

# From understanding to action: A rational approach to type 2 diabetes

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# Disclosures

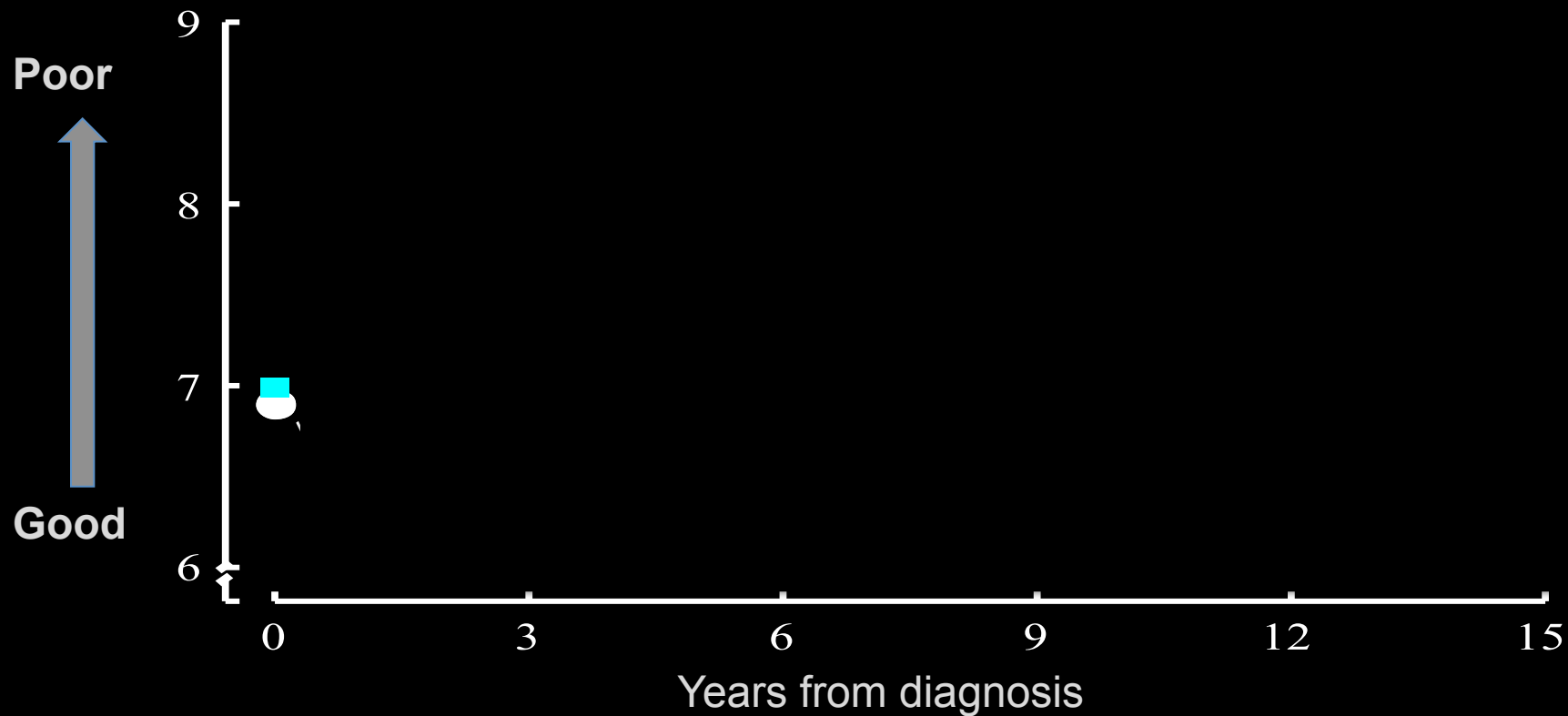
**Member of SACN working group on low carbohydrate diets – all opinions in this lecture are personal**

**Lecture fees from Novartis, Lilly**

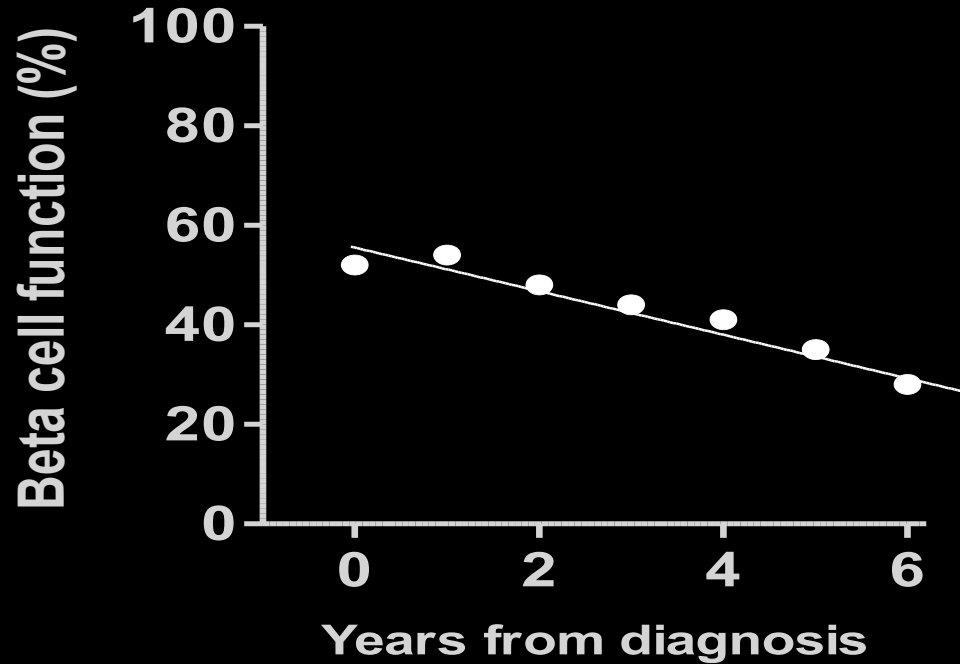
**Provision of low calorie products from Nestle and  
Cambridge Weight Plan**

# The nature of type 2 diabetes:

## UKPDS- Loss of control over time



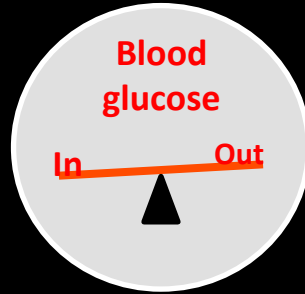
## Beta cell function in type 2 diabetes



# Staying alive overnight



Liver glucose  
production



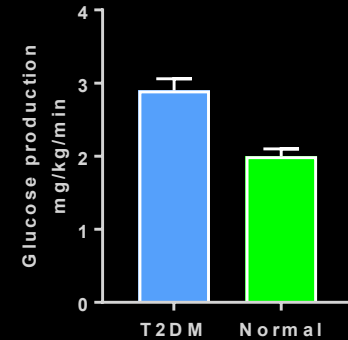
Oxidise for  
energy

**Glucose produced by liver in 1 hour during overnight fast:**  
**Non-diabetic 70kg person**



# Glucose produced by liver in 1 hour during overnight fast:

Type 2 diabetes cf. normal



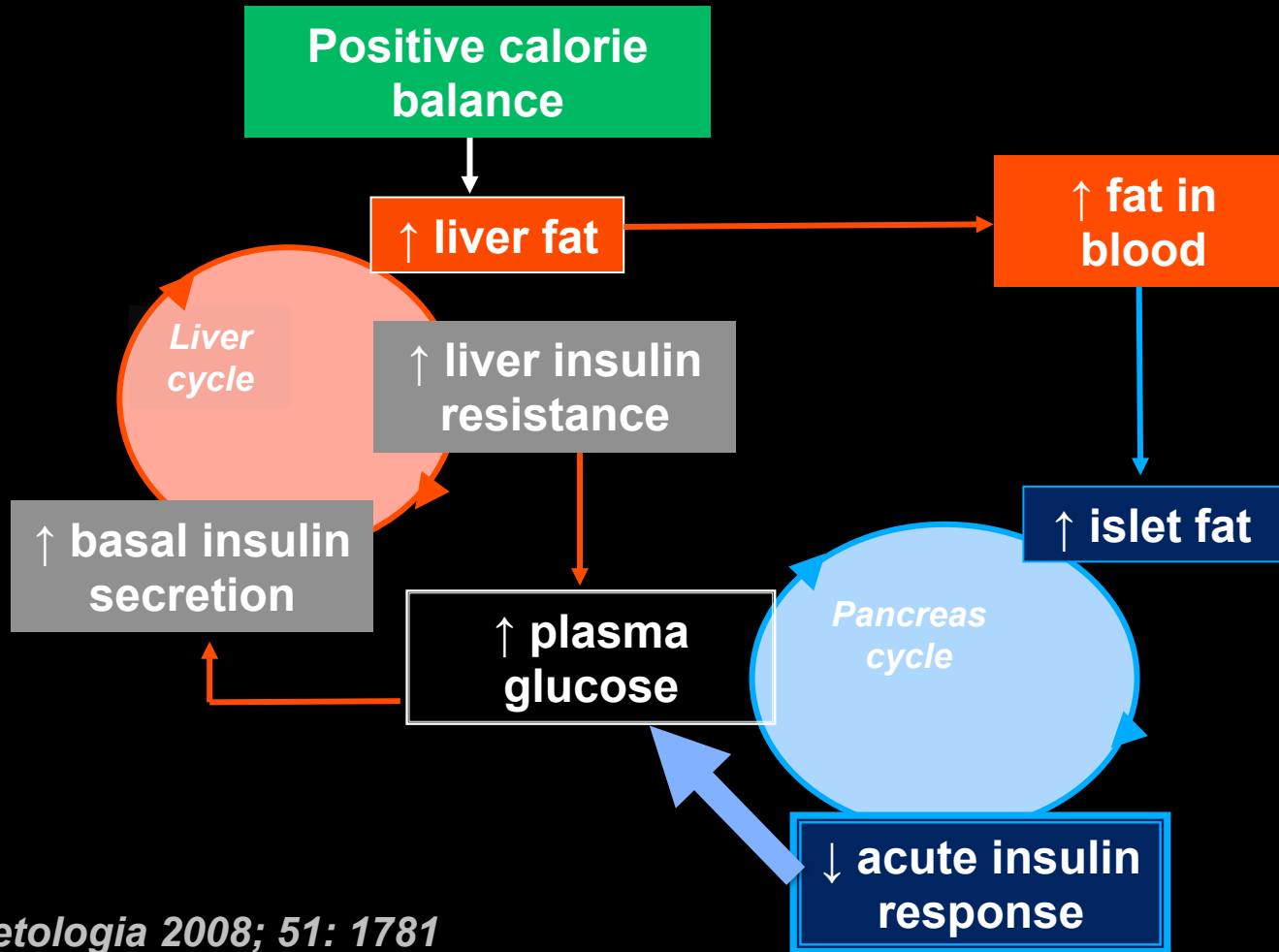


## Six hours of liver glucose production in T2DM

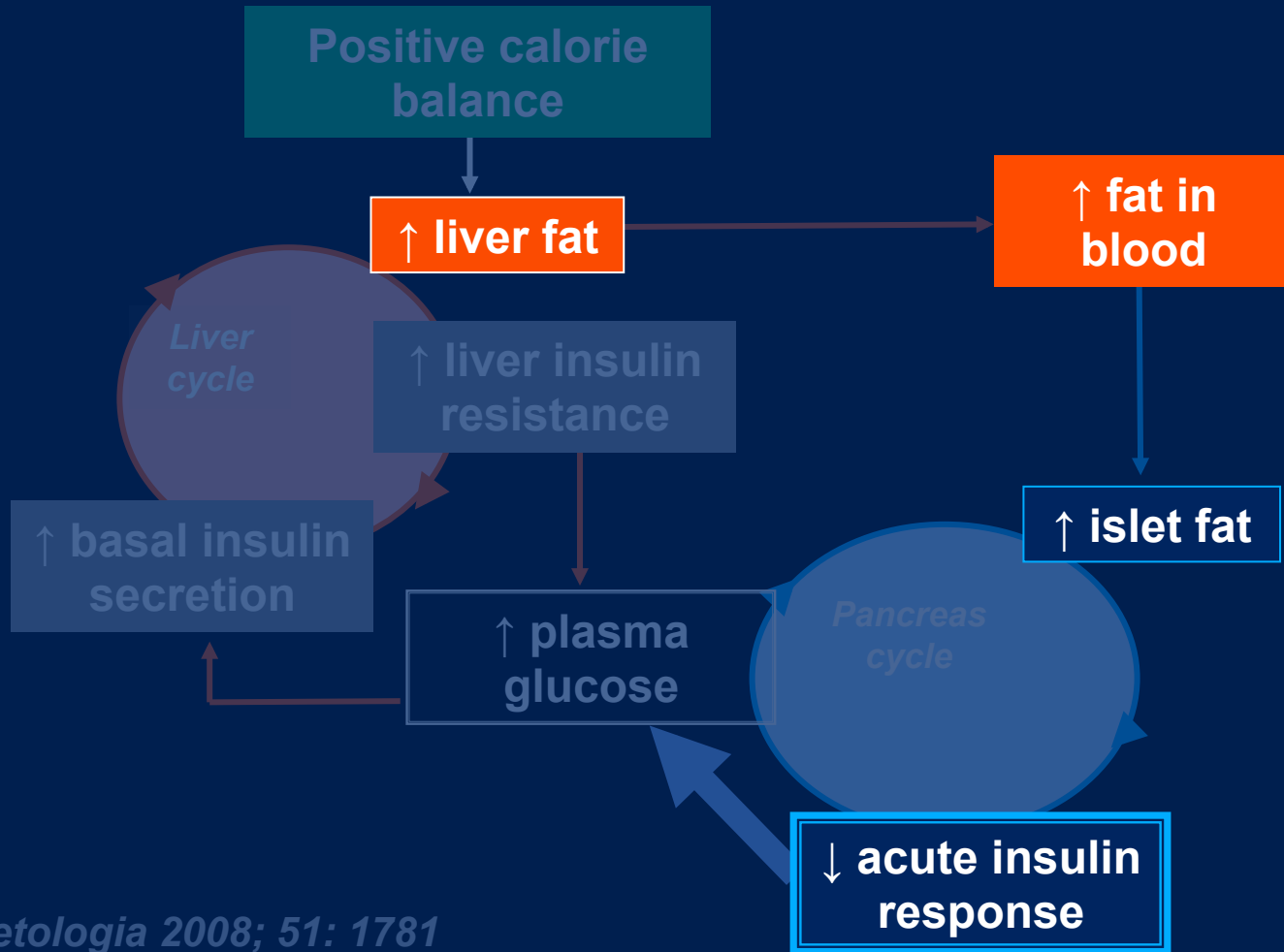




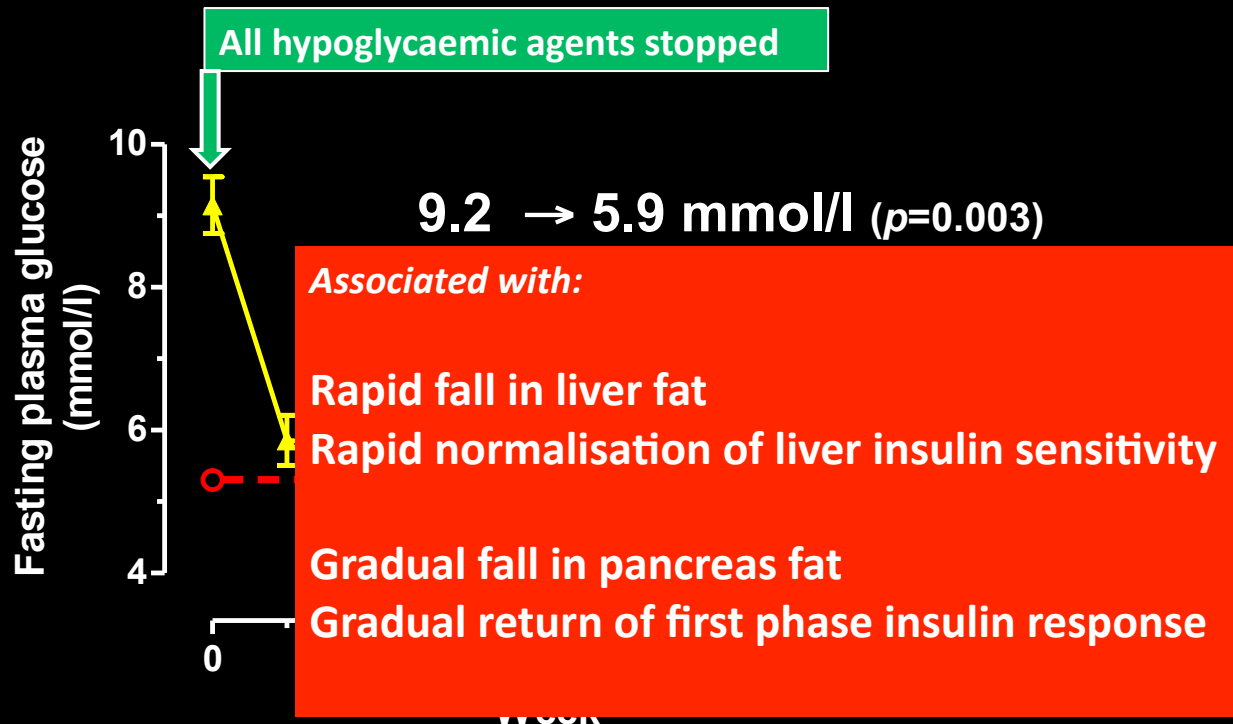
# The twin-cycle hypothesis: type 2 diabetes



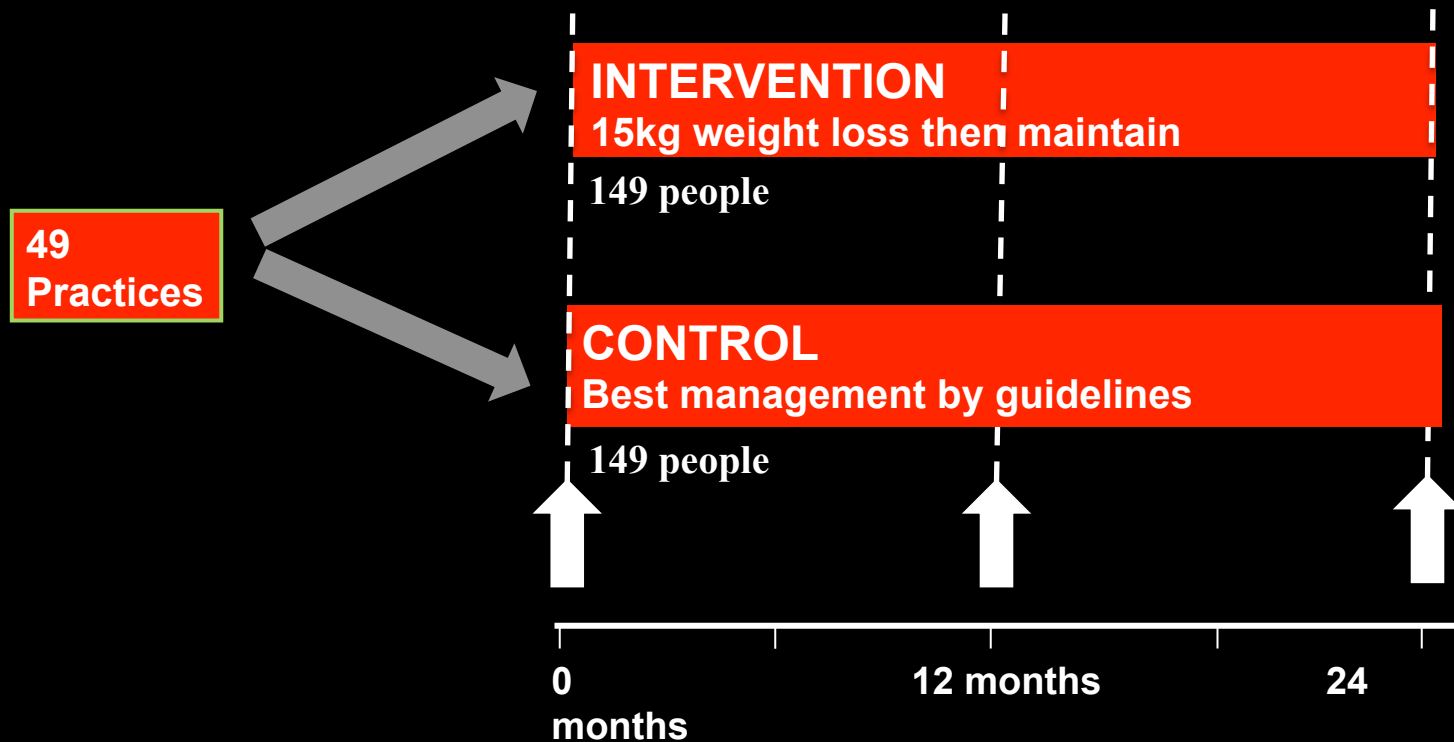
# The twin-cycle hypothesis: type 2 diabetes



# Using a very low calorie diet as a tool to understand aetiology of type 2 diabetes: Testing the Twin Cycle Hypothesis



# DiRECT – a study in routine NHS General Practice



## Results: weight changes over 12 months

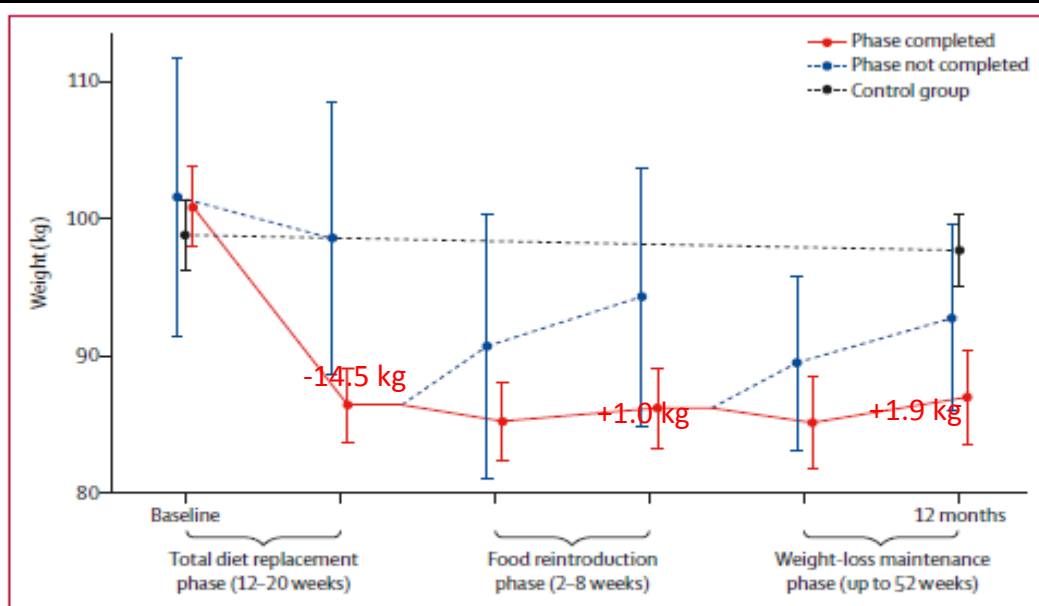


Figure 2: Change in weight of participants who remained in the trial and those who dropped out during each phase of the intervention  
Error bars represent 95% CIs.

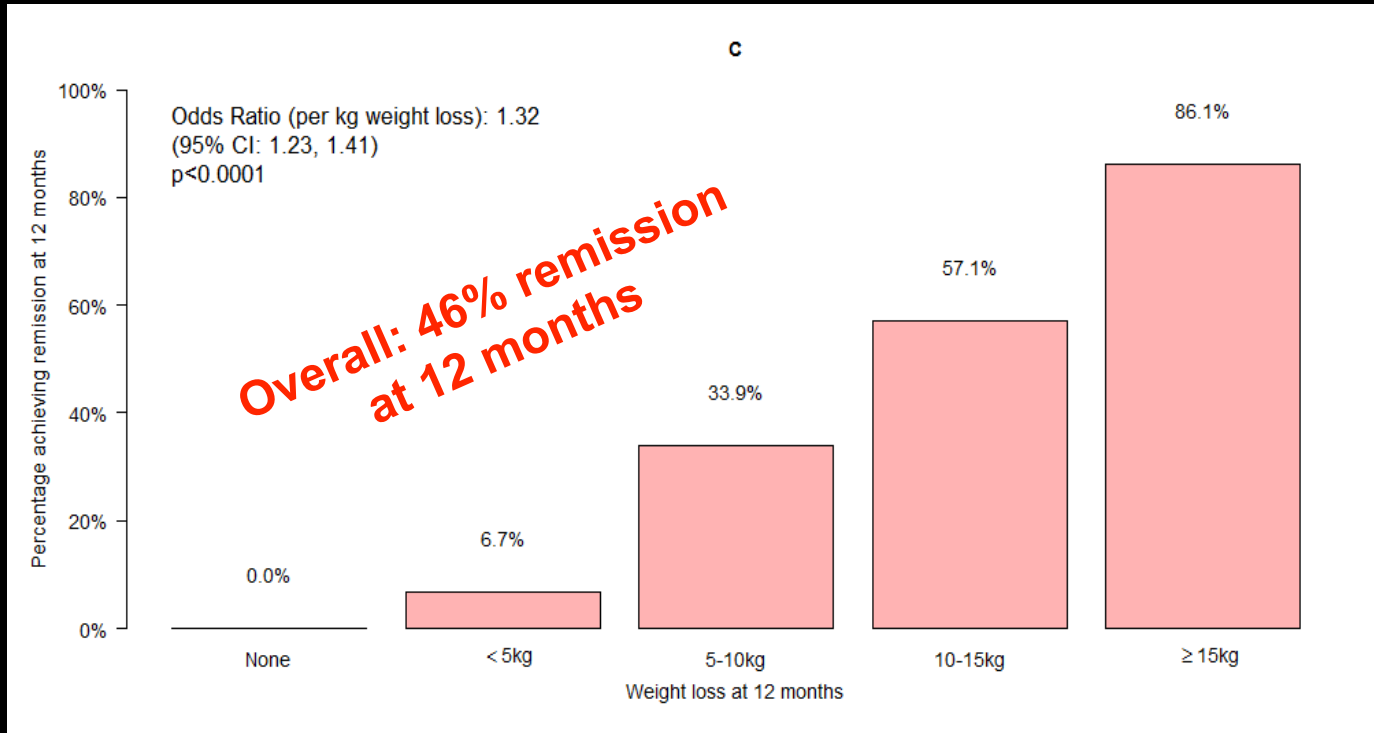
**Before**



**After**

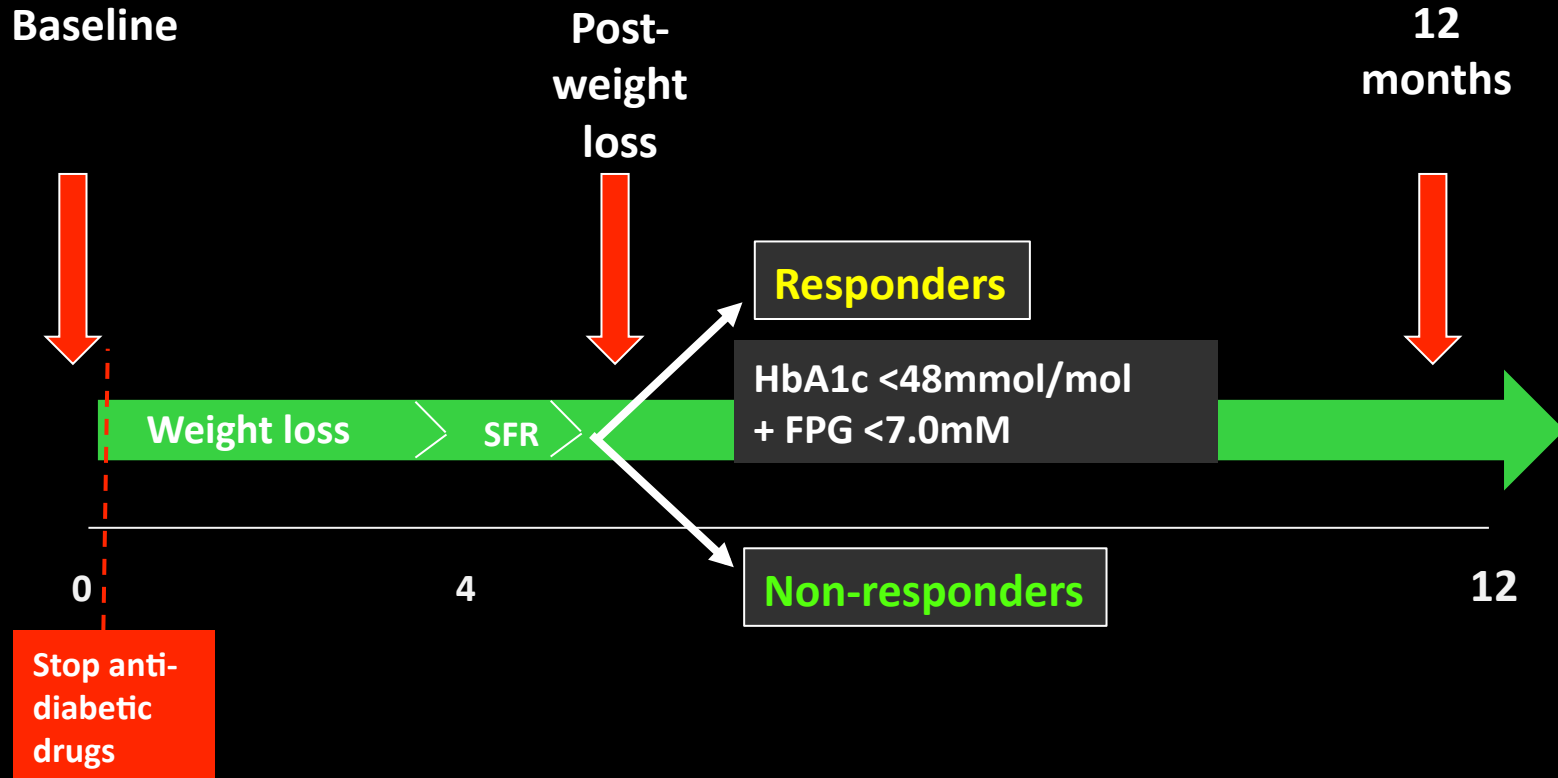


# Remissions by weight-loss category at 12 months

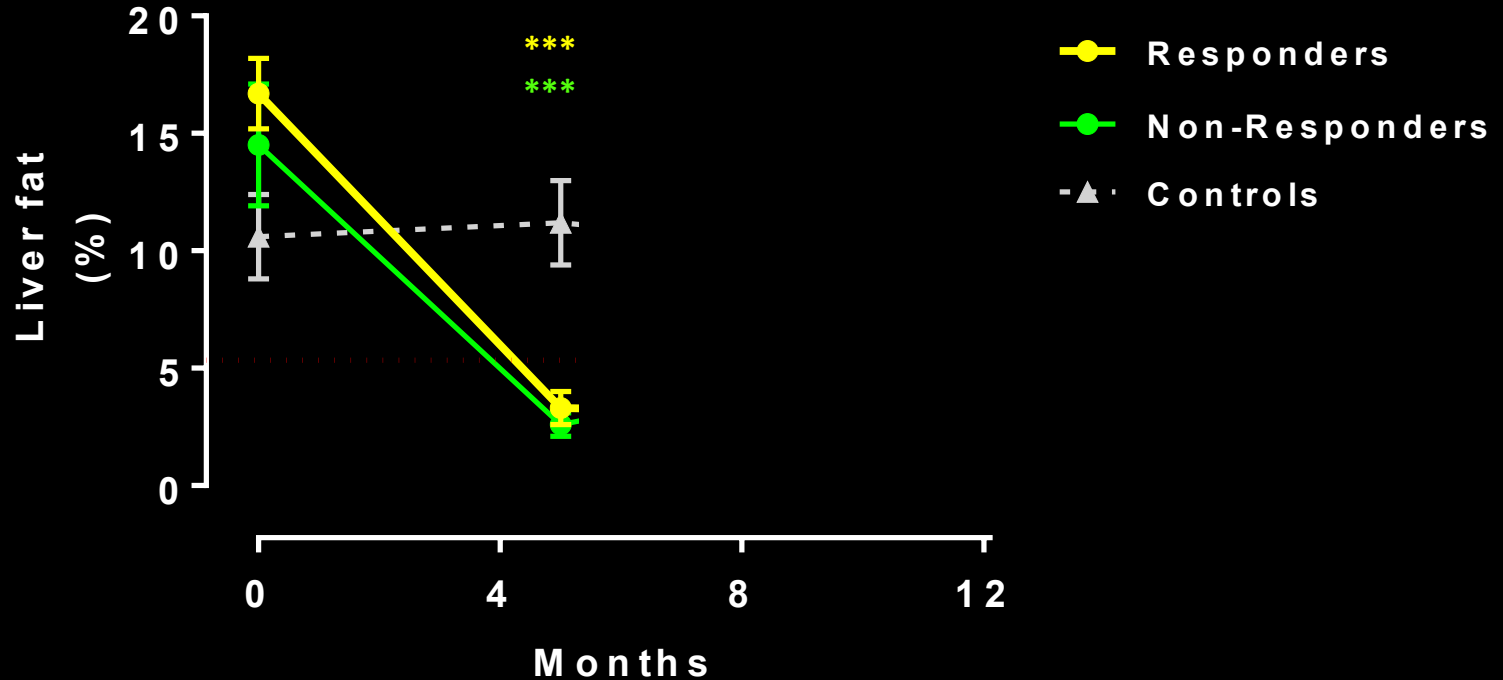




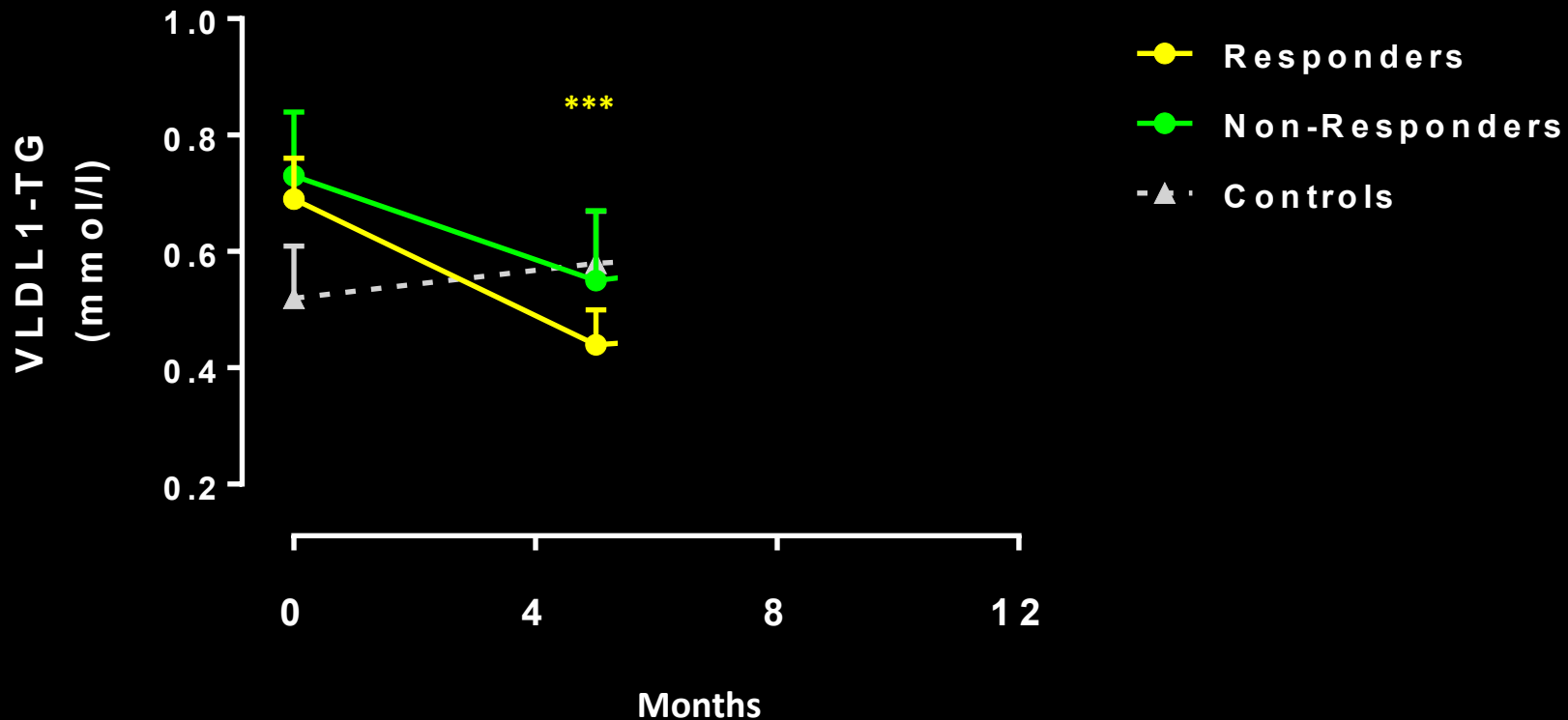
# Protocol for pathophysiological studies



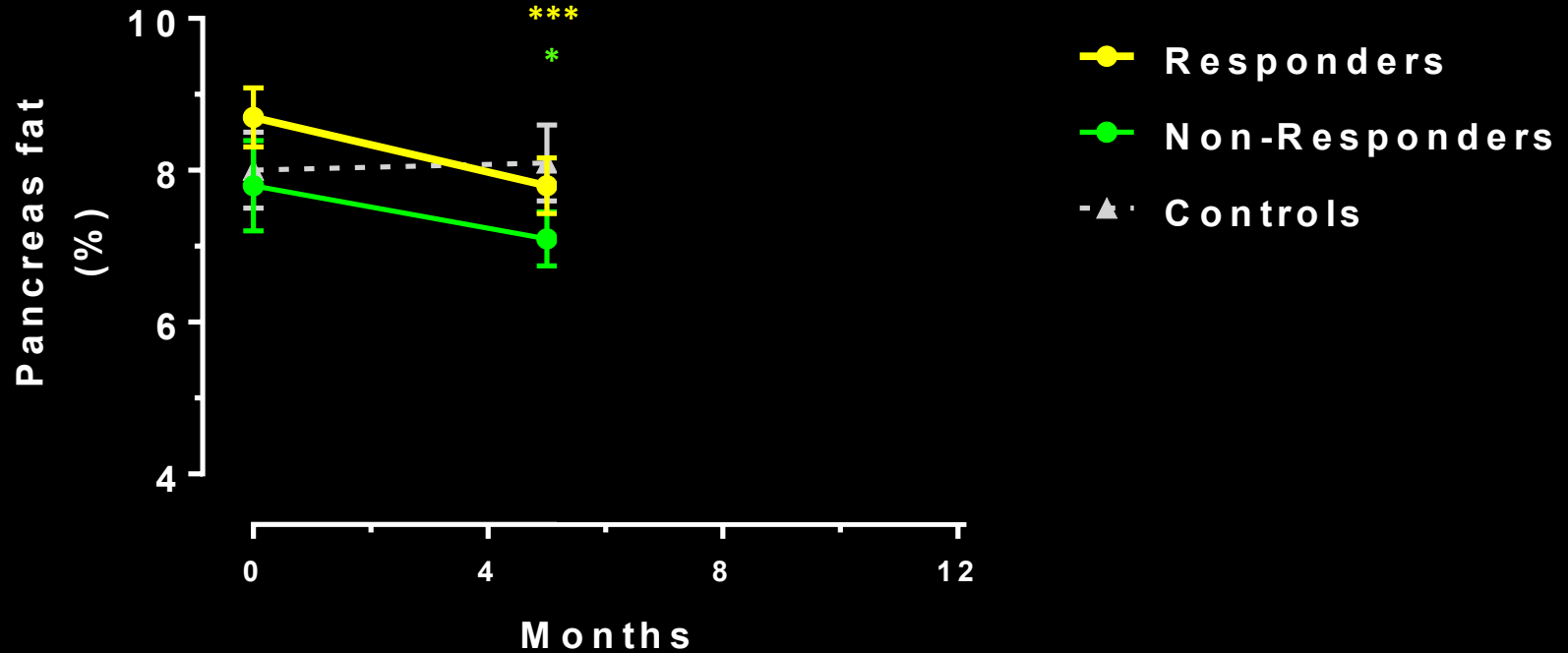
# Change in liver fat



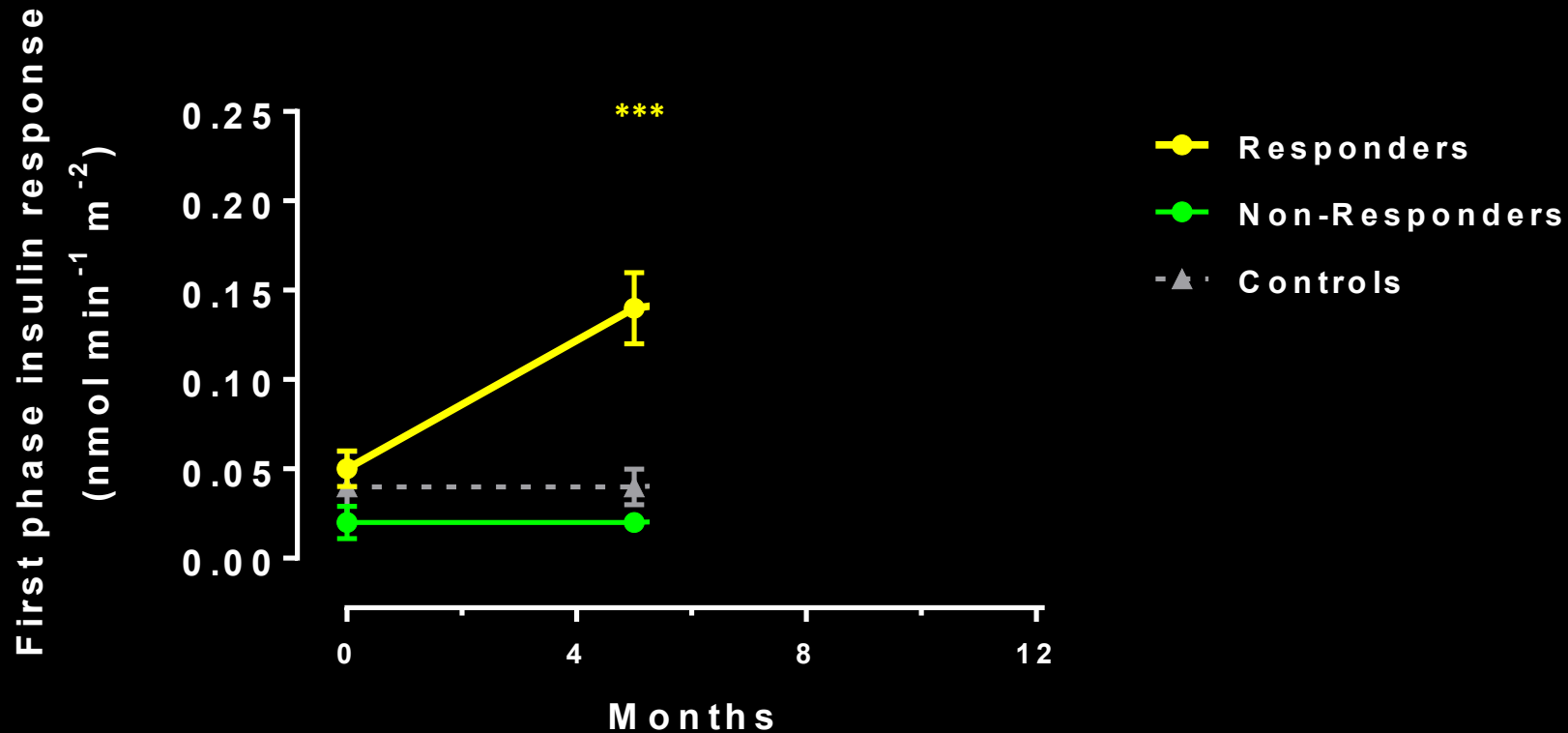
# Change in plasma VLDL1-triglyceride concentration



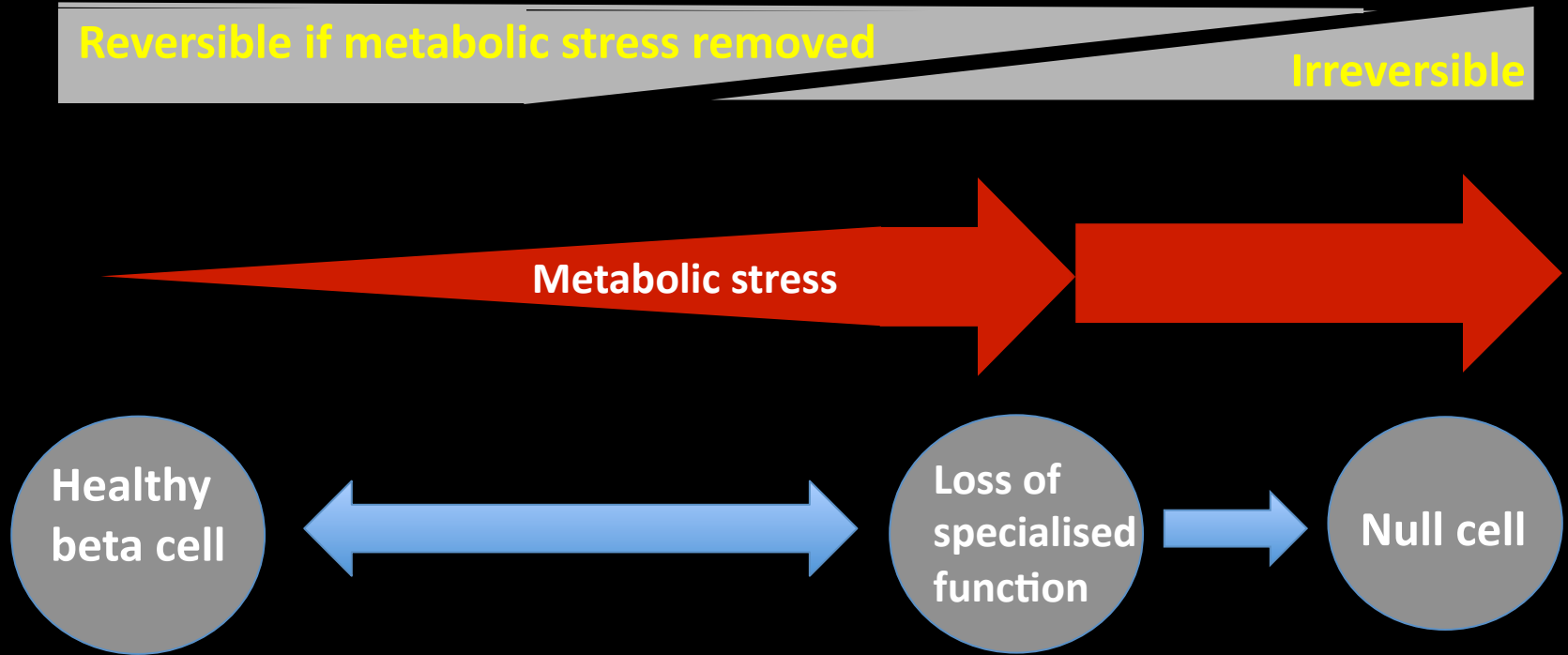
# Change in pancreas fat



# Change in acute insulin secretion



# Dedifferentiation explains the beta cell in type 2 diabetes









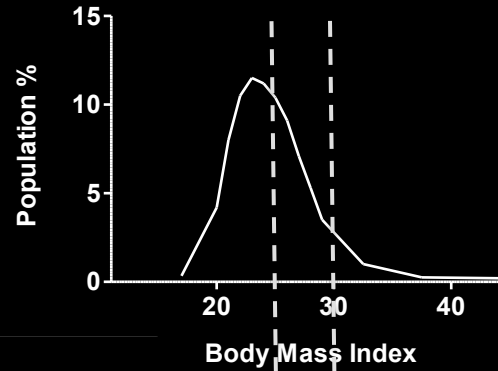
Newcastle ladies ~1980



Newcastle ladies – Daily Mail 2010

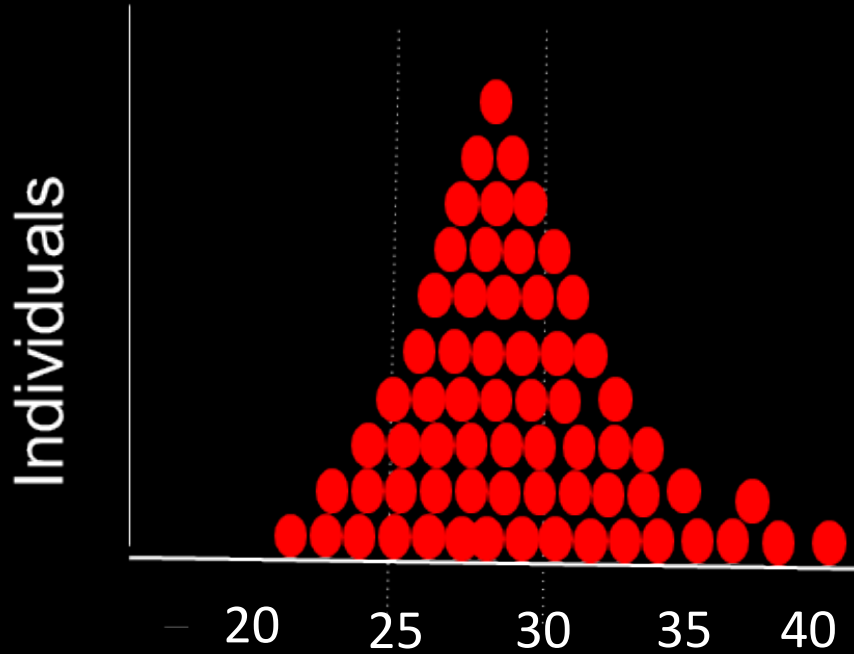
# BMI distribution in UK – 1980 and 2010

1980

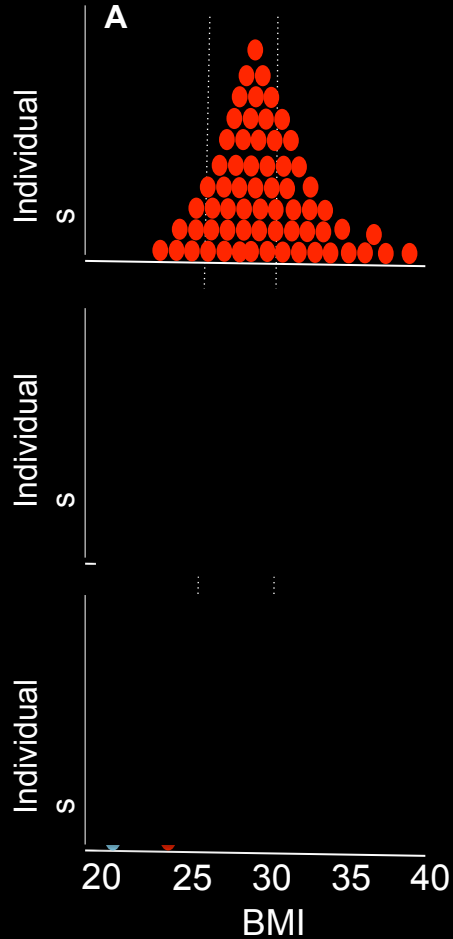


36% - over 25  
7% - over 30

## BMI distribution of individuals with type 2 diabetes



# Personal vs population



# Personal vs population









**Reid code when the processes underlying T2DM  
have been reversed?**

~~Diabetes resolved – 21263 or 212H~~

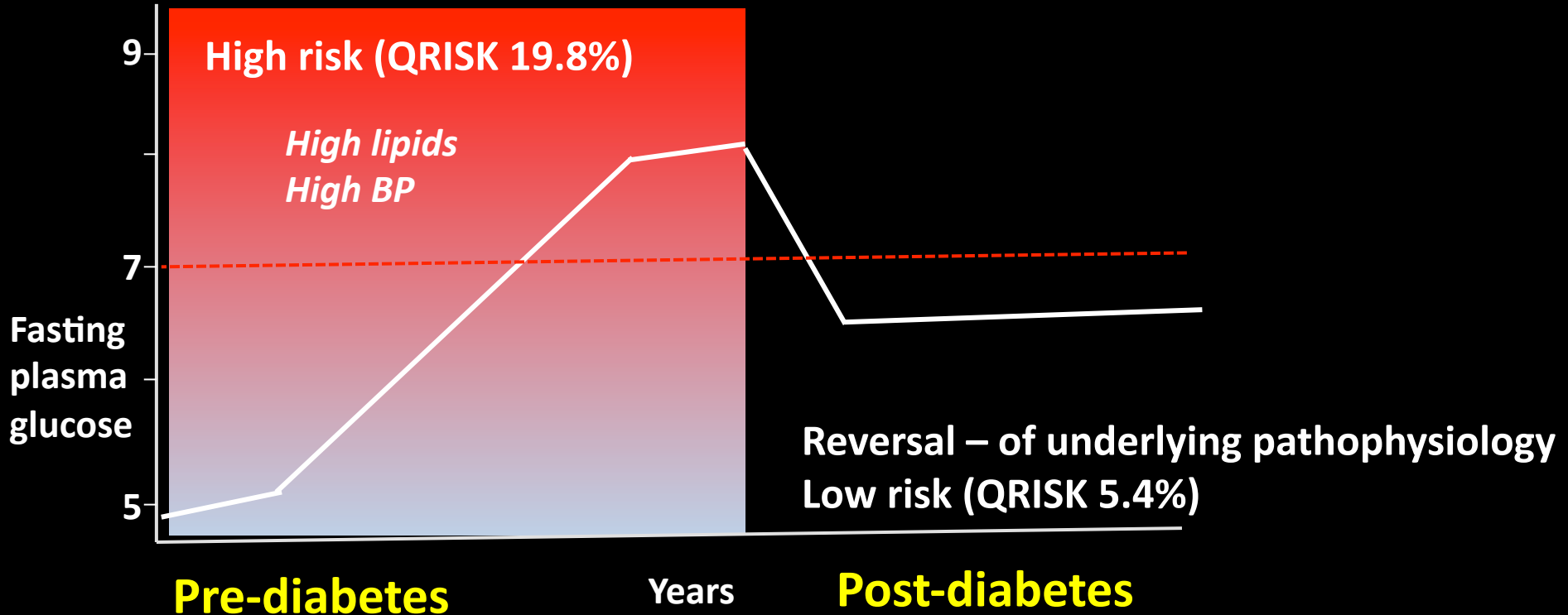
**Diabetes in remission – C10P**

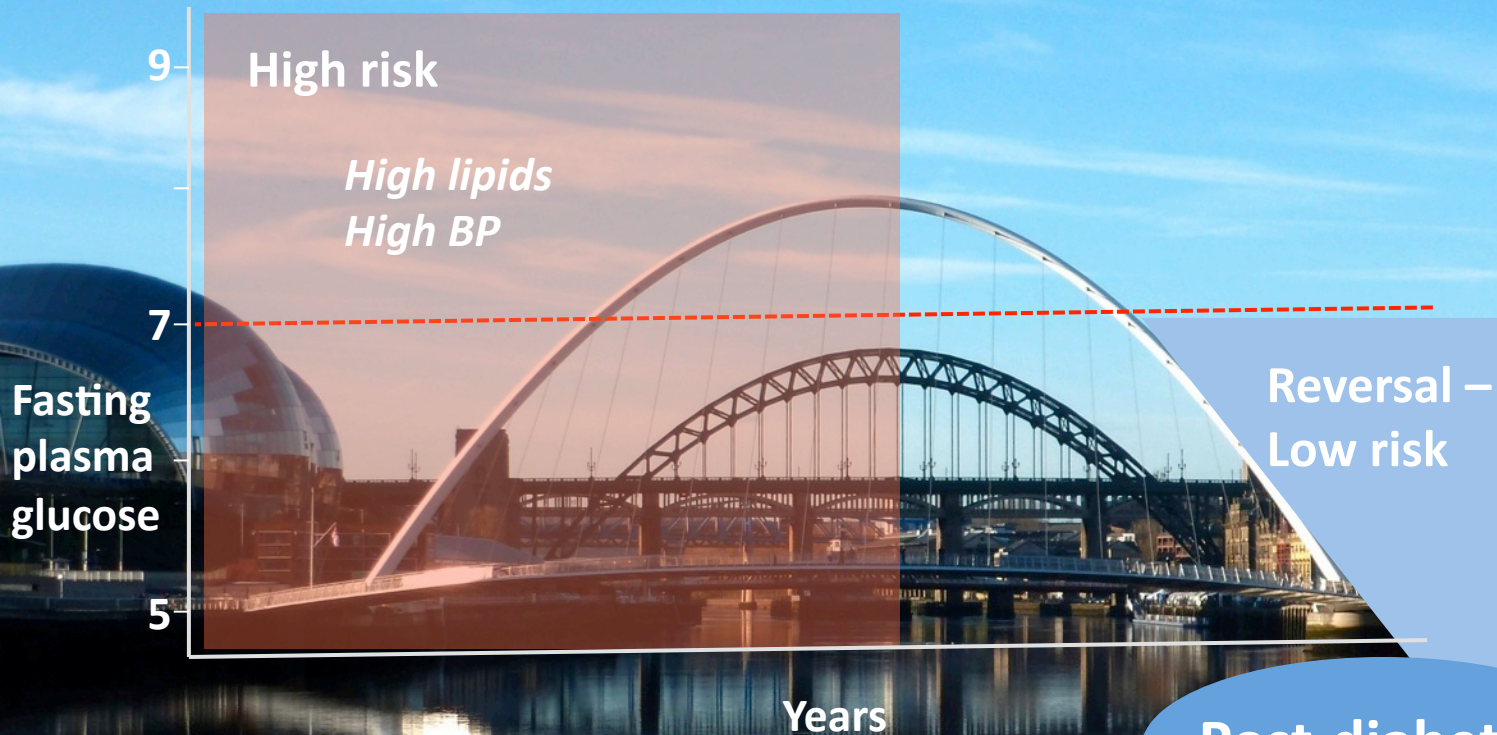
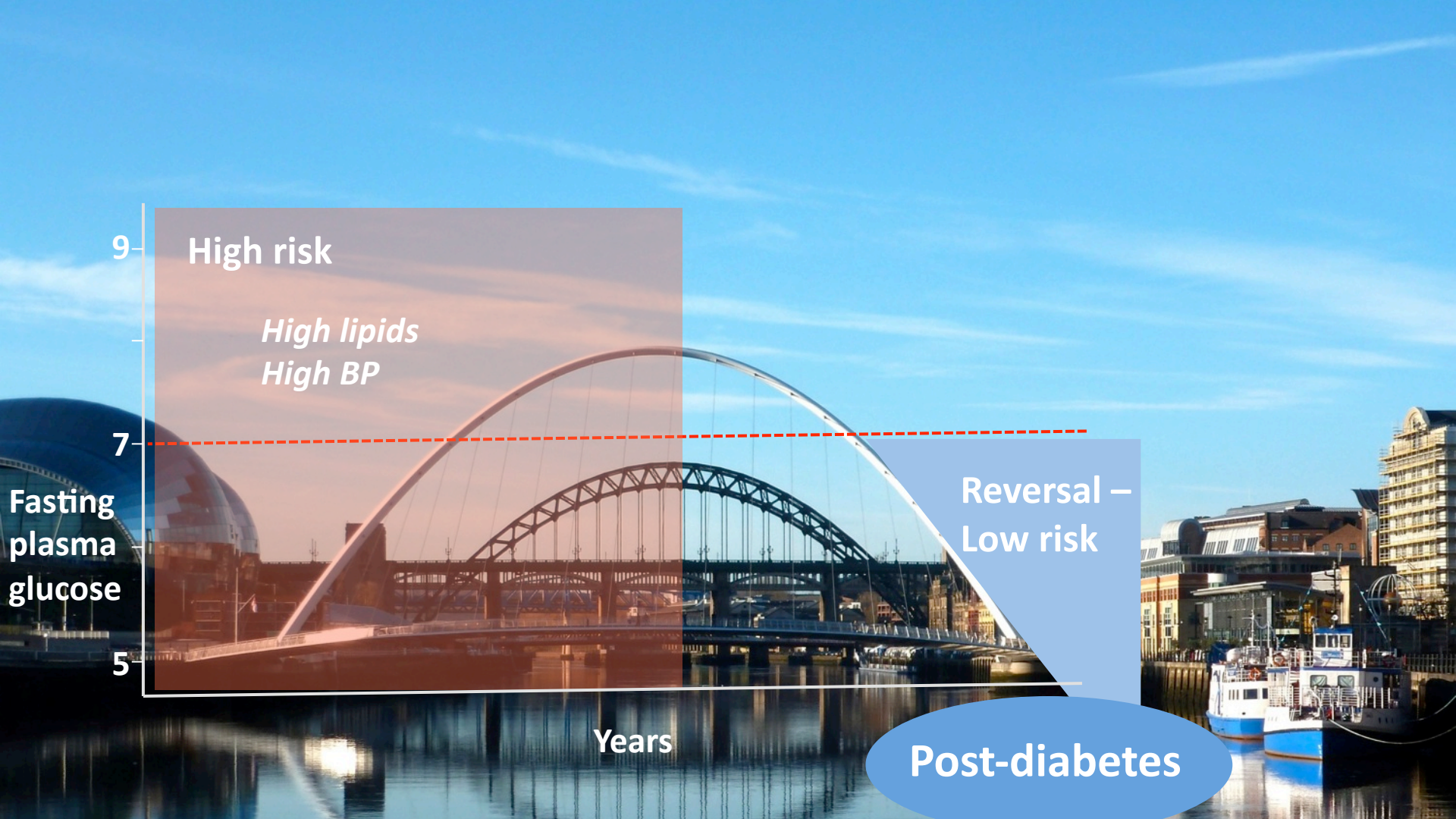
# Current definition of diabetes

ADA 1997 and WHO 1999

Fasting venous plasma glucose  $\geq 7.0$  mmol/l  
or  
HbA1c  $\geq 6.5\%$  ( $\geq 48$  mmol/mol)

# Pre-diabetes, diabetes and post-diabetes





Post-diabetes

# Defining remission of diabetes

Fasting venous plasma glucose  $<7.0$  mmol/l

HbA1c  $<48$  mmol/mol ( $<6.5\%$ )

Two non-diabetic test results, at least 2 months apart  
then reviewed annually

# Options for practical roll-out across UK

## Single-practice model

Re-badge some Clinics  
Minimal GP time input –  
stopping medication.

## Establish GP 'hubs'

With regular Diabetes  
Clinics  
Efficient

**Together with regulatory action on: hidden sugar in  
processed foods, advertising, portion size**

## Phased roll out

Enrol practices in phases

## Out-source

eg to providers of successful  
DPP systems  
Must include funded training  
for long term weight  
maintenance in Primary Care





**Aetiology of T2DM is now clear**

***T2DM is potentially reversible in Primary Care***

***Action required to provide support for all with T2DM***

***Regulatory control of food provision essential***