Understanding and management of type 2 diabetes into the future

Roy Taylor

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

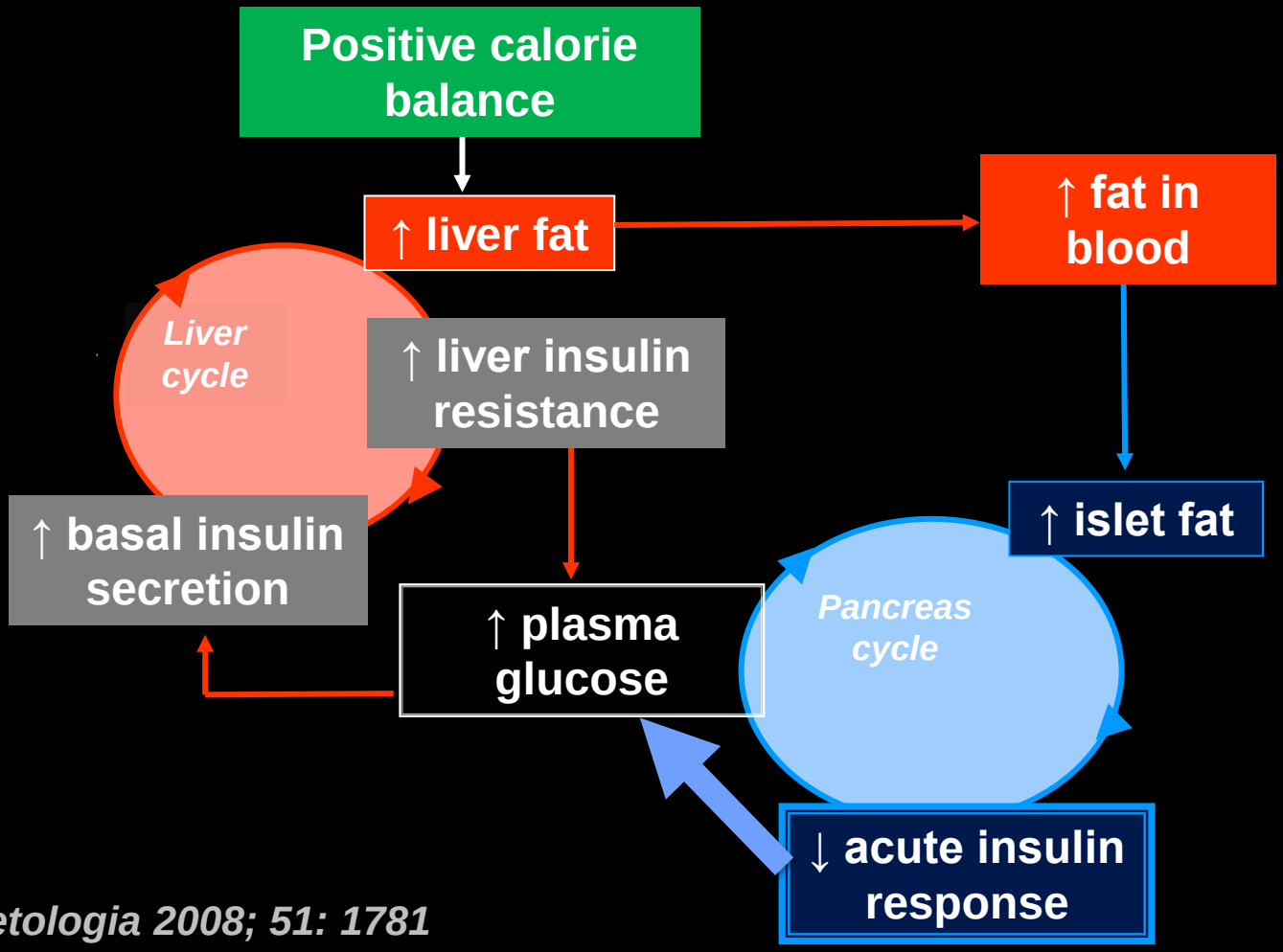
ABCD 2010 Last slide

How long will glucose remain normal after the 8 week intervention?

What stage of T2D becomes irreversible?

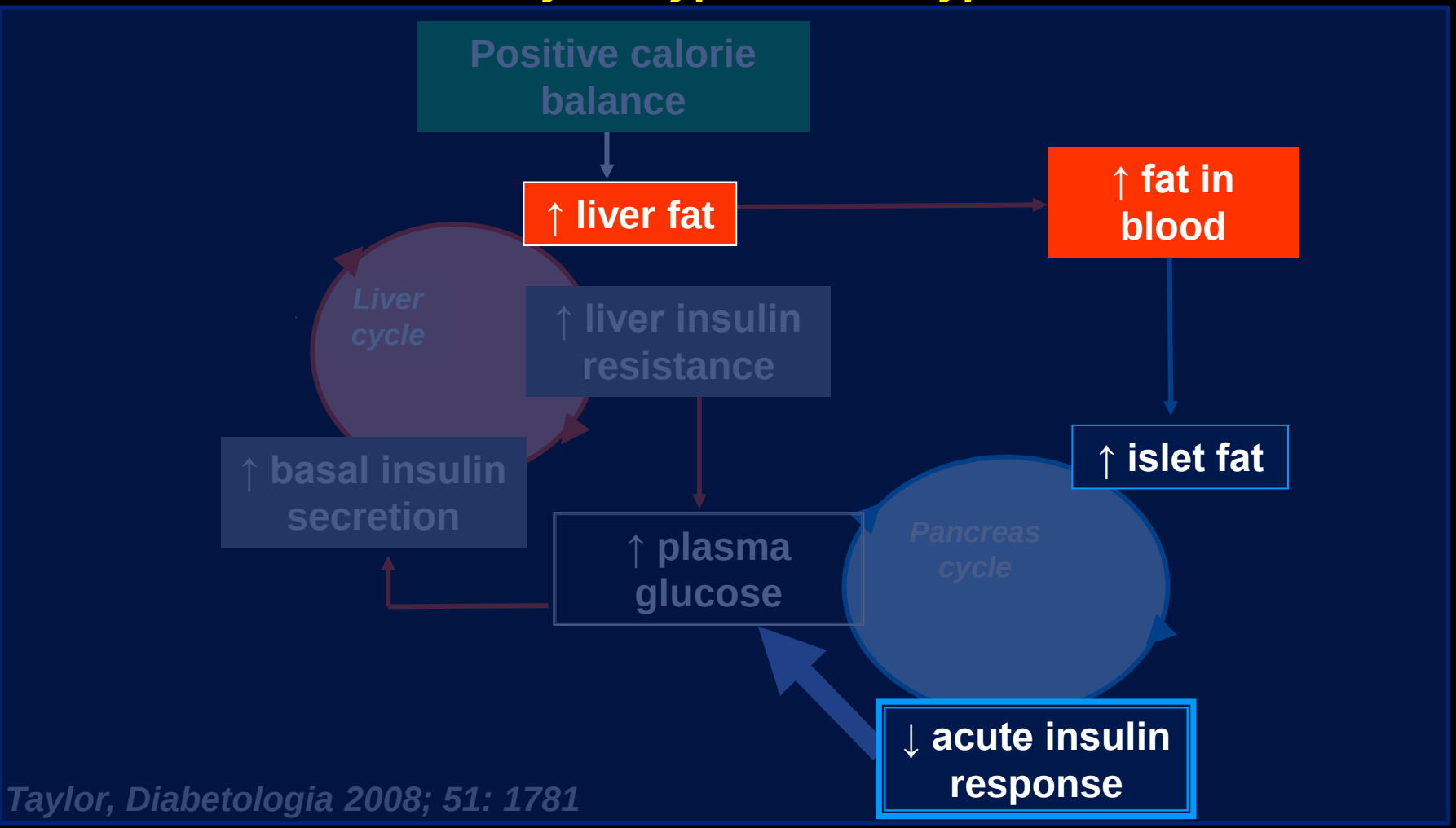
How can these observations be applied in clinical practice?

The twin-cycle hypothesis: type 2 diabetes



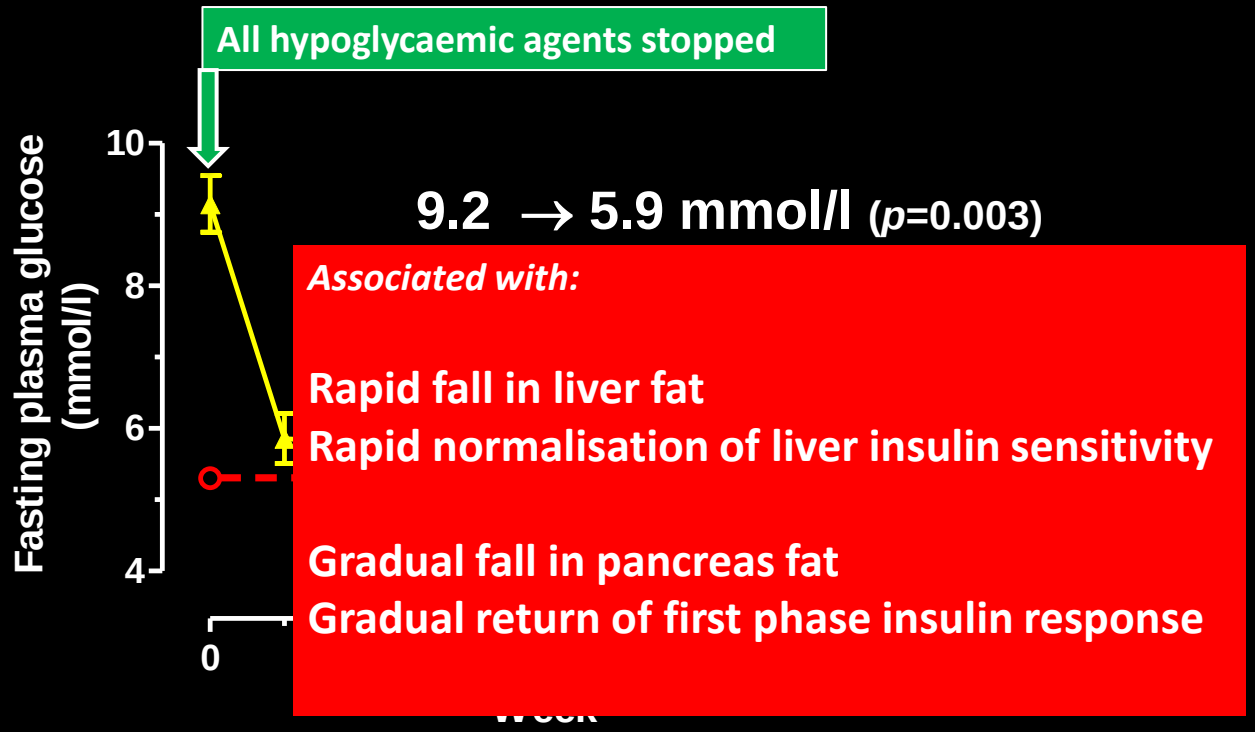
Taylor, Diabetologia 2008; 51: 1781

The twin-cycle hypothesis: type 2 diabetes



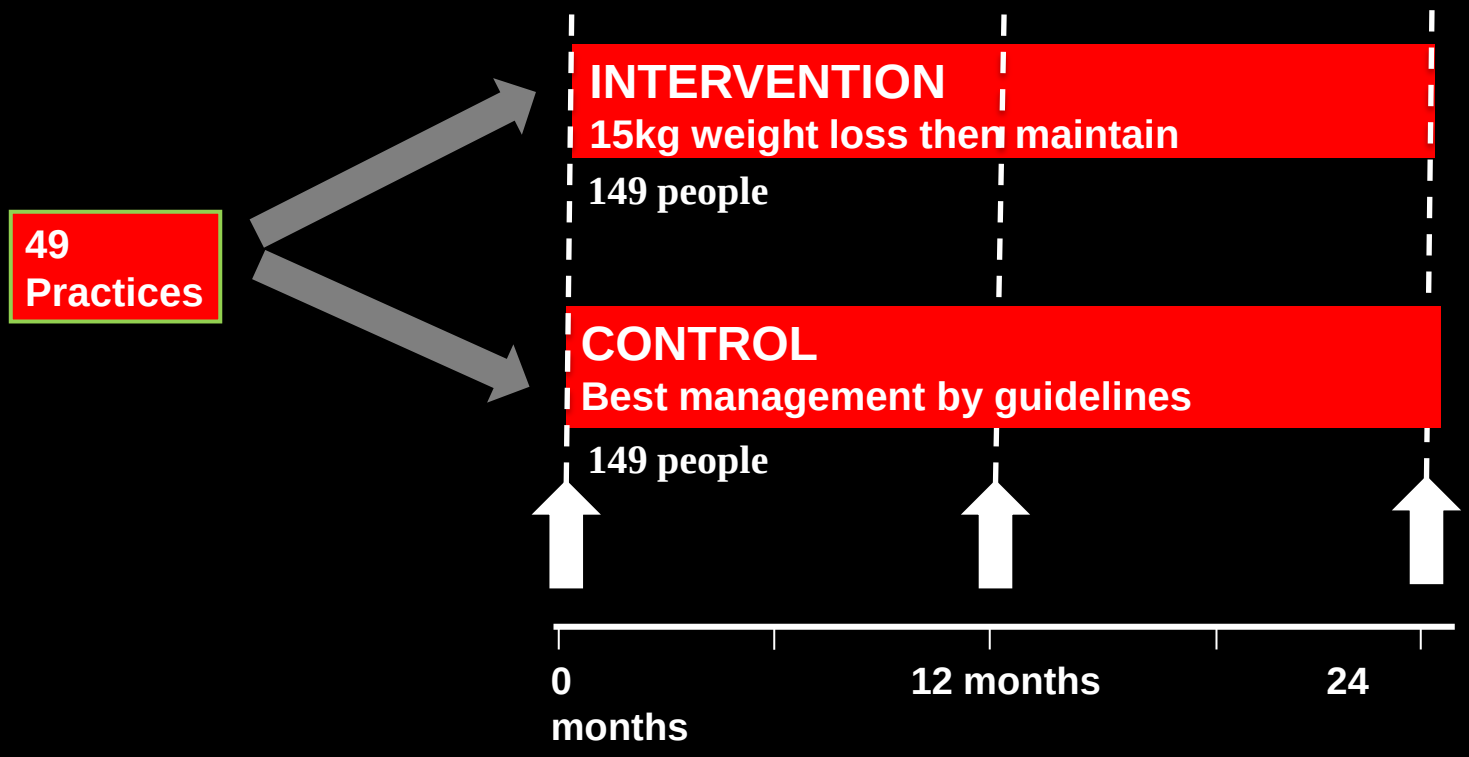
Taylor, Diabetologia 2008; 51: 1781

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



Lim et al, Diabetologia 2011

DiRECT – a study in routine NHS General Practice



Results: weight changes over 12 months

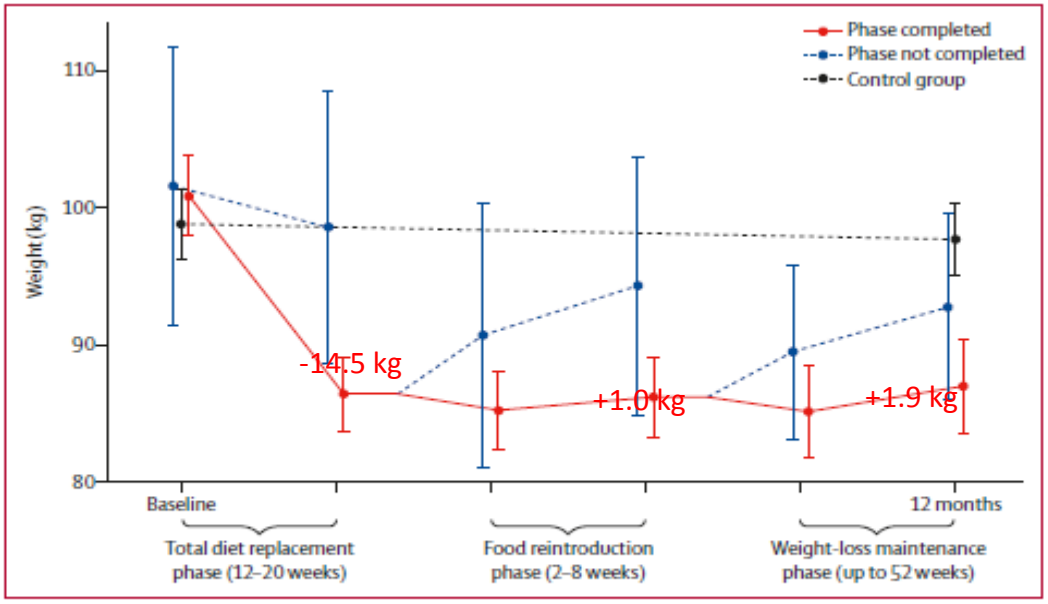
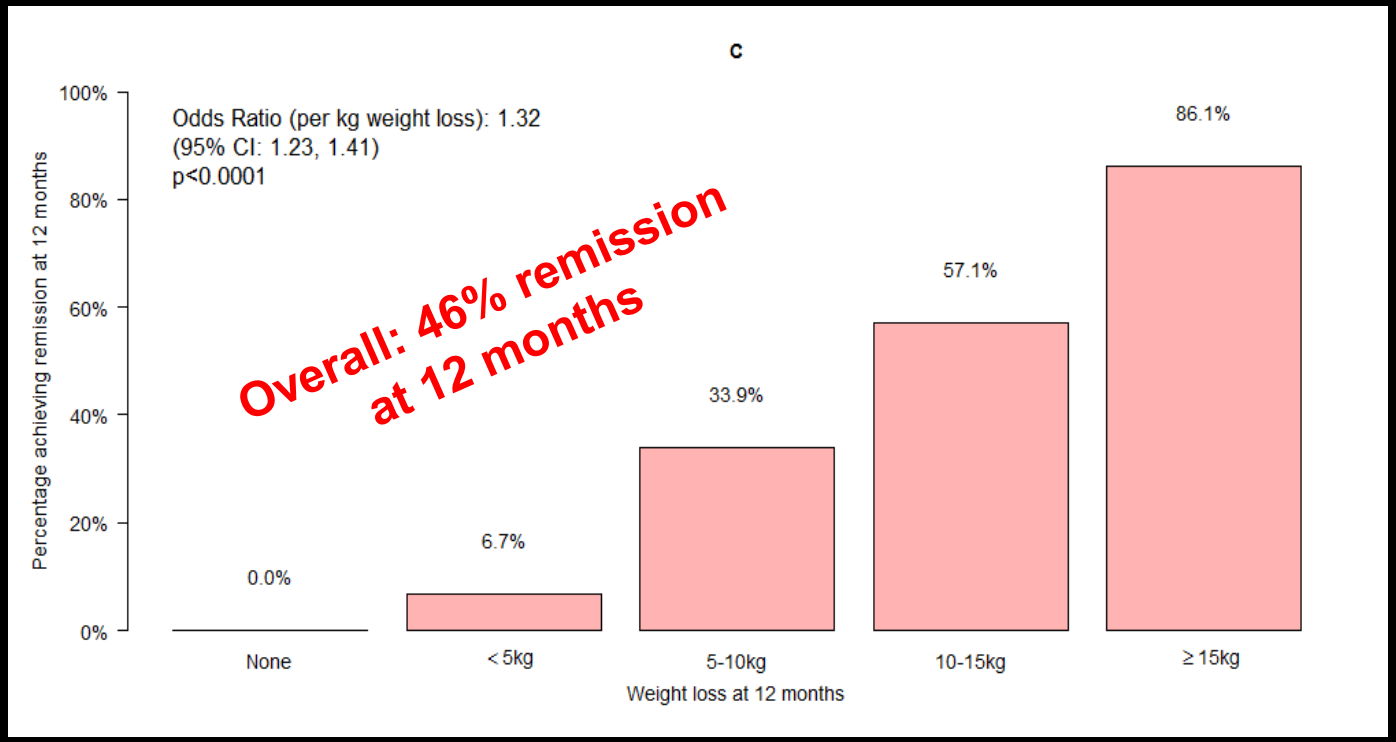


Figure 2: **Change in weight of participants who remained in the trial and those who dropped out during each phase of the intervention**
Error bars represent 95% CIs.

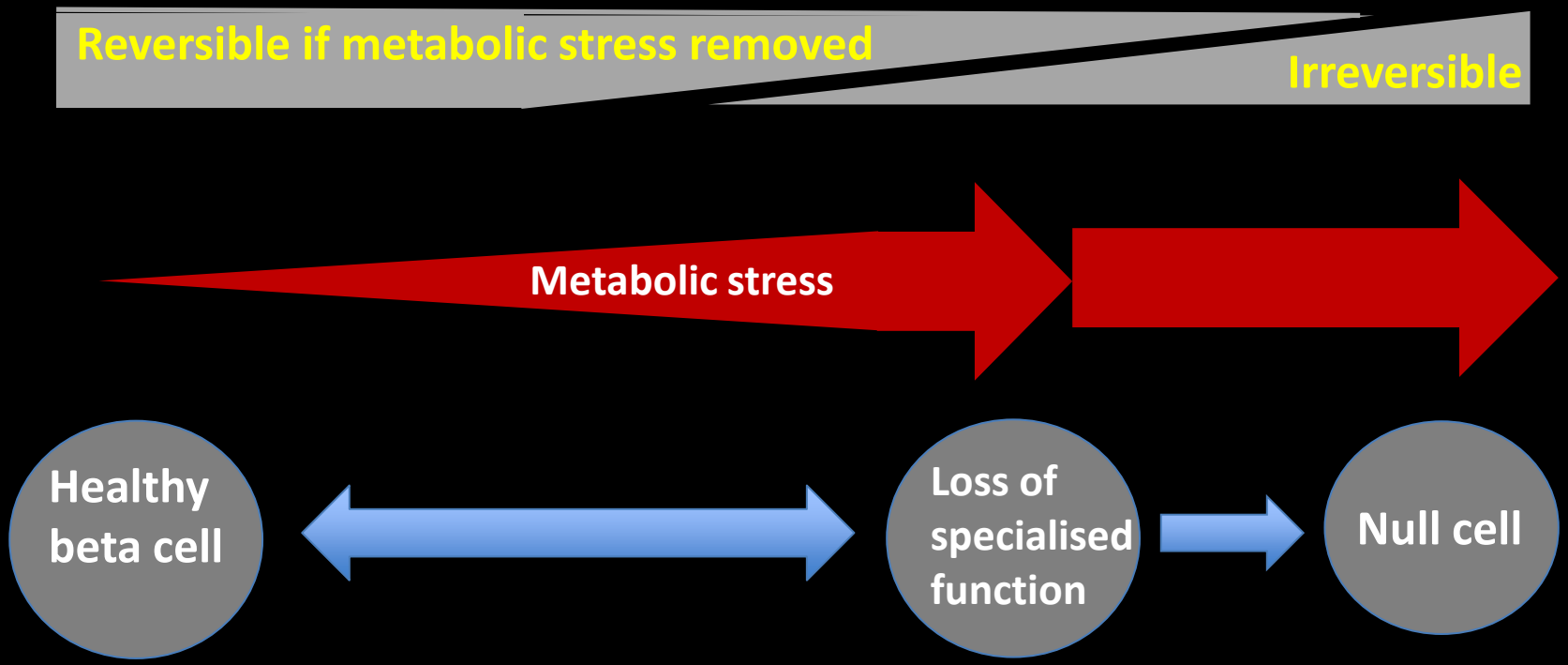
Remissions by weight-loss category at 12 months



DiRECT Diabetes Remission Clinical Trial

Lean et al, Lancet 2017

Dedifferentiation explains the beta cell in type 2 diabetes



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

Anecdote 1 – From 2010

54y old diagnosed with type 2 diabetes

BMI 26.5; HbA1c 6.5%; Fasting glucose 7.2

“I do not want this. How can I get rid of it?”

Advice.

	BMI	*HbA_{1c}*	*FBG*
6 mo	20.2	5.5	4.9
1y	19.4	5.3	4.8
6y	19.4	5.4	4.9

2013

Weight 126kg

HbA1c 9.2%

2014:

Weight 94kg

HbA1c 6.2%

2017

Weight 83kg

HbA1c 5.7%

Reid code when the processes underlying T2DM have been reversed?

~~Diabetes resolved~~ ~~21263 or 212H~~

Diabetes in remission – C10P

Current definition of diabetes

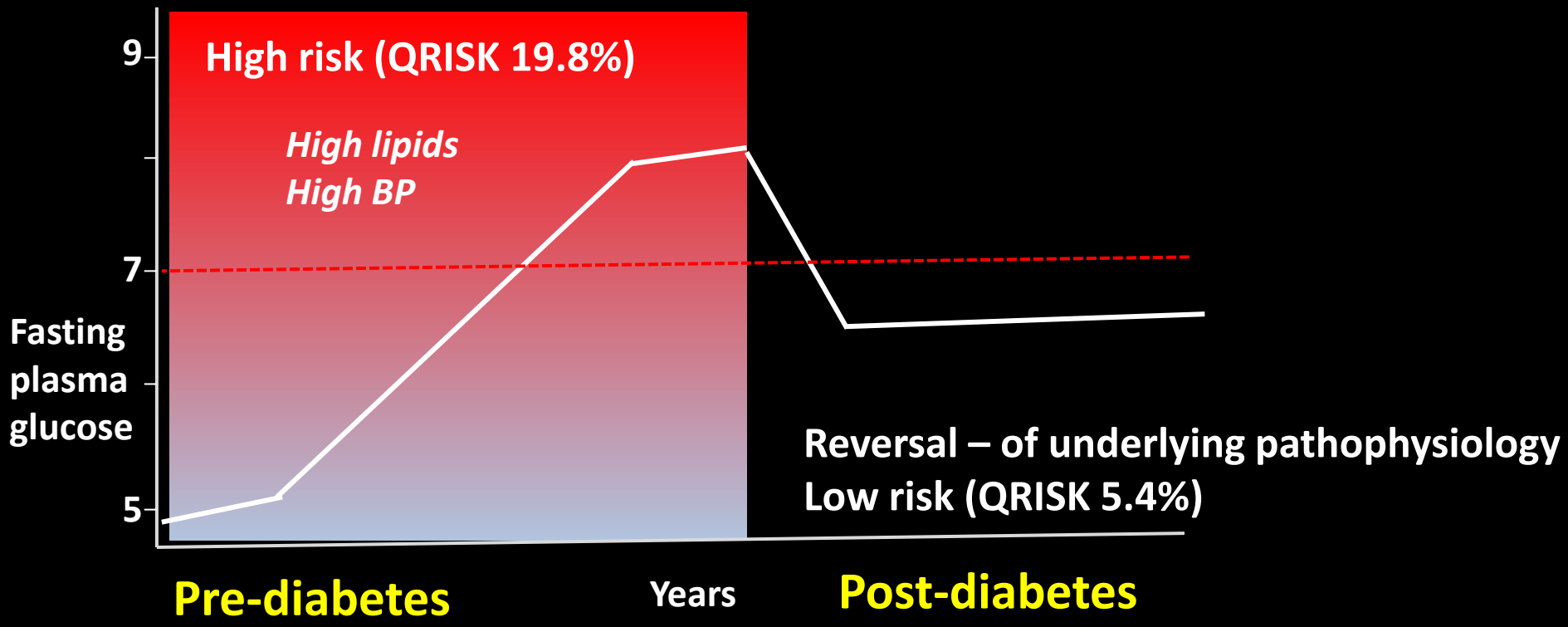
ADA 1997 and WHO 1999

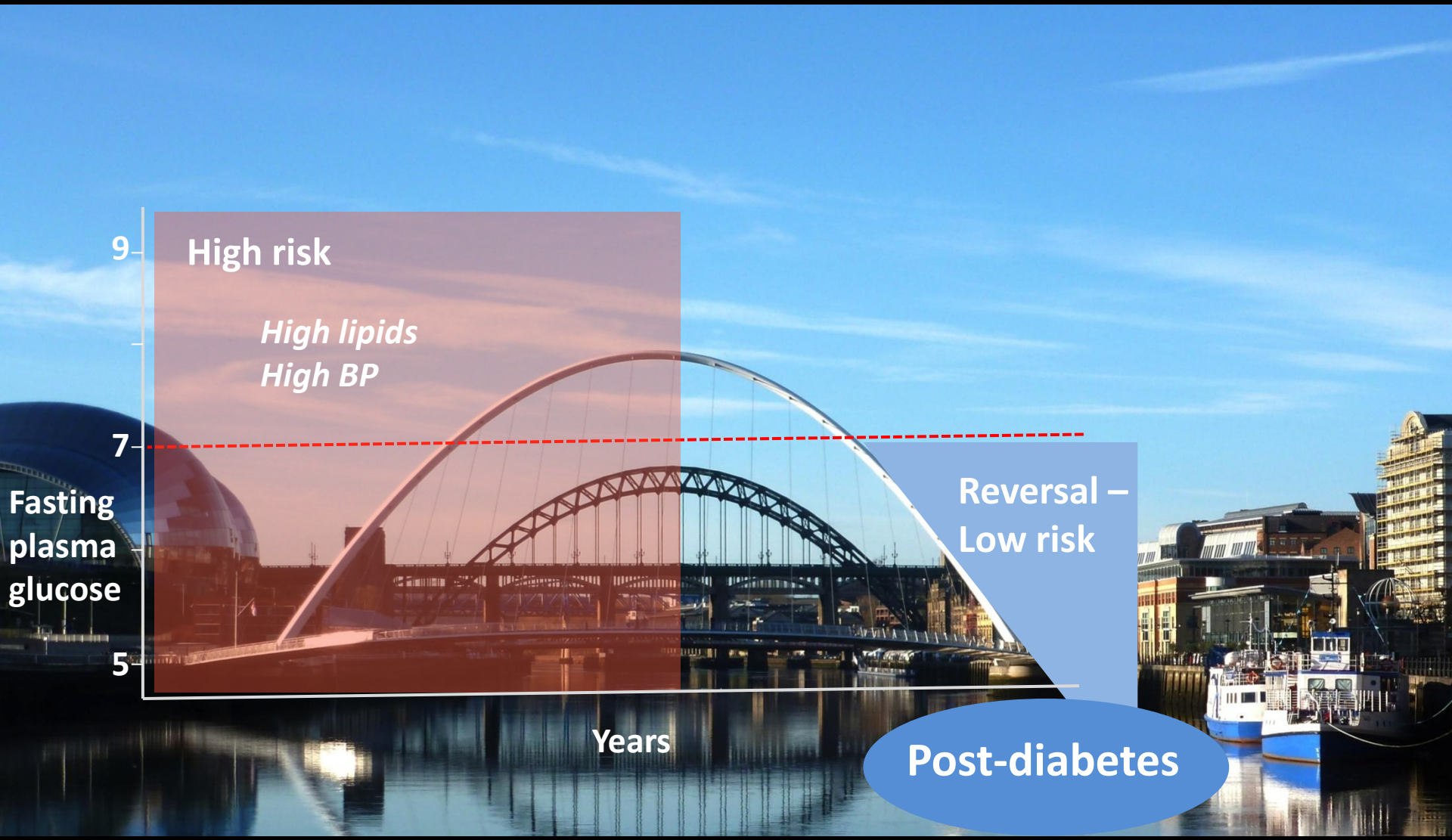
Fasting venous plasma glucose ≥7.0 mmol/l

or

HbA1c ≥ 6.5% (≥ 48mmol/mol)

Pre-diabetes, diabetes and post-diabetes




9
7
5
Fasting plasma glucose
High risk
High lipids
High BP
Reversal – Low risk
Years
Post-diabetes

Defining remission of diabetes

Fasting venous plasma glucose <7.0 mmol/l

HbA1c <48mmol/mol (<6.5%)

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

McCombie et al, BMJ 2017; 358: J4030

Benefits of coding remission of diabetes

For patients

- Motivates maintenance of substantial weight loss
- Removes stigmatisation as “diabetic”
- Life/travel insurance costs no longer 50% higher

For GPs

- Decrease in demands for medical input yet continued payment
- Application of knowledge of how the body works – rather than just being a pill pusher
- Broader application of knowledge

For health systems

- Identifies a valuable indicator of success in healthcare
- Allows better analysis of long term morbidity and mortality risks
- Tracking of major financial benefit

Pathophysiology of T2DM is now clear

T2DM is potentially reversible in Primary Care

Endorsement of definition of remission essential

Advise motivated individuals – it is a choice

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 Remission Clinics
Efficiencies and economies

Staged national roll out

Enrol practices in phases

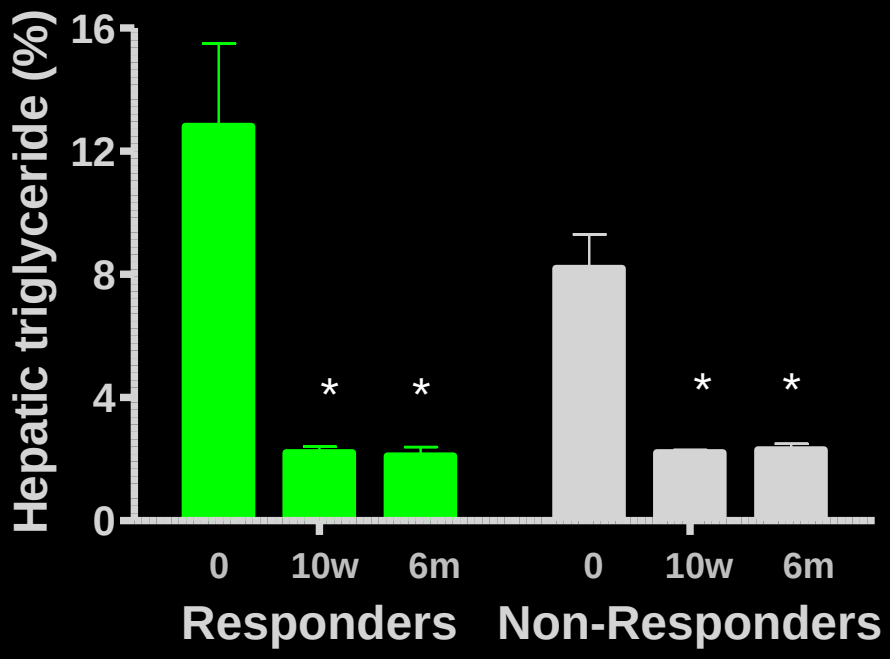
Out-source

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

Before

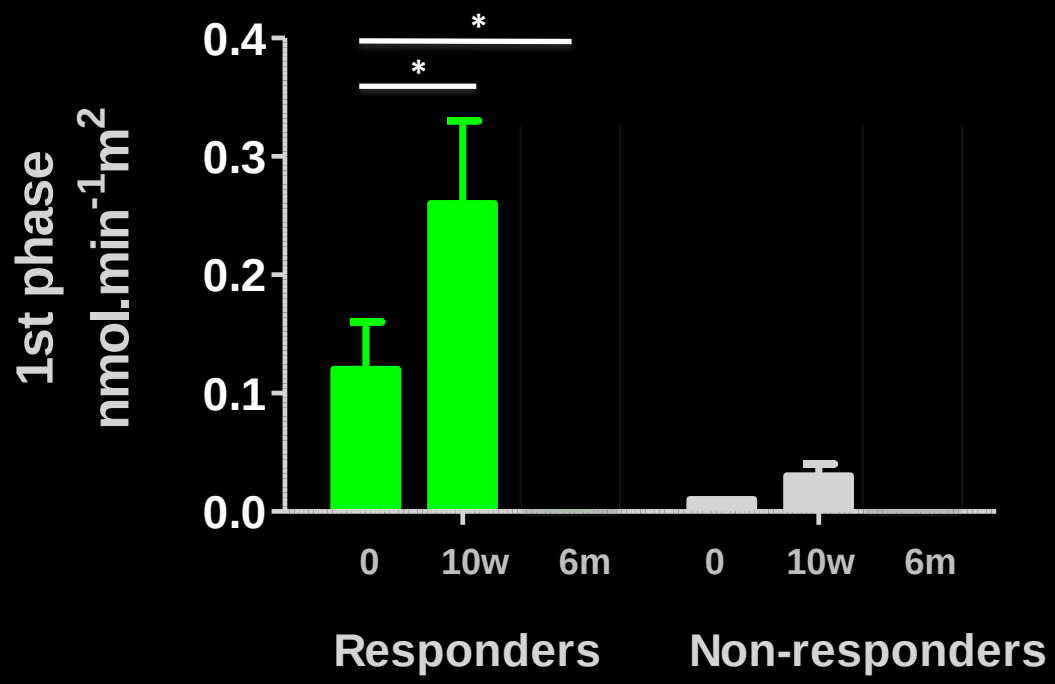
After

Counterbalance: Hepatic triglyceride



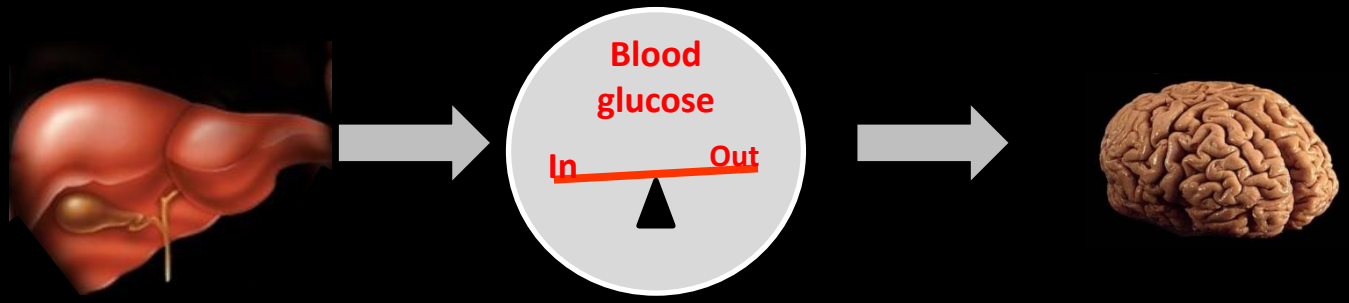
Steven et al. Diabetes Care 2016 39:808-15

Counterbalance: 1st phase insulin secretion



Steven et al. Diabetes Care 2016 39:808-15

Staying alive overnight



Liver glucose production

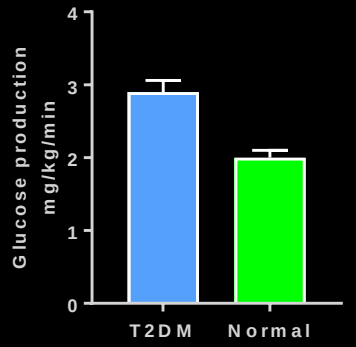
Oxidise for energy

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



Taylor et al, JCI 1996; Singal et al AJP 2002

Six hours of liver glucose production in T2DM