Obesity: a looming cardiovascular threat - pathophysiology, diagnosis, and impact

University of Glasgow

School of Cardiovascular & Metabolic Health

Naveed Sattar
Professor of
Cardiometabolic Medicine

British Heart Foundation

Duality of Interest Declaration

Consulting/speaker honoraria:

Abbott Laboratories, Abbvie, Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Hanmi Pharmaceuticals, Janssen, Menarini-Ricerche, Novartis, Novo Nordisk, Pfizer, Roche Diagnostics, Sanofi

Grant: AstraZeneca, Boehringer Ingelheim, Novartis, Roche Diagnostics

Obesity diagnosis

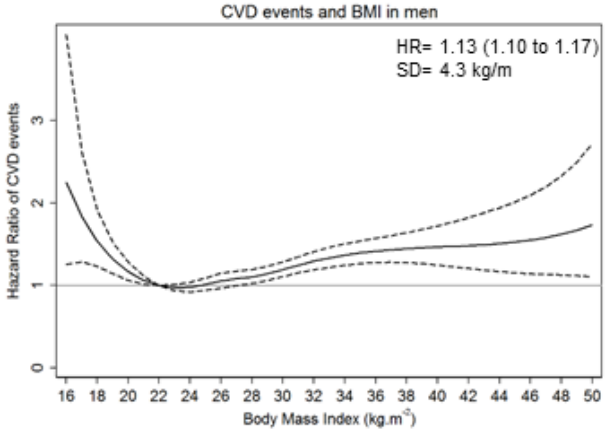
- BMI traditional >30 = obesity (kg/m^2)
- But waist to height ratio better – more predictive for many outcomes
- OR with comorbidities /symptoms linked to obesity
- New Lancet commission coming
- As ASCVD down, obesity up and up – and threatening to reverse CV gains

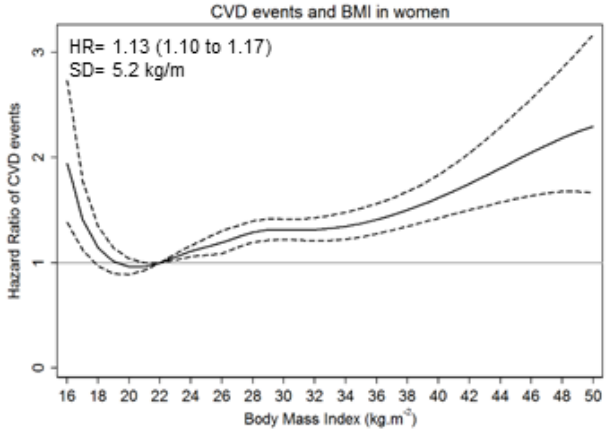
Adiposity to CVD evidence from many places

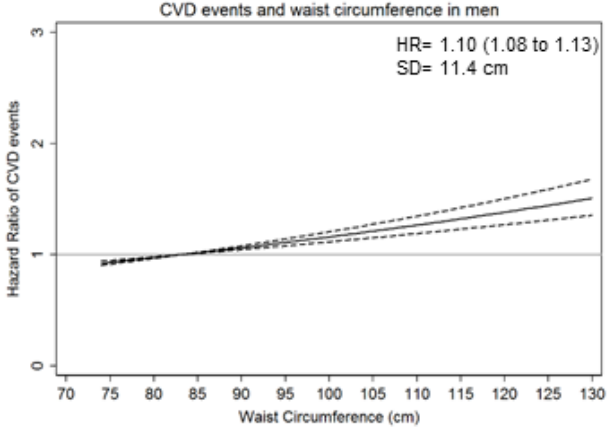
- 1. Epi for MI, and then HF
- 2. Genetics
- 3. Pathways to ASCVD
- 4. Wt loss and outcomes

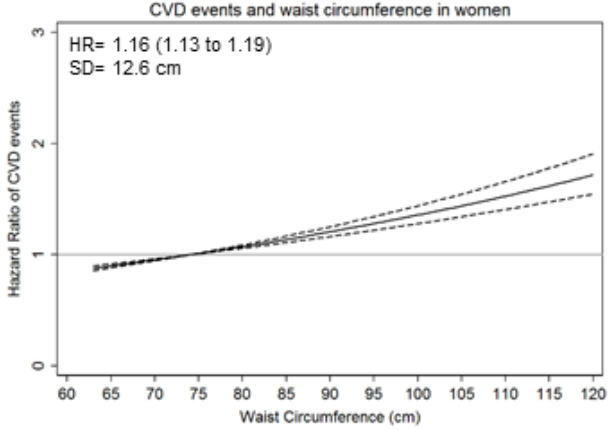
Adiposity and MI /stroke associations modest

EHJ (2018) Only BMI shows U shape









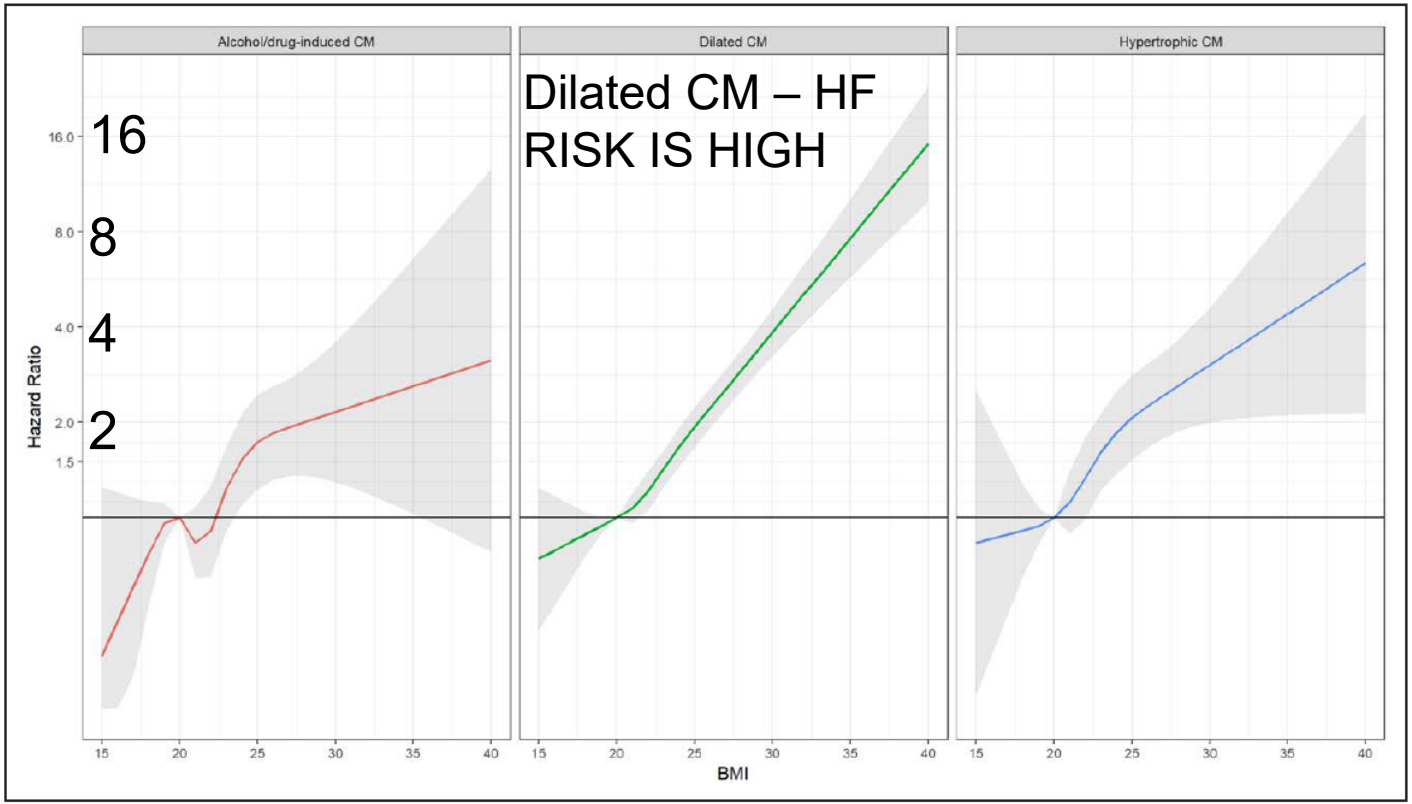
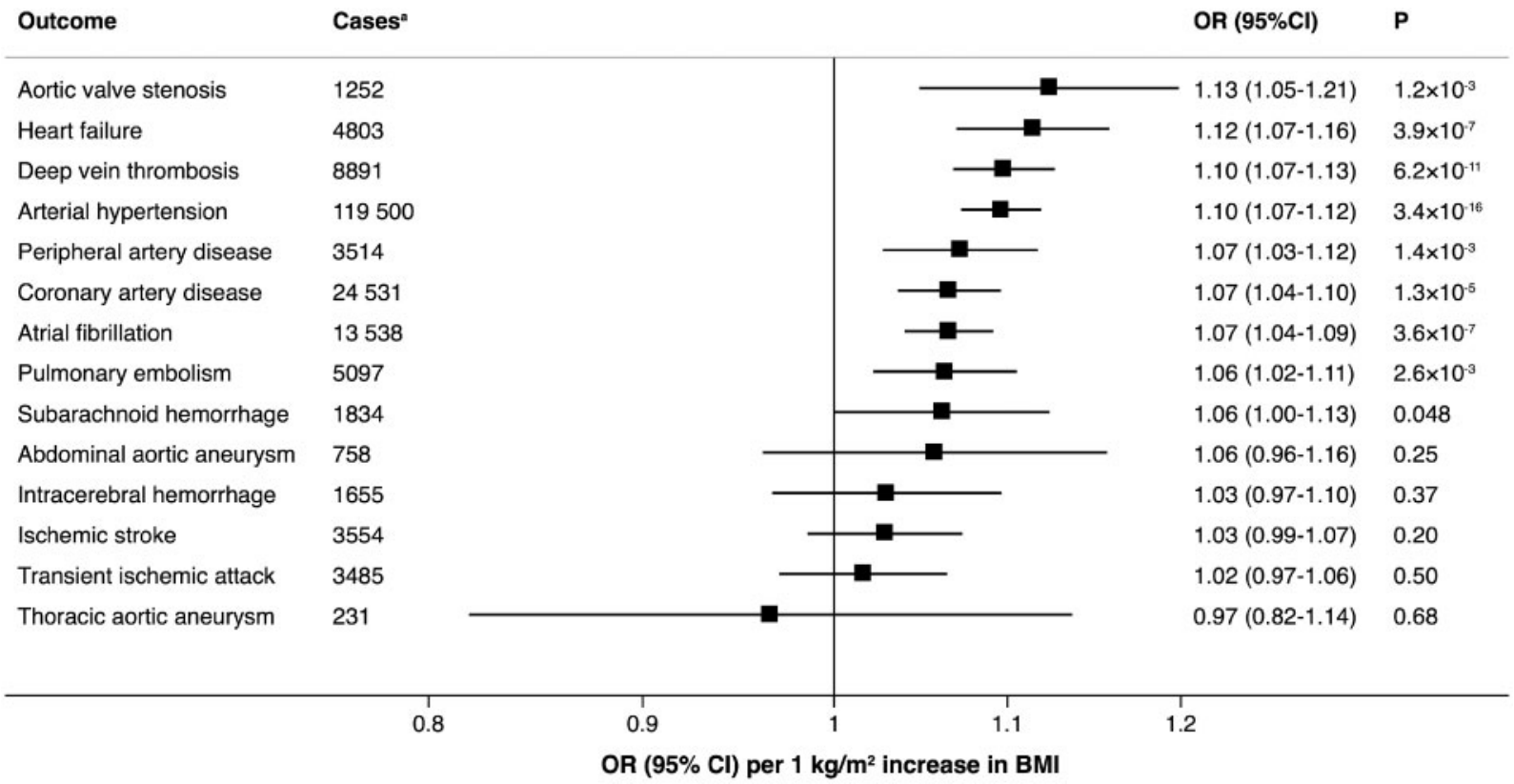


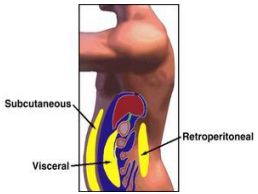
Figure. Association between body mass index (BMI) at conscription and risk for cardiomyopathy (CM).
The model was adjusted for age, conscription year (as a spline with knots at 5%, 35%, 65%, and 95%, ie, 1971, 1982, 1992, and 2004), test center, and baseline comorbidities (diabetes mellitus, hypertension, congenital heart disease), systolic blood pressure, diastolic blood pressure, cardiorespiratory fitness, muscle strength, parental education, and alcohol or substance use disorder (n=773 679). BMI was restricted to BMI between 15 and 40 kg/m² and modeled as a restricted cubic spline with knots at 5%, 35%, 65%, and 95% (ie, 18.0, 20.5, 22.4, and 27.5 kg/m²), with BMI of 20 kg/m² as reference. The unadjusted model is presented in Figure II in the online-only Data Supplement.

Robertson et al (2019) Circulation Higher BMI adolescence vs midlife CM risks

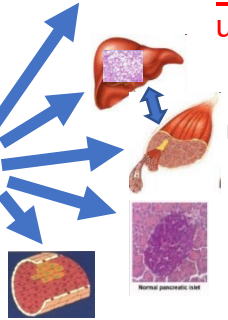
Genetically higher BMI and CVD outcomes
Larsson et al (2019) EHJ



WEIGHT GAIN
Upstream (speed central fat gain dependent on age, sex ethnicity, genes)



FAT
'Spill over'



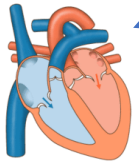
muscle

pancreatic beta cell

higher <u>TG</u> / Low HDL-c
<u>ALT</u> /GGT higher than usual

Hyperglycaemia (beta cell failure) **<u>HbA1c</u> rises over time** (broadly linear correlation to BMI at given age)

AF
HF
CAD

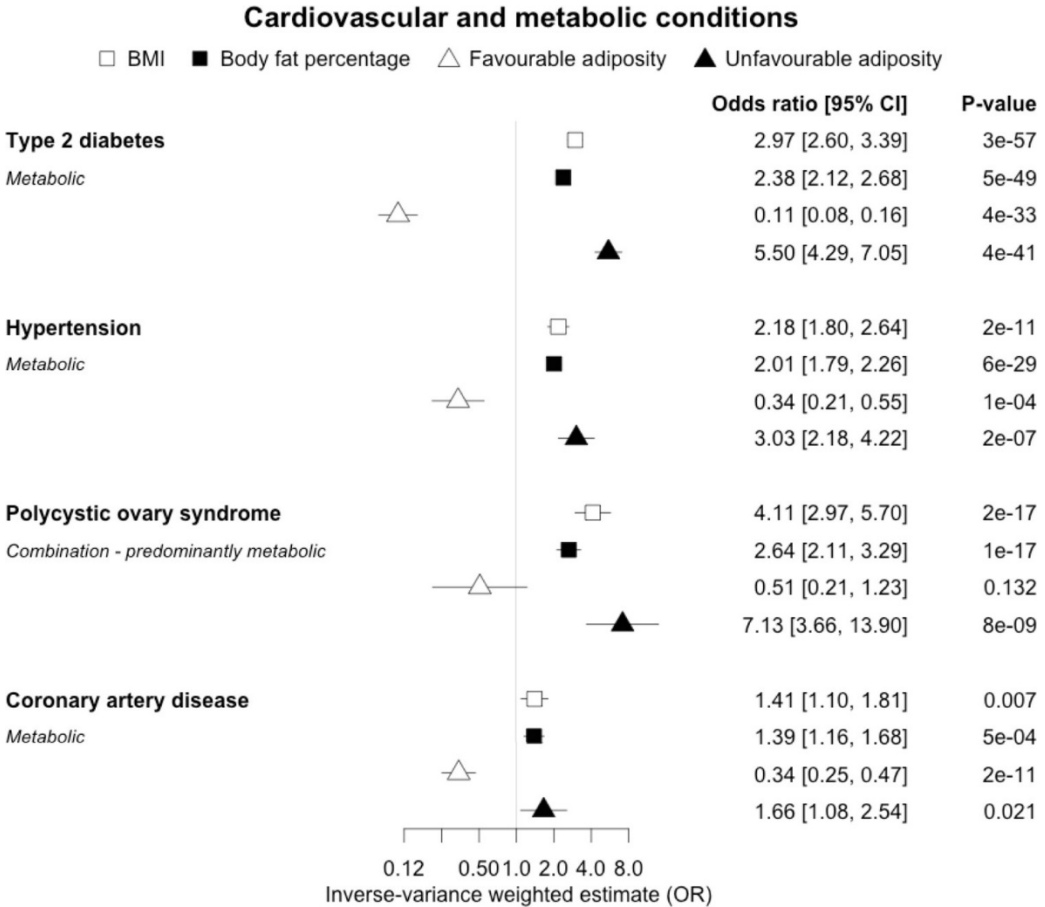


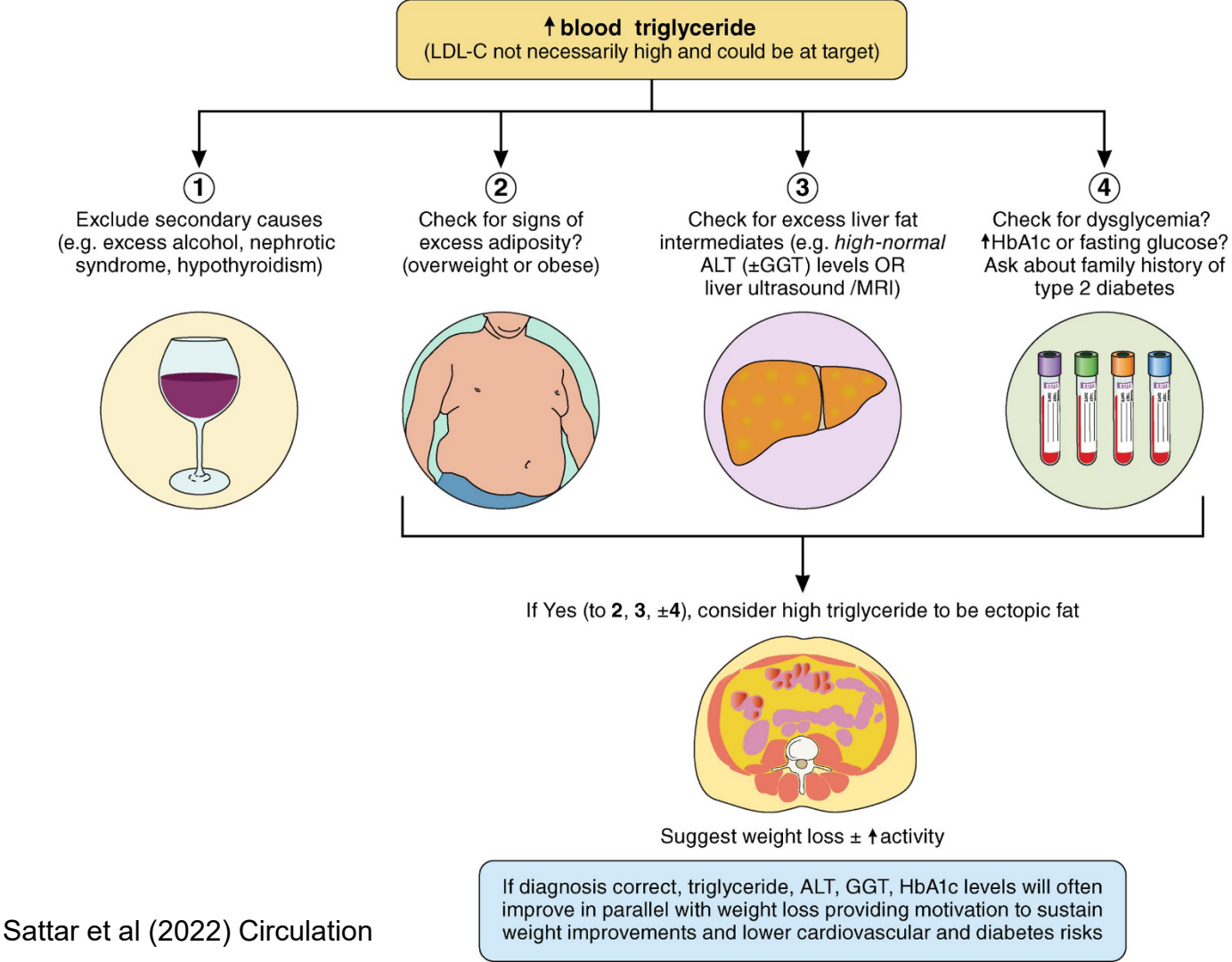
Perivascular fat ⇒ vasocrine signalling
Higher BP
Enhanced by higher salt intake linked to higher calorie intake

Sattar et al (2024 – In press) Diabetes Care

Where you put fat matters

Martin et al (2022) eLife





Sattar et al (2022) Circulation

Trig 18 mmol/l
19kg weight gain

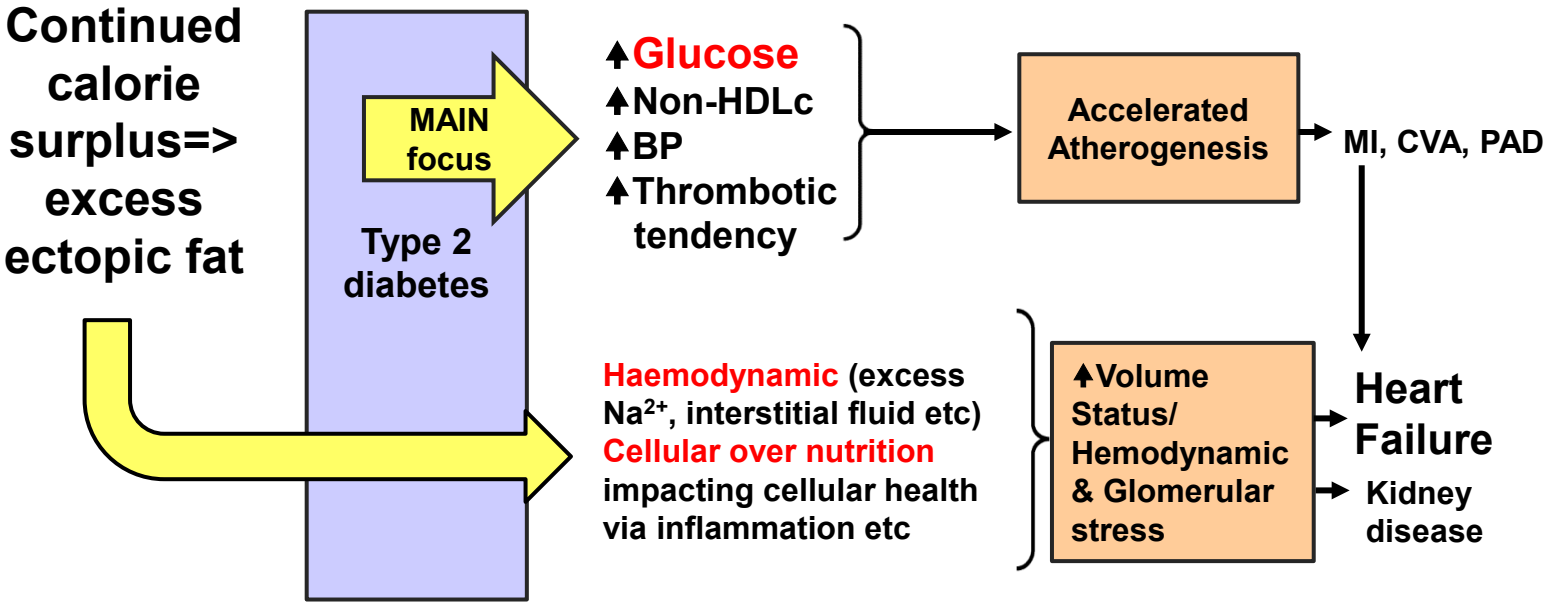
Lost once pandemic abated

Trig back to 2 mmol/l

ALT 81 to 22

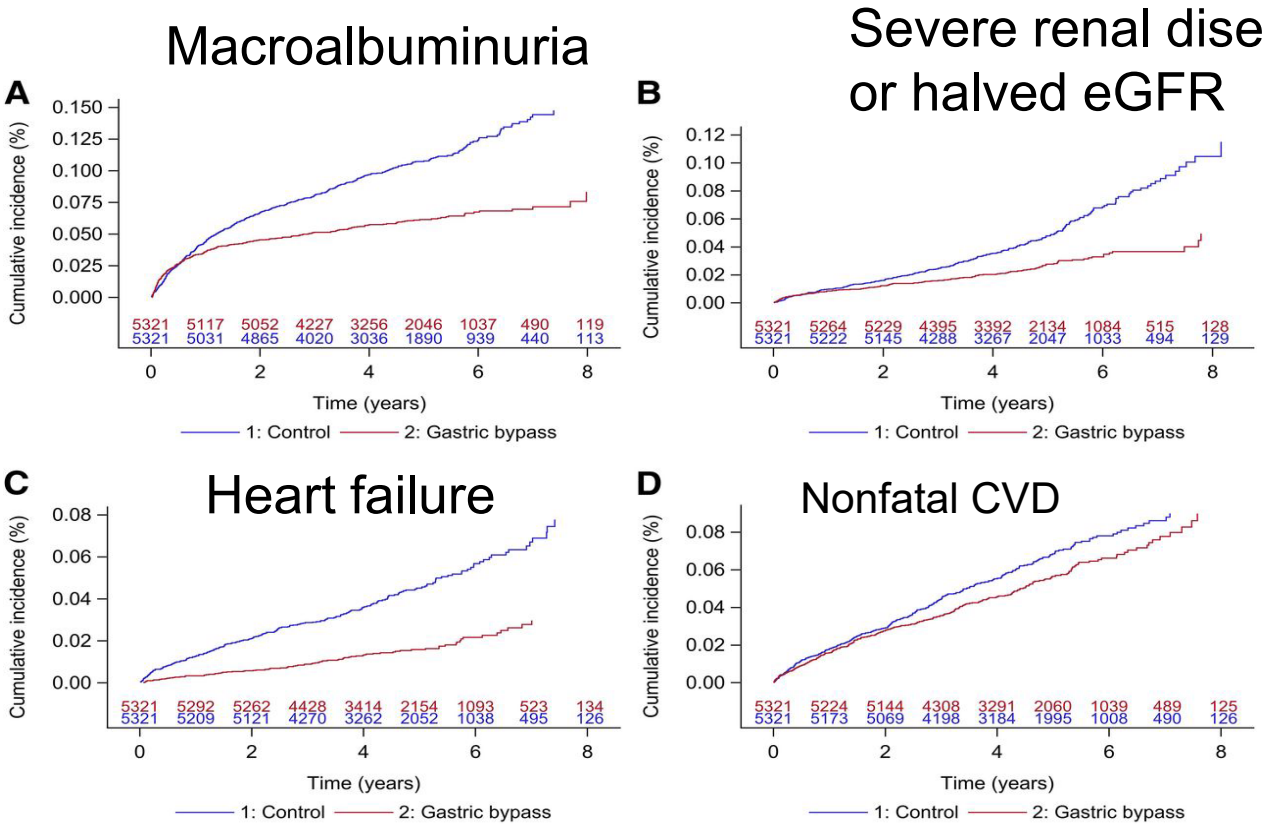
Common risk pathways: BMI link to MACE /HF

Higher BMI over years



Sattar et al (2024) Diabetes Care

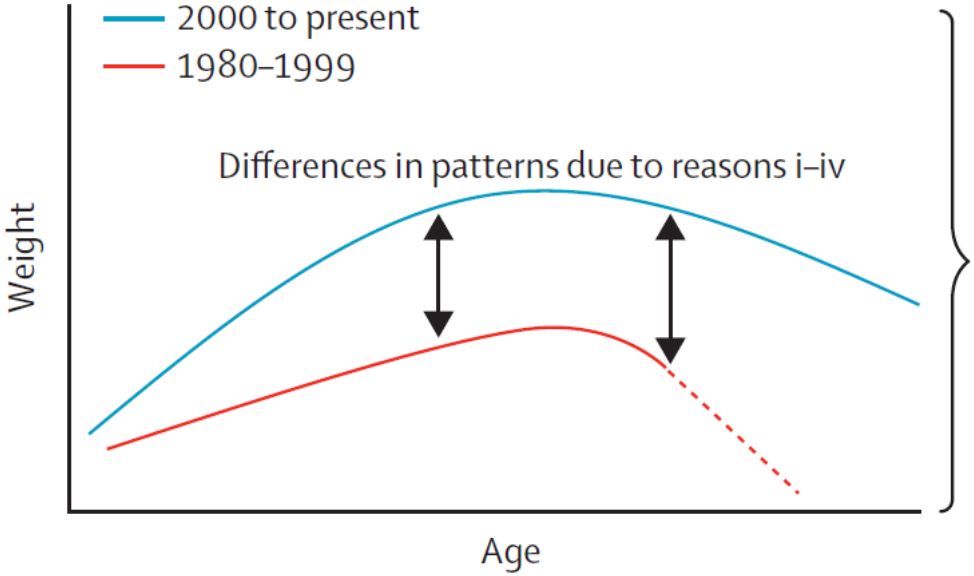
Intentional weight loss bariatric surgery: not randomised – but give optimism?



Liakopoulos et al (2020) Diabetes Care

Treating chronic diseases without tackling excess adiposity promotes multimorbidity

Naveed Sattar, John J V McMurray, Iain B McInnes, Vanita R Aroda, Mike E J Lean



Presence of excess adiposity for longer and later in life
Excess adiposity present for longer and later in life in more people with one condition

Greater risks of second, third, and subsequent comorbidities and symptoms due to effects of excess adiposity that are :
- Metabolic
- Physical
- Haemodynamic
- Inflammatory
- Cellular

Solution

Target weight management much earlier in many chronic conditions and upscale preventive policies

Sattar et al (2022) Lancet D/E