

De olifant in de kamer: obesitas. Een nieuw behandeldoel?

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Disclosures

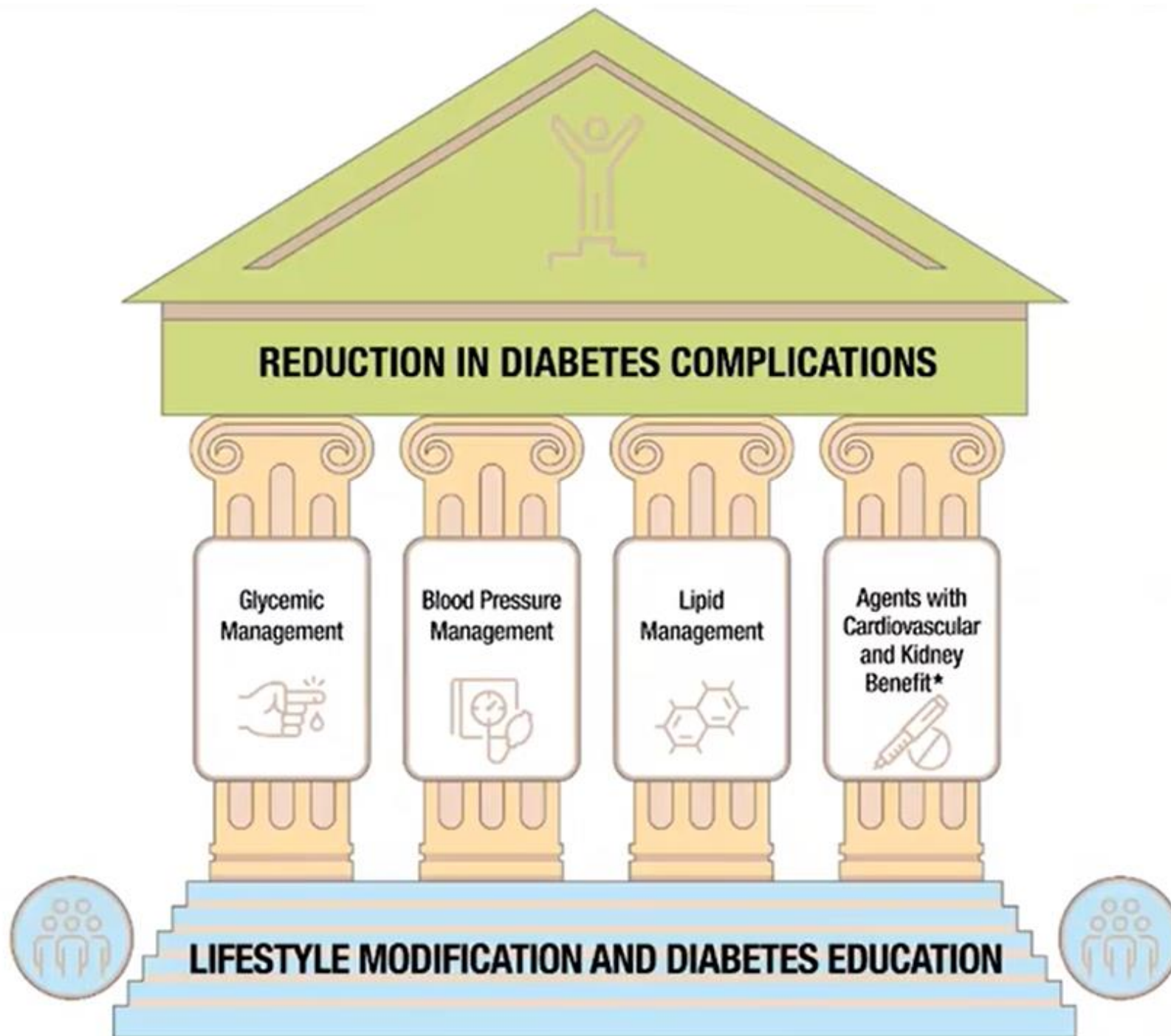
Research contracts:	NONE
Consulting / lectures:	NovoNordisk, BI, Bayer, Lilly
Employment in industry:	NONE
Stockholder of a healthcare company:	NONE
Owner of a healthcare company:	NONE

JOURNAL ARTICLE

GUIDELINES

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes: Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC)

Nikolaus Marx , Massimo Federici , Katharina Schütt,
Dirk Müller-Wieland, Ramzi A Ajjan, Manuel J Antunes,



Een ideaal anti-diabetes geneesmiddel...

- Verlaagt nuchtere glucose 30-50%
- Verlaagt bloeddruk meer dan 10 mm Hg
- Gunstige werking op lipiden:
 - 30% daling triglyceriden
 - 10% daling totaal cholesterol
 - 15% daling LDL-cholesterol
 - 8% stijging HDL-cholesterol

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 - 30% daling triglyceriden
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- Je voelt je beter en wordt aantrekkelijker voor het andere geslacht

Dit geneesmiddel bestaat al!

10 kg afvallen

Benefits of 10 kg Weight Loss

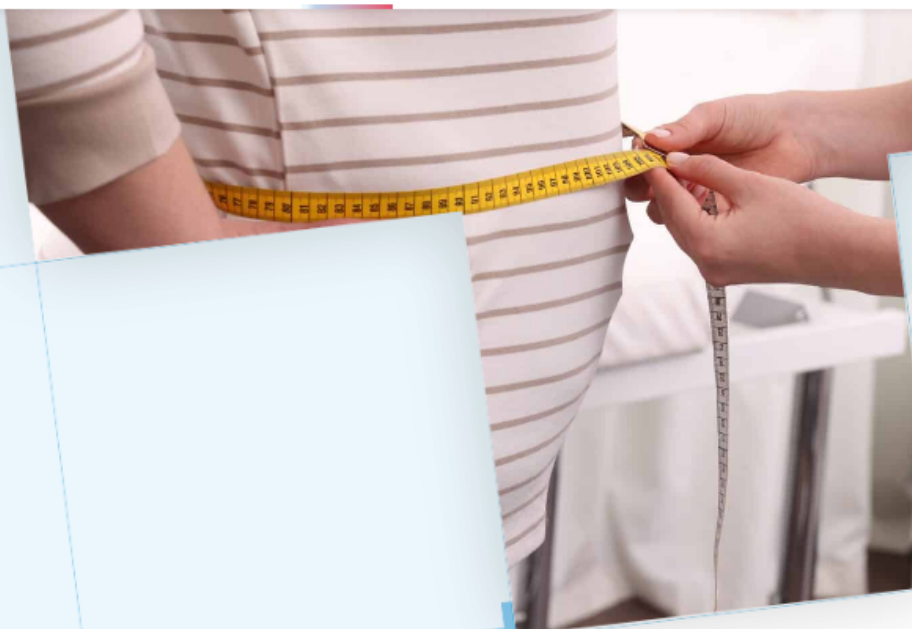
Blood Pressure	Fall of 10mm Hg systolic pressure Fall of 20 mm Hg diastolic pressure
Angina	91% reduction in symptoms 33% increase in exercise tolerance
Lipids	10% fall in total cholesterol 15% fall in LDL-cholesterol 30% fall in triglycerides 8% increase in HDL-cholesterol
Diabetes	>50% risk of developing 30-50% fall in fasting blood glucose 15% fall in glycated Hb



27 juli 2023

Herziene multidisciplinaire richtlijn Obesitas en overgewicht

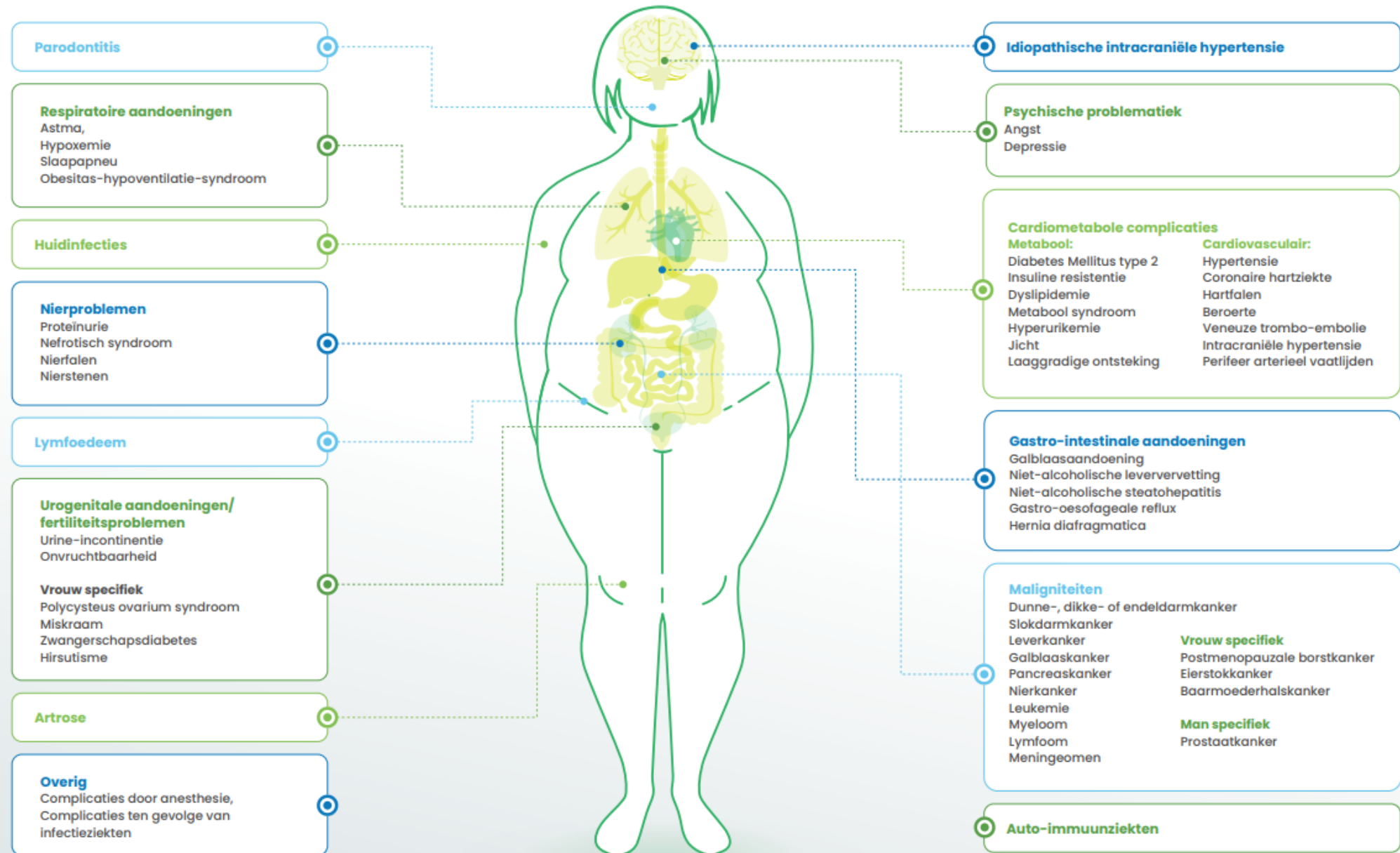
De herziene multidisciplinaire richtlijn Obesitas en overgewicht bij volwassenen is gepubliceerd. Het NHG heeft hieraan meegewerkt. De richtlijn is van belang, omdat meer dan de helft van de Nederlandse volwassenen overgewicht heeft en een aanzienlijk deel daarvan kampt met obesitas. Een samenvatting van de belangrijkste aanbevelingen uit de richtlijn wordt gepubliceerd in Huisarts en Wetenschap.



Diagnose en gepersonaliseerde zorg


- Obesitas heeft grote fysieke, psychosociale en maatschappelijke gevolgen, op de korte en lange termijn.
- Een groot deel van de patiënten zal bij vragen of problemen als gevolg van overgewicht en obesitas aankloppen bij de huisartsenpraktijk.
- De richtlijn geeft adviezen voor het stellen van de diagnose, het gebruik van de juiste uitkomstmaten, gepersonaliseerde zorg en organisatie van zorg.

Figuur 13.1. Overzicht consequenties van overgewicht en obesitas (zie module 'Obesitas-gerelateerde comorbiditeiten')




Risk of mortality and cardiovascular events

Comparison of seven popular structured dietary programmes

Summary  In those at increased cardiovascular risk, evidence indicates that diet programmes, such as Mediterranean and low fat, reduce outcomes including all cause mortality, and non-fatal myocardial infarction

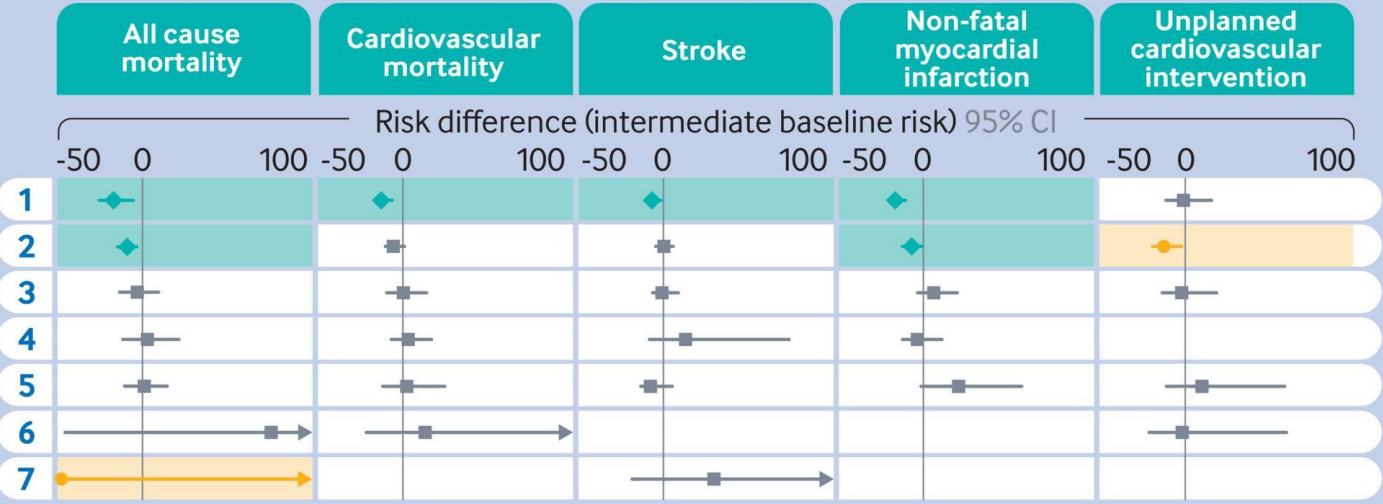
Study design  Systematic review with network meta-analysis | Adults with cardiovascular disease or with at least two cardiovascular risk factors




Data sources  40 randomised controlled trials |  35 548 participants

Comparison  Seven popular structured dietary programmes with or without co-interventions such as exercise or psychological support



Outcomes  Summary of results in patients with intermediate cardiovascular risk

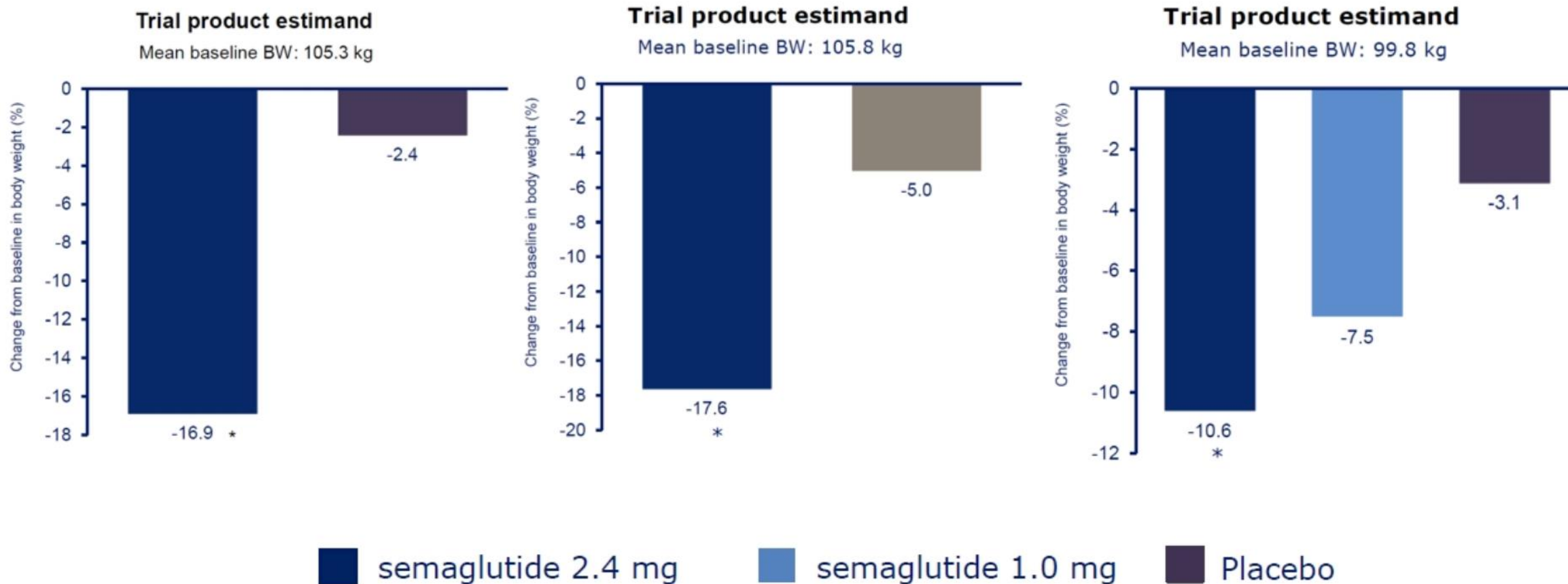


 Superior to minimal intervention Moderate-high certainty
 Maybe superior to minimal intervention Very low-low certainty
 Little or no benefit relative to minimal intervention

Semaglutide for weight loss efficacy

+ intensive behavioural therapy

+ Type 2 diabetes



The NEW ENGLAND JOURNAL of MEDICINE

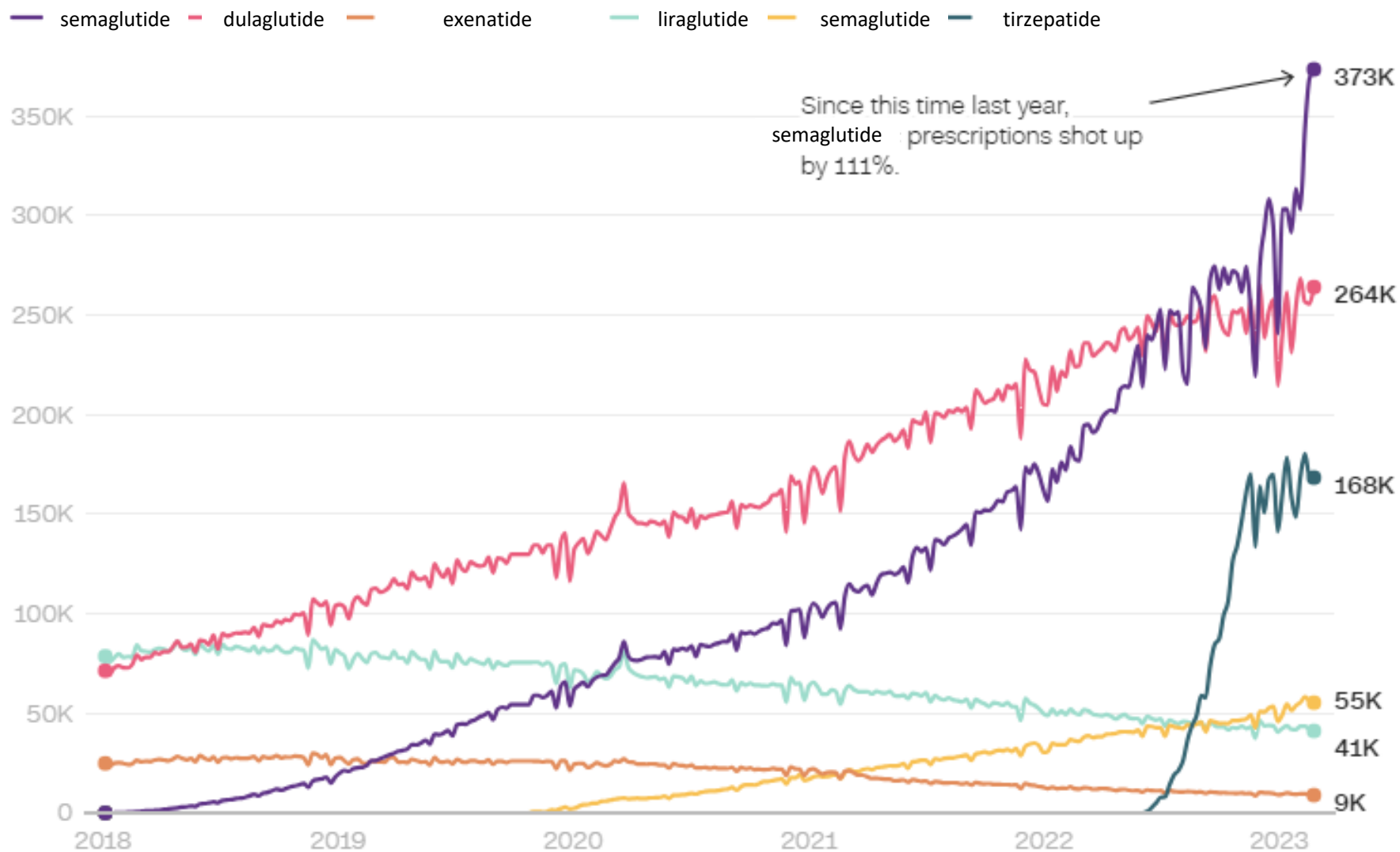
EDITORIAL



Shifting Tides Offer New Hope For Obesity

Clifford J. Rosen, M.D., and Julie R. Ingelfinger, M.D.

Number of prescriptions by drug



Note: The Byetta franchise includes both Byetta and Bydureon.

ORIGINAL ARTICLE

Tirzepatide Once Weekly for the Treatment of Obesity

Ania M. Jastreboff, M.D., Ph.D., Louis J. Aronne, M.D.,
Nadia N. Ahmad, M.D., M.P.H., Sean Wharton, M.D., Pharm.D.,
Lisa Connery, M.D., Breno Alves, M.D., Arihiro Kiyosue, M.D., Ph.D.,
Shuyu Zhang, M.S., Bing Liu, Ph.D., Mathijs C. Bunck, M.D., Ph.D.,
and Adam Stefanski, M.D., Ph.D., for the SURMOUNT-1 Investigators*

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2022, at NEJM.org.



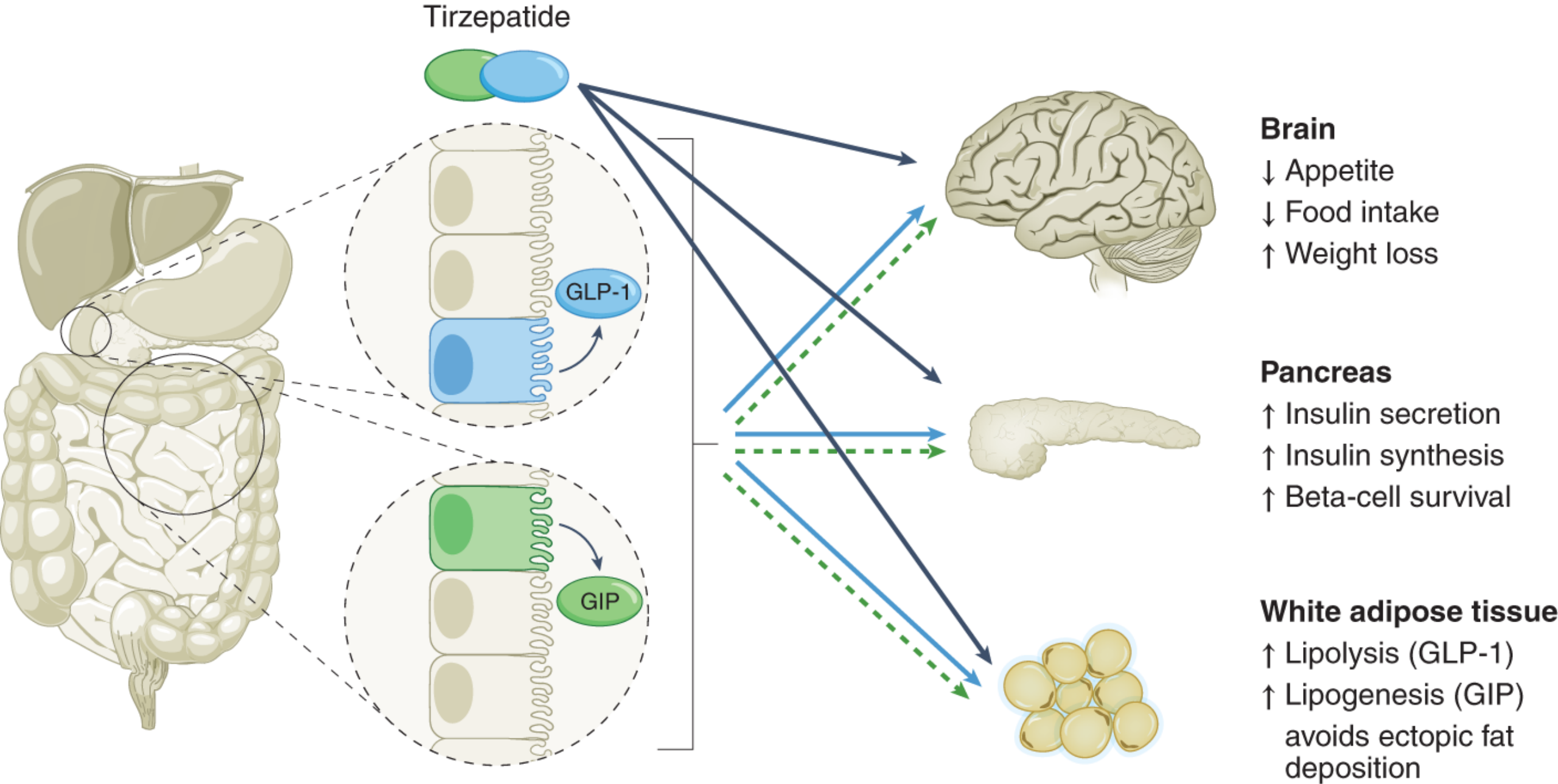
GIP agonism acts through the GIP receptor
GIP enhances the receptor activity of GLP-1
GLP-1 sensitizes the GIPR
GIP desensitizes the GIPR
GLP-1 actions dominate, GIP contributes little



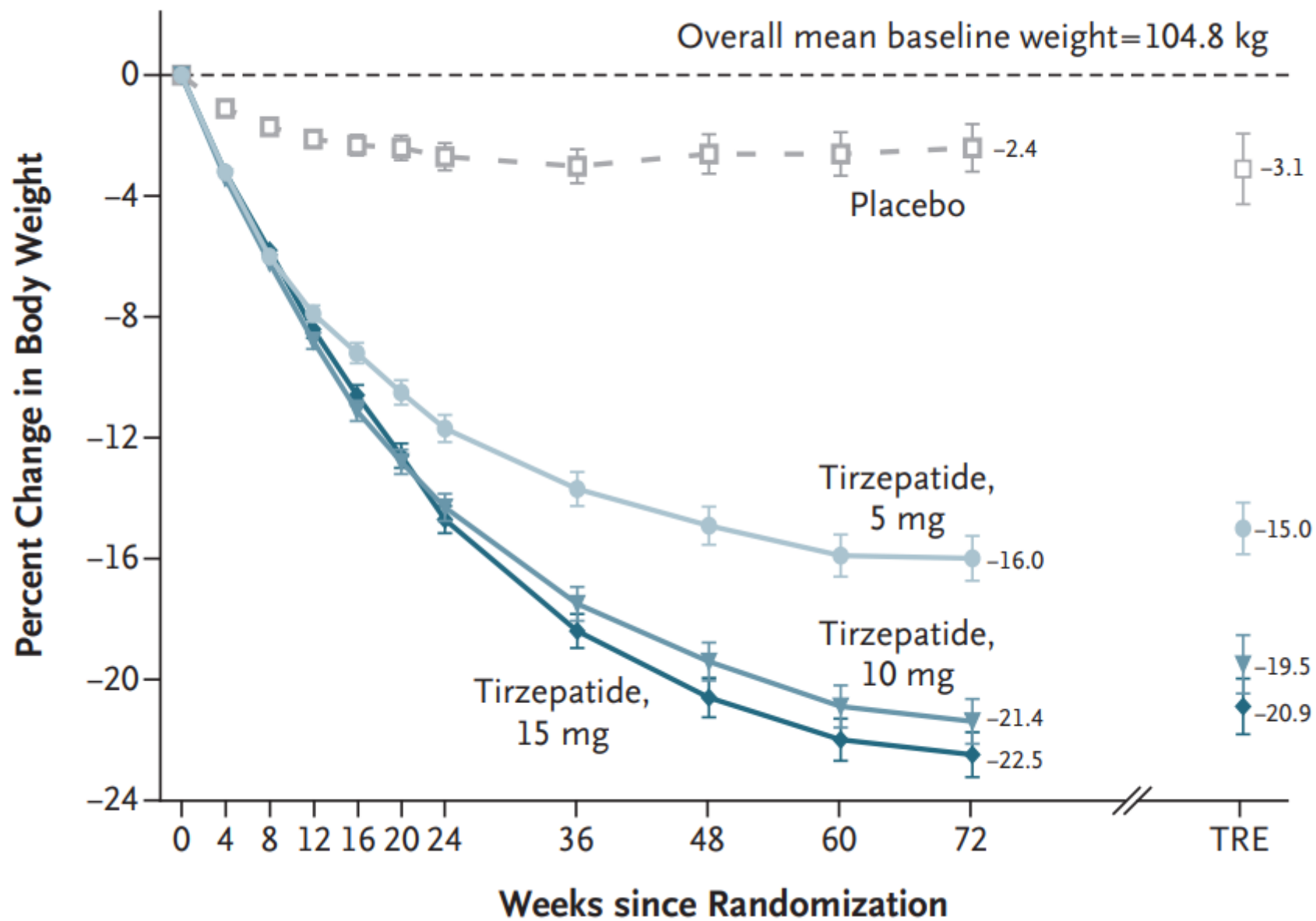
GIPR



GLP1R



B Percent Change in Body Weight by Week (efficacy estimand)



ORIGINAL ARTICLE

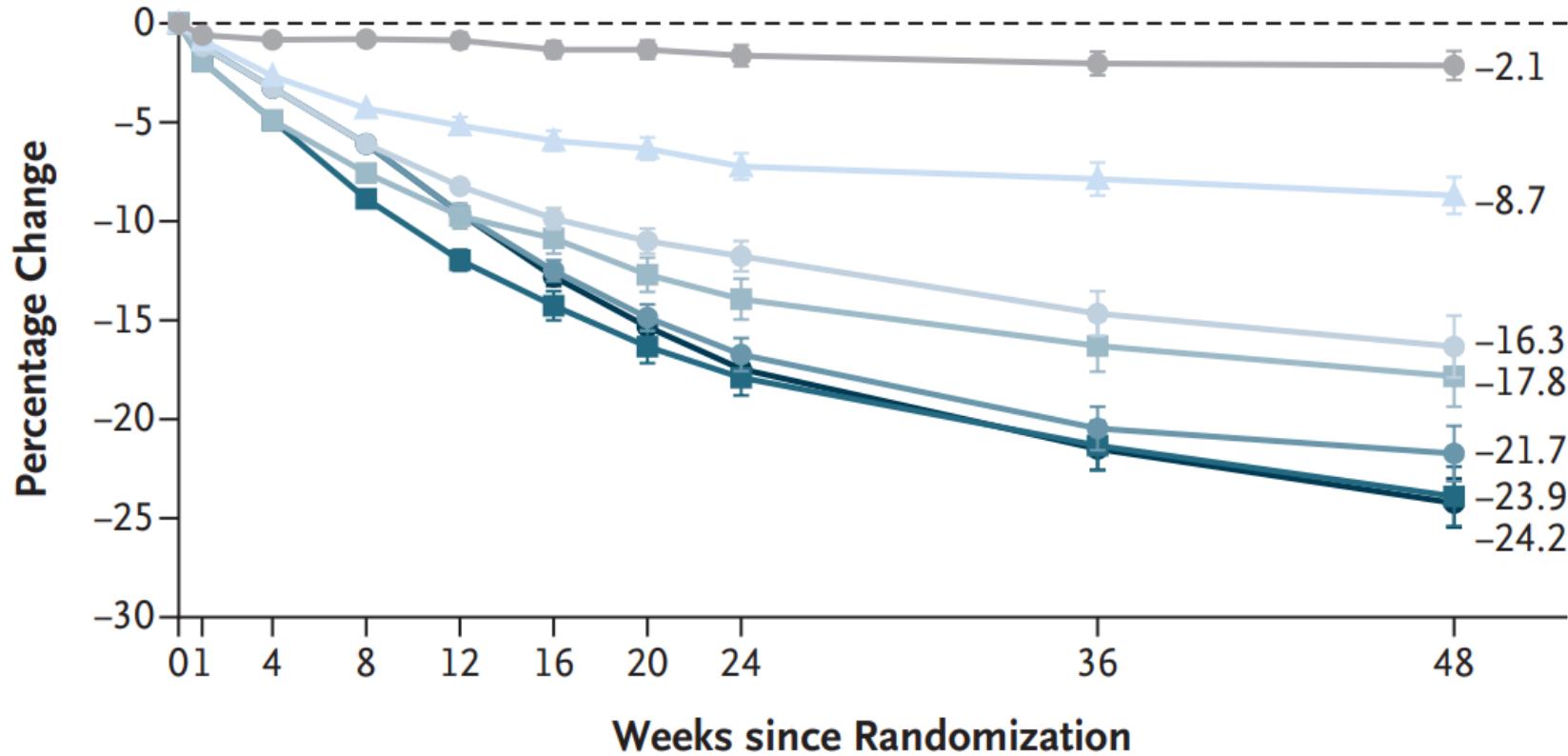
Triple–Hormone-Receptor Agonist Retatrutide for Obesity — A Phase 2 Trial

Ania M. Jastreboff, M.D., Ph.D., Lee M. Kaplan, M.D., Ph.D., Juan P. Frías, M.D.,
Qiwei Wu, Ph.D., Yu Du, Ph.D., Sirel Gurbuz, M.D., Tamer Coskun, M.D., Ph.D.,
Axel Haupt, M.D., Ph.D., Zvonko Milicevic, M.D., and Mark L. Hartman, M.D.,
for the Retatrutide Phase 2 Obesity Trial Investigators*

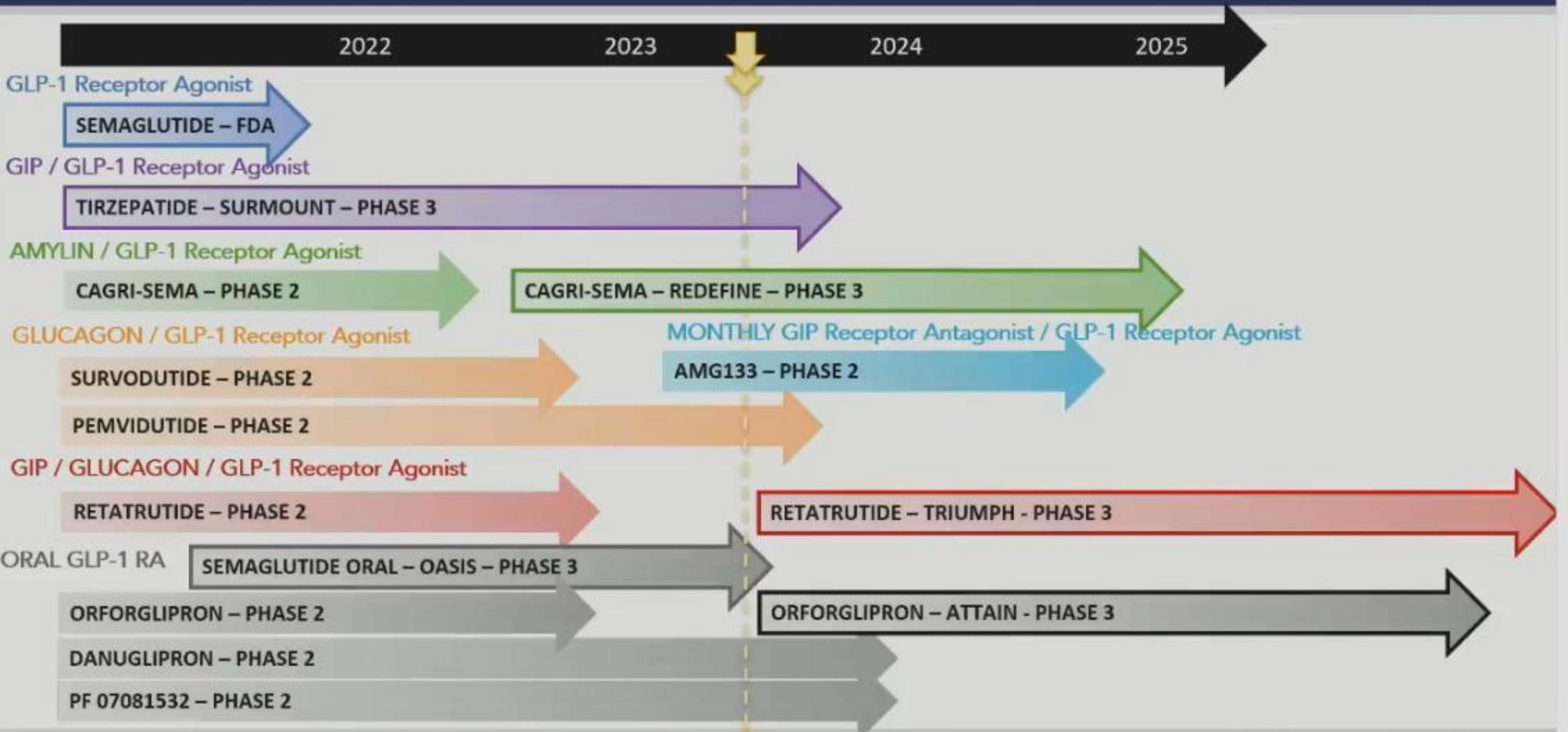
Triple G Agonists — A Home Run for Obesity?

■ Placebo ■ Retatrutide, 1 mg ■ Retatrutide, 4 mg (ID, 2 mg) ■ Retatrutide, 4 mg (ID, 4 mg) ■ Retatrutide, 8 mg (ID, 2 mg) ■ Retatrutide, 8 mg (ID, 4 mg) ■ Retatrutide, 12 mg (ID, 2 mg)

A Changes in Body Weight



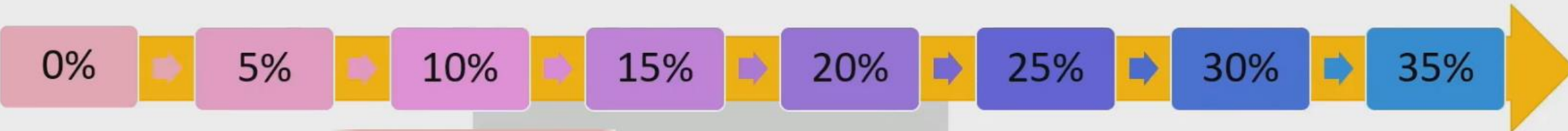
Nutrient-stimulated hormone based therapies



Wat komt eraan

- GLP-1 + GIPra – oa tirzepatide
- GLP-1 + amylin analogues – cagri/sema
- GLP-1 + glucagon agonists – survodutide
- GLP-1 + GIP + glucagon agonist – retatrutide
- Orale GLP-1's - orforglipron
- Overige: PYY, FGF21.....

Efficacy Required to Treat Adiposity-Based Chronic Disease



T2D prevention

Immobility - Physical function

T2D glycemia

CV risk reduction

HTN

Sleep apnea

T2D remission

NAFLD/NASH

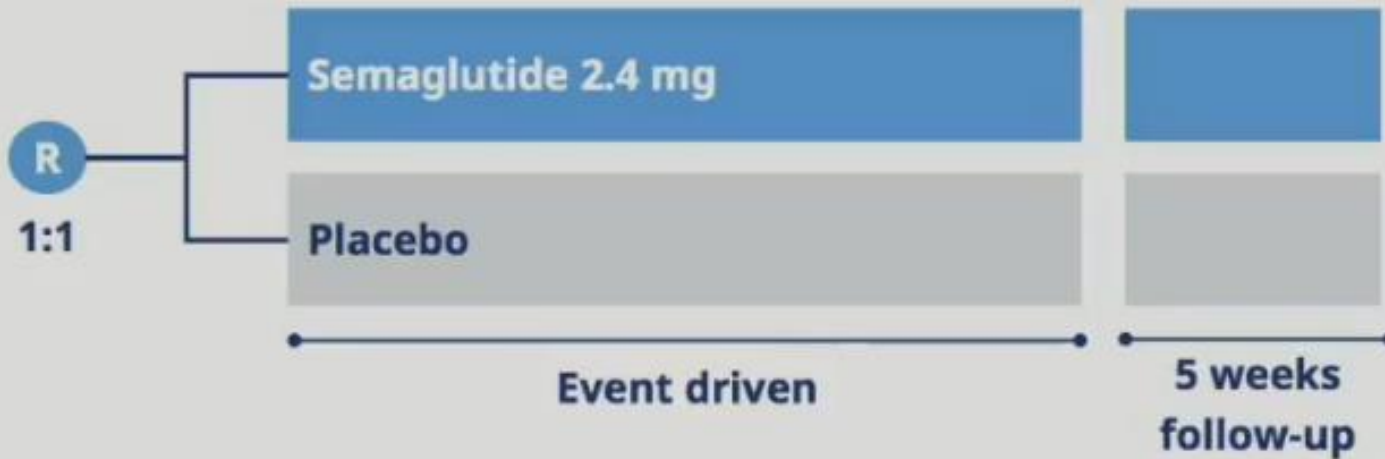
Semaglutide 2.4: SELECT Cardiovascular Outcome Trial

SELECT CVOT

Individuals with Obesity without Type 2 Diabetes



SELECT trial with 17,500 people with obesity



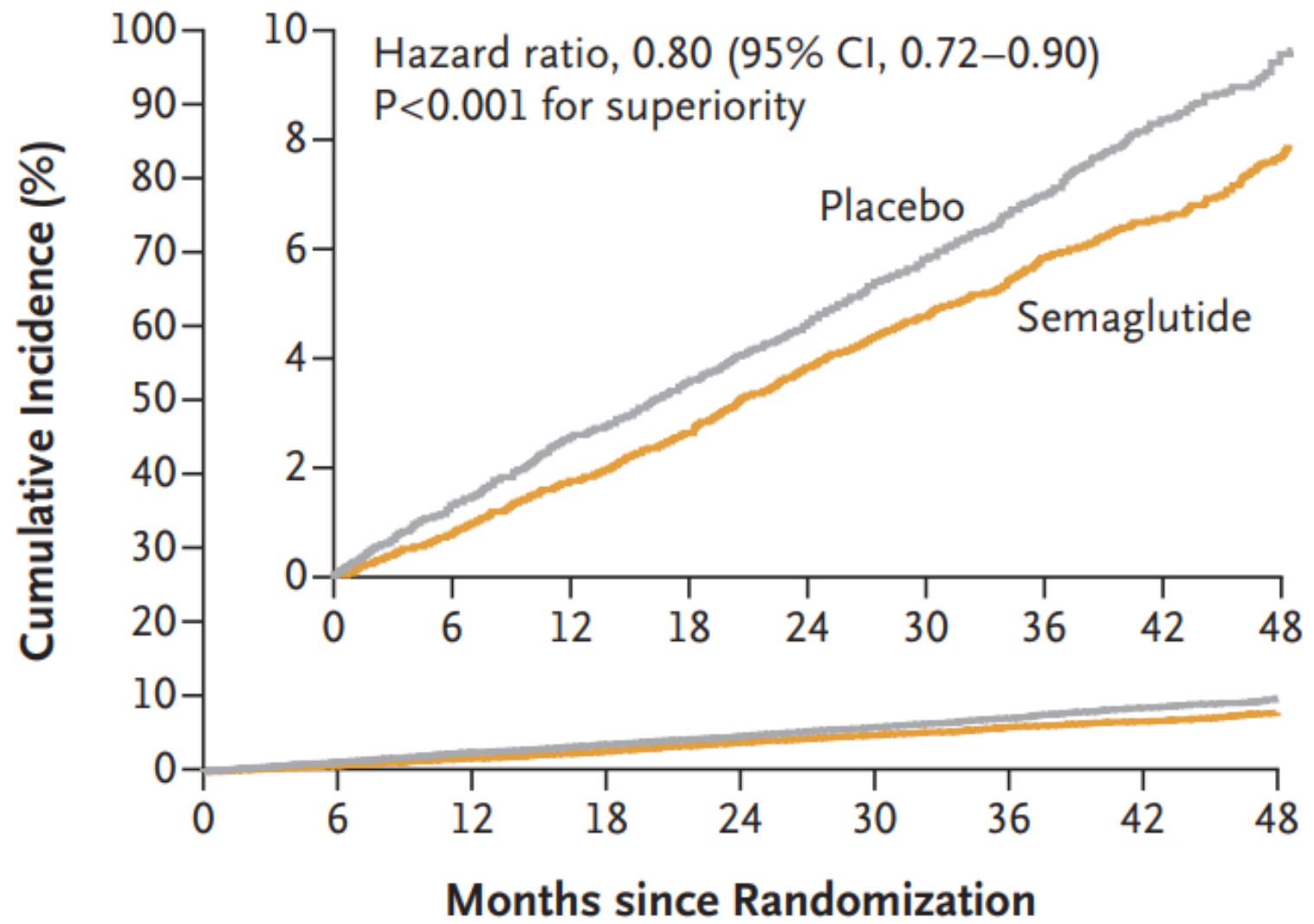
Completion:
2023

ORIGINAL ARTICLE

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

A. Michael Lincoff, M.D., Kirstine Brown-Frandsen, M.D., Helen M. Colhoun, M.D.,
John Deanfield, M.D., Scott S. Emerson, M.D., Ph.D., Sille Esbjerg, M.Sc.,
Søren Hardt-Lindberg, M.D., Ph.D., G. Kees Hovingh, M.D., Ph.D.,
Steven E. Kahn, M.B., Ch.B., Robert F. Kushner, M.D., Ildiko Lingvay, M.D., M.P.H.,
Tugce K. Oral, M.D., Marie M. Michelsen, M.D., Ph.D., Jorge Plutzky, M.D.,
Christoffer W. Tornøe, Ph.D., and Donna H. Ryan, M.D.,
for the SELECT Trial Investigators*

A Primary Cardiovascular Composite End Point



No. at Risk

Placebo	8801	8652	8487	8326	8164	7101	5660	4015	1672
Semaglutide	8803	8695	8561	8427	8254	7229	5777	4126	1734

Weight reduction in patients with diabetes—Section 5.1.1

It is recommended that individuals living with overweight or obesity aim to reduce weight and increase physical exercise to improve metabolic control and overall CVD risk profile.

I

A

Glucose-lowering medications with effects on weight loss (e.g. GLP-1 RAs) should be considered in patients with overweight or obesity to reduce weight.

IIa

B

Bariatric surgery should be considered for high and very high risk patients with BMI ≥ 35 kg/m² (\geq Class II) when repetitive and structured efforts of lifestyle changes combined with weight-reducing medications do not result in maintained weight loss.

IIa

B

Take home

- Farmacotherapie voor obesitas komt naar centre court
- Olifant in de kamer: betaalbaarheid
- Waarschijnlijk vergoeding via obesitas-gerelateerde aandoeningen: DM2, CVD, NASH, SAS, artrose
- (Off-label) gebruik via private sector zal vermoedelijk aanzienlijk toenemen