

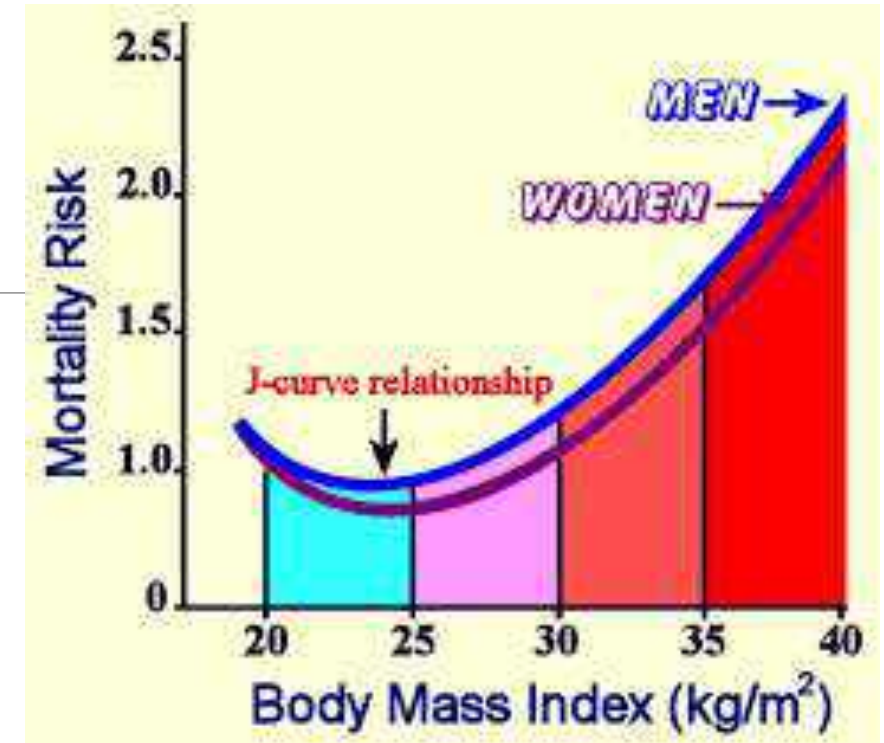
Weight and lack of Testosterone effect men's health

JULIAN J EMMANUEL



What is normal weight and why?

BMI 20-25 is normal- WHO



Every 5 points above 30, loss of 2-4 years in life expectancy

Obesity prevalence

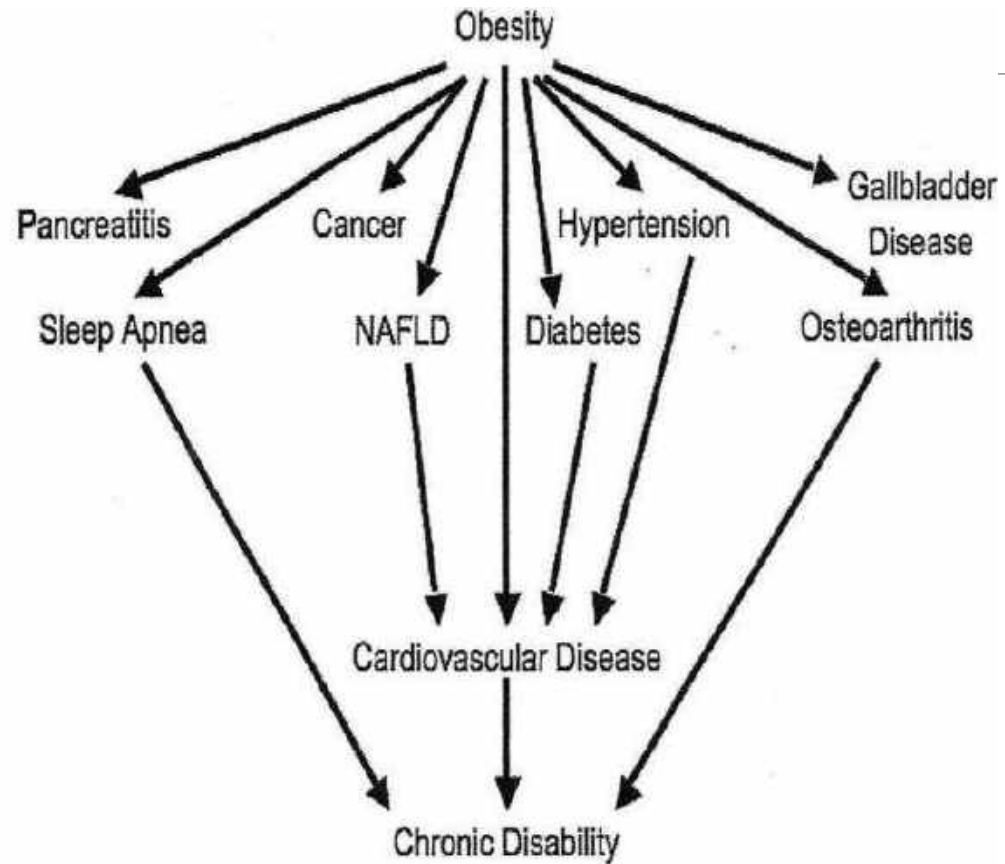
Obesity affects just over a quarter of adults in England (Public Health England, 2016)
http://www.noo.org.uk/NOO_about_obesity

5-10% of the population has T2DM- McCombie L et al; BMJ Sept 2017

Is weight a predictor of poor health?

HOW PREVALENT IS IT?

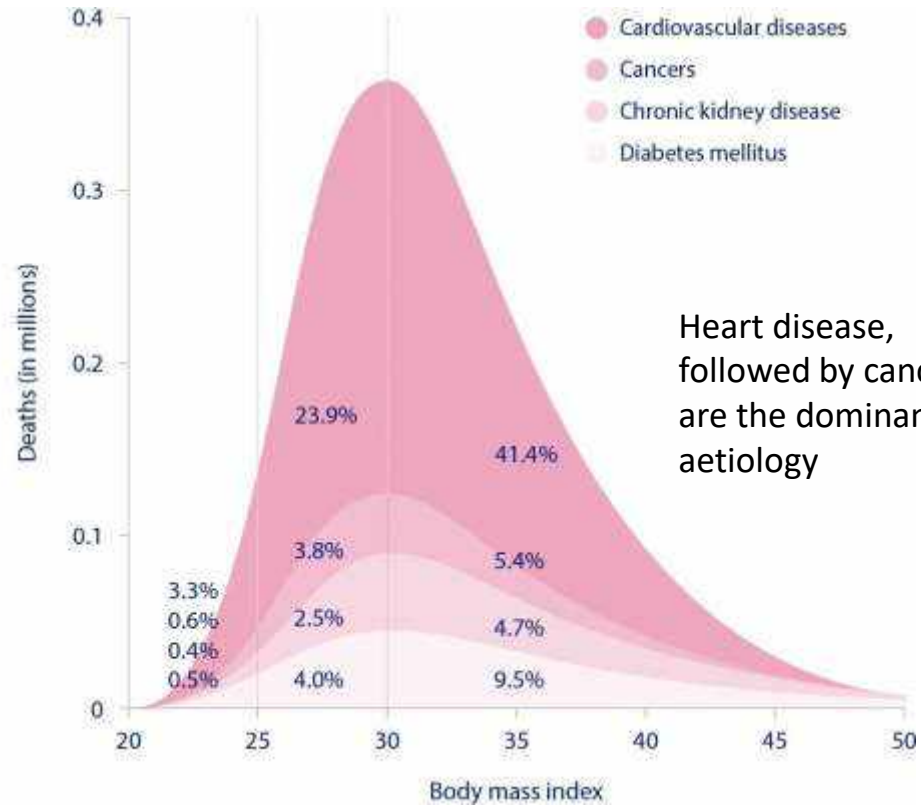
Inflammation
- Fuel in the
wrong place



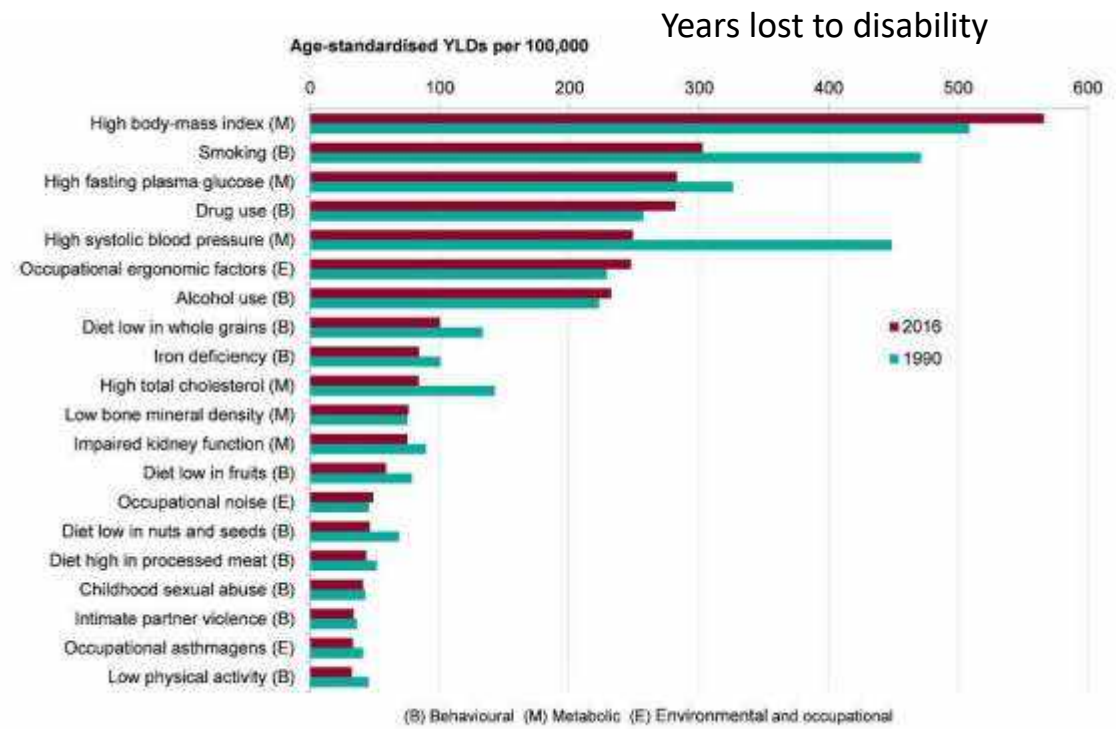
Abbreviation: NAFLD, nonalcoholic fatty liver disease.

Obesity is a predictor of
poor health

AETIOLOGY?



Heart disease,
followed by cancer
are the dominant
aetiology



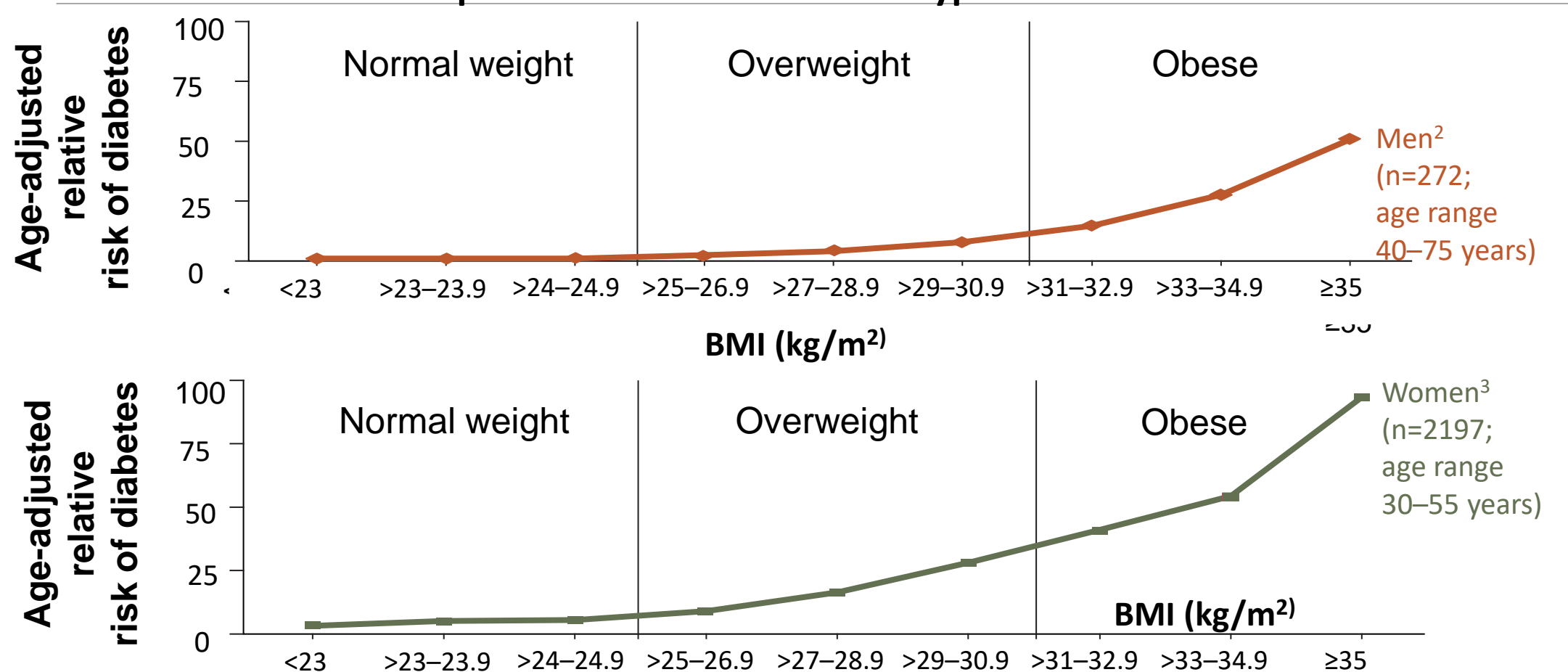
Obesity and (T2) Diabetes are causally linked

DEMAND AND SUPPLY- INSULIN RESISTANCE AND PANCREAS
FAILURE

Diabetes and obesity are closely related

- 90% of individuals with type 2 diabetes are overweight or obese¹

Relationship between BMI and risk of type 2 diabetes

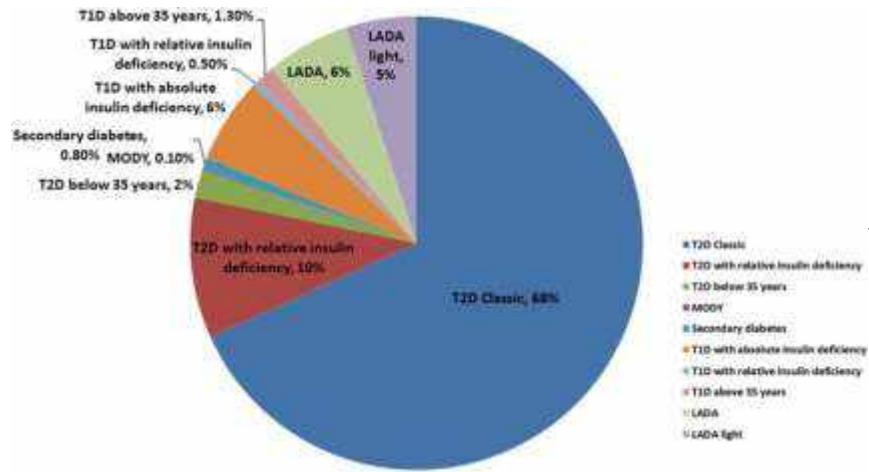


BMI, body mass index.

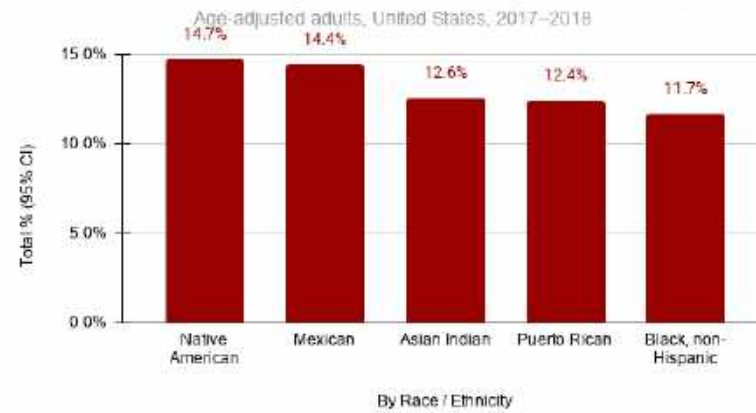
1. WHO (2003) *Obesity and overweight*. Available at: http://www.who.int/dietphysicalactivity/media/en/ssfs_obesity.pdf (accessed 29.01.2014)

1. Chan J *et al. Diabetes Care* 1994;**17**:961-9

2. Colditz GA *et al. Ann Intern Med* 1995;**122**:481-6



Prevalence of Diagnosed Diabetes by Race/ethnicity



Who is at risk



What is normal average sugar and does it correlate to weight?

Obesity and Diabetes do correlate, as does Pre-diabetes and obesity

Treating pre-diabetes has benefits in preventing progression to diabetes; The diabetes prevention programme

HBA1c >48 diabetes, >39/42 pre-diabetes, <30 normal- my opinion, so we can reverse diabetes and cure diabetes, if we intervene early

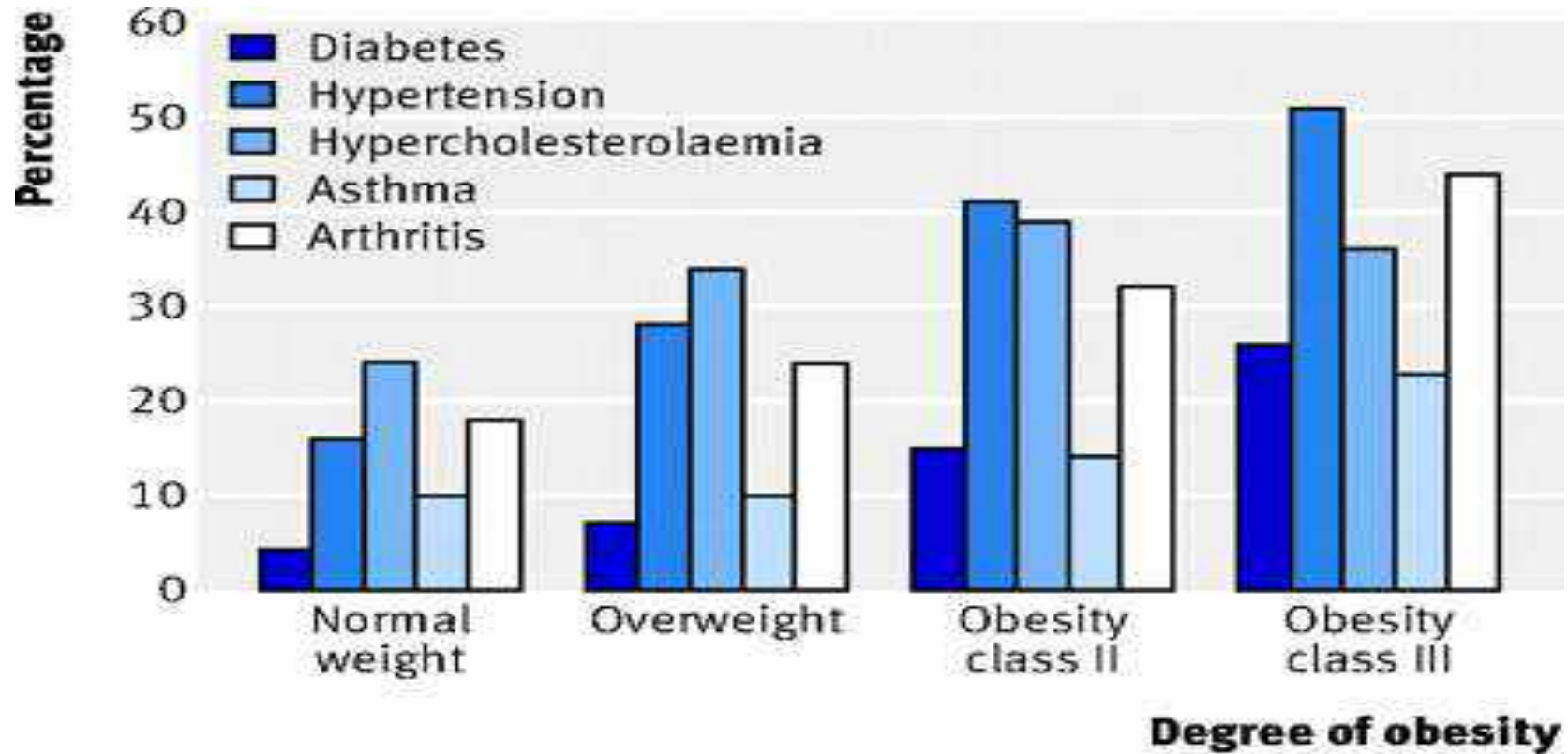
DPP- diabetes prevention programme

Diabetes prevention programme- follow-up 2.8 years, diabetes incidence 11.0 (placebo) 7.8 (metformin a drug) and 4.8 (lifestyle) cases per 100 person-years (2002 NEJM)

Drugs: Metformin (DPP) and now GLP-1 has evidence base for pre-diabetes and obesity

SGLT2 inhibitor- Off Licence- also to treat pre-diabetes and obesity

Degree of obesity is a predictor of risk



Proportion of people with a major co-morbidity, by degree of obesity (Leff and Heath 2009)

Cancer Risk is significantly high

LIKELY INFLAMMATION



Obesity and Cancer risk;

Julian Emmanuel and Simon W Coppack, **Obesity, Bariatric and Metabolic Surgery**

A Practical Guide

Editors Sanjay Agrawal

Springer publishing, 2018

Cancer type	Relative risk Men	Relative risk women	Suggested causal mechanism
Endometrium		1.59	Estrogen excess
Adenocarcinoma esophagus	1.52	1.51	GERD, barrett's esophagus
Thyroid	1.33	1.14	
Adenocarcinoma colon	1.24	1.09	Hyperinsulinemia and/or IGF-1
Renal	1.24	1.34	Hypertension partly
Hepatoma	1.24	1.07	NAFLD, cirrhosis
Breast, estrogen receptor positive		1.18	Estrogen excess
Malignant melanoma	1.17	0.96	
Multiple myeloma	1.11	1.11	Inflammatory cytokines, e.G. Il-6
Rectum	1.09	1.02	
Gall bladder	1.09	1.59	Gall stones
Leukemia	1.08	1.17	Inflammatory cytokines, e.G. Il-6
Pancreas	1.07	1.12	
Non-hodgkin's	1.06	1.07	Inflammatory cytokines, e.G. Il-6
Breast, estrogen receptor negative		1.03	Inflammatory cytokines, e.G. Il-6
Ovary		1.03	
Prostate	1.03		
Stomach	0.97	1.04	
Lung	0.76	0.80	Negative association with smoking
Squamous esophageal	0.71	0.57	Negative association with smoking



Obesity related co-morbidities:

Health Consequences—Obesity Associated Comorbidities: Julian J. Emmanuel and Simon W. Coppack

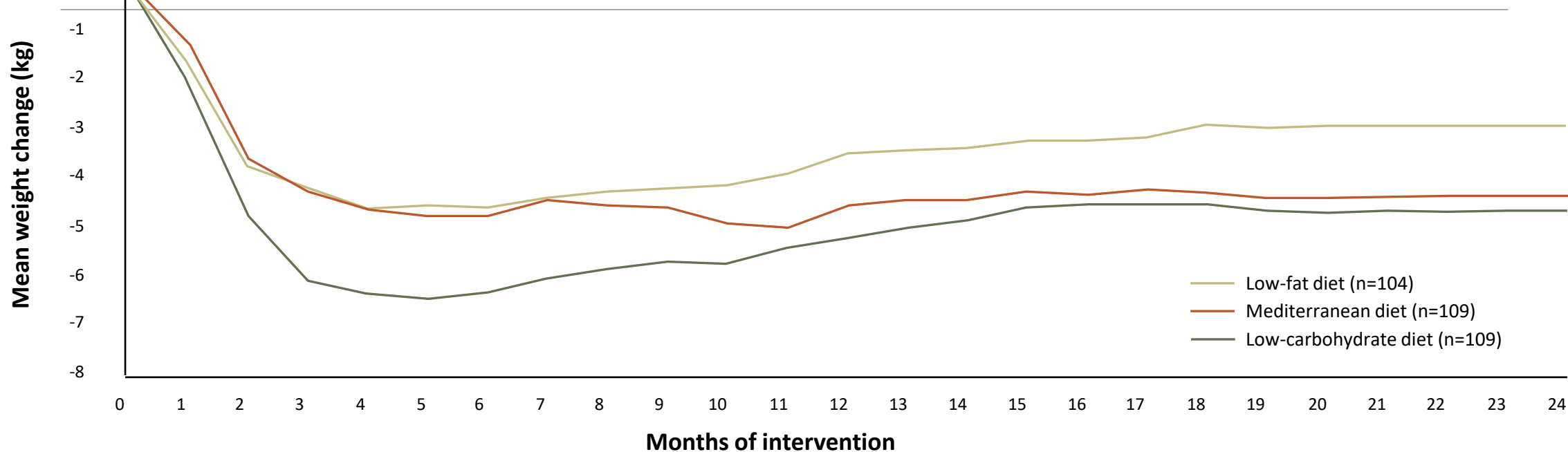
Relative risk	Diseases associated with metabolic consequences (indirect association)	Diseases associated with excess weight (direct association)
Greatly increased risk (>3)	Type 2 diabetes, gallbladder disease, hypertension, dyslipidaemia, insulin resistance, non-alcoholic fatty liver	Sleep apnoea, breathlessness, asthma, social isolation, depression, daytime sleepiness/fatigue
Moderately increased risk (2-3)	Coronary heart disease, stroke, gout	Osteoarthritis, respiratory disease, hernia, psychological problems
Slight increased risk (1-2)	Cancer, impaired fertility, polycystic ovaries, skin complications, cataract	Varicose veins, musculoskeletal problems, backache, stress incontinence, oedema/cellulitis

What interventions are beneficial

Are Lifestyle interventions useful?

What % weight loss do they achieve and maintain?

Different dietary compositions and their effect on weight loss



Baseline mean weight (all, n=322) = 91.4 kg

$P < 0.001$ for both comparisons with the low-fat diet

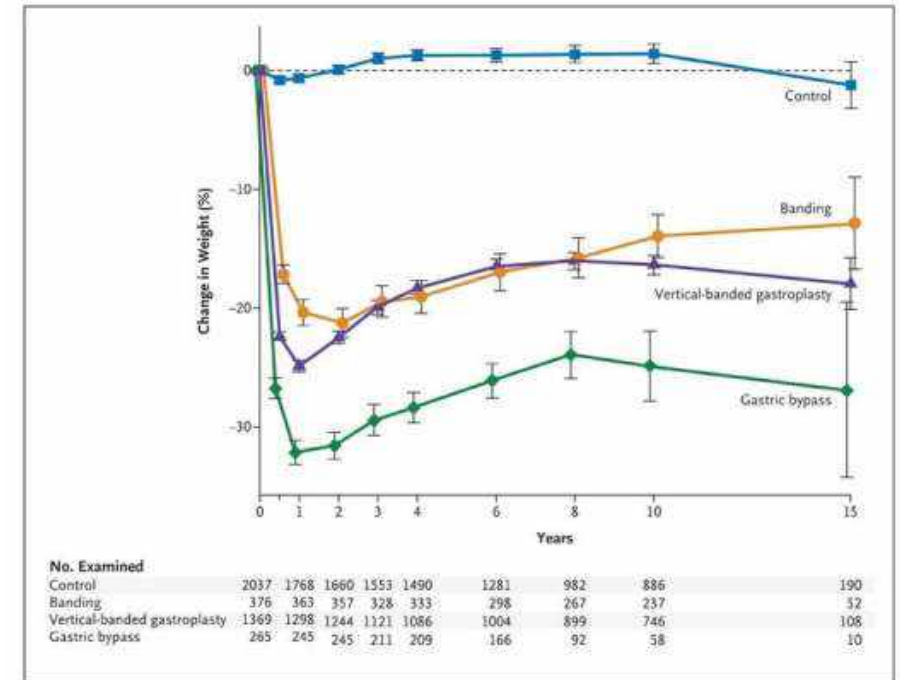
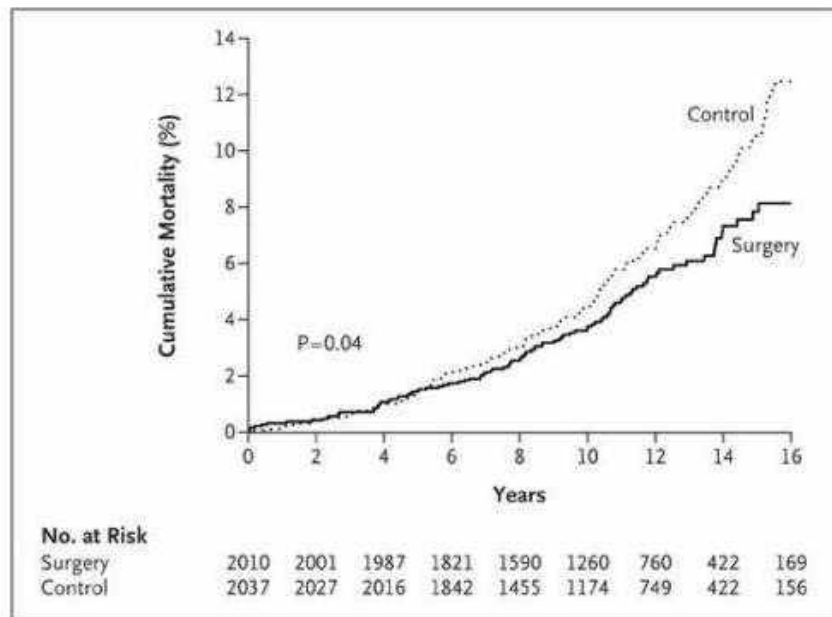
In this 2-year trial, 322 moderately obese subjects (mean age 52 years, mean BMI 31 kg/m², mean baseline weight 91.4 kg, male 86%) were randomly assigned to one of three diets: Low fat, restricted calorie; Mediterranean, restricted calorie; or low carbohydrate, non-calorie restricted.

BMI: body mass index.

Shai I, et al. *N Engl J Med* 2008;359:229-41

SOS

Lars Sjöström, M.D., Ph.D
N Engl J Med 2007; 357:741-752



NICE 2023- GLP-1

Semaglutide recommended for weight management, alongside lifestyle:

- Maximum of 2 years, and within a specialist weight management service in MDT
- 1 weight-related comorbidity and:
 - BMI of at least 35.0 kg/m², or
 - BMI of 30.0 kg/m² to 34.9 kg/m² and meet the criteria for referral to specialist weight management services

Mild and moderate obesity- UK experience

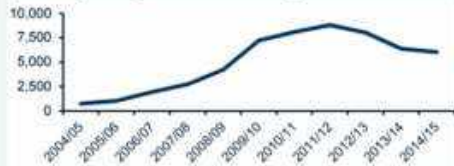
The obesity epidemic has reached the UK, with over one million hospital admissions for obesity last year- 2020

If BMI>50 kg/m², surgical management can be considered as first-line treatment option.

Eligible- 33/1000- 1,980,000 (house of commons library January 2021)

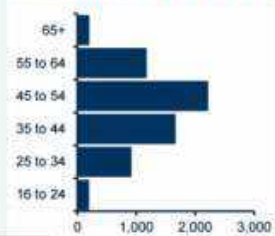
Bariatric surgery, 2014-15

There were **6,032** Finished Consultant Episodes (FCEs) in NHS hospitals with a primary diagnosis of obesity and a main or secondary procedure of bariatric surgery.



This is **31% less** than the peak in 2011/12, but over **8 times more** than ten years ago in 2004/05
(some of the recent fall is attributed to a rise in gastric band maintenance being carried out in an outpatient setting).

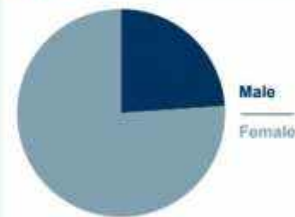
Bariatric Surgery by age



60% of patients were aged between **35 and 54**.

Bariatric Surgery by sex

76% of patients were female.



DPP- diabetes prevention programme

Diabetes prevention programme- follow-up 2.8 years, diabetes incidence 11.0 (placebo) 7.8 (metformin a drug) and 4.8 (lifestyle) cases per 100 person-years (2002 NEJM)

Drugs: Metformin (DPP) and now GLP-1 has evidence base

SGLT2 inhibitor- Off Licence

GLP-1 glucoregulatory effects in humans

Enhances satiety¹

Suppresses postprandial glucagon secretion, which decreases hepatic glucose production^{1,2}

Slows gastric emptying¹

Stimulates glucose-dependent insulin secretion¹



GLP-1 glucagon-like peptide-1.

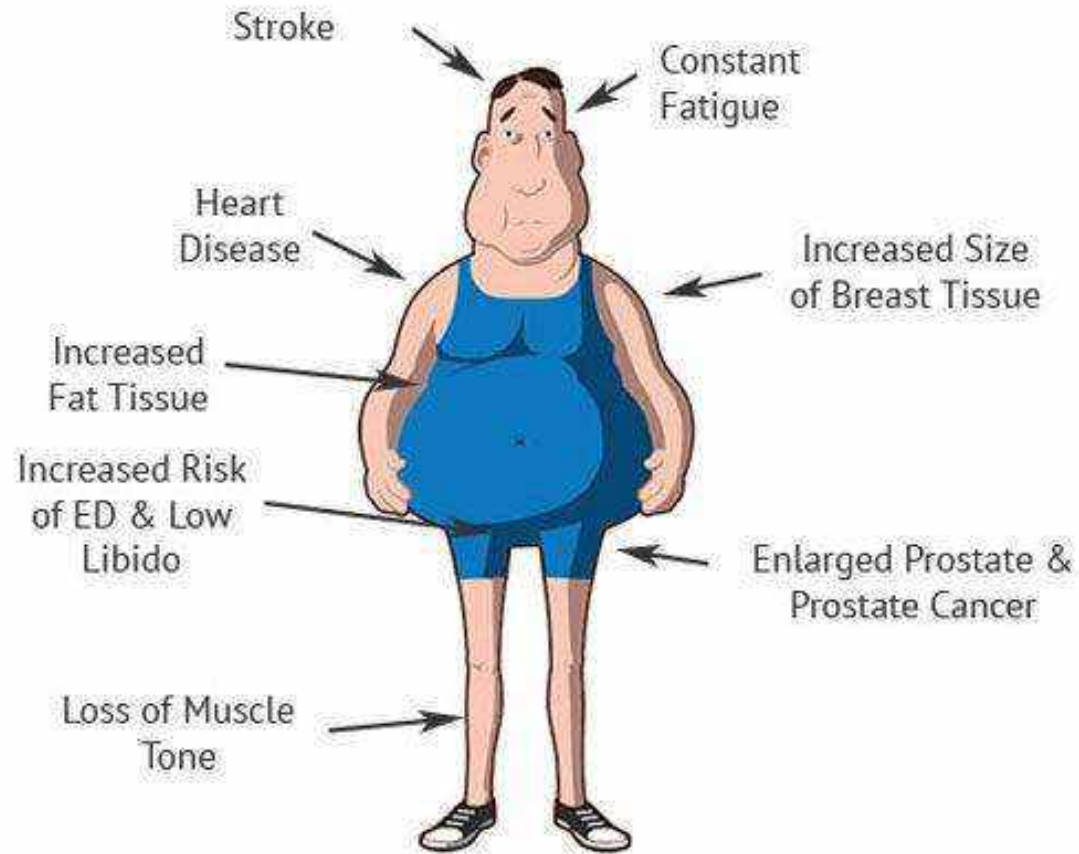
1. Drucker DJ, Nauck MA. *Lancet* 2006;**368**:1696–705; 2. Larsson H, et al. *Acta Physiol Scand* 1997;**160**:413–22.

Does weight and testosterone interact

Obese men (BMI >30 kg/m²) had significantly lower SHBG (binding protein) and total testosterone concentrations, than non-obese men

Low testosterone is associated with increased fat mass, reduced lean mass in men- metabolic dysfunction; testosterone deficiency can lead to energy imbalance, impaired glucose control, reduced insulin sensitivity and dyslipidaemia- high cholesterol.

Signs Of Low Testosterone



Is there a correlation between Testosterone and diabetes and weight

Bi-directional relationship between testosterone and obesity, the hypogonadal-obesity cycle

Weight loss can lead to increased total testosterone levels.

Are there benefits to intervening early

Experience from primary/ secondary gonadal failure:

benefits of Testosterone replacement: Weight loss/
Increased energy levels/ Increase libido/ improved
muscle mass/ fertility

How can we combine these interventions in a synergistic manner

Target weight and Low testosterone- an MDT approach: endocrinologist, urologist and exercise physiologist, dietician and psychologist

A one stop shop- Recommend and start interventions early, and monitor progress under a multi-disciplinary team (Endocrinology, urology, physiologist, and psychology, dietetics to come)