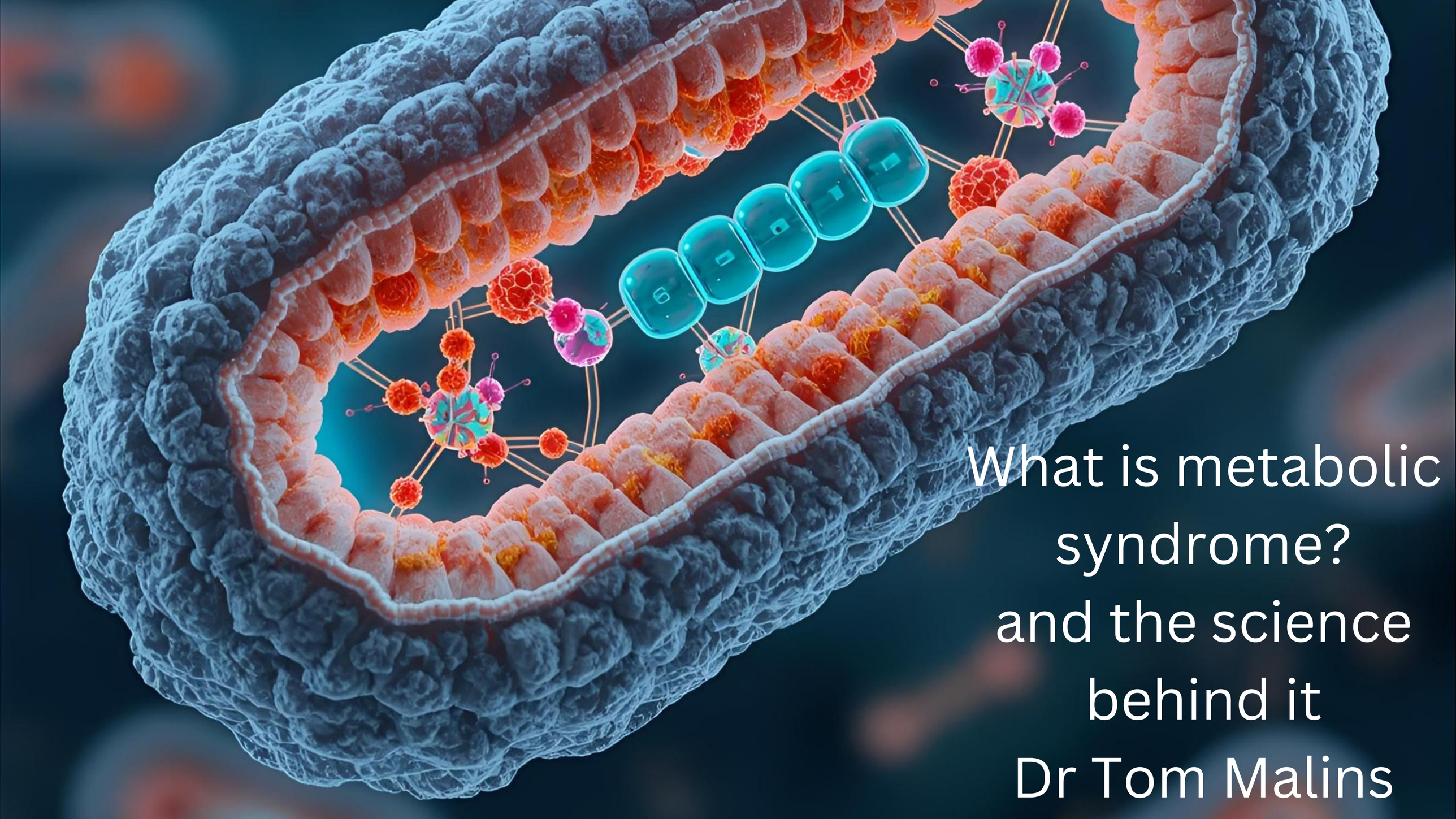


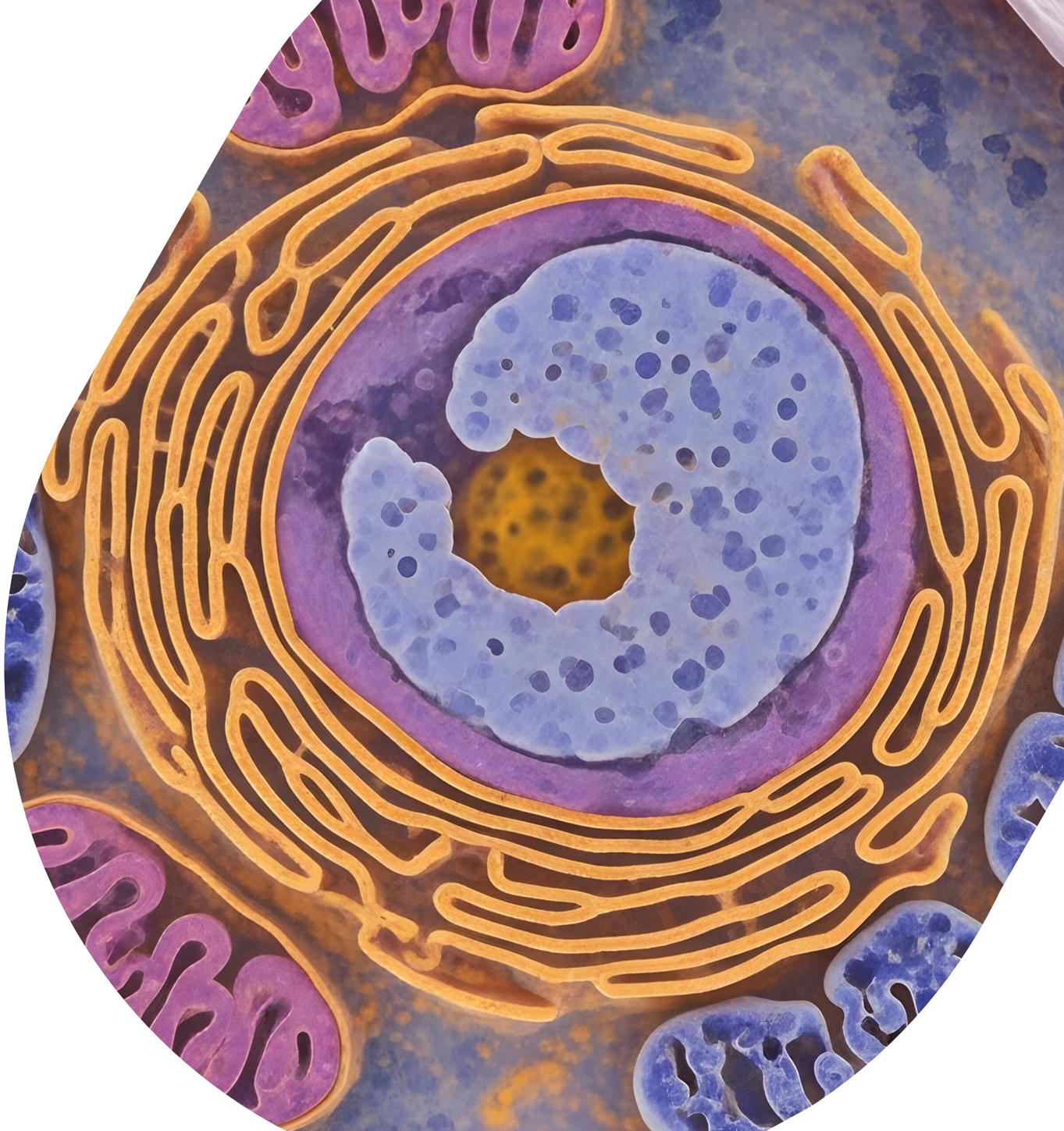
What is metabolic syndrome? and the science behind it

Dr Tom Malins

Content

What is metabolism?

the sum of all the **life-sustaining chemical reactions** that occur within the body, **providing the energy and materials cells need** to function, grow, and repair



Energy Storage & Release

Abdominal obesity
Fatty liver
Sugar cravings
Difficulty losing weight

Glucose & Insulin Regulation

Insulin resistance
High fasting glucose
Energy crashes
Skin tags

Lipid & Cardiovascular Balance

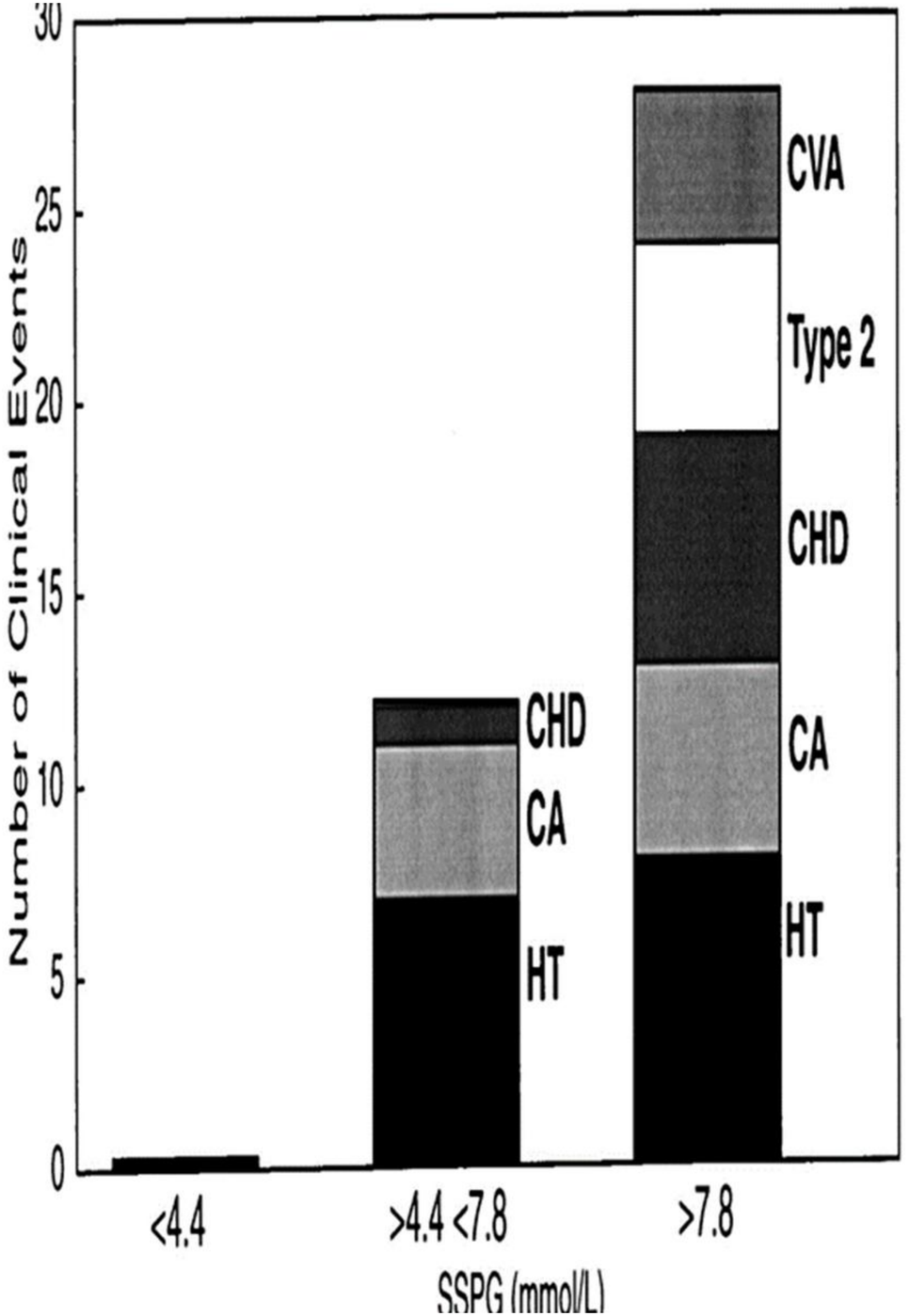
High triglycerides
Low HDL
Hypertension
Reduced exercise tolerance

Cellular Energy Usage

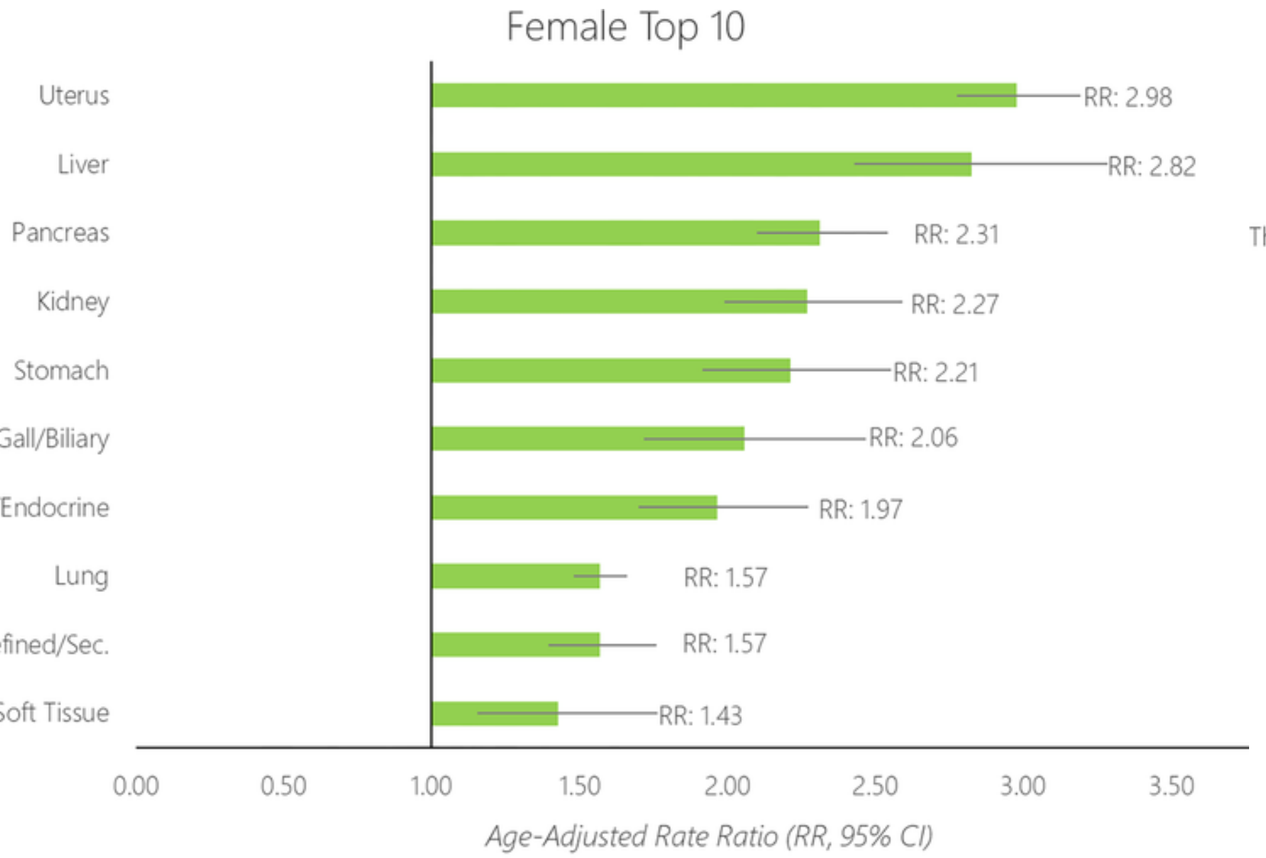
Fatigue
Brain fog
Poor recovery
Muscle weakness

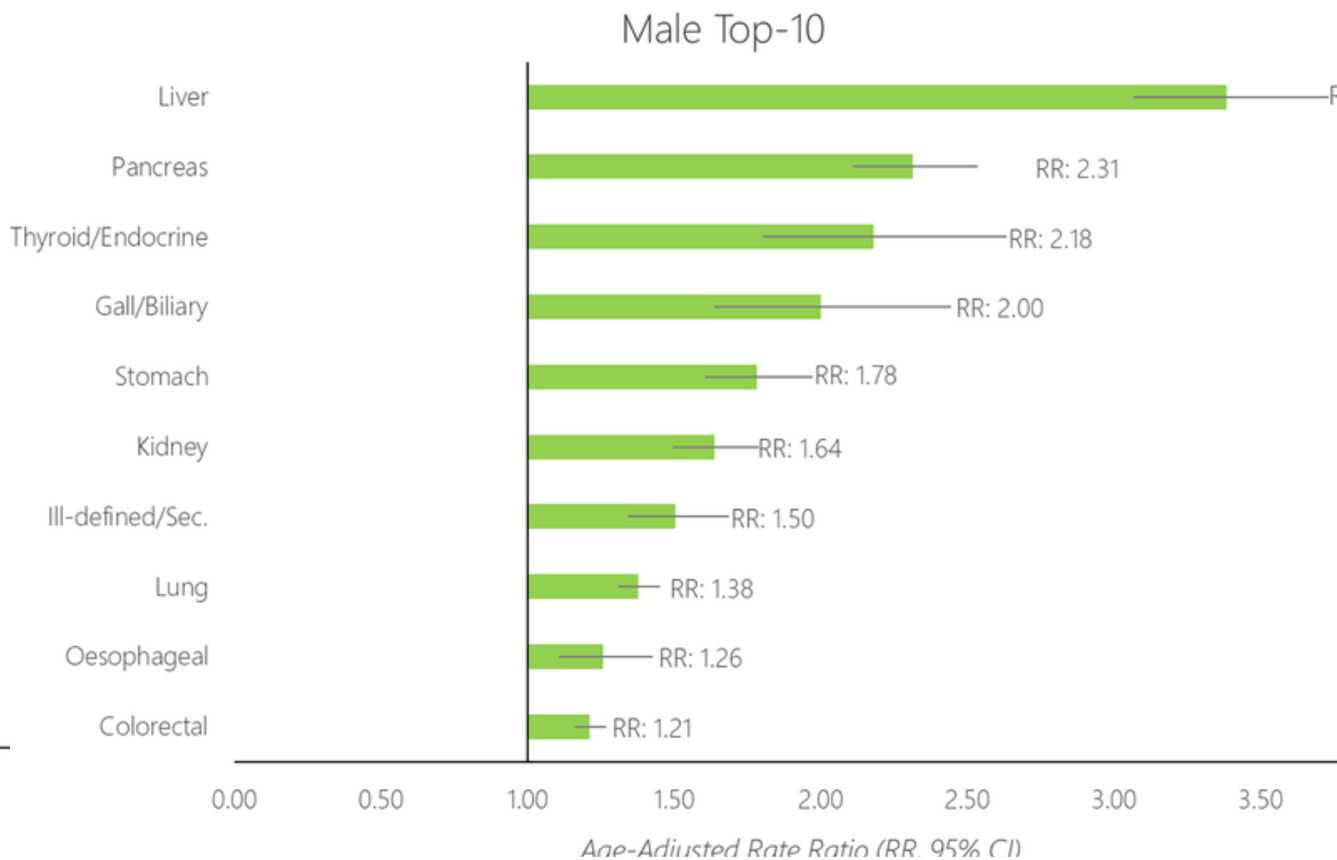
Why Metabolic Health matters

Non-Communicable Disease Risk

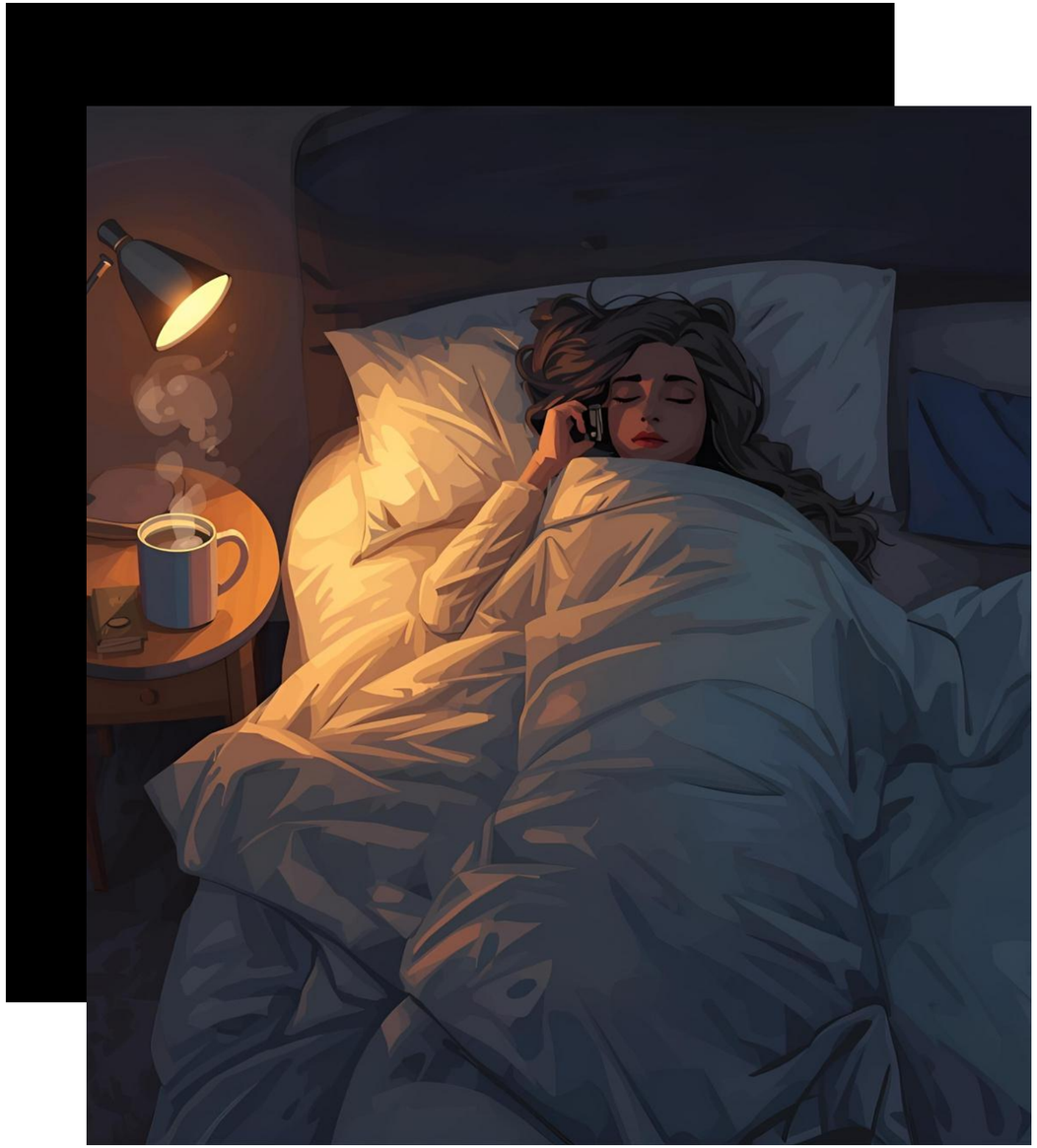


Cancer Risks





DM2 associated Hazard Ratios



Sick Days

Those with T2DM averaged 31.7 sick days per year versus 16.6 for non-diabetic

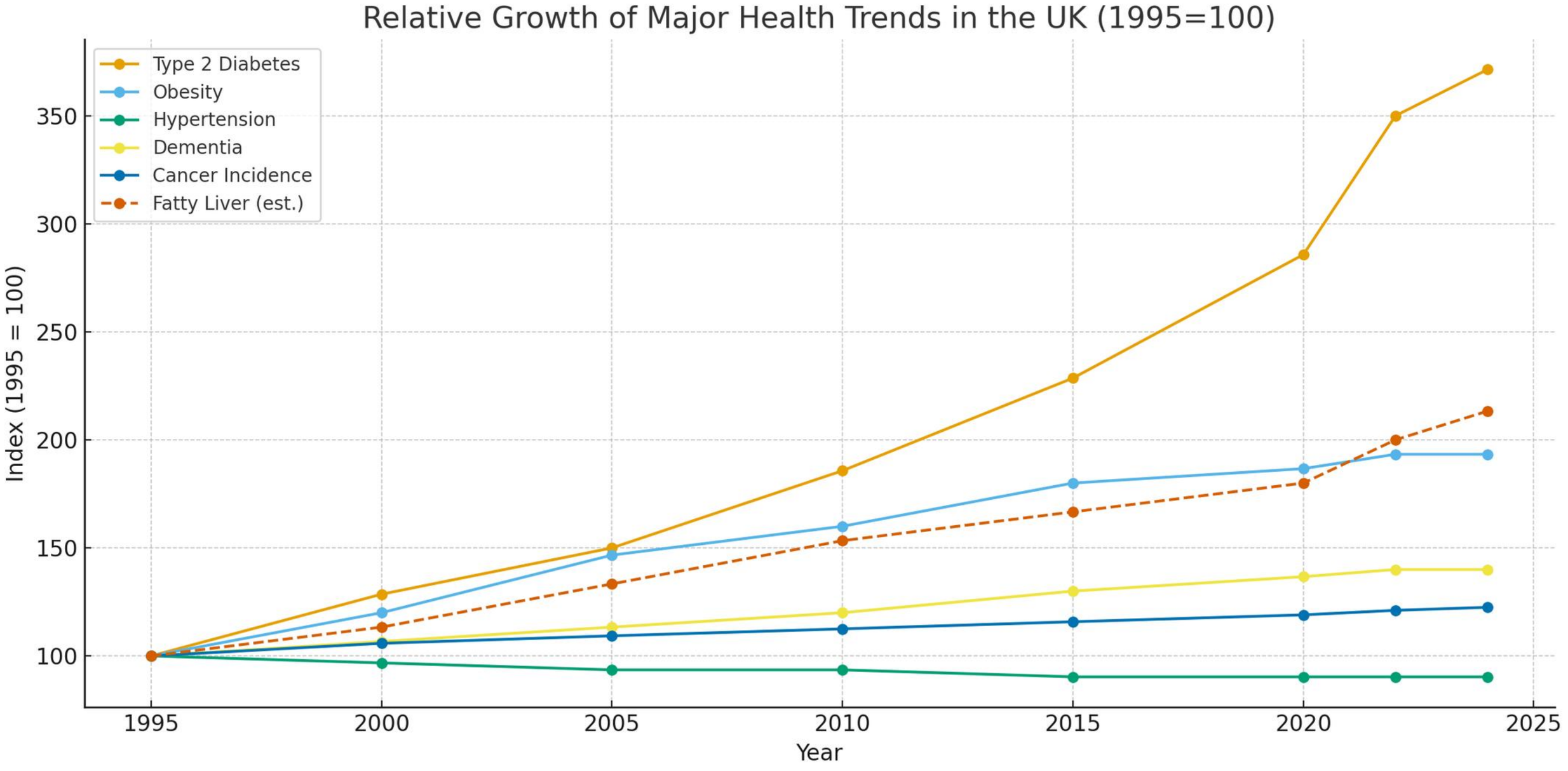
47% of people with type 2 diabetes had any absence versus 26% of controls

Metabolic Syndrome

Criteria

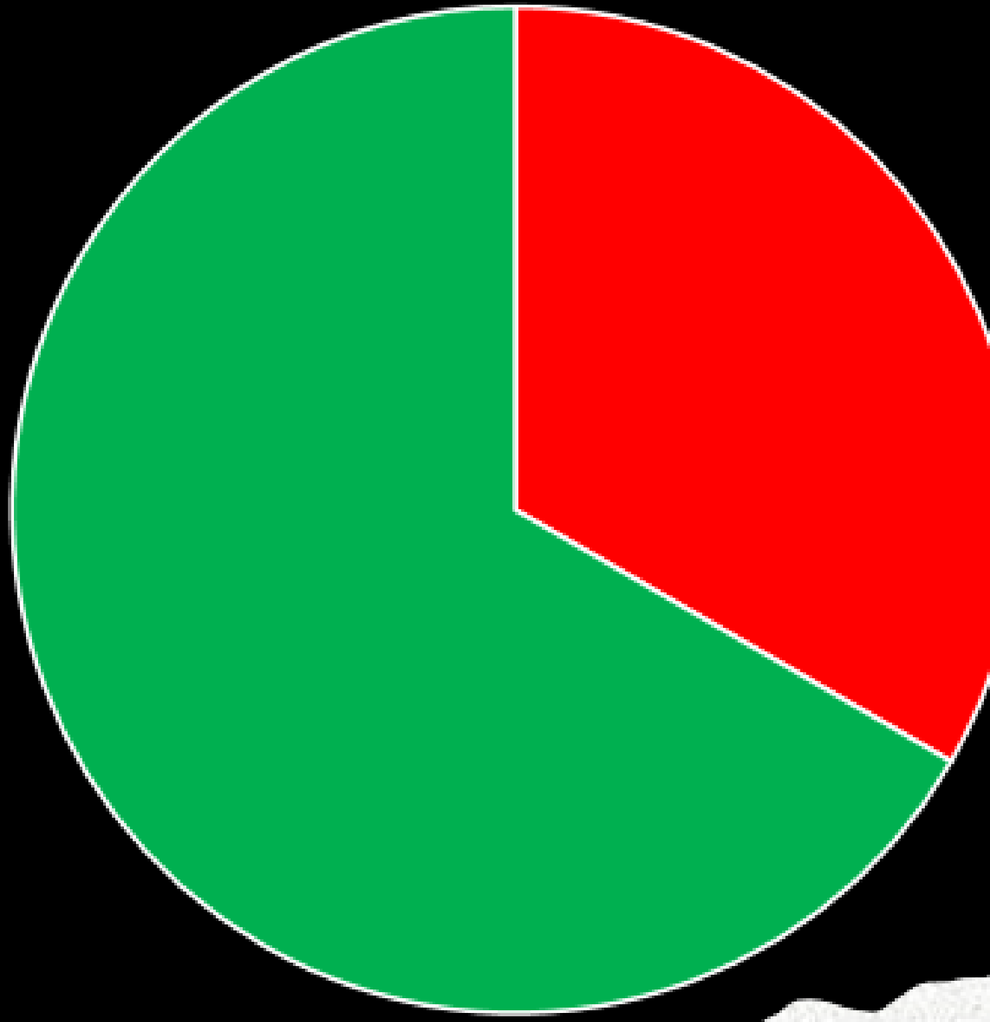
≥3 of the following:

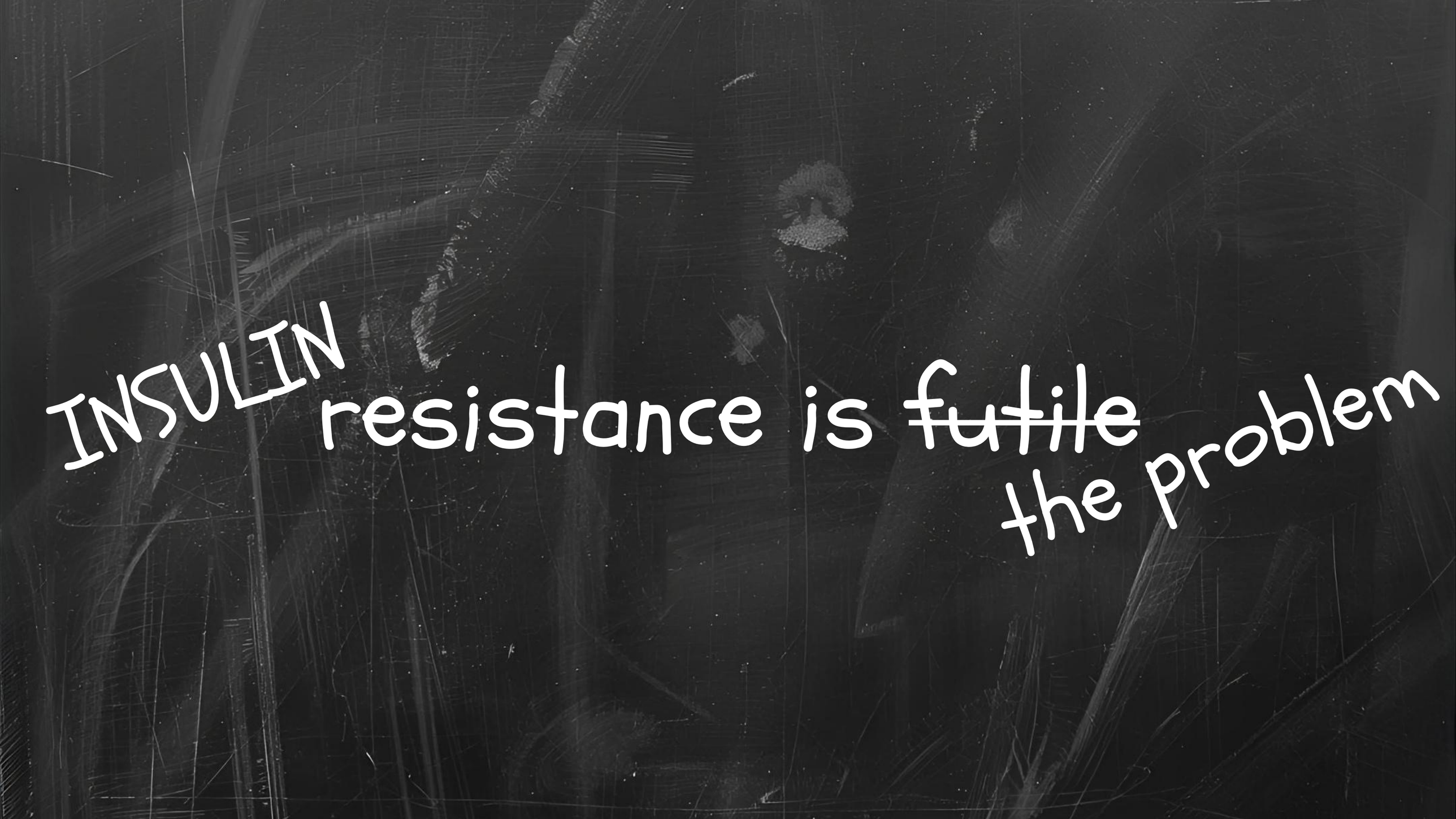
- High blood pressure: Systolic ≥130 mmHg or diastolic ≥85 mmHg, or taking medication to treat high blood pressure.
- High triglyceride levels: ≥1.7 mmol/L
- Low HDL (good) cholesterol: <1.00 mmol/L in men or <1.30 mmol/L in women.
- High blood sugar: Fasting blood glucose ≥6.1 mmol/L or HbA1c ≥42
- Central obesity: A waist circumference of ≥102 cm in men or ≥88 cm in women.


Relative Growth of Major Health Trends in the UK (1995=100)
Type 2 Diabetes
Obesity
Hypertension
Dementia
Cancer Incidence
Fatty Liver (est.)
Index (1995 = 100)
100
150
200
250
300
350
1995
2000
2005
2010
2015
2020
2025
Year

Scale of the problem

1 in 3 adults over 50 in the UK have metabolic syndrome

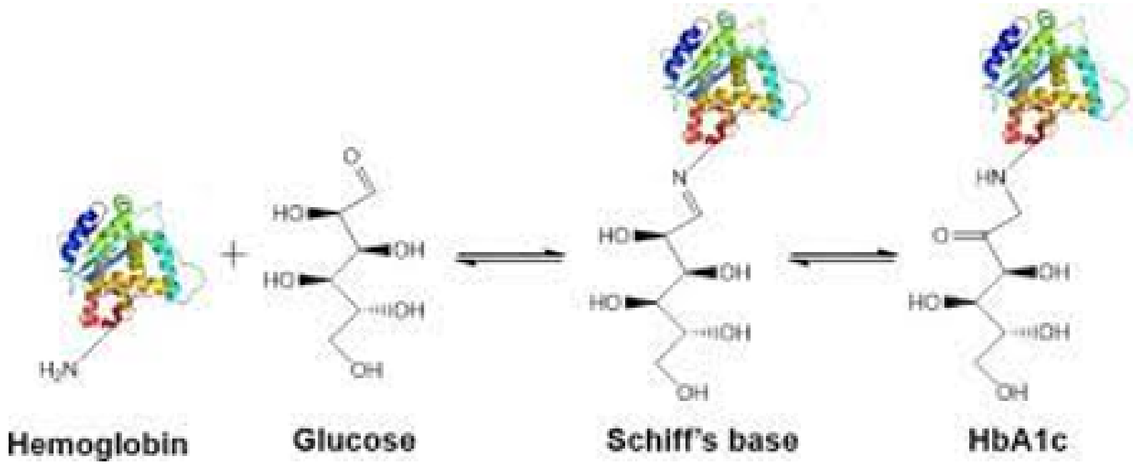



INSULIN
resistance is ~~futile~~
the problem

Hyperinsulinaemia and Insulin Resistance

(the overarching link with Metabolic Syndrome)

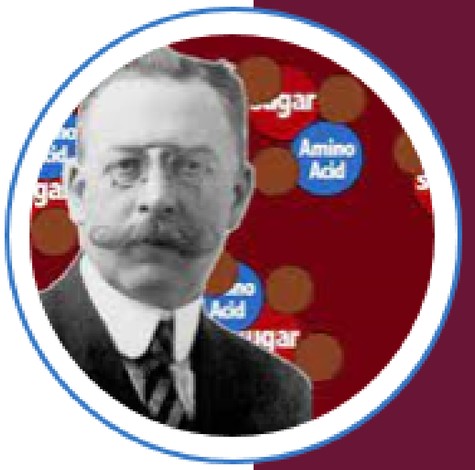
Pre-diabetes



- Pre-diabetes (aka Non-diabetic hyperglycaemia)
  - HbA1c 42-47 mmol/mol
  - Over 48 is termed Diabetes
- A haemoglobin molecule can become ‘sugary’ if exposed to high levels of sugar in the blood.
- An increased HbA1c indicates there have been higher levels of glucose in the bloodstream over the last 3 months.

Maillard Reaction

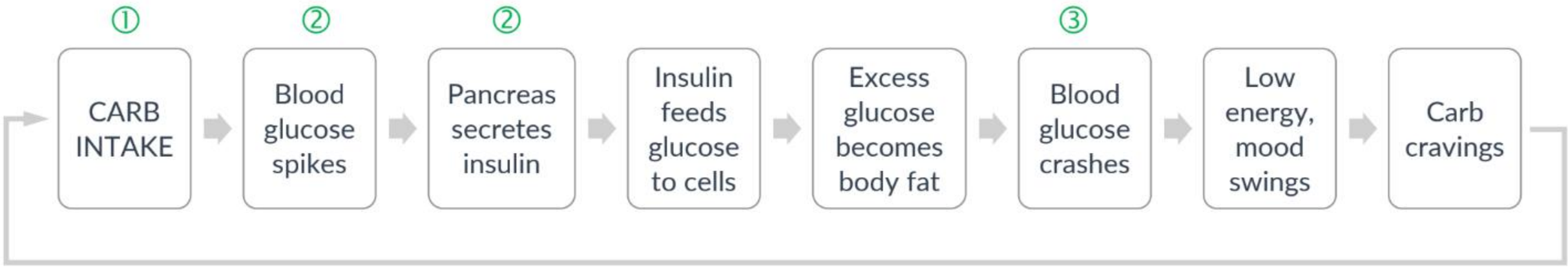
- Louis Camille Maillard (4 February 1878 – 12 May 1936)
- Protein browning reaction e.g. caramelising, meat browning
- In the body, this is essentially part of aging and accelerated by chronically elevated sugar levels – as we age our cartilage shows browning

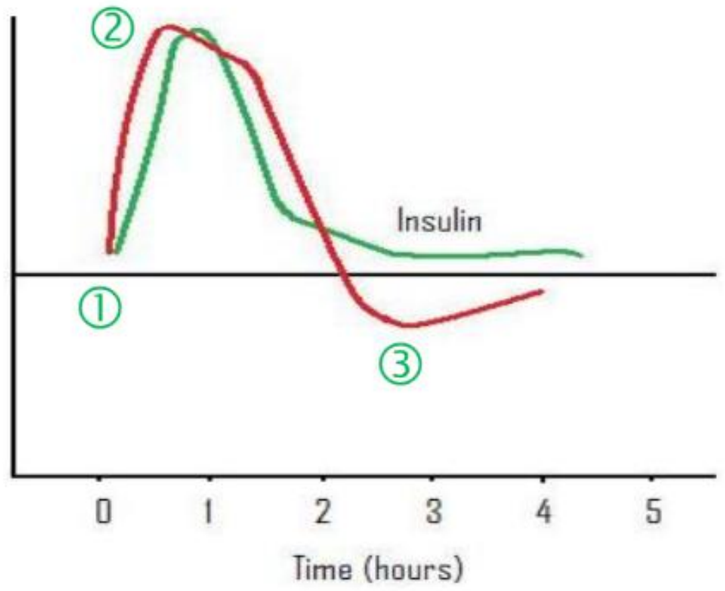


Blood sugar (glucose) levels

- An adult human has approximately 5g of glucose in their blood (5 litres) at any time. The same weight as a 20p piece.
- We get this from our diet, but can also make it within our body
- Our body controls this level tightly to maintain good health

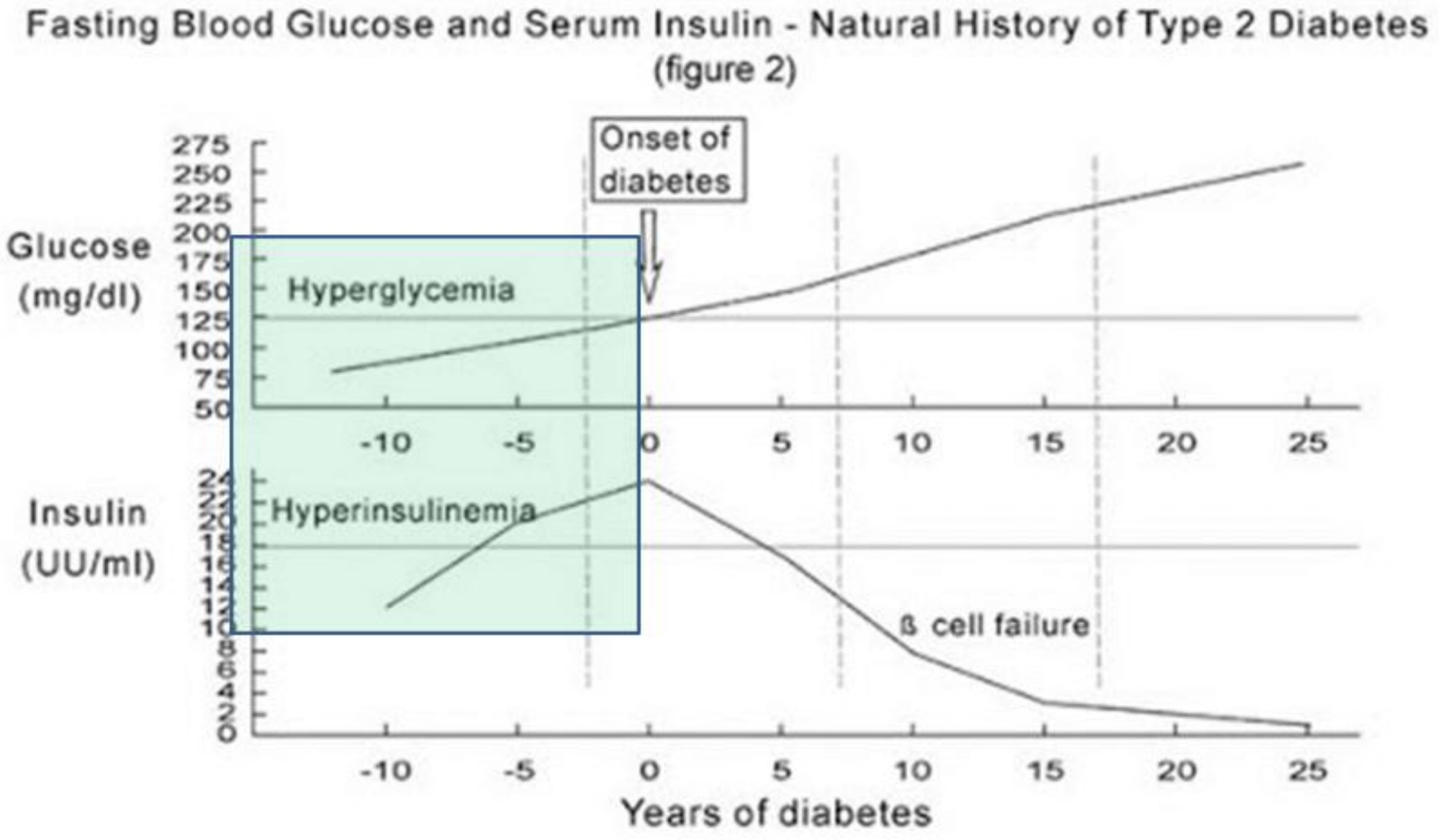
Dietary carbs drive the glucose–insulin–fat cycle





Too much insulin for too long, due to an energy toxic environment leads to insulin resistance and hyperinsulinaemia and downstream NCDs e.g. T2DM

How does Type 2 Diabetes develop?



Glucose-centric v Insulin-centric

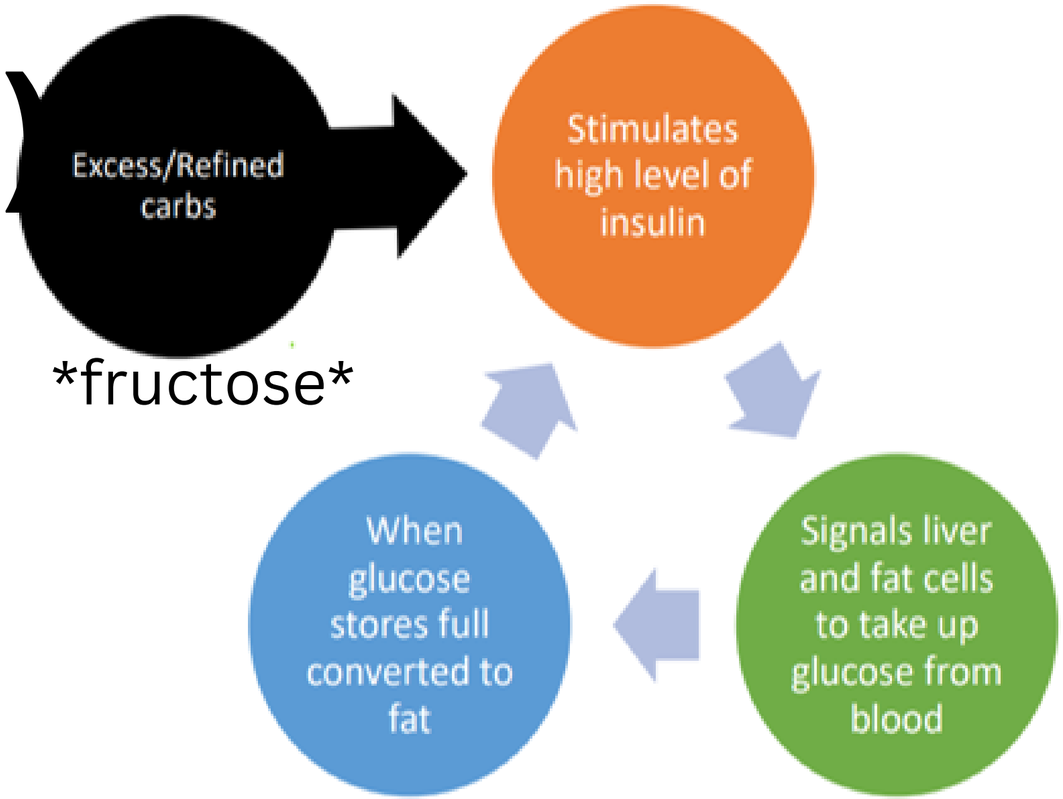
In NHS we measure HbA1c, which may miss many years of deteriorating metabolic health

How should we deal with this?

Be suspicious - if evidence of other metabolic ill health (fatty liver, obesity, low HDL, high trigs etc) - very likely to have insulin resistance and hyperinsulinaemia, even with normal HbA1c.

fatty liver (MASLD)

How does the liver get filled with fat?



fructose

denovo

Fatty Liver = NAFLD = MASLD

- Often diagnosed after abnormal LFTs, on Abdominal USS.
- More signficant biochemical derangements (FIB4) go for Fibroscan.
- Can progress to liver failure (rarely), but is reversible in early stages
- Often a herald sign of other metabolic disease
- Foie Gras - caused by gavaging of grains in geese
- Insulin resistance causes 15x risk of Fatty Liver
- Sadly affecting more children, likely due to high energy processed foods and sedentary lifestyle.
- Be suspicious.

Cholesterol

In the NHS, we measure total cholesterol, LDL, HDL and (if fasted) triglycerides
“Cholesterol” is a misnomer when it comes to LDL, HDL – which are the ‘boats’ that ferry cholesterol around the body

In Metabolic Health:
HDL Should be >1.0 in men and >1.3 in women
Fasting triglycerides should be <1.7

Cholesterol top facts

- A waxy fat
- An essential fat – structurally part of every cell, used for making hormones, bile acids, myelin
- Most cholesterol is made by the liver
- There is no cholesterol in plant foods
- Cholesterol cannot be used for energy
- The most important part of a cholesterol profile blood test is the Total Cholesterol:HDL ratio (and fasting triglycerides)

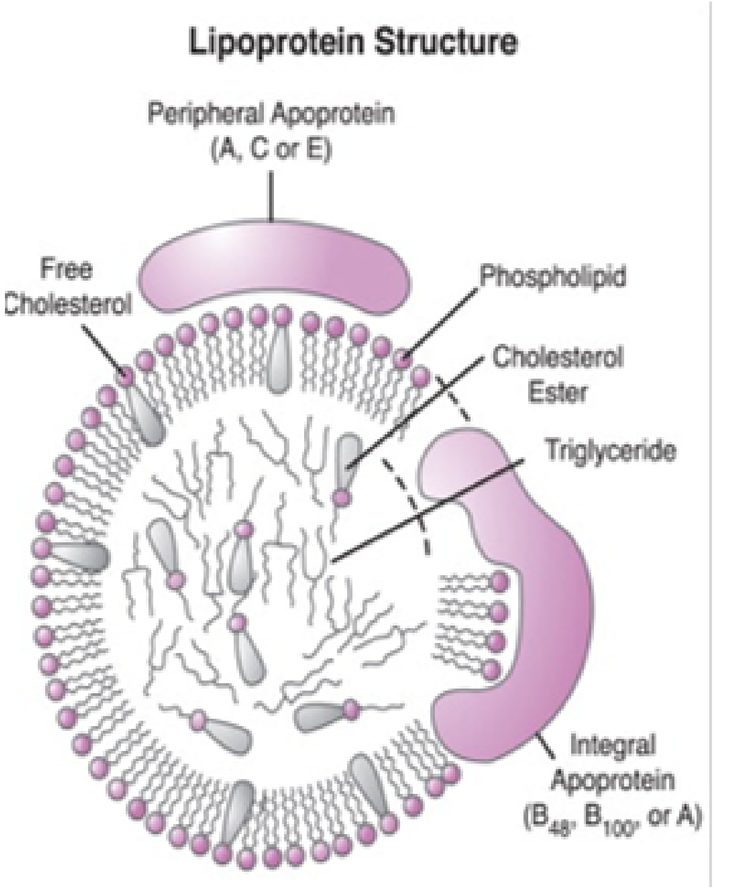
Lipoproteins – the boats

- **Chylomicrons** – low density, transport fatty acids from intestine via lymph to circulation.

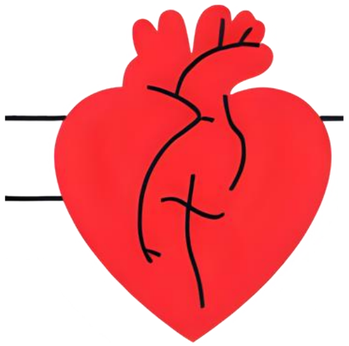
- **VLDL** – transports triglycerides and cholesterol from liver to periphery

- **LDL** – from VLDL – when cholesterol>triglycerides

- **HDL** – made mostly in liver. Transports cholesterol back to liver for recycling



Clinical (GP based) measurements



Total cholesterol : HDL ratio — cardiovascular risk predictor. <4.0 → desirable / lower risk

Triglyceride : HDL ratio — marker of insulin resistance / atherogenic dyslipidaemia. ≤1.5 → favourable / low insulin resistance

Waist to Height Ratio < 0.5 (i.e. waist less than half height)

How to ruin your cholesterol profile...

Eat lots of processed & fried foods (trans + saturated fats)

Load up on sugar & refined carbs

Avoid fibre

Overeat calories daily to maintain energy toxicity

Drink excess alcohol

Be sedentary – no exercise

Gain belly fat

Smoke

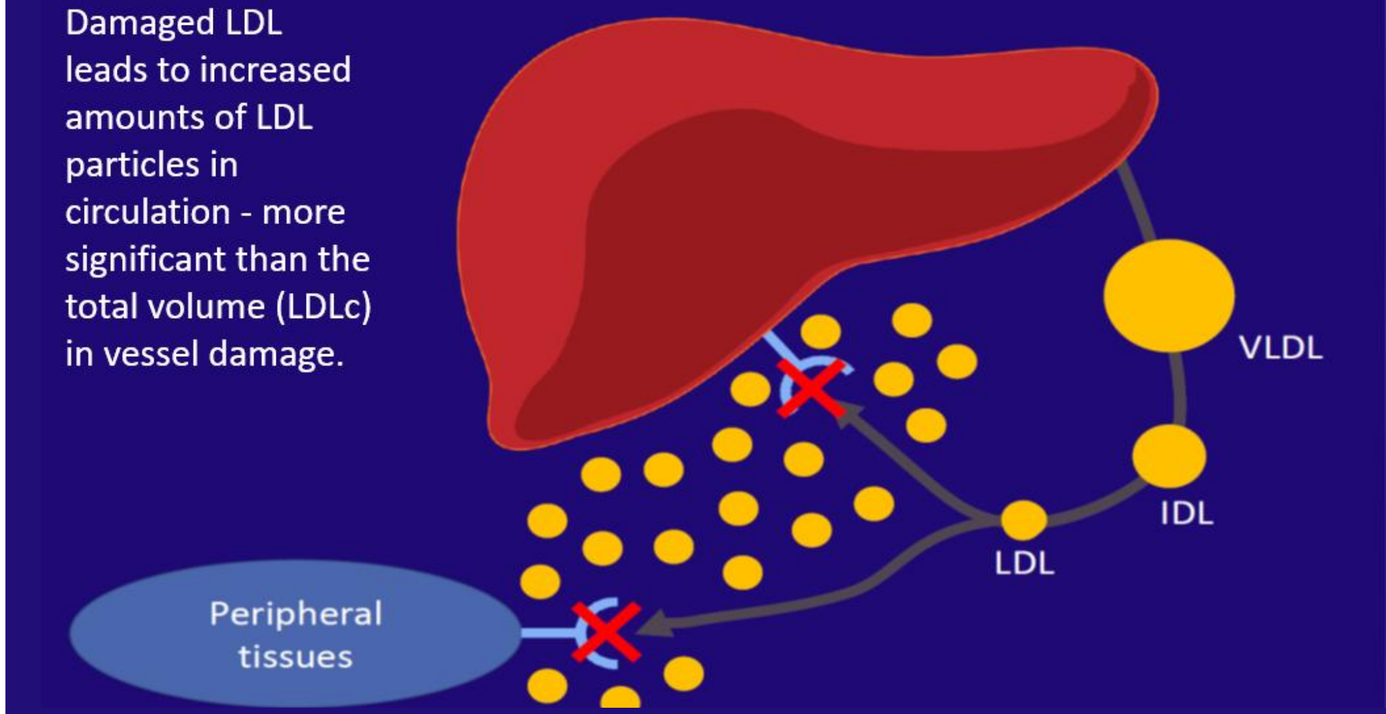
Sleep poorly & stay stressed

Ignore health checks

Healthy v Unhealthy cholesterol

LDL Pattern A
large, buoyant LDL particles.
Associated with a lower risk of cardiovascular disease.

LDL Pattern B
small, dense LDL particles.
higher risk factor for coronary heart disease.
Often linked with higher triglyceride levels, lower HDL cholesterol, and other metabolic issues



obesity

BMI > 30

•64% of English adults overweight or obese (27% in children)

•£6.5 billion – NHS spend on obesity-related ill-health. Projected £9.7billion by 2050

• Causes: genetics, the food environment, increased sedentary behaviours etc

Many downstream sequelae - some obvious and direct e.g. osteoarthritis and some less obvious e.g. PCOS

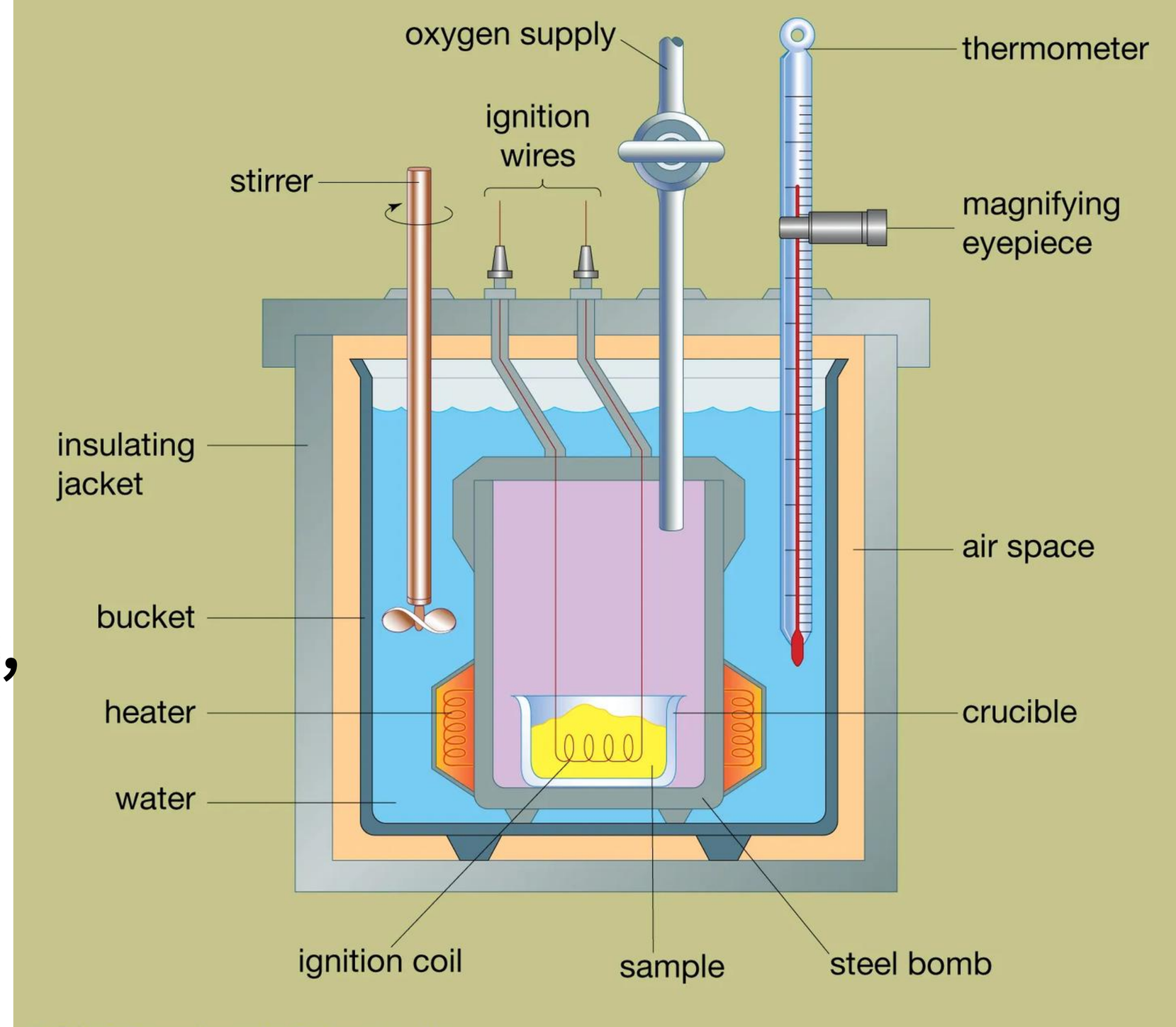
calories in

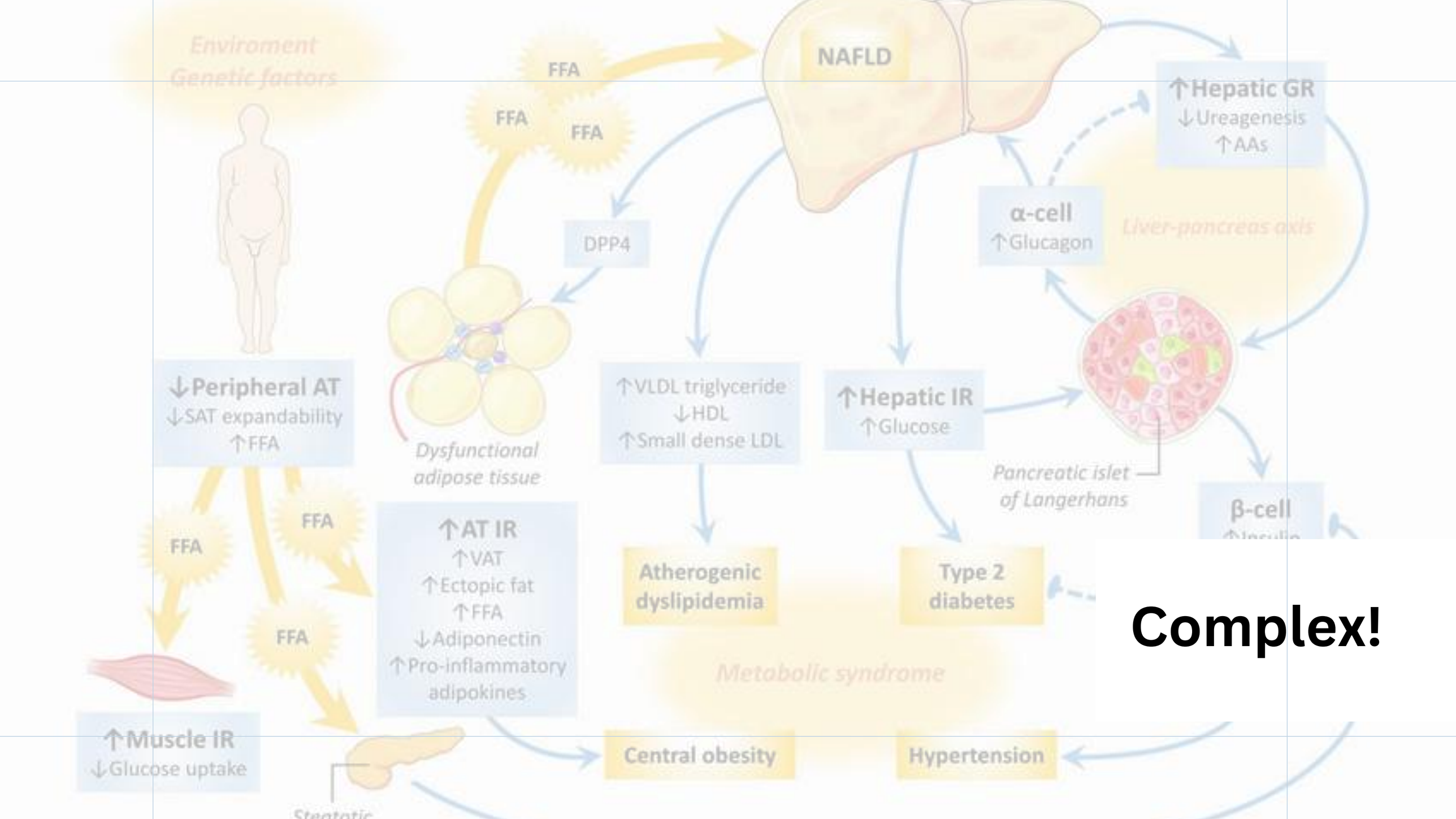
calories out

Yes, but

Humans are not bomb calorimeters

We are complex animals with complex behaviours, hormones, environments, customs etc




Enviroment
Genetic factors
FFA
FFA
FFA
NAFLD
↑Hepatic GR
↓Ureagenesis
↑AAs
DPP4
α-cell
↑Glucagon
Liver-pancreas axis
↓Peripheral AT
↓SAT expandability
↑FFA
Dysfunctional
adipose tissue
↑VLDL triglyceride
↓HDL
↑Small dense LDL
↑Hepatic IR
↑Glucose
Pancreatic islet
of Langerhans
β-cell
FFA
FFA
FFA
↑AT IR
↑VAT
↑Ectopic fat
↑FFA
↓Adiponectin
↑Pro-inflammatory
adipokines
Atherogenic
dyslipidemia
Type 2
diabetes
Metabolic syndrome
↑Muscle IR
↓Glucose uptake
Central obesity
Hypertension
Steatotic

Complex!

Obesity

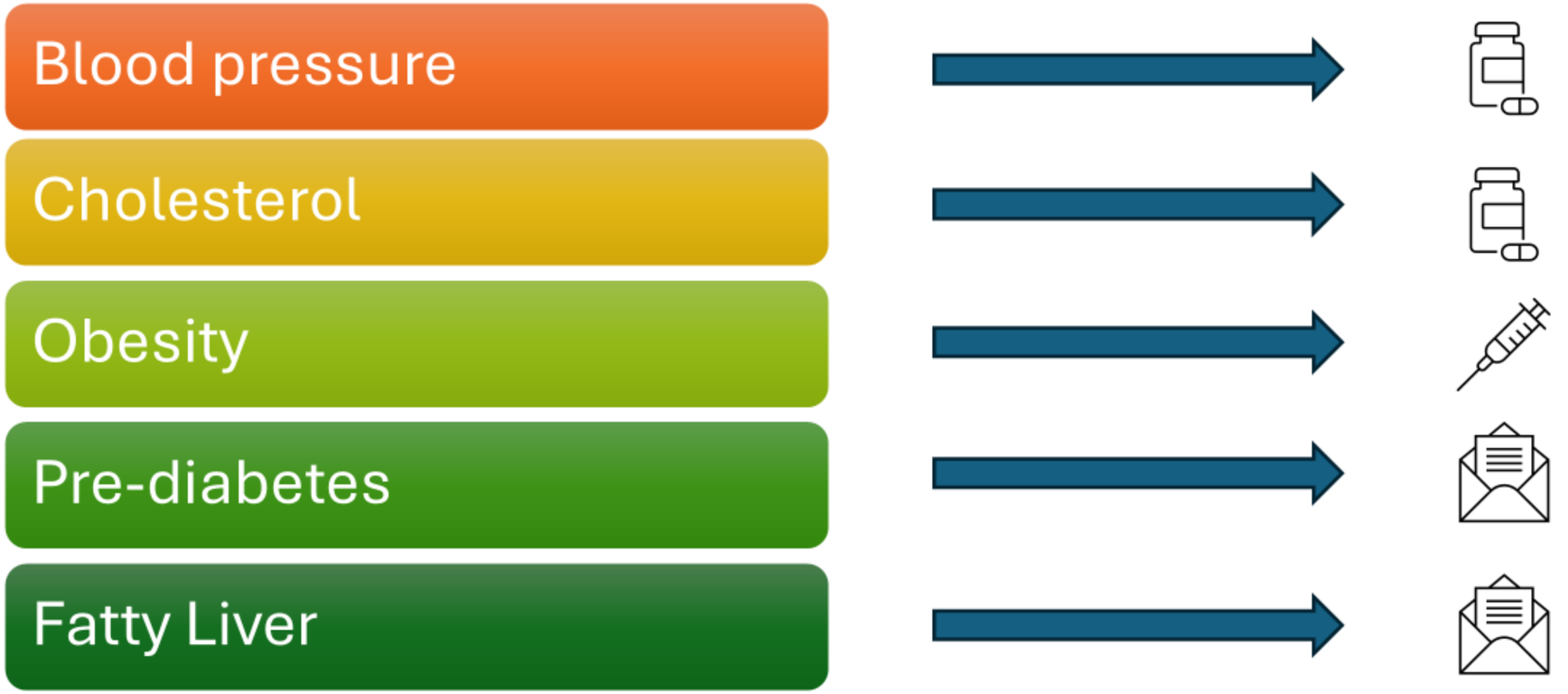
Chronic high levels of insulin (a growth/storage hormone) are associated with obesity
This leads to leptin resistance - increase appetite, cravings etc
Made worse by a high energy, processed food environment

WHAT -CAN- WE DO?

How might we adjust our practice in GP?

Why take a metabolic health approach?

Typical situation:

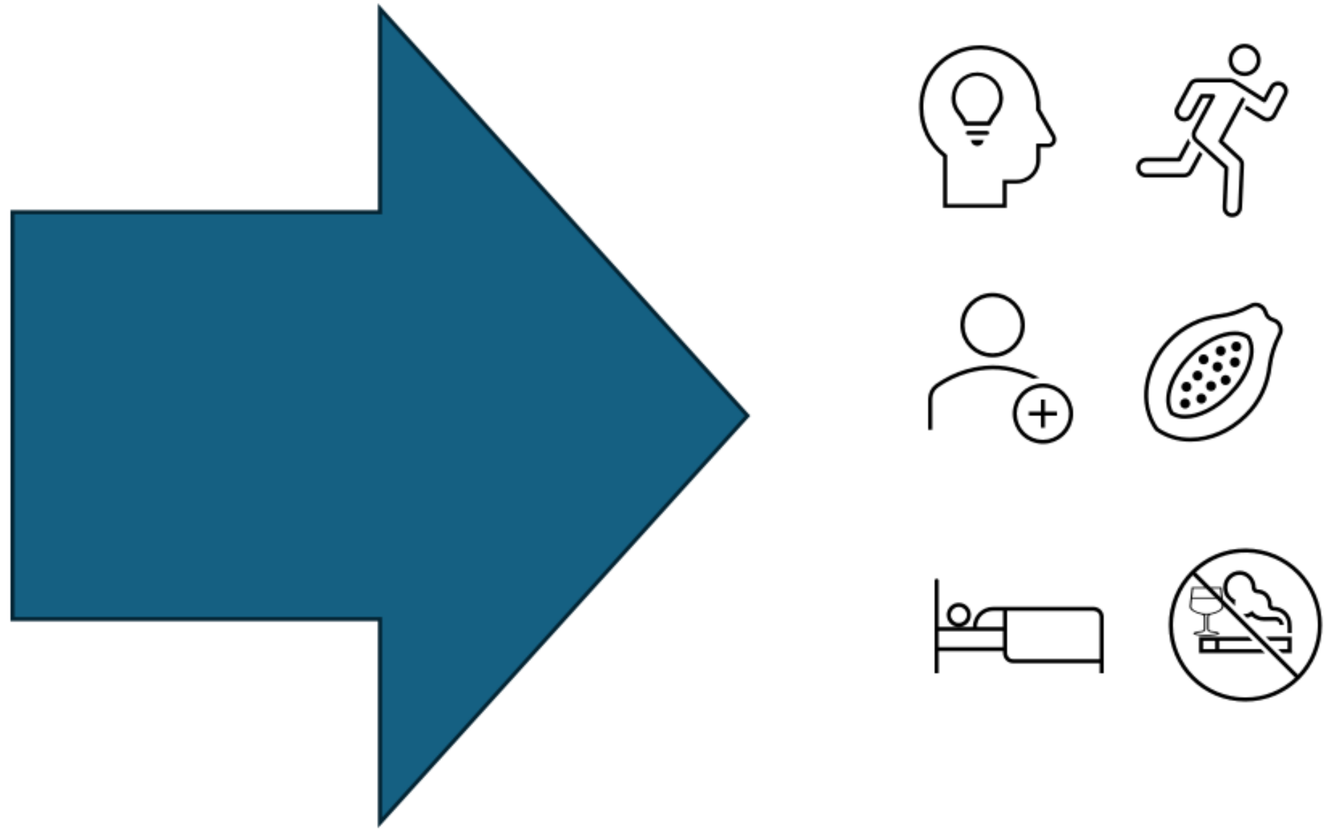


Wait for diagnosis, Treat in silos, Target orientated, Disparate

Why take a metabolic health approach?

A lifestyle and metabolic health approach

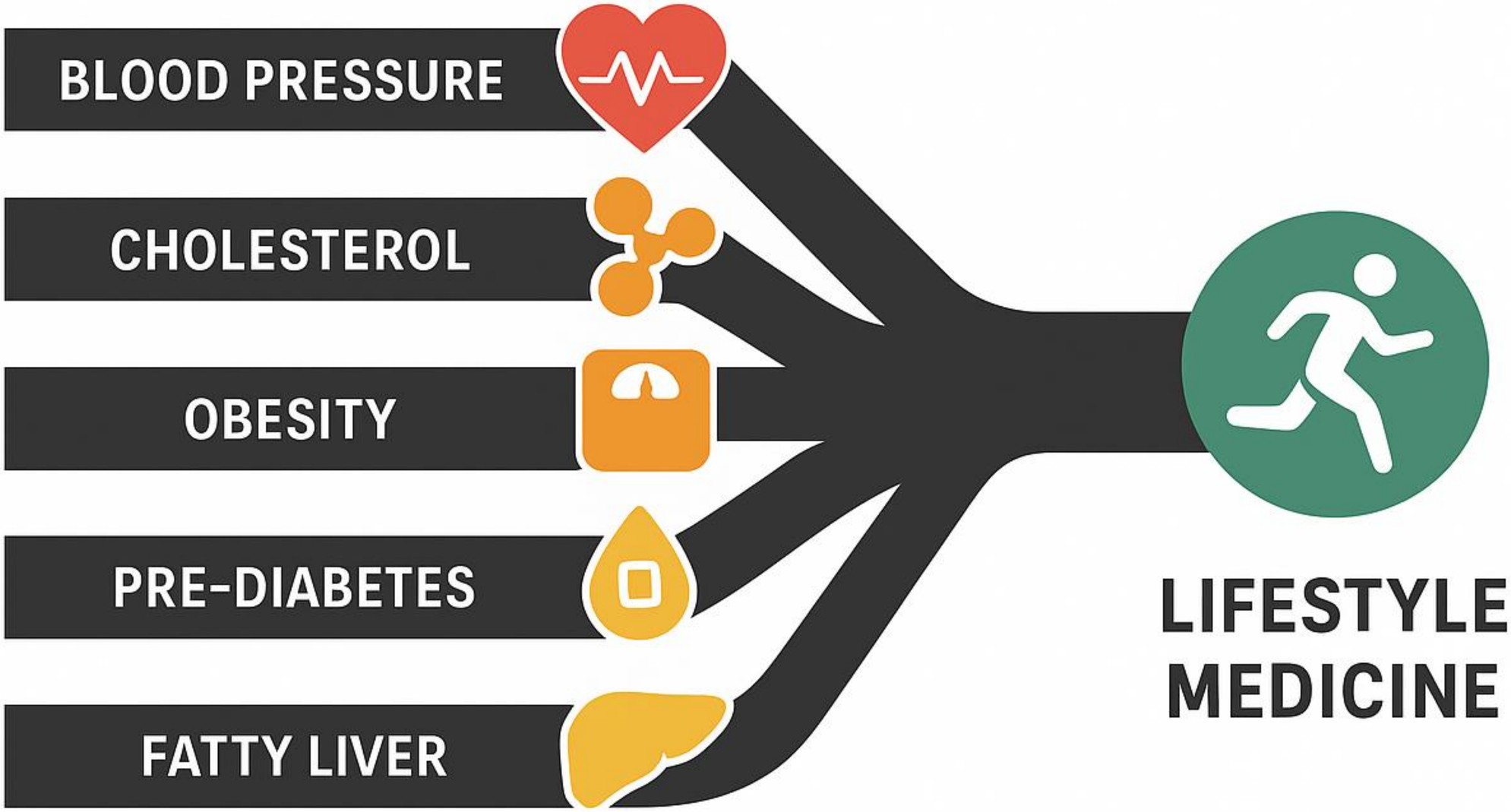
- Blood pressure
- Cholesterol
- Obesity
- Pre-diabetes
- Fatty Liver



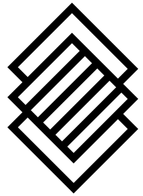
Preventative, Joined up, holistic, person centred

TRADITIONAL CARE

METABOLIC HEALTH EDUCATION

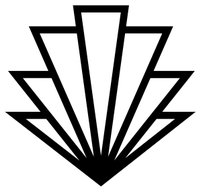


Top tips



Notice patterns e.g. rising normal HbA1c

Triangulate “disparate” diseases e.g. low HDL and obesity



Be suspicious and investigate e.g. liver USS, triglycerides etc.

Share you learning and experiences


Questions?