

# Obesitas\* und Niere

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Obesitas\* = BMI >30; Übergewicht = BMI >25 kg/m<sup>2</sup>

I report the following potential duality/dualities of interest in the field covered by my lecture:

- Consultant:** UpToDate Inc., Bayer, Boehringer, Novo Nordisk,
- Employee:** KfH
- Research Support:** European Union, Canadian Institutes of Health Research, AstraZeneca, Bayer, Boehringer Ingelheim, Novo Nordisk, Sanofi
- Speaker's Bureau:** AstraZeneca, Bayer, Boehringer, Novartis, Novo Nordisk

# Obesitas und Niere

- Erste Fallbeschreibungen
- Epidemiologie
- Therapie der Obesitas
  - Chirurgie
  - Diät
  - Medikamente

# The nephrotic syndrome: a complication of massive obesity

Beschreibt 4 Patienten mit massiver Obesitas und nephrot. Proteinurie. Nach Gewichtsabnahme Verminderung der Proteinurie um 50-80%:

Gew. -48kg, Uprot von 5,2 auf 1g/d

Gew. -49kg, Uprot von 4,2 auf 0,4g/d, Gew + 54kg,  
Uprot 7,3g/d



## **Kidney histology in extremely obese persons (no diabetes) with normal kidney function**

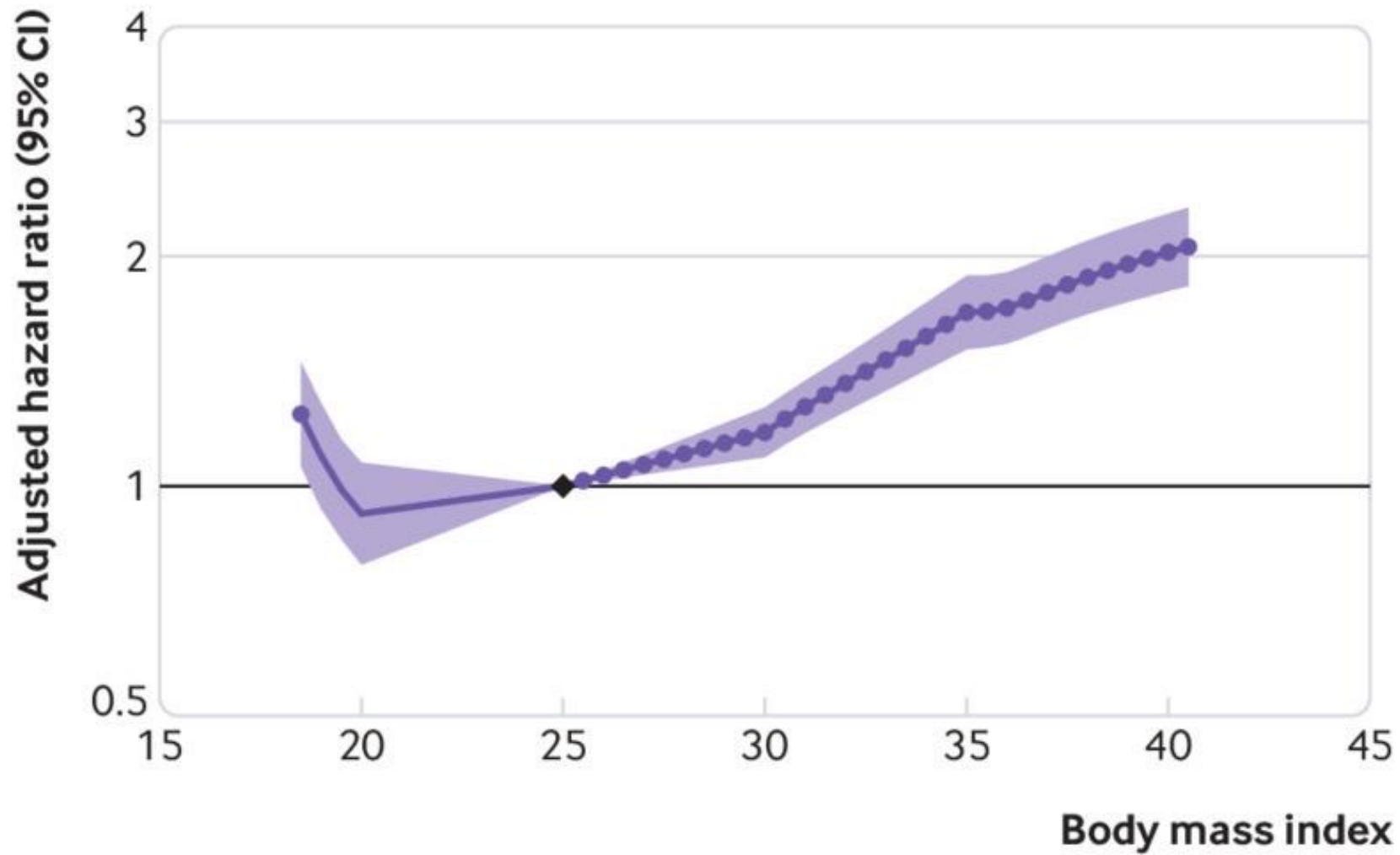
Beschreibt 95 konsekutive Patienten mit BMI  $>40\text{kg/m}^2$  und Nierenpunktion bei bariatrischer Chirurgie. Vergleich: 40 Protokollbiopsien von Nierenspendern bei Transplantation.

- FSGS nur bei 5 Obesitas-Pat. (BMI  $59\text{ kg/m}^2$ , UACR  $<500\text{mg/g}$ )
- Mesangiale Proliferation, Podozytenhypertrophie, Glomerulomegalie bei den meisten Obesitas-Pat., selten bei Kontrollen

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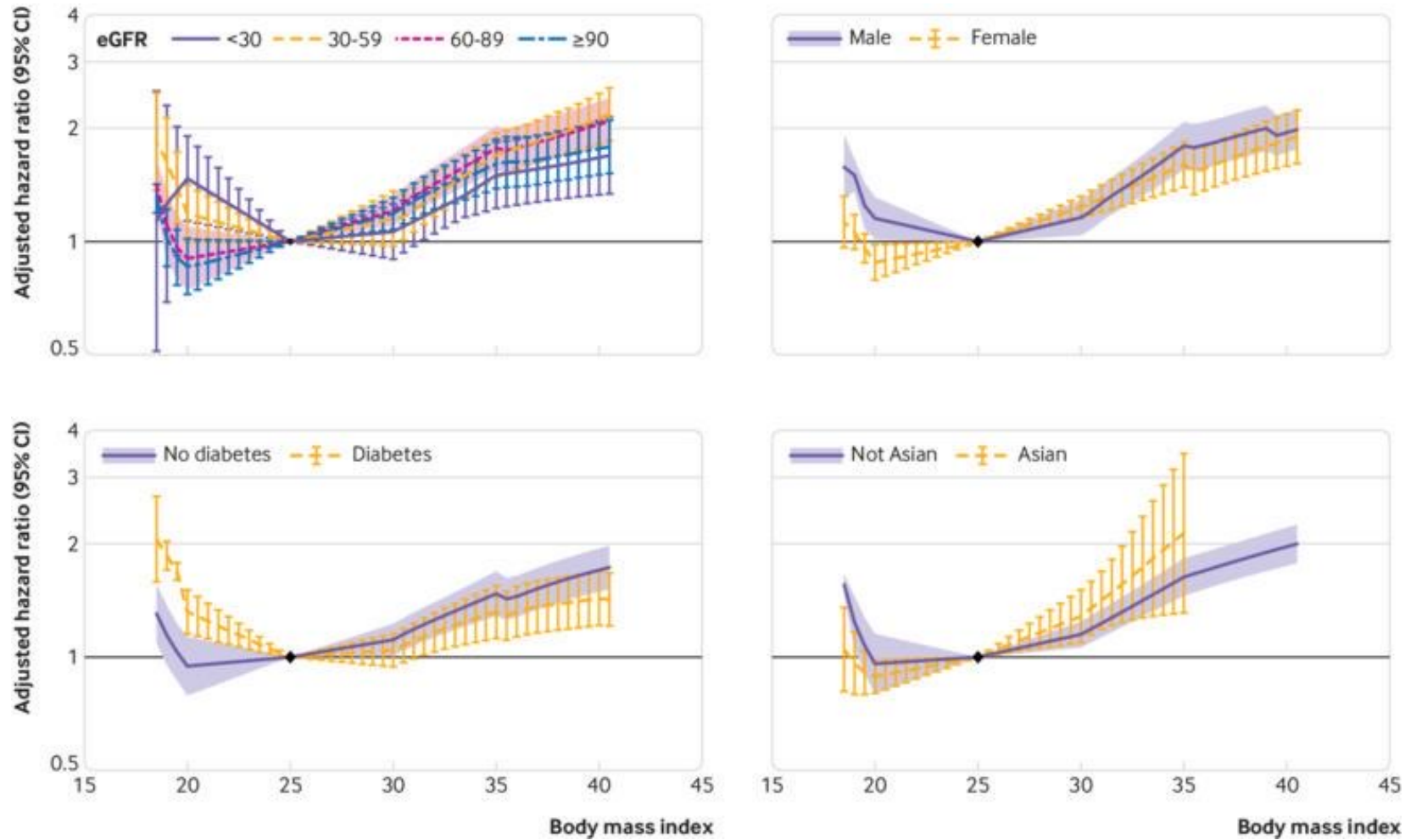
# Association between BMI and GFR decline in general population cohorts



CKD-PC; N= >5 million; Alex R Chang et al. BMJ 2019;364:bmj.k5301



# Association between BMI and GFR decline in general population cohorts: CKD, sex, diabetes, asian



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# Metaanalyse Serumkreatinin vor/nach bariatr. Chirurgie

## Beschreibt 23 Studien mit insgesamt 3015 Patienten

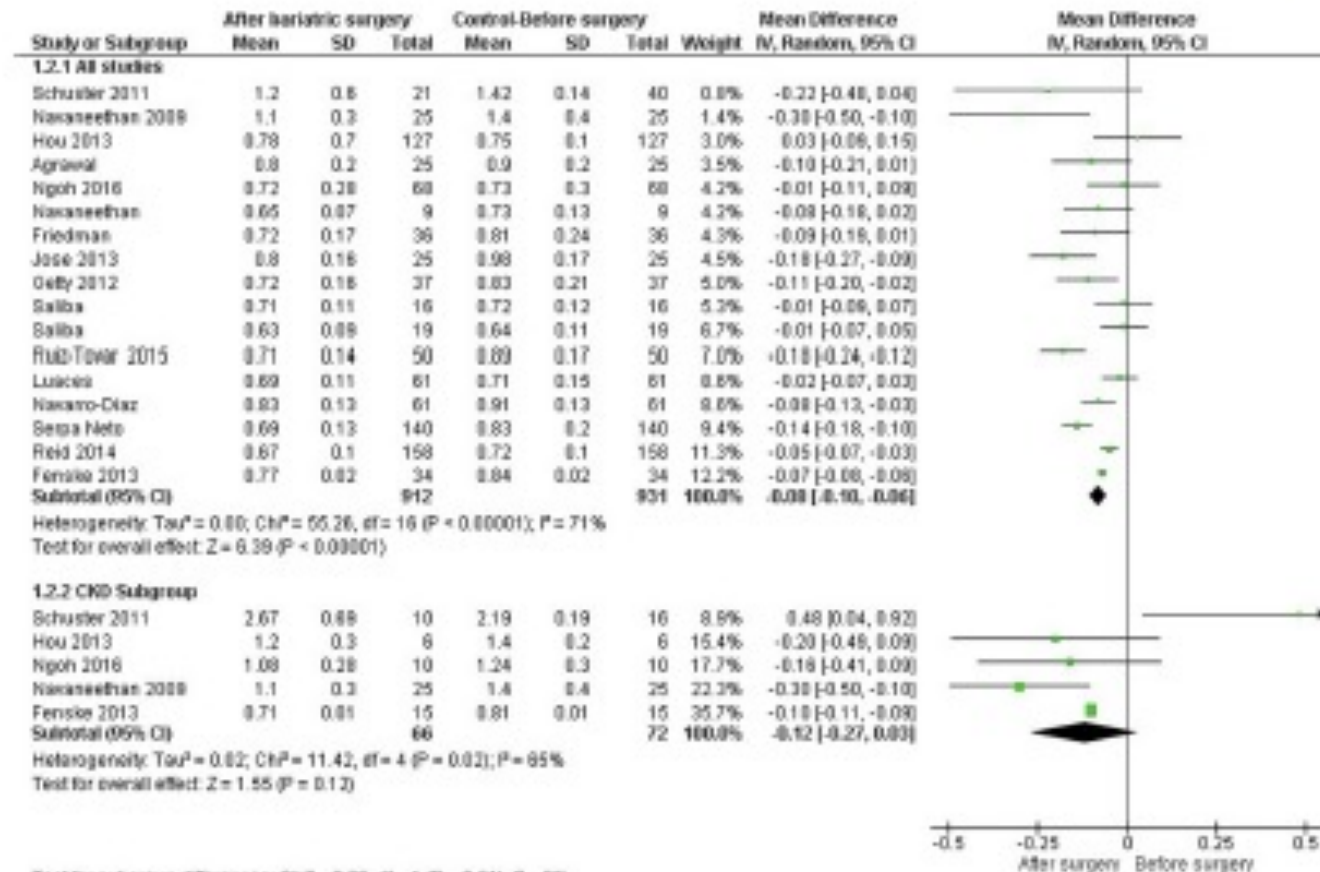


Fig. 2 Forest plot comparing creatinine values before surgery versus after surgery

# Metaana Chirurgi Beschre Kreatinin

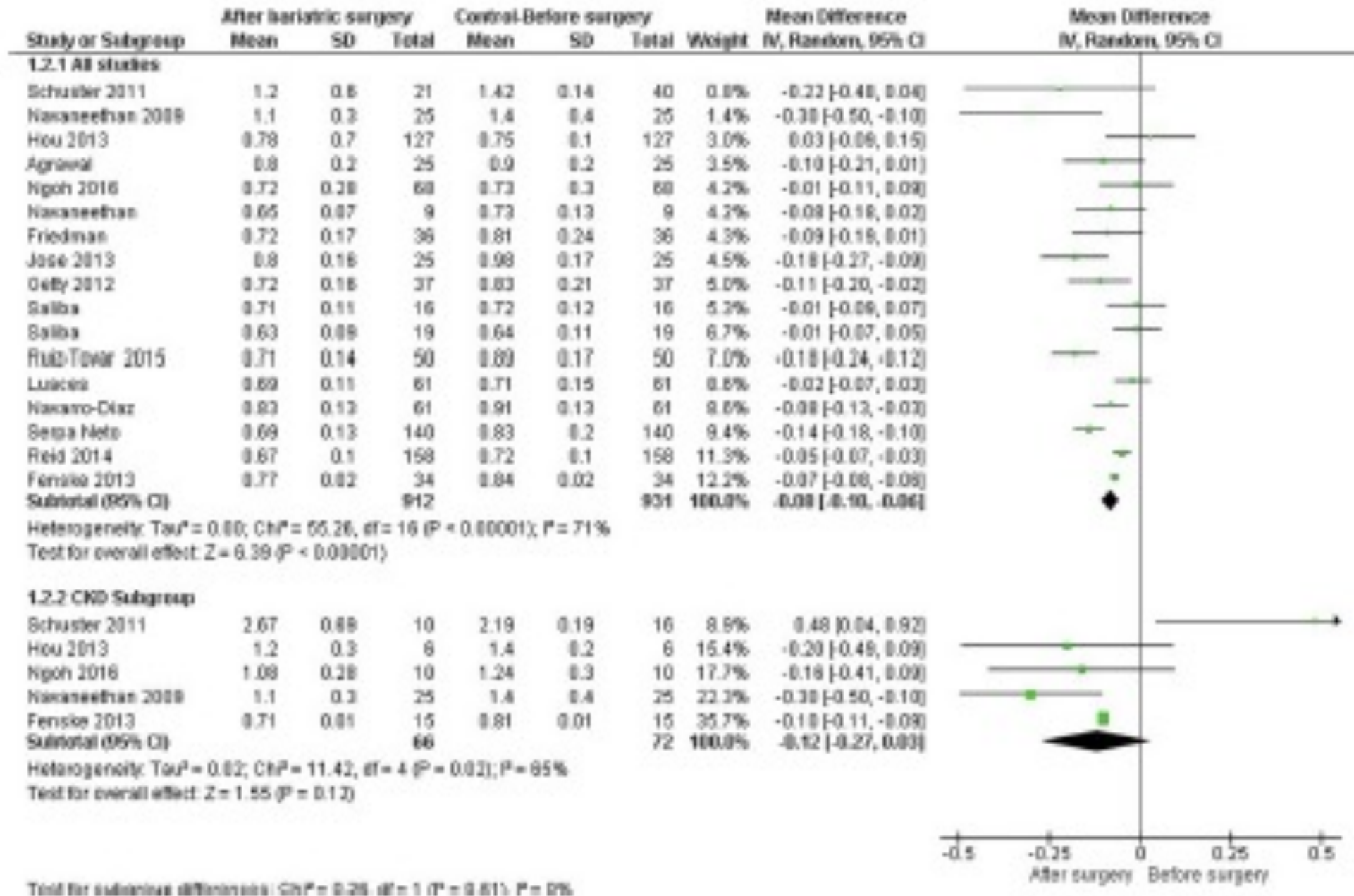


Fig. 2 Forest plot comparing creatinine values before surgery versus after surgery

# Metaana Chirurgie Beschrei eGFR

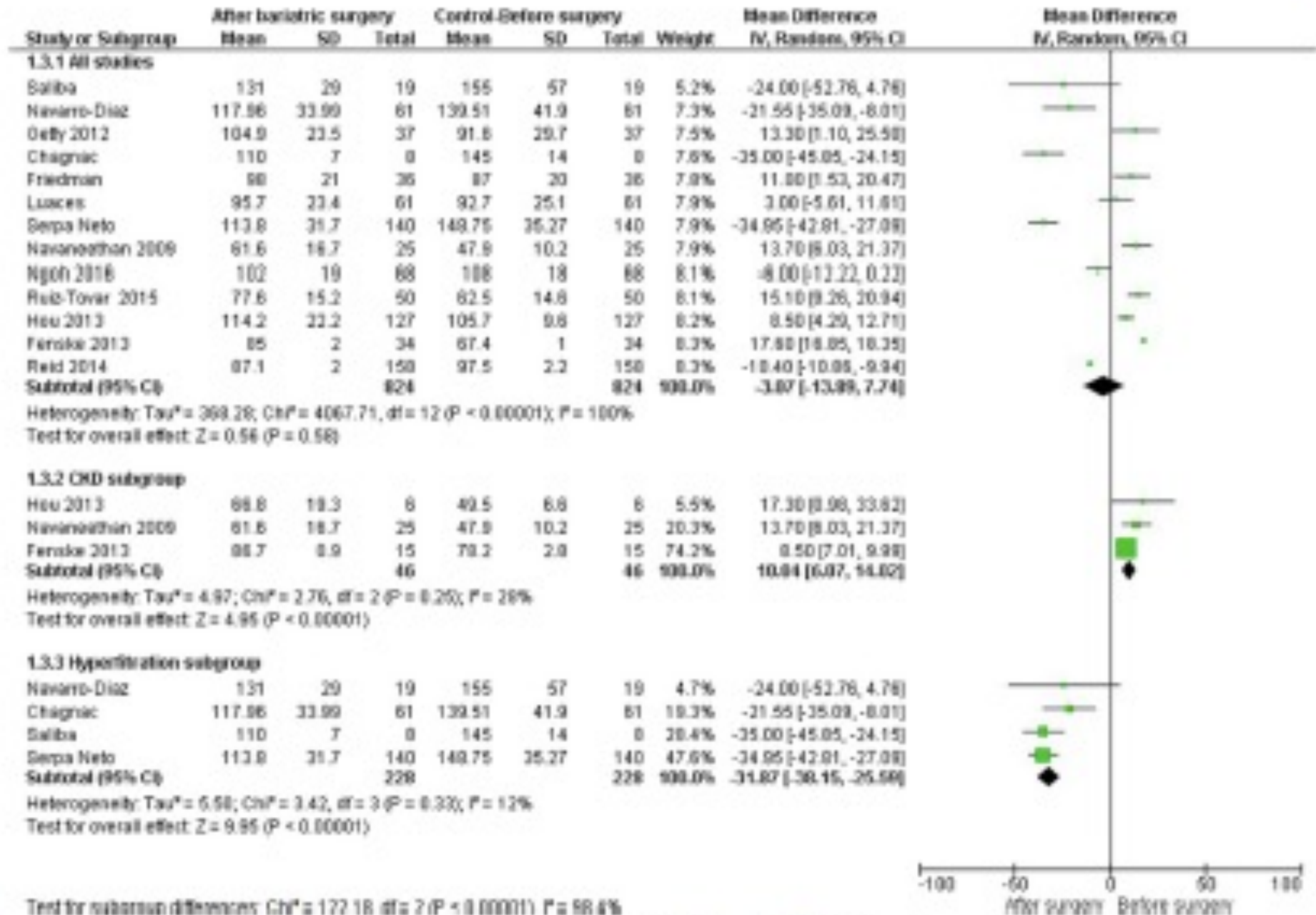
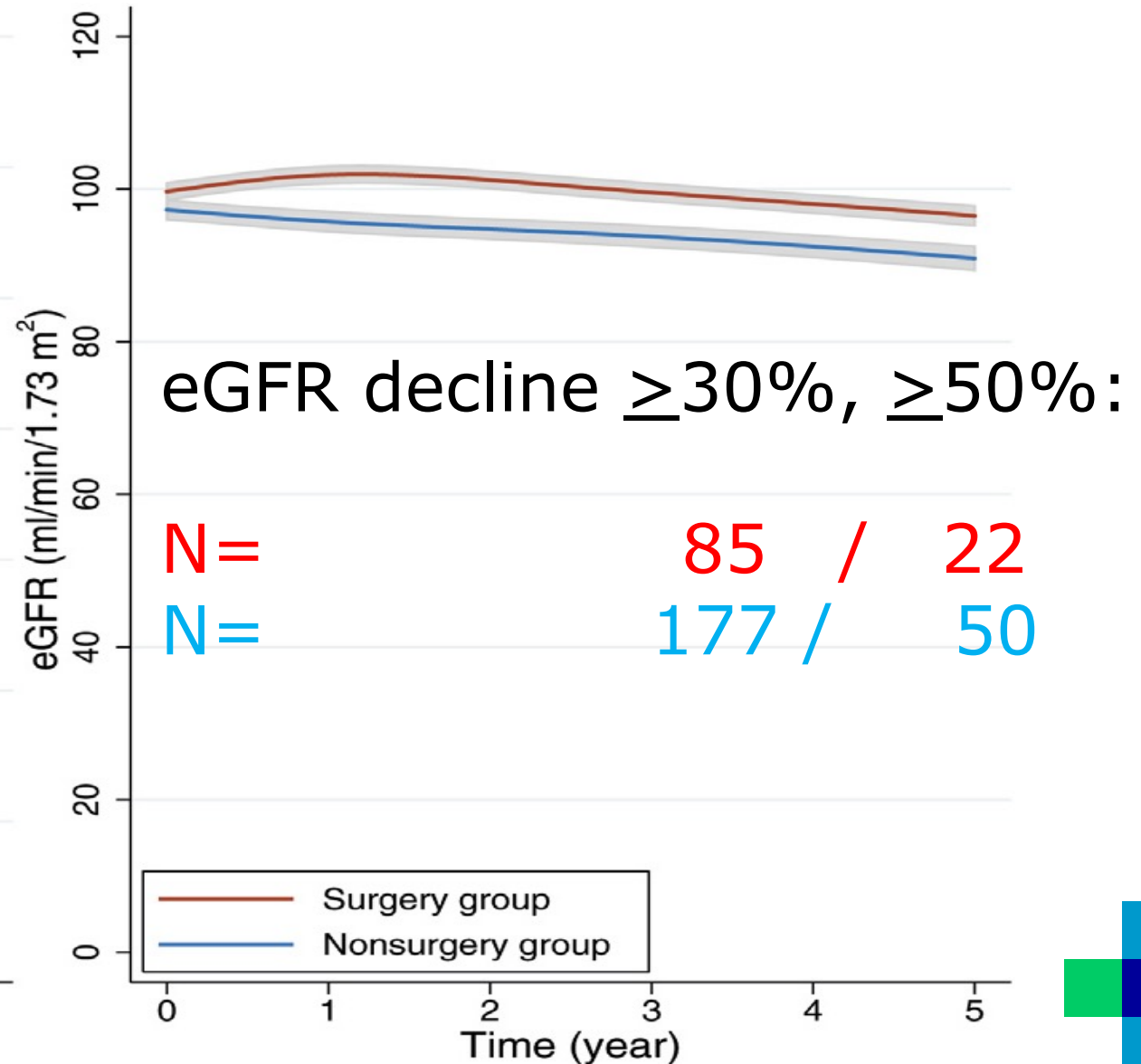
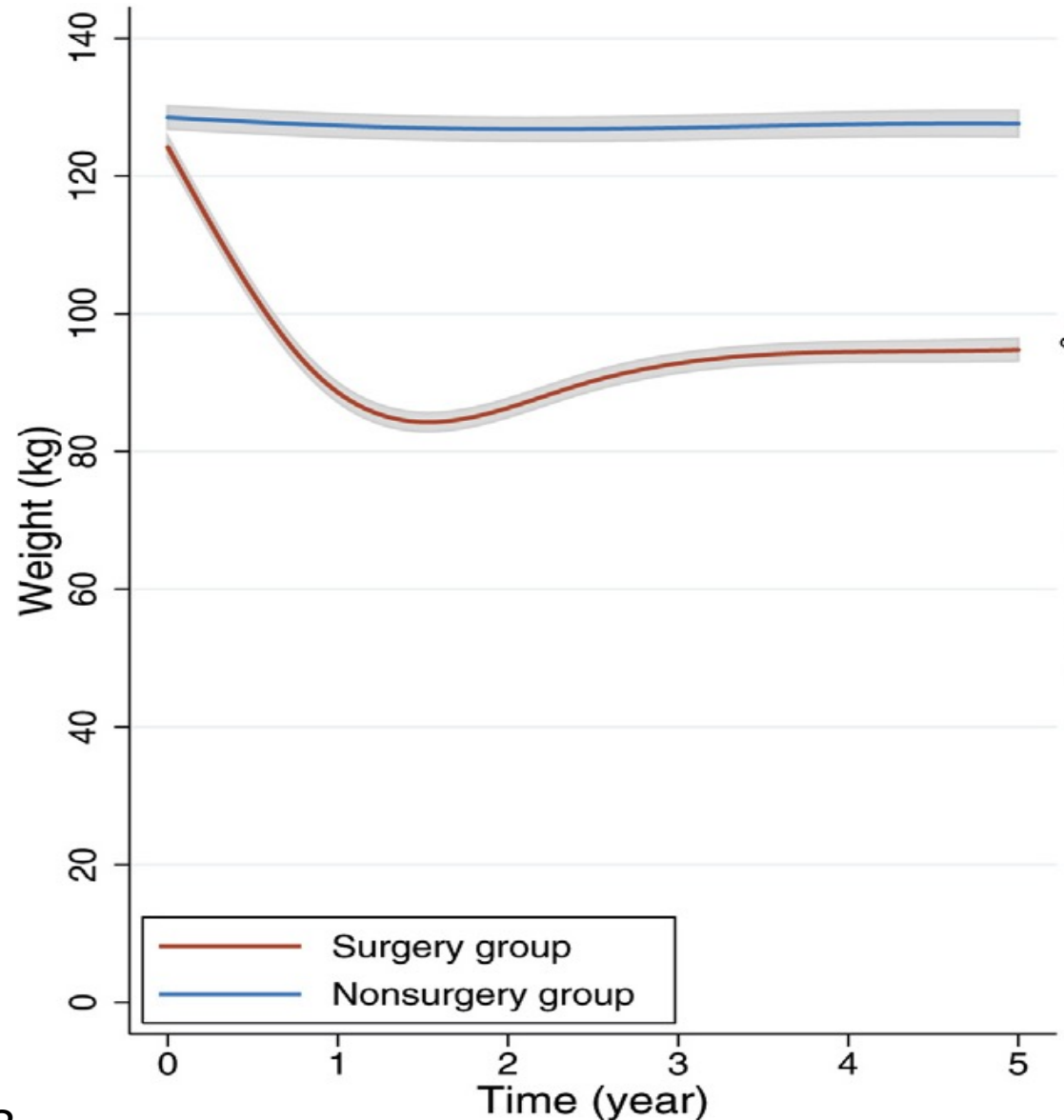


Fig. 3 Forest plot comparing GFR before surgery versus after surgery. GFR, glomerular filtration rate

# Bariatric surgery improves kidney outcomes



## **Kidney function in adolescents before/after bariatric surgery**

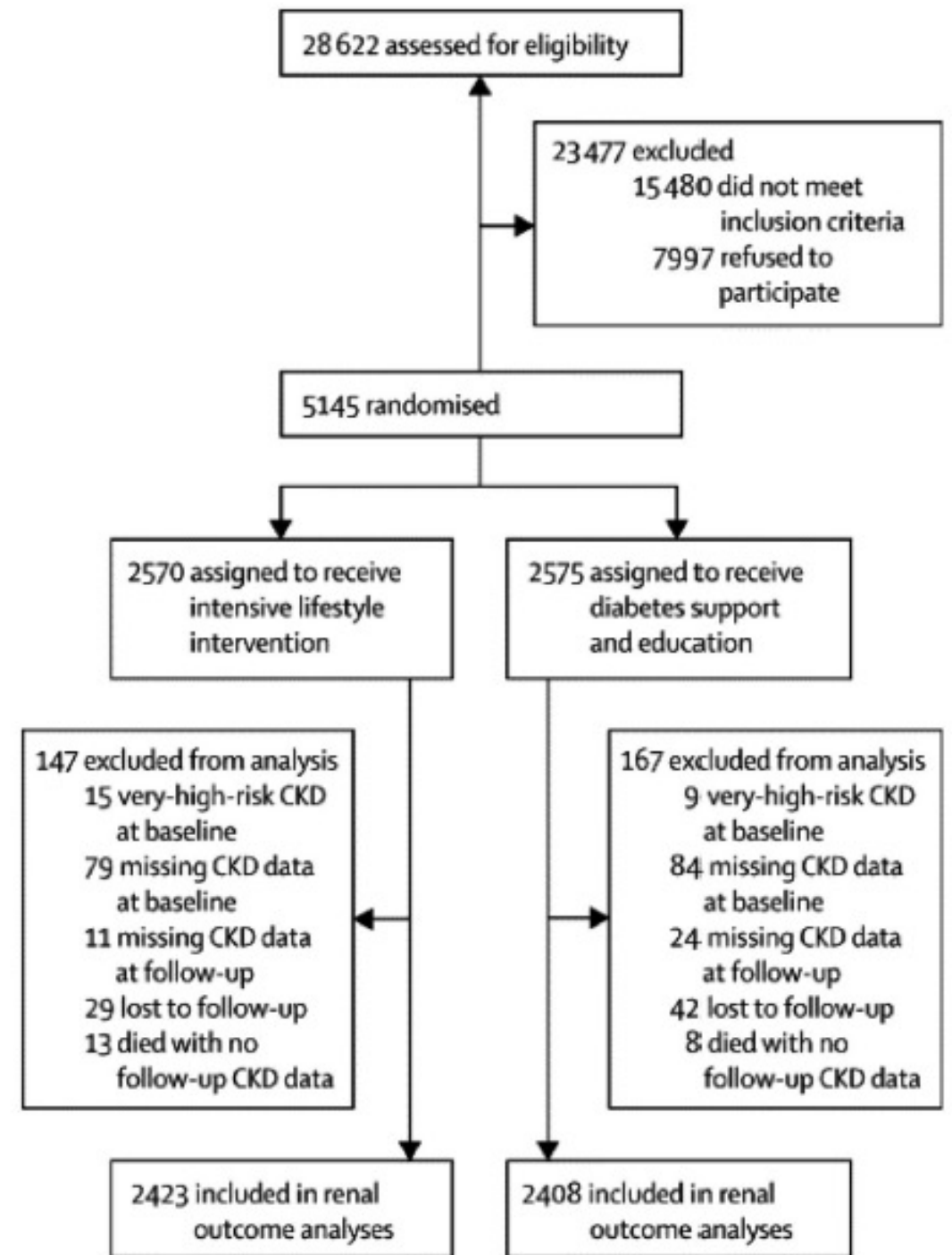
Beschreibt 228 Jugendliche mit Serumkreatinin und Proteinurie vor/nach OP

- 53/228 hatten vor OP eine niedrige GFR und/oder Proteinurie.
- Nach OP: GFR und Proteinurie normal in 46/53



# Look AHEAD trial

Obese, T2D, N= 5145  
control vs intensive life-  
style (follow-up 9.6y;  
weight diff. 4kg, HbA1c  
0.25%, BP 2mmHg, less  
meds, less insulin)

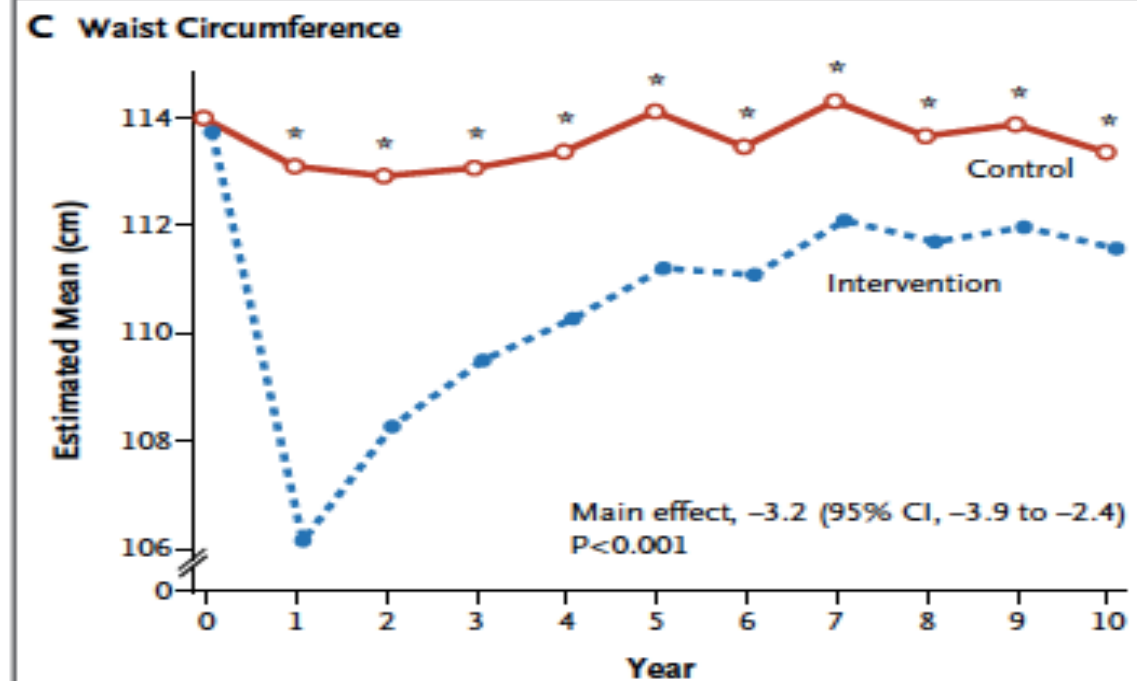
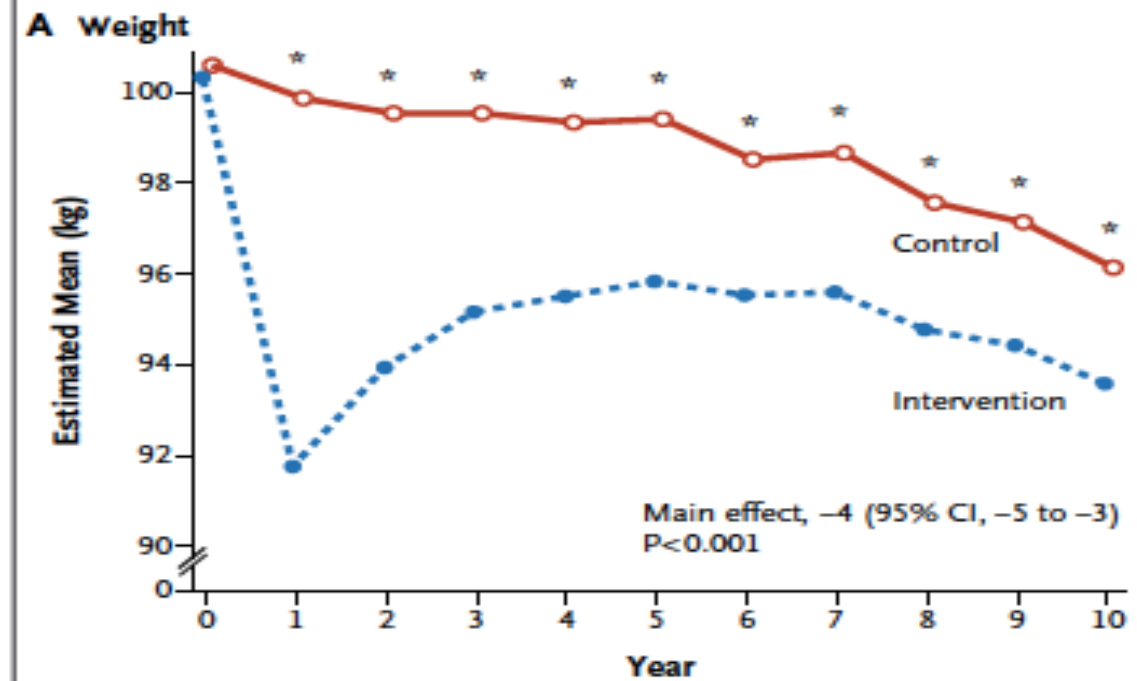


artery, or aortic aneurysm repair). Additional criteria are described elsewhere.<sup>10</sup> The ILI aimed to achieve and maintain weight loss of at least 7% through reduced caloric intake and increased physical activity.<sup>9</sup> Strategies included a calorie goal of 1200 to 1800 kcal per day (with <30% of calories from fat and >15% from protein), meal-replacement products, and at least 175 minutes of moderate-intensity physical activity per week. DSE group sessions focused on diet, exercise, and social support. The study did not set goals for control of

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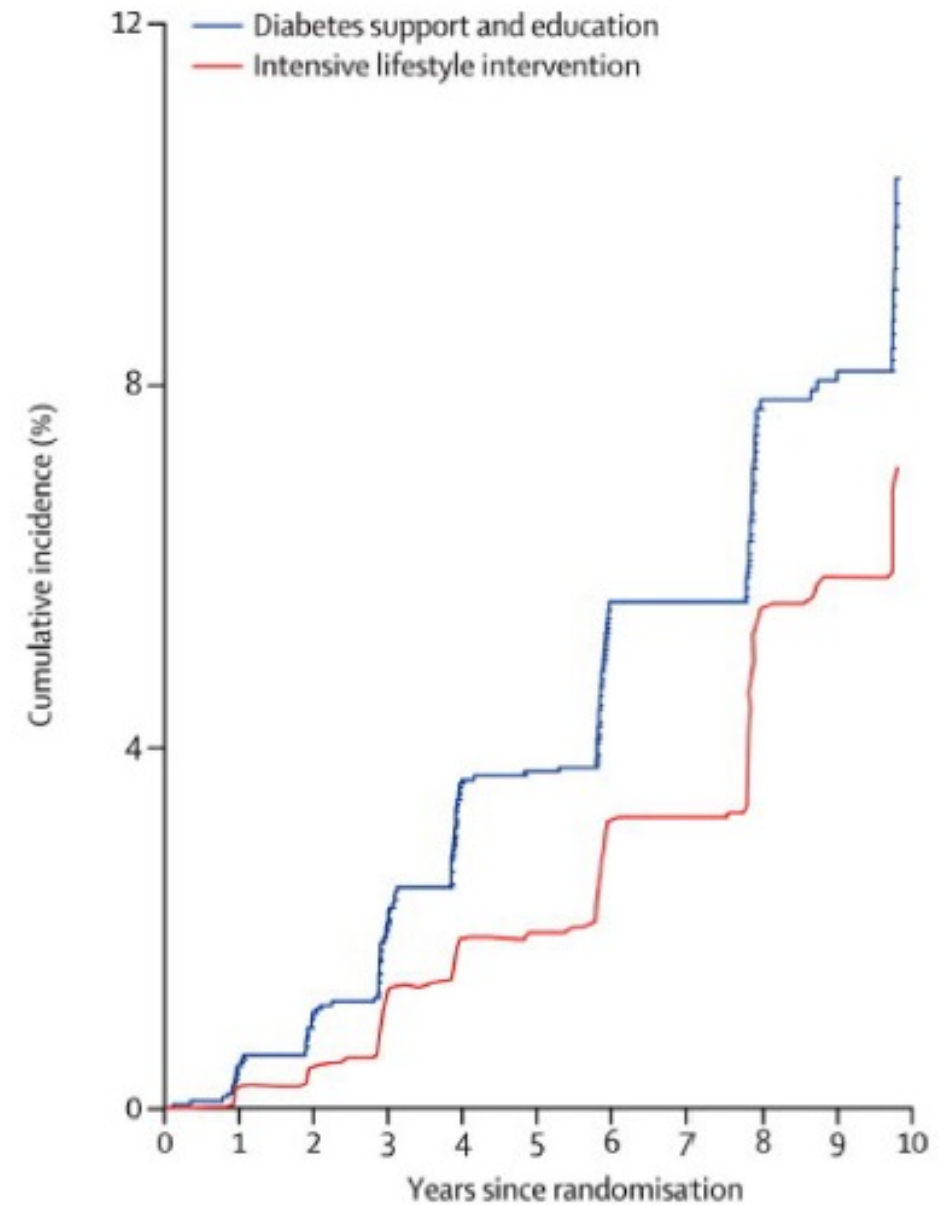
## New kidney disease

- *eGFR* <30 ml/min or
- <45 + *UACR* > 30mg/g or
- <60 + *UACR* >300mg/g\*

Control

Intensive intervention

\*DSC + RRT in 145 vs 120



	0	1	2	3	4	5	6	7	8	9	10
<b>Number at risk</b>											
Diabetes support and education	2408	2325	2203	2092	1914	854					
Intensive lifestyle intervention	2423	2371	2275	2180	1987	889					

# Medikamente zum Abnehmen

## **Nicht mehr verfügbar**

Amphetamine (Pulmonale Hypertonie)

Sibutramin (Vermehrte kardiovask. Todesfälle)

Rimanobant (Depressionen)

## **Verfügbar**

Semaglutid (Übelkeit, Erbrechen, Gallensteine), Orlistat (Durchfall),

in USA: Phentermin-Topiramamat und Bupropion-Naltrexon

## **Zukunft**

Cagri-Sema, Tirzepatid, Survodutid, Retatrutid, Orforglipron, AMG133, Activin receptor inhibitors (Bimagrumab, Taldefgrobep)

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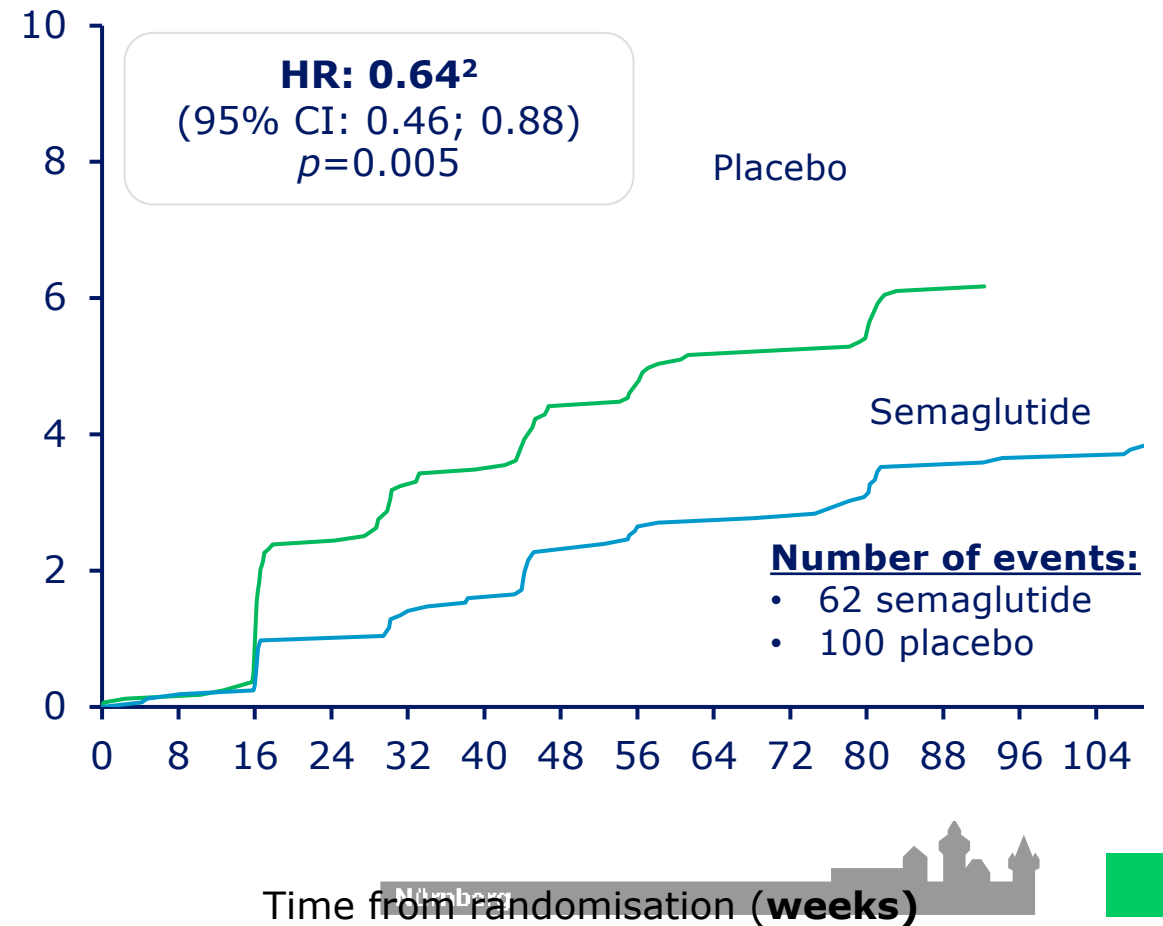
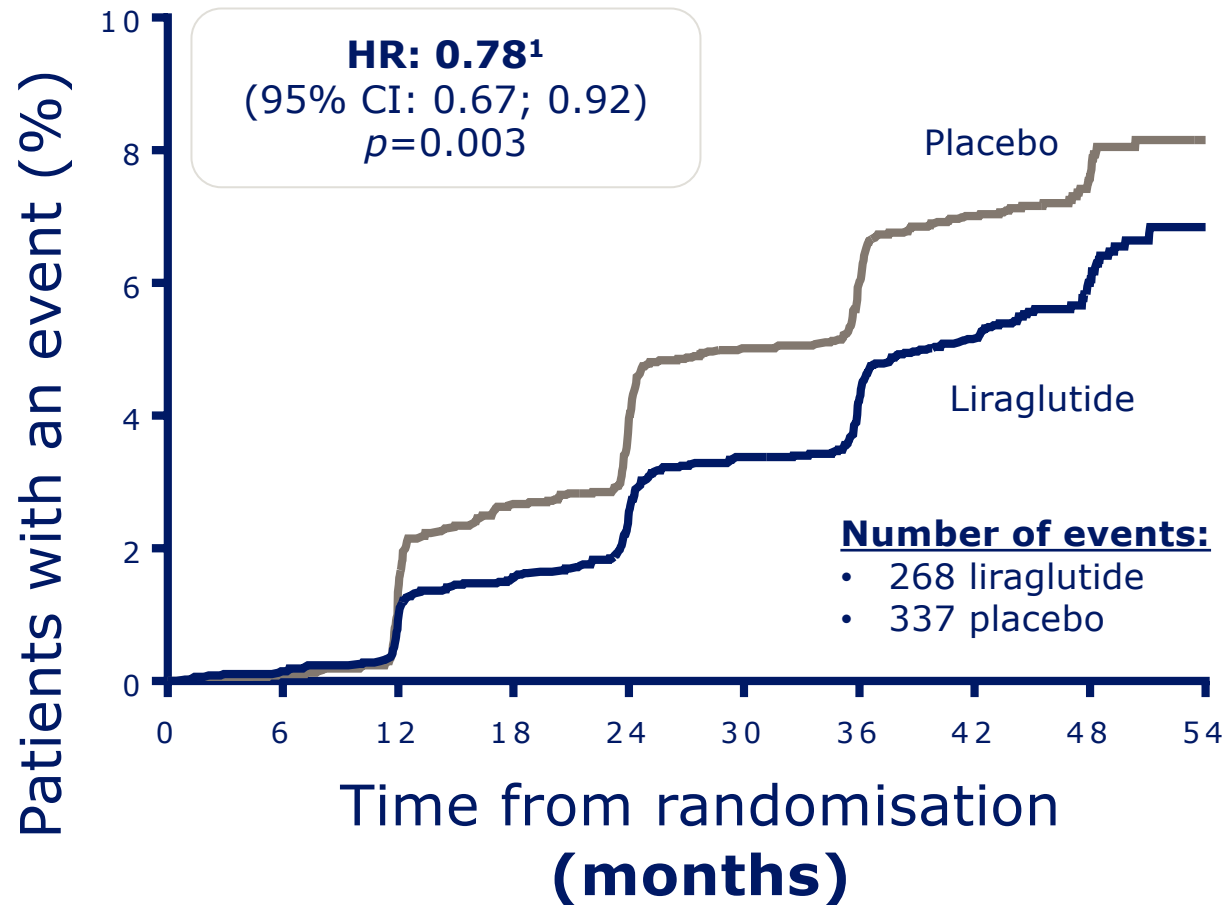
## **Zukunft**

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## Kidney outcomes with semaglutide & liraglutide

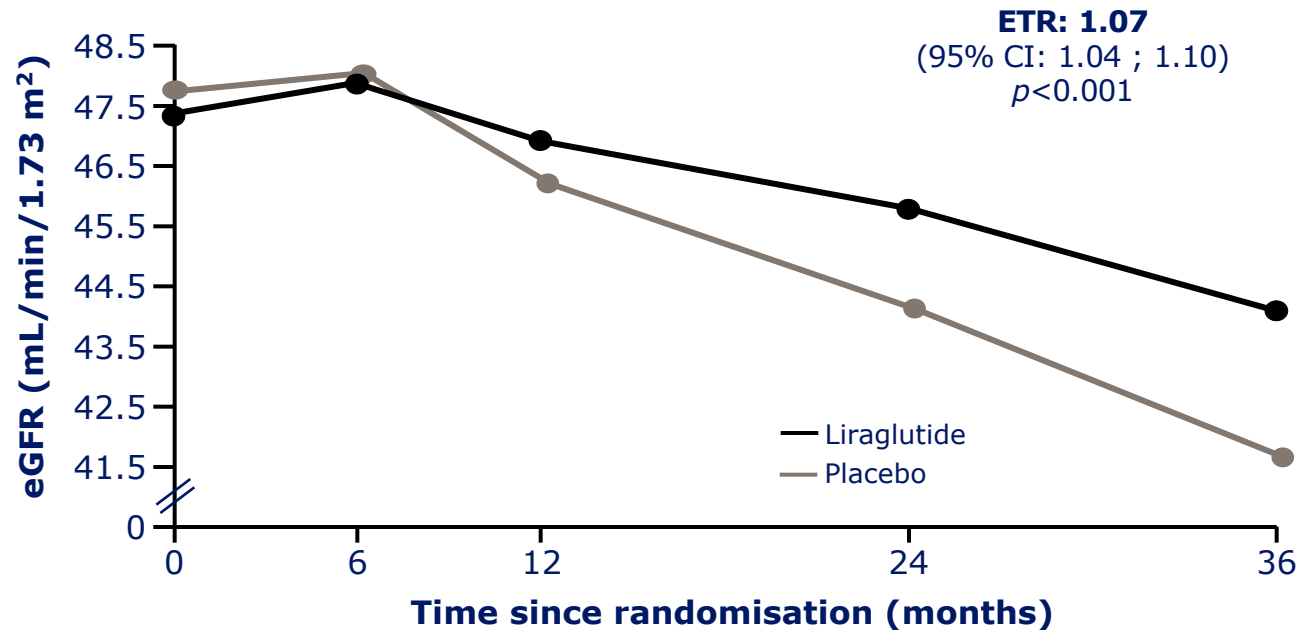
(Macroalbuminuria, doubling of serum creatinine\*, ESRD, renal death)

**LEADER** N=9340 / 605 kidney outcomes **SUSTAIN-6** N=3297 / 162 kidney outc.



## LEADER: eGFR over time

SUBGROUP WITH CKD STAGE 3\*; N=1934



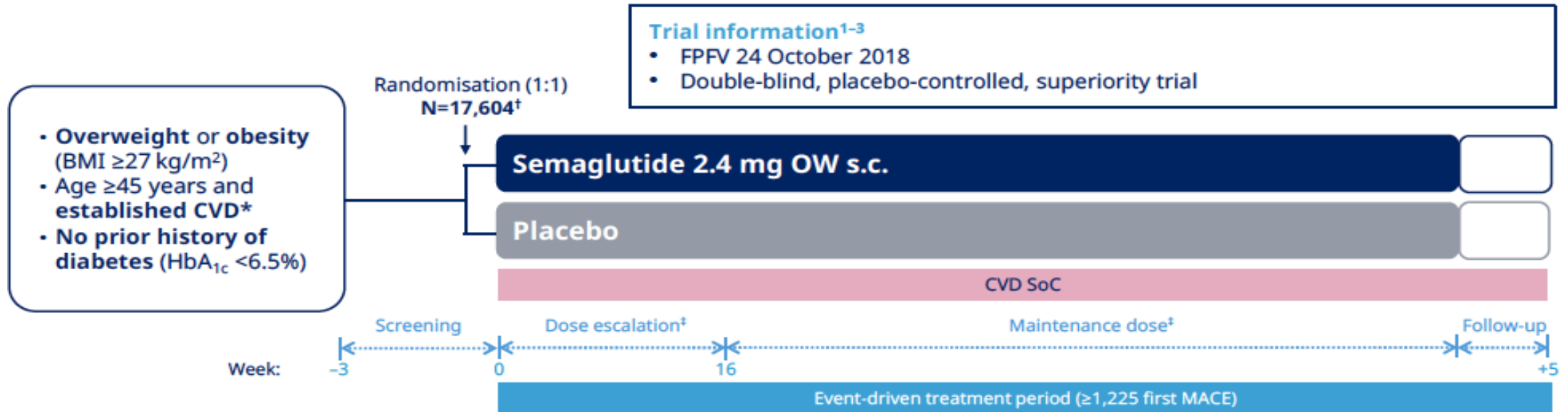
\*Defined as eGFR 30 to <60 mL/min/1.73 m<sup>2</sup>. Estimated geometric means.  
eGFR, estimated glomerular filtration rate; ETR, estimated treatment ratio.

Mann JFE et al. *N Engl J Med* 2017;377:839-848



# SELECT: Semaglutide in obese with CV disease, but without diabetes: **prim. CV outcome** (MI, stroke, CV death)

## Trial design SELECT



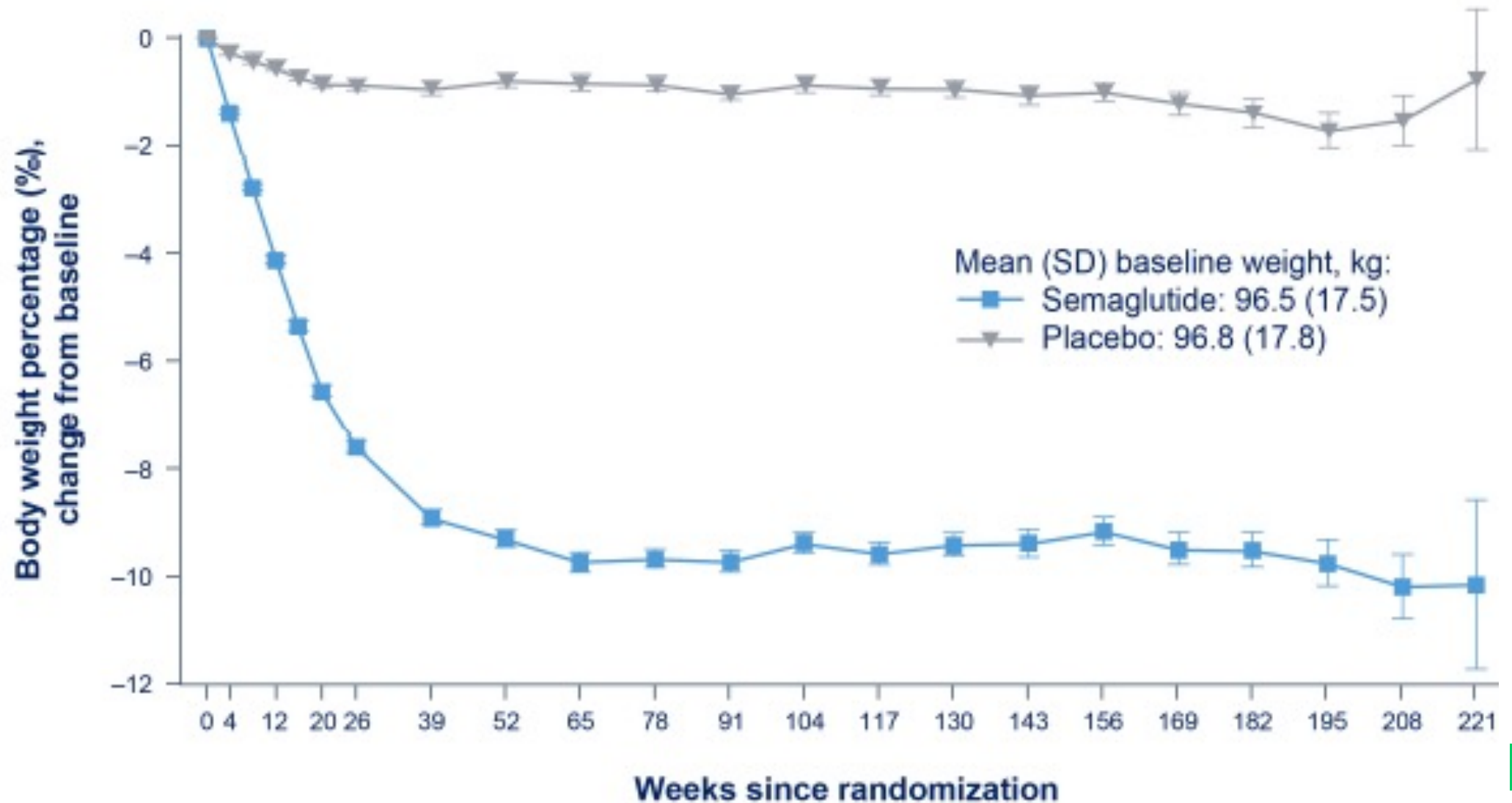
Three-component MACE consisted of non-fatal MI, non-fatal stroke and CV death.

\*Established CVD: MI ≥60 days prior to screening, stroke ≥60 days prior to screening or symptomatic PAD; NYHA class IV excluded. †Number of enrolled participants differs from number reported in baseline publication (17,605) as one participant was randomised twice in error and subsequently removed for the primary analysis. ‡Dose escalation is from week 4 to 16 with intervals of 4 weeks, and maintenance dose is event-driven to end of treatment period.

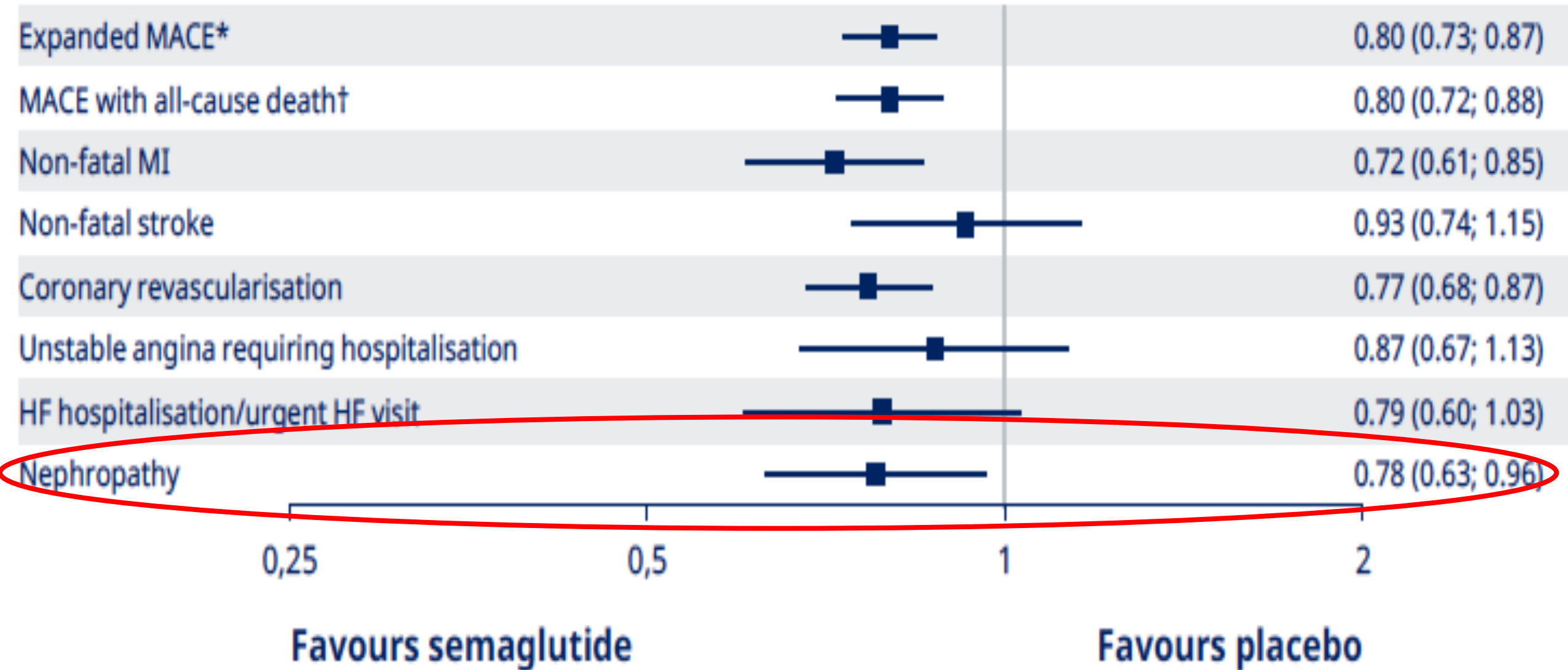
BMI, body mass index; CV, cardiovascular; CVD, cardiovascular disease; FPFV, first patient first visit; HbA<sub>1c</sub>, glycated haemoglobin; MACE, major adverse cardiovascular event; MI, myocardial infarction; NYHA, New York Heart Association; OW, once weekly; PAD, peripheral artery disease; s.c., subcutaneous; SoC, standard of care.

1. Ryan DH et al. Am Heart J 2020;229:61-9; 2. Lingvay I et al. Obesity (Silver Spring) 2023;31:111-22; 3. Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoa2307563.

# SELECT: Semaglutide in obese with CV disease, but without diabetes: **body weight** (% change from 96.6kg)



# SELECT: Semaglutide in obese with CV disease, but without diabetes: **secondary outcomes incl. nephropathy**





SELECT: Semaglutide in obese with CV disease, but without diabetes: **Nephropathy outcome**  
(new macroalb.; eGFR decrease  $\geq 50\%$ ; ESKD\*; Kidney death)

HR 0.78 (0.63-0.96) 155 von 8,803 vs 198 von 8,801

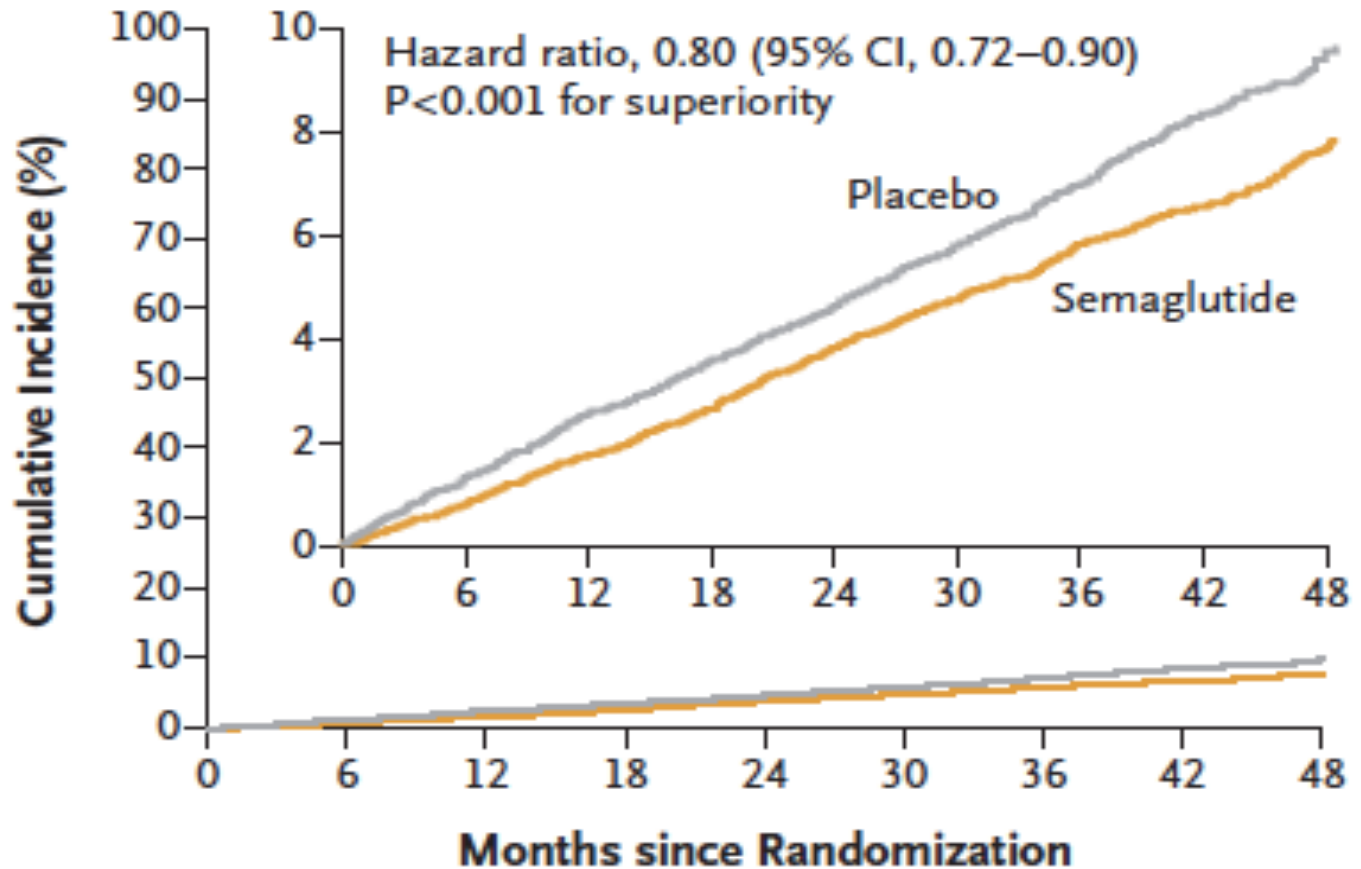
\*ESKD: chron. dialysis or eGFR <15 ml/min

At baseline: mean eGFR 82ml/min; UACR 7 mg/g

(Exclusion criteria: ESKD or dialysis)

# SELECT: Semaglutide in obese with CV disease, but without diabetes: **prim. CV outcome** (MI, stroke, CV death)

**A Primary Cardiovascular Composite End Point**



GFR <60:

HR 0.69 (0.52-0.90)

GFR >60

HR 0.82 (0.72-0.92)

**No. at Risk**

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

# Obesitas und Niere, Zusammenfassung

- Ab einem BMI  $>30$  kg/m<sup>2</sup> steigt das Risiko für das Auftreten einer CKD bzw Beschleunigung einer bestehenden CKD
- Eine Gewichtsabnahme bei Obesitas mit Chirurgie, Diät oder Semaglutid senkt das Risiko für eine CKD
- Ebenso sinkt das CV Risiko mit Chirurgie oder Semaglutid, auch bei CKD
- Lebenslang Abnehmspritze/-pille ??

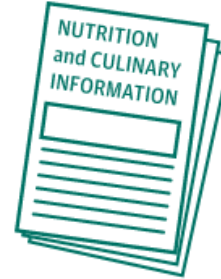
## GLP-1 agonist therapy

- Initial therapy for 12-18 mo to achieve weight loss
- Booster periods over time as needed



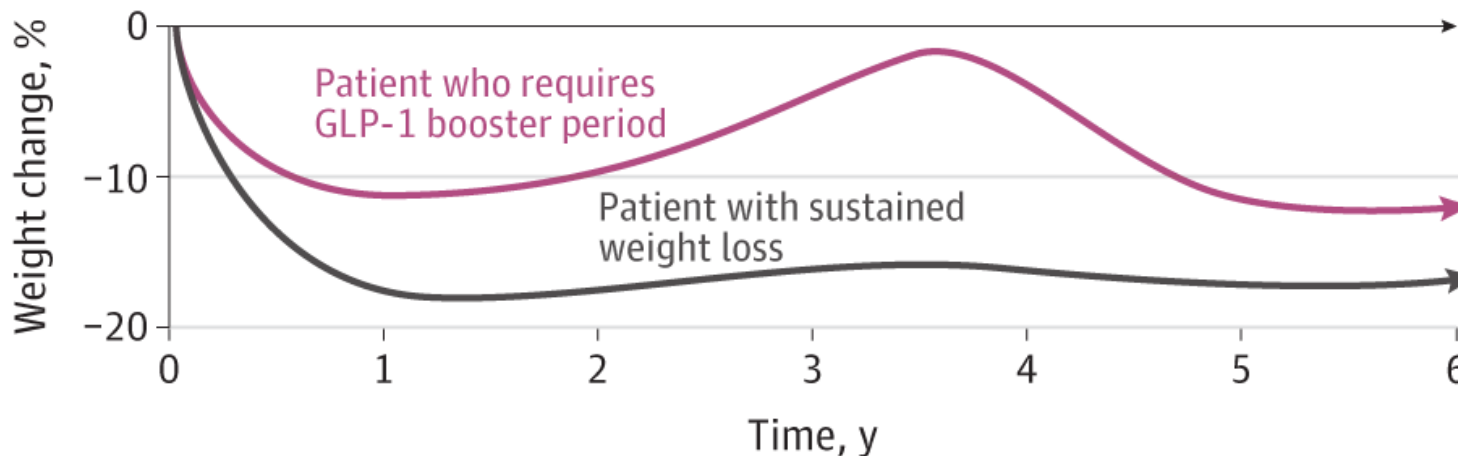
## Lifestyle counseling, including Food Is Medicine

- Nutritionally tailored groceries or meals
- Nutrition and culinary education
- Digital and telehealth behavior support



## Weight trajectory

- Variable patient experiences
- Flexible, individualized treatment plans



Mozaffarian D.

## GLP-1 Agonists for Obesity—A New Recipe for Success?

JAMA. 2024, 29. February

doi:10.1001/  
jama.2024.2252

# Metaanalysis of population studies: obesity and new CKD

