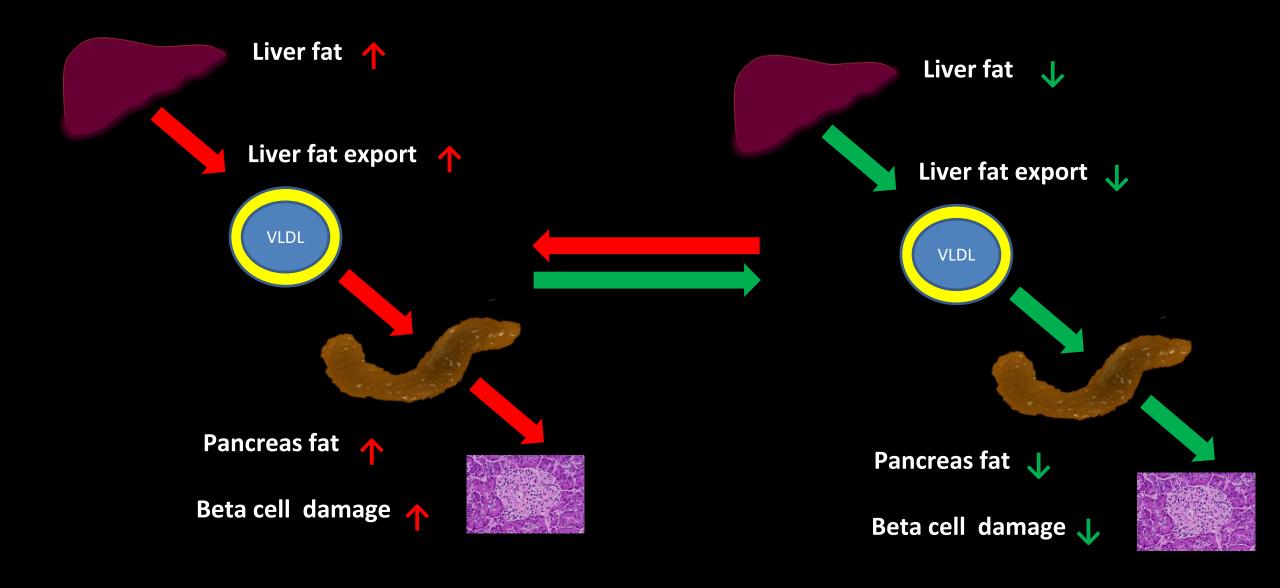
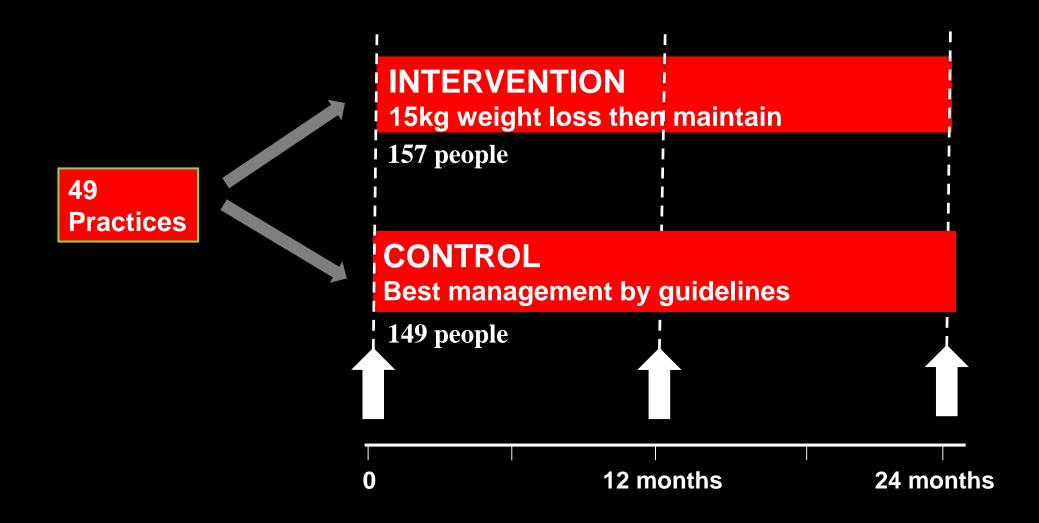
## Summary: Why type 2 diabetes is reversible?



#### **DiRECT – a study in routine NHS General Practice**



## Baseline data: analysed participants

(100%)

Total	l number	298
I O tai	HIGHIDCI	200

Men / women 59% / 41%

Age (years) 54 (SD 7)

Weight (kg) men 106 (SD 16)

women 91 (SD 13)

BMI  $(kg/m^2)$  35 (SD 4)

Duration of T2DM (y)	3.1 (SD 1.7)
HbA1c (mmol/mol)	59 (SD14) (7.6%)

Diet alone 24%

I drug 48%

2+ drugs 28%

Blood Pressure 135/85

Smoking (current) 12%

Former 38%

Never 50%

Intervention and Control groups well balanced for all criteria



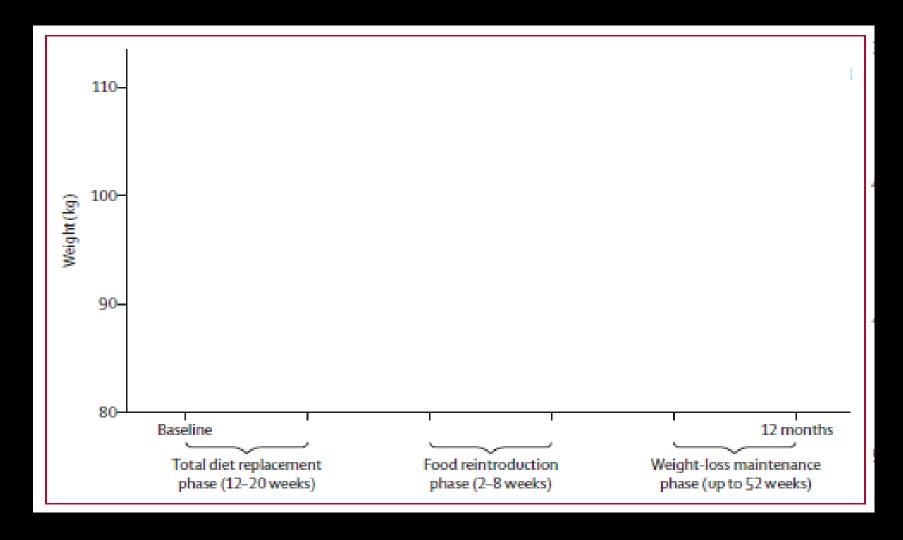






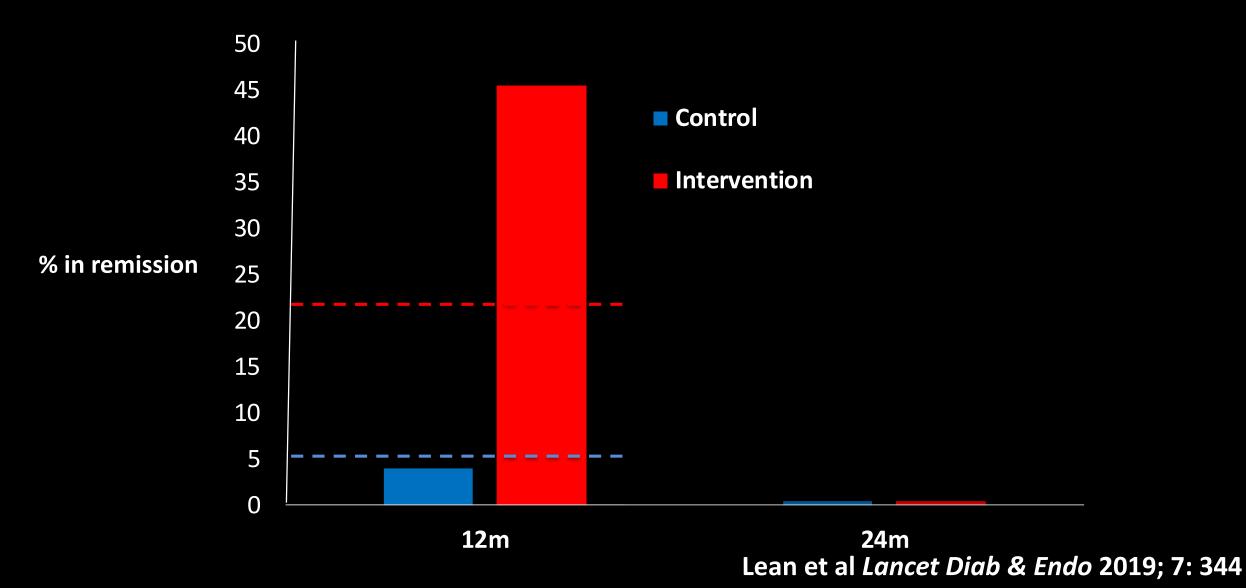


## Results: weight changes over 12 months

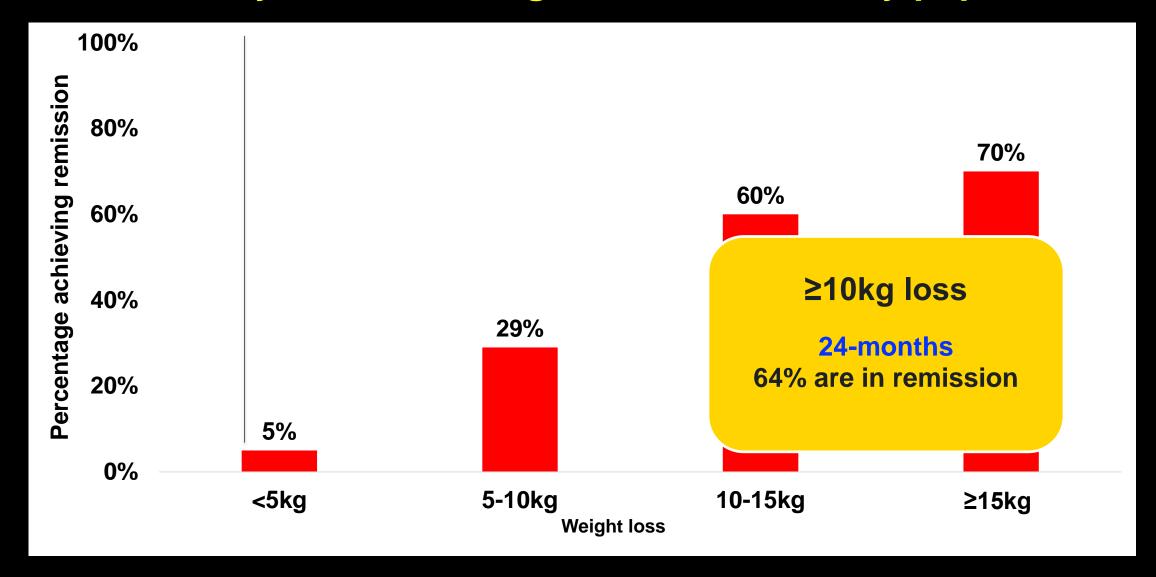




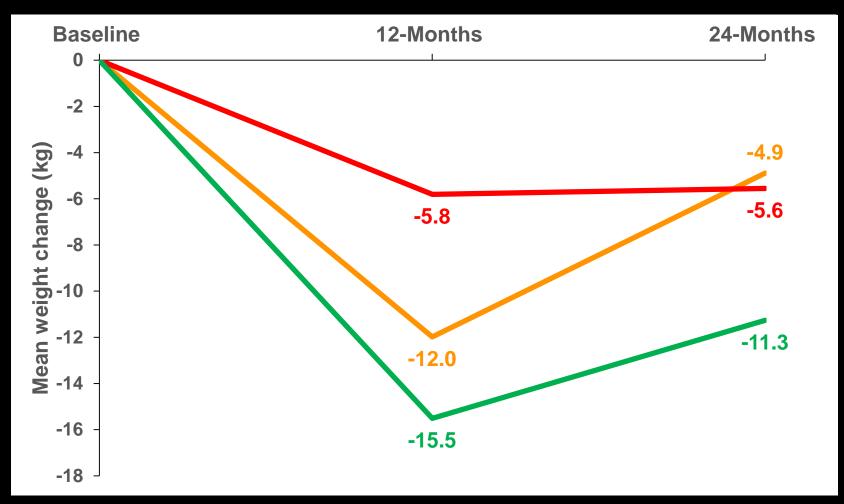
### **Remissions at 12 and 24 months**



### Remissions by 24-month weight loss: entire study population



#### Weight management is critical for T2D remission



**No Remission at 12 or 24-months**n = 62 (42%)

Remission at 12 but not 24-months n = 15 (10%)

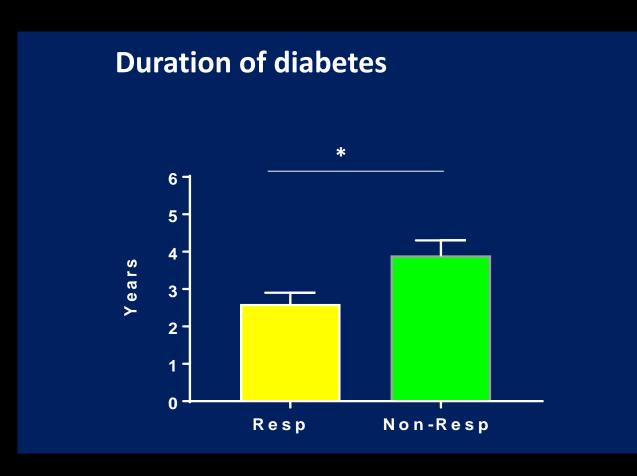
**Remission at 12 and 24-Months**n = 48 (32%)

**DiRECT Intervention group** 



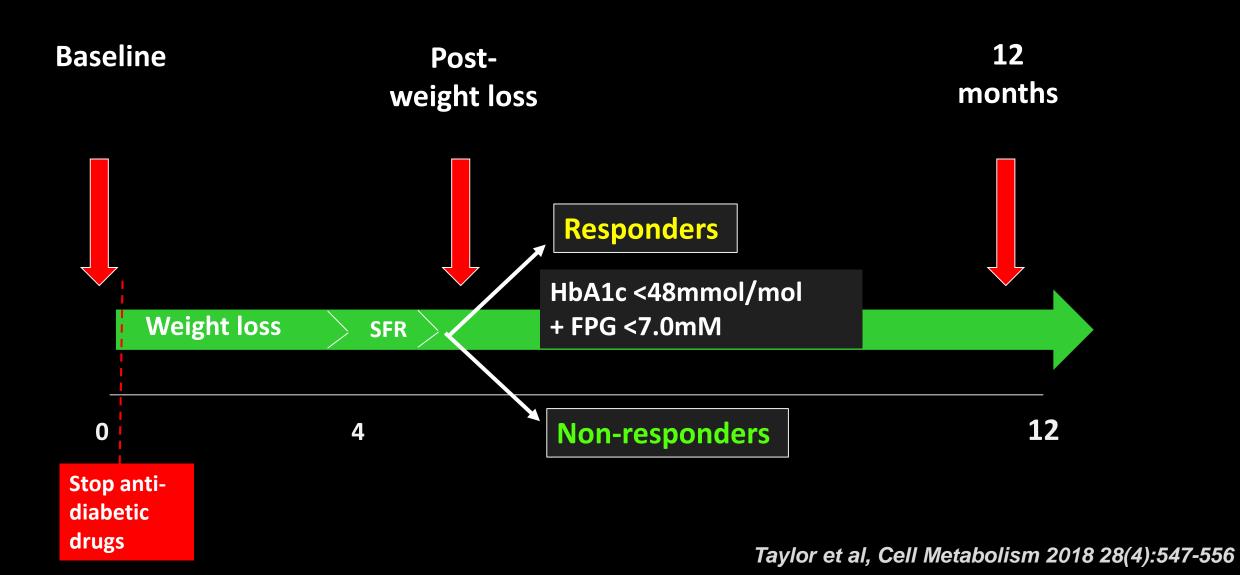
# Baseline determinants of return to non-diabetic glucose control (Tyneside cohort)

	Responder	Non- responder
Age	53 ± 1	53 ± 2
Weight	101 ± 3	102 ± 4
Sex	17/23	9/9
HbA1c	58±2	63±2*
Fasting insulin	108±10	77±9*



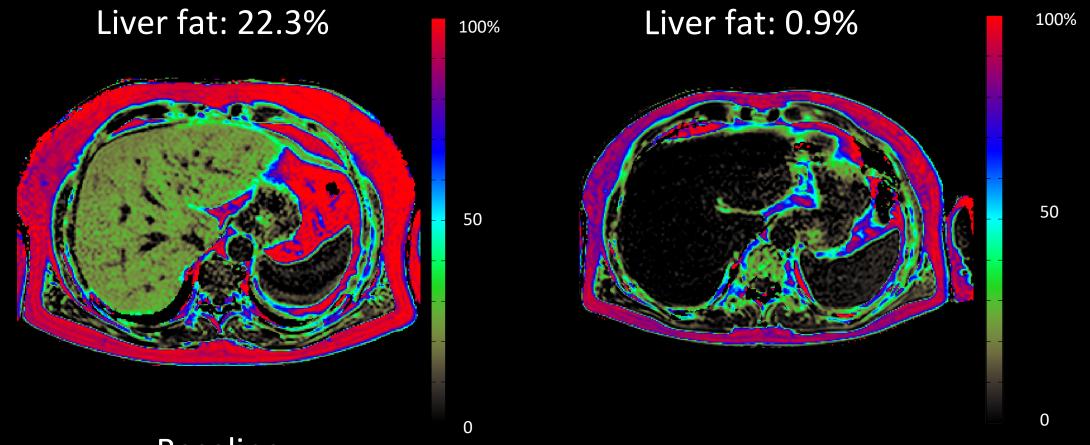
Taylor et al, Cell Metabolism 2018 28(4):547-556

## Protocol for pathophysiological studies





# Methodology – Fat quantification by MRI



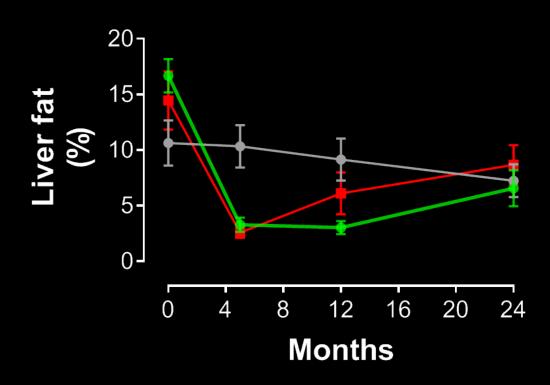
Baseline
Male/58 Years
BMI: 37.9 KG/m<sup>2</sup>

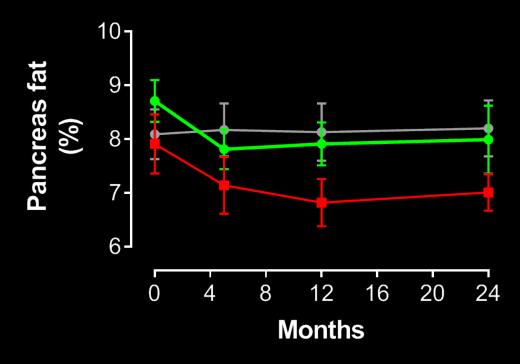
Post weight loss BMI: 28.5 KG/m<sup>2</sup>

Lim et al, Diabetologia 2011 54:2506-2514

# Changes in liver and pancreas fat

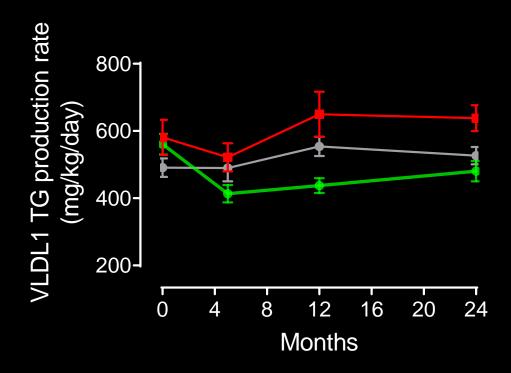
- Non-Responders
- Responders
- Relapsers

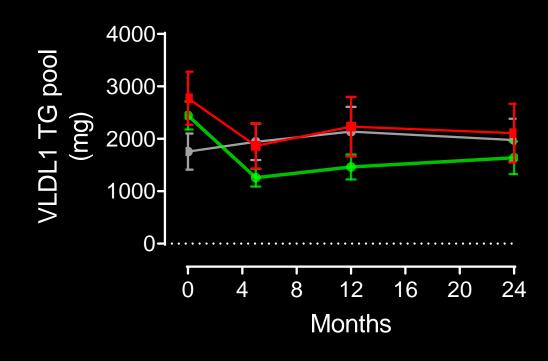




# Change in hepatic triglyceride export

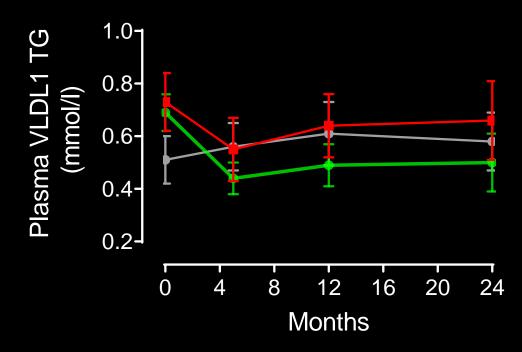
- Responders
- Controls
- Nonresponders

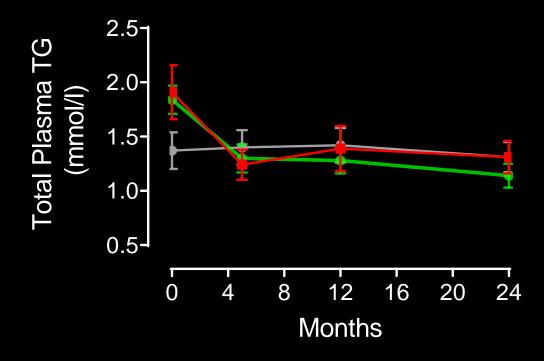




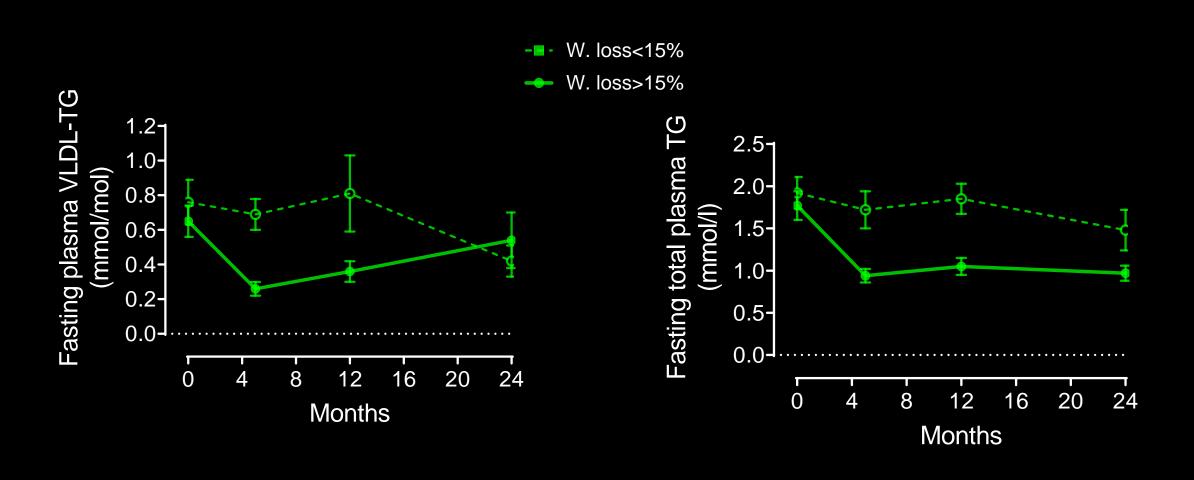
# Change in plasma VLDL1-TG and total triglyceride

- Responders
- Controls
- Nonresponders



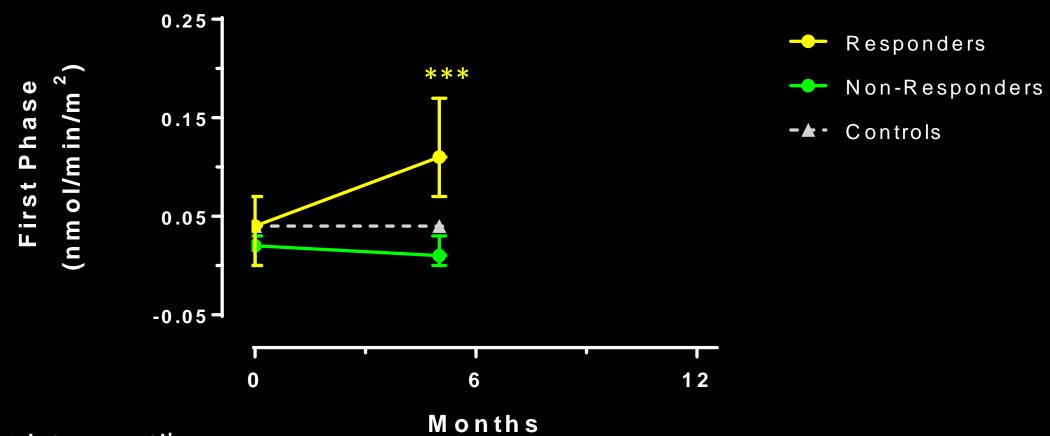


# Effect of degree of weight loss on plasma TG





# Change in acute insulin secretion

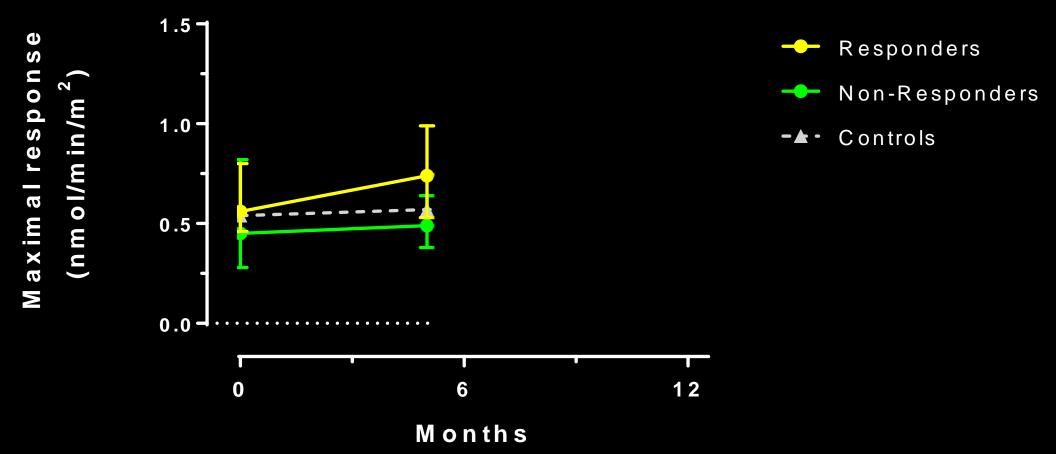


Median ± interquartile

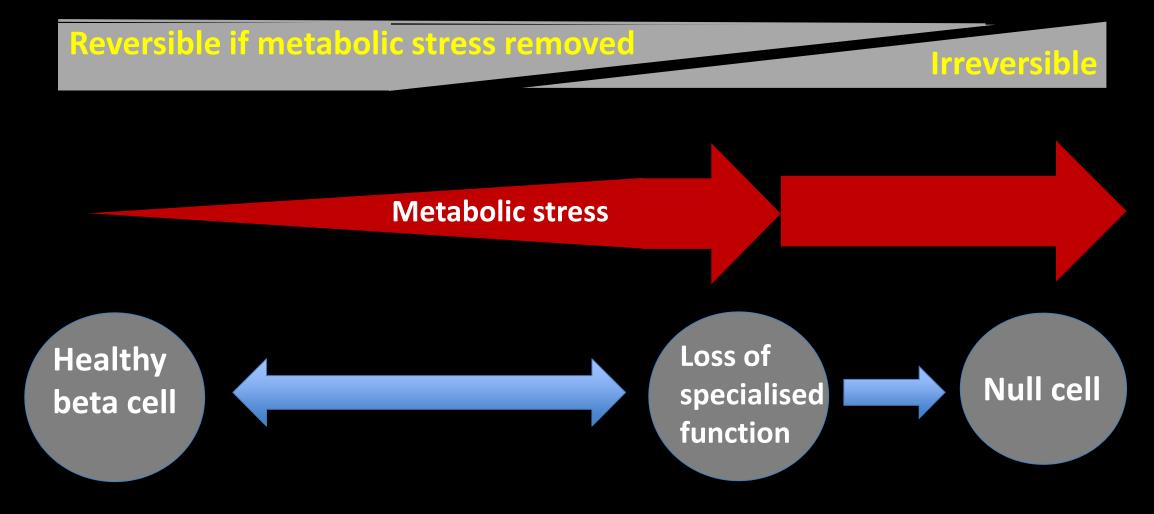
Taylor et al, Cell Metabolism 2018 28(4):547-556



# Change in maximal insulin secretion

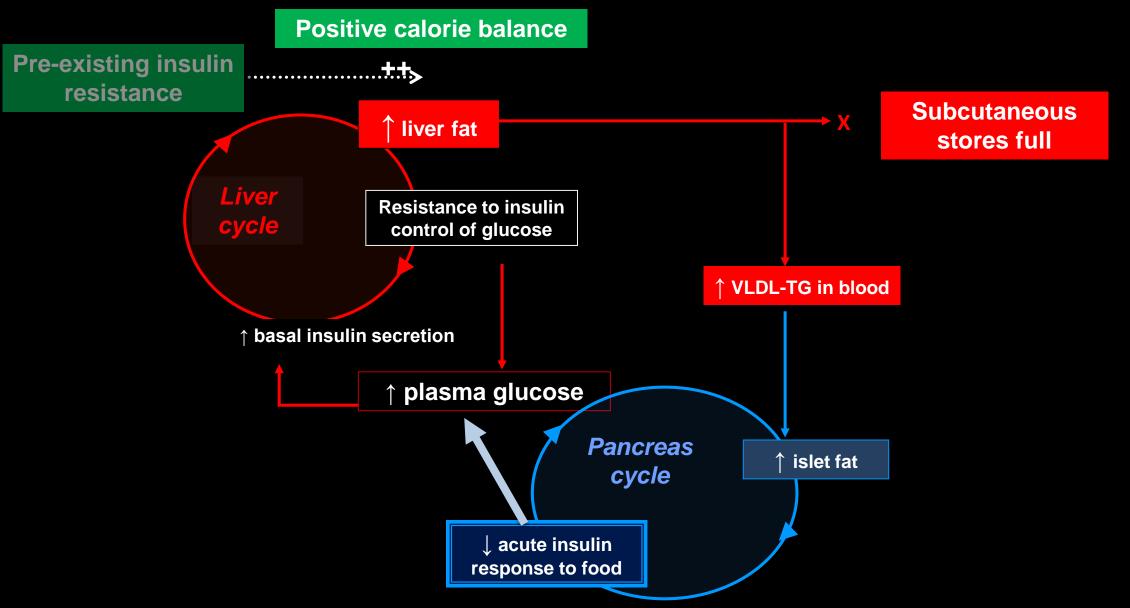


### Dedifferentiation explains the beta cell in type 2 diabetes



Pinnick 2010; Talchai 2012; White 2013; White, Diabetes Care 2016

#### The Twin Cycle Hypothesis: Aetiology of Type 2 diabetes



Taylor R, Diabetologia 2008; 51: 1781

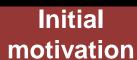
# "Diet" for weight loss

**Simple Practical** Time renders eating renders compensatory eating renders of the compensatory eating ren during weight loss

#### Behaviour-regulation strategies (examples)

- Avoidance,
- Distraction
- Breaking the goal down
- Drinking water
- Modifying the diet

- Reminding oneself of the goals
- Planning,
- Removing food from environment
- Social disclosure
- Weighting up pros and cons



#### **Adherence to the Total Diet Replacement**

Food

# Emotional and cognitive barriers

- Boredom with the regime
- Life events and stress
- Body shape dissatisfaction
- Lack of self-efficacy
- Lack of social support

#### **Environmental barriers**

- Presence of shops with food
- Traveling
- Going out and socializing
- Lack of opportunity to speak with other participants

#### **Process barriers**

- Dissatisfaction with outcomes
- Dislike of the product
- Hunger, cravings, and lapses

#### **Destabilisation**

Re-designing of the "Foodrobe"

Rehackova L et al, Diabetic Medicine 2017; 34: 1554-67

## Summary: Why type 2 diabetes is reversible?

