Leicester Diabetes Centre

Implementation of Obesity Guidelines

Dr Dimitris Papamargaritis, MRCP (UK), MRCP (Diabetes and Endocrinology), PhD, SCOPE certified, EASO National Clinical Fellow, ASO Trustee

Associate Professor in Diabetes and Endocrinology, University of Leicester

Honorary Consultant, University Hospitals of Northamptomshire NHS Group (Kettering General Hospital)

Conflict of Interest

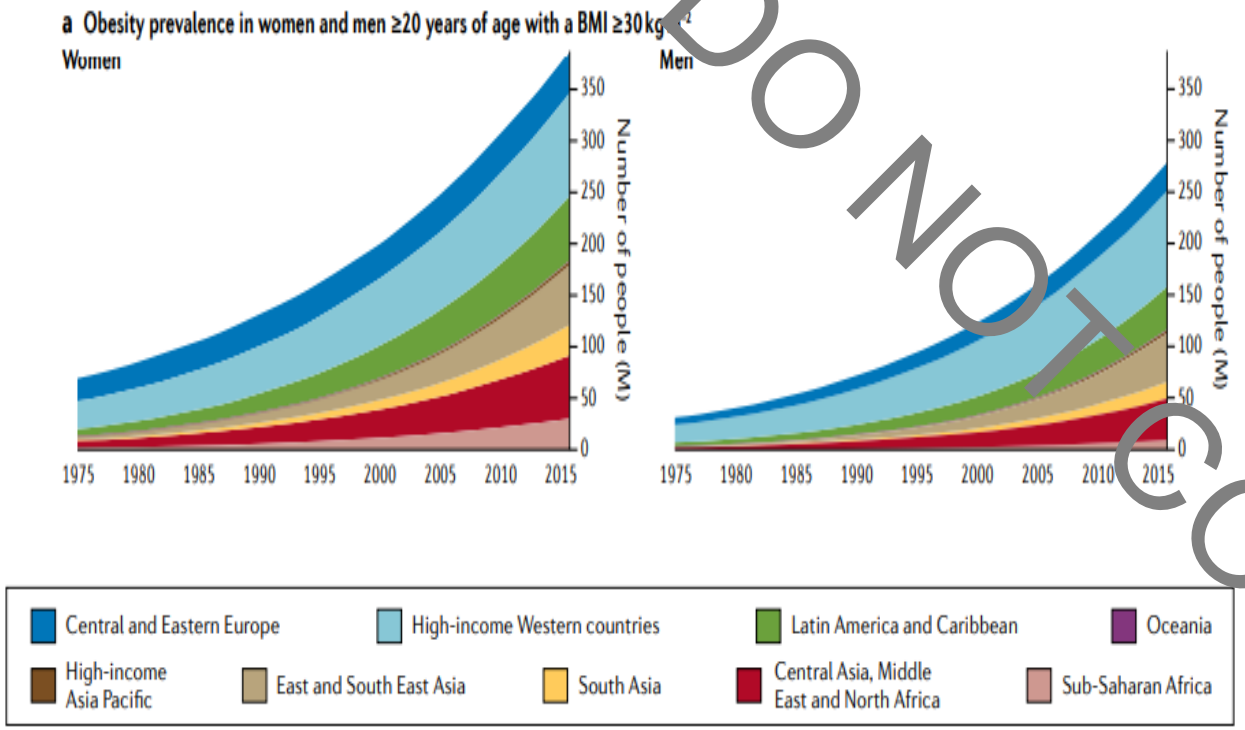
Research grants from

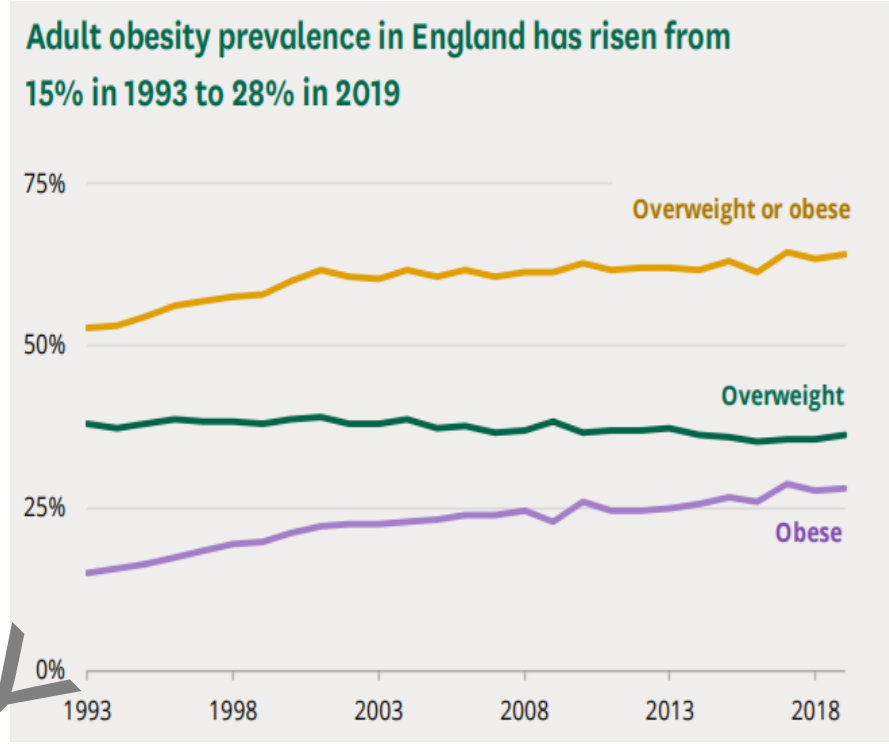
- Novo Nordisk UK Research Foundation
- Novo Nordisk A/S
- Health Education East Midlands
- Academy of Medical Sciences/ Diabetes UK
- National Institute for Health and Care Research (NIHR)

Honoraria/Consultation

- Novo Nordisk UK
- Eli Lilly UK
- Boehringher Ingelheim
- Johnson and Johnson
- Recordati
- Regeneron

Prevalence of obesity worldwide and in England

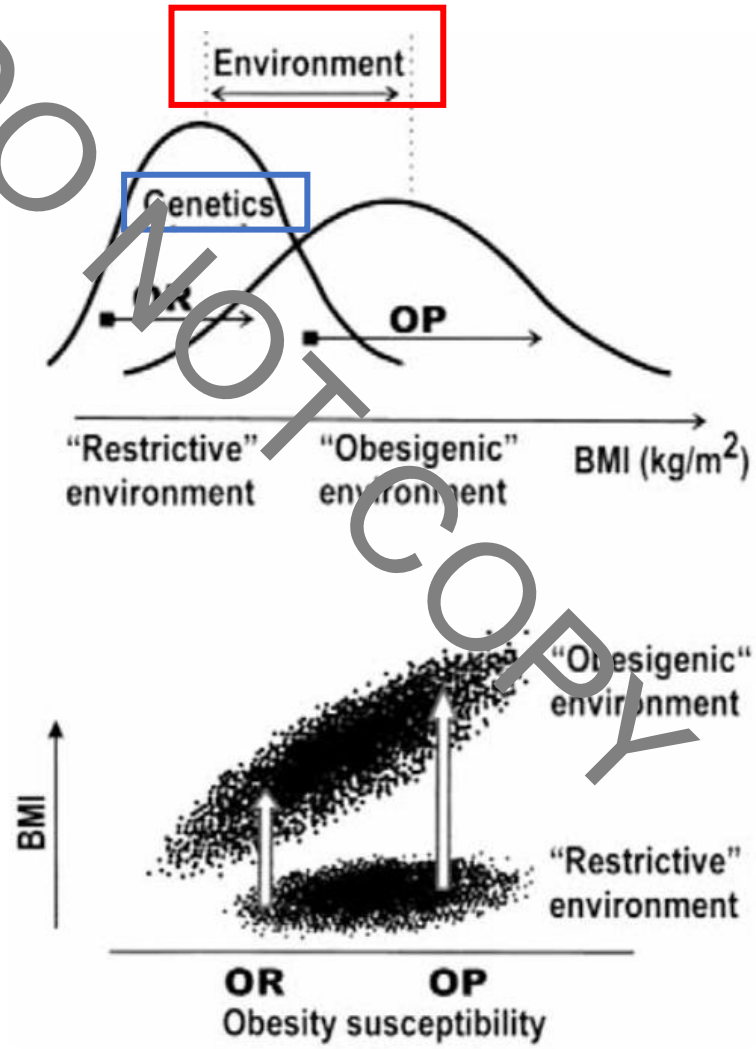




Loos RJF, 2021, Nature Reviews Genetics

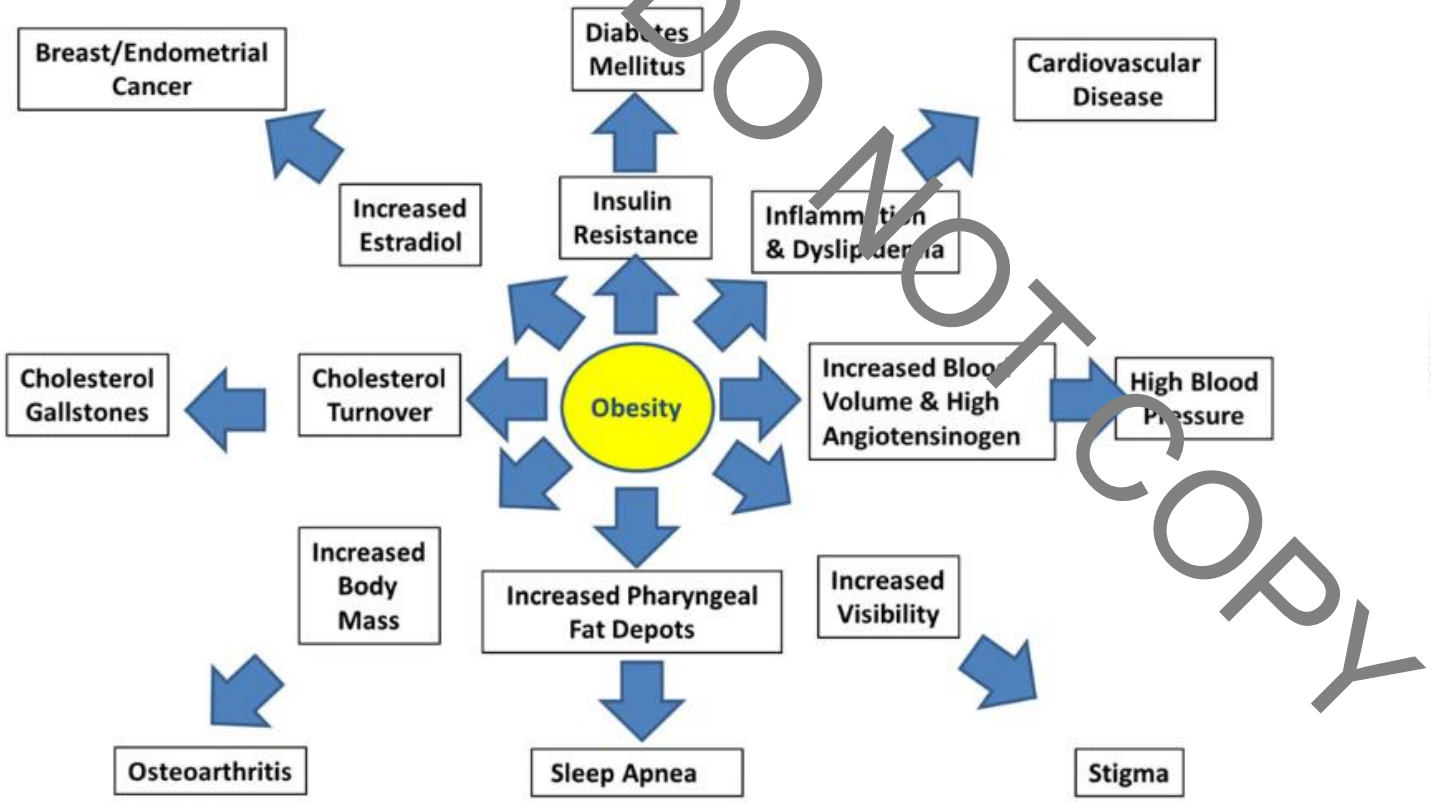
Environment and genetics

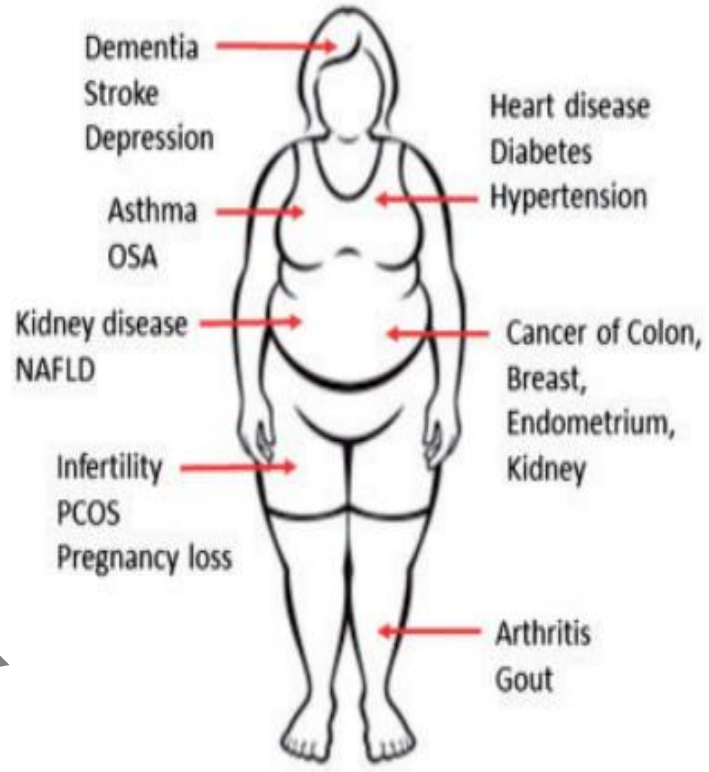
40-70% of our weight is inherited



Ravussin & Bouchard 2000

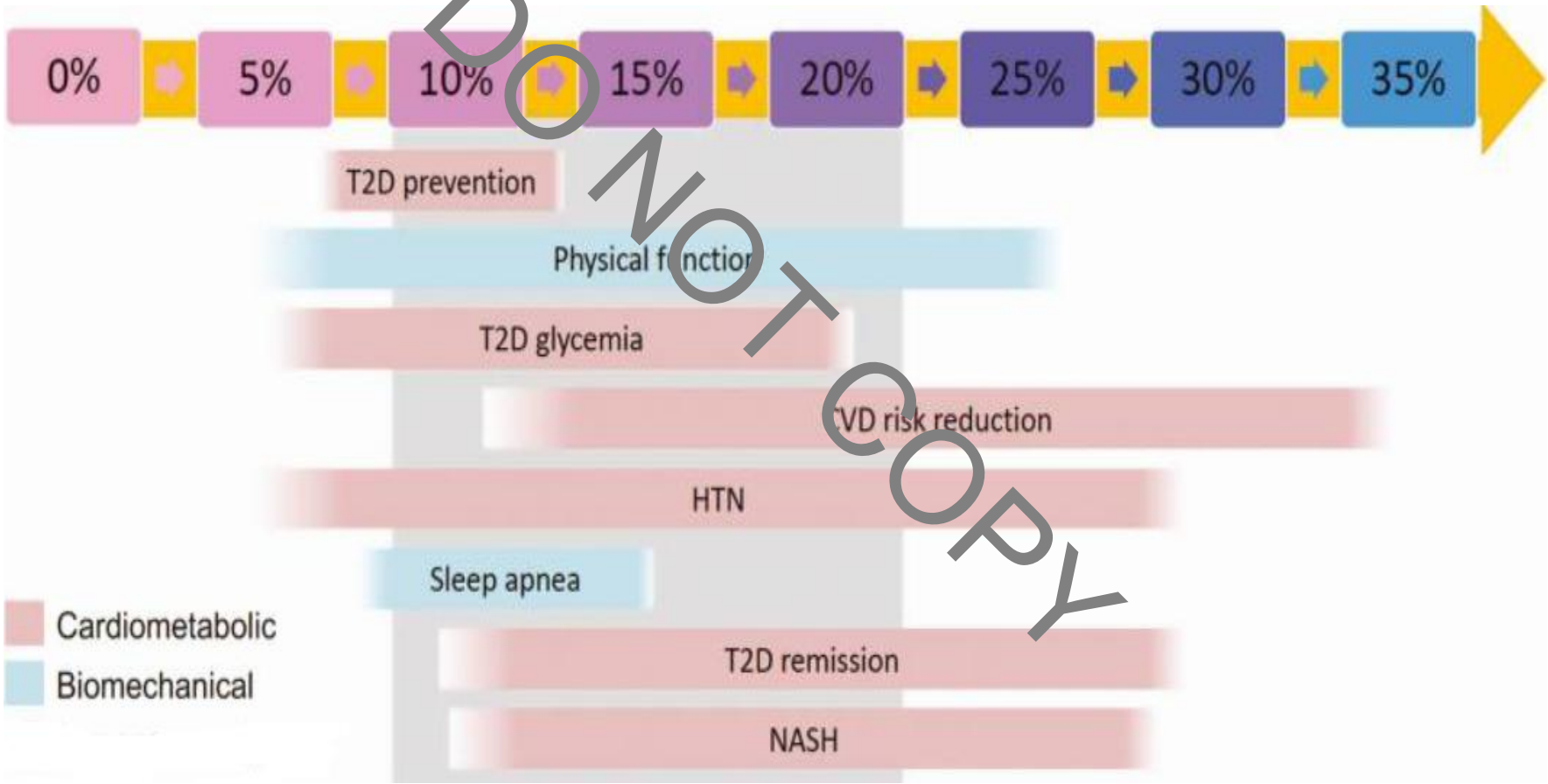
Complications of obesity





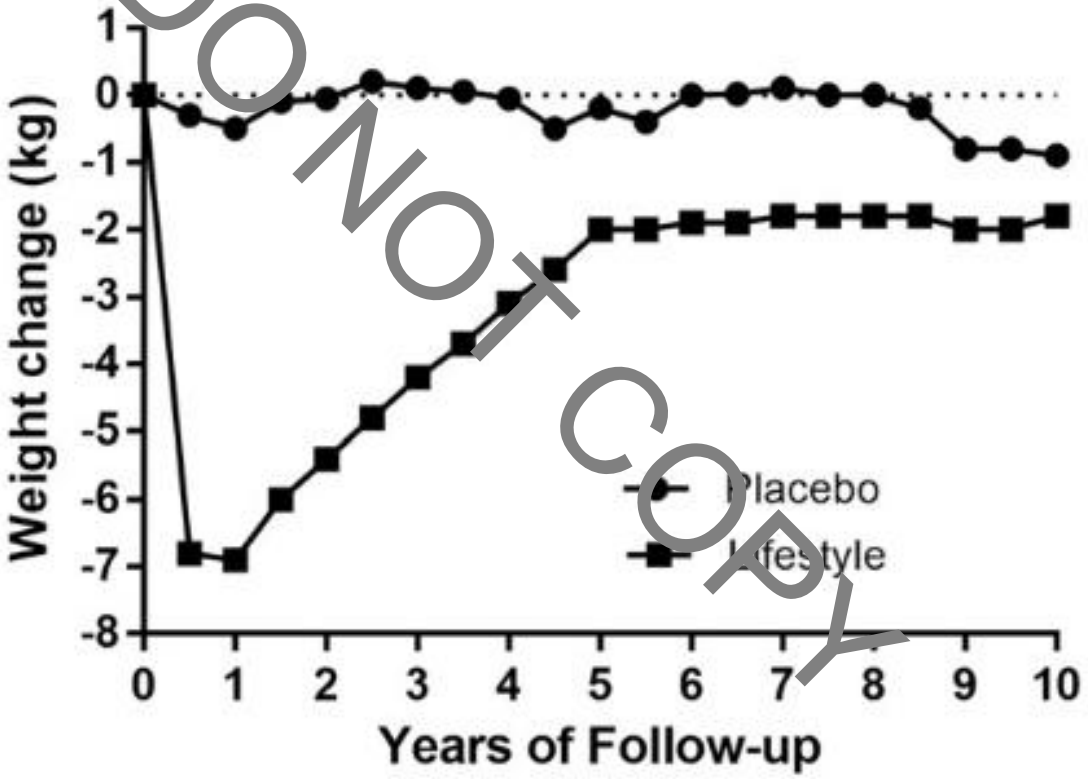
Kinlen D, 2018, QJM/ Bray 2017, DOM

Weight loss required to improve different obesity-related complications



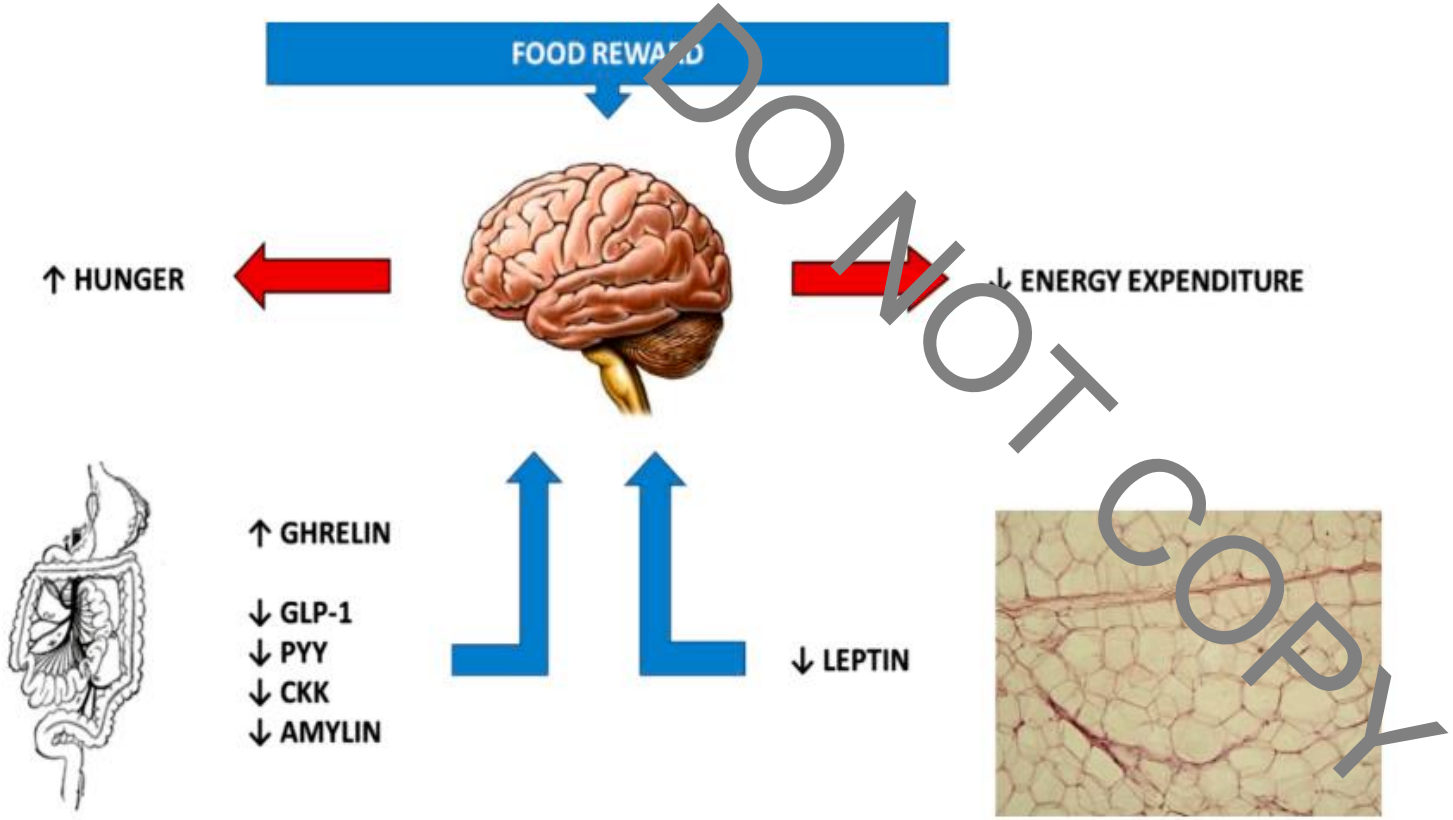
Garvey T, 2022, JCEM

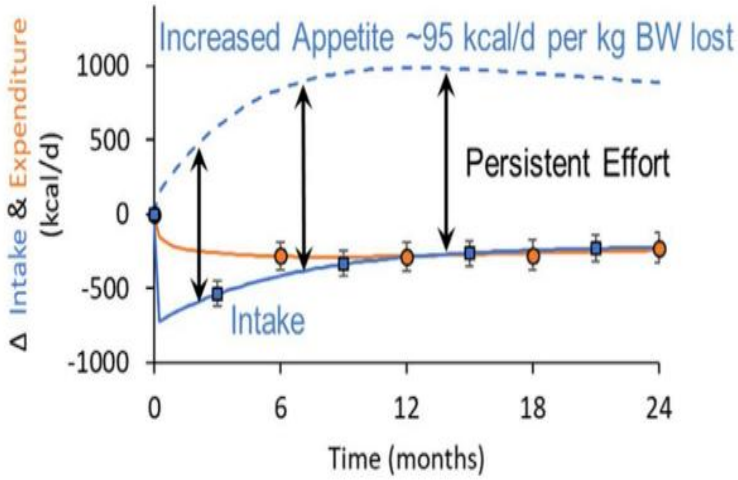
Weight loss and weight loss maintenance is challenging



Adapted from Venditti et al Int J Obes 2008;32:1537-44

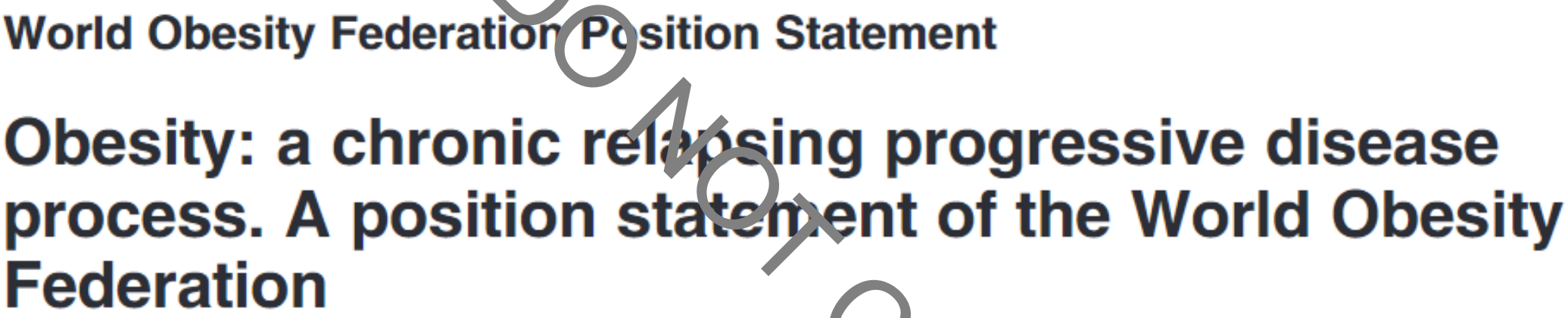
Physiology of weight-loss state





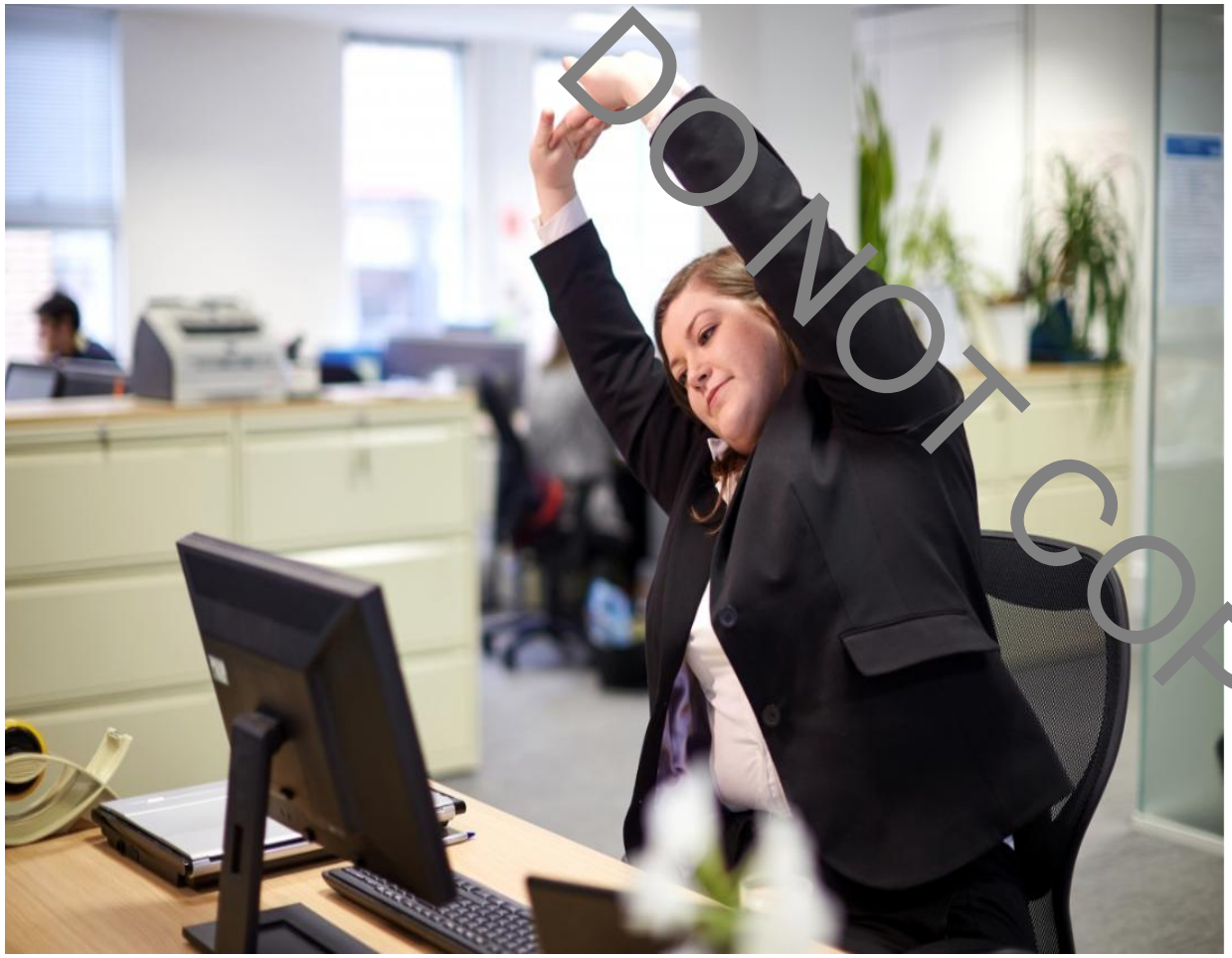
Busetto L, 2021, Eur J Intern Med.

Obesity is a disease



Bray GA, 2017, Obesity Reviews

Case 1 - Catherine



Age: 26 years old

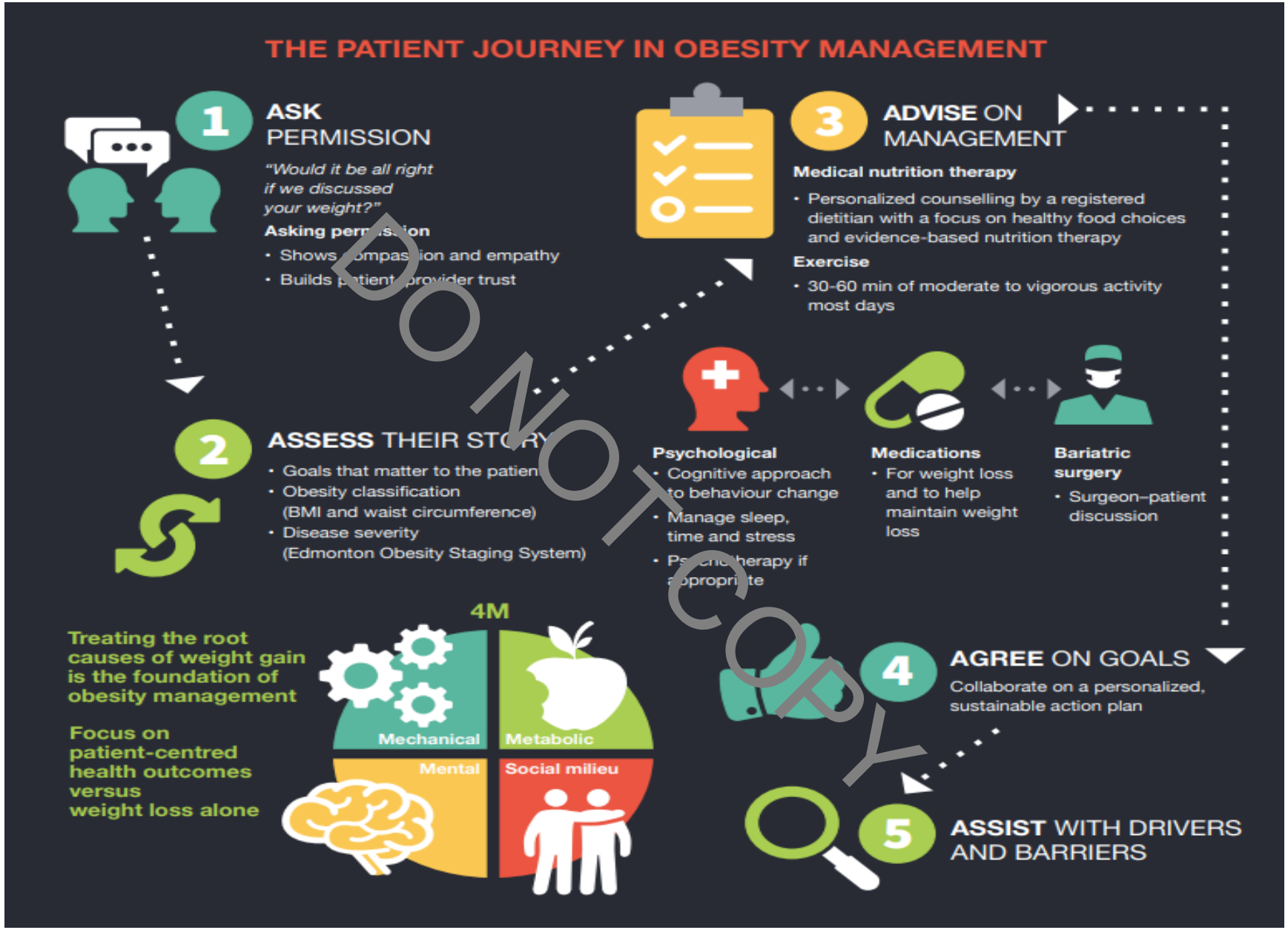
BMI: 33, Weight: 85, Height:1.63cm

Attends for irregular periods

Not currently planning for family, but may consider in the next 2 years – she is getting married in Summer 2026.

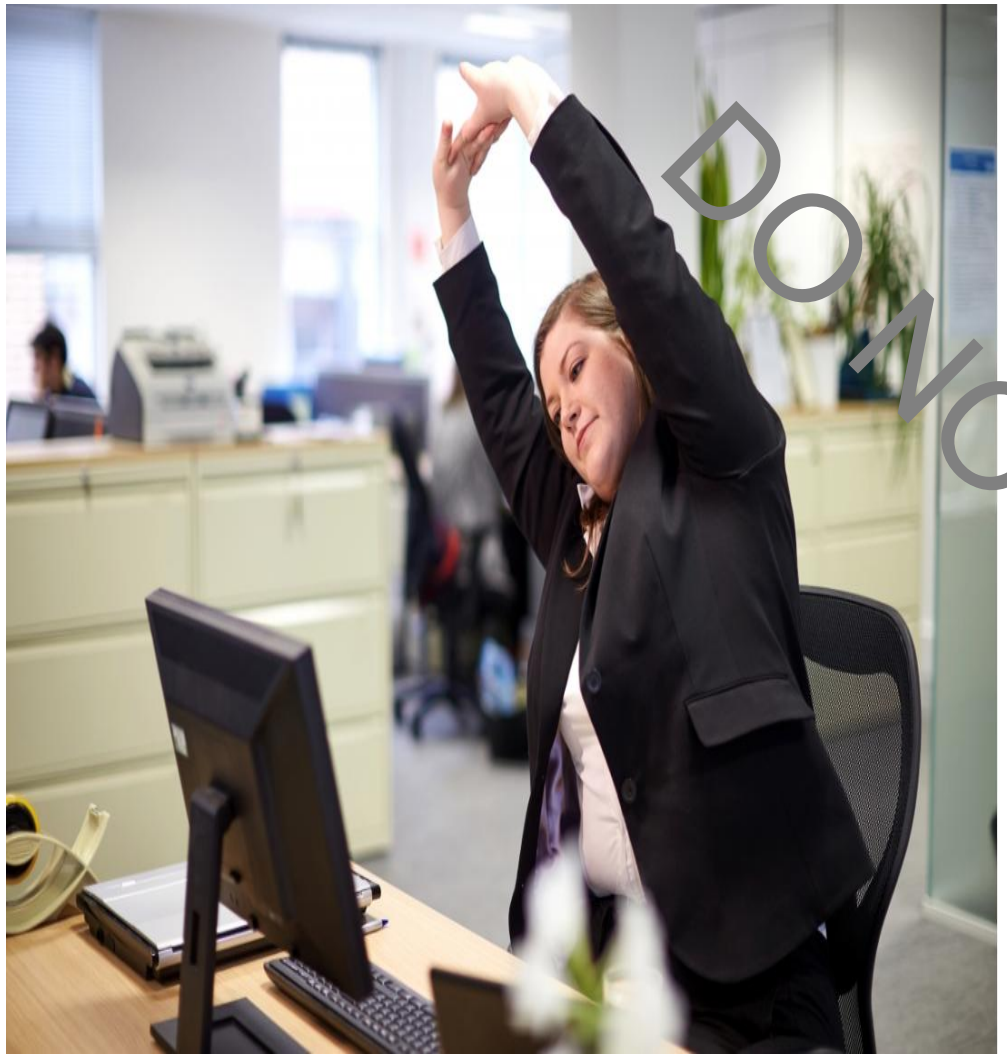
Priority number 1 – Deal with the presenting problem!

Priority number 2 – Get permission to discuss about weight



CMAJ, August 04, 2020 192 (31) E875-E891; DOI: https://doi.org/10.1503/cmaj.191707

Case 1 – Catherine – After investigations for irregular periods, what you want to do?



1.9.8 In adults with BMI below 35 kg/m^2, measure and use their waist-to-height ratio, as well as their BMI, as a practical estimate of central adiposity and use these measurements to help to assess and predict health risks (for example, type 2 diabetes, hypertension or cardiovascular disease). **[2022]**

Waist circumference: 103cm – WHR: 0.63

1.9.14 Classify the degree of central adiposity based on waist-to-height ratio as follows:

- healthy central adiposity: waist-to-height ratio 0.4 to 0.49, indicating no increased health risks
- increased central adiposity: waist-to-height ratio 0.5 to 0.59, indicating increased health risks
- high central adiposity: waist-to-height ratio 0.6 or more, indicating further increased health risks.

These classifications can be used for people with a BMI under 35 kg/m^2 of both sexes and all ethnicities, including adults with high muscle mass.

The health risks associated with higher levels of central adiposity include type 2 diabetes, hypertension and cardiovascular disease. **[2022]**

Assessment for obesity-related complications

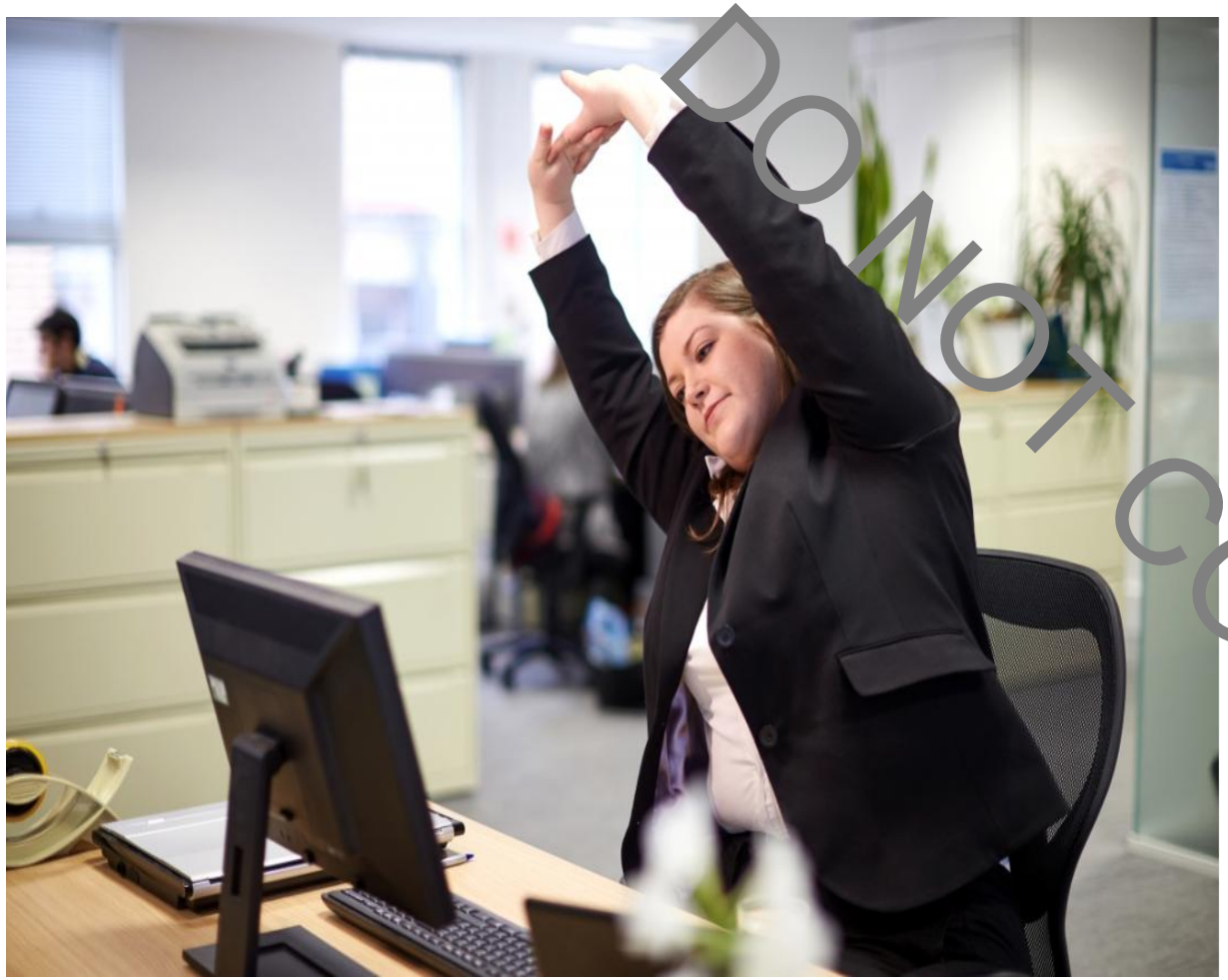
Assessing and managing comorbidities in adults

1.9.16 After the initial assessment of overweight or obesity, identify any comorbidities and other factors that may affect or be affected by the person's weight. Take into account the timing of the assessment, the degree of overweight or obesity, and the results of previous assessments. **[2006]**

1.9.17 Start managing comorbidities as soon as they are identified; do not wait until the person has lost weight. **[2006]**

- Fasting glucose 6.1 mmol/mol, HbA1C: 37, eGFR >90
- BP: 125/80 mmHg
- LDL: 1.7 mmol/l, HDL: 0.9 mmol/l
- TSH: 1.2 (normal)
- **Any other assessments?**

Assessment of obesity



A: Airway (OSA, asthma)
B: BMI
C: Cardiovascular (AF, HTN, dyslipidaemia)
D: Diabetes (HbA1c)
E: Economic impact
F: Functional (does it affect mobility)
G: Gonads (PCOS, infertility)
H: Health status perceived (mental health, quality of life)
: Body image (including binge eating disorder)
Junction gastroesophageal (acid reflux)
K: Kidneys (ACR, eGFR)
L: Liver (FIB-4 for MASH)
M: Medication burden
N: Nutrition (Vitamin deficiencies)
O: Other

Tiered approach in obesity services (UK)

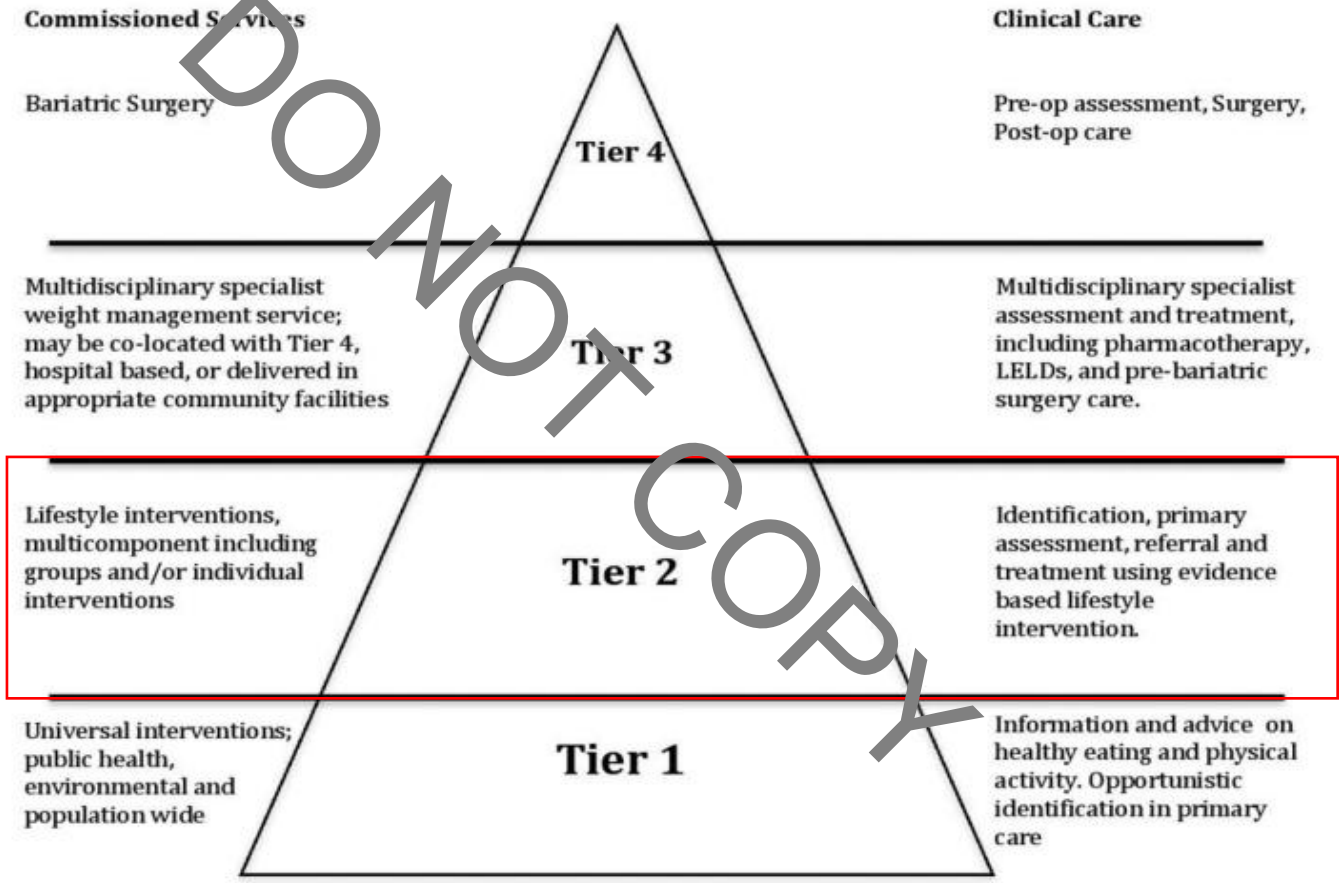


Figure 1 Tiered model of services.

Jennings A, Clinical Obesity, 2014

Catherine

BMI:33, Class 1 obesity

Lifestyle interventions in the community, not eligible for SWMS

Diabetes Prevention Programme

Metformin 1g bd
Orlistat 120mg tds

She lives in Northamptonshire

Northamptonshire Tier 2 level weight management options

Living Well Taking Control

Ready to lose weight and take charge of your health

Living Well Taking Control

Better Health - NHS

Healthy changes start with little changes

Better Health - NHS

NHS Weight Loss Plan

Free 12-week diet and exercise plan

NHS Weight Loss Plan

Type 2 Diabetes

Concerned about developing Type 2 Diabetes

Type 2 Diabetes

https://www.northnorthants.gov.uk/keeping-healthy/weight-management

NICE criteria for Orlistat 120mg tds

Medicine	Starting criteria	Stopping criteria
Orlistat	BMI of: • 30 kg/m^2 or more **or** • 28 kg/m^2 or more with associated risk factors. Use with other drugs aimed at weight reduction is not recommended.	Continue beyond 3 months only if the person has lost at least 5% of their initial body weight since starting orlistat. (See also recommendation 1.9.6 for people with type 2 diabetes.)

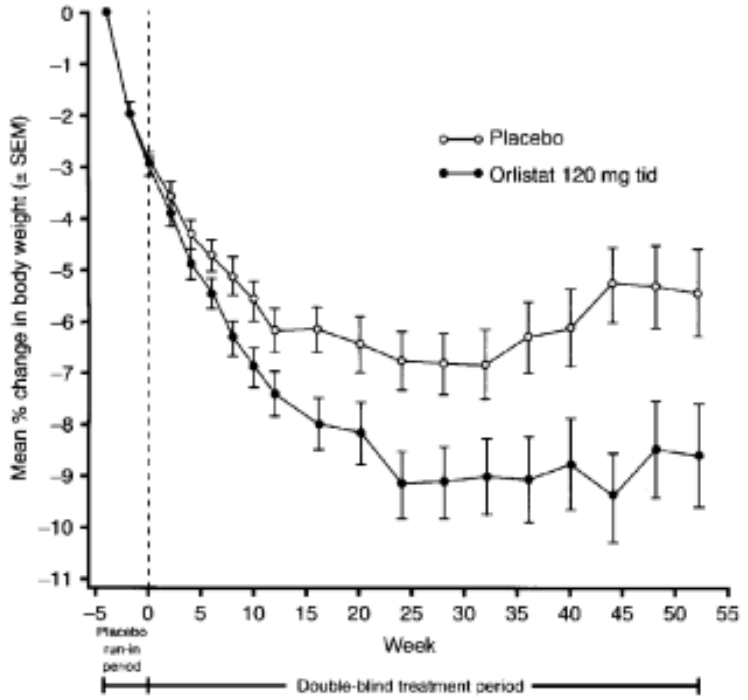


Figure 2 Mean percentage change (±s.e.m.) from initial body weight (intent-to-treat population).

Common side effects: DIARRHOEA (oily)

NICE guidance for obesity (CG 189)/ NICE guidance for T2D prevention (PH38)

Catherine – What if her BMI was 37?

BMI:37 Class 1 obesity

- Prediabetes
- PCOS
- Dyslidipidaemia

Went to diabetes prevention programme – minimum benefit, still fasting glucose: 6.0 mmol/l and HbA1c 37mmol/l/

Potentially (based on local criteria) eligible for SWMS

NICE recommendation Saxenda

Liraglutide is recommended as an option for managing **overweight and obesity** alongside a **reduced-calorie diet and increased physical activity** in adults, only if:

- Patients have a **BMI of at least 35 kg/m²** (or at least 32.5 kg/m² for members of minority ethnic groups known to be at equivalent risk of the consequences of obesity at a lower BMI than the white population)
- Patients have **pre-diabetes**(defined as a HbA_{1c} of 42 mmol/mol to 47 mmol/mol [6.0% to 6.4%] or a fasting plasma glucose level of 5.5 mmol/L to 6.9 mmol/L)
- Patients have a high risk of **cardiovascular disease** based on risk factors such as hypertension and dyslipidaemia
- It is prescribed in **secondary care** by a specialist multidisciplinary tier 3 weight management service for a maximum of 2 years

Liraglutide for managing overweight and obesity (TA664). Guidance NICE. [online] Available at: www.nice.org.uk/guidance/ta664 Accessed 21 July 2021

Tiered approach in obesity services (UK)

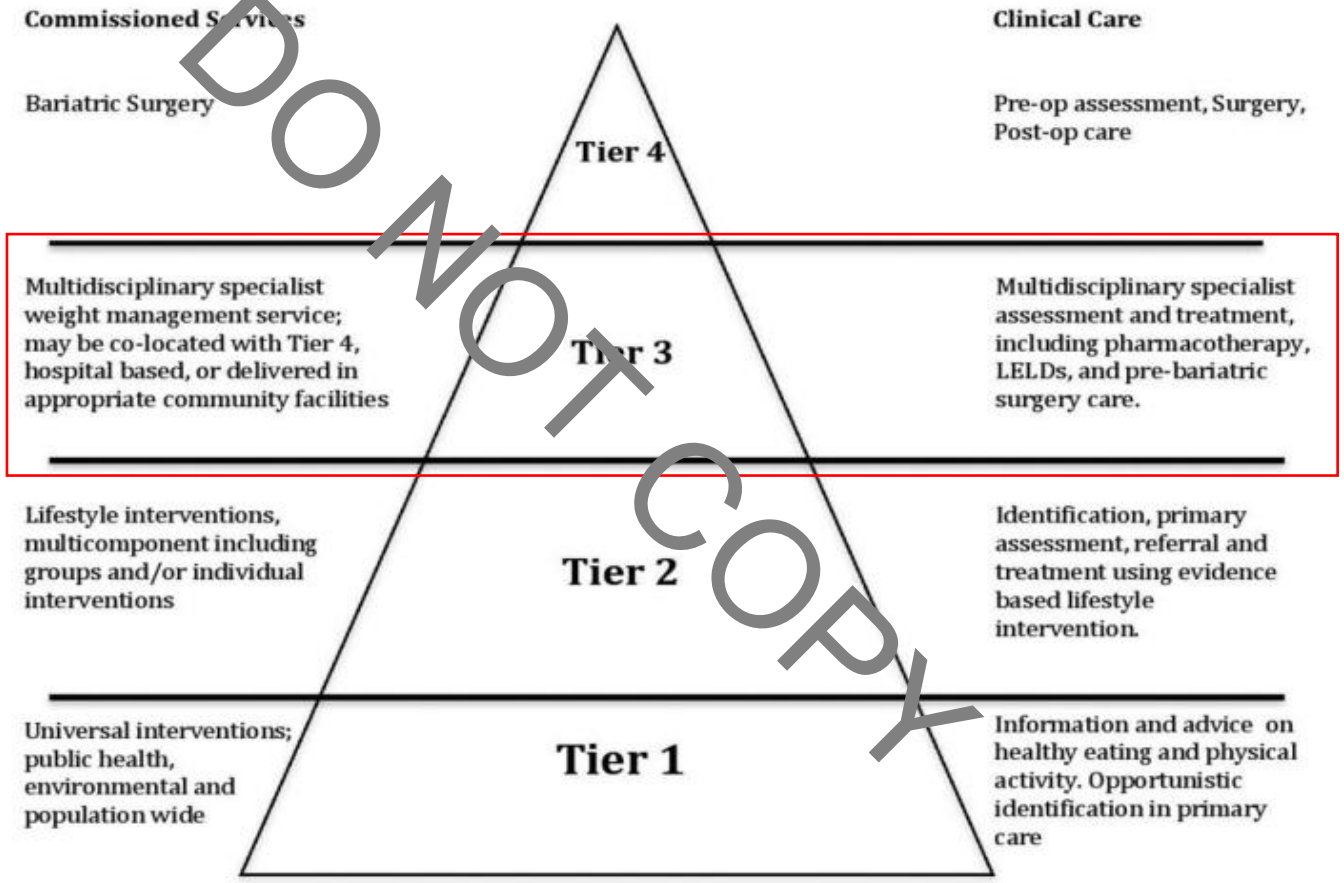
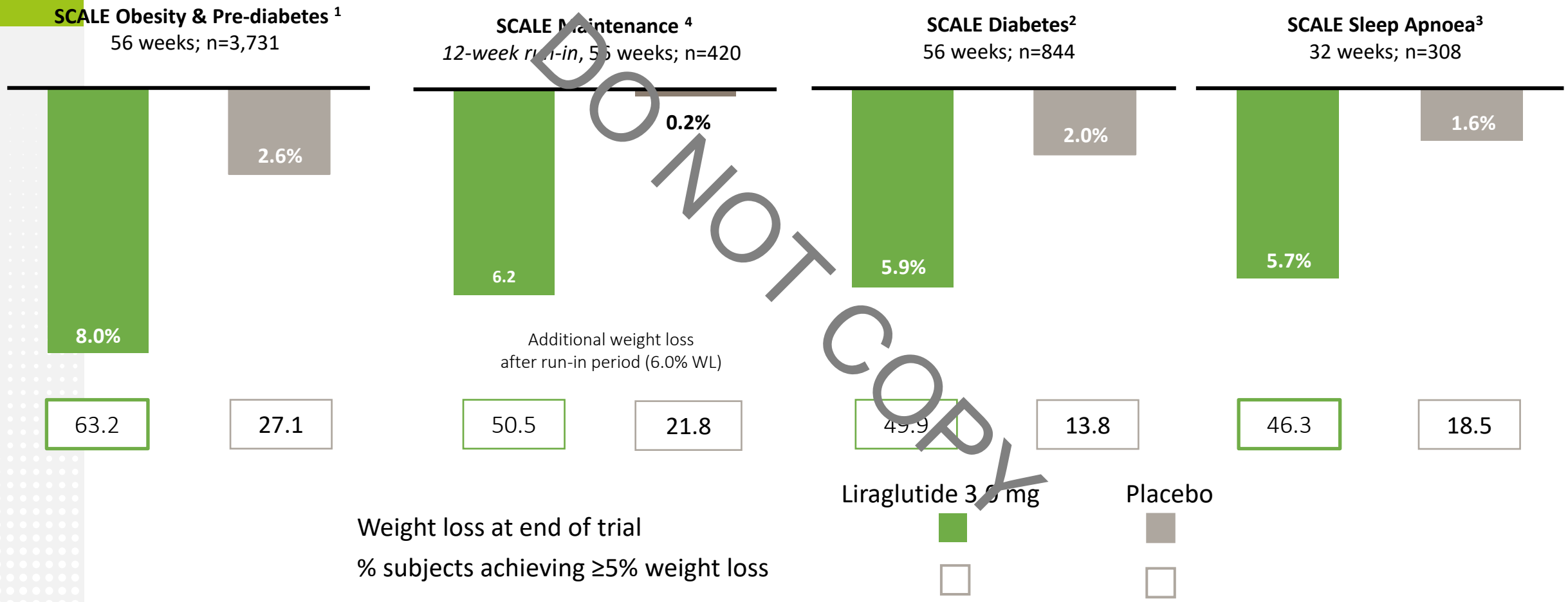


Figure 1 Tiered model of services.

Jennings A, Clinical Obesity, 2014

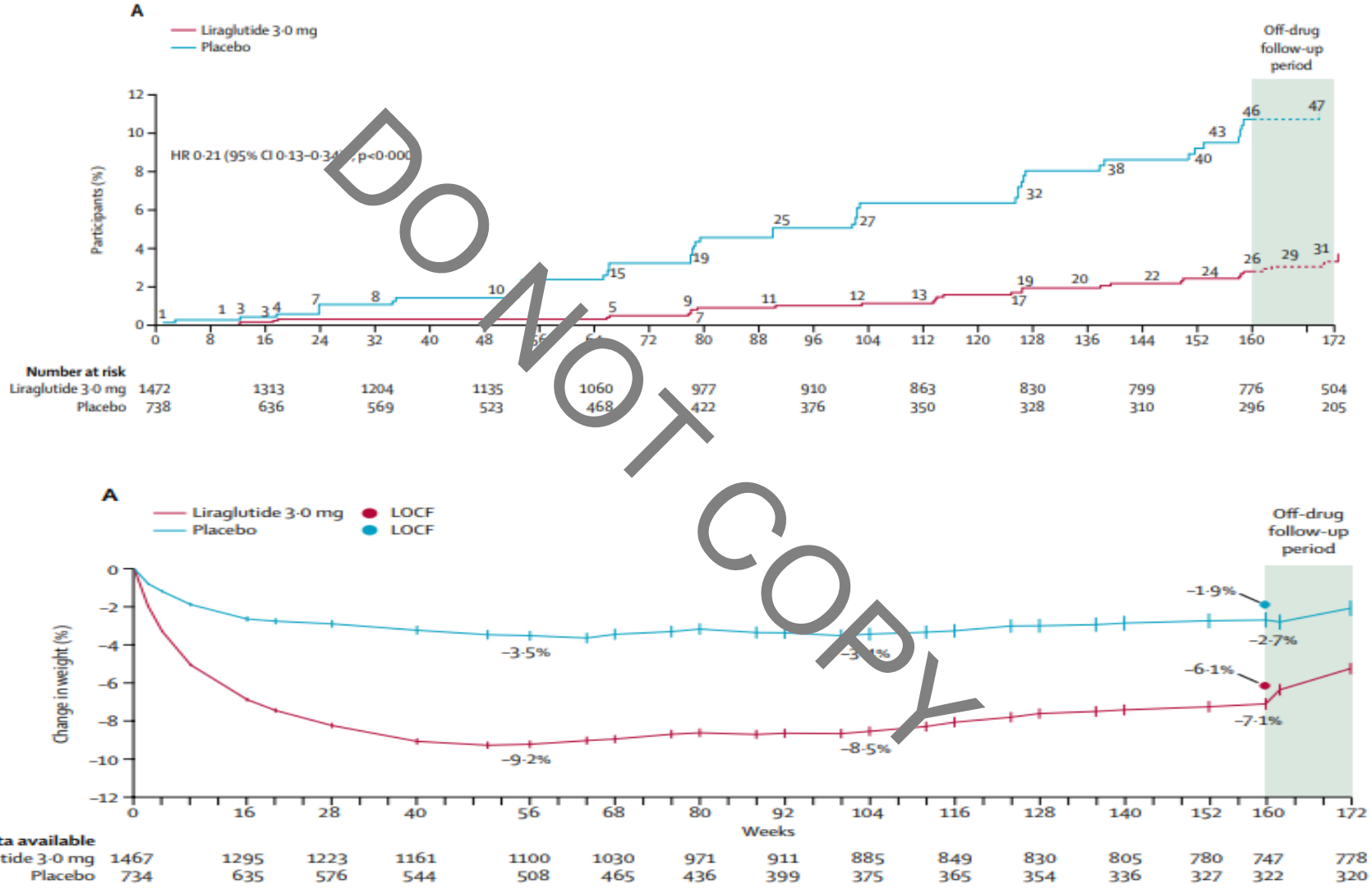
All SCALE trials demonstrate weight loss



Data are observed means; LOCF at end of trial.
LOCF, last observation carried forward.

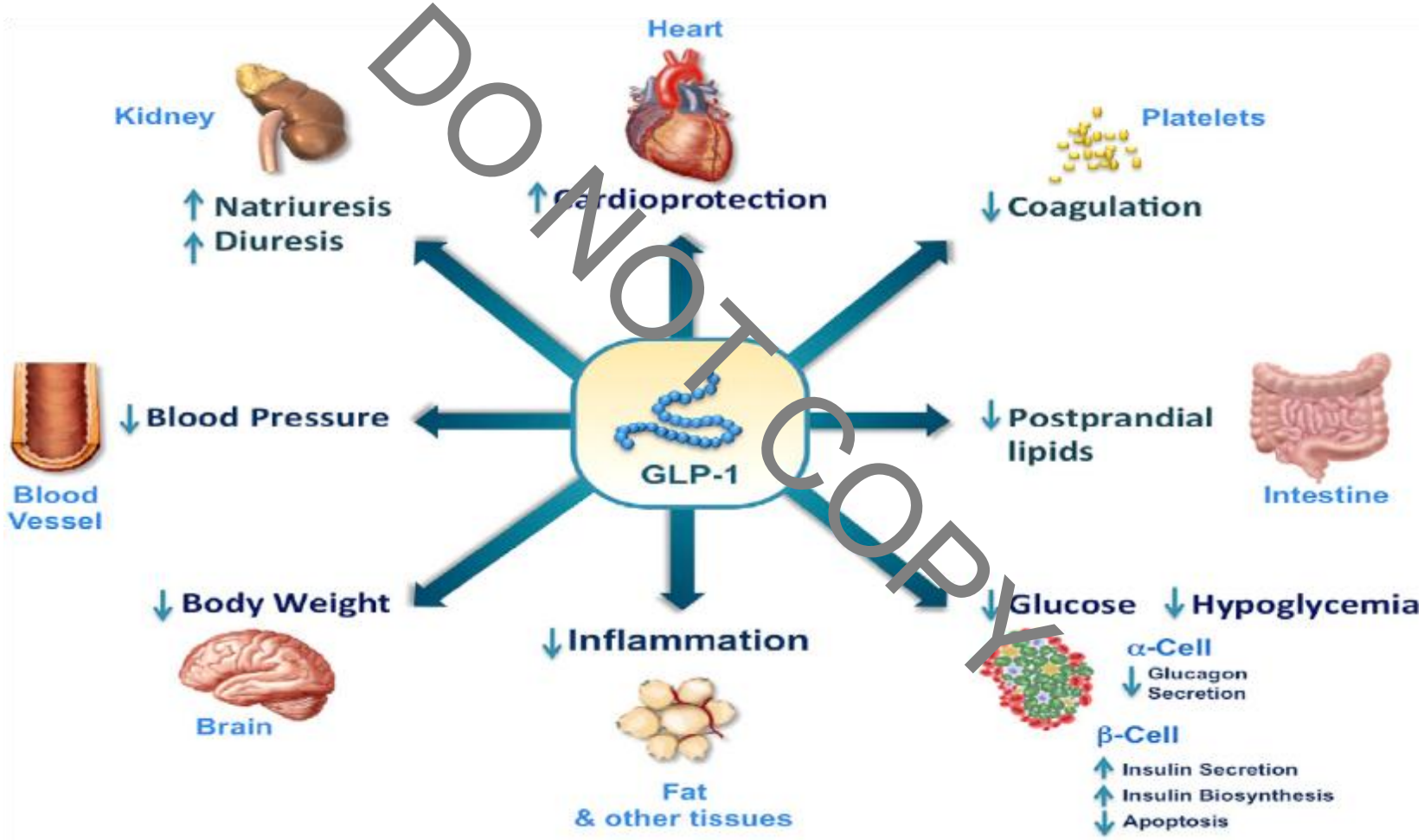
1. Pi-Sunyer X, et al. *N Engl J Med* 2015;373(1):11–22; 2. Davies MJ, et al. *JAMA* 2015;314(7):687–99;
3. Blackman A, et al. *Int J Obes (Lond)* 2016;40(8):1310–9; 4. Wadden TA, et al. *Int J Obes (Lond)* 2013;37(11):1443–51.

Diabetes prevention and liraglutide 3mg



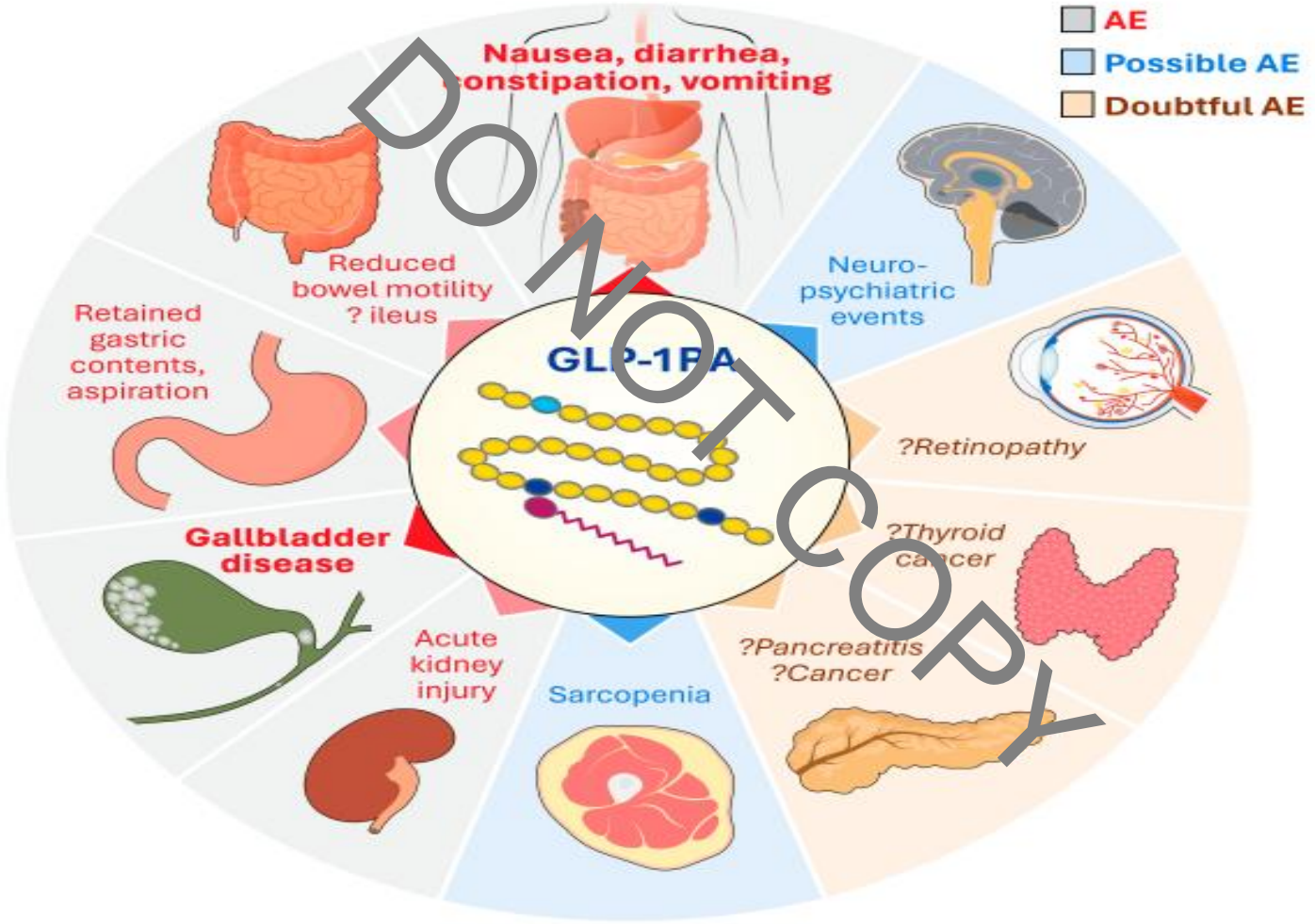
le Roux CW, Lancet, 2017

Pharmacotherapy - GLP-1 Actions in Multiple Organs



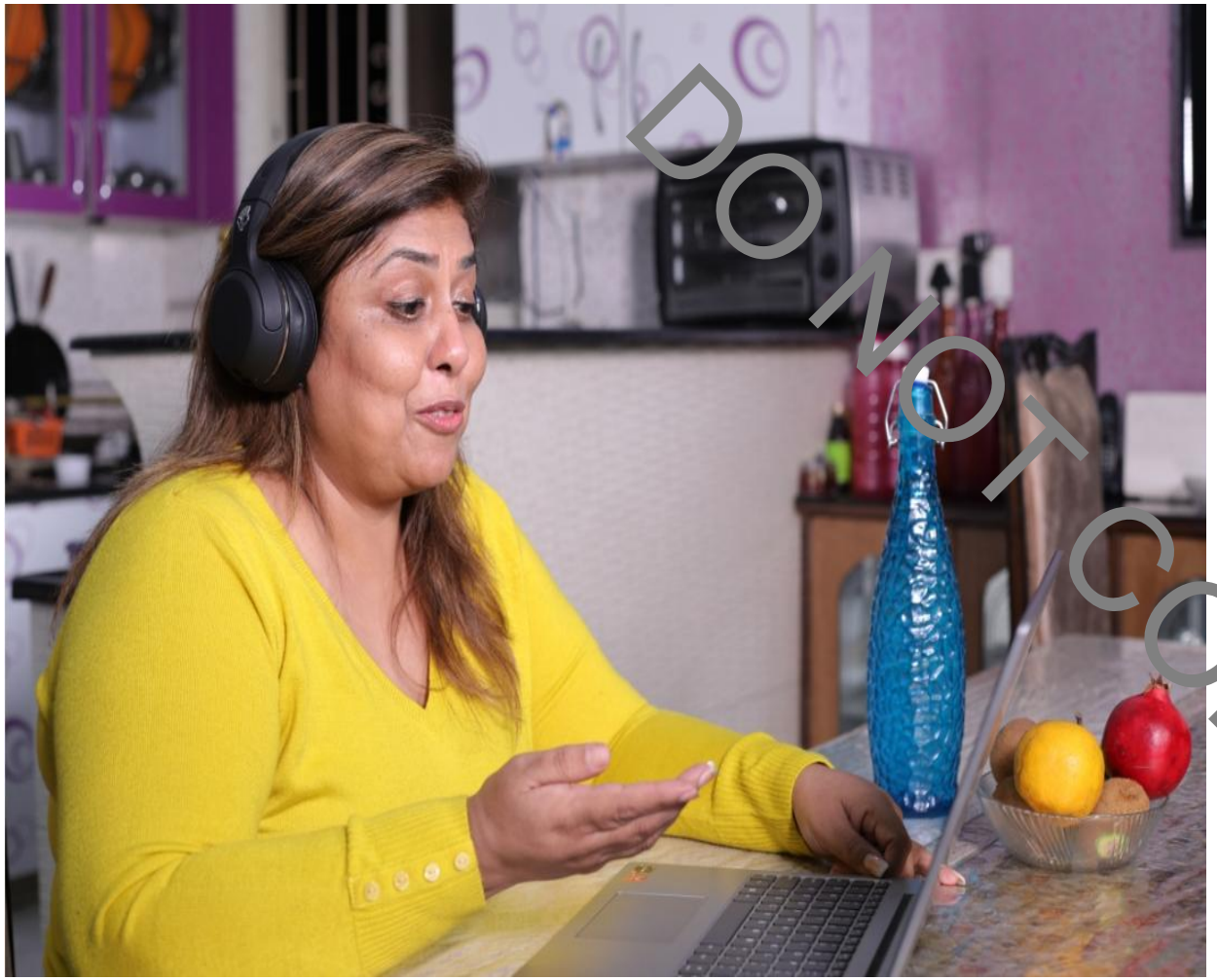
Drucker DJ. The Cardiovascular Biology of Glucagon-like Peptide-1. Cell Metab. 2016; 24(1): 15–30.

GLP-1 RAs and adverse events



Drucker DJ, 2024, Diabetes Care

Case 2 – Anna



Female, 56 years old – South Asian origin

BMI:38, weight:96 kg, Height: 161cm

Attends the clinic for knee pain

What you want to do?

HbA1c: 43 at latest blood test 2 months ago (prediabetes)

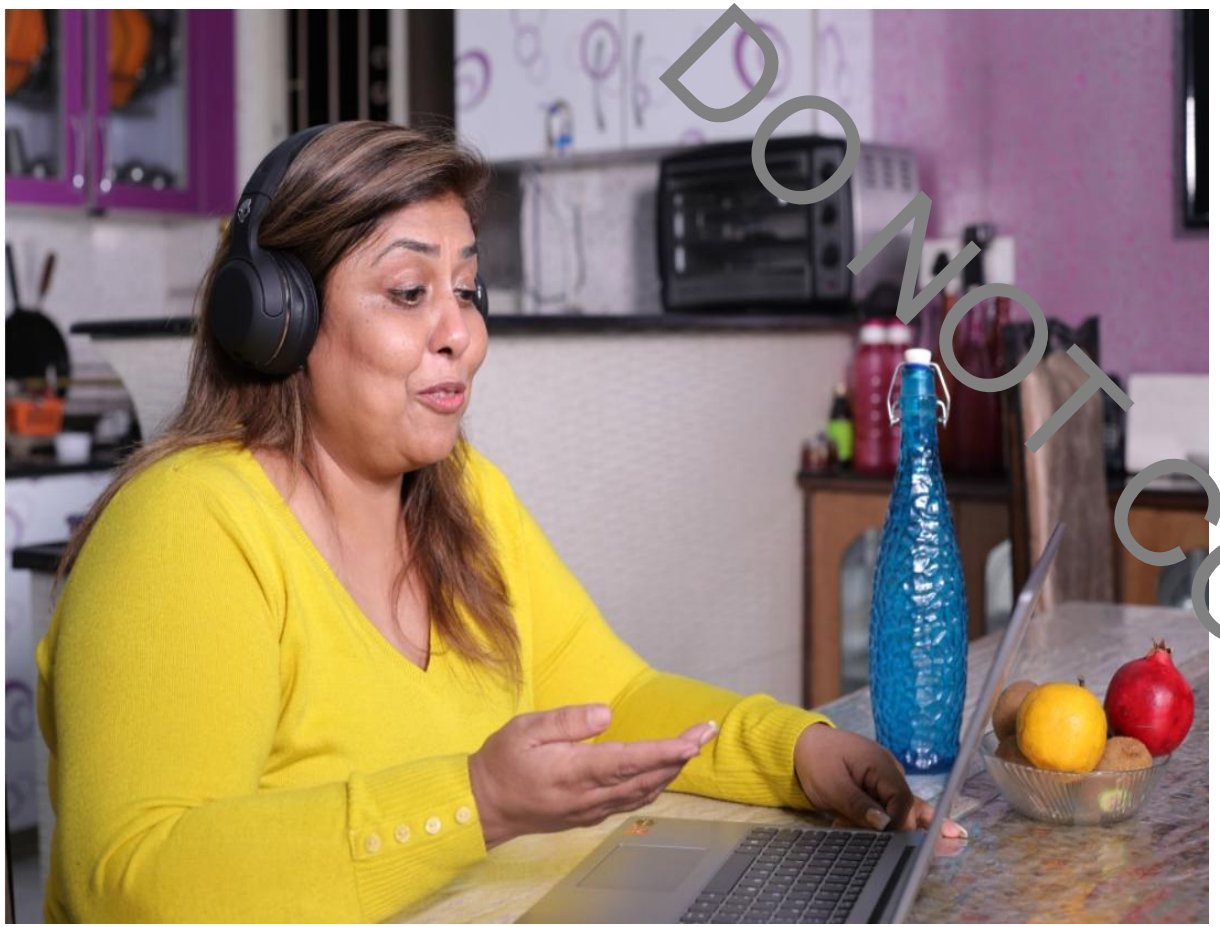
HTN, dyslipidaemia, previous MI 4 years ago

On atorvastatin 80mg, ramipril 5mg once daily, amlodipine 10mg once daily, bisoprolol 2.5mg OD and aspirin 75mg OD.

SBP:120/80, LDL: 1.2 mmol/l

Lives with her husband and 3 children

Assessment



A: Airway (OSA, asthma)
B: BMI
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: Body image (including binge eating disorder)
Junction gastroesophageal (acid reflux)
K: Kidneys (ACR, eGFR)
L: Liver (FIB-4 for MASH)
M: Medication burden
N: Nutrition (Vitamin deficiencies)
O: Other

Case 2 – Anna

Lately my husband complain that I snore and I feel tired all the time.

Epworth sleepiness score: 12
STOP-BANG: 5

Arrange sleep study – 35 AHI/hour (severe OSA)

Am I eligible for obesity treatment?

NICE guideline for tirzepatide

1 Recommendations

1.1 Tirzepatide is recommended as an option for managing overweight and obesi… alongside a reduced-calorie diet and increased physical activity in adult… they have:

- an initial body mass index (BMI) of at least 35 kg/m² a…
- at least 1 weight-related comorbidity and
- the company provides it according to t…

Use a lower BMI threshold (usua… South Asian, Chinese, other Asian, … Caribbean ethnic backgrounds.

1.2 If less than 5% of the initial weight has been … tolerated dose, decide whether to continue tre… benefits and risks of treatment for the person.

NHS England

Interim commissioning guidance

Implementation of the NICE Technology Appraisal TA1026 and the NICE funding variation for tirzepatide (Mounjaro®) for the management of obesity.

https://www.nice.org.uk/guidance/ta1026

Who is eligible for tirzepatide based on implementation plan?

Table 1. Cohort Access Groups for Implementation in primary care Settings.

Funding Variation Year*	Estimated Cohort Duration	Cohorts	Cohort Access Groups	
			Comorbidities	BMI**
Year 1 (2025/26)	12 months	Cohort I	≥4 'qualifying' comorbidities hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease, type 2 diabetes mellitus	≥ 40
Year 2 (2026/27)	9 months	Cohort II	≥4 'qualifying' comorbidities hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease, type 2 diabetes mellitus	≥35 – 39.9
Year 2/3 (2026 and 2027/28)	15 months	Cohort III	3 'qualifying' comorbidities hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease, type 2 diabetes mellitus	≥ 40

*Funding Variation year refers to the financial year.

** Use a lower BMI threshold (usually reduced by 2.5 kg/m^2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean ethnic backgrounds

https://www.england.nhs.uk/wp-content/uploads/2025/03/PRN01879-interim-commissioning-guidance-implementation-of-the-nice-technology-appraisal-ta1026-and-the-NICE-fu.pdf

Table 2. Qualifying Comorbidities and Definitions for initial assessment.

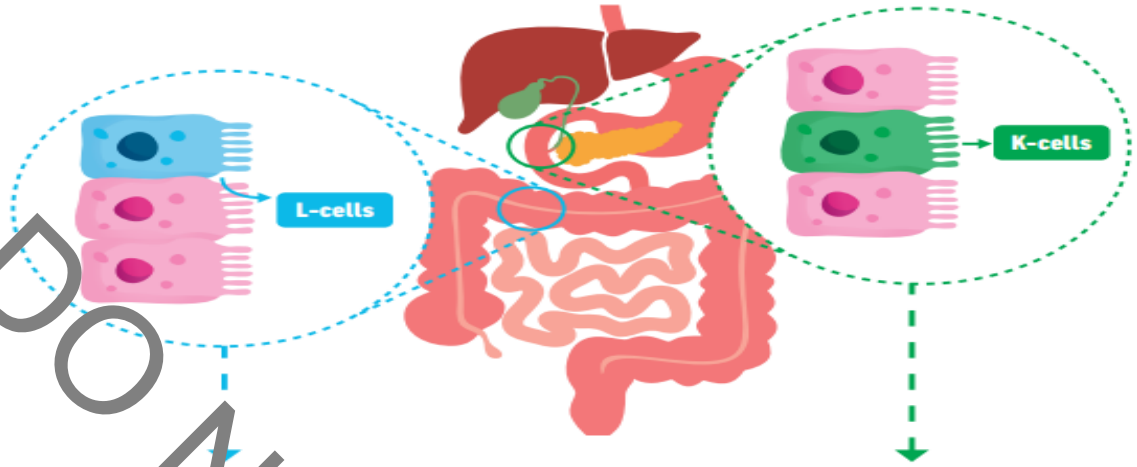
Qualifying Comorbidities	Definition for Initial Assessment
Atherosclerotic cardiovascular disease (ASCVD)	Established atherosclerotic CVD (ischaemic heart disease, cerebrovascular disease, peripheral vascular disease, heart failure)
Hypertension	Established diagnosis of hypertension and requiring blood pressure lowering therapy
Dyslipidaemia	Treated with lipid-lowering therapy, or with low-density lipoprotein (LDL) ≥ 4.1 mmol/L, or high-density lipoprotein (HDL) <1.0 mmol/L for men or HDL<1.3 mmol/L for women, or fasting (where possible) triglycerides ≥1.7 mmol/L
Obstructive Sleep Apnoea (OSA)	Established diagnosis of OSA (sleep clinic confirmation via sleep study) and treatment indicated i.e. meets criteria for continuous positive airway pressure (CPAP) or equivalent
Type 2 diabetes mellitus	Established type 2 diabetes mellitus *

*People with type 2 diabetes can be prescribed tirzepatide (Mounjaro®) for obesity or for glycaemic management in type 2 diabetes if they meet the criteria set out in the recommendations in either:

For the delivery of the NICE Funding Variation in England all patients must be provided wraparound support which incorporates nutritional and dietetic advice as a minimum and access to behavioural change components, as a mandatory requirement to access treatment.

NHS England intends to make centrally funded wraparound care services available to all ICB from 23rd June 2025, which will be accessible from primary care settings. This will be exclusively for use by the identified priority cohort, for each ICB. The access and associated service pathway will be confirmed with all ICBs in May 2025.

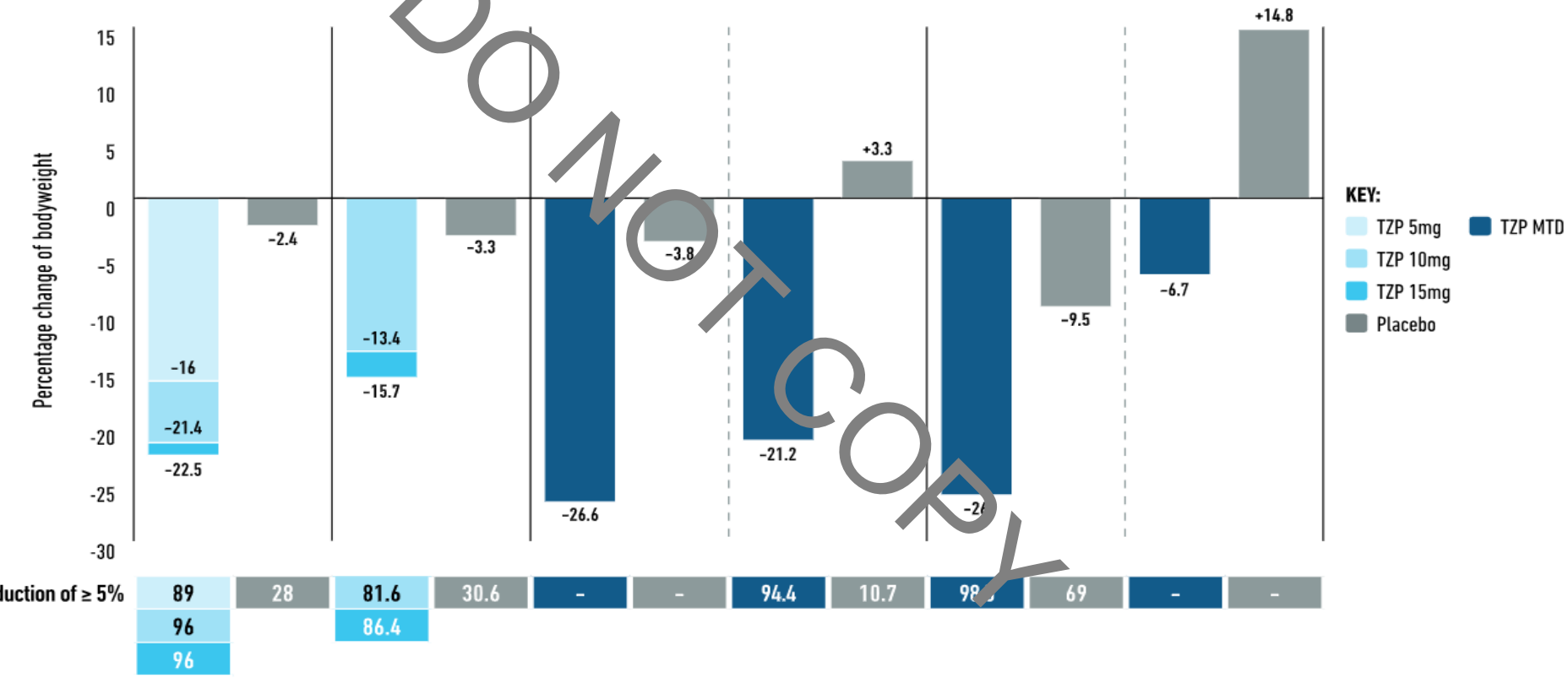
https://www.england.nhs.uk/wp-content/uploads/2025/03/PRN01879-interim-commissioning-guidance-implementation-of-the-nice-technology-appraisal-ta1026-and-the-NICE-fu.pdf



	GLP-1	GIP
Brain	↓ appetite ↓ food intake ↑ nausea	↓ appetite* ↓ food intake* ↓ nausea*
Pancreas	↑ insulin secretion ↓ glucagon	↑ insulin secretion ↑ glucagon
Stomach	↓ gastric emptying	↓ gastric acid secretion
Adipose tissue	↑ lipolysis	↑ lipogenesis ↑ lipid buffering capacity
Bone		↓ bone resorption
Heart	↑ cardioprotection	
Kidney	↑ natriuresis ↑ diuresis	

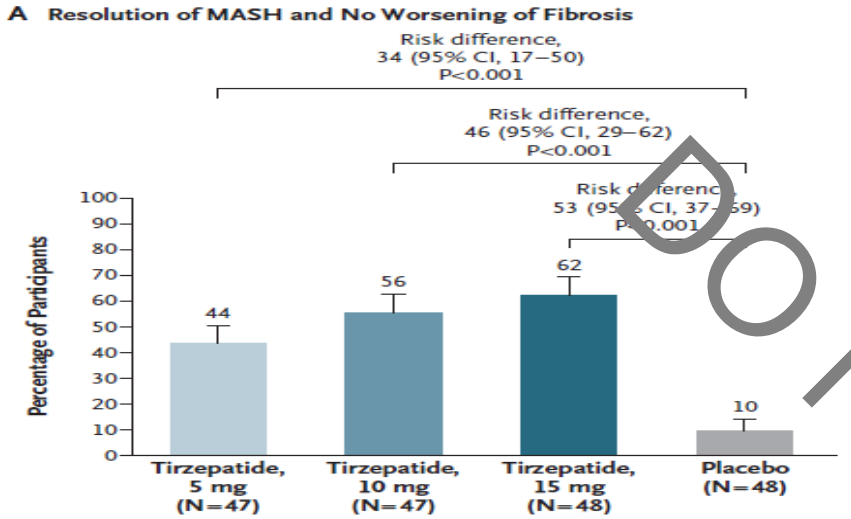
Sinha R, Papamargaritis D et al, 2023, JOMES

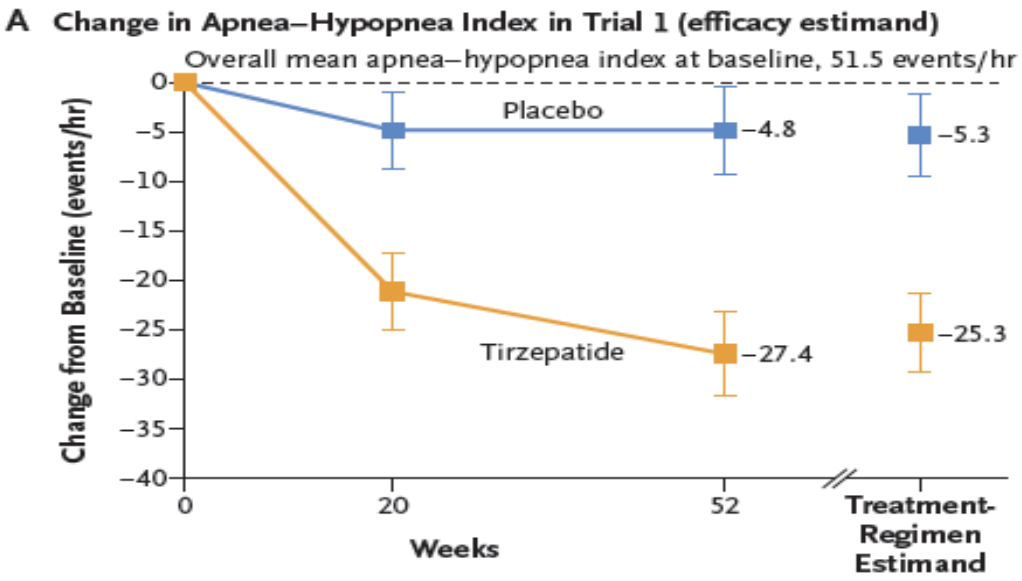
	SURMOUNT-1	SURMOUNT-2	SURMOUNT-3		SURMOUNT-4	
Participants randomised	n=2539	n=938	n=579		n=670	
Trial details	Adults with overweight or obesity without T2D	Adults with overweight or obesity and T2D	Adults with overweight or obesity without T2D who achieved ≥5% WL during the 12 week lead-in period with intensive lifestyle		Adults with overweight or obesity without T2D who reached maximum tolerated TZP dose during the 36-week lead-in period	
Treatment Duration	0-72 weeks	0-72 weeks	0-84 weeks	12-84 weeks (from randomisation)	0-88 weeks	36-88 weeks (from randomisation)
Baseline BW	104.8 kg	100.7 kg	109.5 kg	102.5 kg	107.3 kg	84.6 kg – 85.8 kg

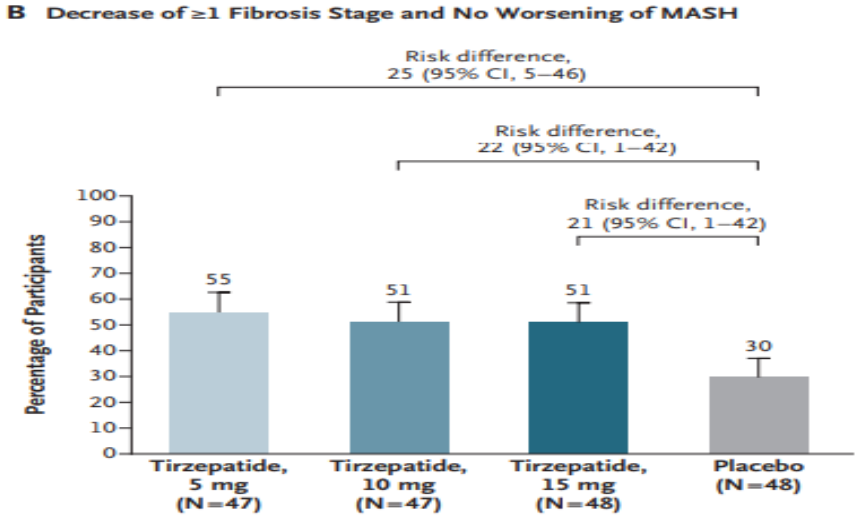


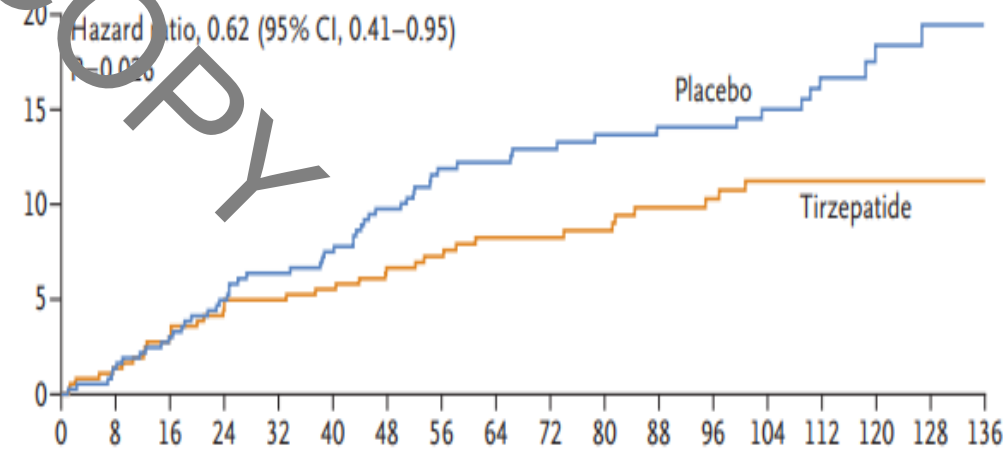
Hamza M, Papamargaritis D, Davies MJ, 2025, Expert Opinion on Pharmacotherapy/ Jastreboff AM, 2025, NEJM

Tirzepatide and obesity-related complications









Loomba R, 2024, NEJM/ Malhotra A, 2024, NEJM/ Packer M, 2025, NEJM

SURPASS-CVOT – Press release

Table II. Baseline clinical characteristics in SURPASS-CVOT.

	SURPASS-CVOT (*N* = 13,299)
Age, years	64.1 ± 8.8
Sex, female	3849 (28.9)
Geography	
North America	1955 (14.7)
South America	3833 (28.8)
Europe	6149 (46.2)
Asia-Pacific	1,362 (10.2)
Weight, kg	92.5 ± 18.8
BMI, kg/m²	32.6 ± 5.5
History	
Coronary artery disease	8,649 (65.0)
Myocardial infarction	6,288 (47.3)
Coronary revascularization procedure	7,630 (57.4)
Stroke	2,541 (19.1)
Peripheral artery disease	3,369 (25.3)
Hypertension	11,986 (90.1)
Dyslipidemia	11,406 (85.8)
Current tobacco use	1,978 (14.9)
Diabetes duration, years	14.7 ± 8.8
Systolic blood pressure, mm Hg	135.0 ± 15.7
Diastolic blood pressure, mm Hg	77.7 ± 9.7
HbA1c, %	8.4 ± 0.9
eGFR (CKD-EPI), mL/Min/1.73 m²	76.5 ± 21.3
<60 mL/Min/1.73 m²	3,029 (22.8)
UACR, mg/g	22.0 (9.0, 83.0)
Microalbuminuria	4,179 (32.0)
Macroalbuminuria	1,503 (11.5)

Data are mean ± SD, n (%), or median (interquartile range).
Percentage is based on number of participants with nonmissing measurement at baseline.
BMI, body mass index; *CKD-EPI*, chronic kidney disease-epidemiology; *eGFR*, estimated glomerular filtration rate; *HbA1c*, glycated hemoglobin A1c; *SD*, standard deviation; *UACR*, urine albumin-creatinine ratio.

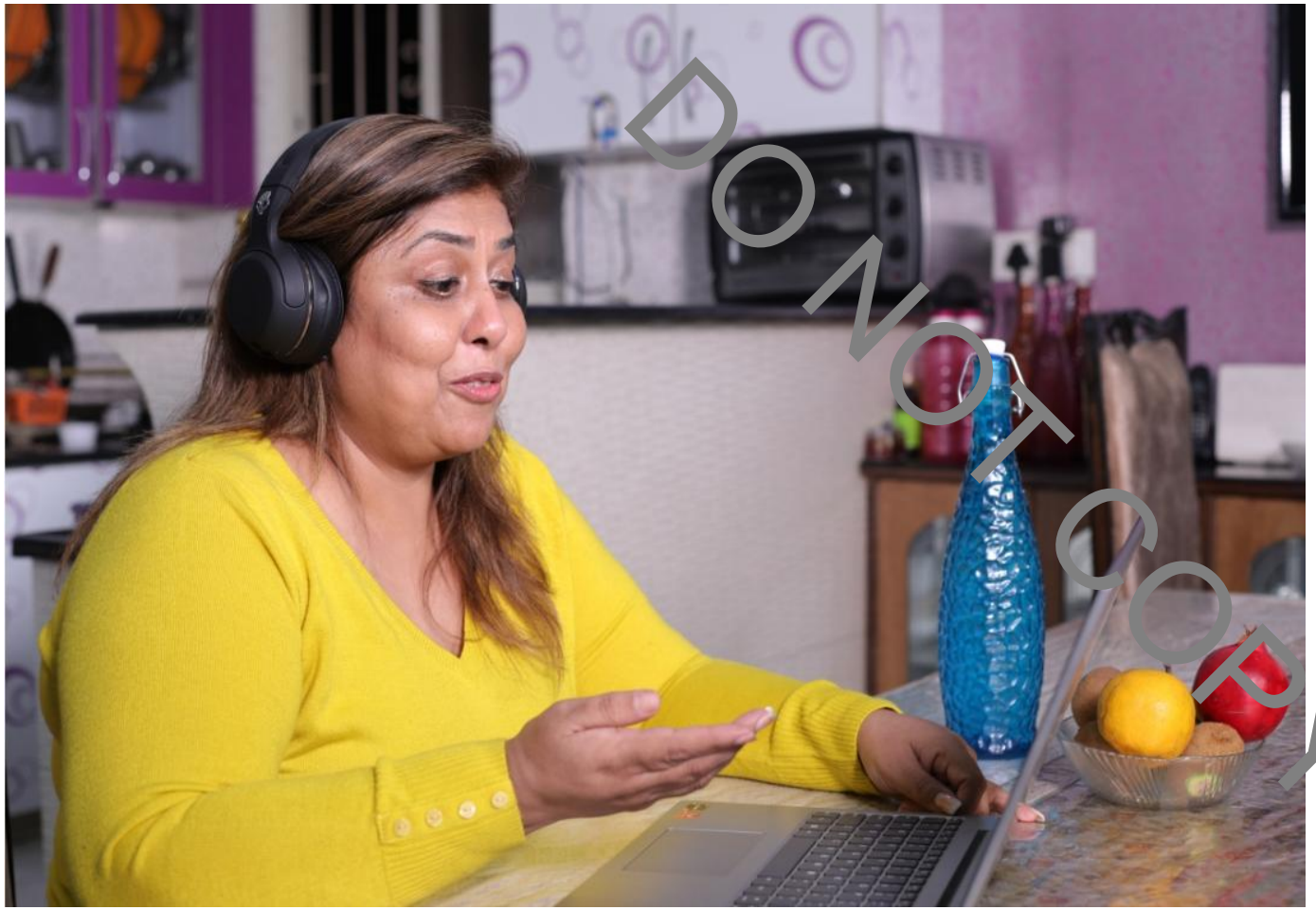
Primary and Select Secondary Endpoints:

	Mounjaro (tirzepatide)	Trulicity (dulaglutide)
Primary Endpoint		
Time-to-first occurrence of MACE-3[i]	Hazard ratio = 0.92 95.3%[ii] CI: 0.83 to 1.01[iii] p = 0.086	
Secondary Endpoints		
Time to all-cause death[i]	Hazard ratio = 0.84 95.0% CI: 0.75 to 0.94 p = 0.002[iv]	
Change in eGFR in chronic kidney disease population from mean baseline of 53.4 mL/min/1.73 m² at 36 months[v]	-4.97 mL/min/1.73 m²	-8.51 mL/min/1.73 m²
	Estimated treatment difference: 3.54 mL/min/1.73 m² (95.0% CI: 2.57 to 4.50) p < 0.001[iv]	
A1C reduction from mean baseline of 8.39% at 36 months[v,vi]	1.73 %	0.90 %
	Estimated treatment difference: -0.83% (95.0% CI: -0.88 to -0.78) p < 0.001[iv]	
Change from mean baseline of 92.6 kg (204.15 lbs) in body weight at 36 months[v,vi]	-12.06% (-11.43 kg / -25.20 lbs)	-4.95% (-4.65 kg / -10.25 lbs)
	Estimated treatment difference: -7.1% (95.0% CI: -7.4 to -6.8) p < 0.001[iv]	

A pre-specified indirect comparison analysis of matched patient-level data from the REWIND and SURPASS-CVOT studies found that Mounjaro reduced the risk of MACE-3 by 28% (hazard ratio: 0.72; 95.0% CI: 0.55 to 0.94) and all-cause mortality by 39% (hazard ratio: 0.61; 95.0% CI: 0.45 to 0.82) compared to a putative placebo.[3,4] In another key pre-specified analysis of participants with high or very-high risk of chronic kidney disease, Mounjaro slowed eGFR decline by 3.54 mL/min/1.73 m² at 36 months vs. Trulicity (95.0% CI: 2.57 to 4.50).[3,5,6]

Nichols SJ, 2024, Am Heart J/ https://investor.lilly.com/news-releases/news-release-details/lillys-mounjaro-tirzepatide-gipglp-1-dual-agonist-demonstrated

Case 2 – Anna



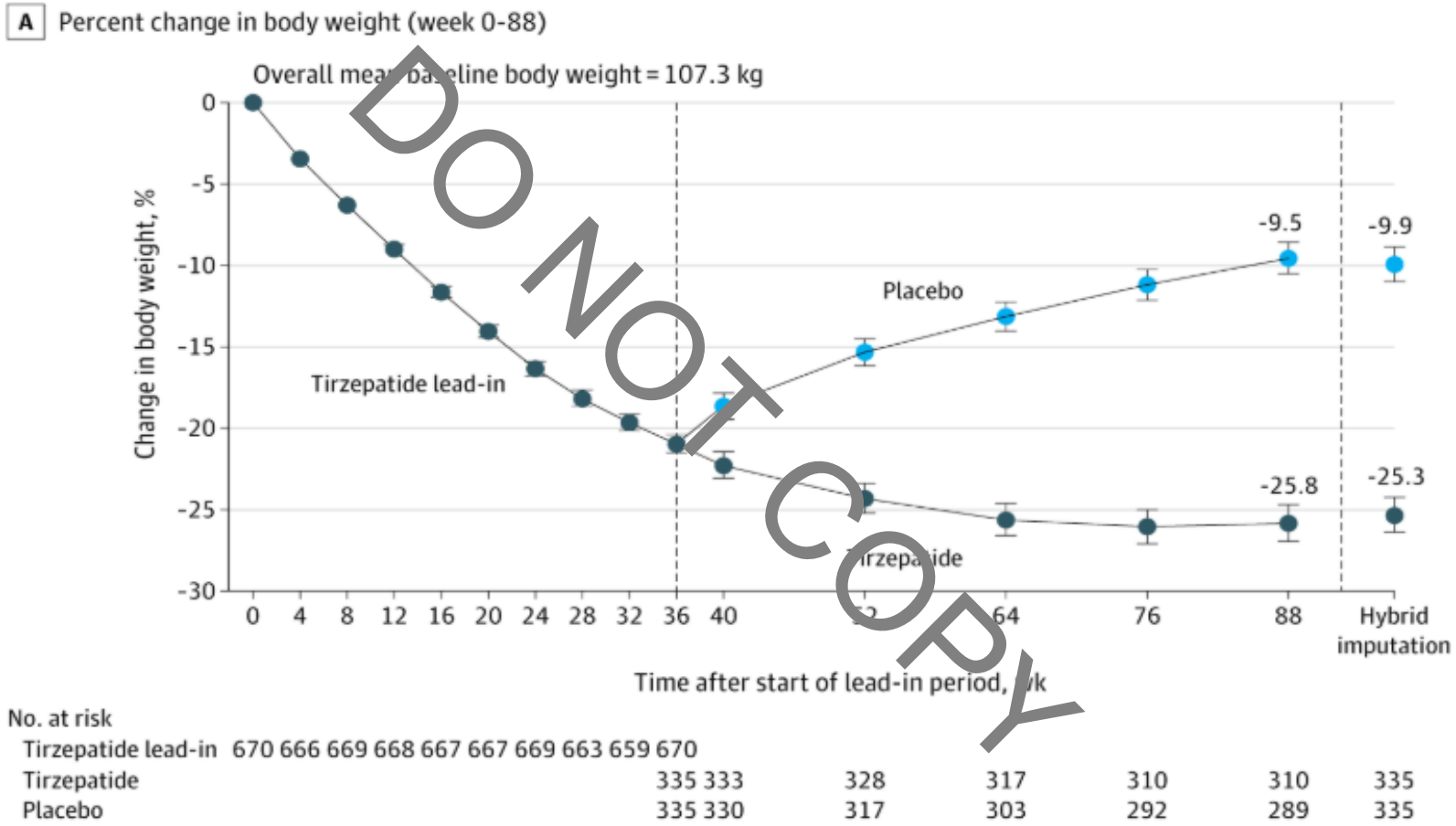
What do you need to tell her on prescription of the medication regarding AEs?

Now, if she was at her 20's or 30's what you would advise regarding contraception? Is tirzepatide safe for pregnancy?

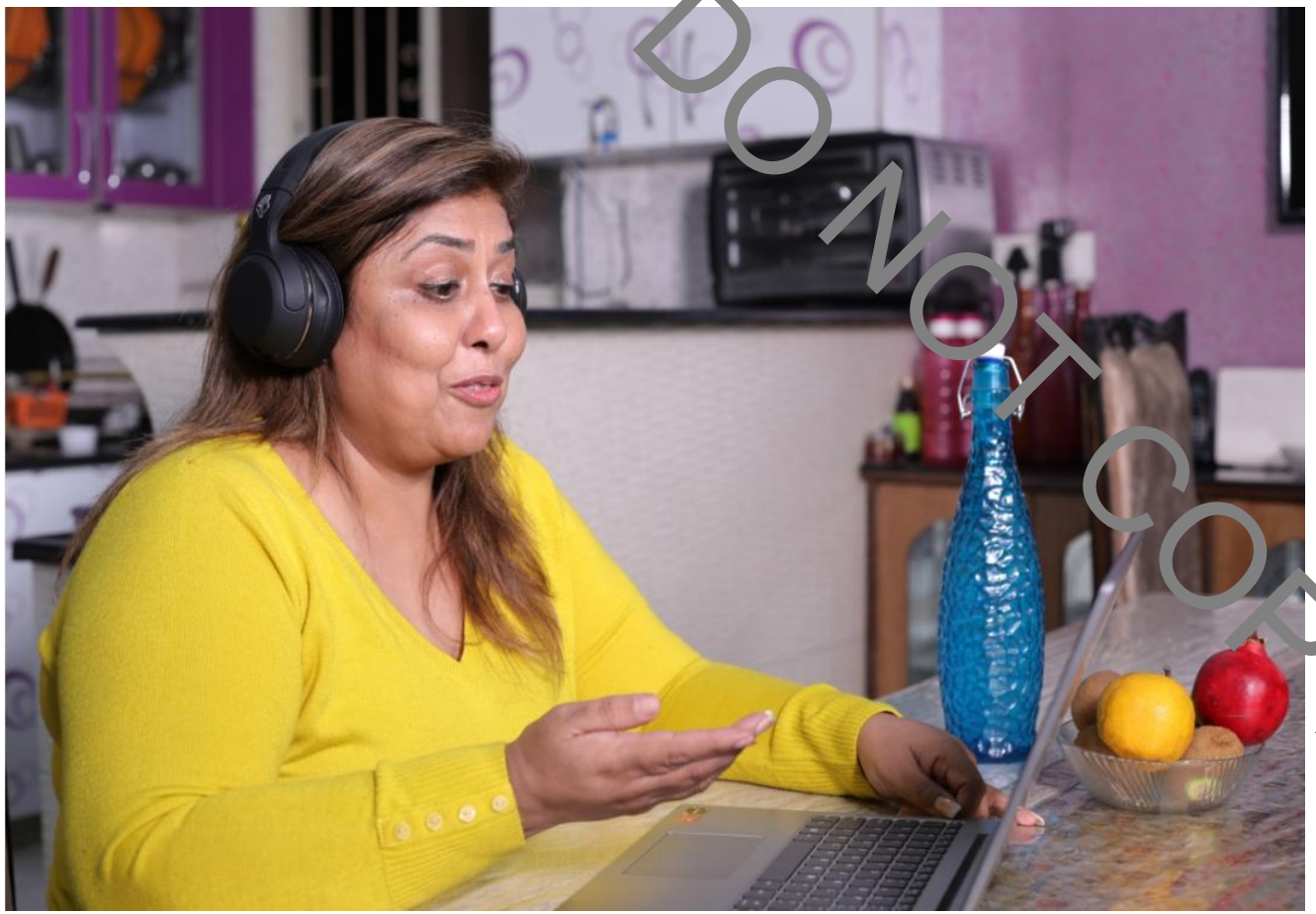
For how long I need to receive this treatment?

And for how long this treatment has been approved under NHS prescription?
I can not fund the medication long-term!

OBESITY IS A CHRONIC DISEASE



What if her BMI was 36? What could you do for her?



HTN
Dyslipidaemia
Previous myocardial infarction
Severe OSA (>30 AHI) – CPAP
Prediabetes

Am I eligible for medication for weight loss?

Referring adults to specialist services

1.11.12 Offer a higher level of intervention to people with weight-related comorbidities (see the section on assessing and managing comorbidities in adults). Adjust the approach depending on the person's clinical needs, for example for people with a BMI over 35 kg/m^2 who have recently developed diabetes or for people with a BMI of 50. **[2022]**

1.11.13 Consider referral to specialist overweight and obesity management services if:

- the underlying causes of overweight or obesity need to be assessed
- the person has complex disease states or needs that cannot be managed adequately in behavioural overweight and obesity management services (for example, the extra support needs of people with learning disabilities)
- less intensive management has been unsuccessful
- specialist interventions (such as a very-low-calorie diet) may be needed
- surgery or certain medicines is being considered.

For more information see specialist overweight and obesity services. **[2006, amended 2025]**

Tiered approach in obesity services (UK)

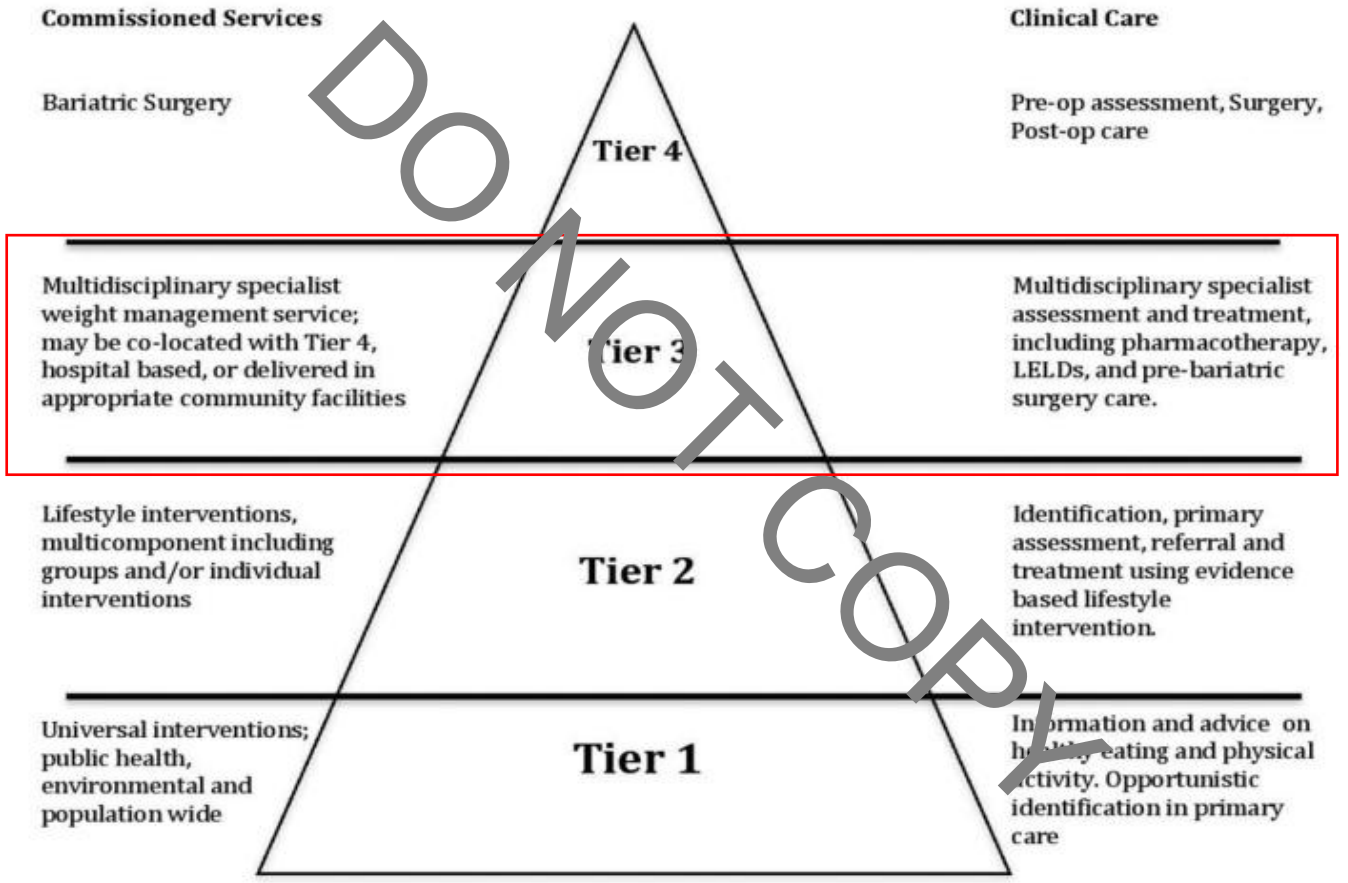


Figure 1 Tiered model of services.

Jennings A, Clinical Obesity, 2014

Semaglutide 2.4mg once weekly

1 Recommendations

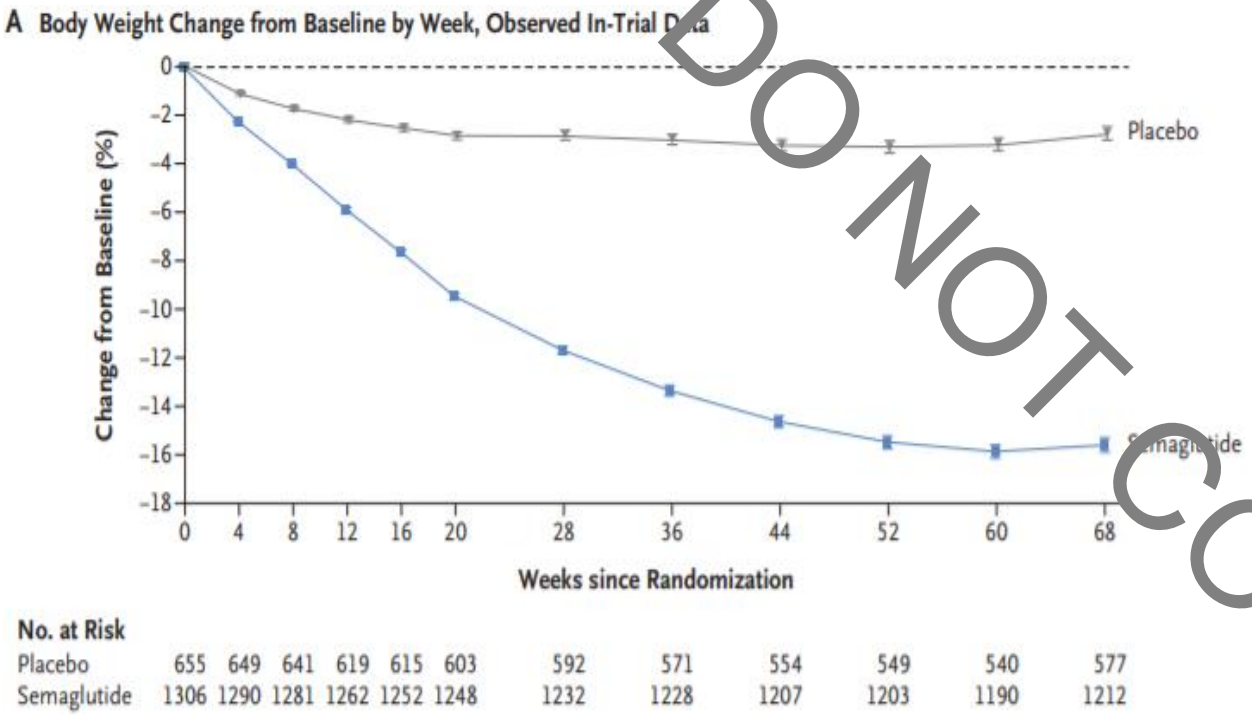
1.1 Semaglutide is recommended as an option for weight management, including weight loss and weight maintenance, alongside a reduced-calorie diet and increased physical activity in adults, only if:

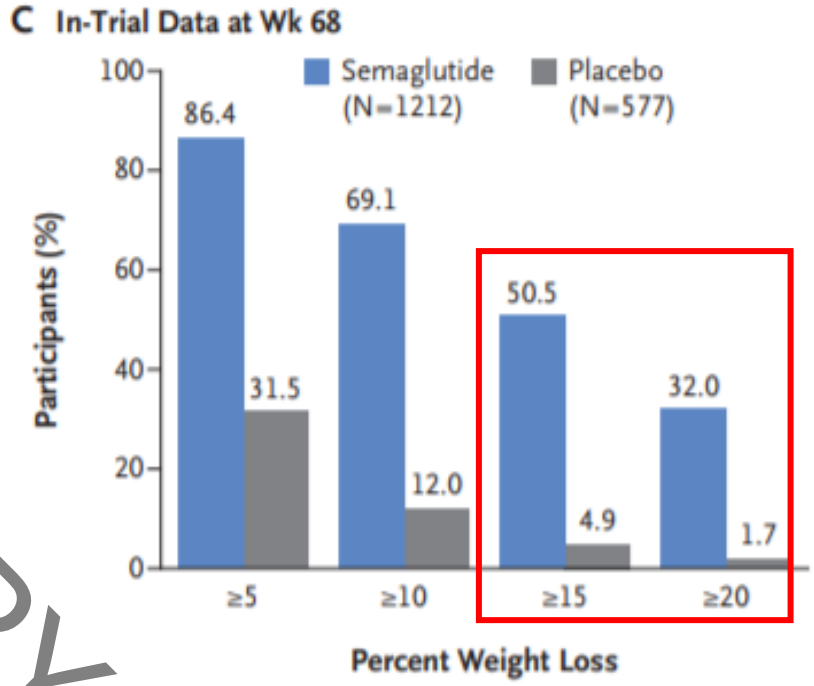
- it is used for a maximum of 2 years, and within a specialist weight management service providing multidisciplinary management of overweight or obesity (including but not limited to tiers 3 and 4), and
- they have at least 1 weight-related comorbidity and:
  - a body mass index (BMI) of at least 35.0 kg/m^2, or
  - a BMI of 30.0 kg/m^2 to 34.9 kg/m^2 and meet the criteria for referral to specialist overweight and obesity management services in NICE's guideline on overweight and obesity management.
- the company provides semaglutide according to the commercial arrangement.

Use lower BMI thresholds (usually reduced by 2.5 kg/m^2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family backgrounds.

1.2 Consider stopping semaglutide if less than 5% of the initial weight has been lost after 6 months of treatment.

Semaglutide 2.4mg once weekly

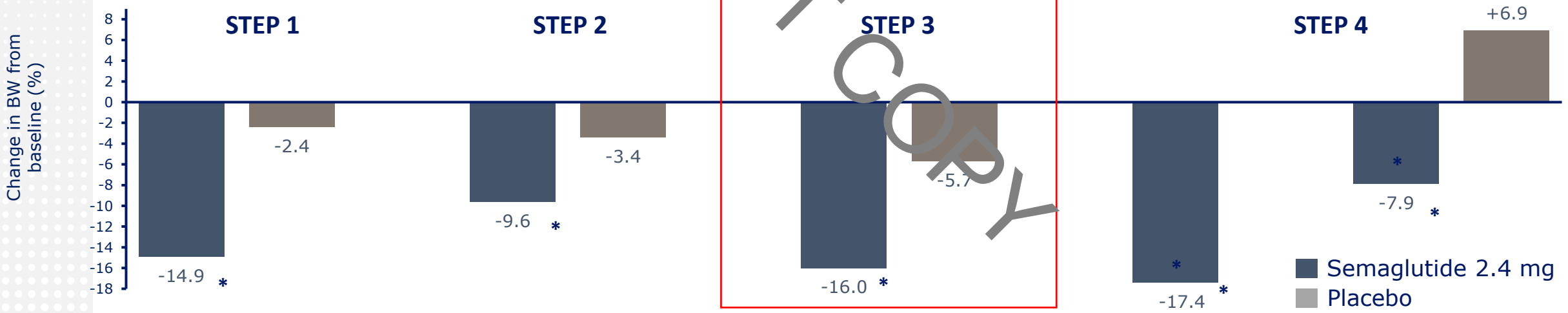




Wilding JPH, 2021, NEJM

Primary endpoint summary for STEP1–4

	Weight management	Weight management in T2D	Weight management with IBT	Sustained weight management	
Trial details	Adults with obesity or overweight without T2D (n=1961)	Adults with obesity or overweight with T2D (n=1210)	Adults with obesity or overweight, without diabetes adjunct to IBT (n=611)	Adults with obesity or overweight without diabetes reaching target dose during run-in (n=902)	Adults with obesity or overweight without diabetes after run-in (n=803)
Duration & Baseline BW	0–68 wks 105.3 kg	0–68 wks 99.8 kg	0–68 wks 105.8 kg	0–68 wks 107.2 kg	20–68 wks 96.1 kg

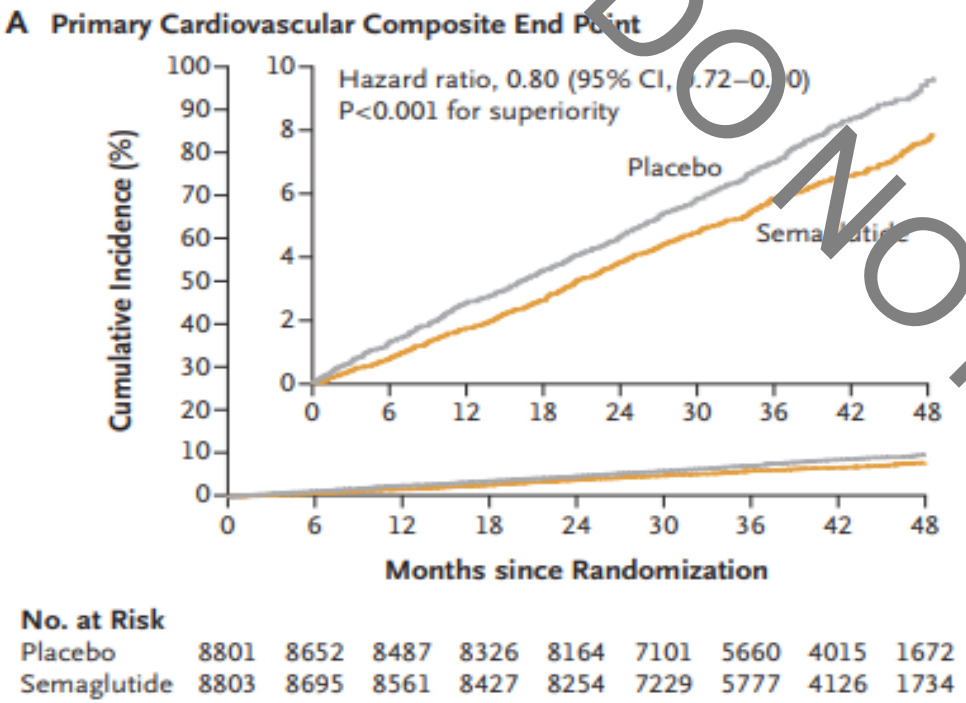


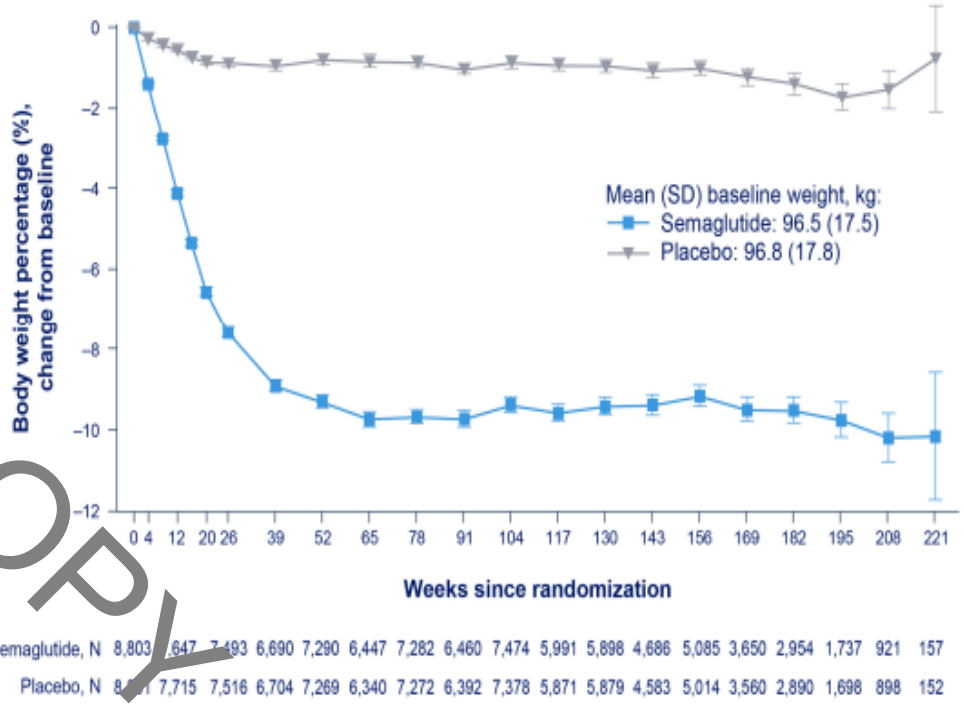
Treatment policy estimand: Evaluates the treatment effect regardless of trial product discontinuation and use of rescue medication

*Lifestyle intervention: –500 kcal/day diet + 150 min/week physical activity. *Participants on sulfonylurea: semaglutide 1.0 mg: 24.6%; semaglutide 2.4 mg: 26.7%; placebo: 24.1% ; IBT, intensive behavioral therapy; LCD, low-calorie diet; OW, once-weekly; STEP, Semaglutide Treatment Effect in People with obesity; T2D, type 2 diabetes.

1. Wilding *et al. N Engl J Med* 2021;384:989; 2. Wadden *et al. JAMA* 2021; doi:10.1001/jama.2021.1831; 3. Rubino *et al. JAMA* 2021; doi:10.1001/jama.2021.3224;
4. Davies *et al. Lancet* 2021;397:971−84.

Cardiovascular outcomes of semaglutide 2.4mg once weekly vs placebo in people with obesity and established CVD (without T2D) – SELECT





Lincoff MA, 2023, NEJM

OBESITY MANAGEMENT Collaborative UK

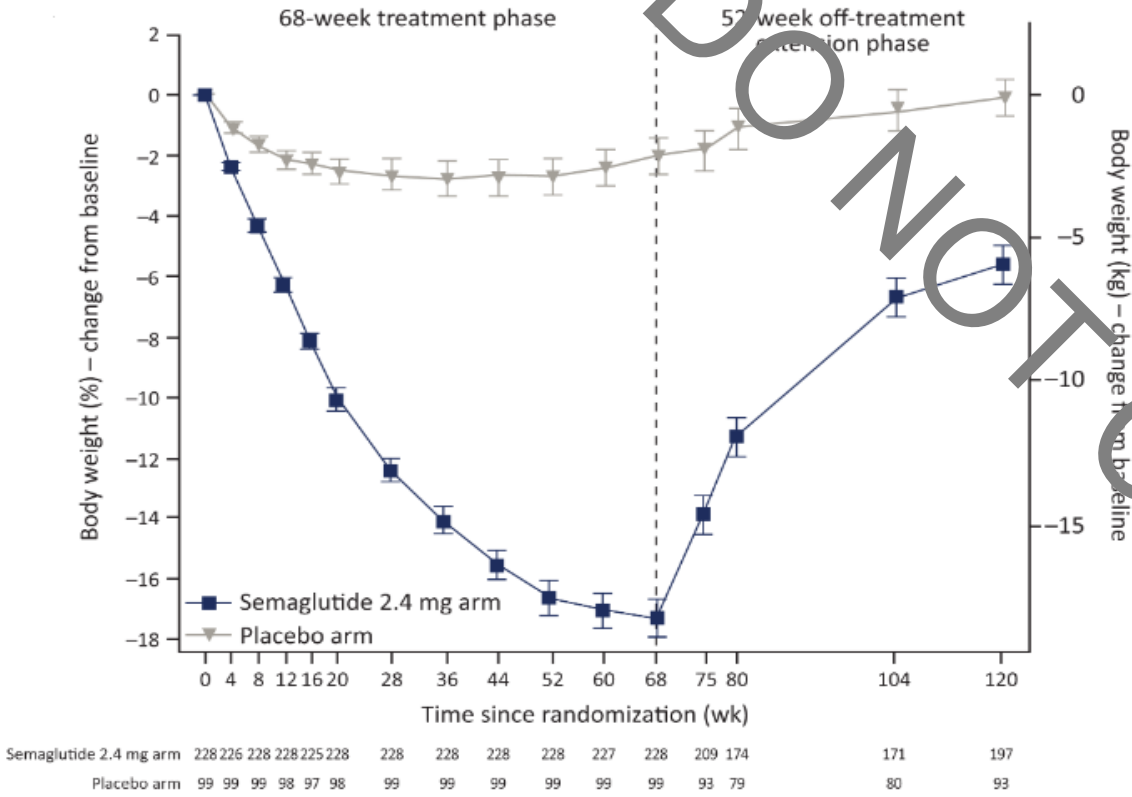
Society for Endocrinology
a world-leading authority on hormones

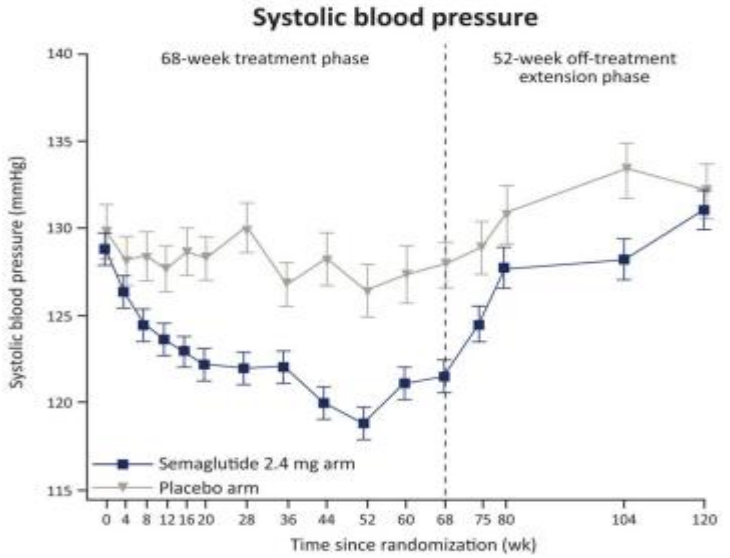
Guidance for the phased introduction of new medical therapies for weight management: A joint position statement by the Society for Endocrinology and Obesity Management Collaborative UK*

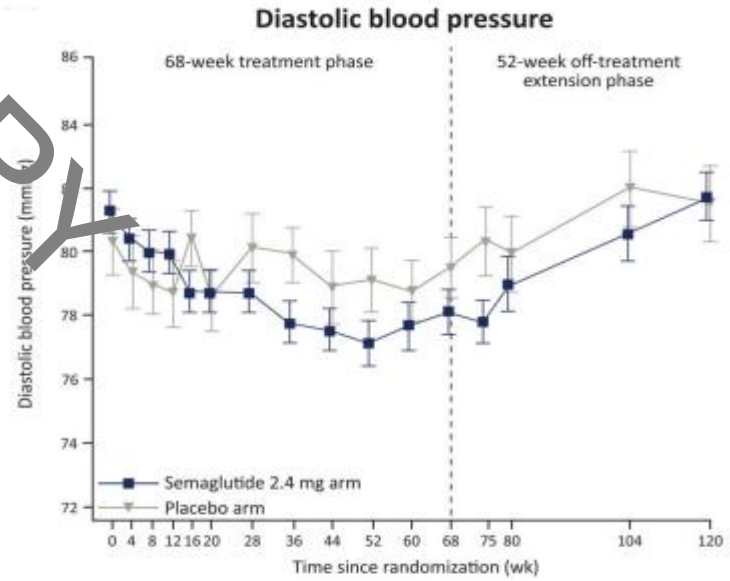
Patient cohort	Eligibility
Phase 1	Precancerous or cancerous conditions in which weight loss would improve outcomes or aid access to therapies Patients requiring urgent weight loss for organ transplant Idiopathic intracranial hypertension (IIH) requiring frequent lumbar punctures and/or with visual compromise Patients undergoing planned time-sensitive surgery (including bariatric surgery) for life-limiting conditions, where high BMI is the primary barrier to surgery and weight loss would be beneficial Weight loss required for assisted conception in women under the care of a fertility service, in cases where weight loss would be beneficial** Severe obstructive sleep apnoea (OSA), obesity hypoventilation syndrome (OHS) and/or severe asthma Proven genetic cause of obesity and not eligible for Setmelanotide (Imcivree®)
Phase 2	Living with obesity and 3 or more weight related co-morbidities, including: • Chronic kidney disease (stages 3 or 4) • Pre-existing cardiovascular disease[3] • Hypertension • IIH • Metabolic dysfunction-associated steatohepatitis (MASH) • Moderate OSA • PCOS • Pre-diabetes or T2DM • Restricted mobility affecting quality of life

https://www.endocrinology.org/media/sjdpporx/joint-position-statement-on-medical-therapies-for-obesity_final-resubmitted-sfe-211223.pdf

Long-term clinical effectiveness - STEP-1 trial extension

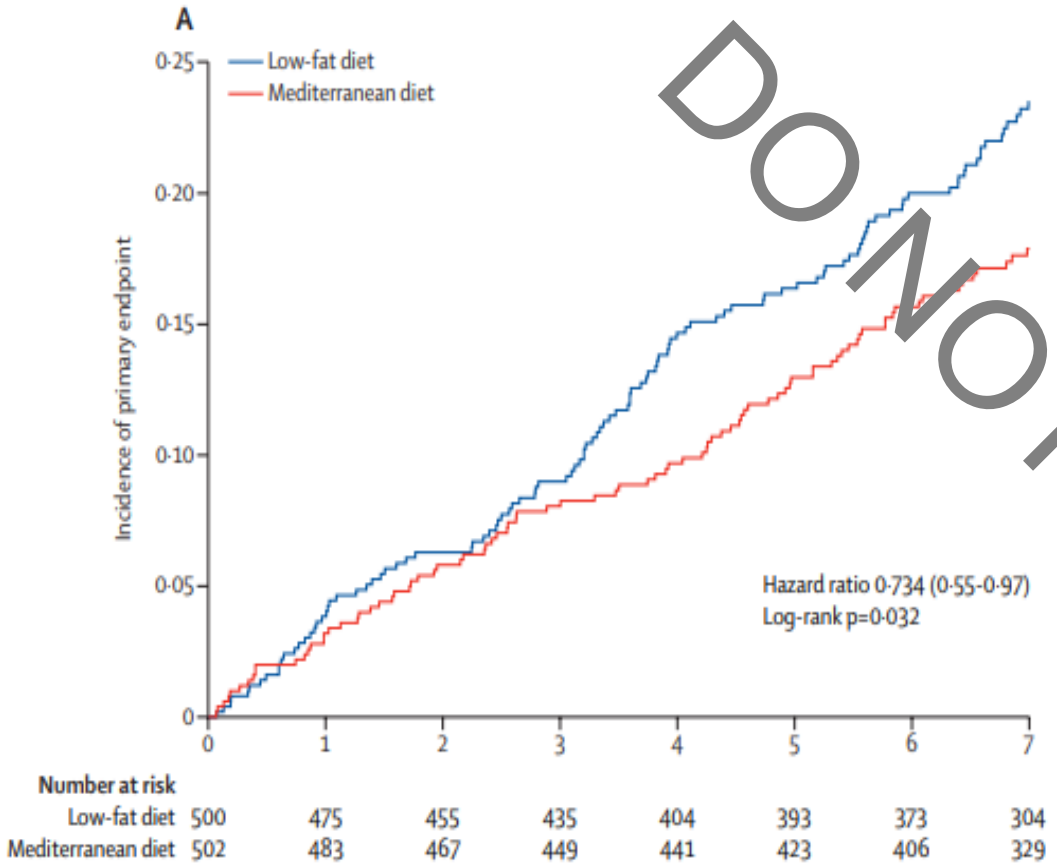


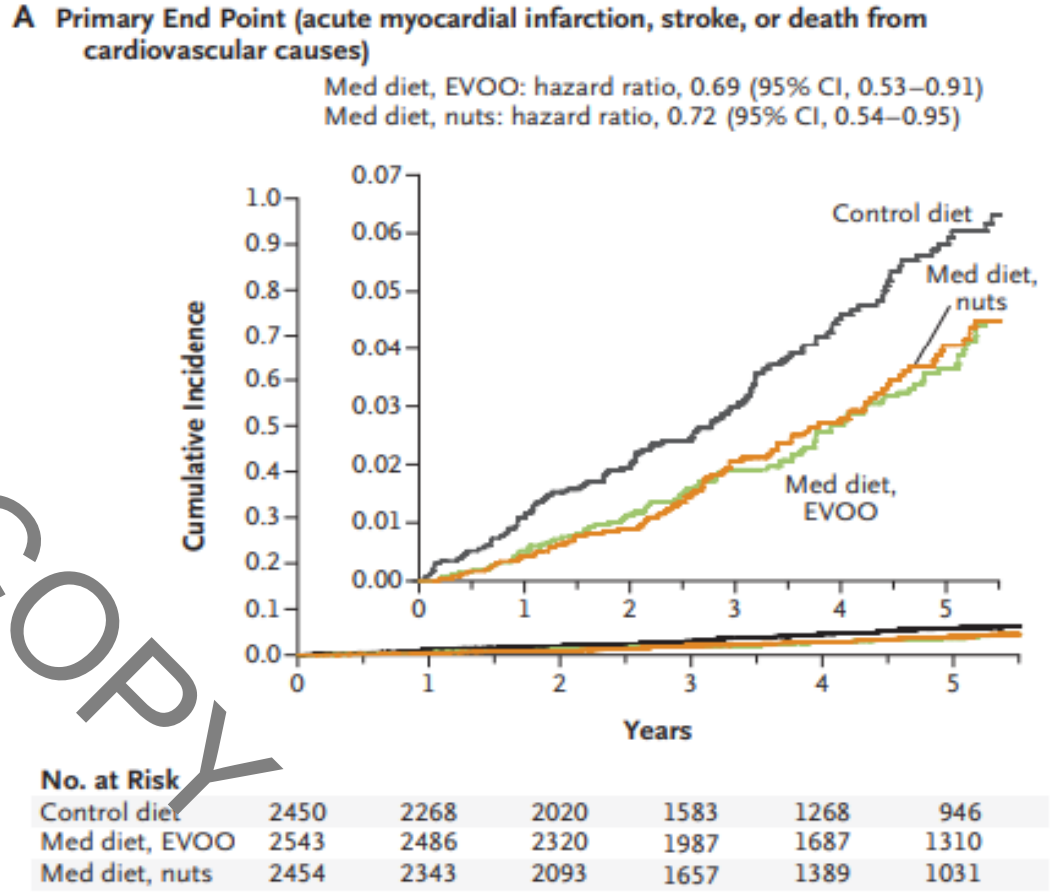




Wilding JPH, DOM, 2022

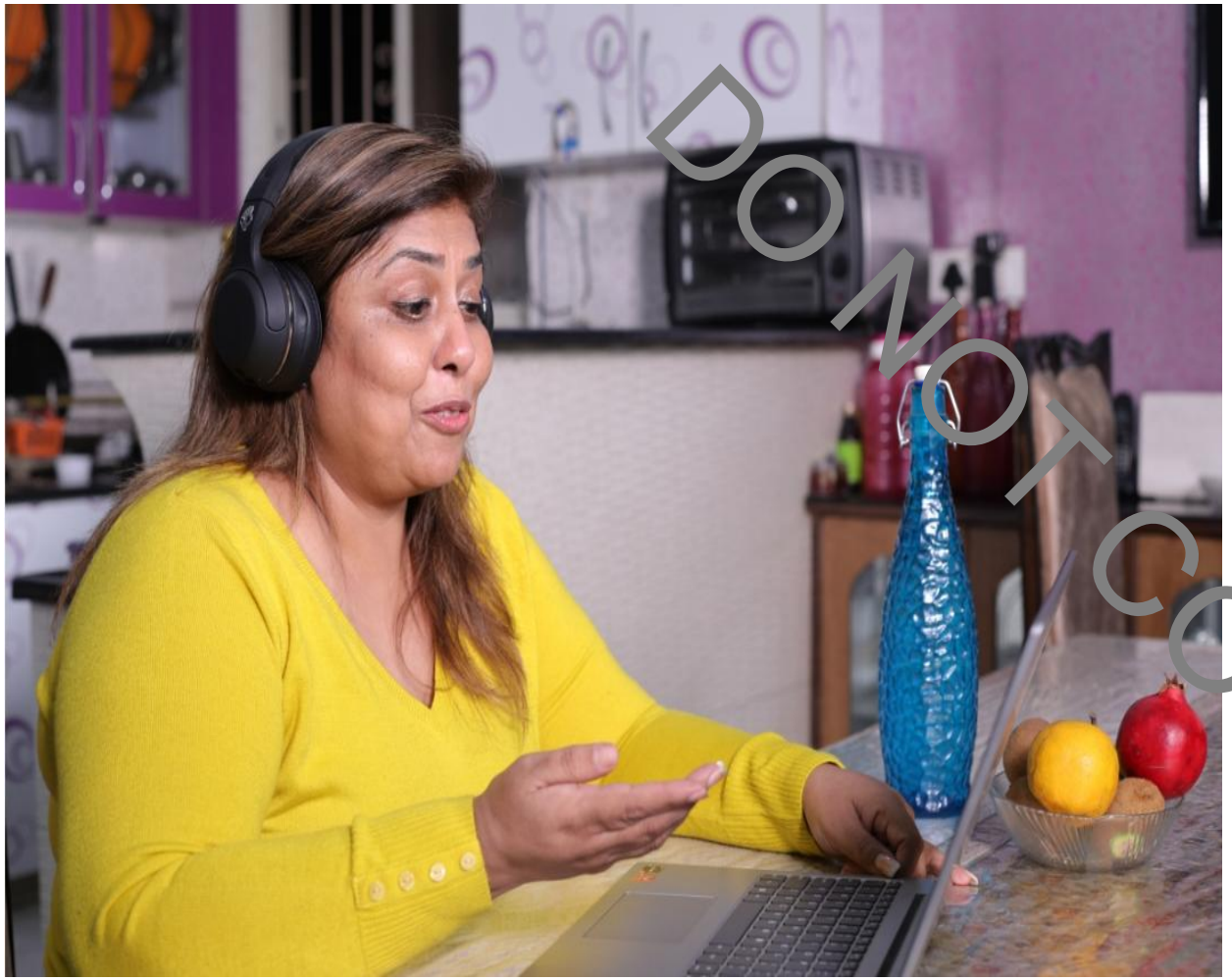
Importance of healthy eating – Mediterranean diet





Delgado-Lista J, Lancet 2022/ Estruch R, NEJM, 2018

What if we do not have locally a SWMS that can prescribe obesity treatment?



Option 1. Wait for next year and prioritise her for prescription of tirzepatide (BMI ≥35 plus 4 obesity-related complications)

Option 2. Explore also the option of bariatric surgery!

Is she eligible?

Is it something that she would consider?

Take into account her wishes – if she will consider it, refer her to the SWMS.

NICE for bariatric surgery

1.10 Surgical interventions

When to refer adults for assessment for bariatric surgery

1.10.1 Offer adults a referral for a comprehensive assessment by specialist weight management services providing multidisciplinary management of obesity to see whether bariatric surgery is suitable for them if they:

- have a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 39.9 kg/m^2 with a significant health condition that could be improved if they lost weight (see box 2 for examples) **and**
- agree to the necessary long-term follow up after surgery (for example, lifelong annual reviews). **[2023]**

1.10.2 Consider referral for people of South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family background using a lower BMI threshold (reduced by 2.5 kg/m^2) than in recommendation 1.10.1 to account for the fact that these groups are prone to central adiposity and their cardiometabolic risk occurs at a lower BMI. **[2023]**

Box 2 Examples of common health conditions that can improve after bariatric surgery

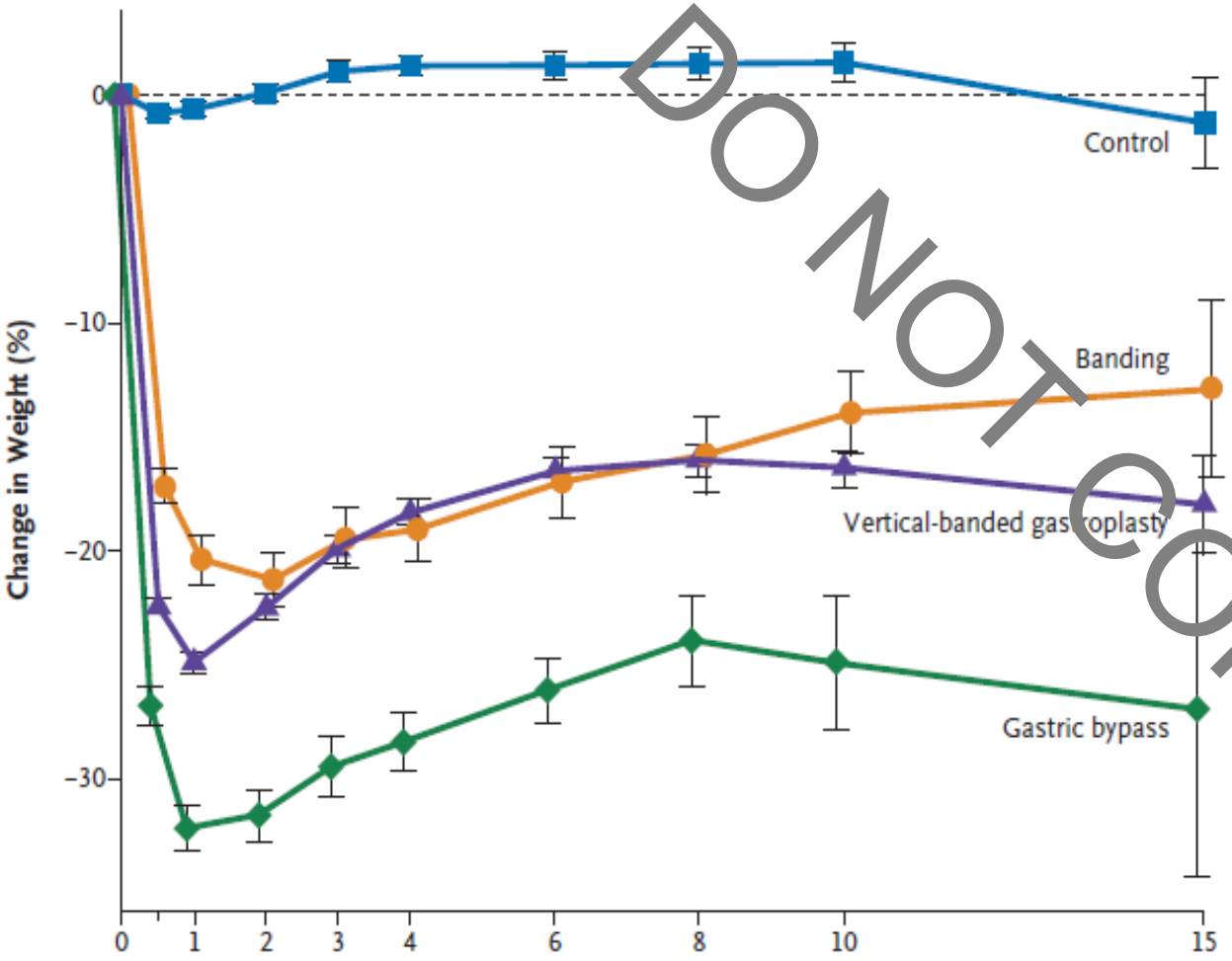
Some conditions that can improve after bariatric surgery include:

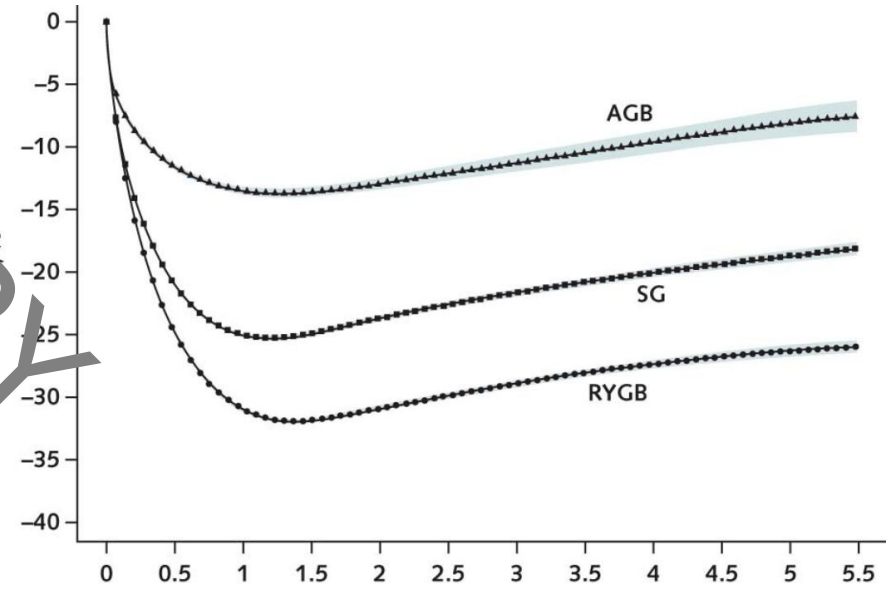
- cardiovascular disease
- hypertension
- idiopathic intracranial hypertension
- non-alcoholic fatty liver disease with or without steatohepatitis
- obstructive sleep apnoea
- type 2 diabetes.

These examples are based on the evidence identified for this guideline and the list is not exhaustive.

NICE CG189

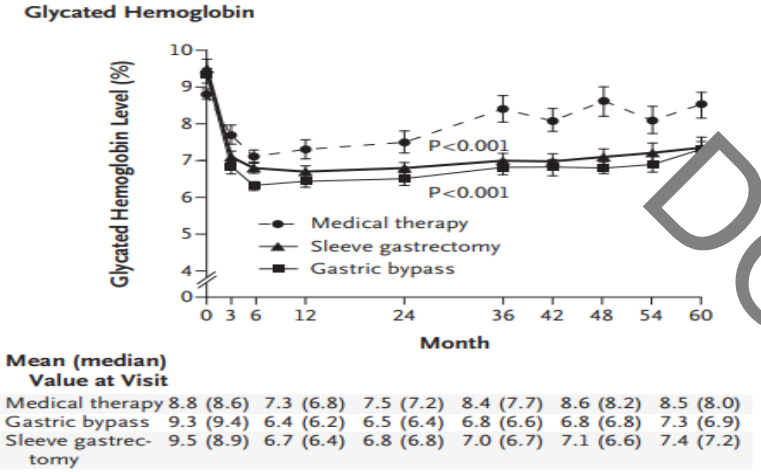
Bariatric surgery - Long term weight loss maintenance





Sjöström, L. et al. N Engl J Med 2007/ Arterburn 2018, Annals of Internal Medicine

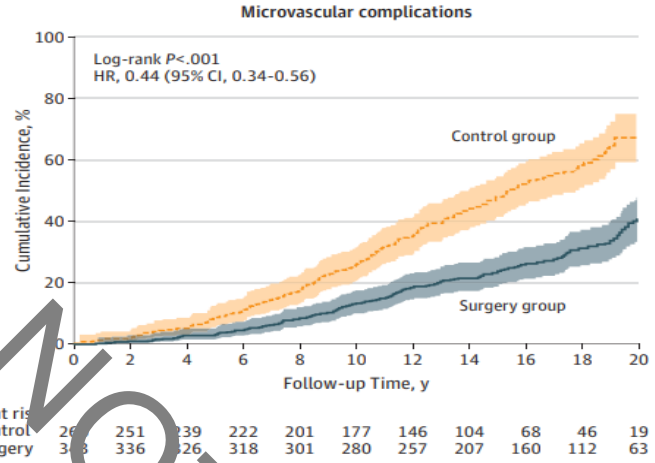
Bariatric surgery and cardiometabolic complications

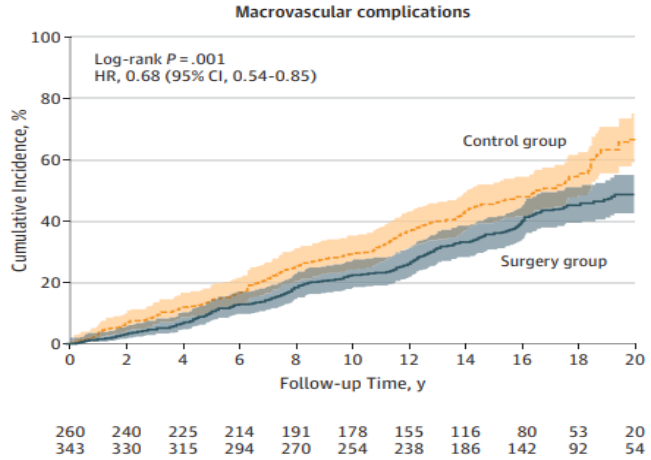


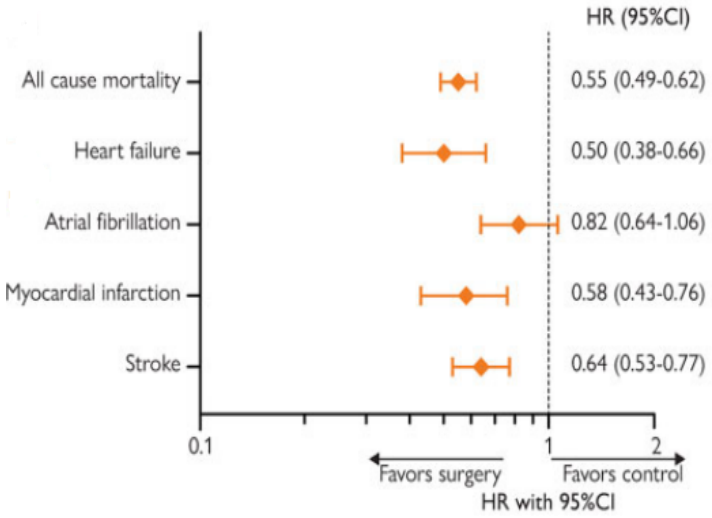
Mean (median) Value at Visit

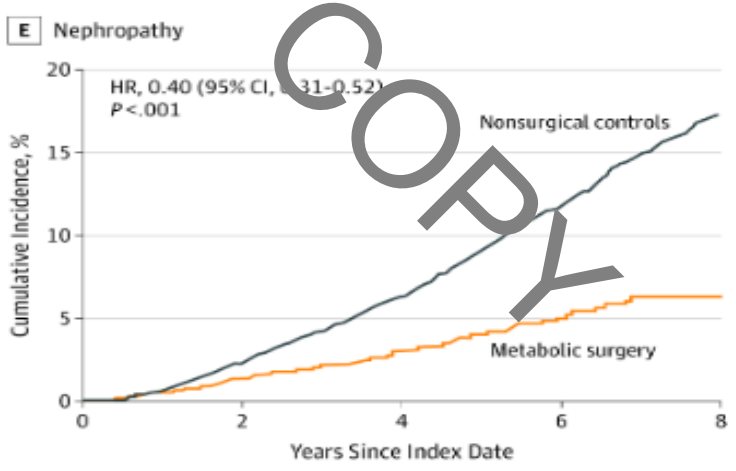
Medical therapy	8.8 (8.6)	7.3 (6.8)	7.5 (7.2)	8.4 (7.7)	8.6 (8.2)	8.5 (8.0)
Gastric bypass	9.3 (9.4)	6.4 (6.2)	6.5 (6.4)	6.8 (6.6)	6.8 (6.8)	7.3 (6.9)
Sleeve gastrectomy	9.5 (8.9)	6.7 (6.4)	6.8 (6.8)	7.0 (6.7)	7.1 (6.6)	7.4 (7.2)

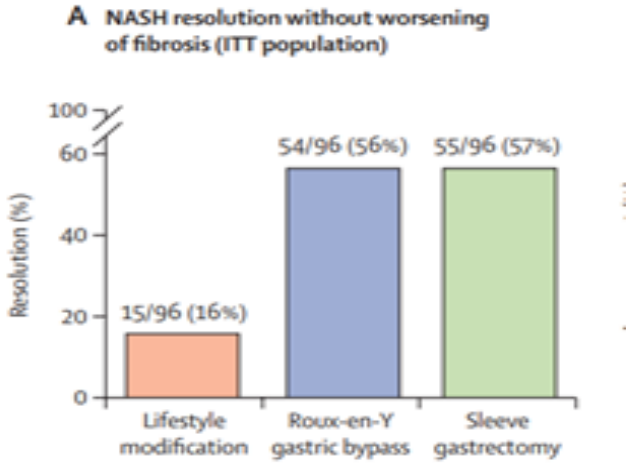
Figure 3. Cumulative Incidence of Microvascular and Macrovascular Diabetes Complications in the Surgery and Control Groups











Schauer, 2017, NEJM/ Sjostrom, JAMA, 2014/ Van Veldhuisen SL, European Heart Journal, 2022/ Aminian, JAMA, 2019/ Verrastro O, 2023, Lancet

Case 3 - George

Primary care – Diabetes clinic

- He is 38 years old
- BMI: 47, weight:150kg
- He has tried multiple times to lose weight and he has done the slimming world programme for 12 weeks – able to achieve 5% weight loss, but minimal improvement at his quality of life.

Case 3 – George

He is 38 years old

BMI: 47, weight:150kg, height: 1.79m

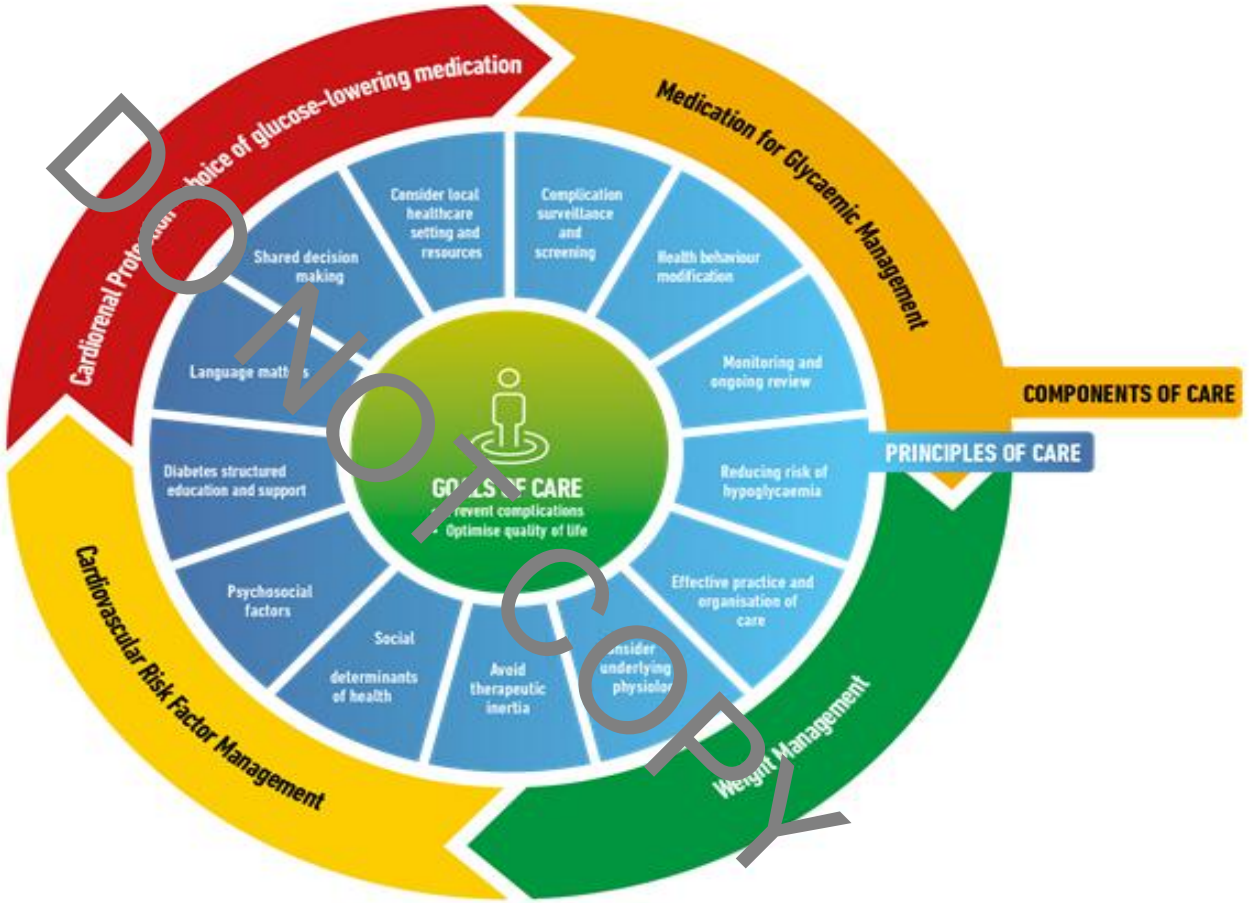
T2D for last 5 years on metformin 1g bd, SGLT-2i (Empagliflozin 25mg once daily), linagliptin 5mg, HbA1c 8%

Hypertension, MASH (under the hepatology team), microalbuminuria (ACR:13, eGFR:82)

Also on ramipril 5mg OD and atorvastatin 20mg OD

What you want to do next?

FIGURE 4: HOLISTIC PERSON-CENTRED APPROACH TO T2DM MANAGEMENT



Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

Diabetes Care 2022; https://doi.org/10.2337/dci22-0034. *Diabetologia* 2022; https://doi.org/10.1007/s00125-022-05787-2.

1 Recommendations

1.1 Tirzepatide is recommended for treating type 2 diabetes alongside diet and exercise in adults when it is insufficiently controlled only if:

- triple therapy with metformin and 2 other oral antidiabetic drugs is ineffective, not tolerated or contraindicated, and
- they have a body mass index (BMI) of 35 kg/m^2 or more, and specific psychological or other medical problems associated with obesity, or
- they have a BMI of less than 35 kg/m^2, and:
  - insulin therapy would have significant occupational implications, or
  - weight loss would benefit other significant obesity-related complications.

  Use lower BMI thresholds (usually reduced by 2.5 kg/m^2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean family backgrounds.

  Tirzepatide is only recommended if the company provides it according to the commercial arrangement.

Case 3 – George – What if he was on insulin?

He is 38 years old

BMI: 47, weight:150kg, height: 1.79m

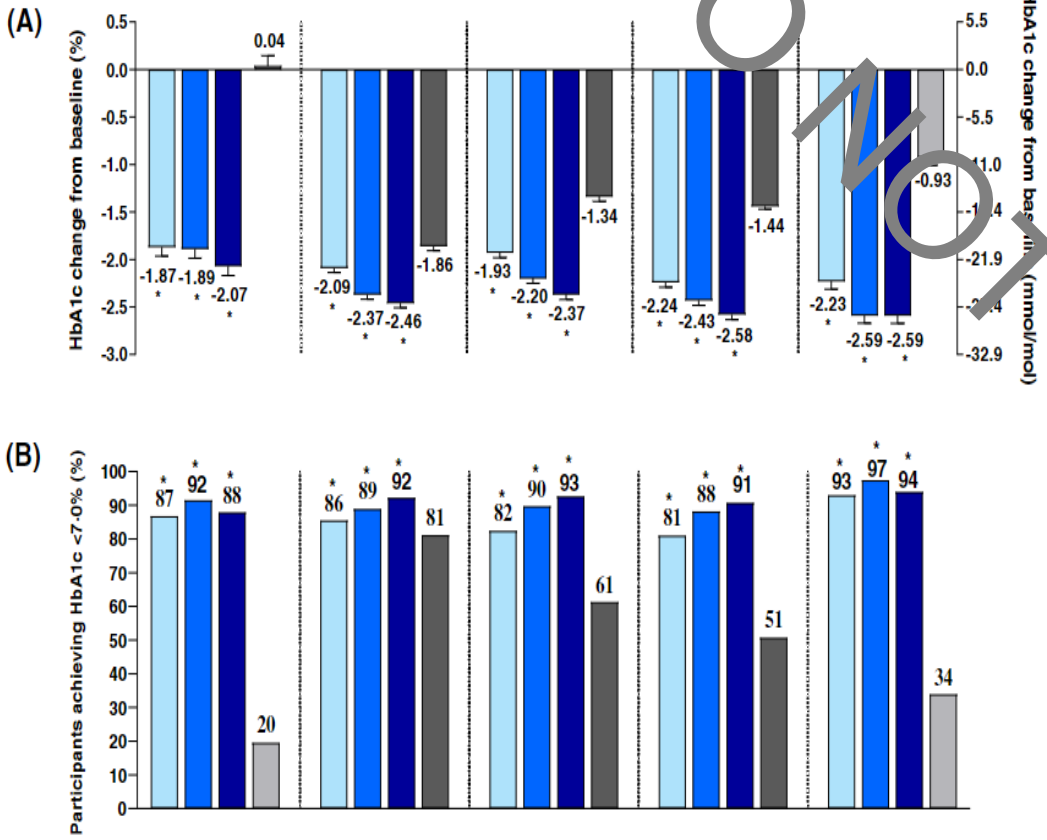
T2D for last 5 years on
metformin 1g bd,
Empagliflozin 25mg once daily
Humulin I 40 units twice daily
HbA1c 8%.

What is your advise to him regarding insulin on initiation of tirzepatide?

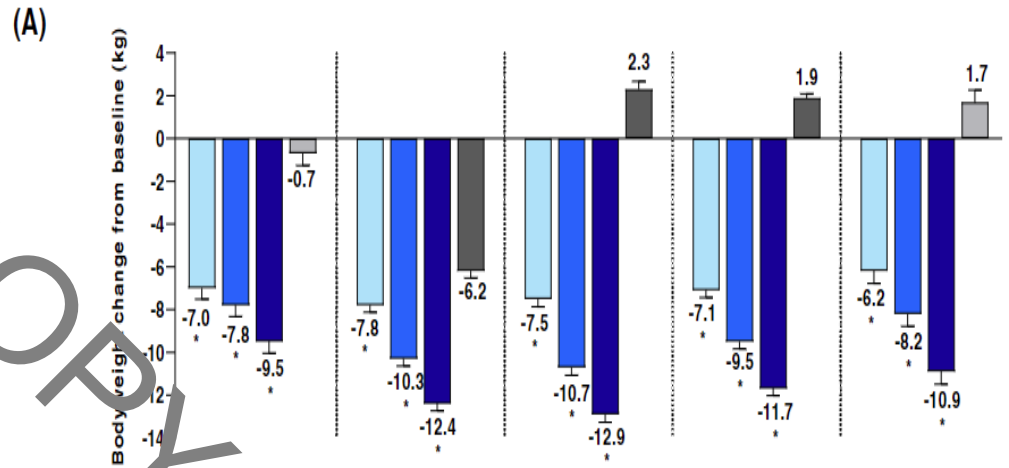
What about retinal screening? (R1M0 bilaterally)

Tirzepatide - SURPASS programme

	SURPASS-1	SURPASS-2	SURPASS-3	SURPASS-4	SURPASS-5
N	478	1878	1437	1995	475
Add-on to	Monotherapy	MET	MET ± SGLT-2i	MET, SGLT2i, or SU	IGlar ± MET
Timepoint (weeks)	40	40	52	52	40
Comparator	PBO	Sema 1 mg	IDeg	IGlar	PBO

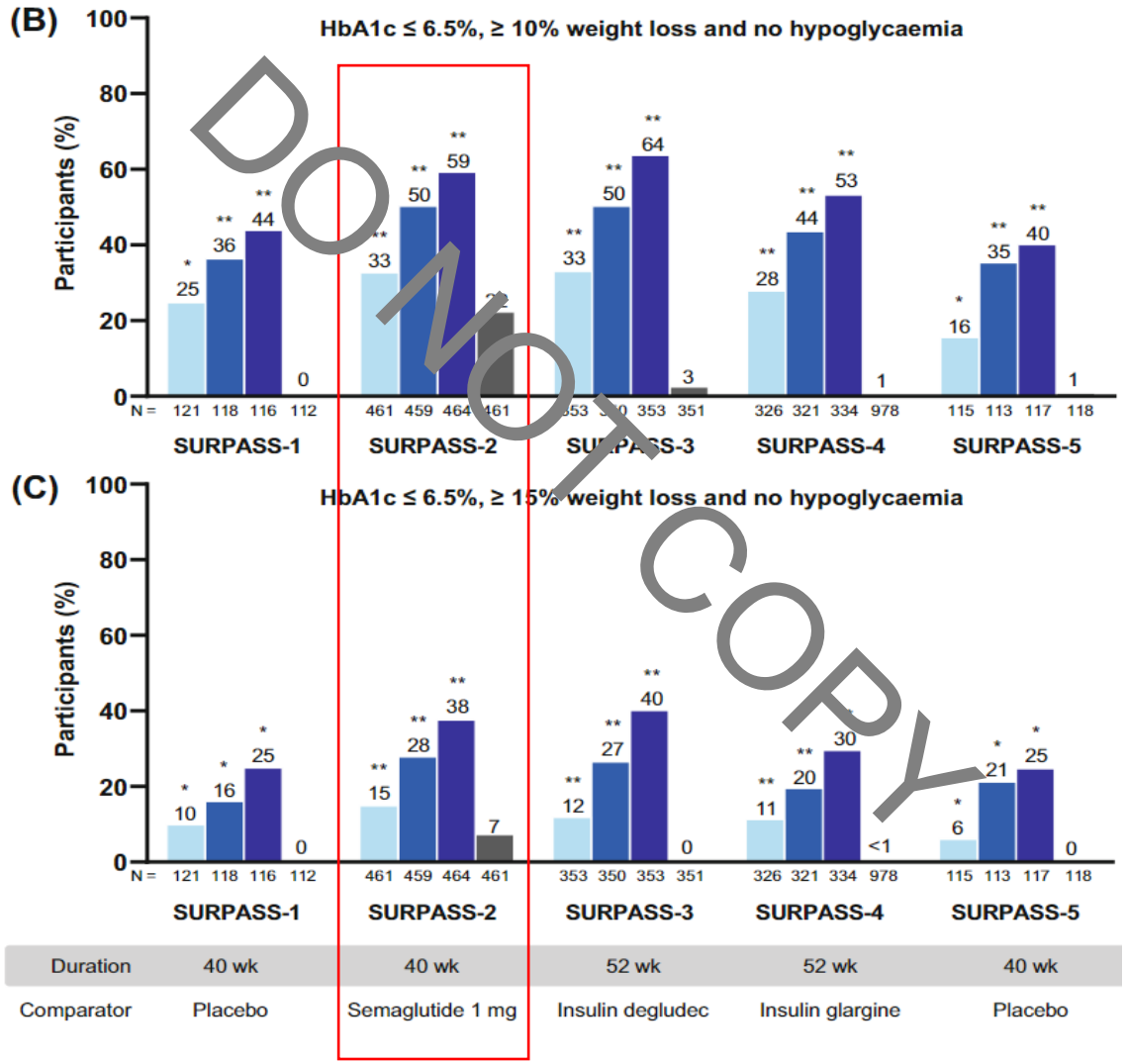


	SURPASS-1	SURPASS-2	SURPASS-3	SURPASS-4	SURPASS-5
N	478	1878	1437	1995	475
Add-on to	Monotherapy	MET	MET ± SGLT-2i	MET, SGLT2i, or SU	IGlar ± MET
Timepoint (weeks)	40	40	52	52	40
Comparator	PBO	Sema 1 mg	IDeg	IGlar	PBO

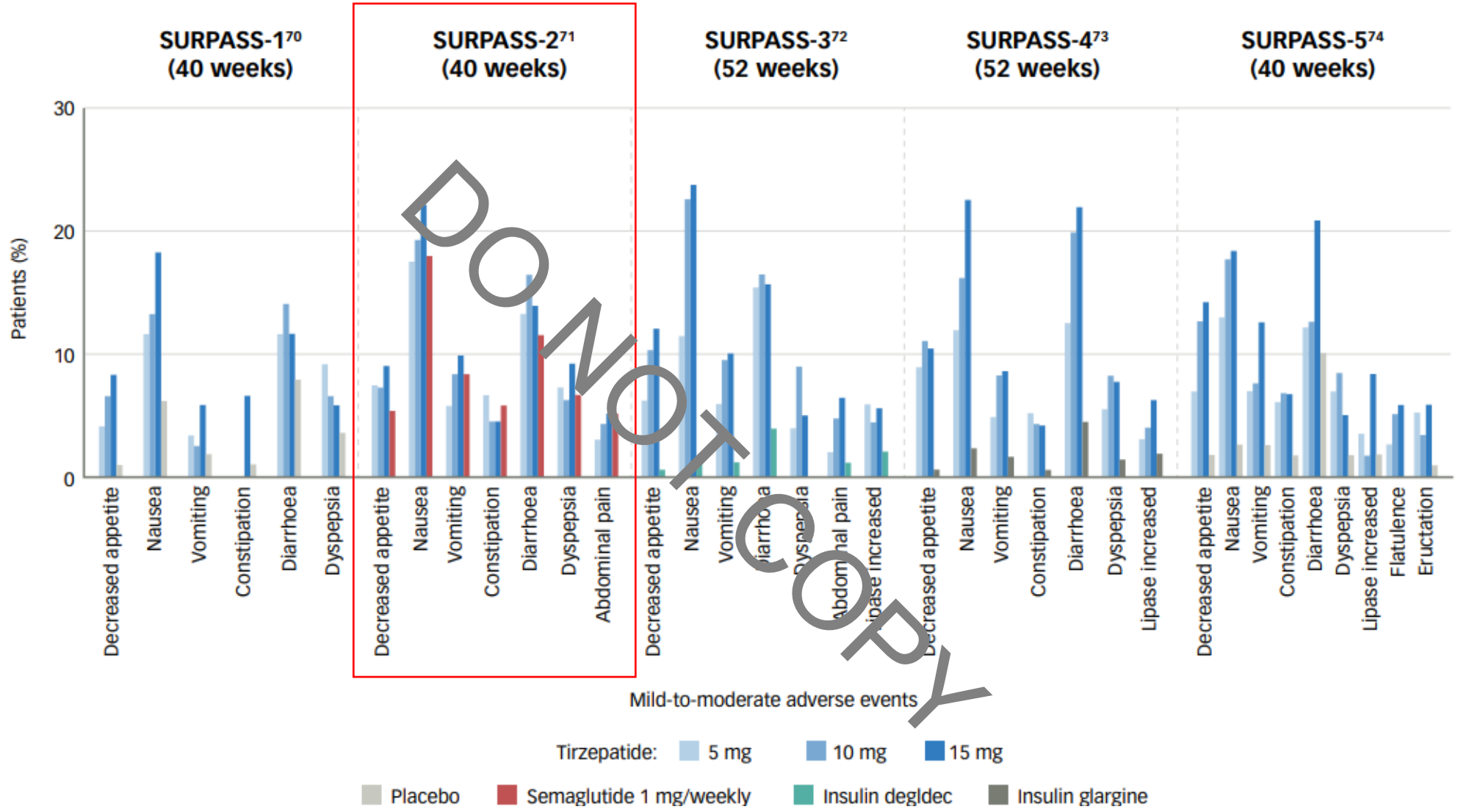


De Block C, 2023, DOM

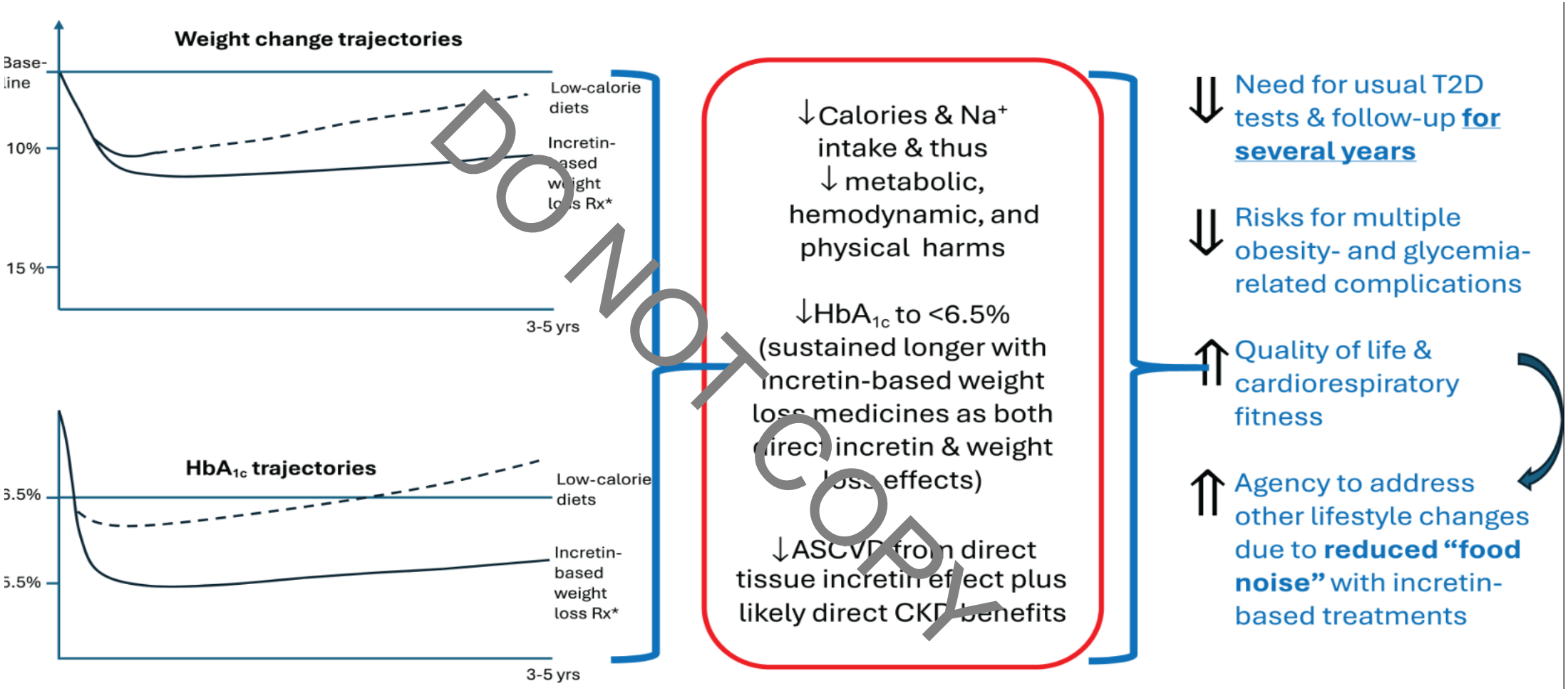
Achieving the triple target (HbA1c, WL and hypoglycaemia)



Linvay, DOM, 2023



Kaneko S, touchREV Endocrinol, 2022



Sattar N, Diabetes Care, 2025

3 months down the line –On tirzepatide 5mg once weekly – HbA1c 6.2% and **4% weight loss (weight 144 kg)**.

You have achieved the glycaemic target **– Are you going to continue titrating the medication?**

Still MASH, hypertension and microalbuminuria…

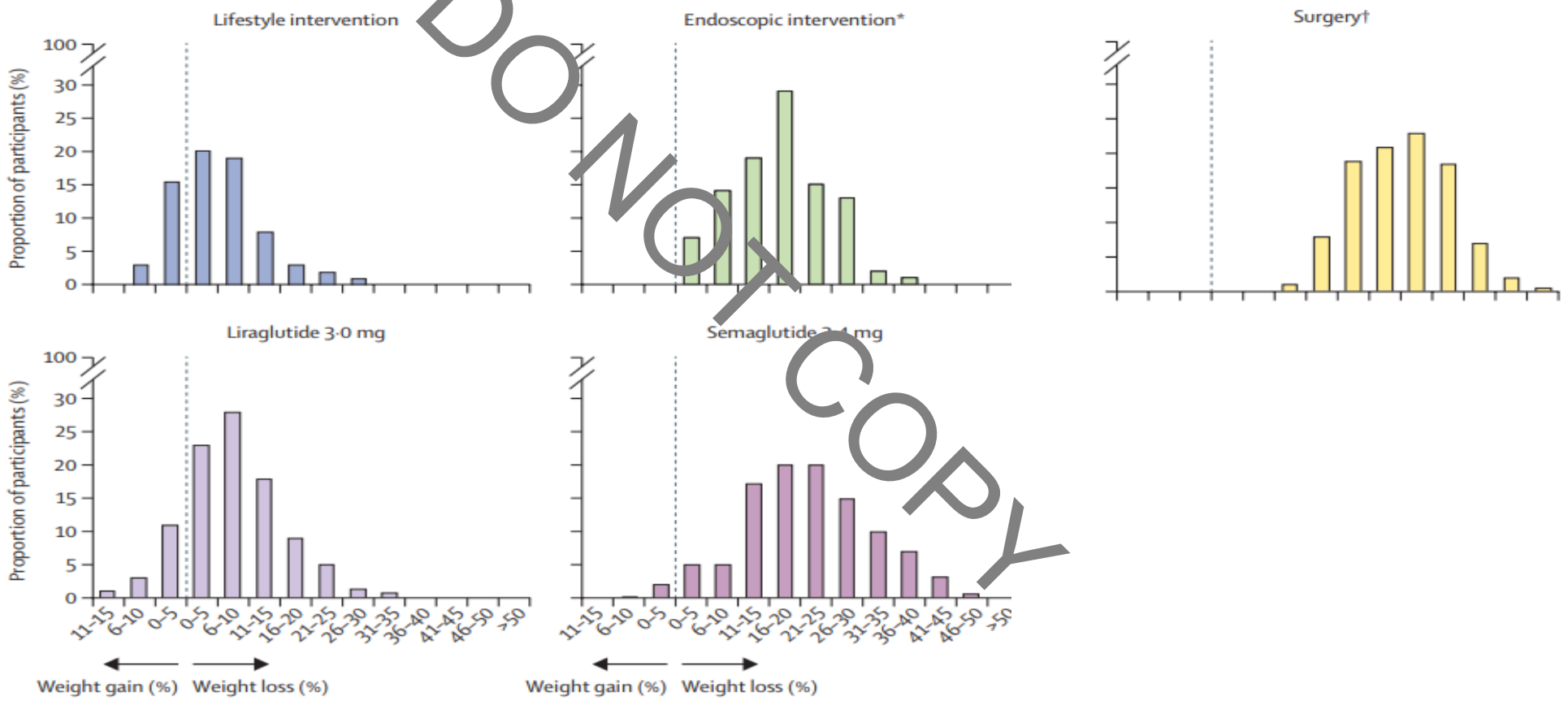
10 months down the line –On tirzepatide 10mg once weekly (not able to tolerate higher doses)– HbA1c 5.9% and **8% weight loss (weight 138 kg)**.

I was hoping to achieve more weight loss?

Is there something wrong with me?

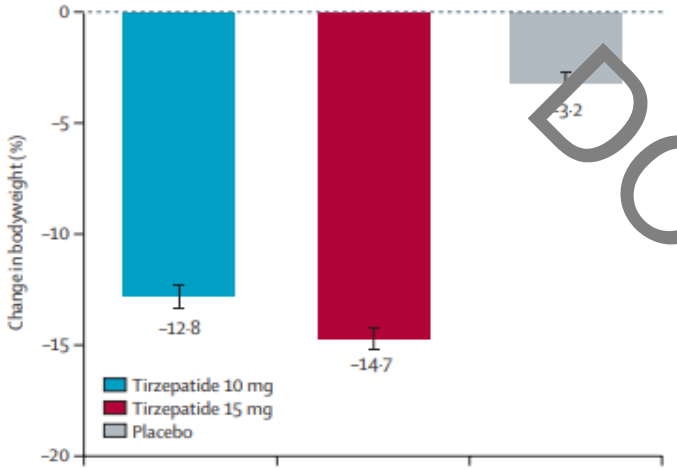
Is there any other option?

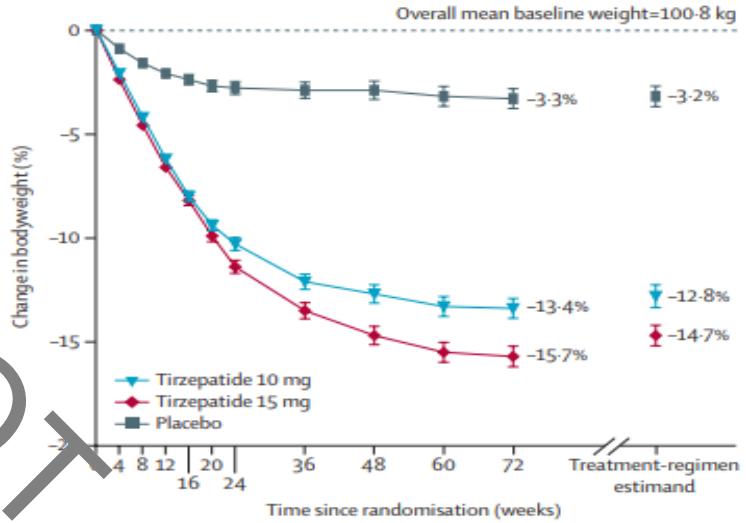
Response to weight loss treatments is heterogeneous

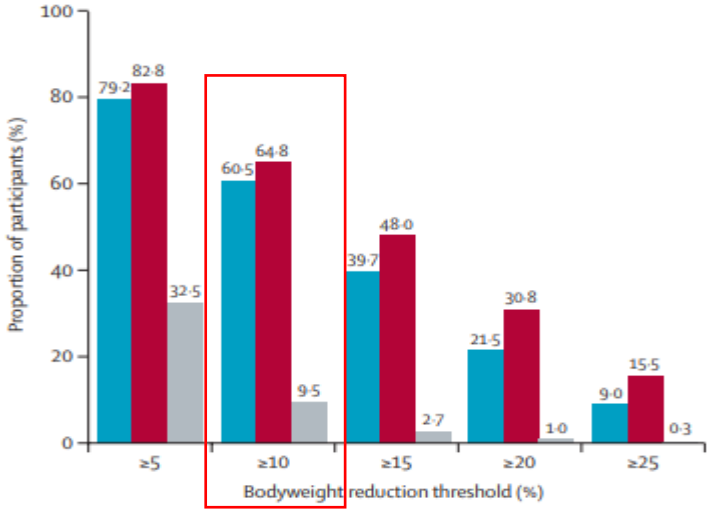


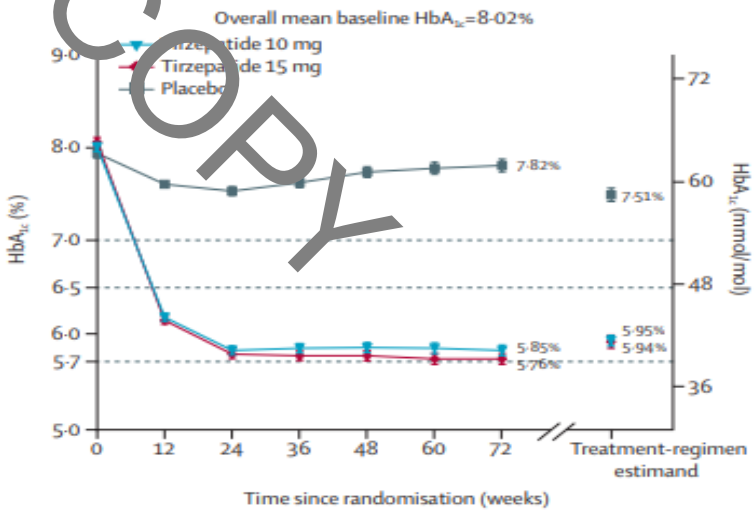
Perdomo CM, Lancet, 2023

SURMOUNT-2 (people with obesity and T2DM)









Garvey et al, Lancet, 2023

Tiered approach in obesity services (UK)

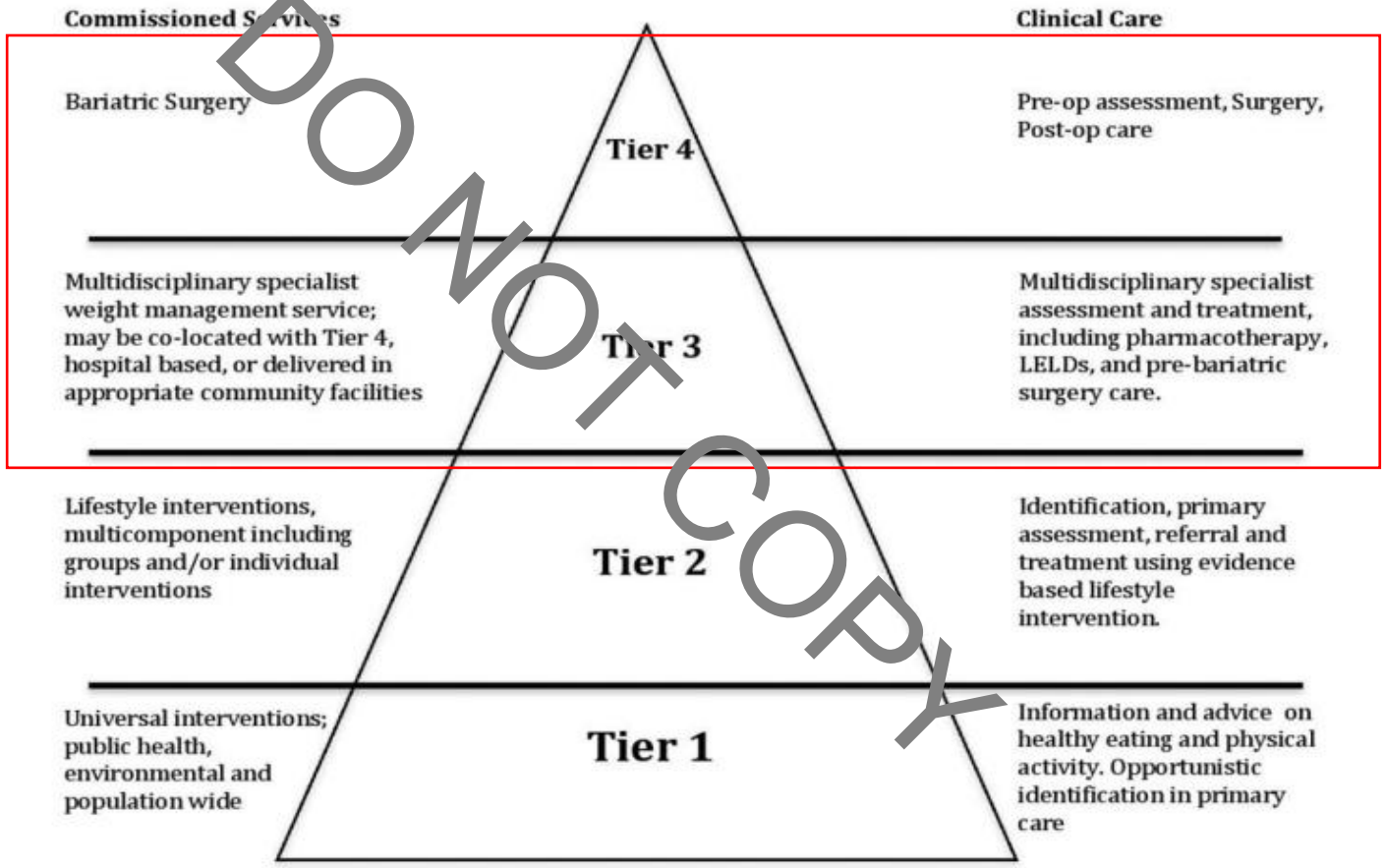


Figure 1 Tiered model of services.

Jennings A, Clinical Obesity, 2014

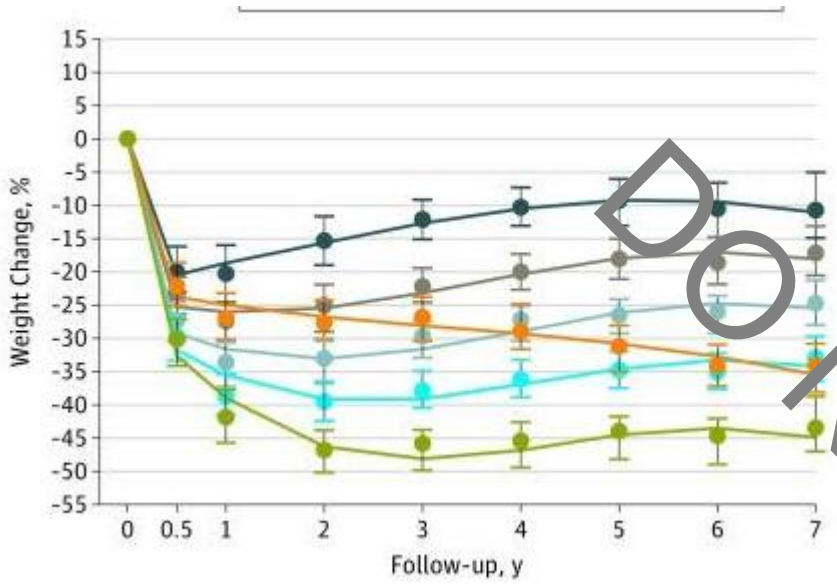
Underwent RYGB – Achieved 25% weight loss at 2 years (112kg)

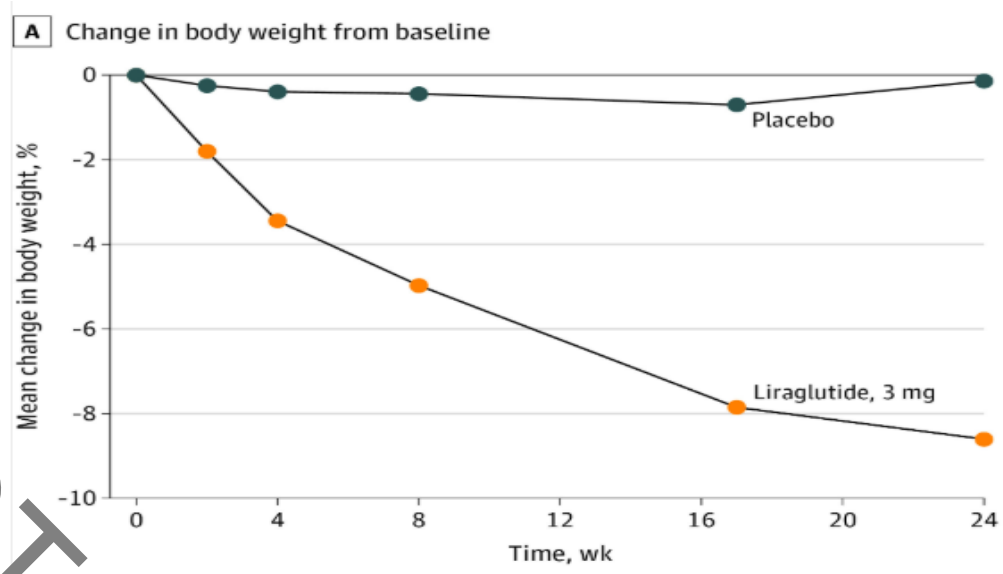
Stopped medications for T2D – Latest HbA1c: 5.6%

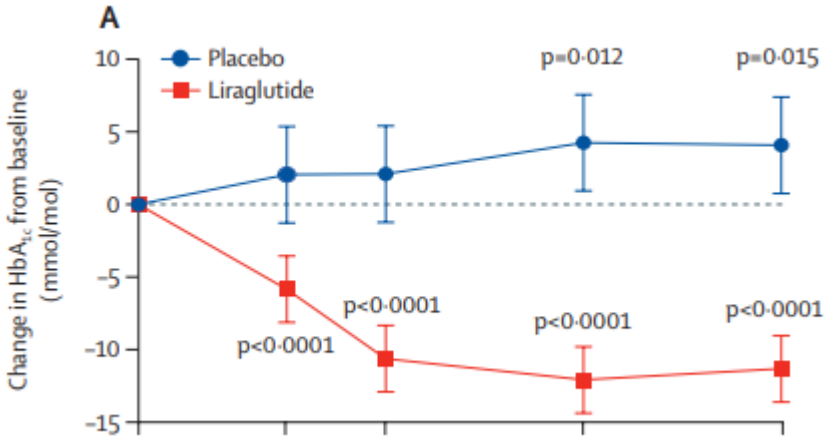
MASH improved

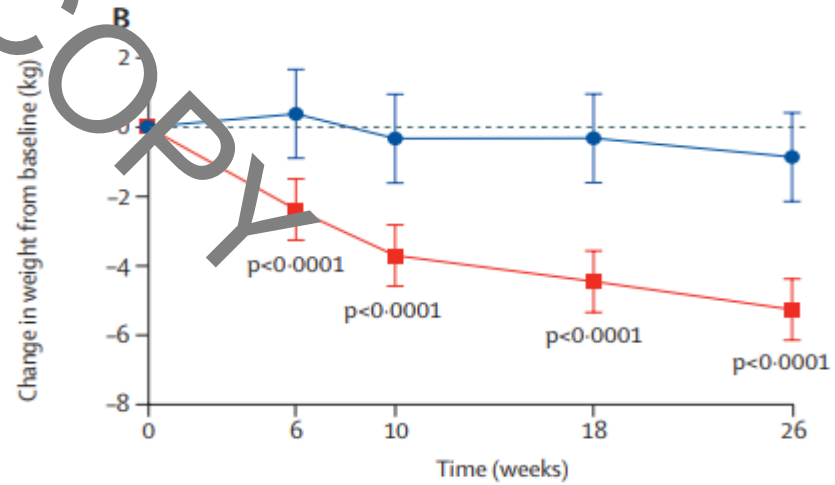
I feel much better – but if I regain weight, is the WL medications still an option for me? Do they still work?

Combining bariatric surgery with medications









Courcoulas AP, 2018, JAMA Surg/ Mok et al, 2024, JAMA Surgery

Role of physical activity in people with severe obesity (treatment of obesity) in the era of new pharmacotherapies

- It is not about weight loss!
- The aim should be to optimise health and weight loss quality (including improving cardiorespiratory fitness, body composition, physical function and quality of life)
- Support weight maintenance after weight loss
- Reduce surgical risk and enhancing recovery (improve CRF)

Grannell A, Clin Obes, 2022

Conclusion

- **Know your local services and pathways** so you can guide patients effectively.
- **Ask permission** before raising weight—start with what matters to them.
- **Assess for obesity-related complications** to understand risk and treatment urgency.
- **Know the national, but mainly the local criteria** for lifestyle programmes, medications, and bariatric surgery – try to navigate between T2D and obesity pathways for tirzepatide.
- **And remember:** novel obesity treatments are set to transform cardiometabolic medicine.

https://www.cheshireandmerseyside.nhs.uk/your-health/prescribing/statements/mounjaro-tirzepatide/

Thank you for your attention

dp421@leicester.ac.uk

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