

# Clinical aspects of long term remission of type 2 diabetes



# Disclosures – Roy Taylor

- **Member of UK government (SACN) working group on low carbohydrate diets – all opinions in this lecture are personal**
- **Author of book: Life Without Diabetes**
- **Lecture fees from Novartis, Lilly & Janssen**
- **Research funding from Diabetes UK**



# **“Diet” for weight loss**

**Simple**

**Practical**

**Spouse/partner on board**

**Duration limited and planned**

**No additional exercise during this time**

# **“Diet” for weight loss**

**Simple**

**Practical**

**Spouse/partner on board**

**Duration limited and planned**

**Compensatory eating  
renders exercise counterproductive  
during weight loss**

# Weight loss then weight maintenance

## Step 1 Low calorie weight loss

600kcal/day liquid formula diet + nonstarchy vegetables  
(or 800kcal/day liquid formula only)

## Step 2 Step-wise return to normal eating

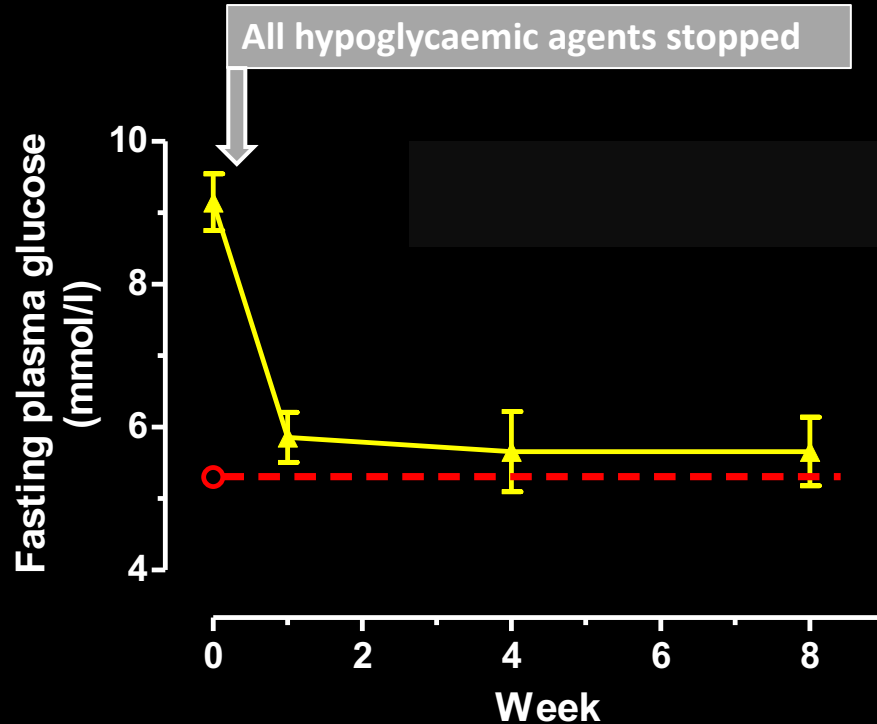
Replace liquid formula with normal food, one meal at a time. Aiming for  $\pm 1500$ kcal/day

## Step 3 Long term support to limit calorie intake and encourage increased physical activity

# Effect of very low calorie diet on fasting glucose

## The COUNTERPOINT study

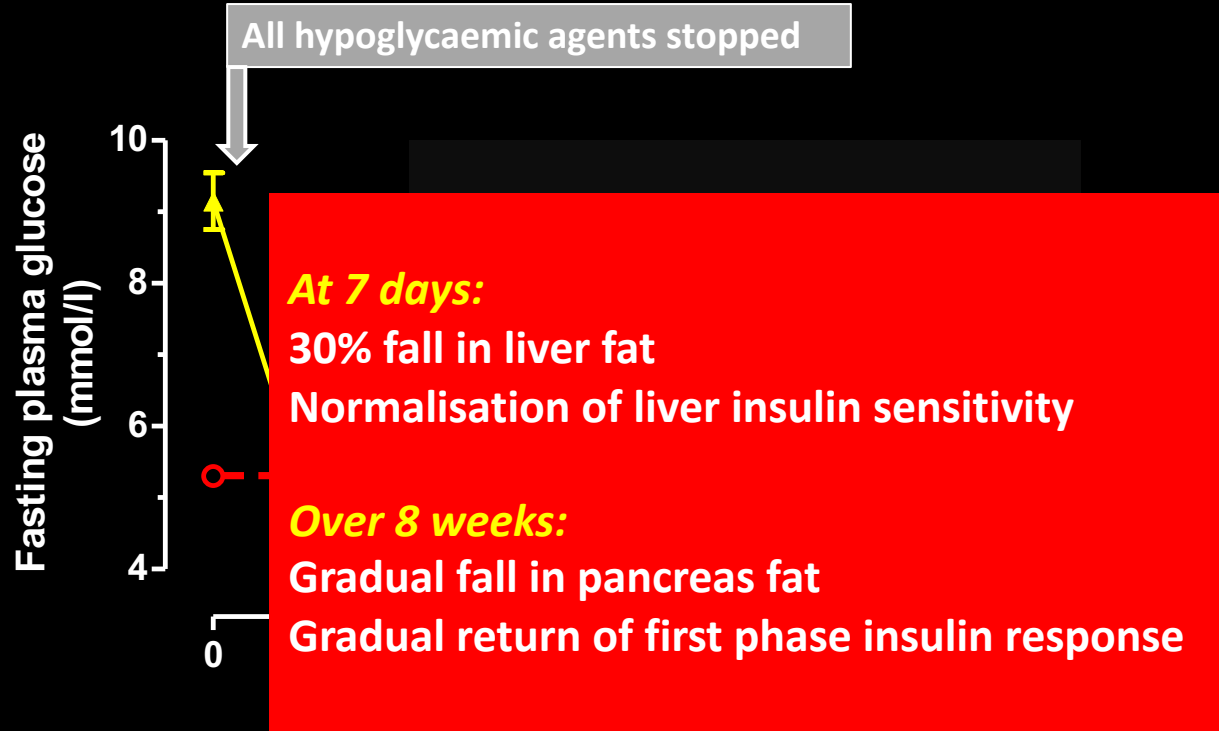
Type 2 diabetes  
0-4 years duration



# Effect of very low calorie diet on fasting glucose

## The COUNTERPOINT study

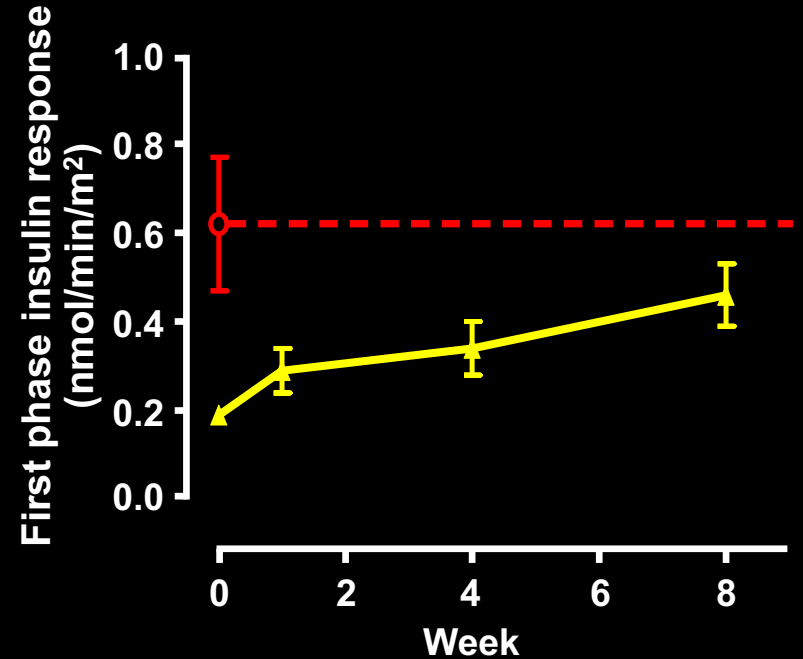
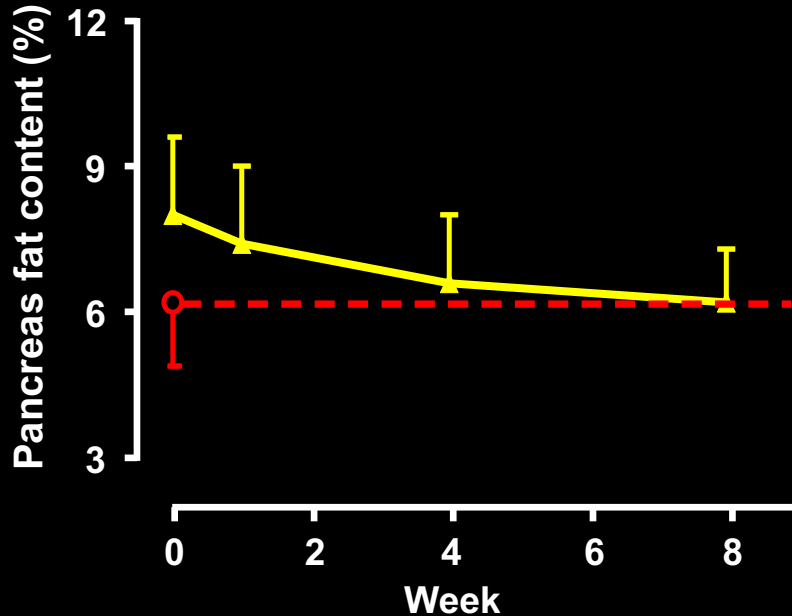
Type 2 diabetes  
0-4 years duration





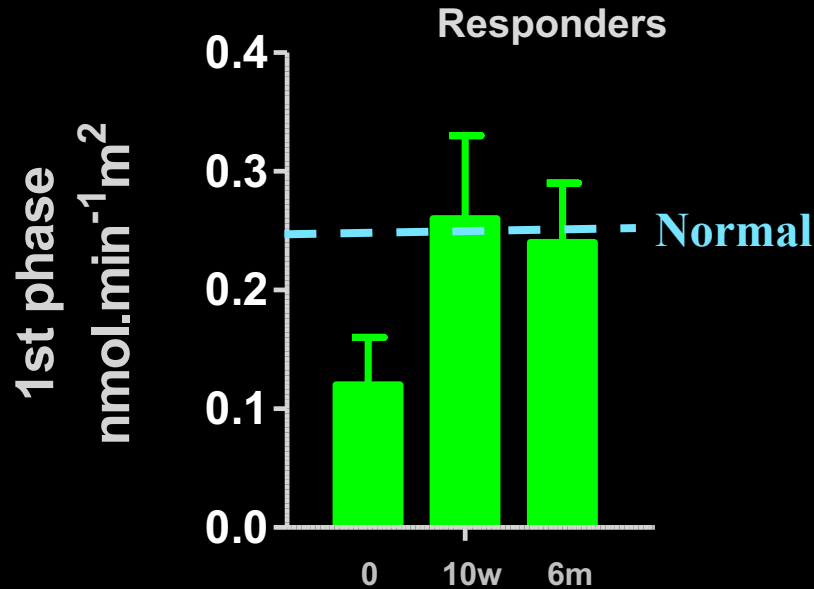
# Counterpoint:

## Change in intra-pancreatic fat & first phase insulin secretion



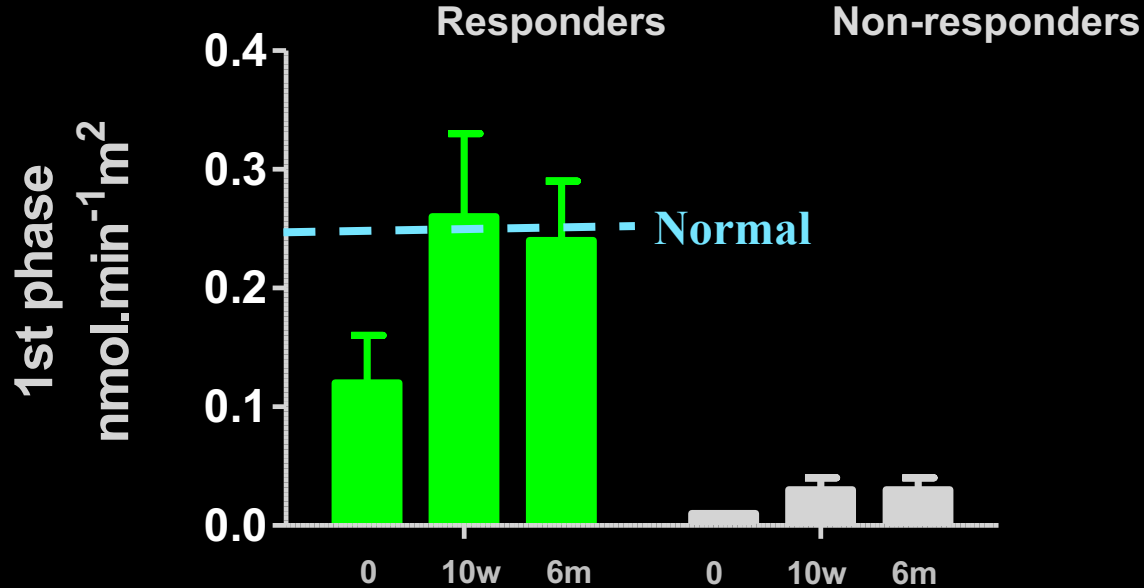
# CounterBALANCE – Does duration of T2DM matter?

Effect of VLCD then 6 months isocaloric eating on first phase insulin secretion



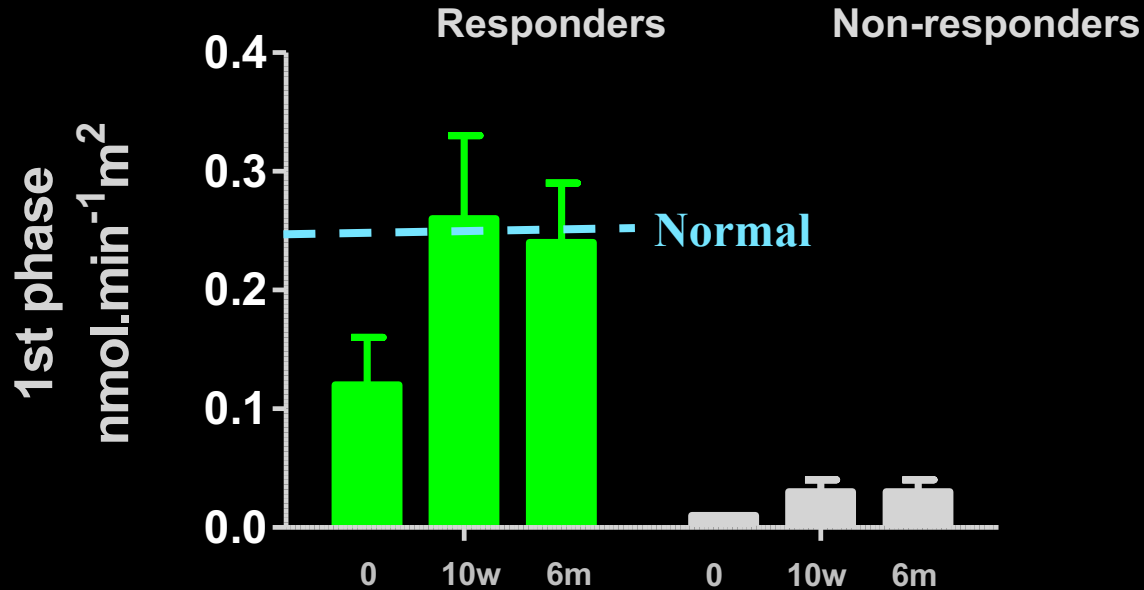
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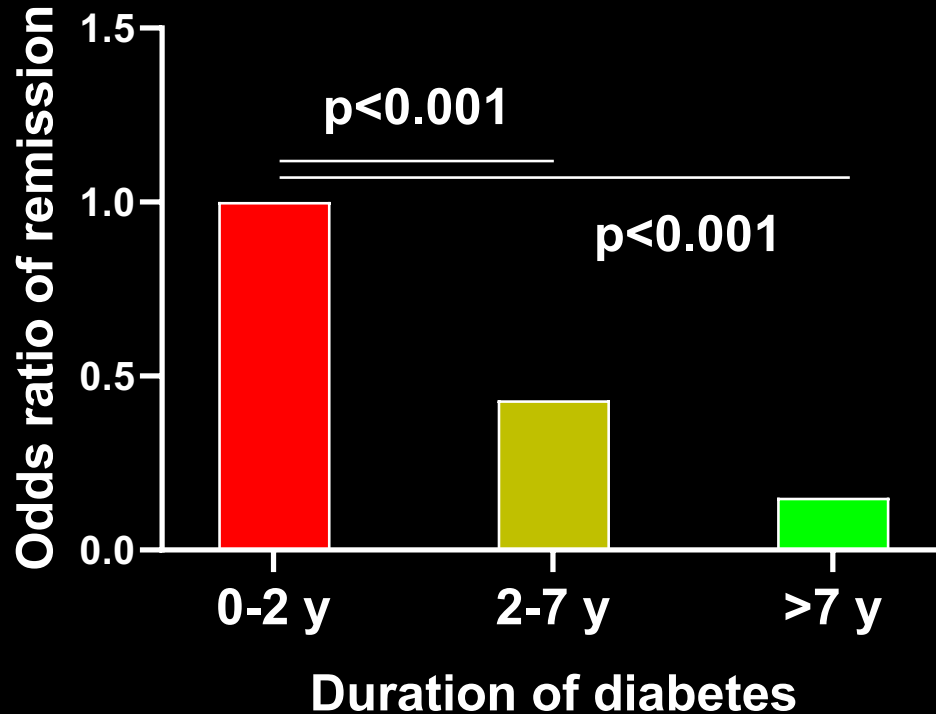
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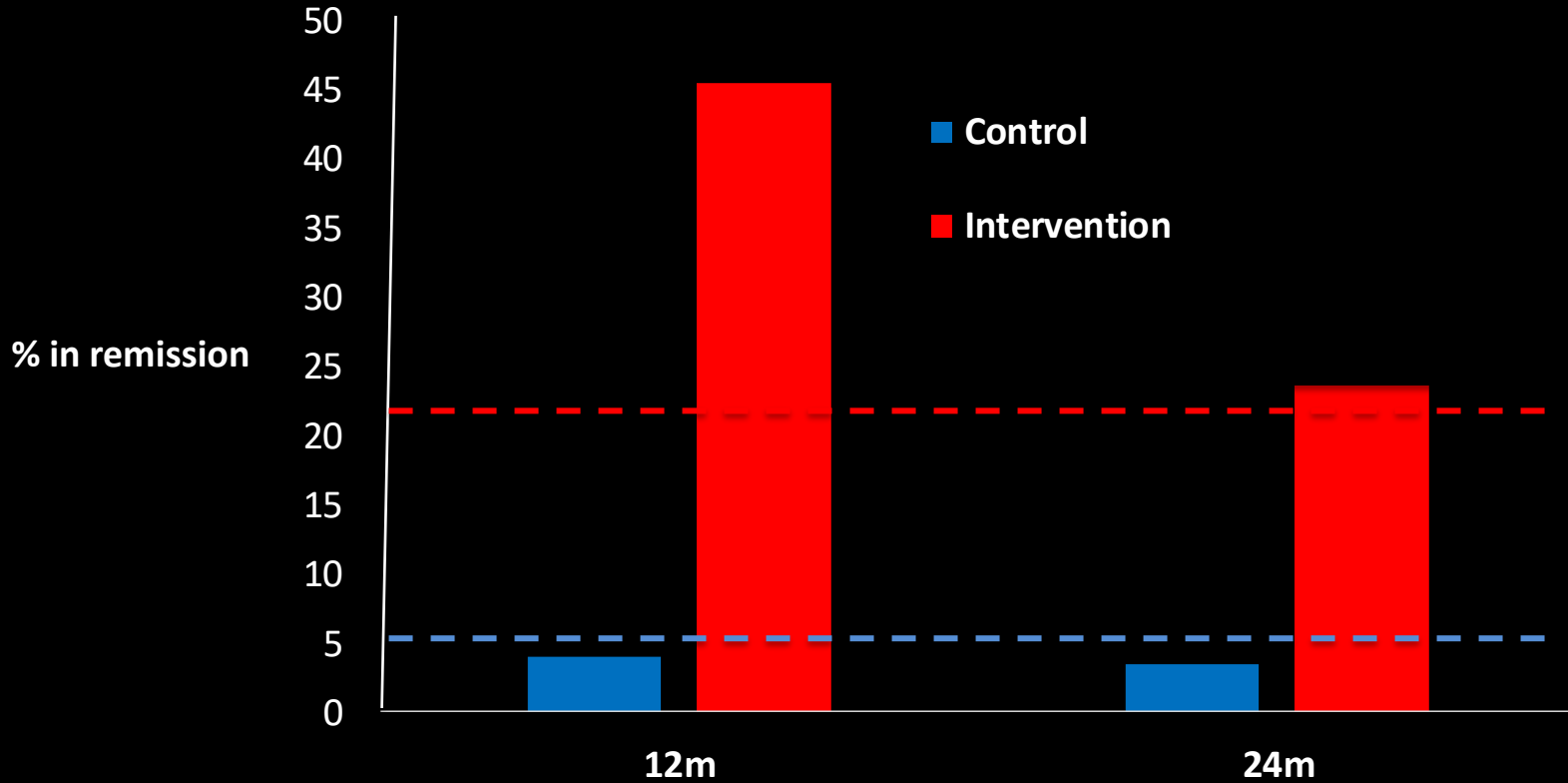


HbA1c (%)	7.1	5.8	5.9	8.4	8.0	7.8
Duration (years)	3.8±1.0			9.8±1.6		

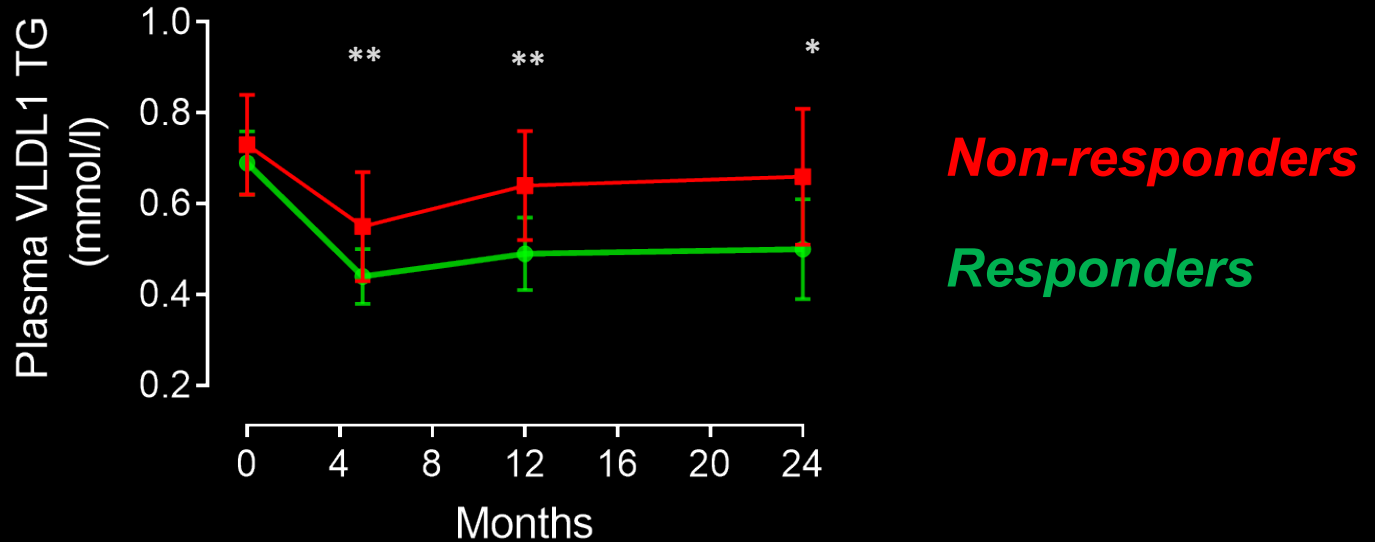
## Look Ahead – Multivariate analysis to identify effect of duration of type 2 diabetes on odds ratio of remission



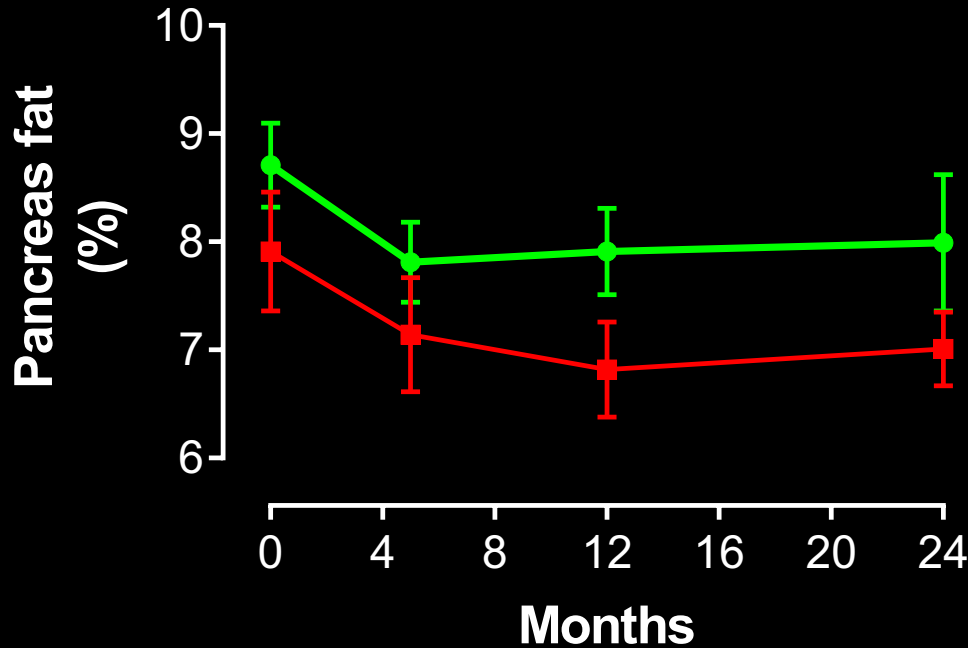
# Remissions at 12 and 24 months



# DiRECT: Decreased VLDL-TG output from the liver

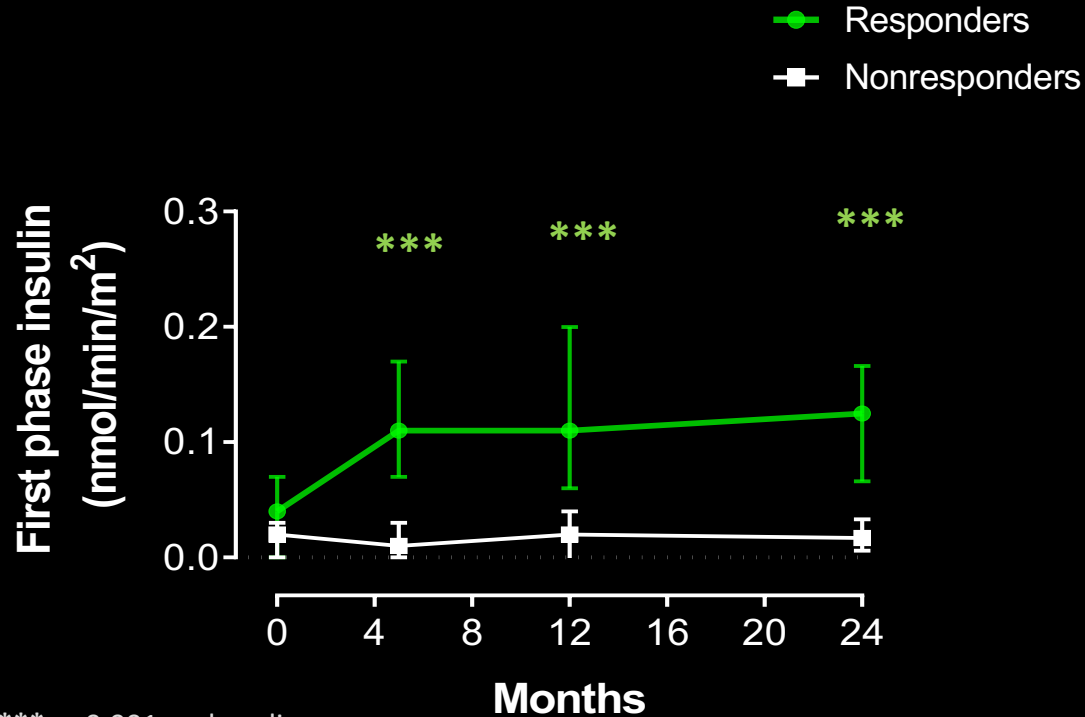


# DiRECT: Pancreas fat content in T2DM falls with weight loss irrespective of remission





# Remission depends on capacity of beta cells to recover once lipid excess is removed



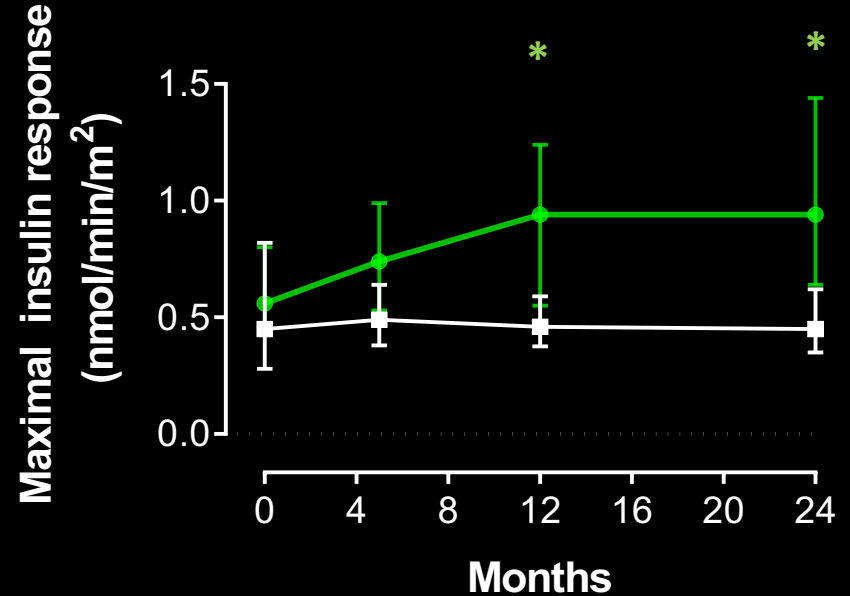
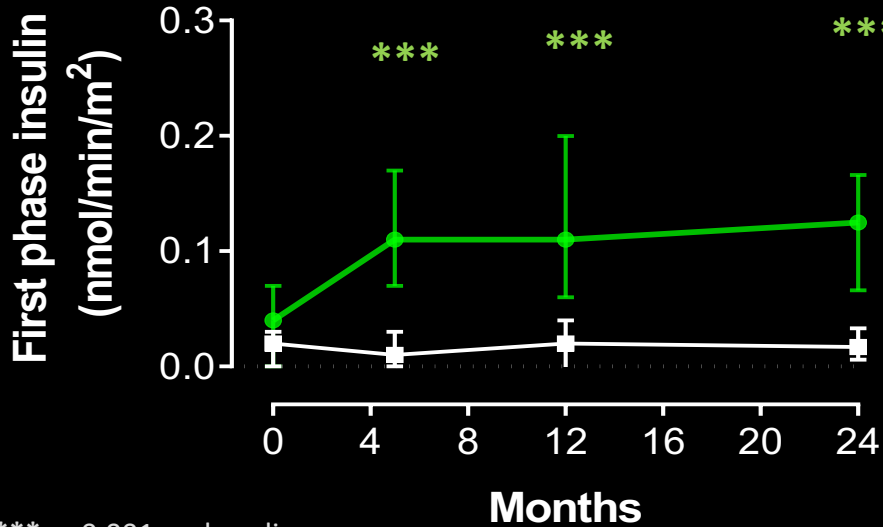
\*\*\* p<0.001 vs. baseline,

\*\* p<0.01 vs. baseline,

\* p<0.05 vs. baseline

# Remission depends on capacity of beta cells to recover once lipid excess is removed

● Responders  
■ Nonresponders



\*\*\* p<0.001 vs. baseline,

\*\* p<0.01 vs. baseline,

\* p<0.05 vs. baseline

# The pancreas in T2DM is 25% smaller than normal

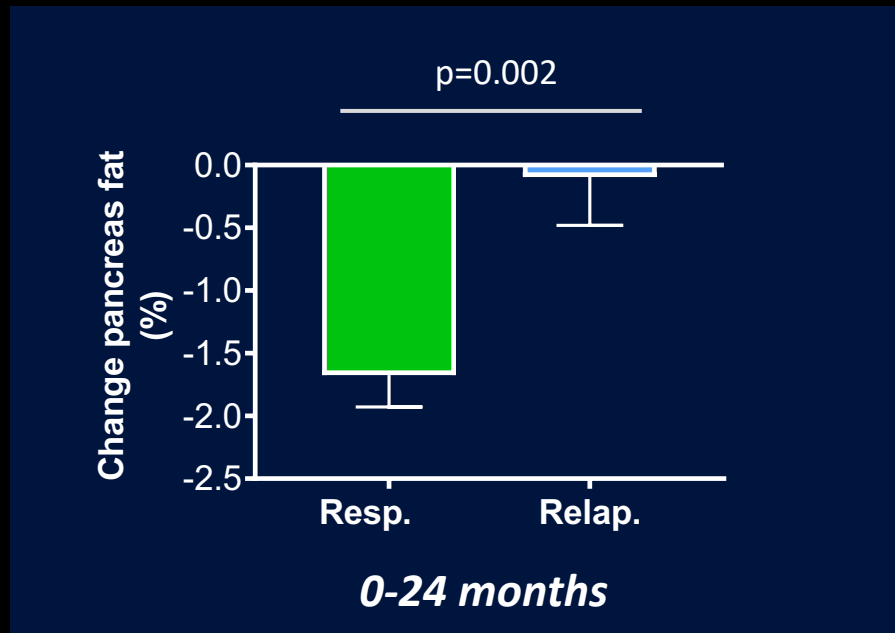
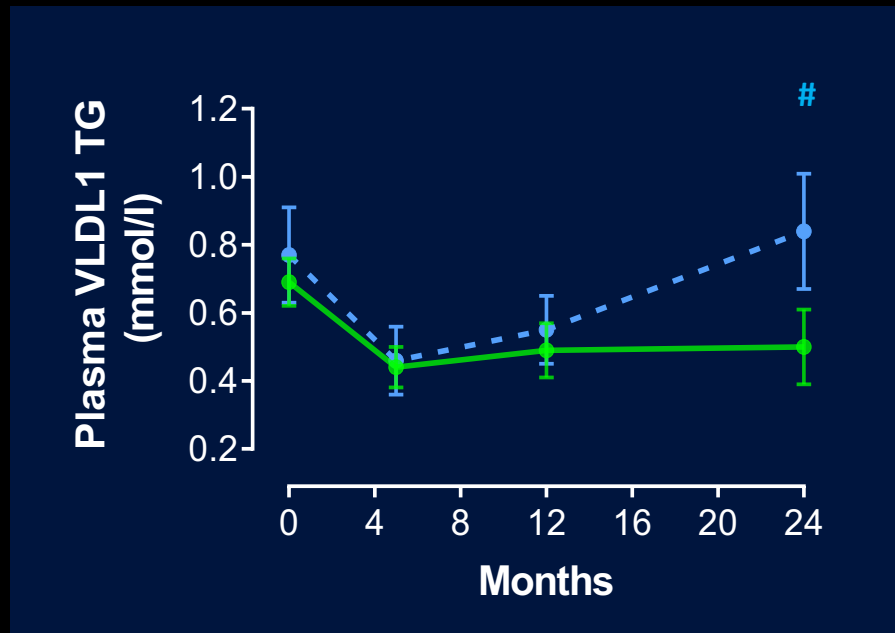
Does it return towards normal size with remission?



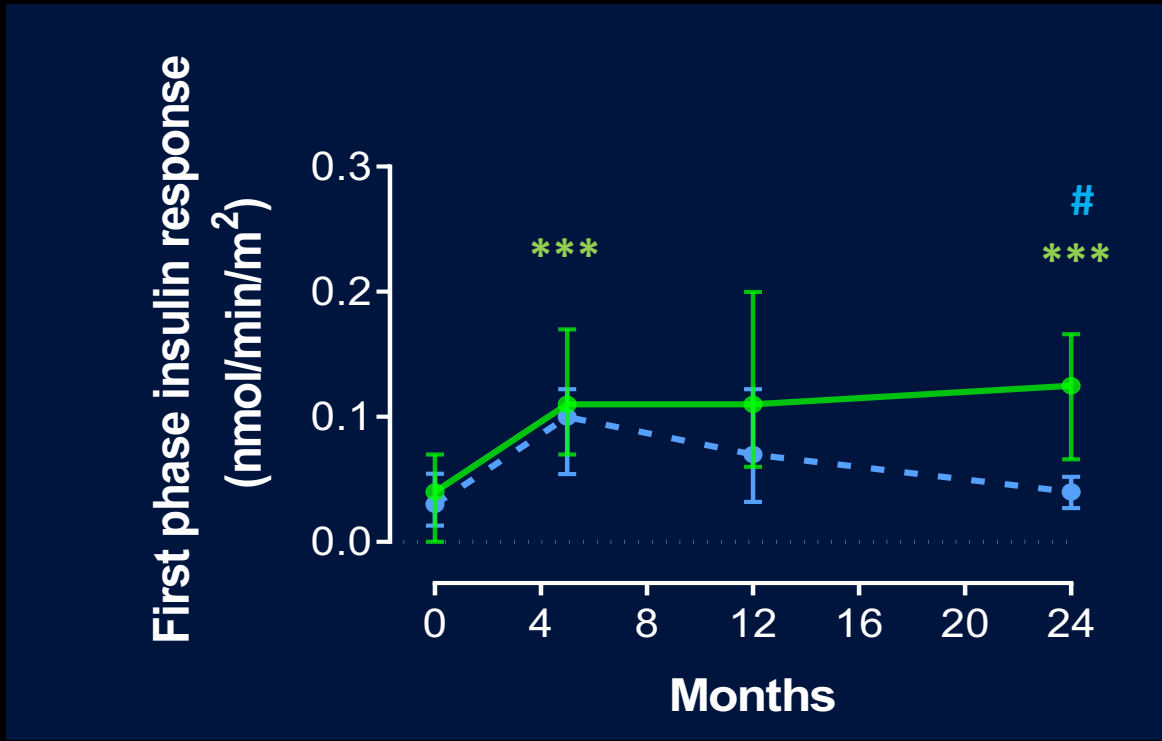
*Macauley et al, PLOS One 2015; 10:e0126825*  
*Al-Mrabeih et al, Diabetologia 2016; 59:1753*

# With weight regain: observing T2DM develop

- Responders
- Relapsers



# With weight regain: observing T2DM develop



\*\* p<0.01 vs. baseline, \*\*\* p<0.001 vs. baseline  
# p<0.05 vs. 5 months, ## p<0.05 vs. 5 months

# The twin cycle hypothesis

Negative calorie balance in people with type 2 diabetes will:

## *Liver*

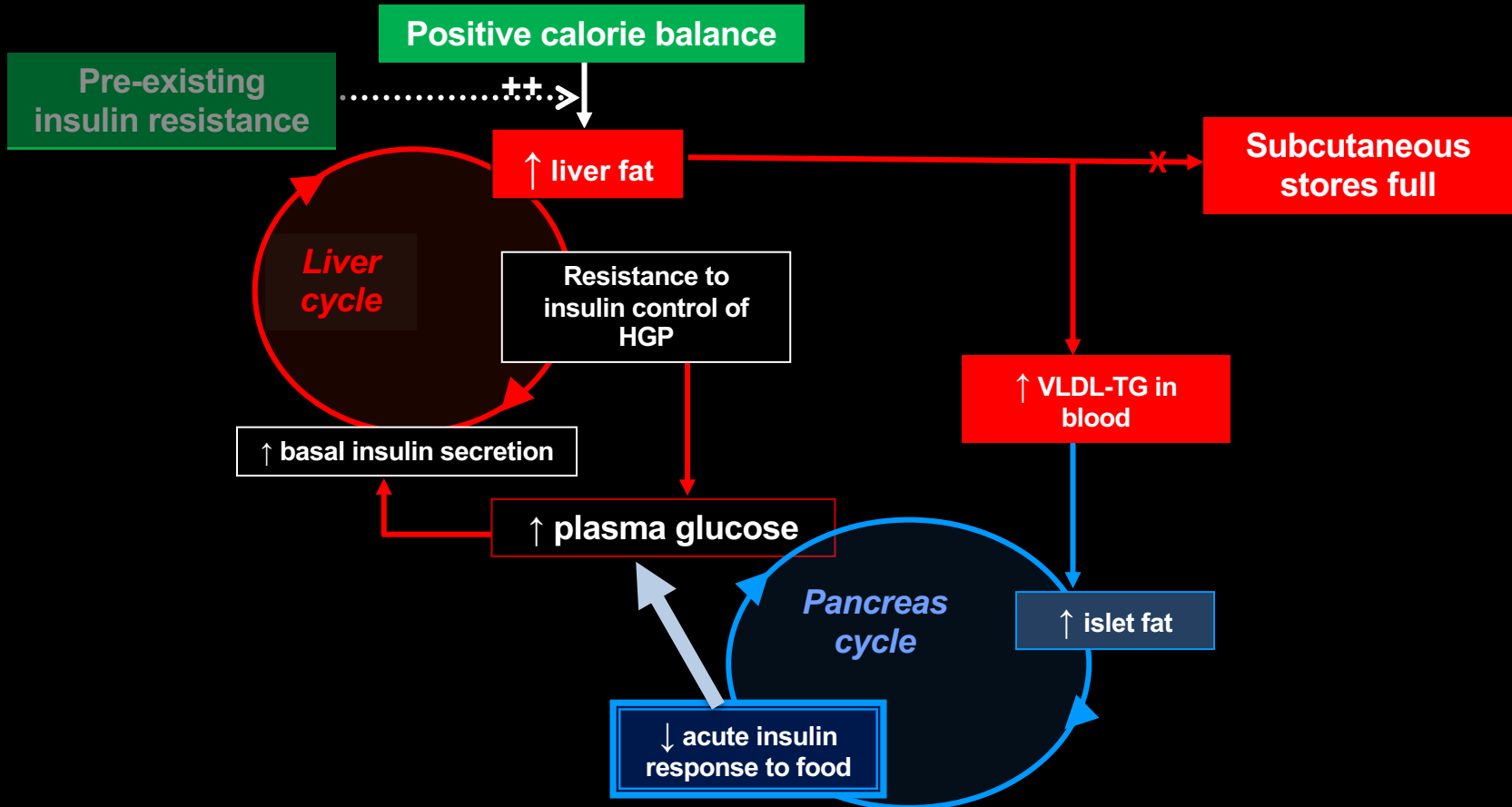
Decrease fat –  
improve insulin action  
and  
normalise overnight blood  
sugar

*and*

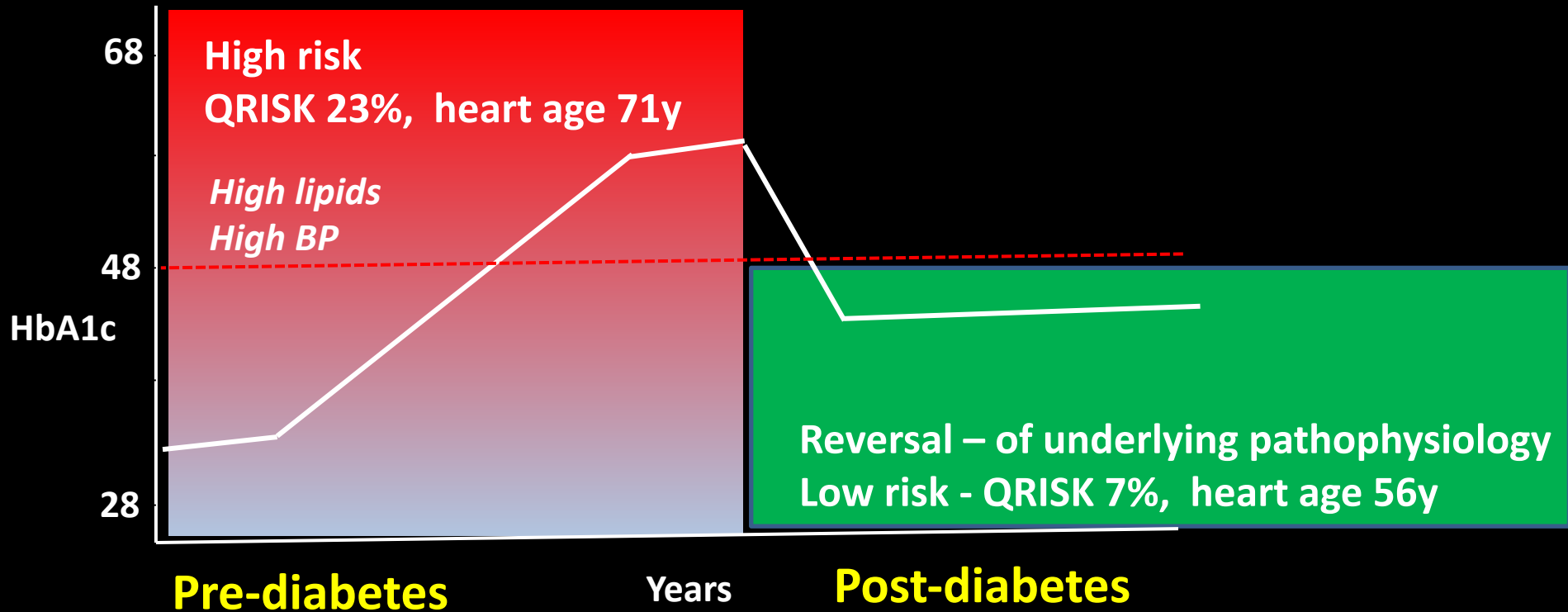
## *Pancreas*

Decrease fat –  
normalise the insulin  
response to eating

# The Twin Cycle Hypothesis: Aetiology of Type 2 diabetes

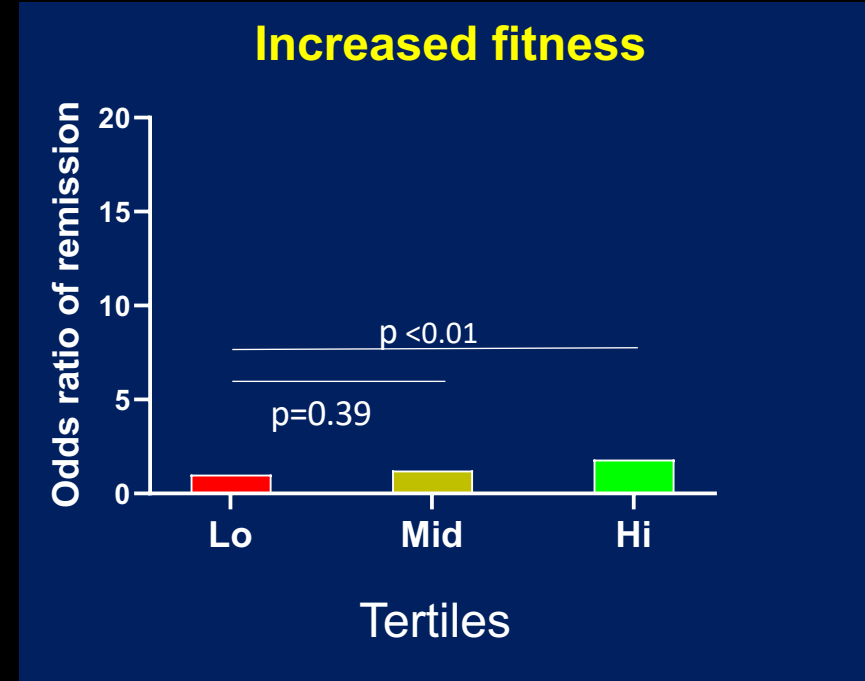
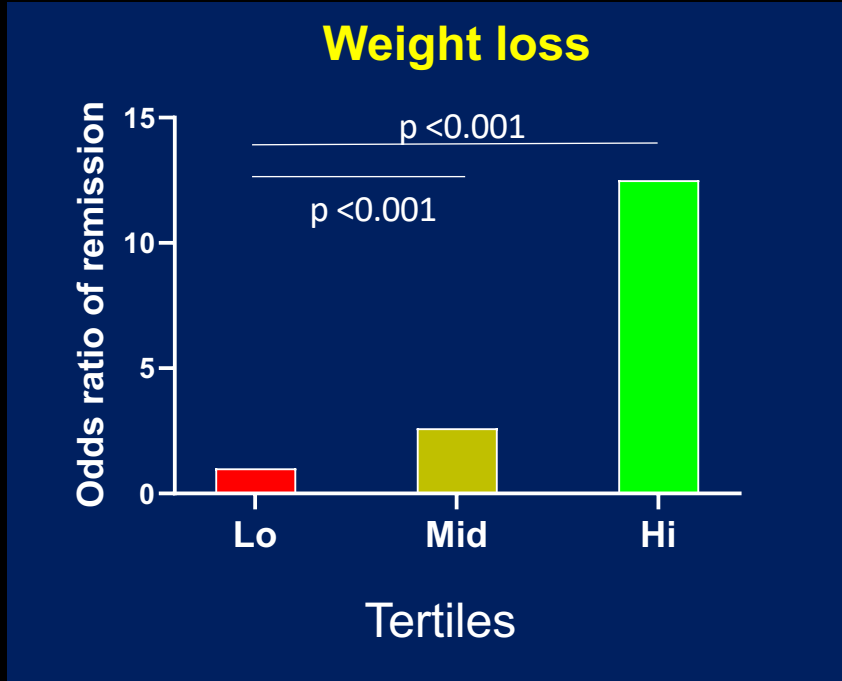


# Pre-diabetes, diabetes and post-diabetes





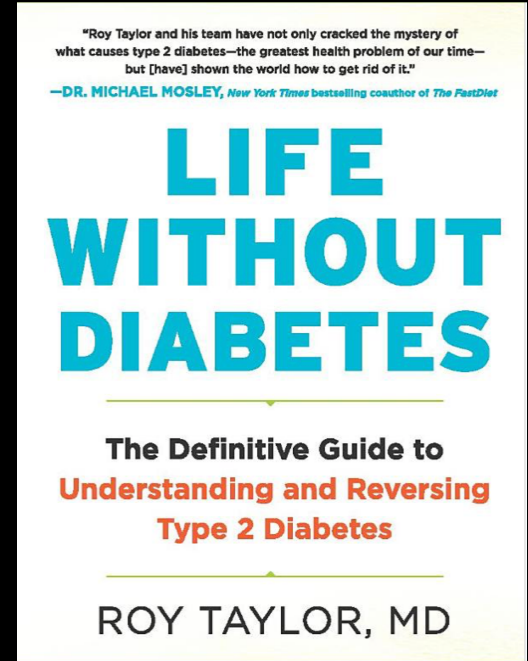
# Look Ahead – Multivariate analysis to identify major factors underlying remission of type 2 diabetes (11.5% at 1y)

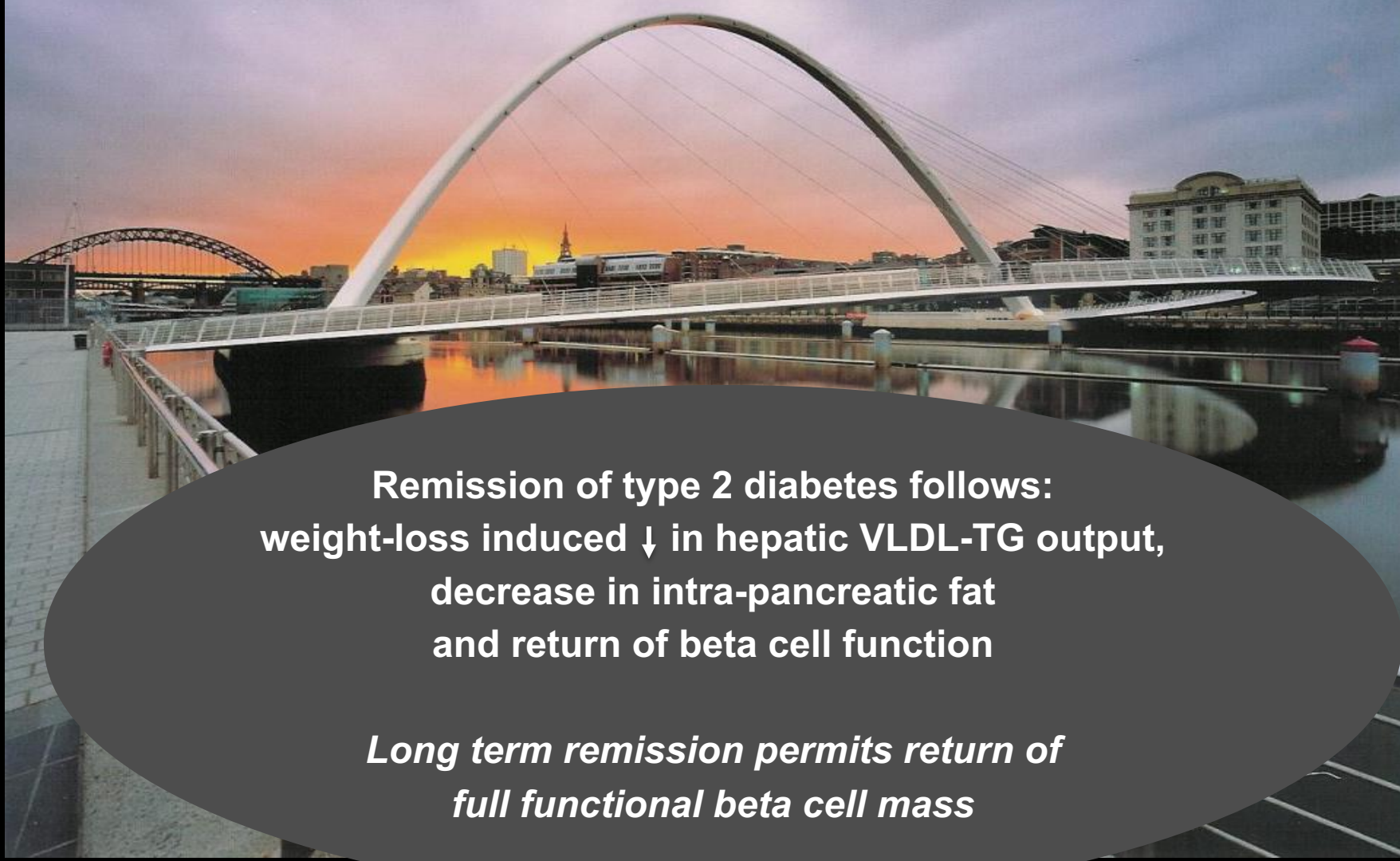


**Website  
on how-to-do-it**

[go.ncl.ac.uk/diabetes-reversal](http://go.ncl.ac.uk/diabetes-reversal)

**Book**





**Remission of type 2 diabetes follows:  
weight-loss induced ↓ in hepatic VLDL-TG output,  
decrease in intra-pancreatic fat  
and return of beta cell function**

***Long term remission permits return of  
full functional beta cell mass***