Kardiovaskuläre Risikoprävention

.....there is no glory in prevention
Lei(d)tsatz der Präventionsmedizin

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Transparenzerklärung

Hiermit lege ich offen, dass ich von folgenden Firmen finanzielle Untersützung erhalten habe, die sich auf Vorträge, Beratertätigkeit, ungebundene Forschungs-unterstützung oder sonstige medizinisch-wissenschaftliche Leistungen bezieht

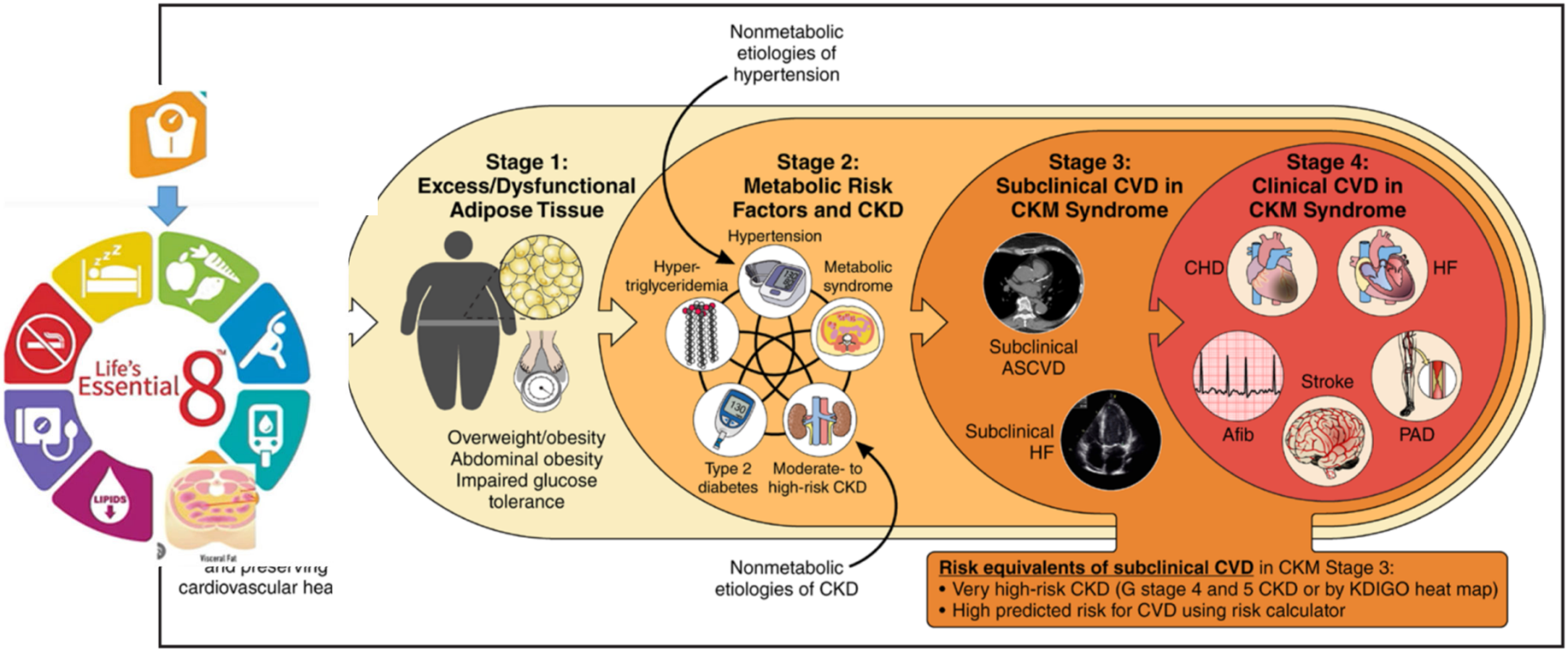
- Berlin Chemie
- Sanofi
- Lilly
- Novo Nordisk
- astra
- Bayer
- Aristo
- Medical Tribune
- Medfora
- Miaglossa

Unentgeltliche Aktivitäten

- Deutsche Gesellschaft für Kardiologie
- Deutsche Hochdruckliga
- Akademie der Deutschen Hochdruckliga
- International Society of Preeclampsia
- Gutachter für nationale – und internationale Forschungsgemeinschaften und Fachzeitschriften

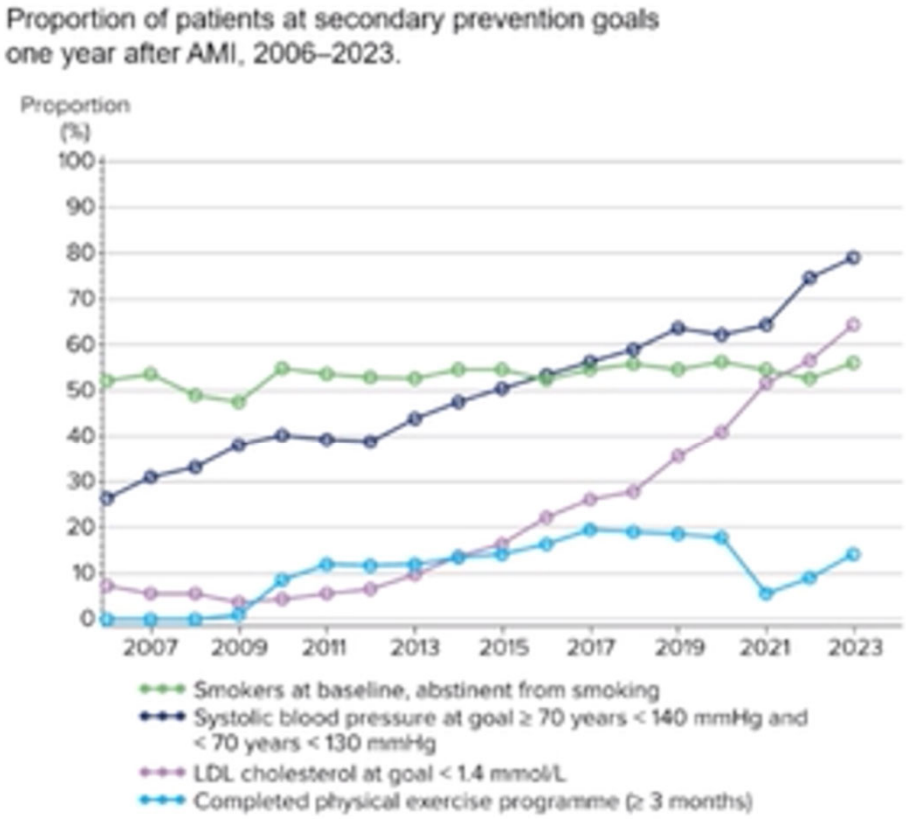
übergeordnete Bedeutung der Adipositas aus der Kardiologie

AHA PRESIDENTIAL ADVISORY: EXCESS/DYSFUNCIONAL ADIPOSE TISSUE IS THE DETERMINANT OF CARDIOVASCULAR-KIDNEY-METABOLIC DERANGEMENT

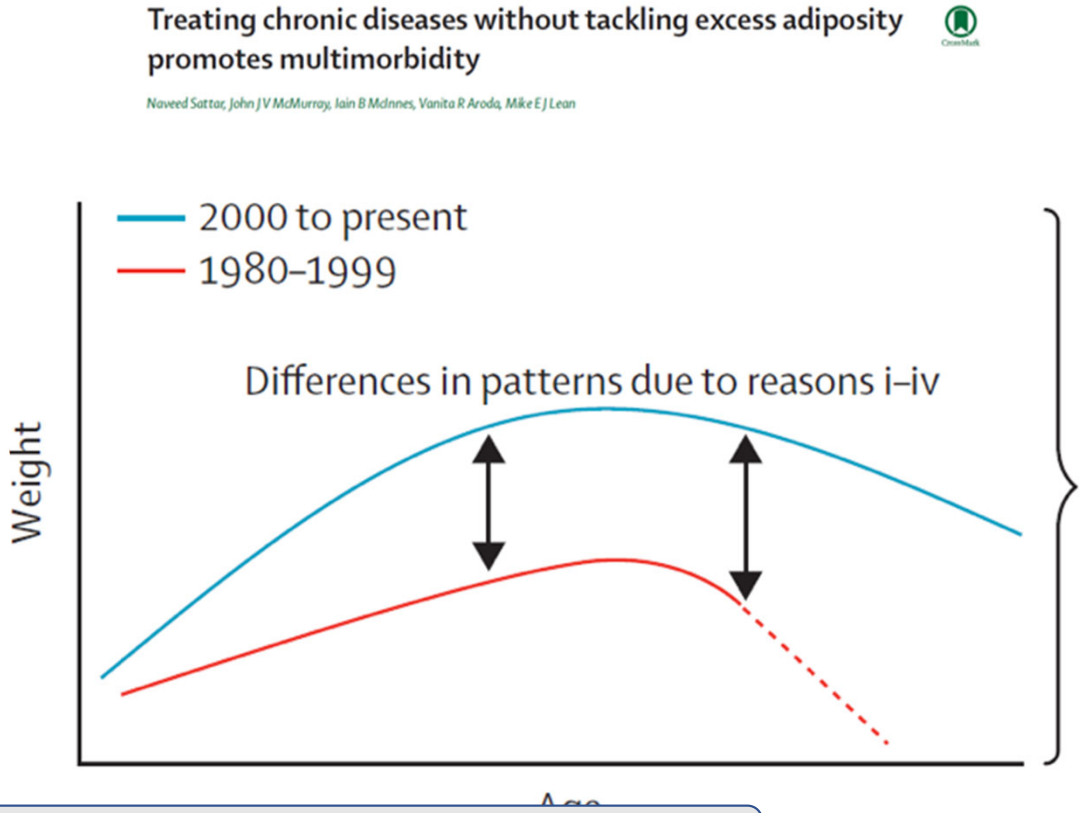


Ndumele CE et al, Circulation 2023

übergeordnete Bedeutung der Adipositas aus der Kardiologie



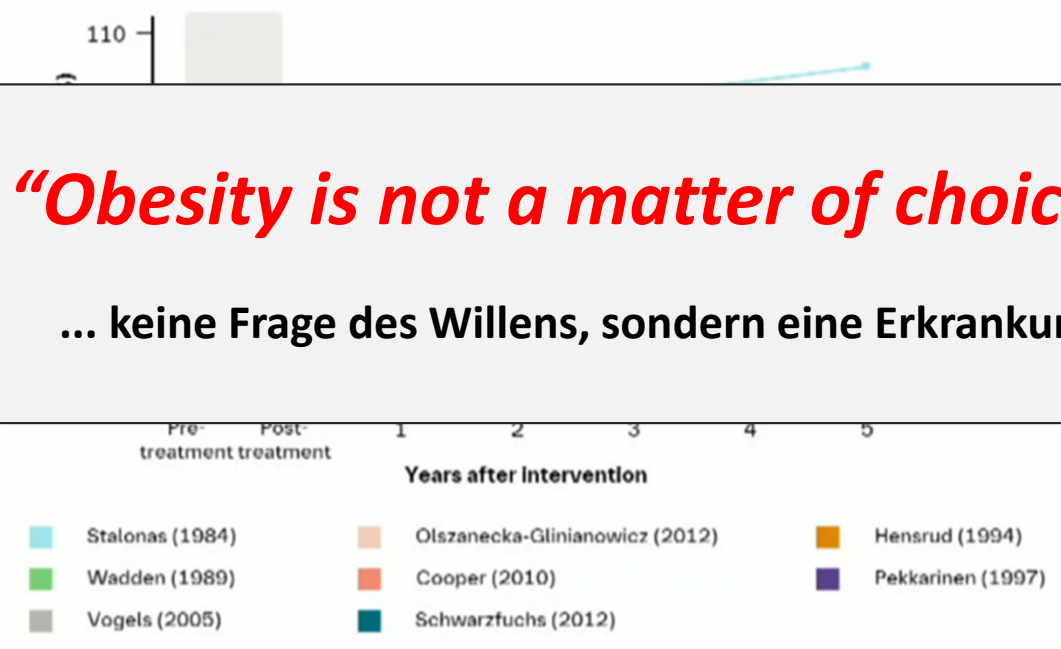
Swedeheart 2



erfolgreiche kardiovaskuläre Prävention führt zu mehr Adipositas

Sattar et al. Lancet 2022

die Probleme des Abnehmens



"Obesity is not a matter of choice"

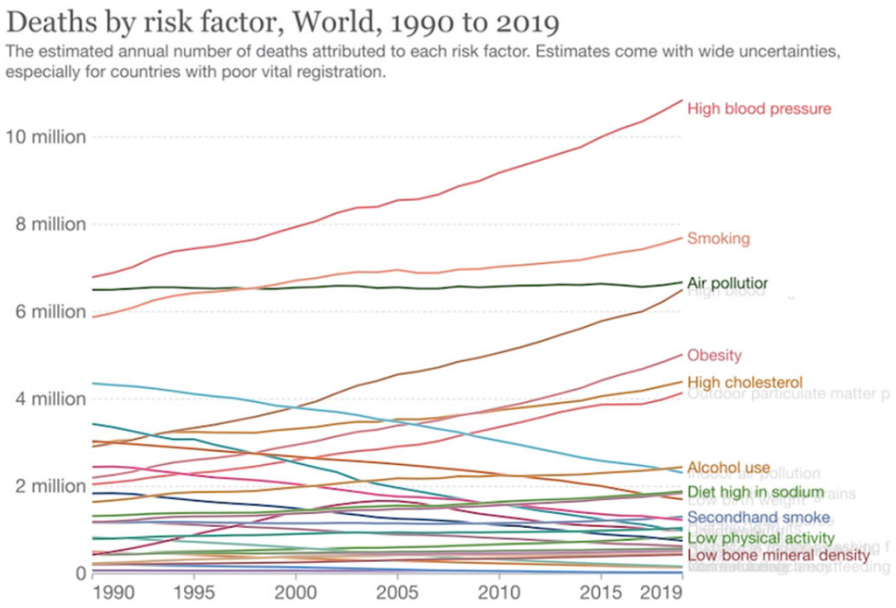
... keine Frage des Willens, sondern eine Erkrankung

....die Gewichtsabnahme durch Lebensstilveränderung / Diät

ist im Allgemeinen bescheiden und langfristig nicht nachhaltig

Nordmo et al Obes Rev 2020a nd Horn et al. Postgrad Med 2022

Adipositas eine Erkrankung oder ein Risikofaktor ?



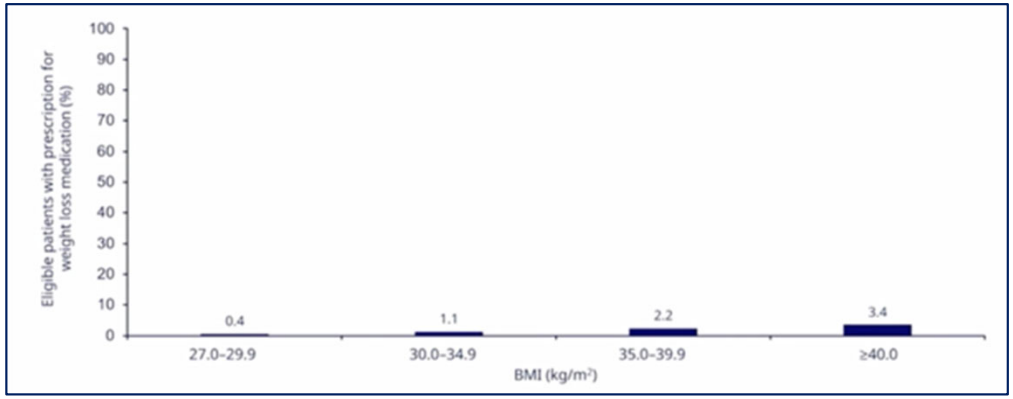
NCD Risk Factor Collaboration: Lancet 2017

Kommunikation ist die Kunst, auf das Herz zu zielen, um den Kopf zu treffen.

Nichts ist einfacher als in der Kommunikation zu scheitern.

Adipositas ist kein kosmetisches Problem
...es tötet

die traurige Realität



<1% der Patienten bekommen ein Angebot

Saxon DR et al. Obesity 2019

Probleme der Adipositastherapie

Iss weniger !

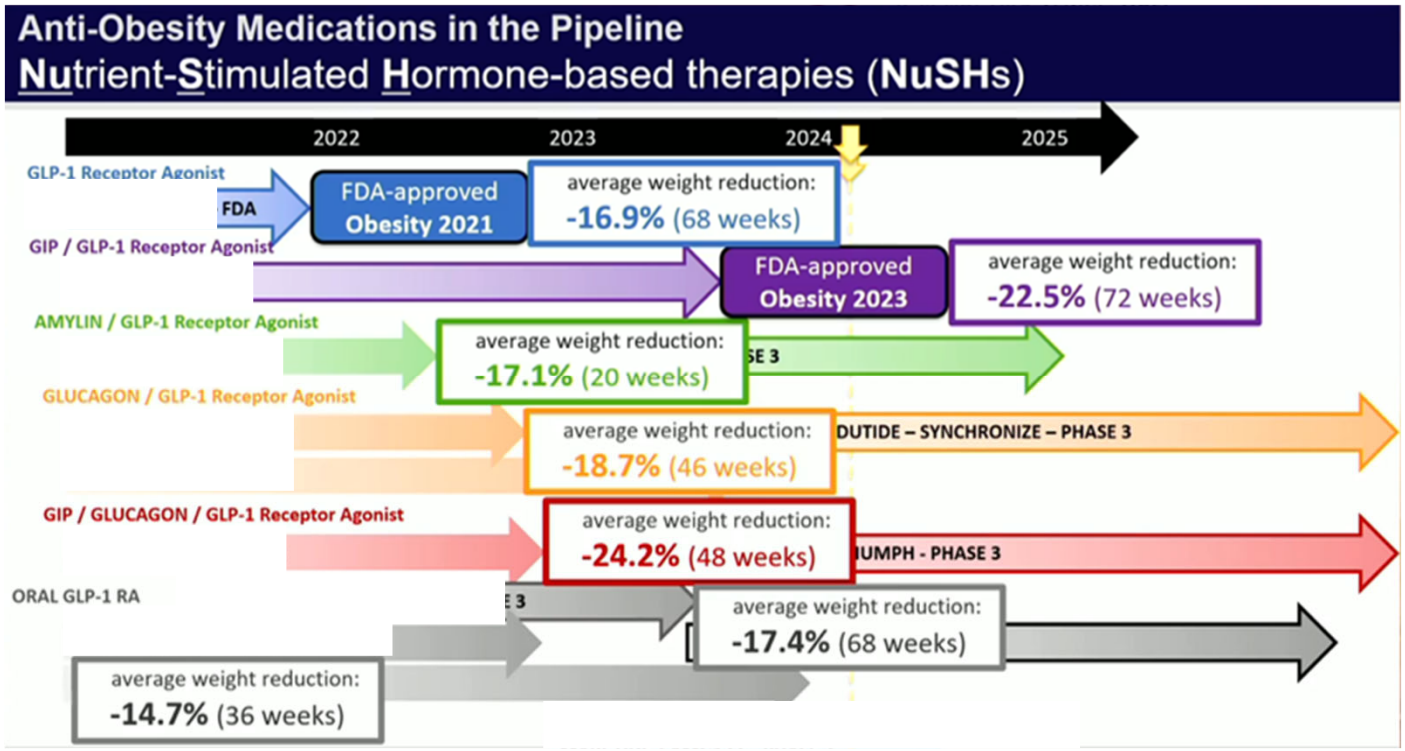
Beweg Dich mehr !

Streng Dich mehr an !!

- **viel zu viele nicht-evidenzbasierte Therapien**
- **einzigartiges Chaos**

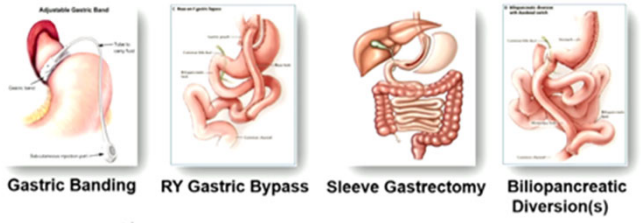
- **zu wenig Kommunikation zu dem Thema**
- **Patient fühlt sich selbstverantwortlich dafür**
- **voller Frust, Trauer, Enttäuschung,**

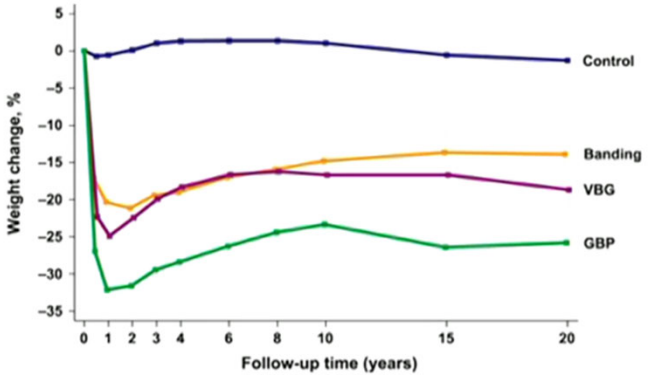
Adipositastherapie: eine Revolution



Adipositas ist zwar nicht heilbar, aber es is jetzt behandelbar

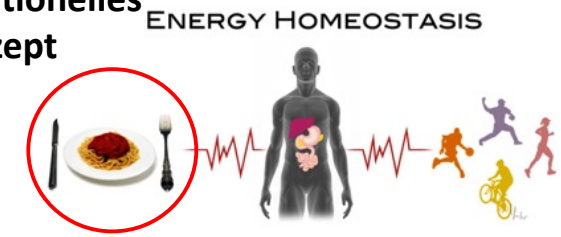
Barische Chirugie: überzeugende Langzeitdaten





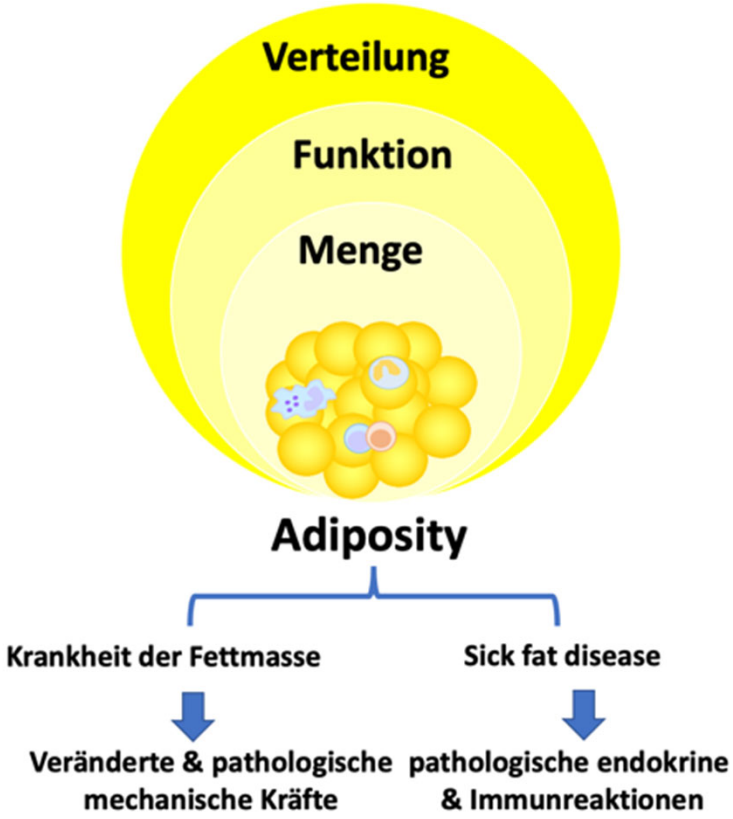
	Diät	RYGB
Energieverbrauch	↓	↑
Appetit	↑	↓
Hunger	↑	↓
Sättigung	↓	↑
Belohnungsessen	↑	↓
Stress-Antwort	↑	↓
Darmpeptide		
Hunger Hormone (Ghrelin)	↑	↓
Sättigungs- Hormone (GLP-1, PYY, CCK, amylin)	↓	↑

traditionelles Konzept



"Physiology, not mechanics"

Charakterisierung und Staging/Therapieziel bei Adipositas



	Stage 0	Stage 1	Stage 2	Stage 3
	"Normal health"	*"At risk"*	*"Established disease"*	*"Advanced disease"*
Airways	Normal	Snoring	Require CPAP	Cor pulmonale
Body mass index	<35	35-40	40-60	>60
Cardiovascular	<10% risk	10-20% risk	Heart disease	Heart failure
Diabetes	Normal	Impaired fasting	Type 2 diabetes	Uncontrolled type 2 diabetes
Economic	Normal	Expensive travel/clothes	Workplace discrimination	Unemployed due to obesity
Functional	Can manage 3 flights of stairs	Manages 1 or 2 flights of stairs	Requires walking aids or wheel chair	House bound
Gonadal	Normal	PCOS	Infertility	Sexual dysfunction
Health perceived	Normal	Low mood or QoL	Depression or poor QoL	Severe depression
body Image	Normal	Dislikes body	Body image dysphoria	Eating disorder

Was ist das Therapieziel für uns Kardiologen / Nephrologen ?

Gomez-Ambrosi et al. Eur J Intern Med 2024, Frühbeck G et al. Eur Heart J 2024, Lingavy et al. Lancet 2022

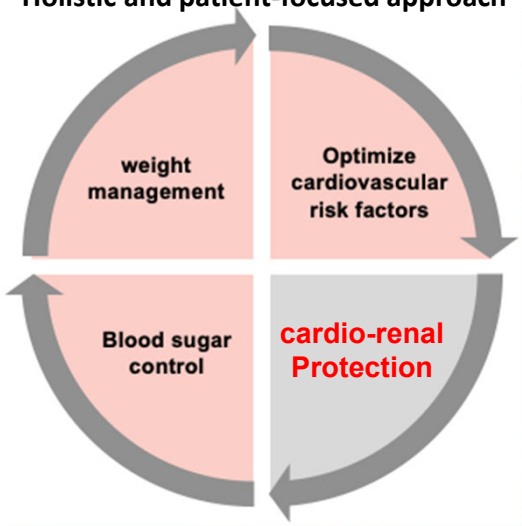
Ein provokantes, aber überzeugendes Konzept

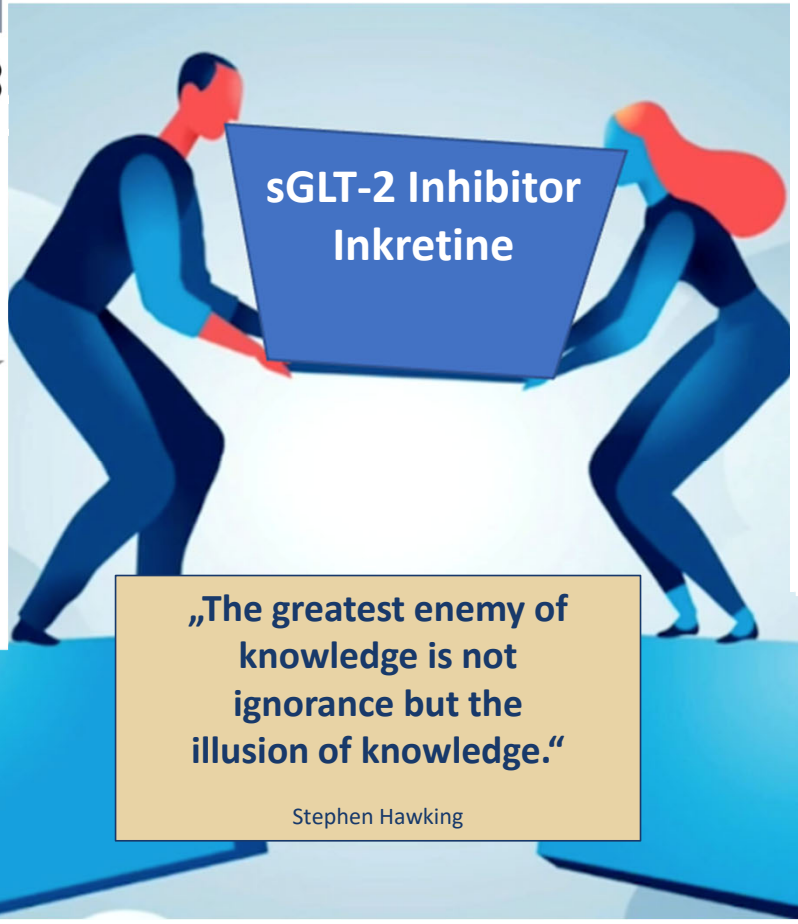
Kardiologen und Diabetologen im Spannungsfeld

Diabetes Care — American Diabetes Association

Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Holistic and patient-focused approach





„The greatest enemy of knowledge is not ignorance but the illusion of knowledge.“

Stephen Hawking

Diabetes
Diabesity
Adipositas

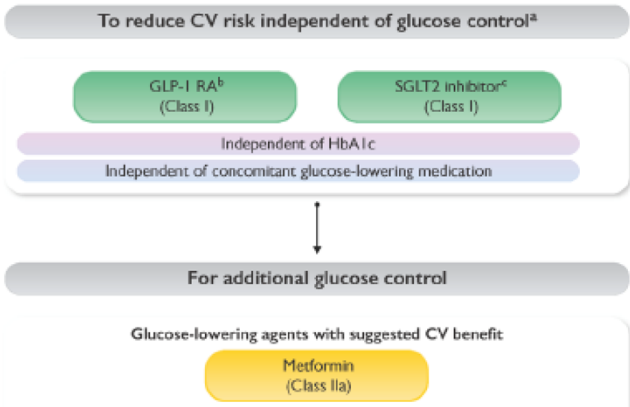
KHK
Herzinsuffizienz

ESC European Society of Cardiology — European Heart Journal (2023) 00, 1–98 https://doi.org/10.1093/eurheartj/ehad192

ESC GUIDELINES

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

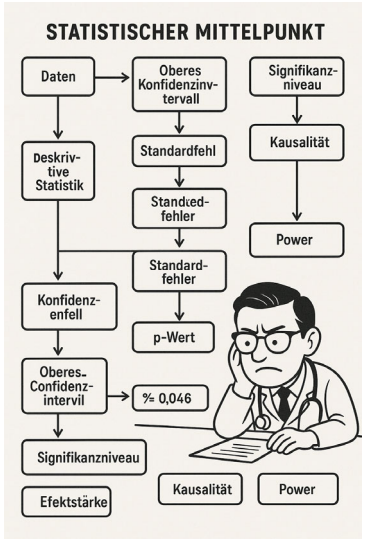
Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC)

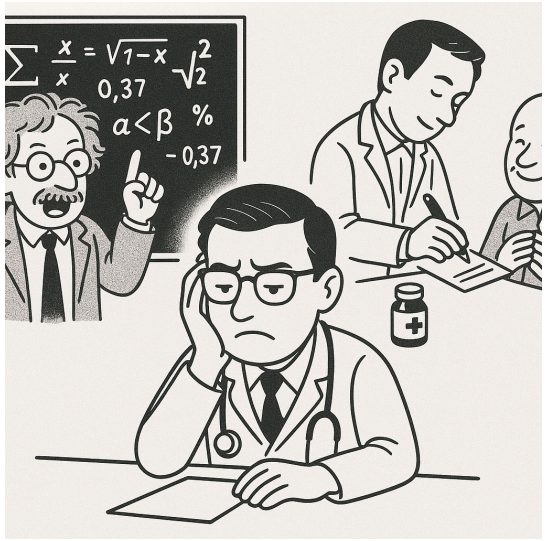


vieles hat sich geändert

das Bild der Kollegen
und der eigenen Fachrichtung

das Studiendesign



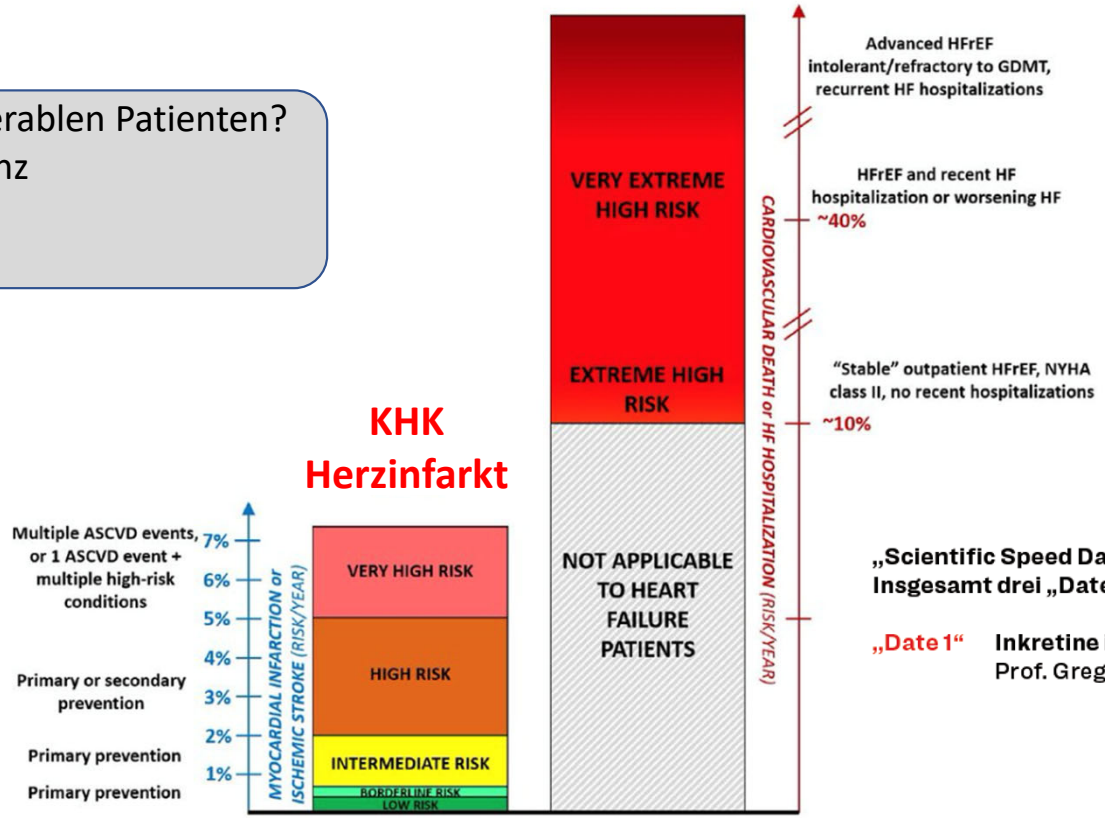


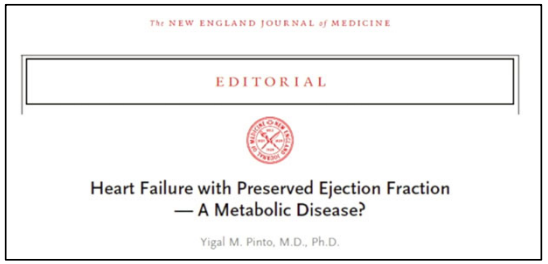
signifikant bedeutet nicht automatisch relevant und umgekehrt

die Situation in der Kardiologie

Wer sind die vulnerablen Patienten?
- Niereninsuffizienz
- Ältere
- Diabetes

Herzinsuffizienz



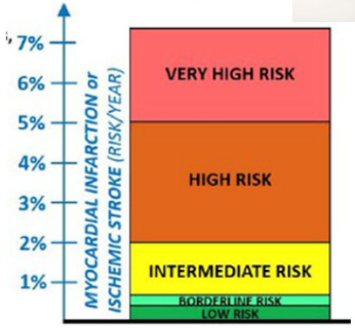


„Scientific Speed Dating" in Arbeitsgruppen
Insgesamt drei „Dates" pro Teilnehmer, jeweils 45 Minuten

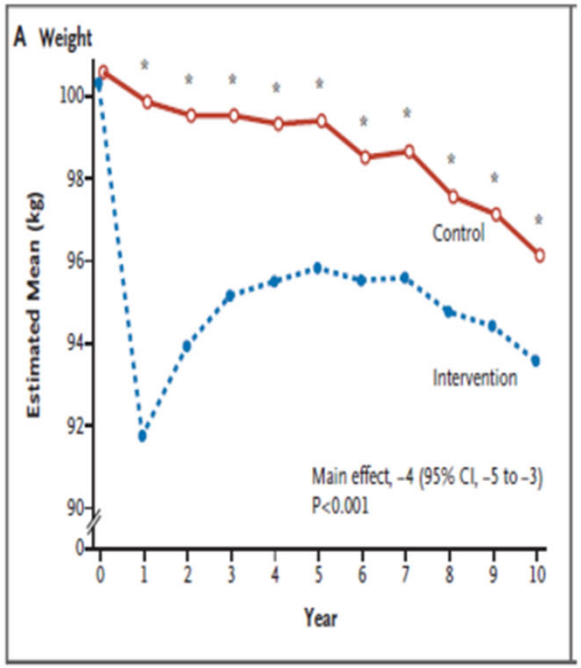
„Date 1" **Inkretine in der Kardiologie: Endpunktstudien im Fokus**
Prof. Gregor Simonis

Kardiovaskuläre Endpunkstudien bei Adipositas bis 202

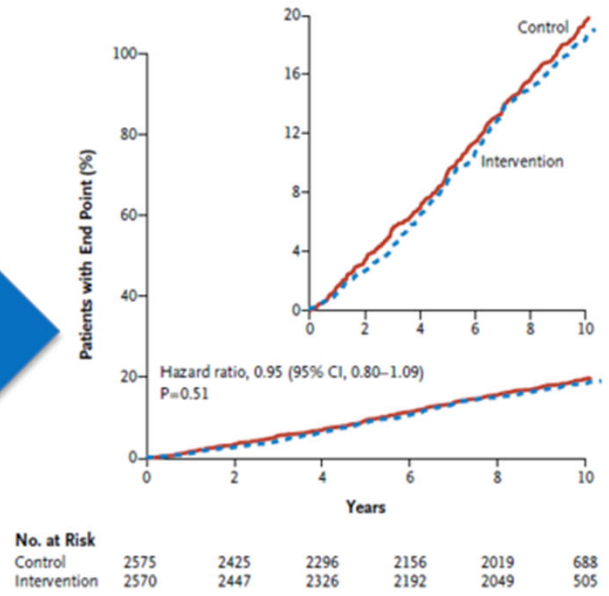
KHK
Herzinfarkt



Gewichtsreduktion durch Lifestyle und kardiovaskuläre Endpunkte



7% Weight ↓



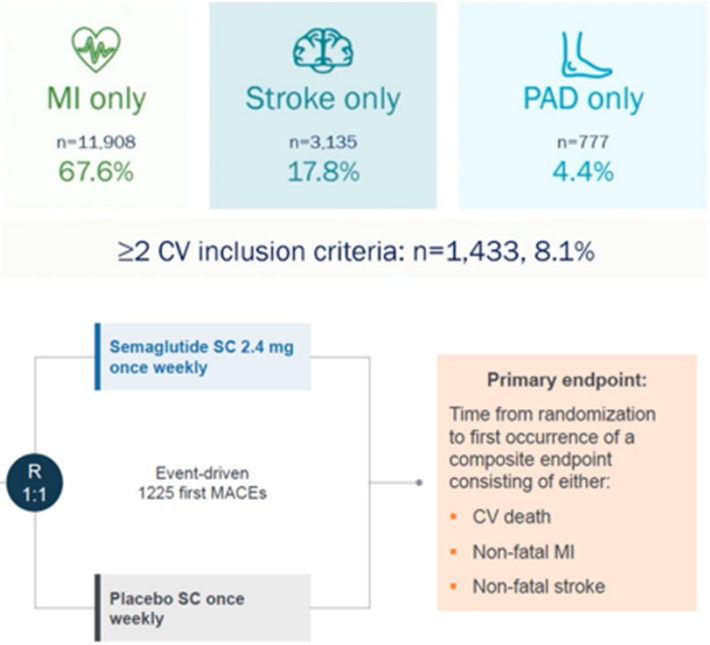
Look Ahead: N Engl J Med 2013

Kardiovaskuläre Endpunkstudien bei Adipositas nach 2023

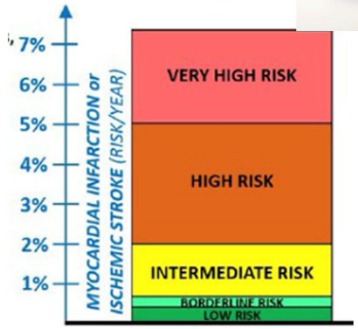
Bis August 2023 hatten wir keine Beweise,

daß Gewichtsreduktion kardiovaskuläre Endpunkte reduzieren kann

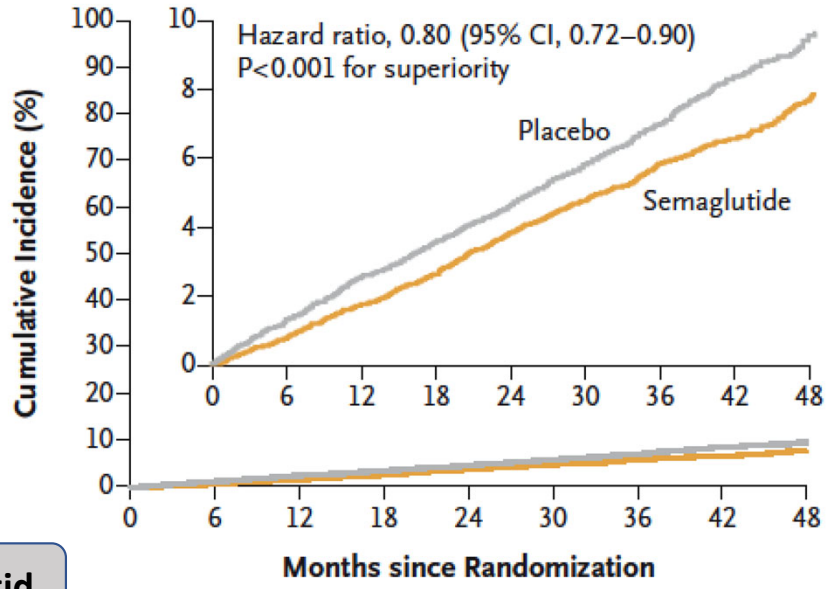
- **17605 Patienten**
- **weiblich: 27.8 %**
- **Alter 61.6 jahre**
- **BMI: 33.5**
- **EF: ≥45 %**
- **LDL: 78 mg/dl**
- **RR : 131/79 mm Hg**
- **kein Diabetes**



KHK Herzinfarkt



Primary Cardiovascular Composite End Point

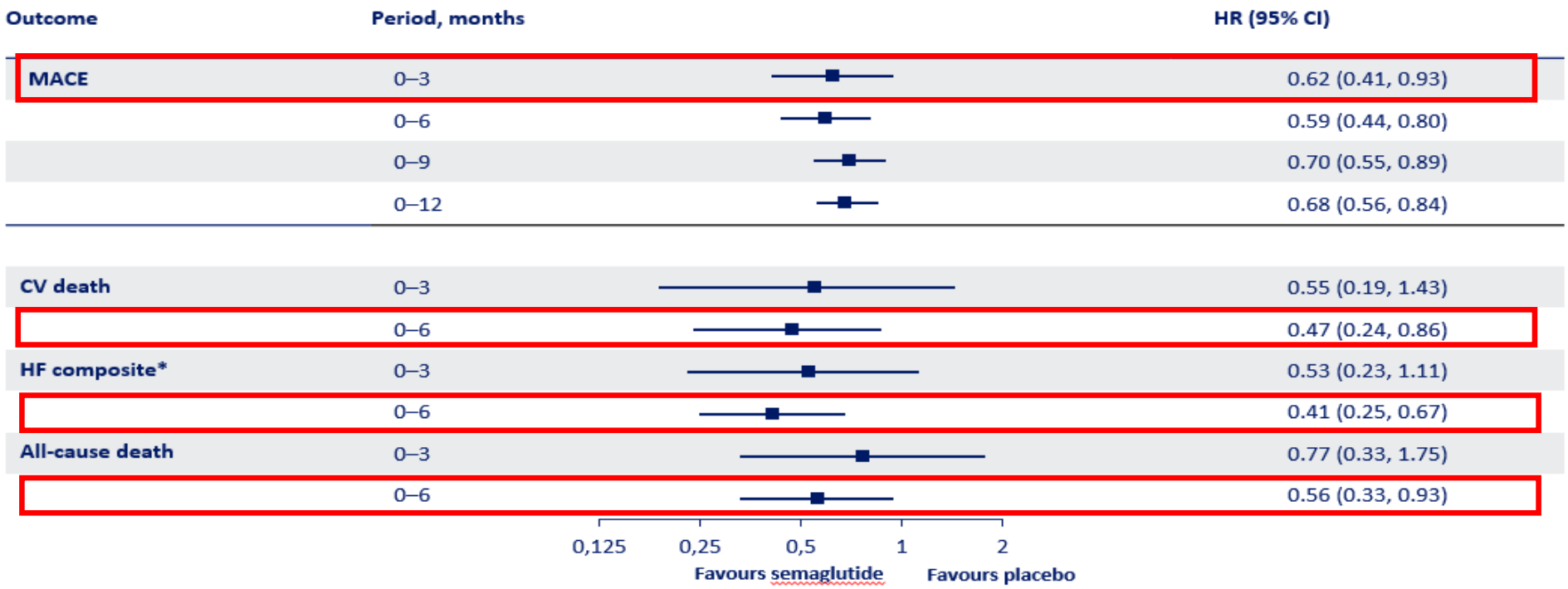


2026 Ergebnisse der SURMOUNT-MMO mit Tirzepatid

Lincoff et al. NEJM 2023

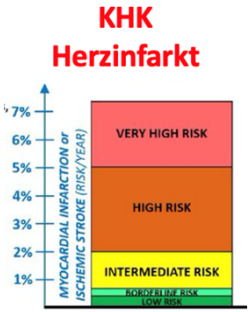
Frühzeitiger Nutzen auf kardiovaskuläre Endpunkte

- erster statistischer signifikanter Effekt: Tag 20
- nachhaltig ab Tag 86



Plutzky J. Early Clinical Benefit of Semaglutide in Adults with Overweight or Obesity and Cardiovascular Disease: A Secondary Analysis of the SELECT Trial. ECO 11. – 14. Mai 2025, Malaga, Spanien

Kardiovaskuläre Endpunkstudien bei Diabetes



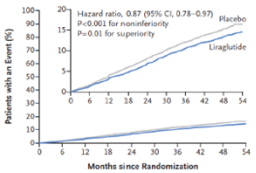
Rationale der SURPASS-CVOT Studie :

SURPASS-CVOT
Tirzepatid
vs.
Dulaglutid

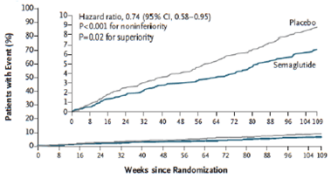
2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2025

JETZT

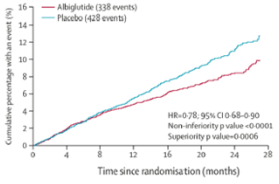
LEADER[1]



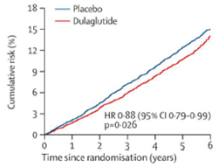
SUSTAIN-6[2]



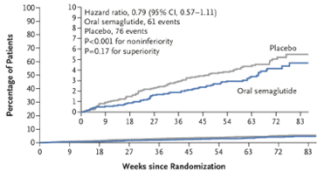
Harmony Outcomes[3]



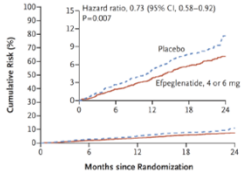
REWIND[4]



PIONEER 6[5]

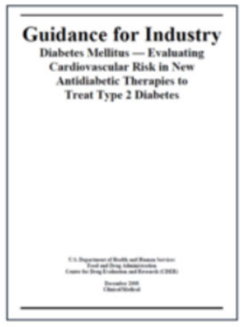


AMPLITUDE-O[6]



McGuire DK, et al. *Cardiovasc Diabetol*. 2022; Nicholls SJ, et al. Am Heart J. 2023 Zinman B. et al. N Engl J Med 2015
Marso et al. N Engl J Med 2016 Marso et al. N Engl J Med. 2016 7. Gerstein HC et al. Lancet. 2019

FDA requirements for CV outcome studies for new anti-diabetic agents



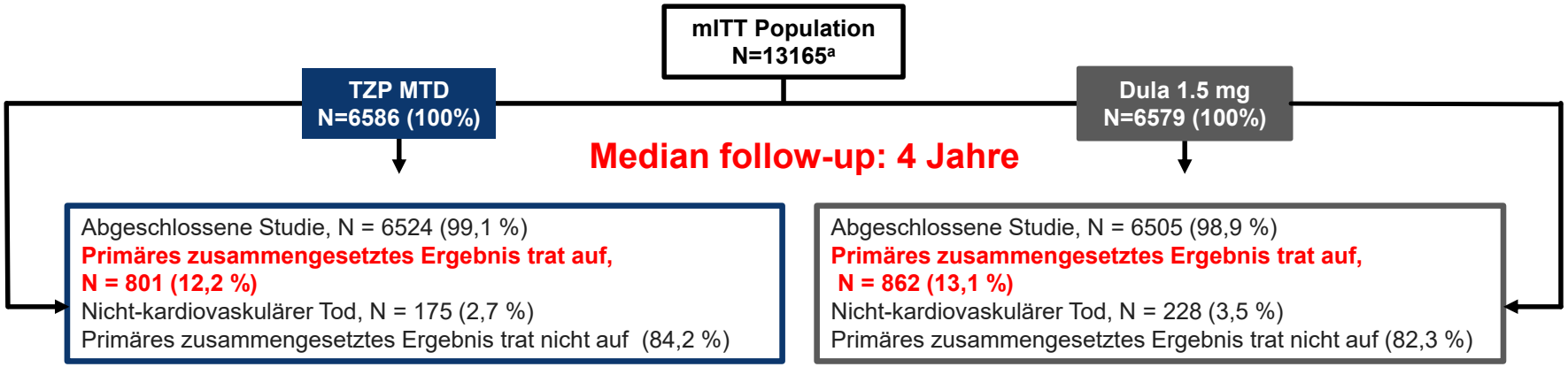
2008 FDA guidelines substantially raised the threshold for approval of antidiabetes drugs from proof of glucose lowering to robust assessment of cardiovascular safety

CV risk assessment on phase 2/3 data for all marketed and pipeline antidiabetes treatments: requisite upper bound of two-sided 95% CI for estimated risk ratio

>1.8:	the data are inadequate to support approval; a large safety trial should be conducted
1.3–1.8:	potential for CV harm might still exist; an adequately powered and designed post-marketing trial is necessary to show an upper bound <1.3
<1.3:	overall risk-benefit analysis supports approval; a post-marketing trial is generally not necessary

SURPASS-CVOT mündliche Präsentation auf dem EASD-Kongress in Wien, Österreich, am 18. September 2025

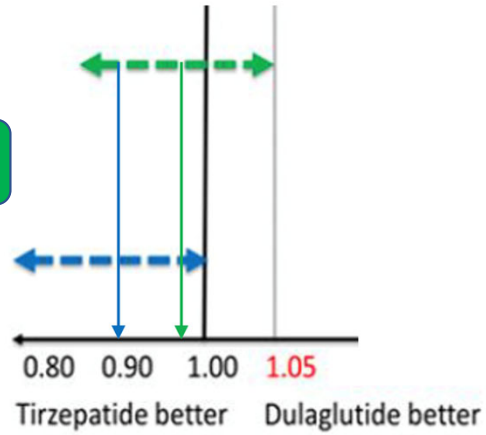
Studienaufbau



NI vs dulaglutide

Label: kardioprotektiv (FDA)

Superiority vs dulaglutide

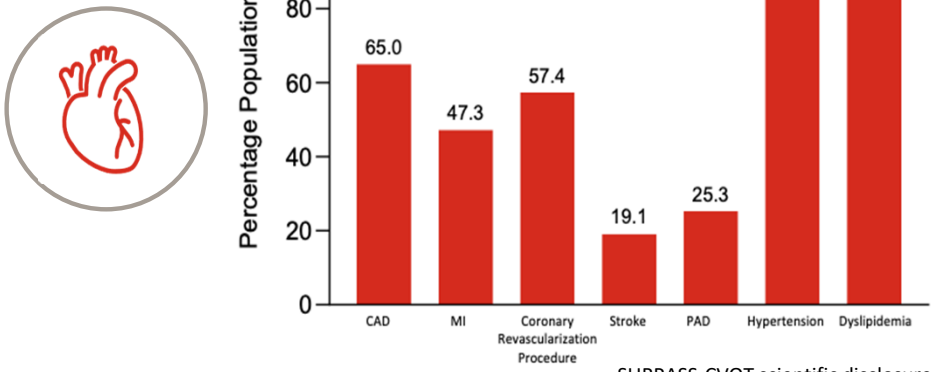


SURPASS-CVOT scientific disclosure, oral presentation at EASD Congress Vienna, Austria, on 18th September 2025

Basisparameter

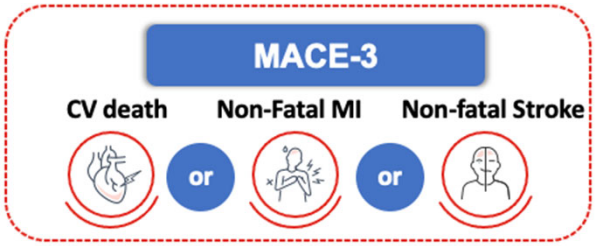
Parameter	TZP MTD (N=6586)	Dula 1.5 mg (N=6579)
Cardiovascular risk factors		
Weight, mean, kg	92.6	92.5
BMI, mean, kg/m²	32.6	32.6
Systolic blood pressure, mean, mmHg	135.1	135.5
HbA1c, mean, % (mmol/mol)	8.4 (68.4)	8.4 (68.1)
LDL cholesterol, mean, mg/dL (mmol/L)	80.5 (2.1)	80.7 (2.1)
Triglycerides, median, mg/dL (mmol/L)	160.3 (1.81)	159.4 (1.80)
eGFR, mean, mL/min/1.73 m²	78.5	79.2
UACR, median, mg/g	22.0	22.0

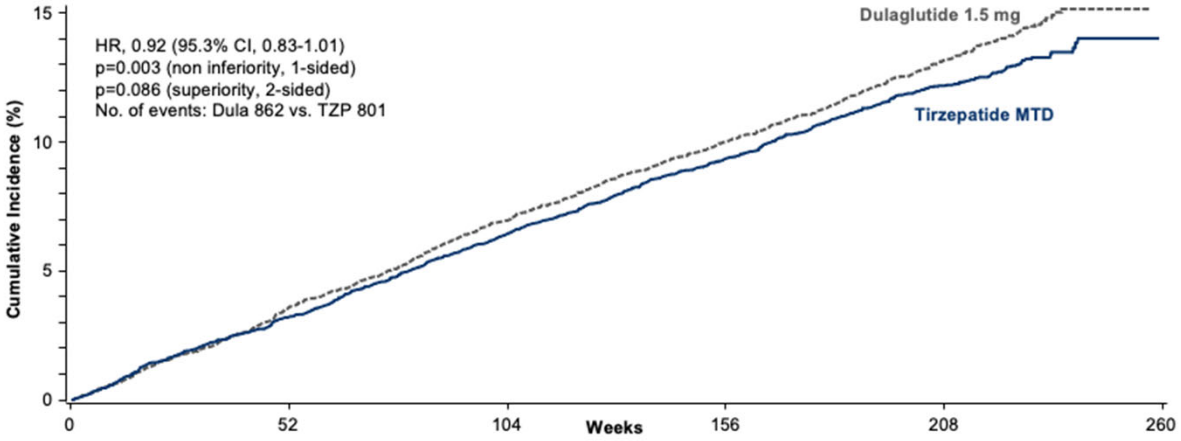
Parameter, %	TZP MTD (N=6586)	Dula 1.5 mg (N=6579)
Statin	86.0	85.6
Antihypertensive medications		
ACE inhibitor	40.3	39.4
ARB	40.0	40.9
Mineralocorticoid receptor antagonist	9.7	9.3
Antihyperglycaemic medications		
Metformin	81.1	81.7
SGLT-2 inhibitor	30.4	30.8
Sulfonylurea	21.3	22.0
DPP-4 inhibitor	5.8	5.7
Thiazolidinedione	2.4	2.7
Alpha-glucosidase inhibitor	1.7	1.6
Insulin	49.4	48.3

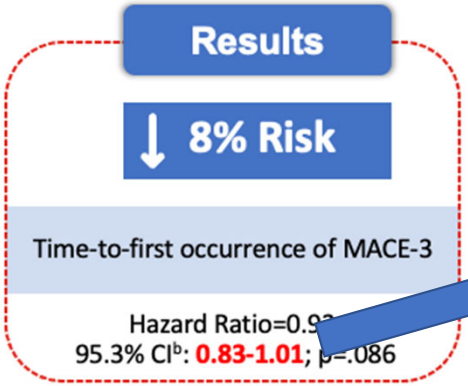


SURPASS-CVOT scientific disclosure, oral presentation at EASD Congress Vienna, Austria, on 18th September 2025

Primäre Endpunkt: kardiovaskuläre Mortalität, Herzinfarkt, Schlaganfall







Upper Limit of 95.3%[a] CI of HR for MACE-3 for TZP vs. Dulaglutide	Interpretation	Clinical Implications
<1.00	TZP is superior to dulaglutide	TZP has more cardioprotective effects than dulaglutide
≥1.00 but <1.05	TZP non-inferior to dulaglutide, and superior to putative placebo	TZP and dulaglutide are cardioprotective
≥1.05 but <1.23	TZP non-inferior to putative placebo	TZP confers no increased CV risk

Tirzepatide zeigte konsistente Ergebnisse über alle drei Komponenten des MACE-3-Kompositeindpunkts hinweg.

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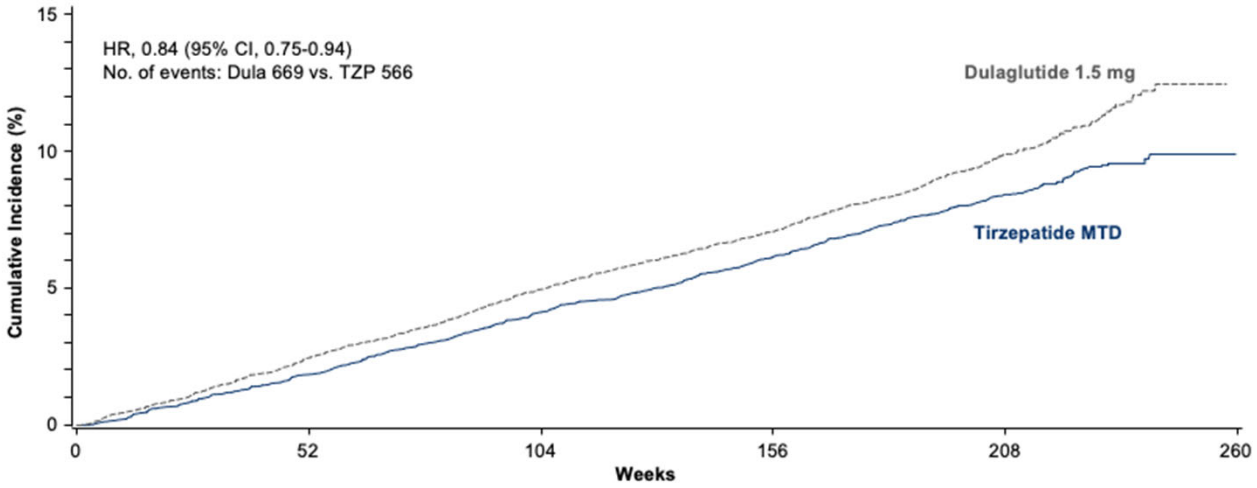
Gesamtsterblichkeit



Time to all-cause death[1]

↓ 16% Risk

Tirzepatide vs. dulaglutide

Hazard Ratio=0.84
95.0% CI: 0.75-0.94; p=.002

nur hypothesengenerierend

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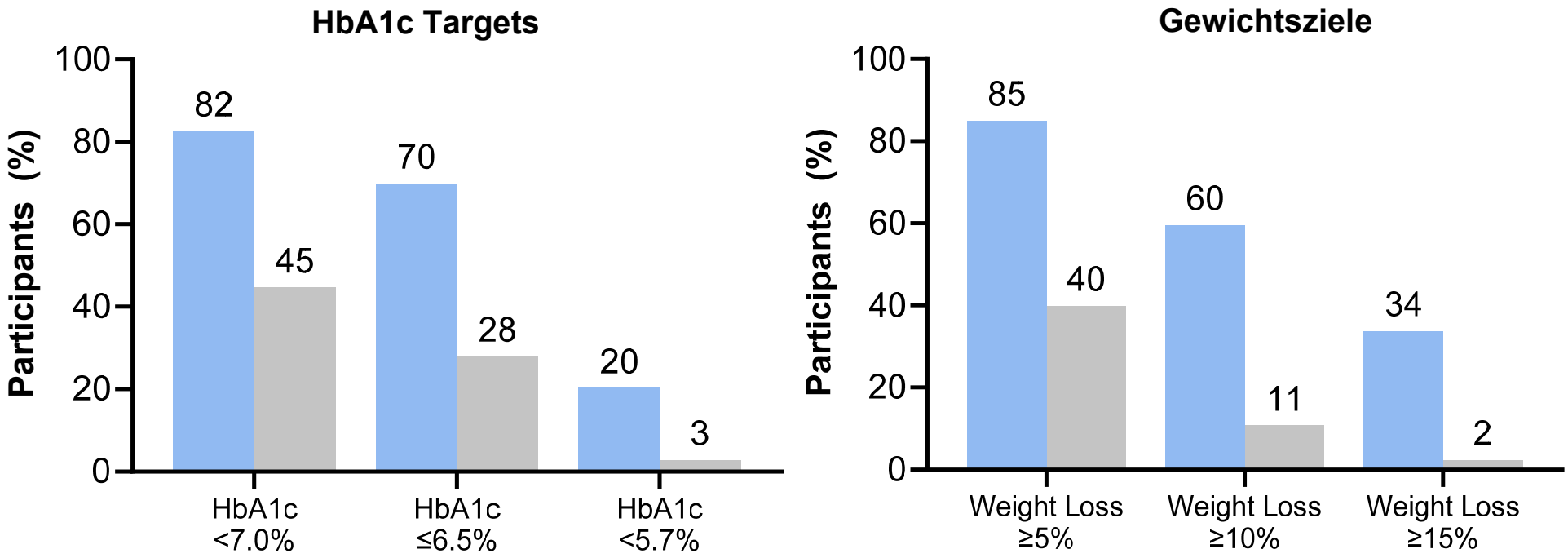
Anzahl der Patienten, die die Zielwerte erreichen



Target achieved at W24 (HbA1c) and W52 (body weight) : TZP MTD Dula 1.5 mg

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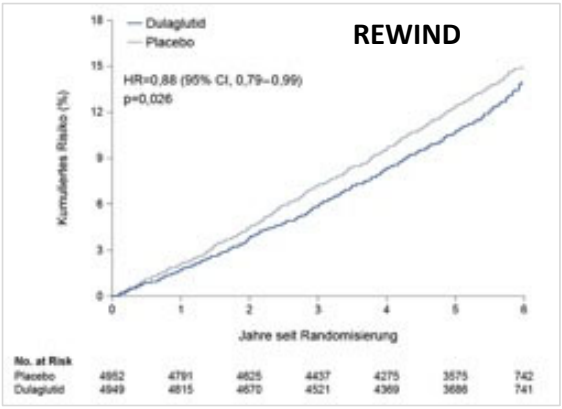
Präspezfische Analyse: Tirzepatid gegen Placebo
Wortschöpfung: putative (errechnet) Placebo



Dies ist eine Studie mit aktivem Komparator

Eine vorab festgelegte indirekte Vergleichsanalyse von aufeinander abgestimmten Patientendaten
aus den Studien REWIND und SURPASS-CVOT ergab, dass TZP Folgendes reduzierte:

MACE-3

↓ **28% Risk**

Hazard Ratio=0.72
95.0% CI: 0.55 to 0.94

vs. errechneten Placebo

Gesamt sterblichkeit

↓ **39% Risk**

Hazard Ratio=0.61
95.0% CI: 0.45 to 0.82

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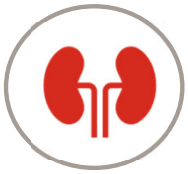
renale Endpunkte



- eGFR (CKD-EPI) 76.5 ±21.3 mL/min/1.73m^2
- <60 mL/min/1.73m^2 22.8%
- UACR 22 mg/g
- Microalbuminuria 32%
- Macroalbuminuria 11.5%

Major Kidney Outcomes	Primary Composite Kidney Endpoint
Persistent macroalbuminuria	✓
Persistent ≥50% reduction in eGFR	✓
ESKD[a]	✓
Death from kidney disease	✓

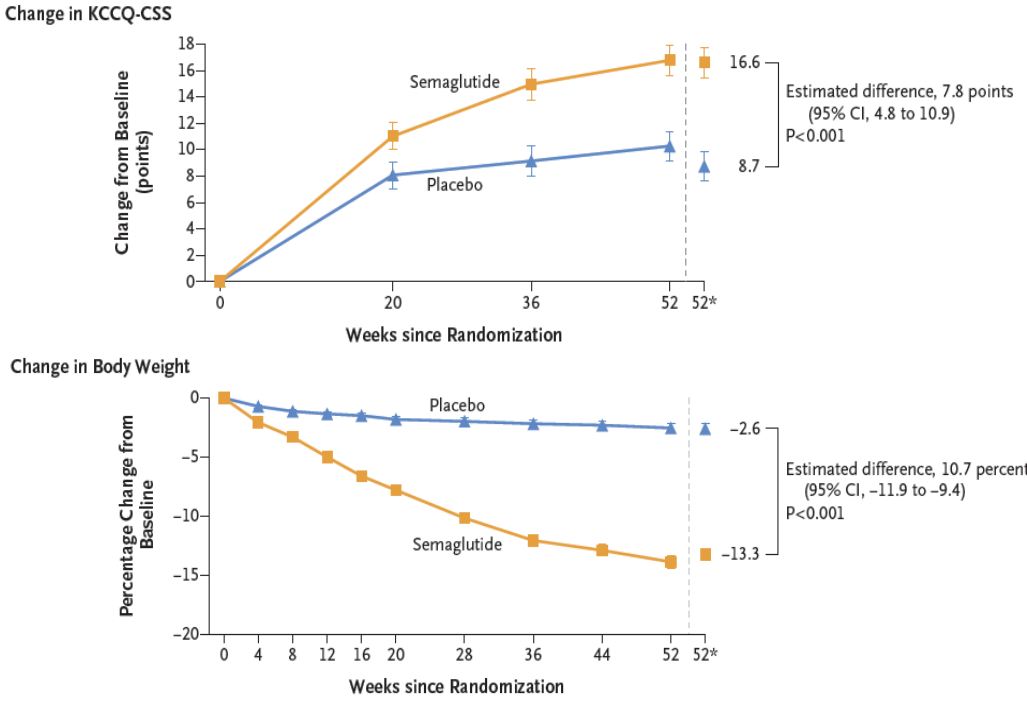
	Overall Population			
Parameter	**TZP MTD (N=6586)**	**Dula 1.5 mg (N=6579)**	**Hazard Ratio (95% CI)**	**p-value**
Primary composite kidney endpoint	441 (6.7)	532 (8.1)	0.81 (0.71 to 0.92)	**<0.001**
Components				
Persistent macroalbuminuria	238 (3.6)	322 (4.9)	0.72 (0.61 to 0.86)	**<0.001**
Persistent ≥50% reduction in eGFR	163 (2.5)	181 (2.8)	0.88 (0.71 to 1.09)	0.24
ESKD	106 (1.6)	93 (1.4)	1.12 (0.85 to 1.48)	0.42
Death from kidney disease	4 (0.1)	5 (0.1)		

SURPASS-CVOT scientific disclosure, oral presentation at EASD Congress Vienna, Austria, on 18th September 2025

Semaglutid bei HFpEF mit Adipositas: STEP-HFpEF und STEP-HFpEF-DM

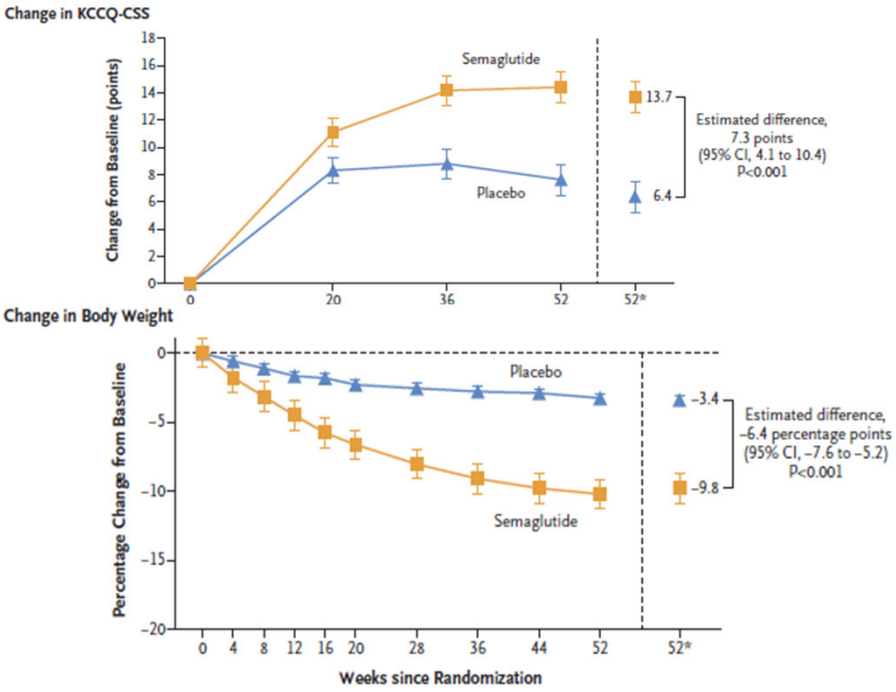
Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

M.N. Kosiborod, S.Z. Abildstrøm, B.A. Borlaug, J. Butler, S. Rasmussen, M. Davies, G.K. Hovingh, D.W. Kitzman, M.L. Lindegaard, D.V. Møller, S.J. Shah, M.B. Treppendahl, S. Verma, W. Abhayaratna, F.Z. Ahmed, V. Chopra, J. Ezekowitz, M. Fu, H. Ito, M. Lelonek, V. Melenovsky, B. Merkely, J. Núñez, E. Perna, M. Schou, M. Senni, K. Sharma, P. Van der Meer, D. von Lewinski, D. Wolf, and M.C Petrie, for the STEP-HFpEF Trial Committees and Investigators*



Semaglutide in Patients with Obesity-Related Heart Failure and Type 2 Diabetes

M.N. Kosiborod, M.C. Petrie, B.A. Borlaug, J. Butler, M.J. Davies, G.K. Hovingh, D.W. Kitzman, D.V. Møller, M.B. Treppendahl, S. Verma, T.J. Jensen, K. Liisberg, M.L. Lindegaard, W. Abhayaratna, F.Z. Ahmed, T. Ben-Gal, V. Chopra, J.A. Ezekowitz, M. Fu, H. Ito, M. Lelonek, V. Melenovský, B. Merkely, J. Núñez, E. Perna, M. Schou, M. Senni, K. Sharma, P. van der Meer, D. Von Lewinski, D. Wolf, and S.J. Shah, for the STEP-HFpEF DM Trial Committees and Investigators*



SUMMIT: Tirzepatid bei adipositasgetriebener HFpEF

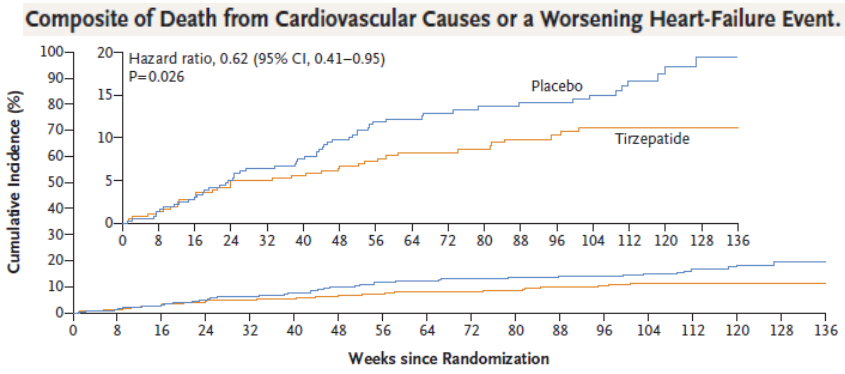
ORIGINAL ARTICLE

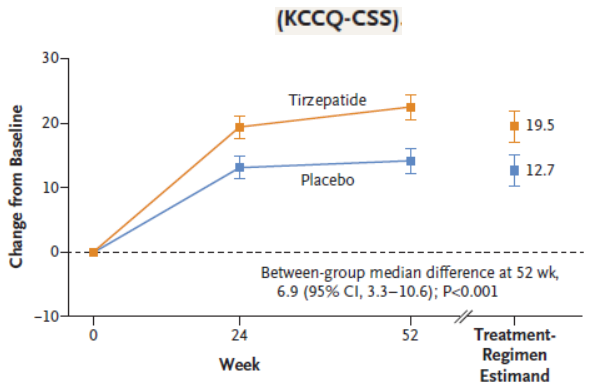
Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity

Milton Packer, M.D., Michael R. Zile, M.D., Christopher M. Kramer, M.D., Seth J. Baum, M.D., Sheldon E. Litwin, M.D., Venu Menon, M.D., Junbo Ge, M.D., Govinda J. Weerakkody, Ph.D., Yang Ou, Ph.D., Mathijs C. Bunck, M.D., Karla C. Hurt, B.S.N., Masahiro Murakami, M.D., and Barry A. Borlaug, M.D., for the SUMMIT Trial Study Group*

DOI: 10.1056/NEJMoa2410027

Einschlusskriterien: >40 Jahre, EF ≥50%, BMI >30 kg/m², NYHA II-IV
Rx: Tirzepatid (MTD: 5, 10 oder 15 mg) vs. Placebo
1: CV Tod oder Verschlechterung der Herzinsuffizienz, KCCQ-CCS
Eingeschlossen: 731 Patienten, ~ 65 Jahre, ~ BMI 38 kg/m², ~ 30% KHK, NT-proBNP ~ 180 pg/ml, ~ 25% Vorhofflimmern, **~ 47% Diabetes**
Medianes F/U 104 Wochen





End Point	Tirzepatide (N=364) Value	Tirzepatide (N=364) Events/100 patient-yr	Placebo (N=367) Value	Placebo (N=367) Events/100 patient-yr	Hazard Ratio or Difference (95% CI)†	P Value
Change at 52 weeks in 6-minute walk distance — m	26.0±3.8	—	10.1±3.9	—	18.3 (9.9 to 26.7)‡	<0.001§
Percent change at 52 weeks in body weight — %	−13.9±0.4	—	−2.2±0.5	—	−11.6 (−12.9 to −10.4)	<0.001

Tirzepatid effektiv bei adipositasgetriebener HFpEF

Ein provokantes, aber überzeugendes Konzept