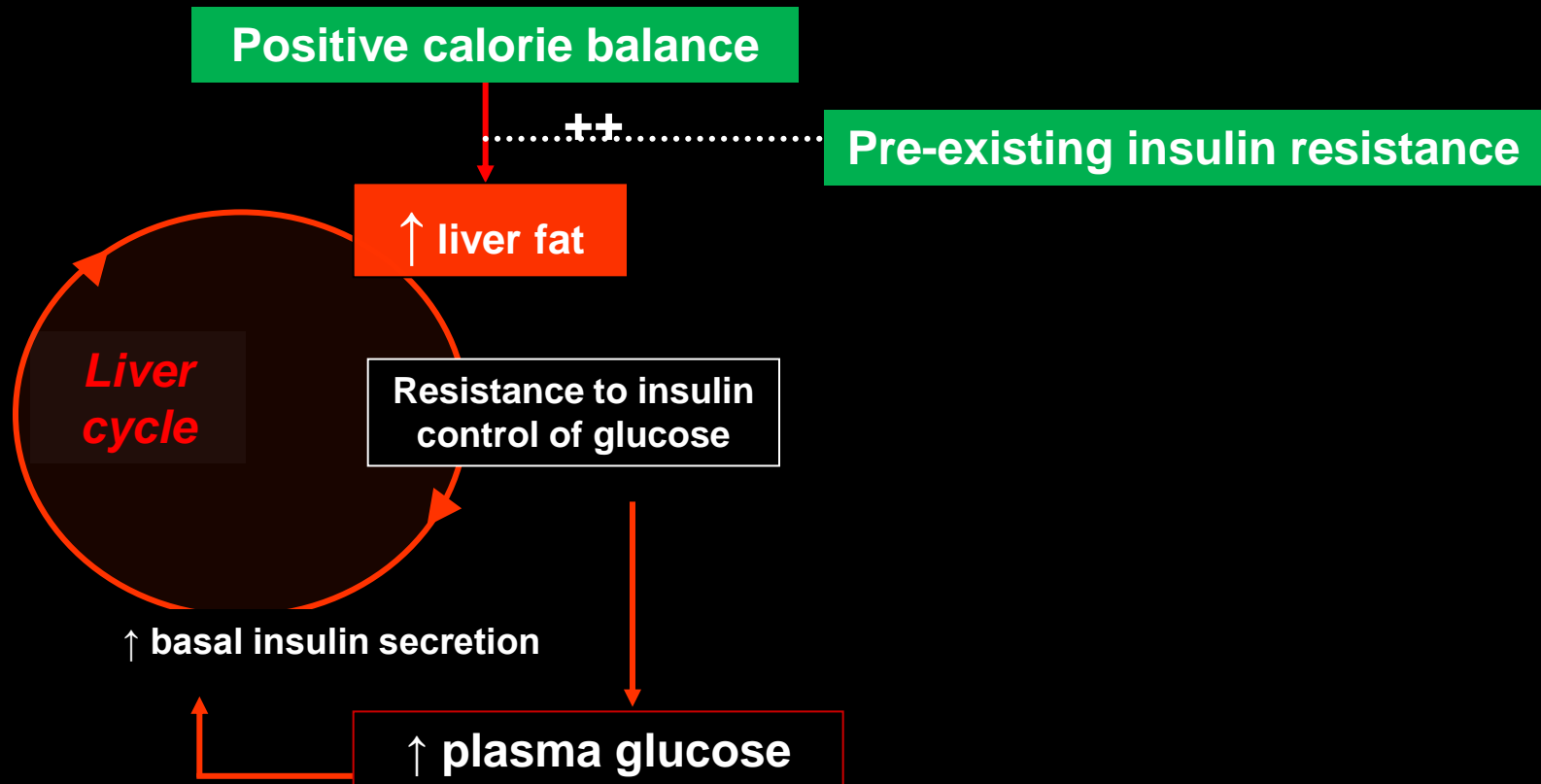
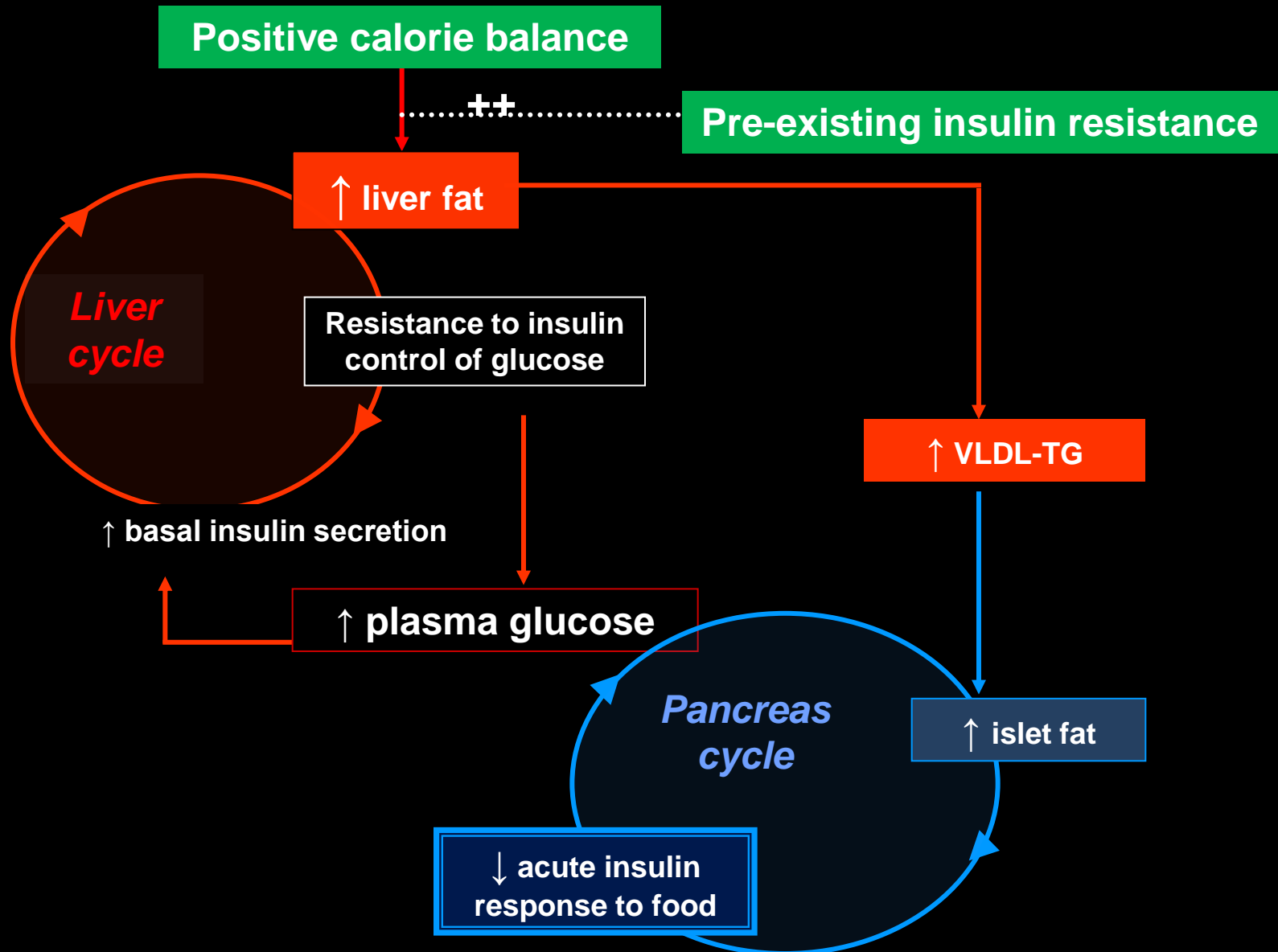


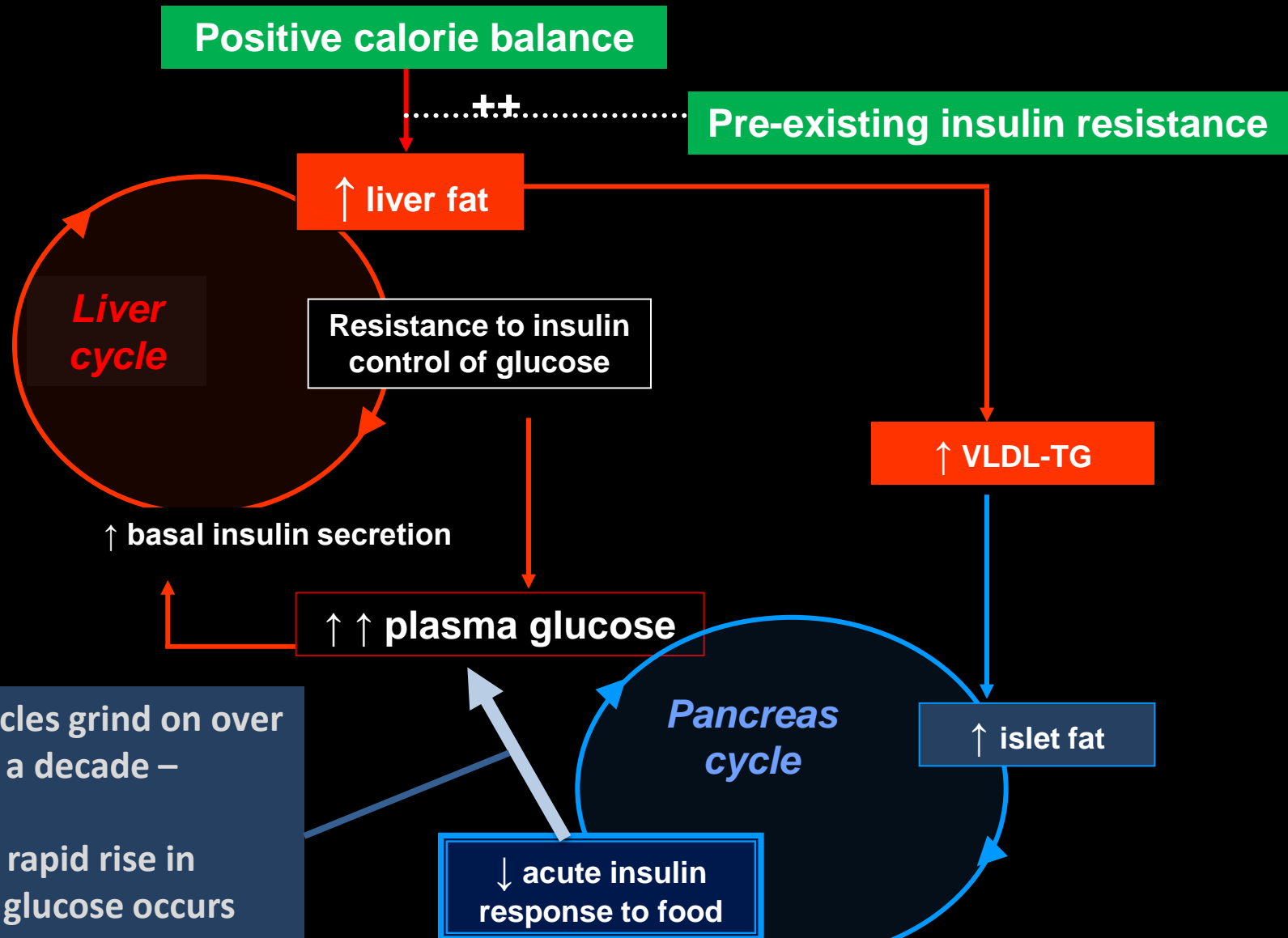
# The twin-cycle hypothesis: type 2 diabetes



# The twin-cycle hypothesis: type 2 diabetes



# The twin-cycle hypothesis: type 2 diabetes



# The twin cycle hypothesis

Substantial weight loss in people with type 2 diabetes will:

## *Liver*

Decrease fat –  
improve insulin action  
and  
normalise overnight  
blood sugar

*and*

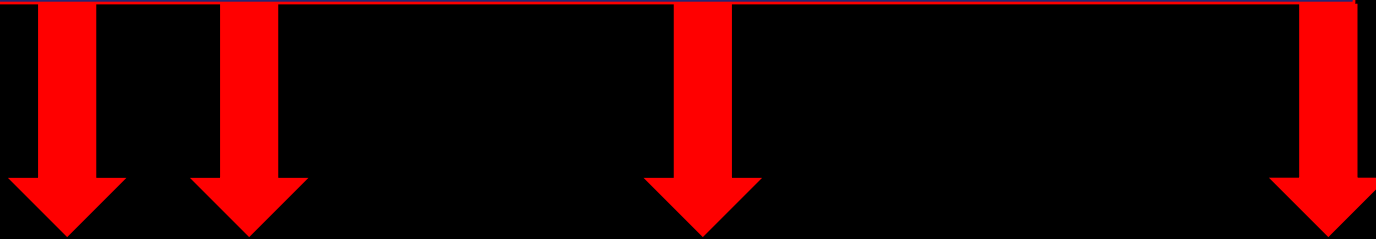
## *Pancreas*

Decrease fat –  
normalise the insulin  
response to eating

# The Counterpoint Study

(Counteracting Pancreatic inhibitiOn of Insulin secretion by Triglyceride)

***Tests of:*** Beta cell function  
Liver and muscle insulin sensitivity  
Liver and pancreas fat

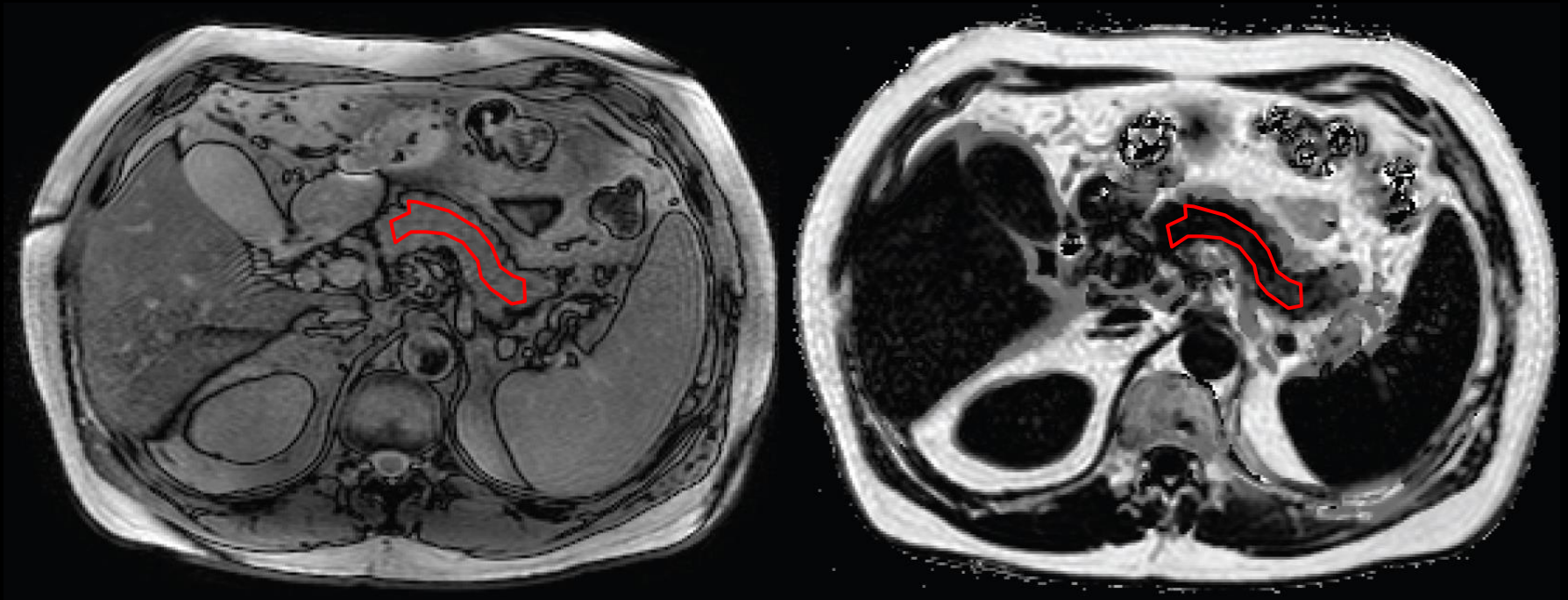


Very low calorie diet  
(~800 kcal/day)

0 1 4 8

Weeks

# New magnetic resonance method allows measurement of organ fat content



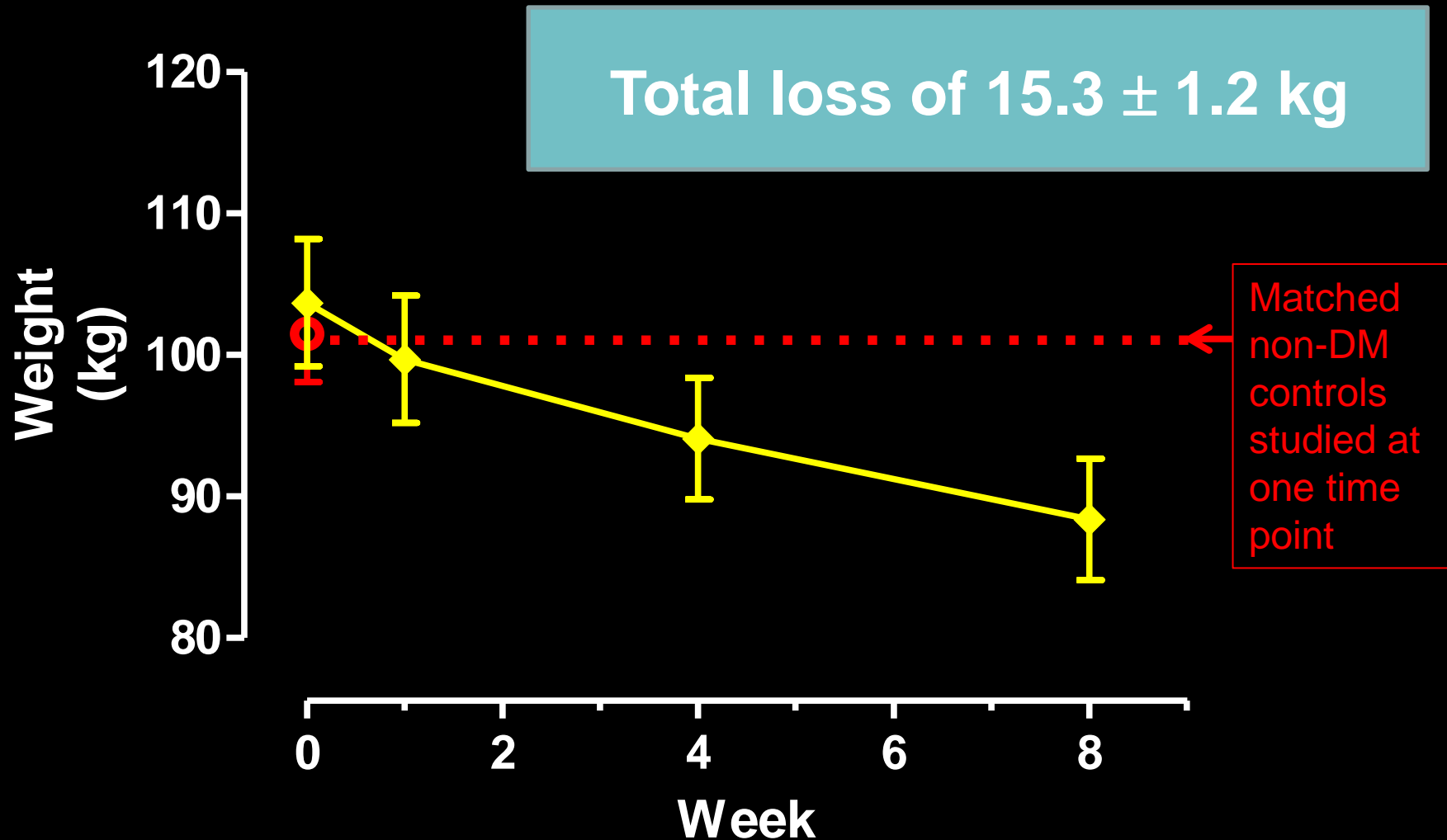
Detailed anatomical MRI scan

Fat map co-localised with scan

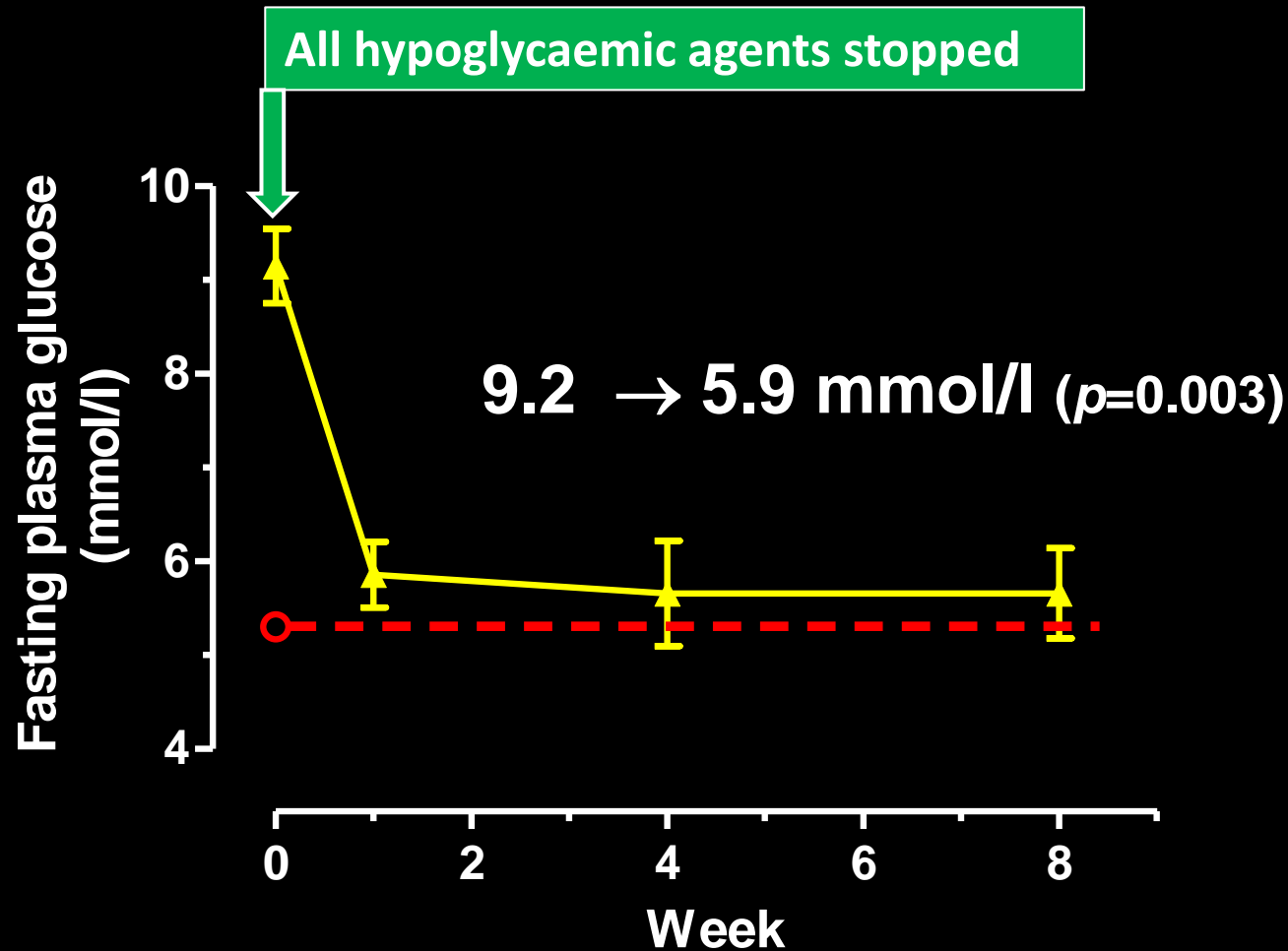
Bland-Altman reproducibility coefficients: Liver 0.5; Pancreas 0.9

Method based on 3-point Dixon developed by Dr Kieren Hollingsworth

# Body weight change during Counterpoint

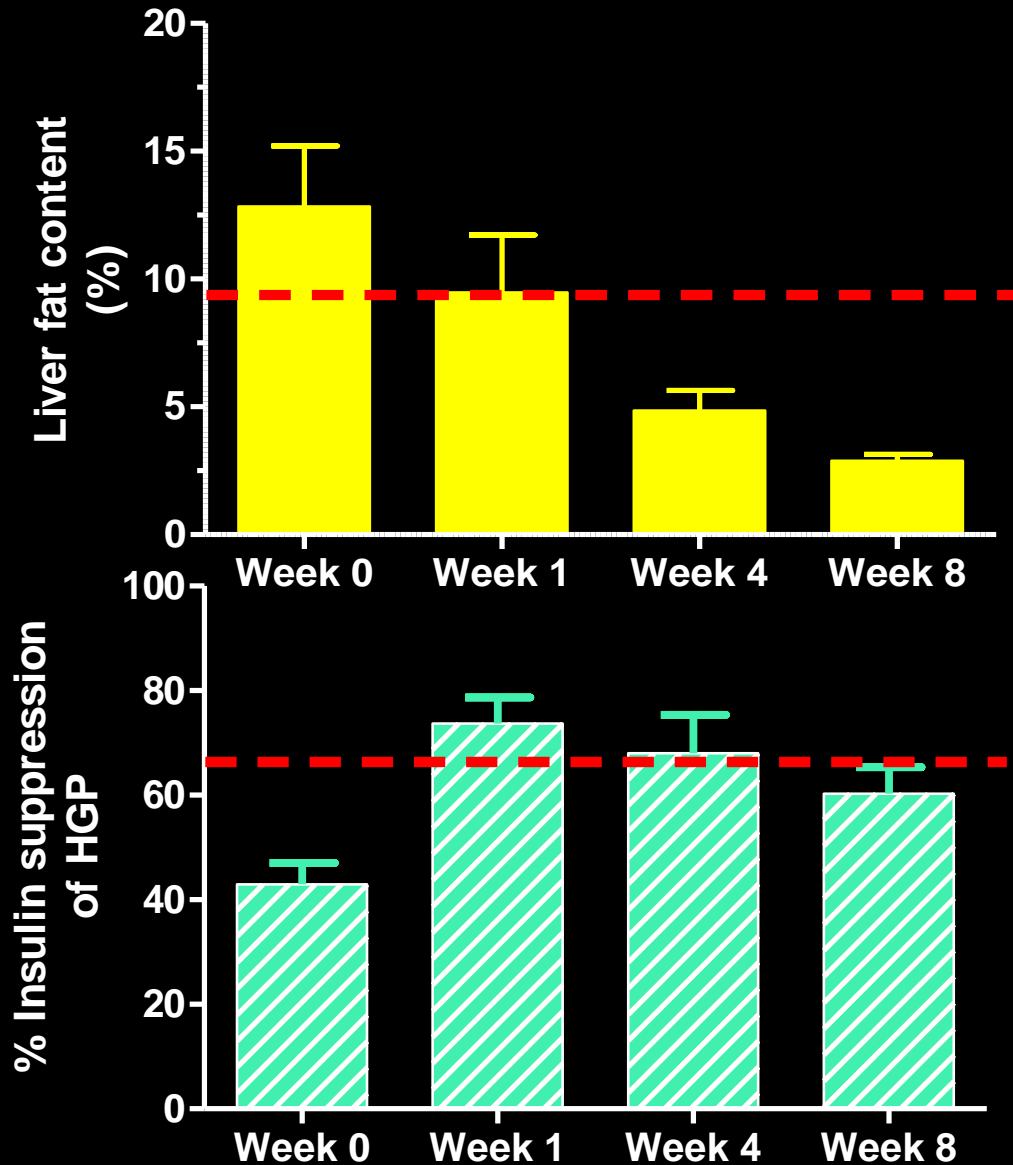


# Counterpoint: Effect of VLCD on fasting glucose





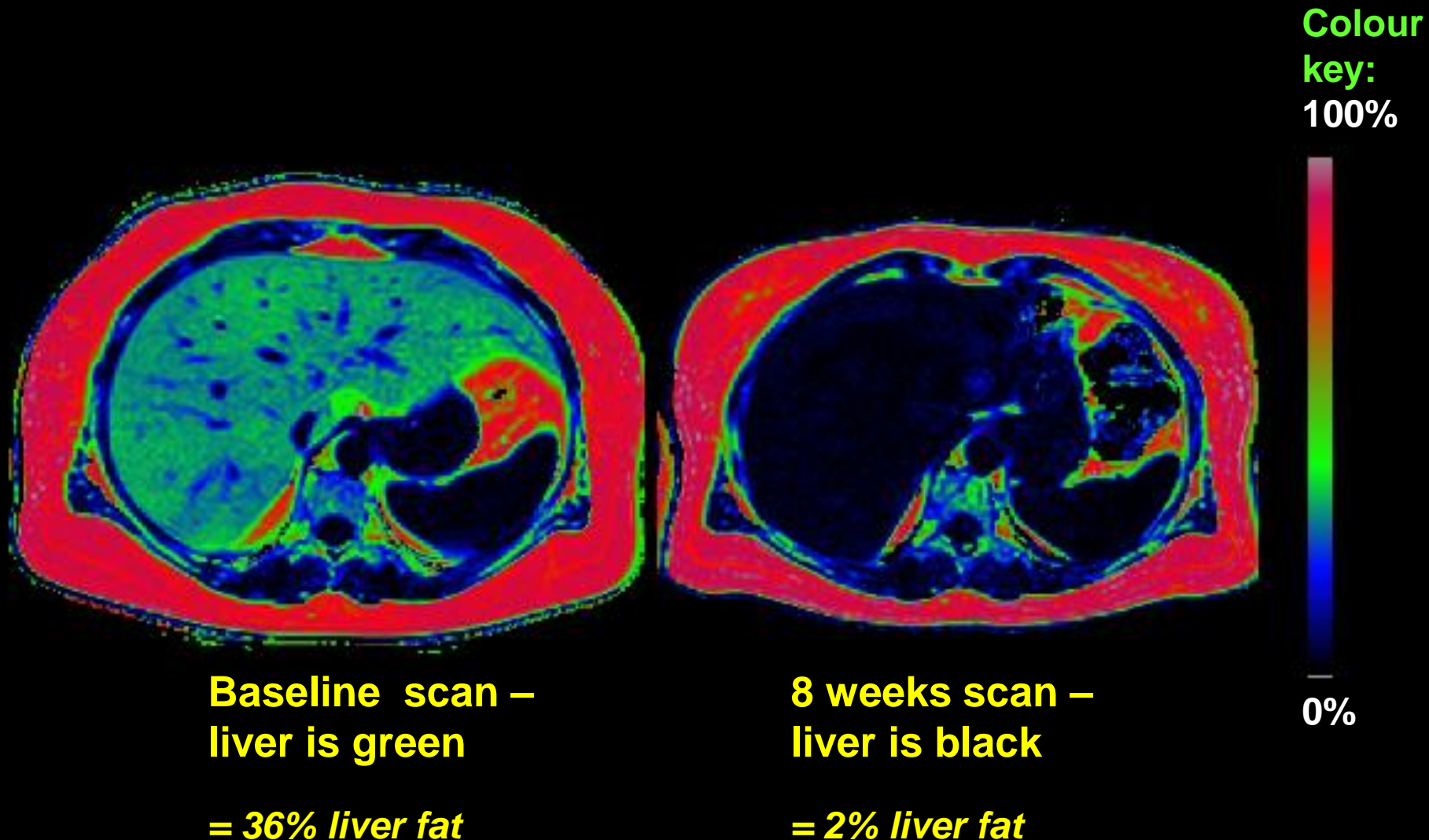
# Liver fat and liver insulin sensitivity - Counterpoint



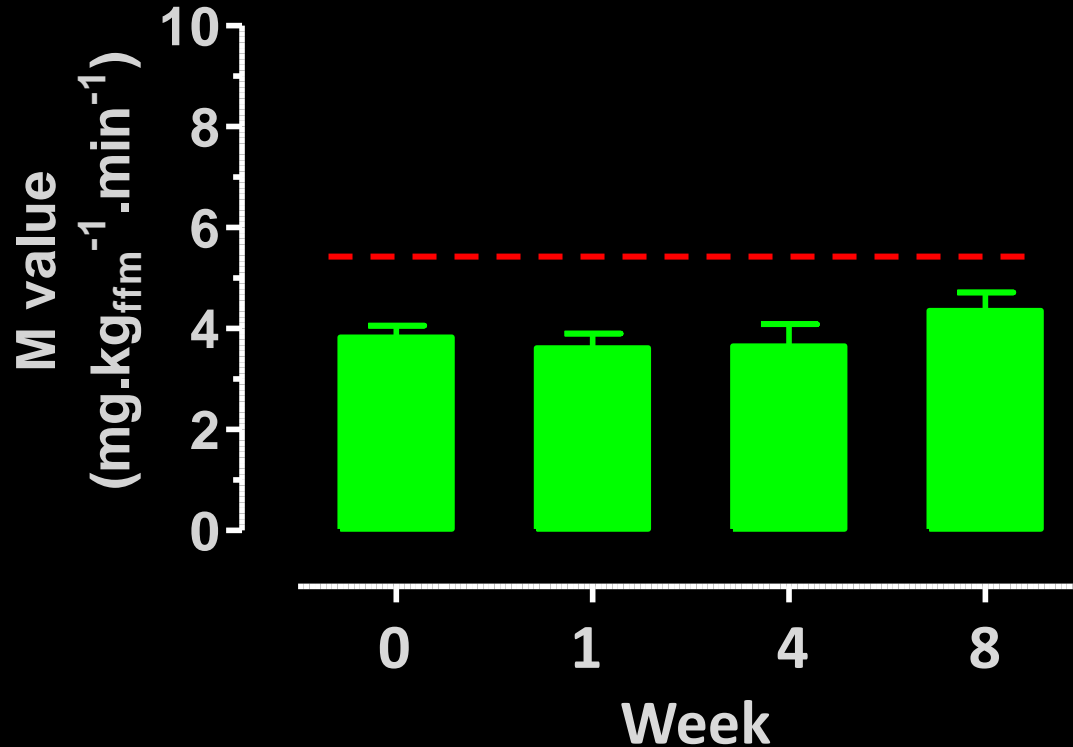
Dotted red lines  
show non-diabetic  
matched control  
data

As liver fat  
normalised -  
so did liver  
insulin  
sensitivity

# Change in liver fat during 8 weeks of low calorie diet and reversal of Type 2 diabetes to normal



# Muscle insulin sensitivity assessed by isoglycaemic hyperinsulinaemic clamp during Counterpoint

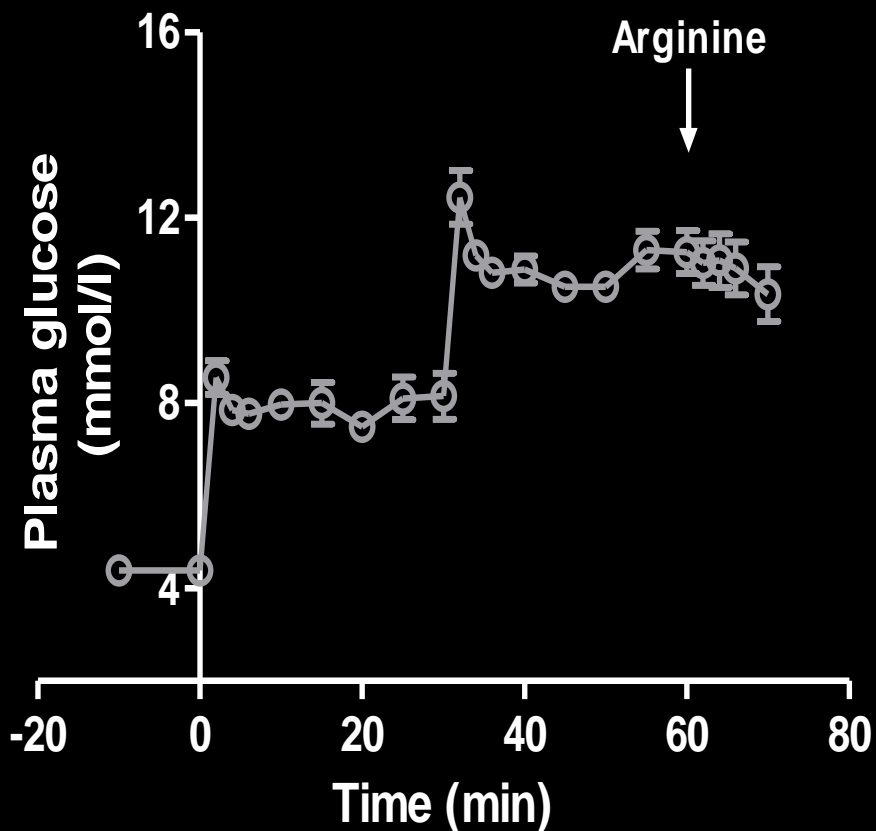


No change in muscle despite reversal of diabetes

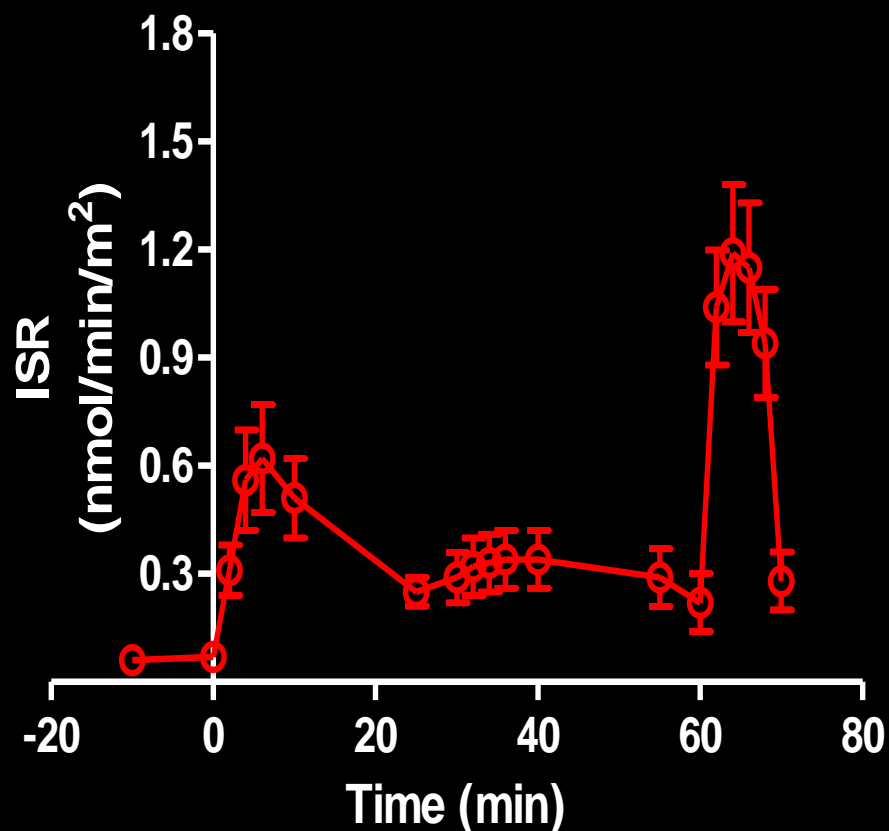
# Beta cell function: Control subjects

## Stepped Insulin Secretion Test with Arginine (SISTA)

IV glucose infused to achieve this plasma glucose profile:

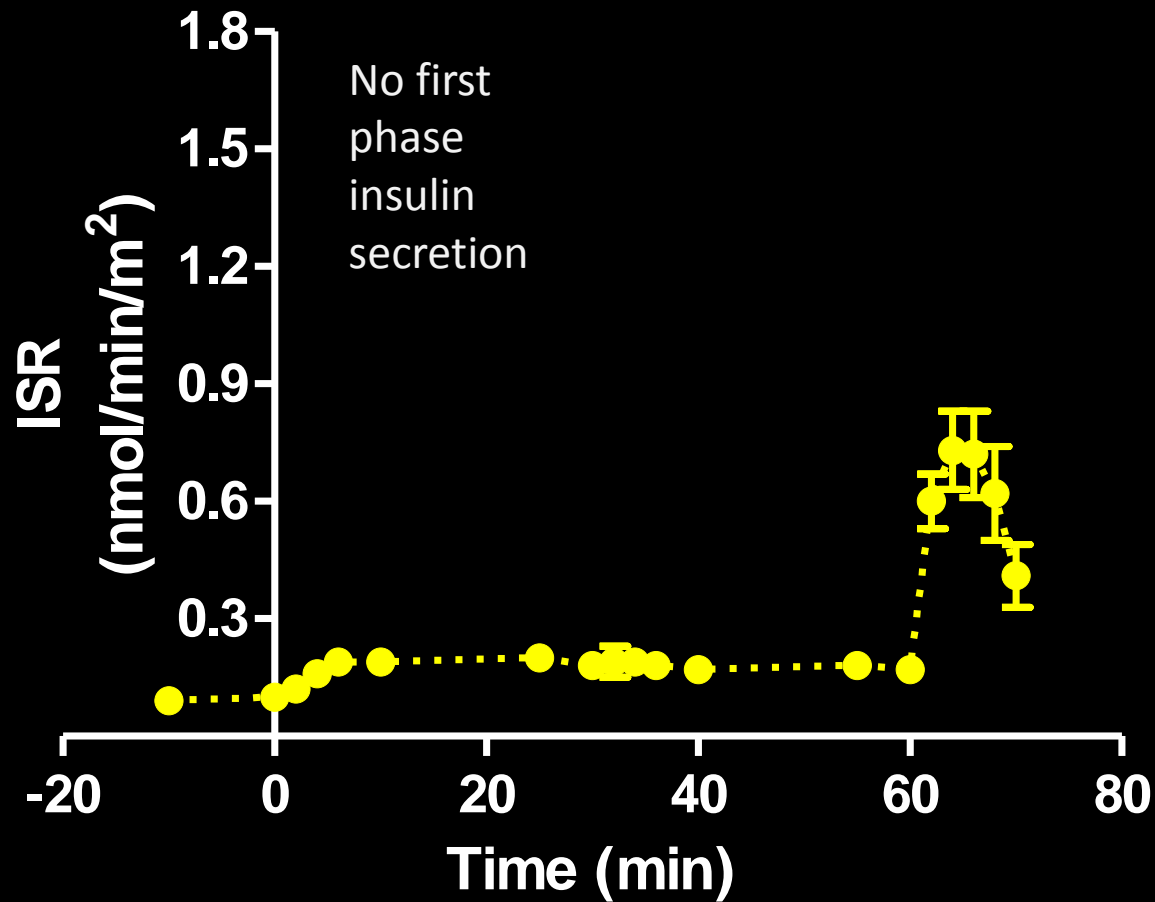


Observed insulin secretion rate:



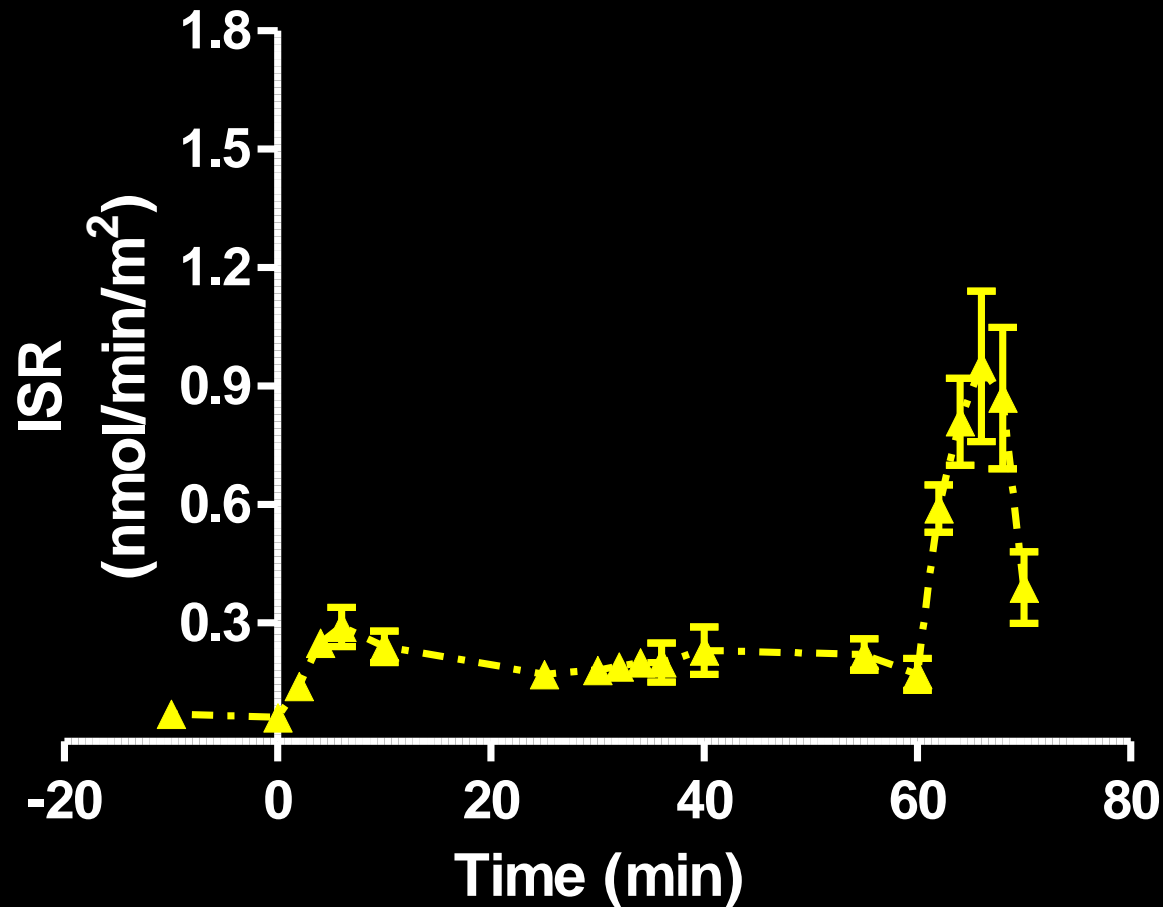
# Beta cell function: Diabetes subjects

## Baseline



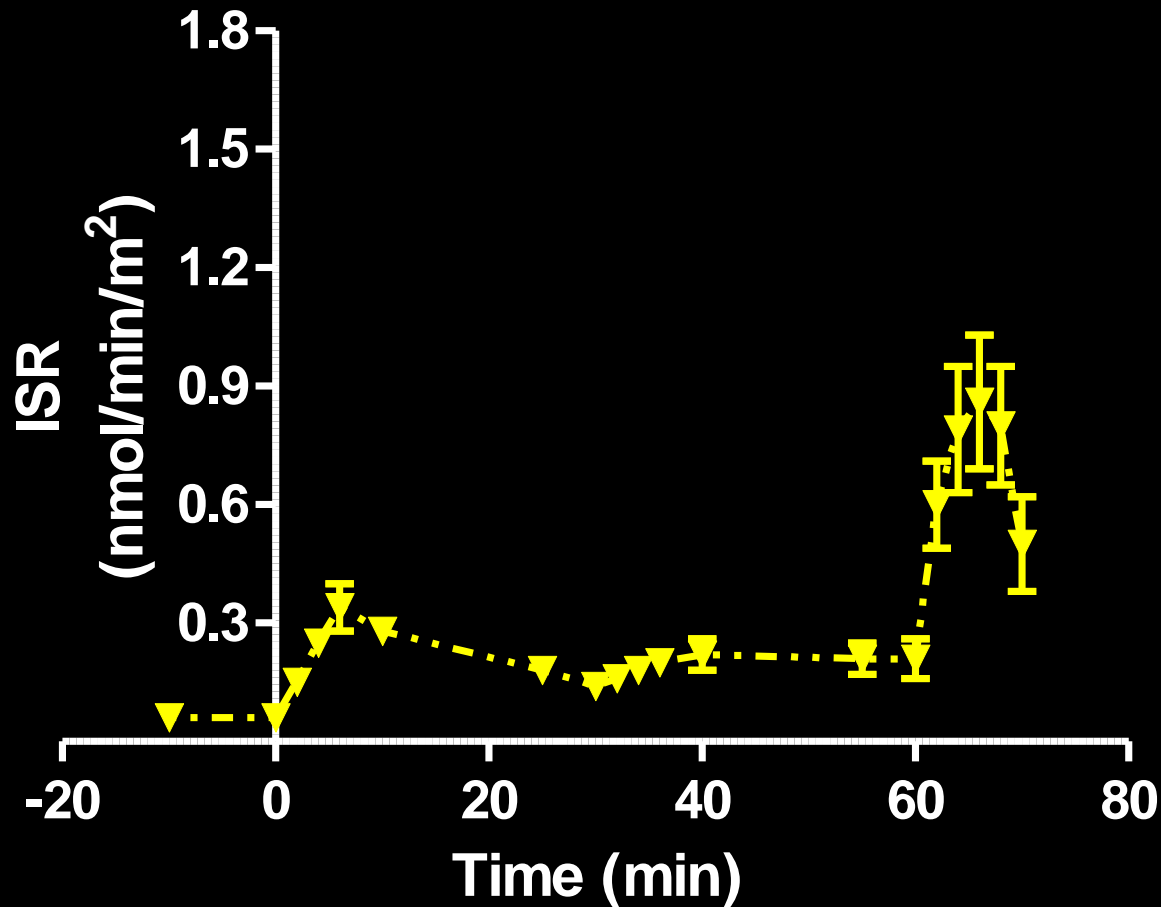
# Beta cell function: Diabetes subjects

Week 1



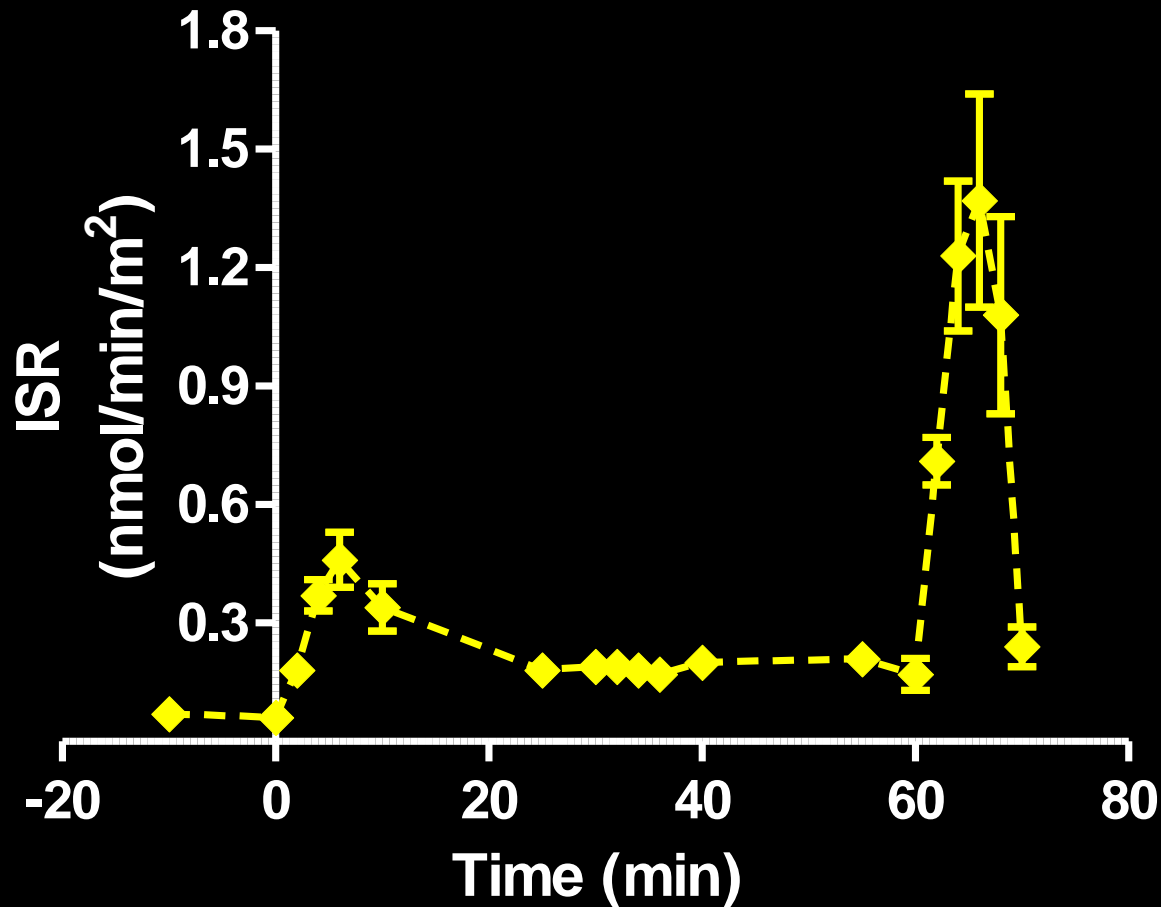
# Beta cell function: Diabetes subjects

Week 4



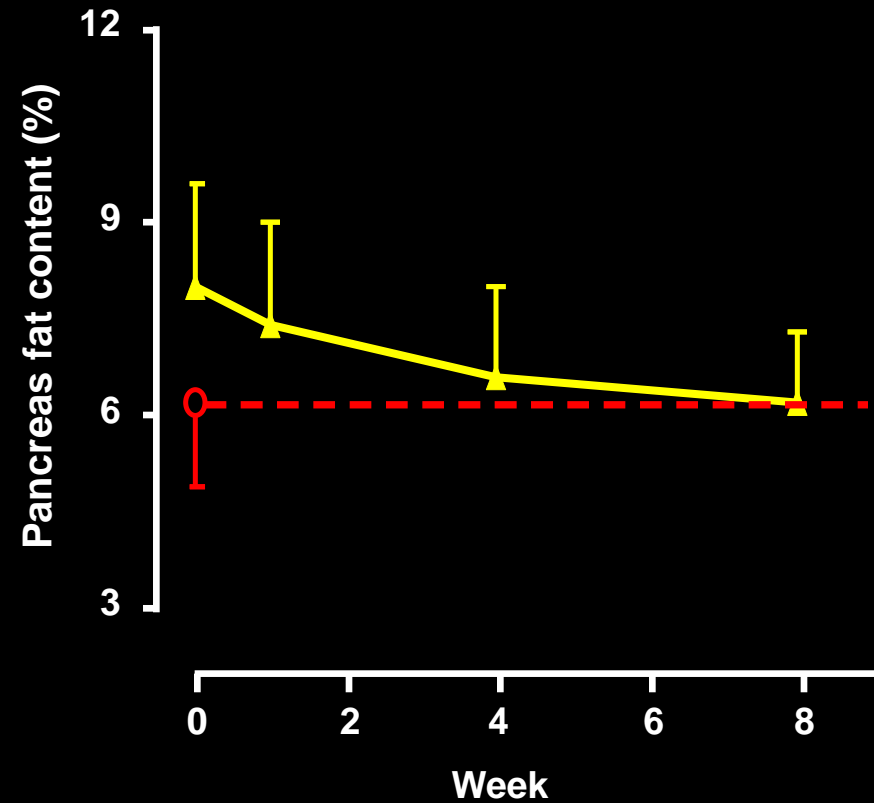
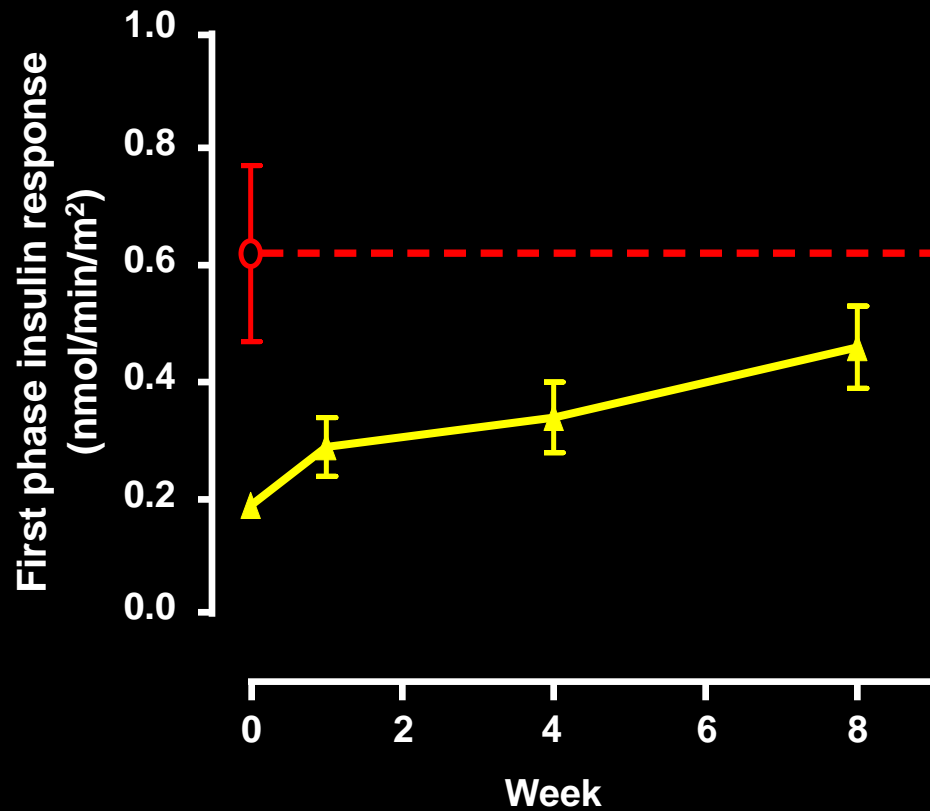
# Beta cell function: Diabetes subjects

Week 8





# Change in beta-cell function and pancreas fat



# **Reversing the twin cycles of type 2 diabetes**

**Type 2 diabetes is a simple condition of fat excess to which some people are more susceptible than others**

**Health-motivated people can reverse their diabetes**

**This knowledge must not be used as a stick with which to beat people who do not want to change their lives**