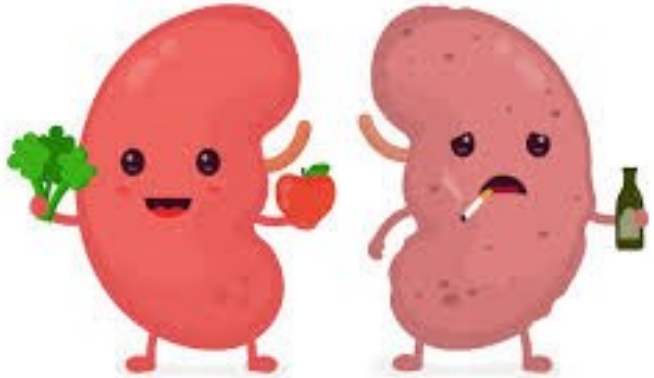
Medicinsk behandling av övervikt – med visst njurfokus



/Niclas Abrahamsson
Endokrin, Akademiska

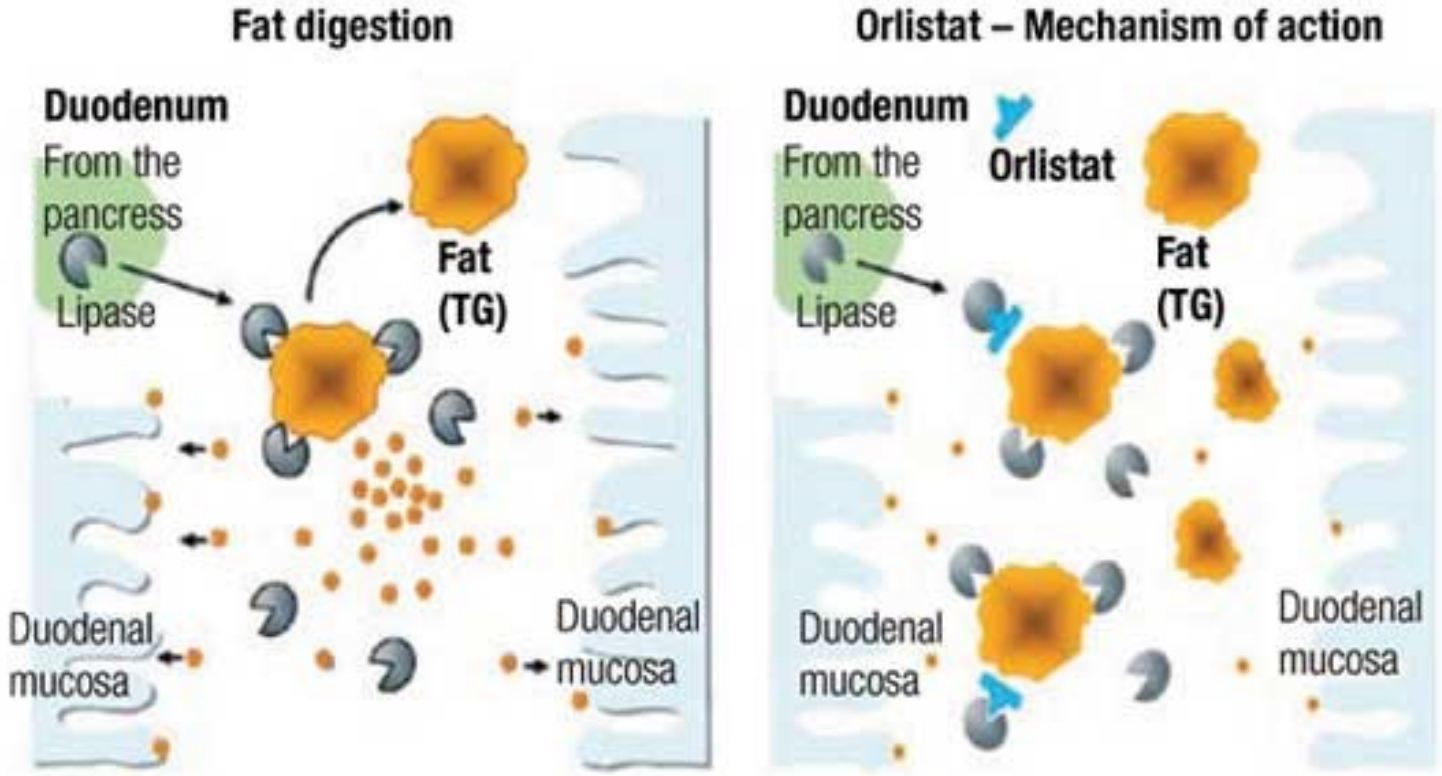
Mediciner

- **Orlistat** (Xenixal, Alli)
- **Naltrexon/Bupropion** (Mysimba)

- **Inkretiner: GLP-1-analoger** (Semaglutide) & **GLP-1/GIP-analoger** (Tirzepatide)

Orlistat (Xenical/Alli)

- Hämmar pankreatiskt lipas och därmed fettupptag, c:a 30% ut icke nedbrytet i feces
- Effekt = bieffekt = fettiga (explosiva) diarrer
- En utöver placebo viktnedgång om **-2,63kg**
- 180kr/mån
- Njurfunktion: ”Effekten av orlistat har inte studerats på patienter med nedsatt lever- och/eller njurfunktion, barn och äldre.”
- ”Användning av orlistat kan förknippas med hyperoxaluri och oxalatnefropati som ibland leder till njursvikt



Orlistat – mechanism of action.

BMJ Case Rep. 2017 Nov 12;2017

Orlistat-induced oxalate nephropathy: an under-recognised cause of chronic kidney disease

Laurence Richard Solomon [1], Andrew Christopher Nixon [1], Leanne Ogden [1], Beena Nair [2]

Two patients developed kidney failure due to oxalate deposition in the kidney while taking orlistat. Cessation of orlistat was followed by partial recovery of kidney function. The

Naltrexon/Bupropion (Mysimba)

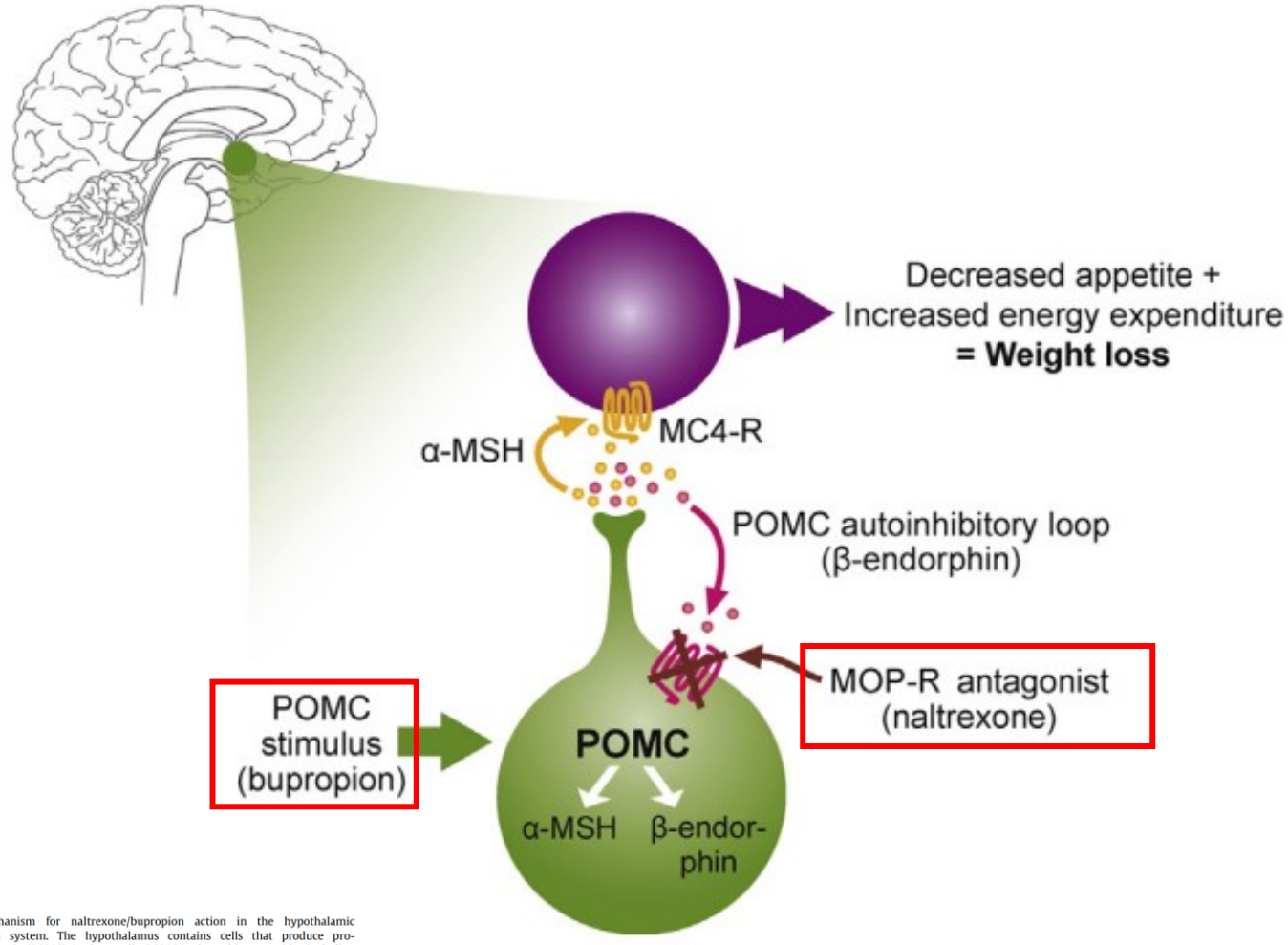


Fig. 3. Mechanism for naltrexone/bupropion action in the hypothalamic melanocortin system. The hypothalamus contains cells that produce pro-opiomelanocortin (POMC). In these cells, POMC is cleaved into peptides including α-melanocyte stimulating hormone (α-MSH) and β-endorphin, which are co-released from POMC cells. α-MSH stimulates the melanocortin-4 receptor (MC4R), which leads to decreased food intake, increased energy expenditure and weight loss. β-Endorphin binds to the inhibitory μ-opioid receptor (MOP-R) on POMC cells and acts like a brake to reduce activity of POMC cells. Bupropion stimulates activity of POMC cells, increasing POMC production and release of α-MSH and β-endorphin. Naltrexone blocks the MOP-R and prevents the β-endorphin-mediated feedback autoinhibition of POMC cells. Together, the naltrexone/bupropion combination produces a greater increase in POMC activity than either drug alone. This increased POMC activity is thought to contribute to weight loss in humans.

Pharmacological Research 84 (2014) 1–11

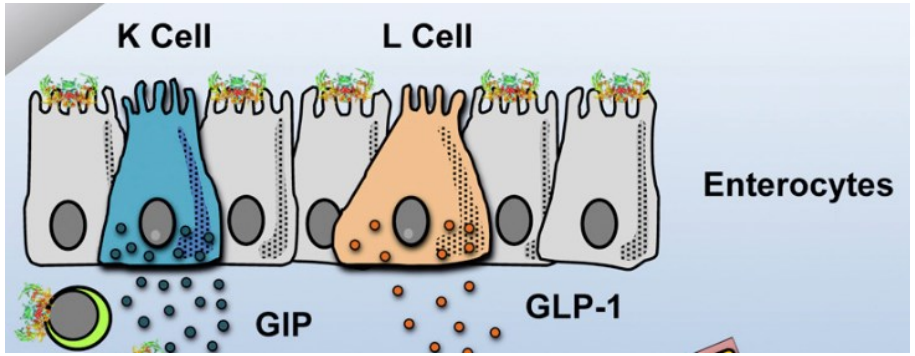
Naltrexone/bupropion for obesity: An investigational combination pharmacotherapy for weight loss

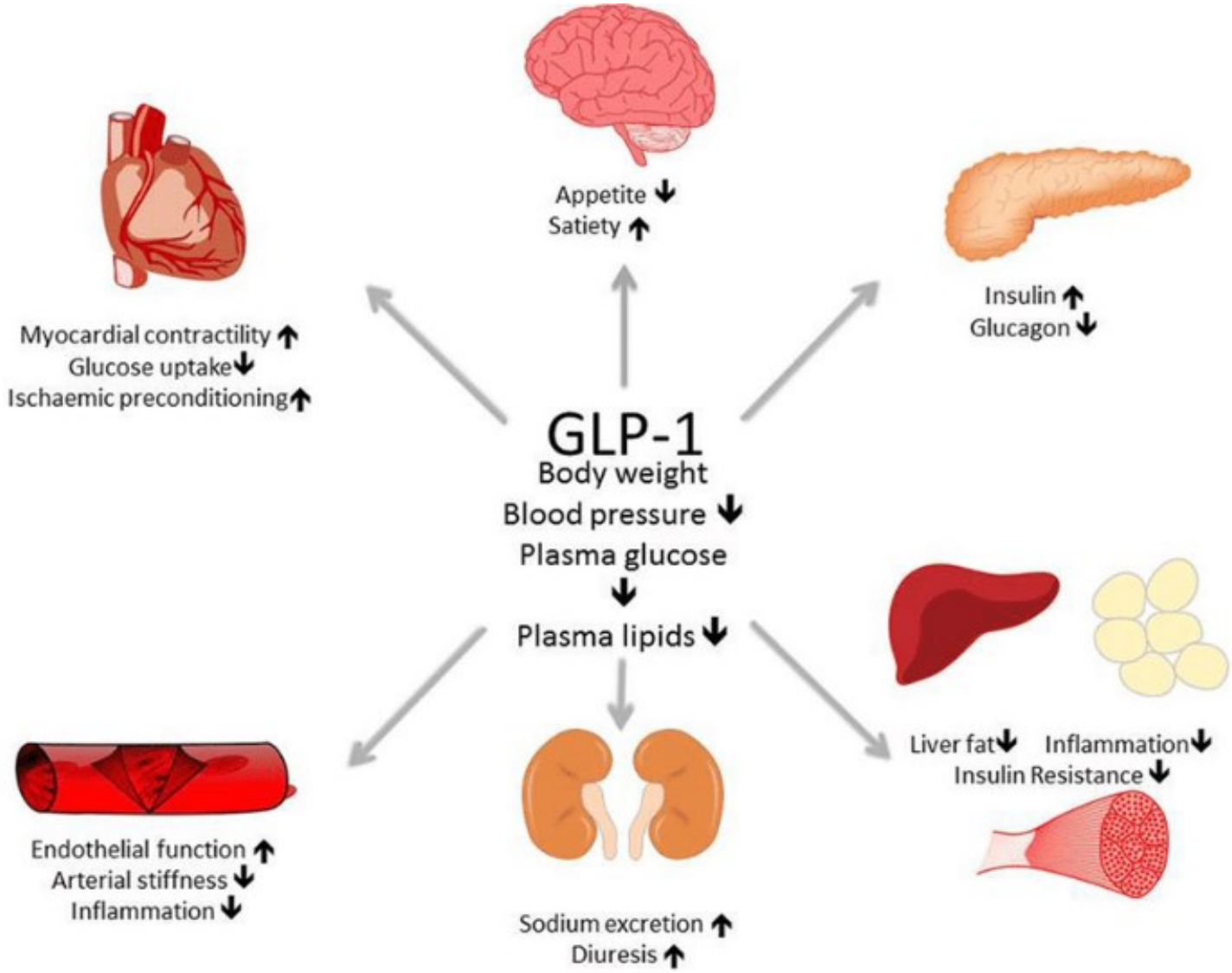
Sonja K. Billes[a], Puspha Sinnayah[b], Michael A. Cowley[c,*]

- Viktnedgång jmf med placebo. 5,0 % (32mg) resp 3,7 % (16mg)
- Biv: ångest, sömnproblem, huvudvärk, yrsel, pulsökning, illamående
- Kontraind: Terminal njursvikt
- Om måttligt/svårt nedsatt njurfunktion halverad dos
- Utan subvention, 1100kr/mån

GLP-1-analoger

- Förlångsammar magsäckstömning
- Sänker aptit, craving, reward, smakhöjare

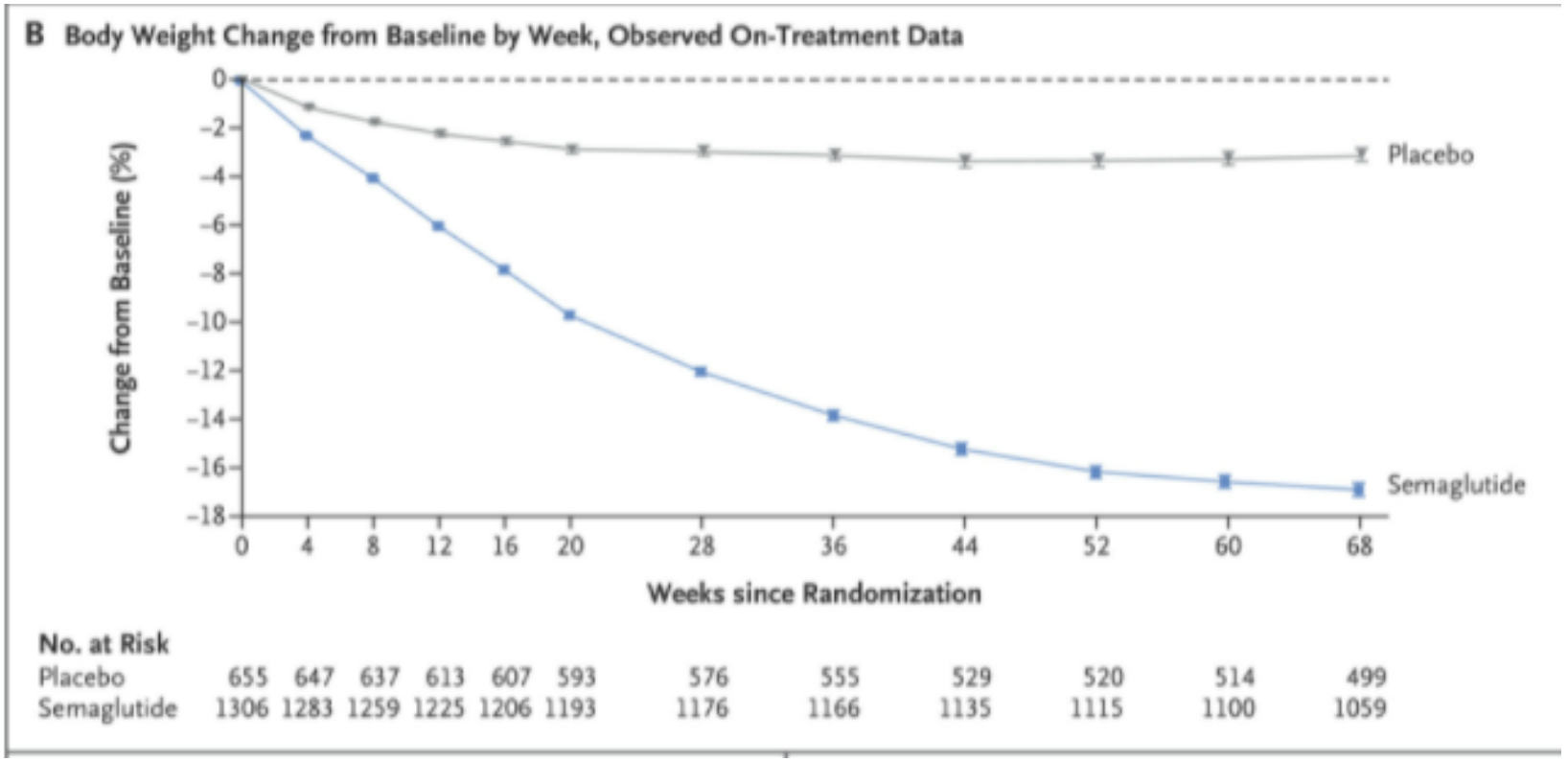




Semaglutide (Ozempic©/Wegovy©)

- N1900
- 68v
- 2,4mg/v (högdosen)
- Ca 3.200kr/mån

Fass:
Ingen dosjustering krävs för patienter med lindrig, måttlig eller svår nedsättning av njurfunktionen. Erfarenheten från användning av semaglutid hos patienter med terminal njursjukdom är begränsad.

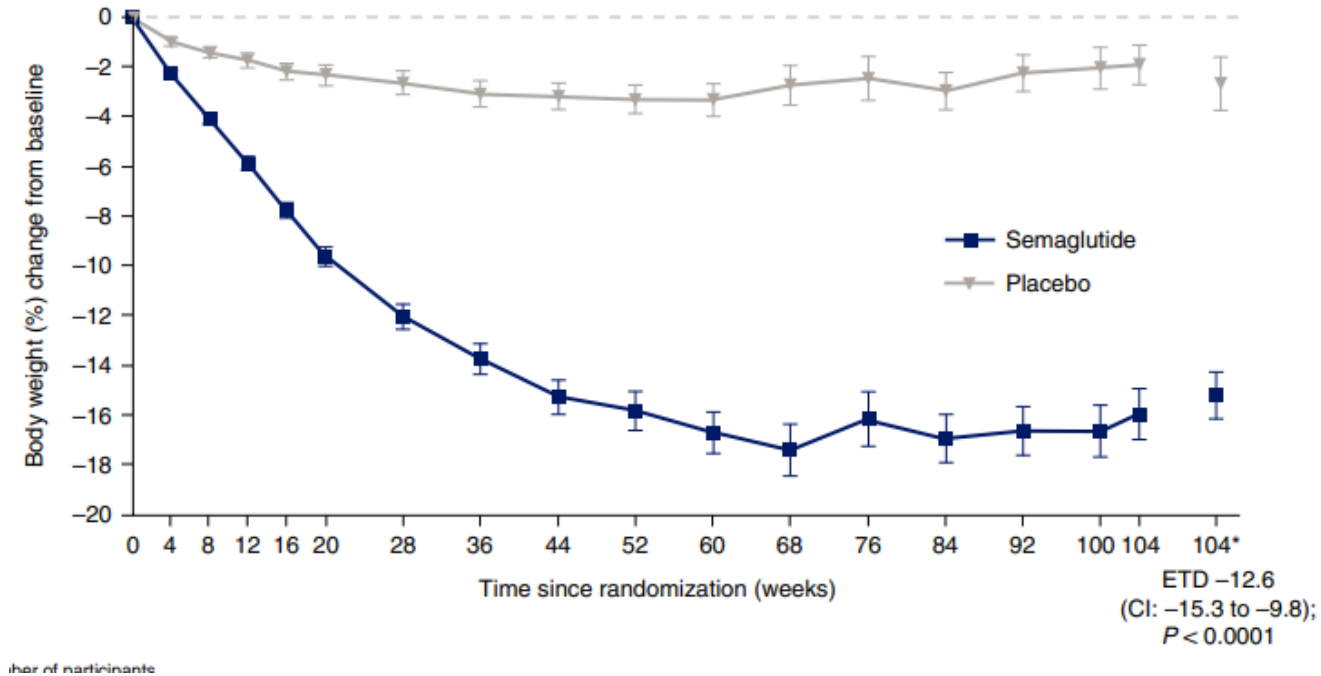


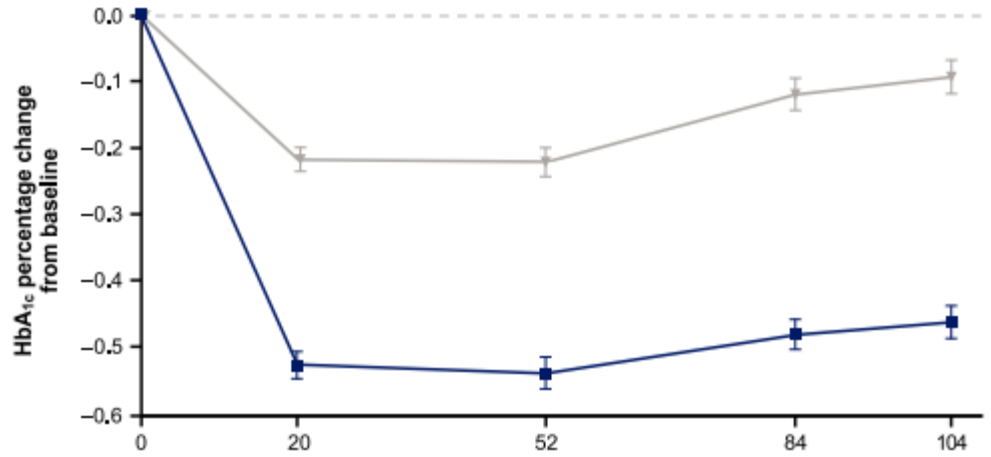
(STEP-1)

Once-Weekly Semaglutide in Adults with Overweight or Obesity

John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D., Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D., Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D., Sean Wharton, M.D., Pharm.D., Koutaro Yokote, M.D., Ph.D., et al., for the STEP 1 Study Group*

Långtidsdata



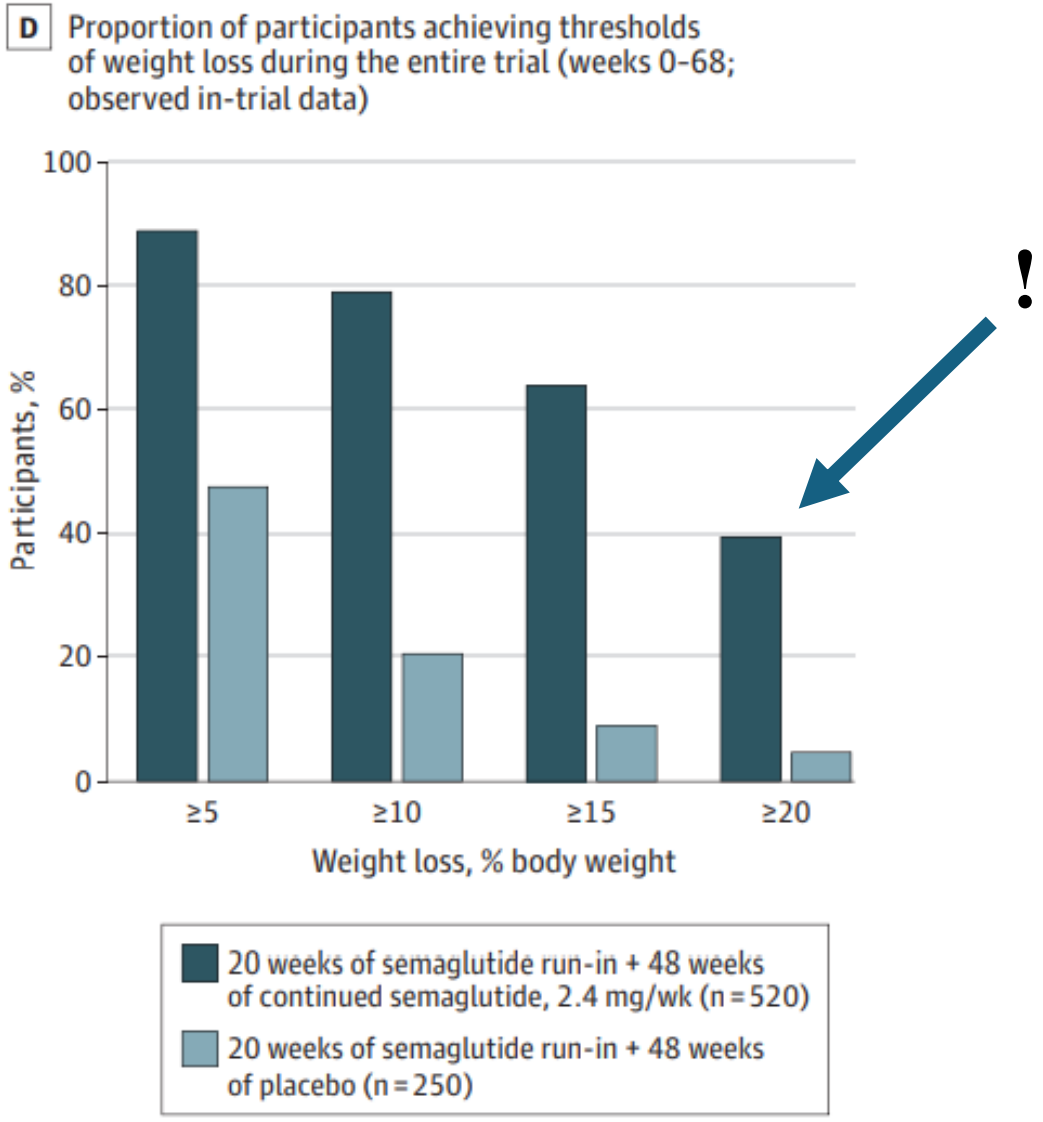


Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial

Nature Medicine | Volume 28 | October 2022 | 2083–2091

Semaglutide - STEP-4

- N900
- 68v
- alla beh i 20v
- sedan 2,4mg/v vs placebo



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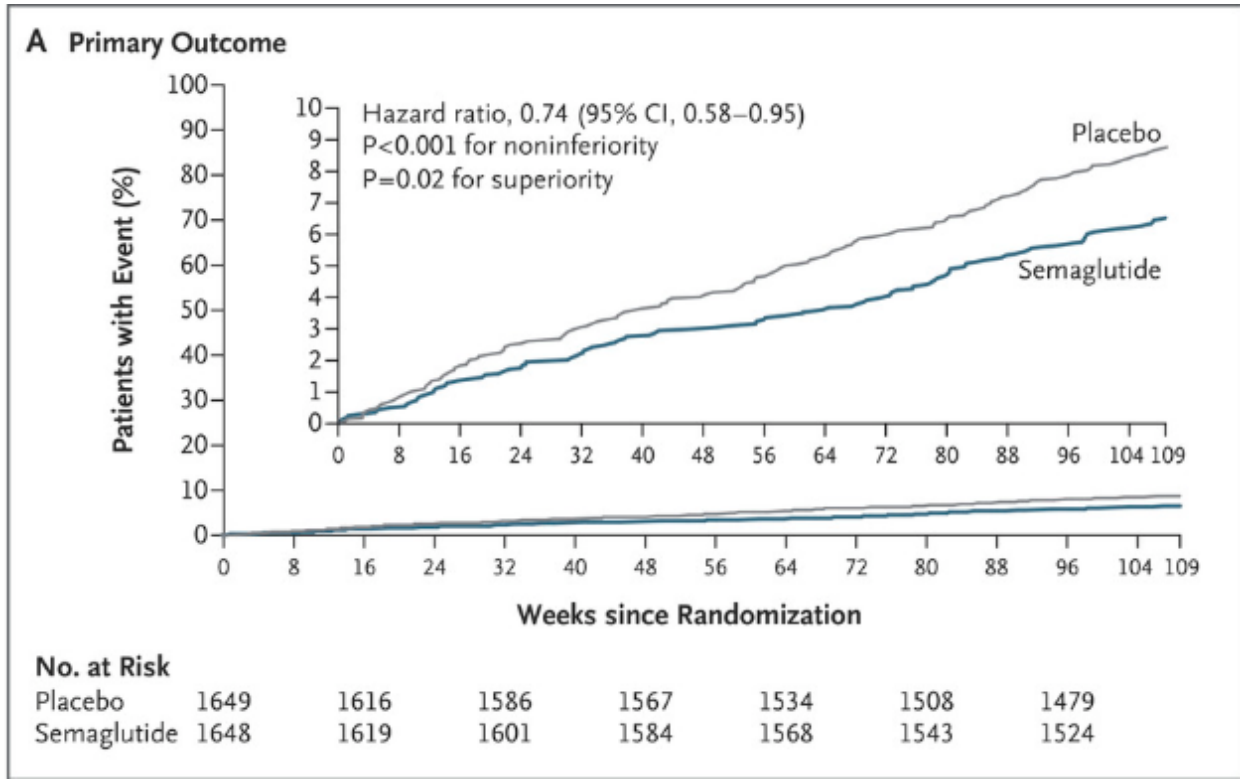
Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity
The STEP 4 Randomized Clinical Trial

Domenica Rubino, MD[1]; Niclas Abrahamsson, MD[2]; Melanie Davies, MD[3,4]; et al

Semaglutide –mortalitet hos:

Diabetiker



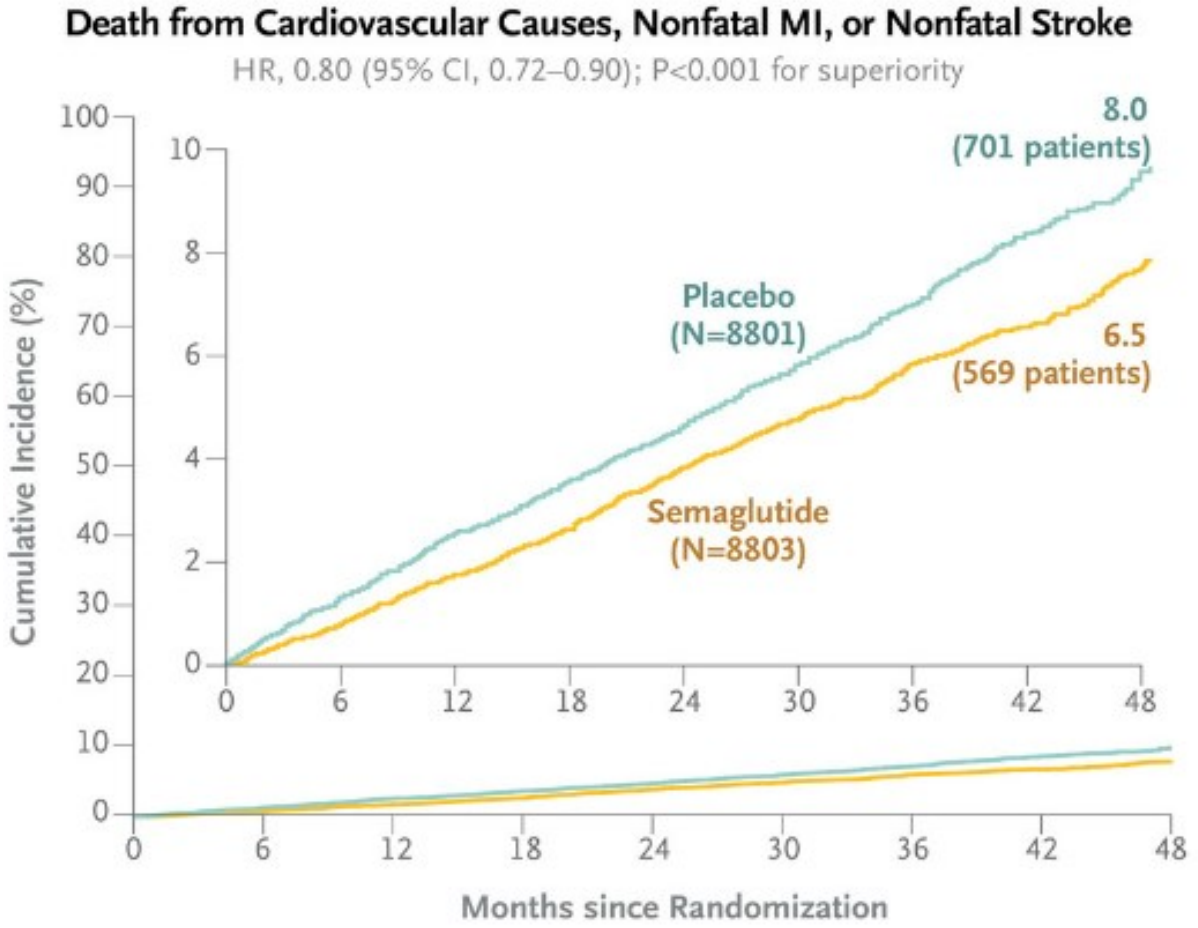
- N3300
- 2 år
- a composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke)

NEJM 2016

Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Steven P. Marso, M.D., Stephen C. Bain, M.D., Agostino Consoli, M.D., Freddy G. Eliaschewitz, M.D., Esteban Jódar, M.D., Lawrence A. Leiter, M.D.,

Icke-Diabetiker

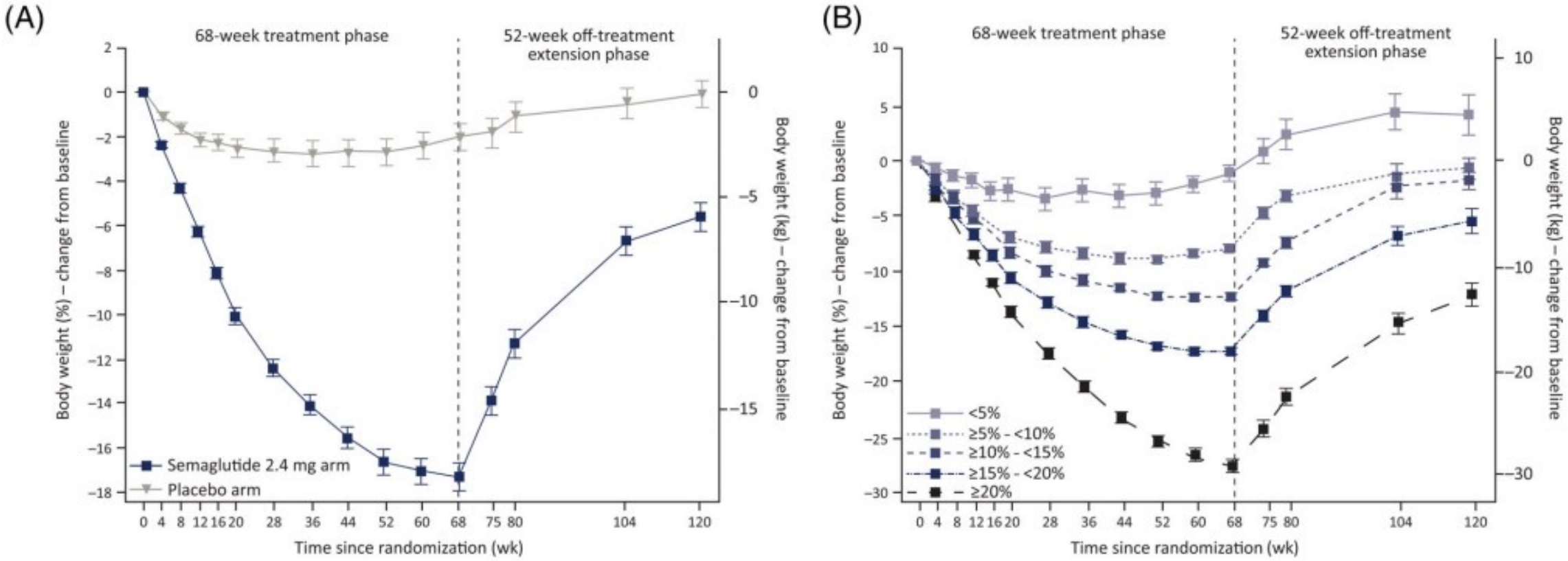


Sekundärprofylax

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

Lincoff AM et al. DOI: 10.1056/NEJMoa2307563

Vad händer efter studien...

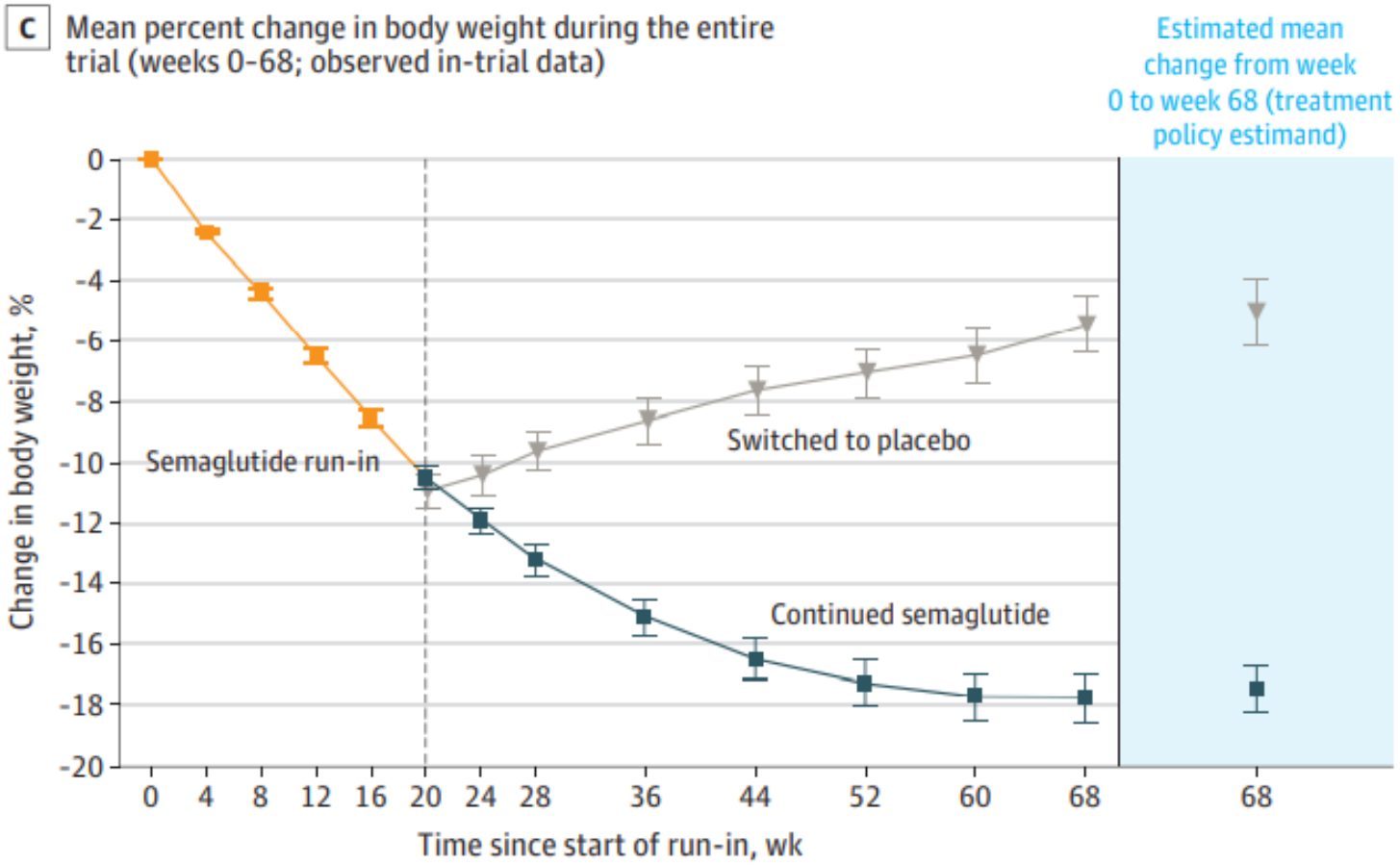


Diabetes Obes Metab. 2022;24:1553–1564.

Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension

Vad händer om man sätter ut GLP-1-analog-behandling, men fortsatt levnadsvanebehandling? (STEP-4)

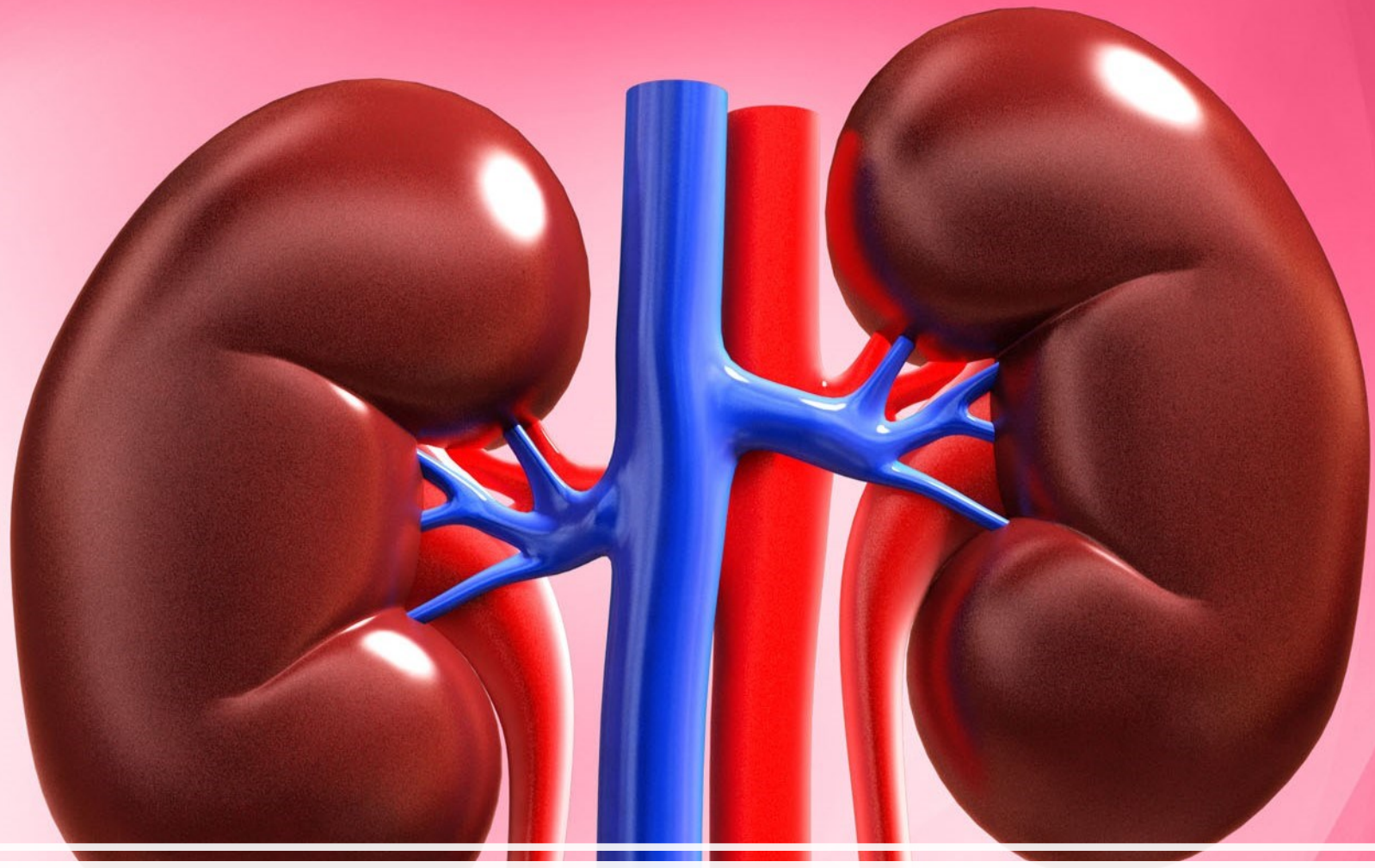
- N900
- 68v
- alla beh i 20v
- sedan 2,4mg/v vs placebo



Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity

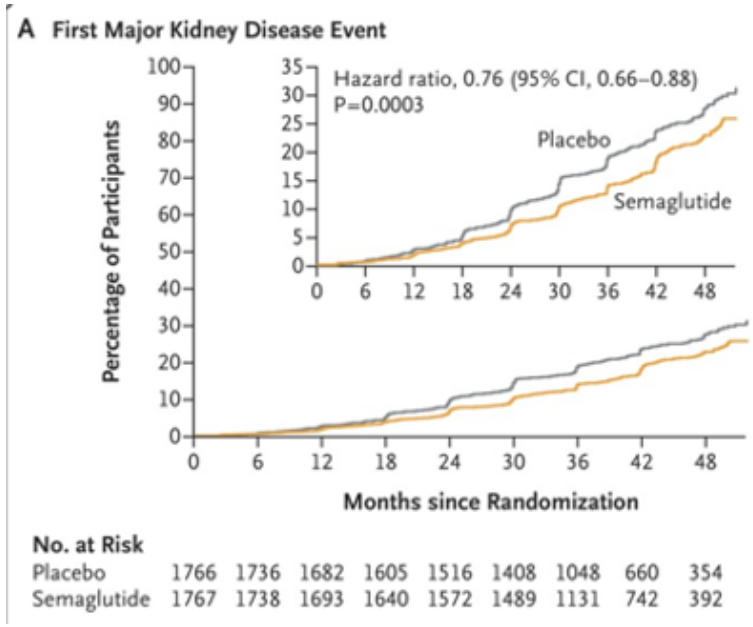
The STEP 4 Randomized Clinical Trial

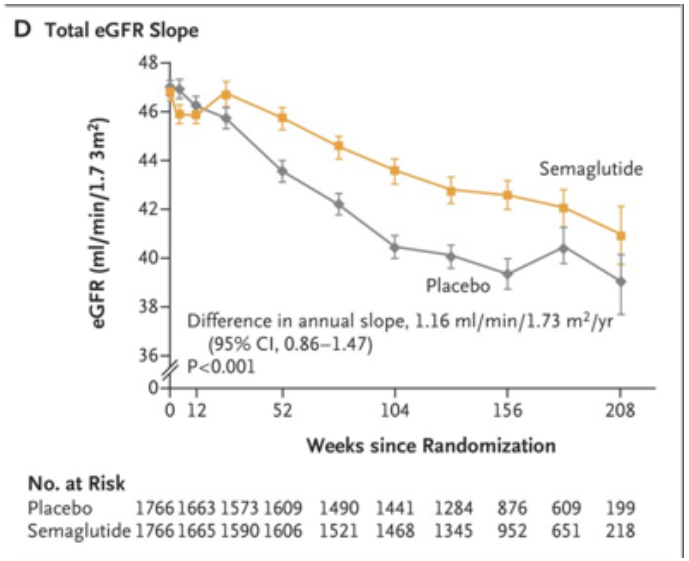
Domenica Rubino, MD[1]; Niclas Abrahamsson, MD[2]; Melanie Davies, MD[3,4]; et al

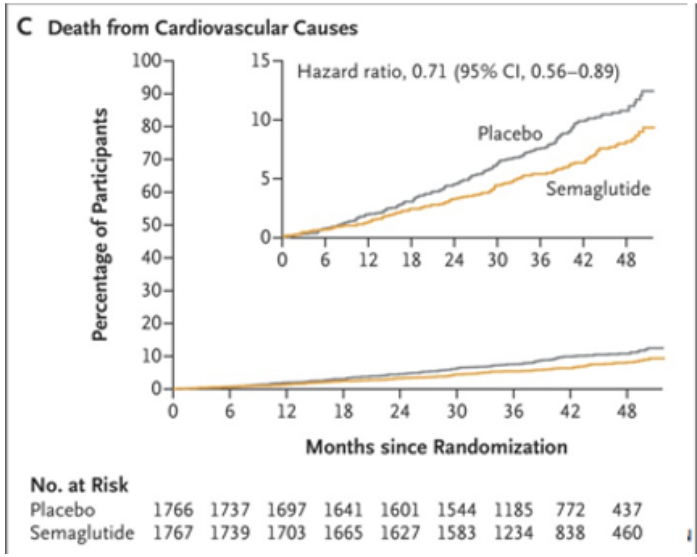


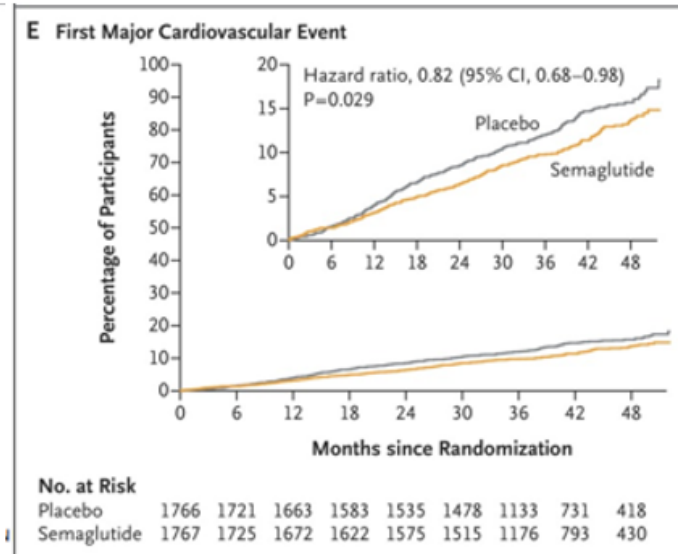
Semaglutide & Kronisk njursjukdom

Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes









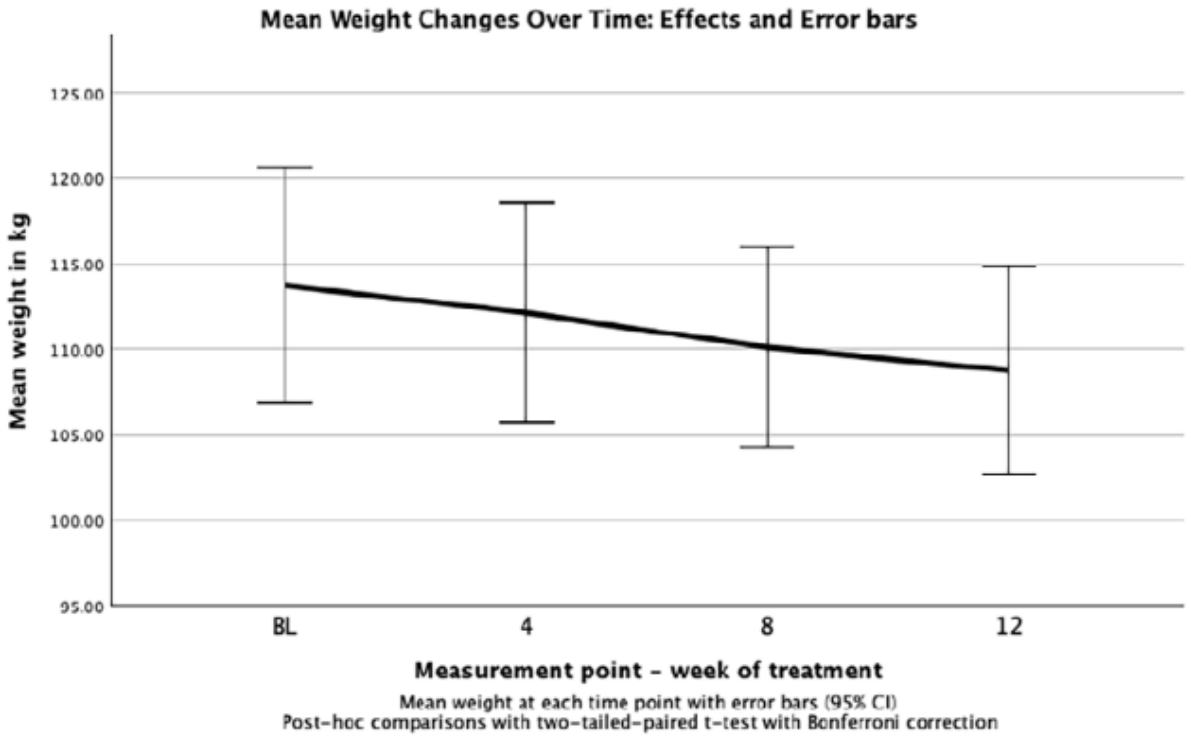
- N3500
- T2DM+njursvikt i alla grader
- Composite (dialysstart, njurTx, eGFR <15, 50% reduktion av eGFR, njurrelaterad död

Twenty people would need to be treated with semaglutide over a 3-year period to prevent one major kidney disease event.

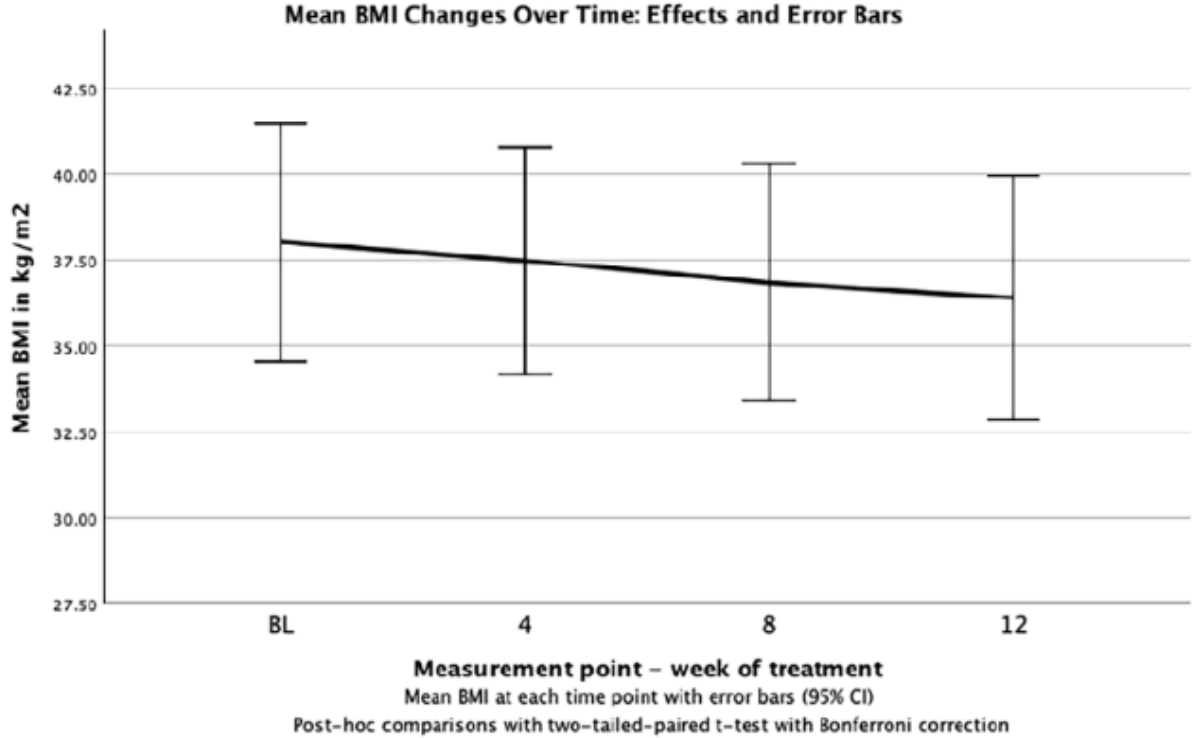
Pre-transplantation

Semaglutide in patients with kidney failure and obesity undergoing dialysis and wishing to be transplanted: A prospective, observational, open-label study

(C)



(F)



N13
BMI>30kg/m2
HD
Semaglutide 1,0mg.

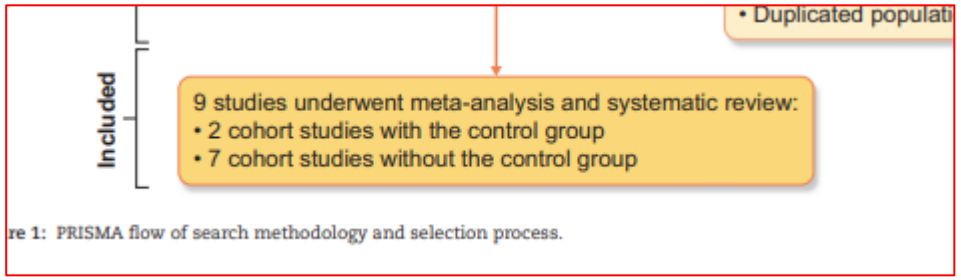
Milda biv; GI framförallt, 1 pat avslutade, resten nöjda

Lenka Vanek MD[1,2] | Amelie Kurnikowski MD[2] | Simon Krenn MD[2,3]
Sebastian Mussnig MD[1,2] | Manfred Hecking PhD[1,2,4]

Diabetes Obes Metab. 2024;26:5931–5941

Semaglutide post-Transplantation

Safety and efficacy of glucagon-like peptide-1 receptor agonists among kidney transplant recipients: a systematic review and meta-analysis



re 1: PRISMA flow of search methodology and selection process.

Table 2: Adverse events

Adverse events	Patients evaluated, *n*	Incidence, *n* (%)
Drug discontinuation due to any cause	140	14 (10)
Nausea and vomiting	119	21 (17.6)
Diarrhoea	79	6 (7.6)
Injection site pain	37	2 (5.4)
Hypoglycaemia	79	3 (3.8)
Pancreatitis	154	1 (0.6)
Pancreas cancer	154	1 (0.6)

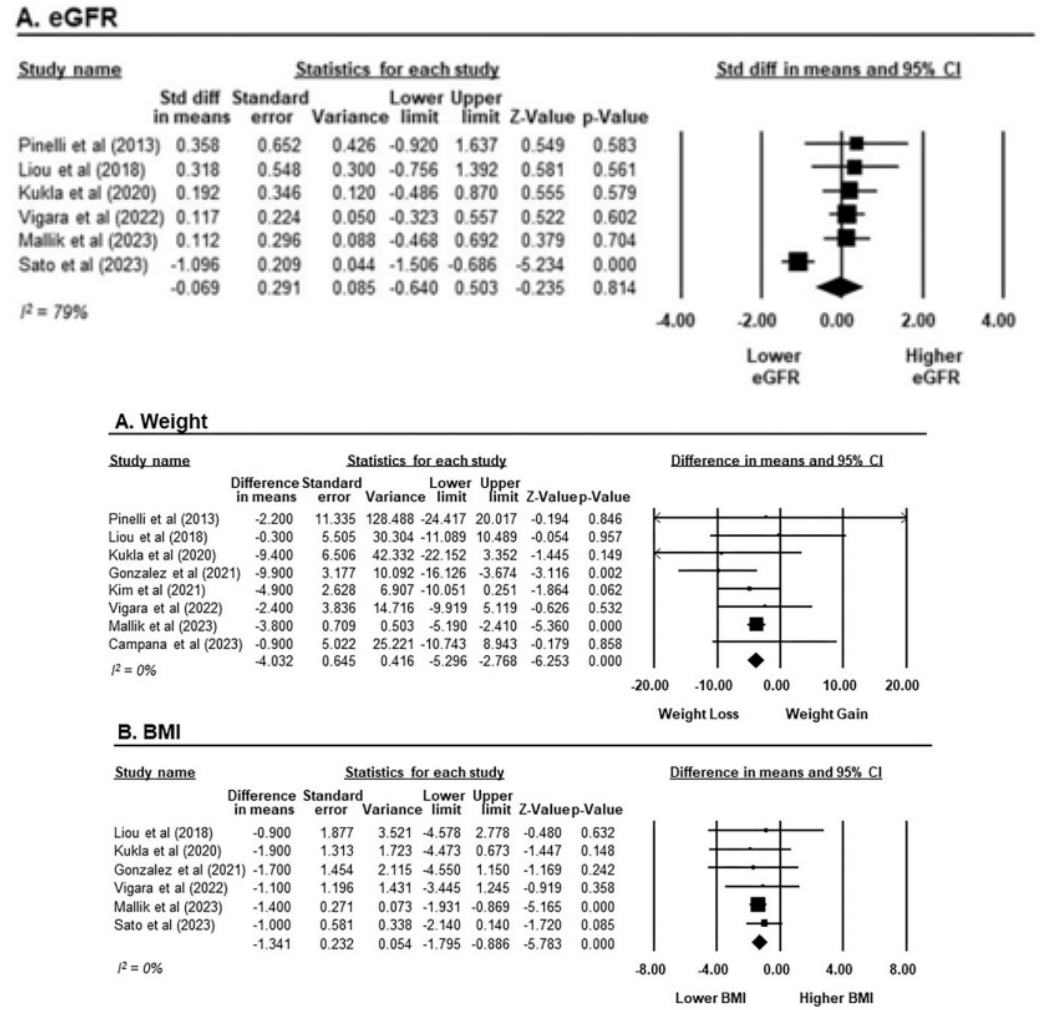


Figure 5: The changes in weight and BMI from baseline after GLP-1RAs treatment in KTRs. **(A)** Weight presented on a scale ranging from −20 to 20 kg. **(B)** BMI presented on a scale ranging from −8 to 8 kg/m². Studies are identified by the name of the first author and the year of publication. MDs were determined using the random effects model.

Mikrodosering...

Example of Microdosing Schedule:

1. **Week 1-4**: 0.05 mg weekly.
2. **5-8**: 0.1 mg weekly.
3. **9-12**: 0.2 mg weekly.
4. Gradually increase by 0.1 mg every 4 weeks until reaching the effective dose.

0,25/0,5/1,0mgx4st=1100kr. 0,05mg=55kr
2,4mg ca 3200kr/månad

Tirzepatide -GLP-1/GIP-analog Mounjaro/Zepbound

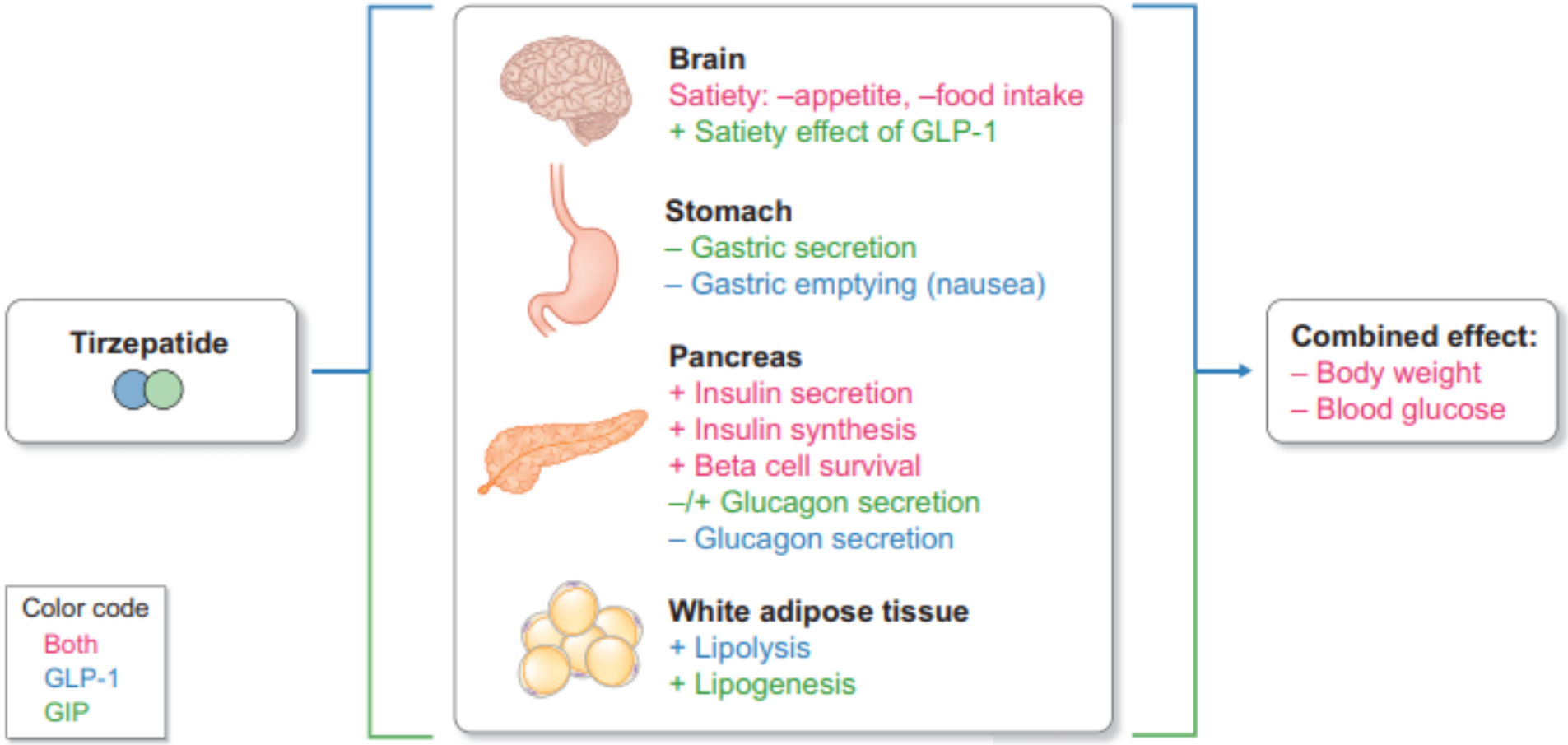
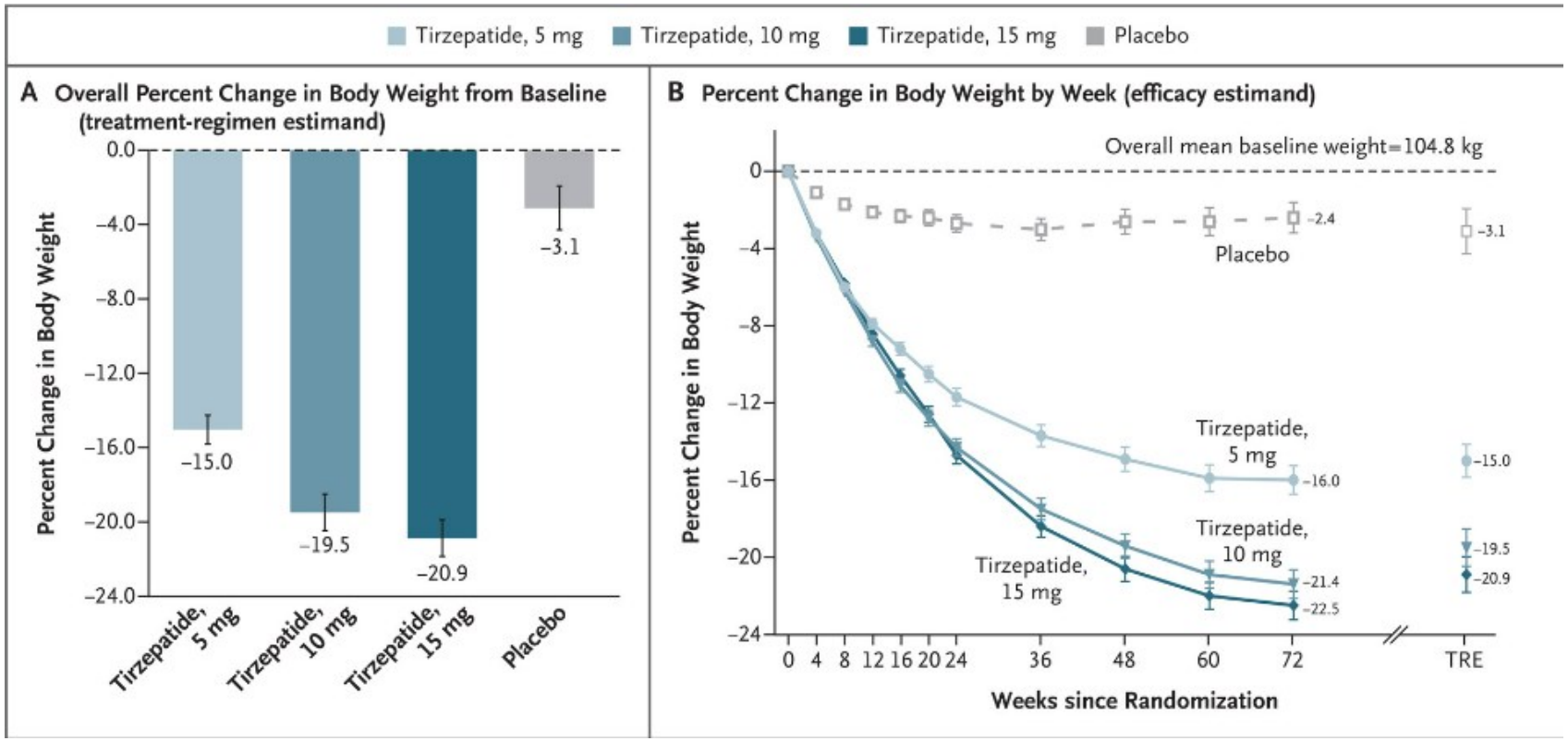


Figure 3: Shared and unique actions by GIP and GLP1 in key target organs that may be reproduced by tirzepatide.

Clinical Kidney Journal, 2023, vol. 16, no. 5, 797–808

Tirzepatide -vikteffekt

Högdos
4500kr/mån



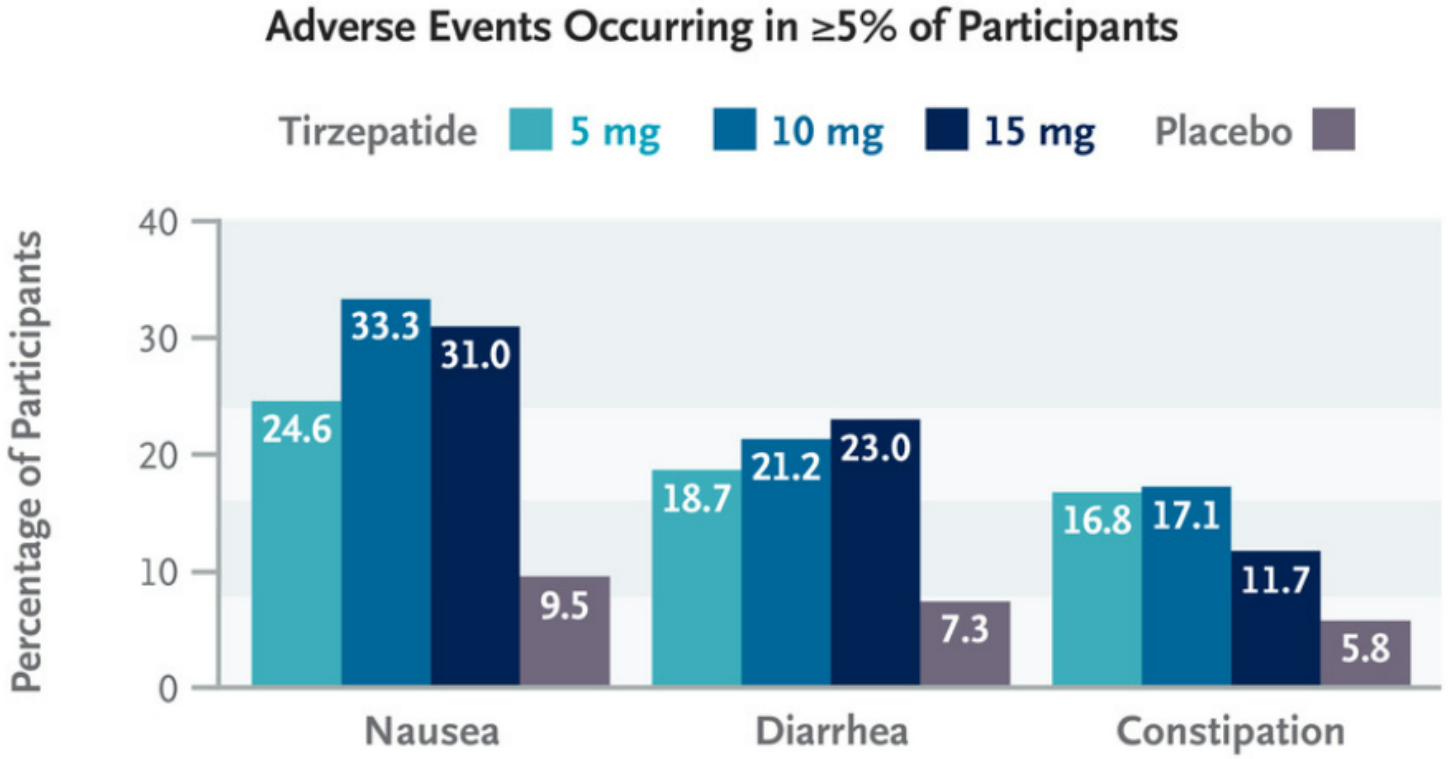
- N2500
- bmi 30 or 27 with comorbidity
- non-diabetics

N Engl J Med 2022; 387:205-216

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*

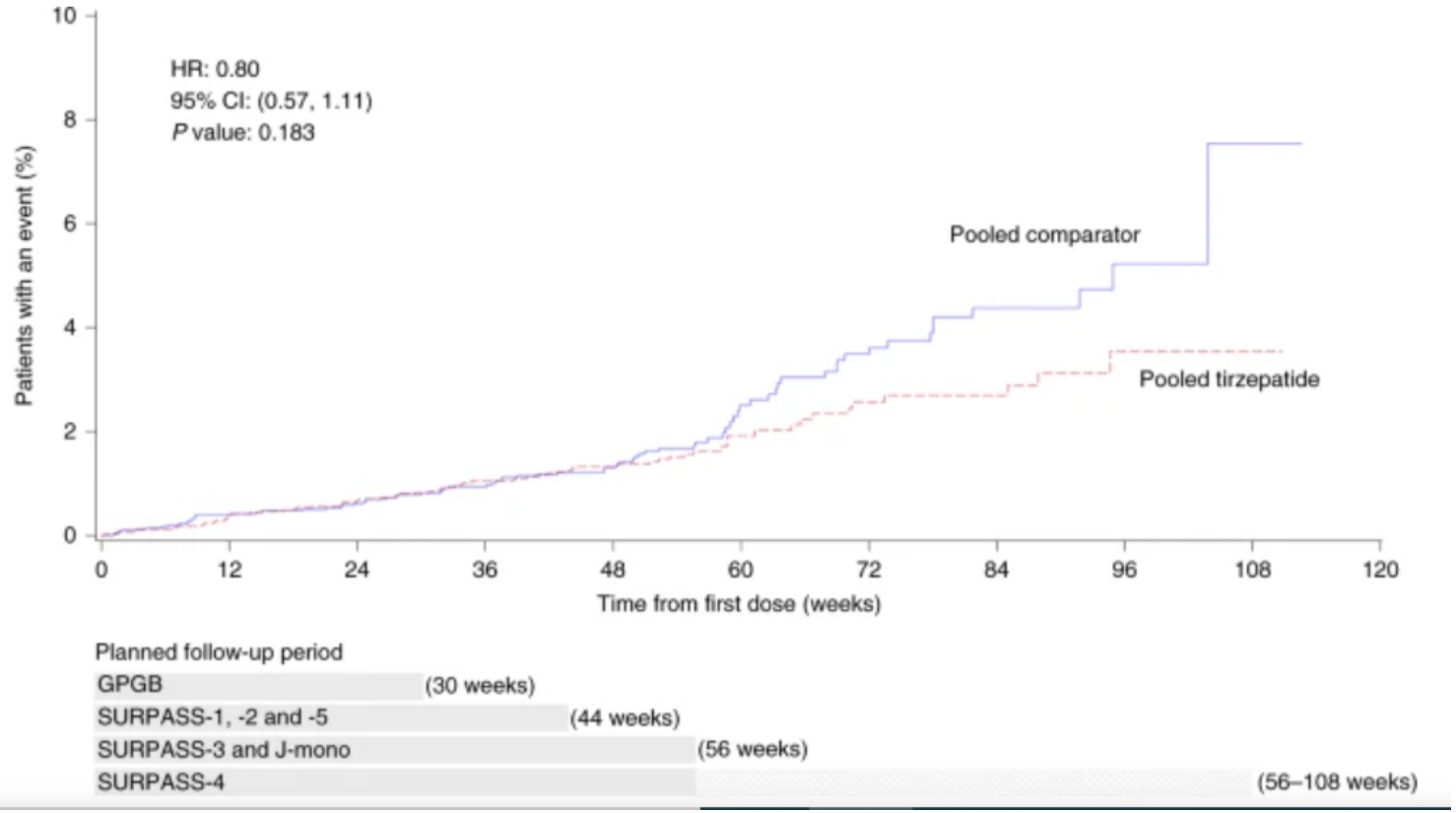
Tirzepatide - biverkningar



Variable	Tirzepatide, 5 mg (N=630)	Tirzepatide, 10 mg (N=636)	Tirzepatide, 15 mg (N=630)	Placebo (N=643)
		number (percent)		
Participants with ≥1 adverse event during treatment period	510 (81.0)	520 (81.8)	497 (78.9)	463 (72.0)

Tirzepatide - mortalitetsdata

Fig. 2: Adjusted Kaplan–Meier plot of pooled tirzepatide versus pooled comparator effect on time to first occurrence of adjudication-confirmed MACE-4 (primary outcome).



Tirzepatide cardiovascular event risk assessment: a pre-specified meta-analysis

Naveed Sattar, Darren K. McGuire, Imre Pavo, Govinda J. Weerakkody, Hiroshi Nishiyama, Russell J. Wiese & Sophia Zoungas

Nature Medicine **28**, 591–598 (2022) | Cite this article

Vilken är bäst då?

- N751, 72 veckor
- Tirzepatide 10-15mg vs Semaglutide 1,7-2,4mg

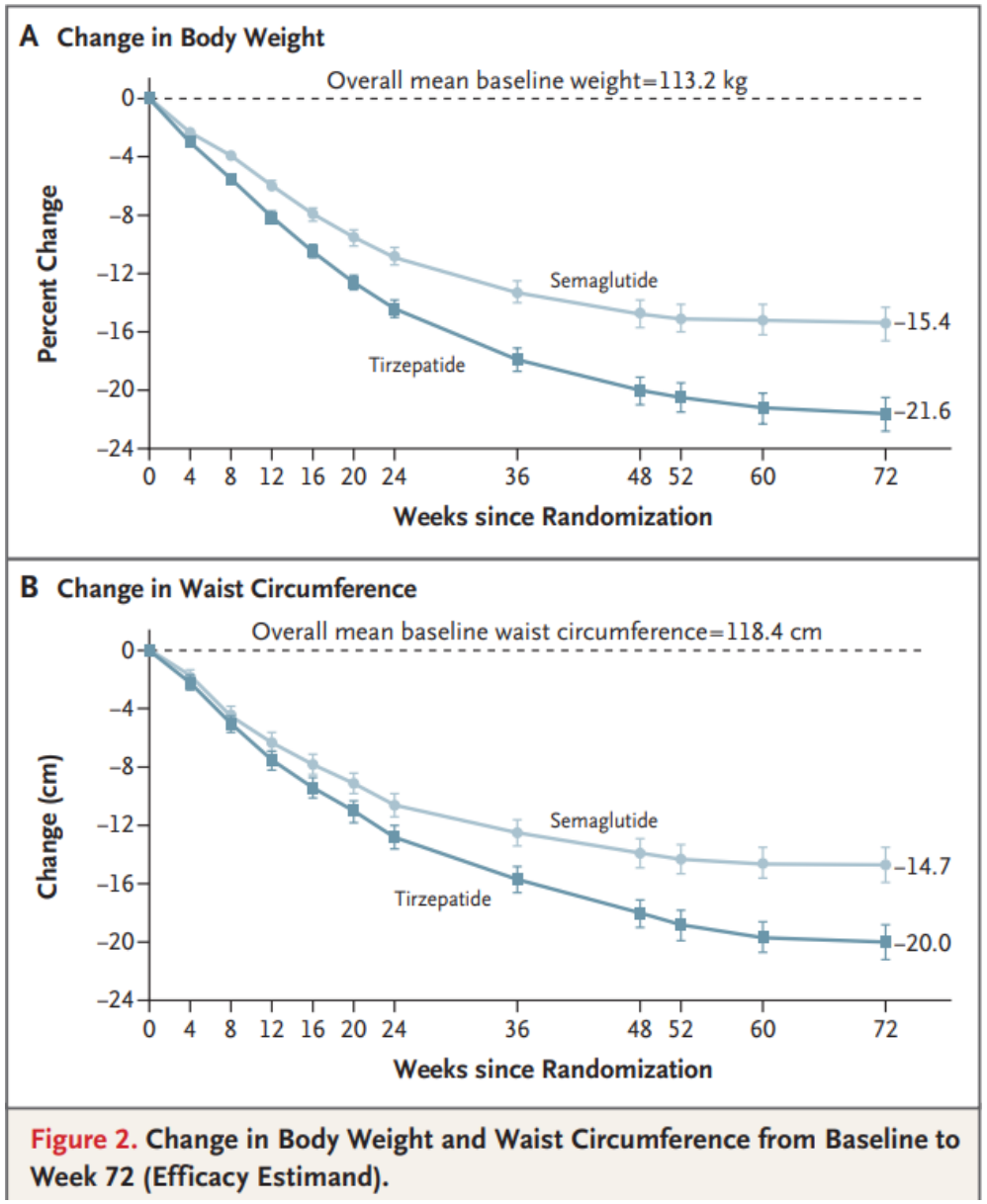


Figure 2. Change in Body Weight and Waist Circumference from Baseline to Week 72 (Efficacy Estimand).

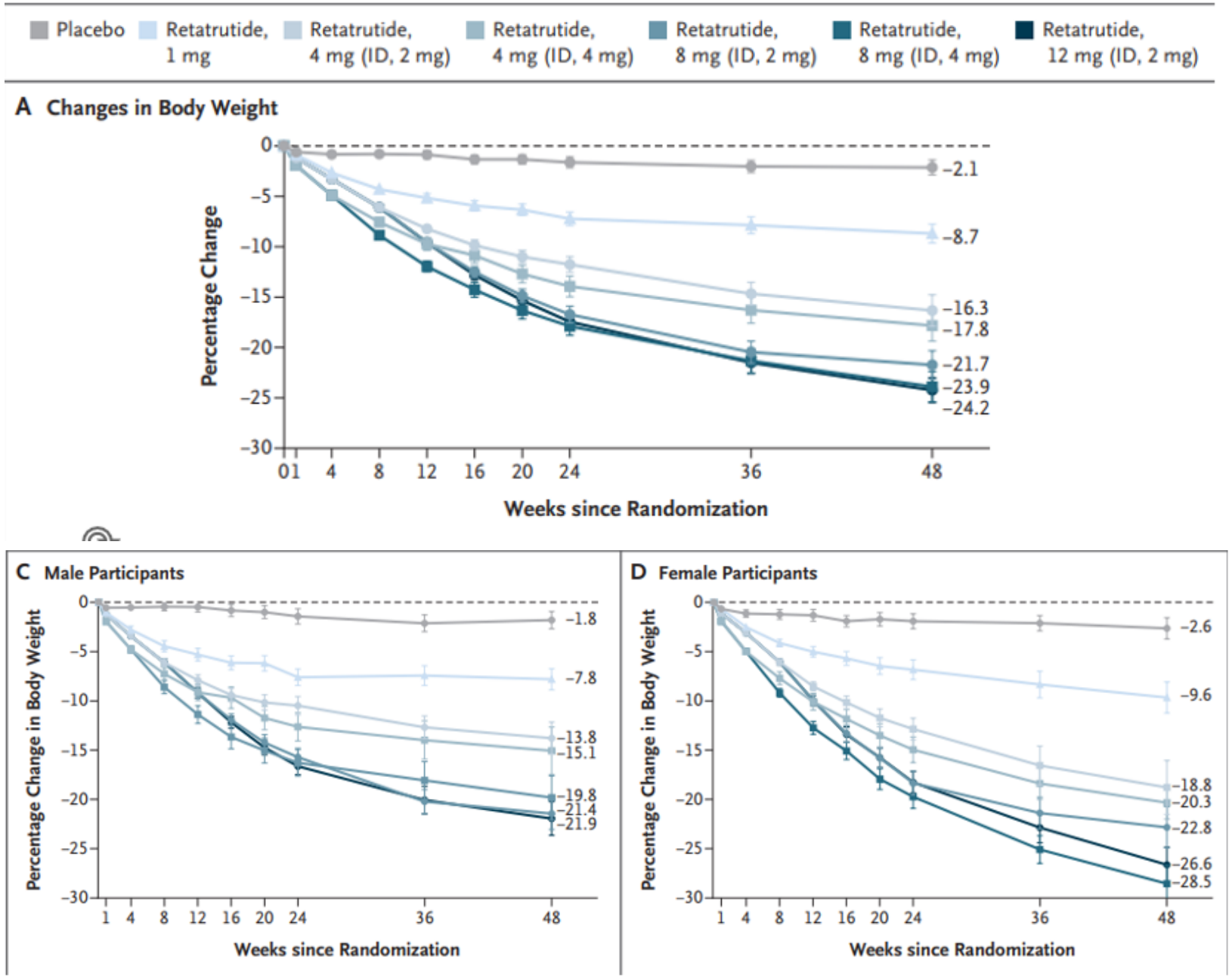
Tirzepatide as Compared with Semaglutide for the Treatment of Obesity

This article was published on May 11, 2025, at NEJM.org.

Vad finns runt hörnet...

Retatrutide –
GLP-1/GIP/Glukagon-agonist – ”Trippelagonist”

- RCT, n 338
- 48veckor
- 1 inj/vecka
- BMI 37



N Engl J Med 2023;389:514-26.

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