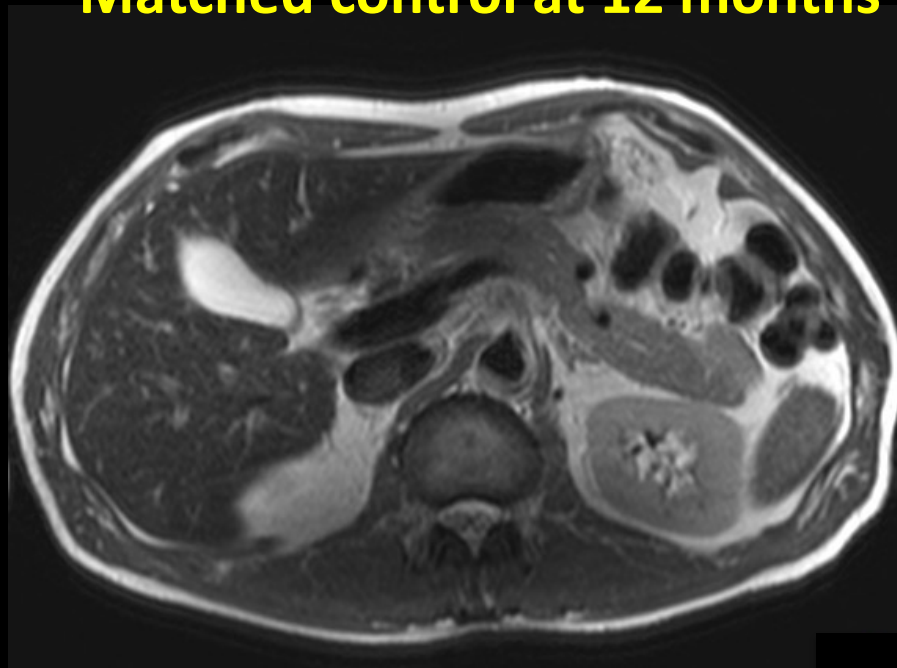
*** $p < 0.001$

MRI fat maps of abdomen

Ex-T2DM at 12 months

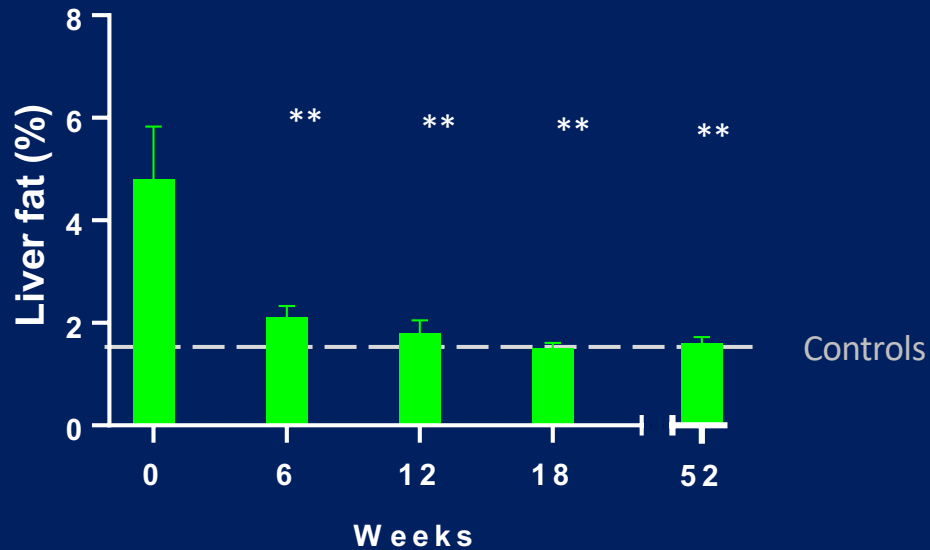


Matched control at 12 months



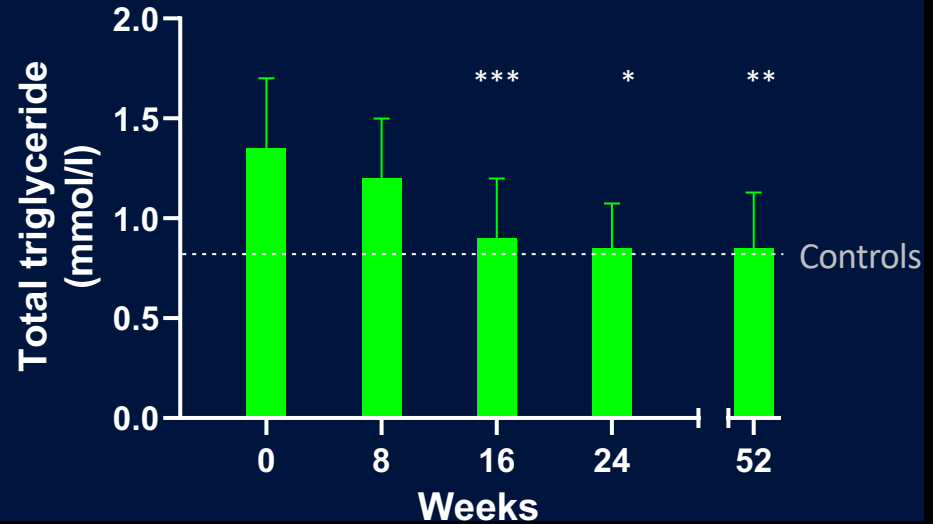
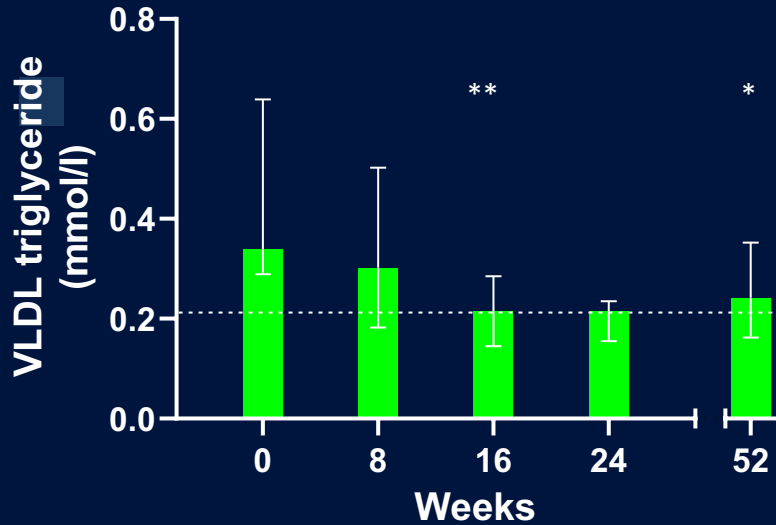
% Body fat – 32% at baseline; 28% at 1 year [controls 25%]

Liver fat



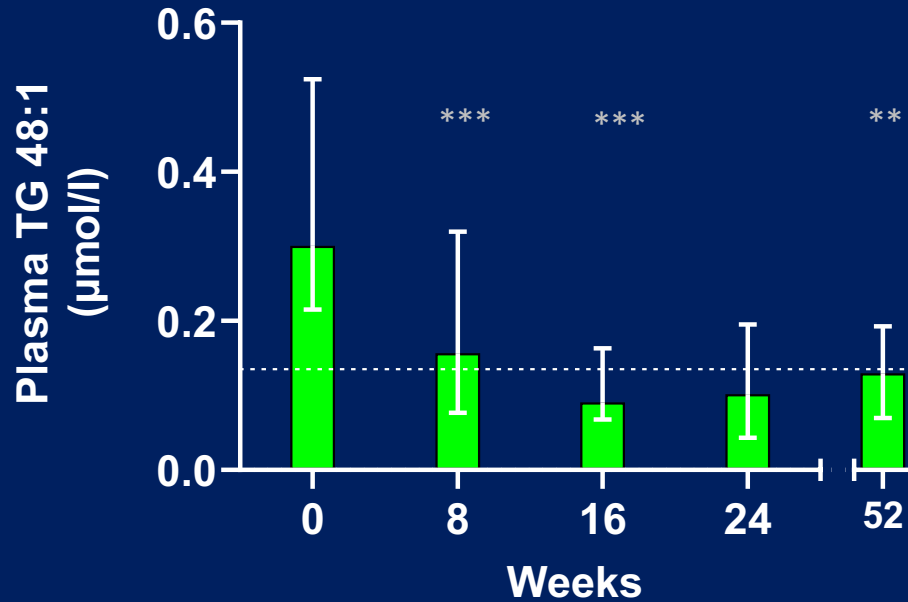
**p<0.01

Plasma VLDL triglyceride

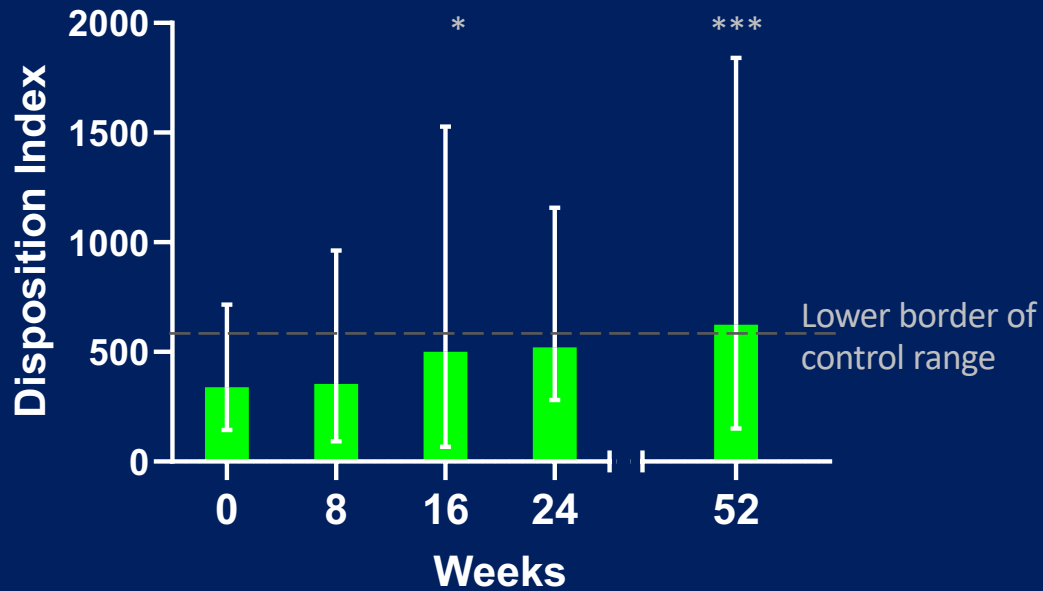


*p<0.05 **p<0.01 ***p<0.001

Measure of *de novo* lipogenesis



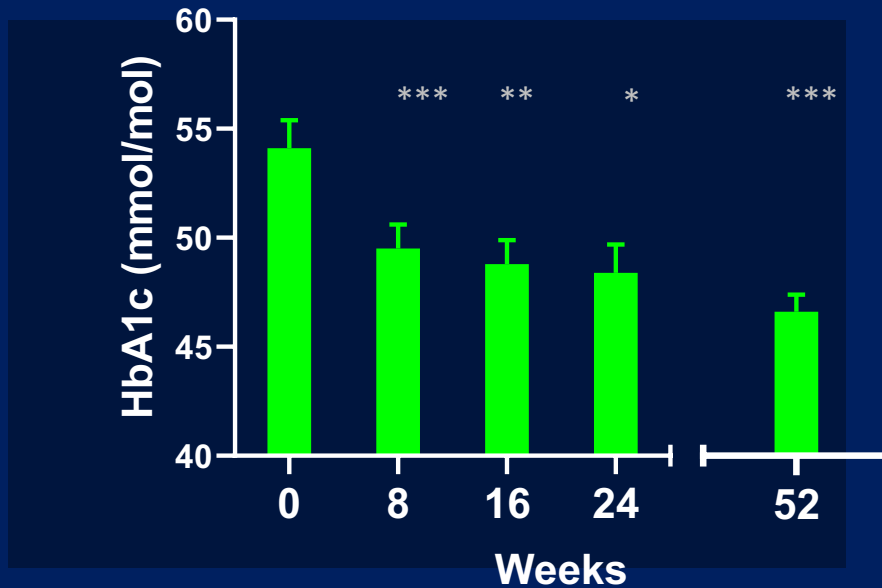
Change in Insulin Secretion



* $p < 0.02$

** $p = 0.005$

Change in HbA1c

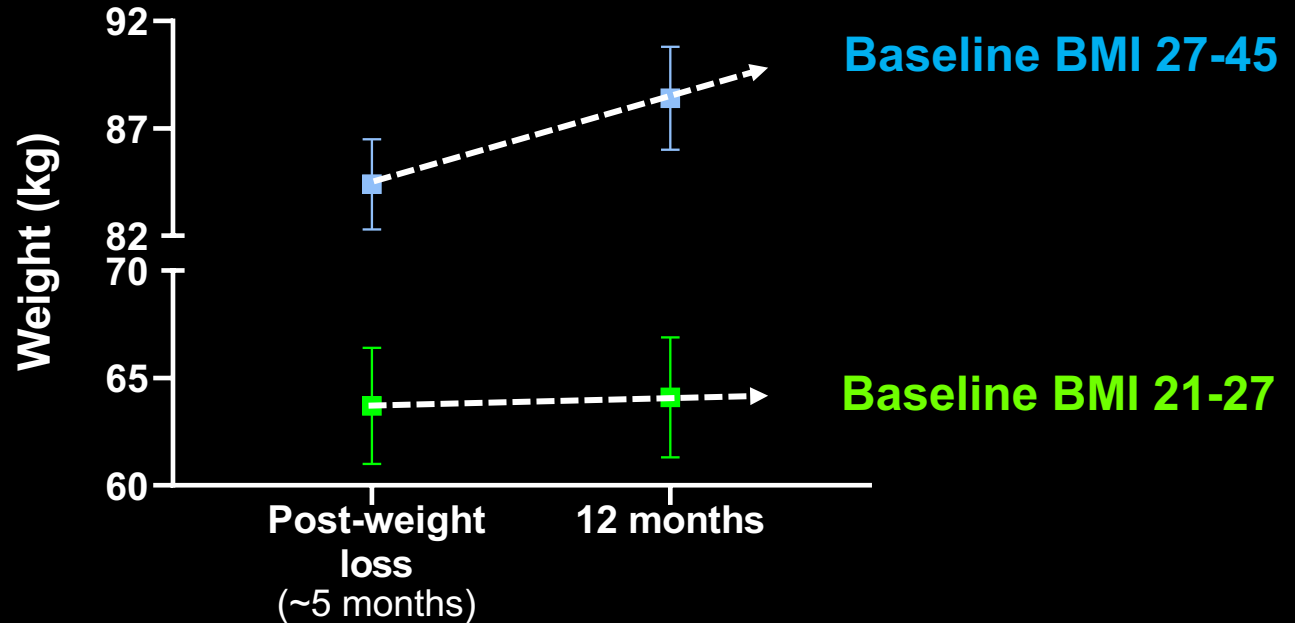


Change in HbA1c



70% of 'slim' people achieved remission with weight loss

Slimmer people have no problem in preventing weight regain under similar follow up



Implications for T2DM management in 'normal' and raised BMI

Information at diagnosis

Offer a choice - ?return to health

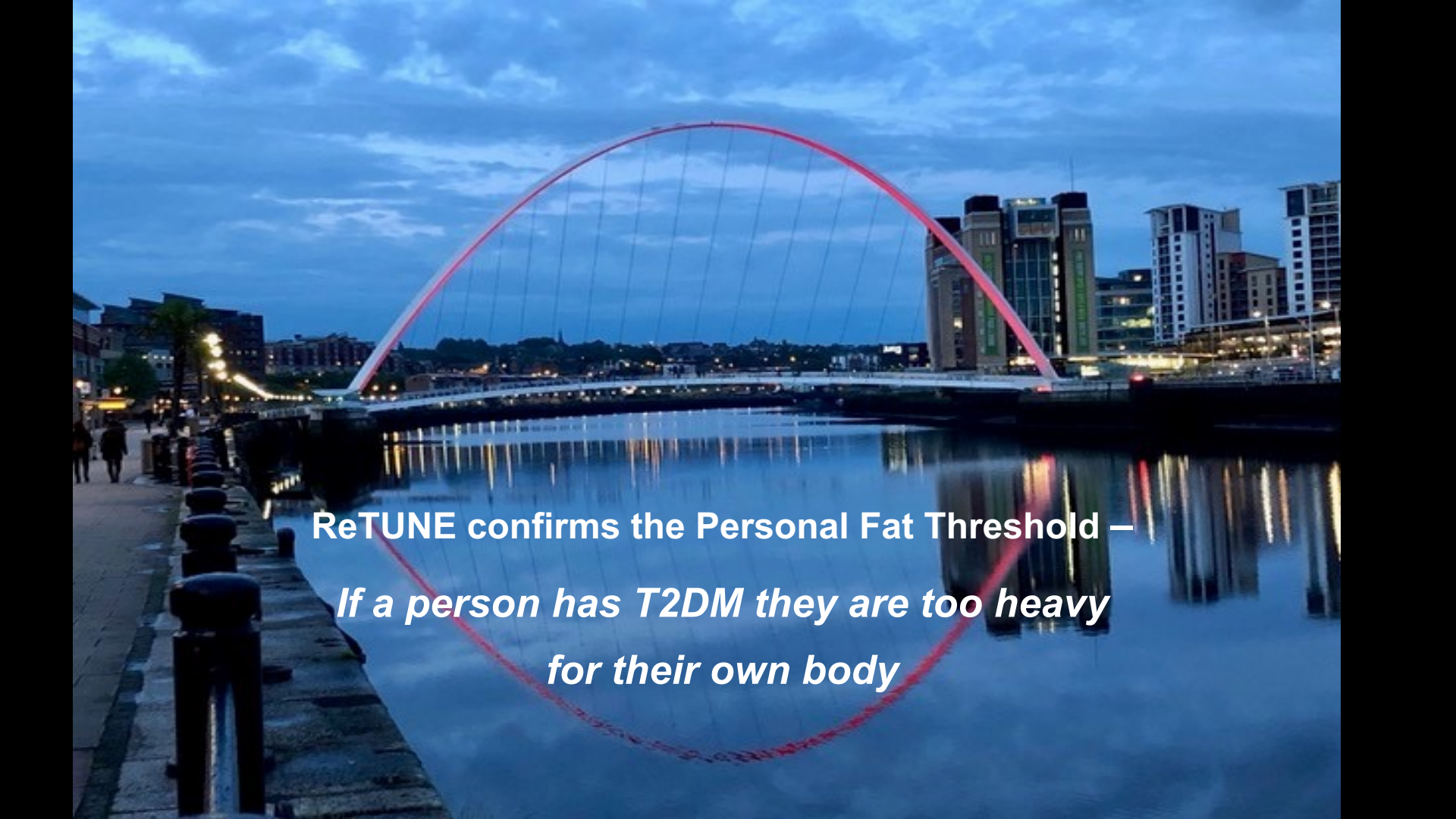
Approach to target-driven weight loss

Choice of hypoglycaemic agent

What is T2DM ?

T2DM
is a state of
excess fat inside
liver and pancreas

In people with
susceptible beta cells



ReTUNE confirms the Personal Fat Threshold –
If a person has T2DM they are too heavy
for their own body