INluks

«Quer durch den Bauch»

17. Juni 2025

Fett-weg-Spritze oder Messer (1)

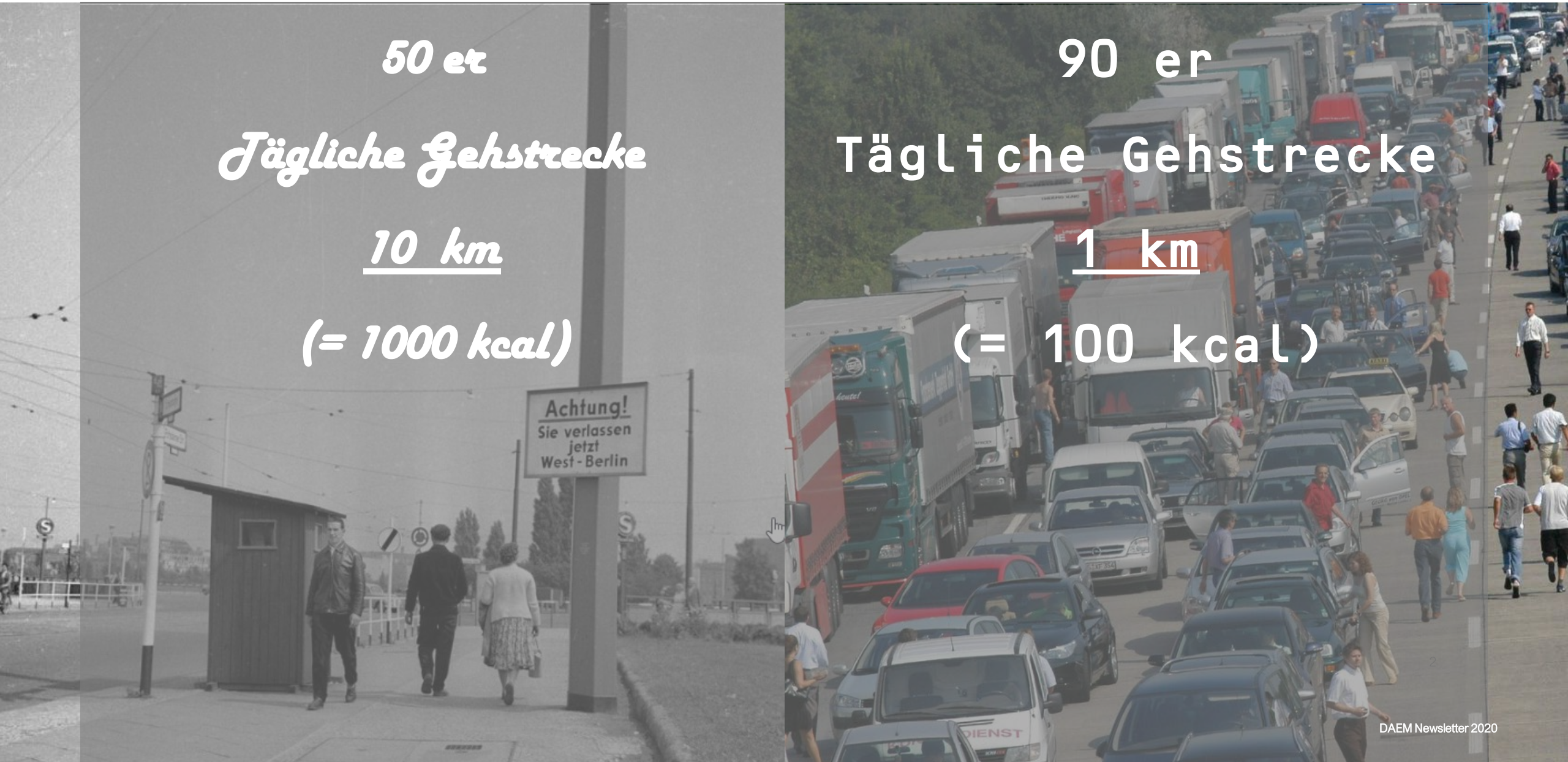
Dr. med. Lukas Burget

Leitender Arzt Endokrinologie/Diabetologie, LUKS

Co-Leiter Adipositaszentrum Zentralschweiz

Ursache (1) Bewegung – *nicht alles wird besser*

luzerner kantonsspital
LUZERN SURSEE WOLHUSEN



Ursache (2) Kalorien – *gute Korrelation mit BMI*

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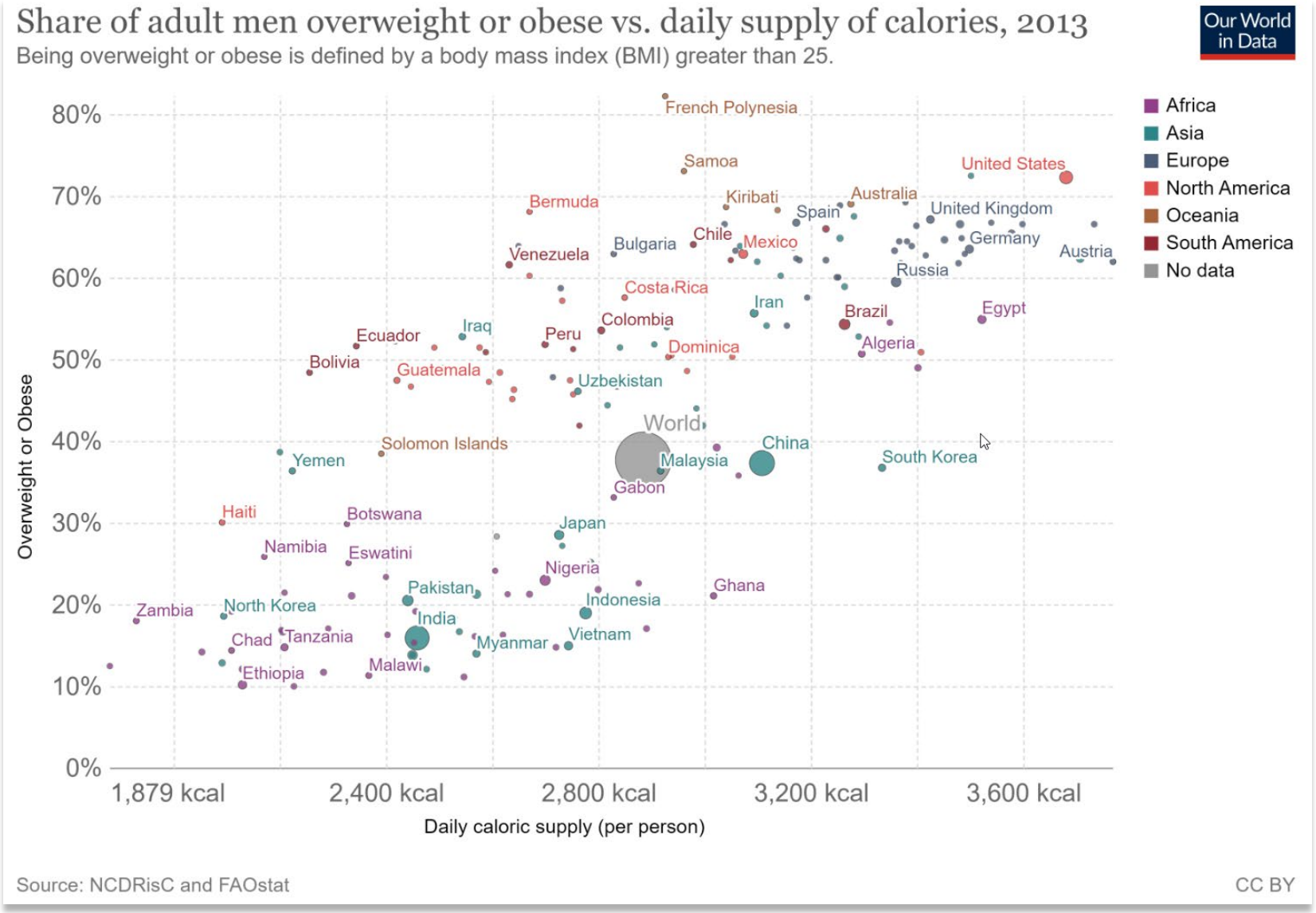
LUZERN SURSEE WOLHUSEN



Ursache (3) Genetik

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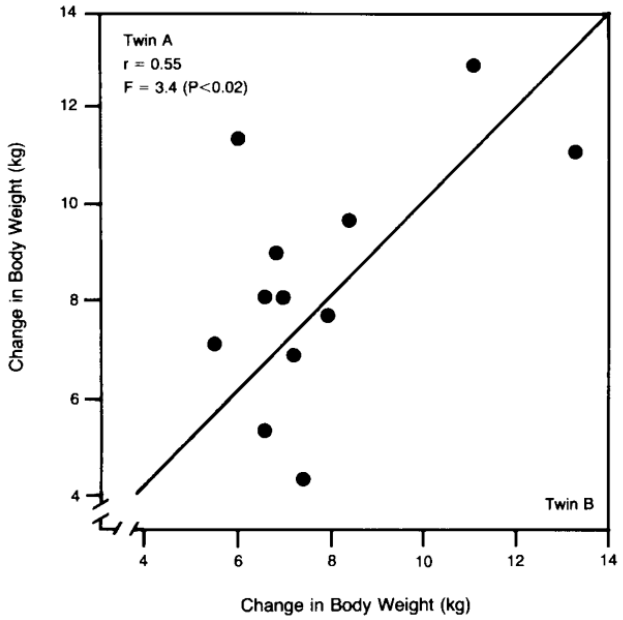
LUZERN SURSEE WOLHUSEN

THE RESPONSE TO LONG-TERM OVERFEEDING IN IDENTICAL TWINS

CLAUDE BOUCHARD, PH.D., ANGELO TREMBLAY, PH.D., JEAN-PIERRE DESPRÉS, PH.D., ANDRÉ NADEAU, M.D., PAUL J. LUPIEN, M.D., PH.D., GERMAIN THÉRIAULT, M.D., JEAN DUSSAULT, M.D., SITAL MOORJANI, PH.D., SYLVIE PINAULT, M.D., AND GUY FOURNIER, B.SC.

12 eineiige Zwillingspaare > 6 Wochen hyperkalorische Ernährung (+ 1000 kcal vs. Baseline)



Gewichtszunahmen zwischen 4 und 13 kg mit signifikant geringerer Varianz *innerhalb* der Paare vs. *zwischen* den Paaren

NEJM 1990

«Greenwashing»

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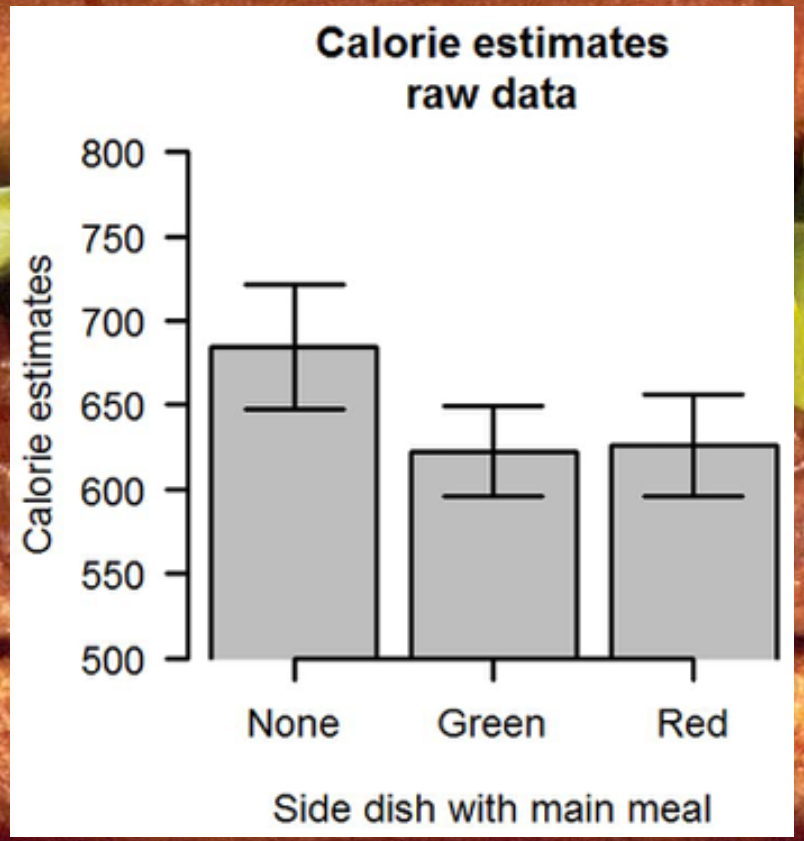
LUZERN SURSEE WOLHUSEN

Underestimating Calorie Content When Healthy Foods Are Present: An Averaging Effect or a Reference-Dependent Anchoring Effect?

Suzanna E. Forwood[1]*, Amy Ahern[2], Gareth J. Hollands[1], Paul C. Fletcher[3], Theresa M. Marteau[1]

1 Behaviour and Health Research Unit, Department for Public Health and Primary Care, University of Cambridge, Cambridge, United Kingdom, **2** Medical Research Council Human Nutrition Research, Cambridge, United Kingdom, **3** Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom



PLOS one 2013

«Convenience oder Küche ?»

Cell Metabolism
Clinical and Translational Report

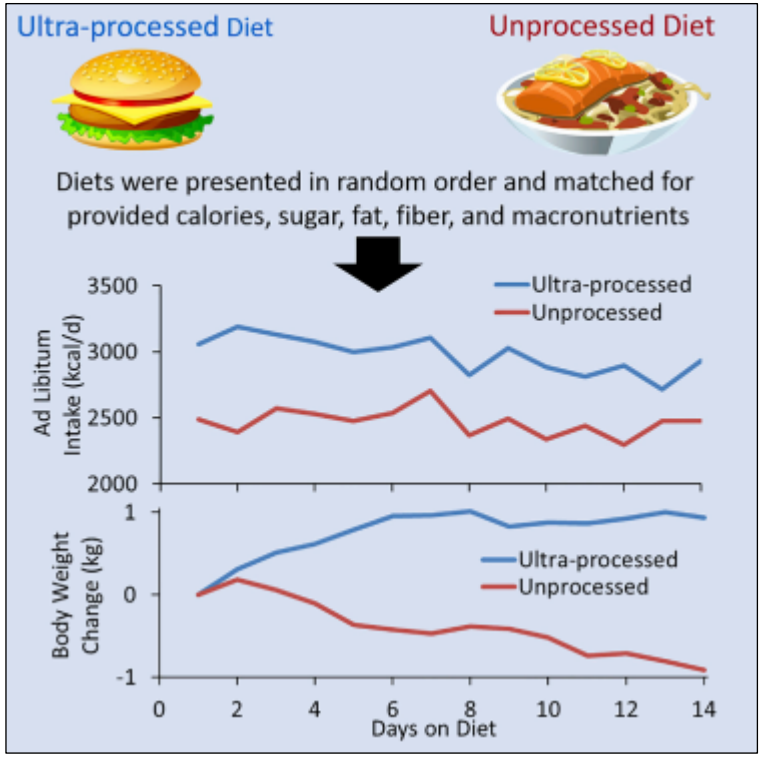
Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of *Ad Libitum* Food Intake

Kevin D. Hall,[1,5,*] Alexis Ayuketah,[1] Robert Brychta,[1] Hongyi Cai,[1] Thomas Cassimatis,[1] Kong Y. Chen,[1] Stephanie T. Chung,[1] Elise Costa,[1] Amber Courville,[2] Valerie Darcey,[1] Laura A. Fletcher,[1] Ciaran G. Forde,[4] Ahmed M. Gharib,[1] Juen Guo,[1] Rebecca Howard,[1] Paule V. Joseph,[3] Suzanne McGehee,[1] Ronald Ouwerkerk,[1] Klaudia Raisinger,[2] Irene Rozga,[1] Michael Stagliano,[1] Mary Walter,[1] Peter J. Walter,[1] Shanna Yang,[2] and Megan Zhou[1]

20 übergewichtige Probanden, «Junkfood» vs. frisch gekocht (ad libitum)

106 $ / W

+ Zucker
+ Ω 6 / Ω 3
+ Ges. Fettsäuren
- Ballaststoffe

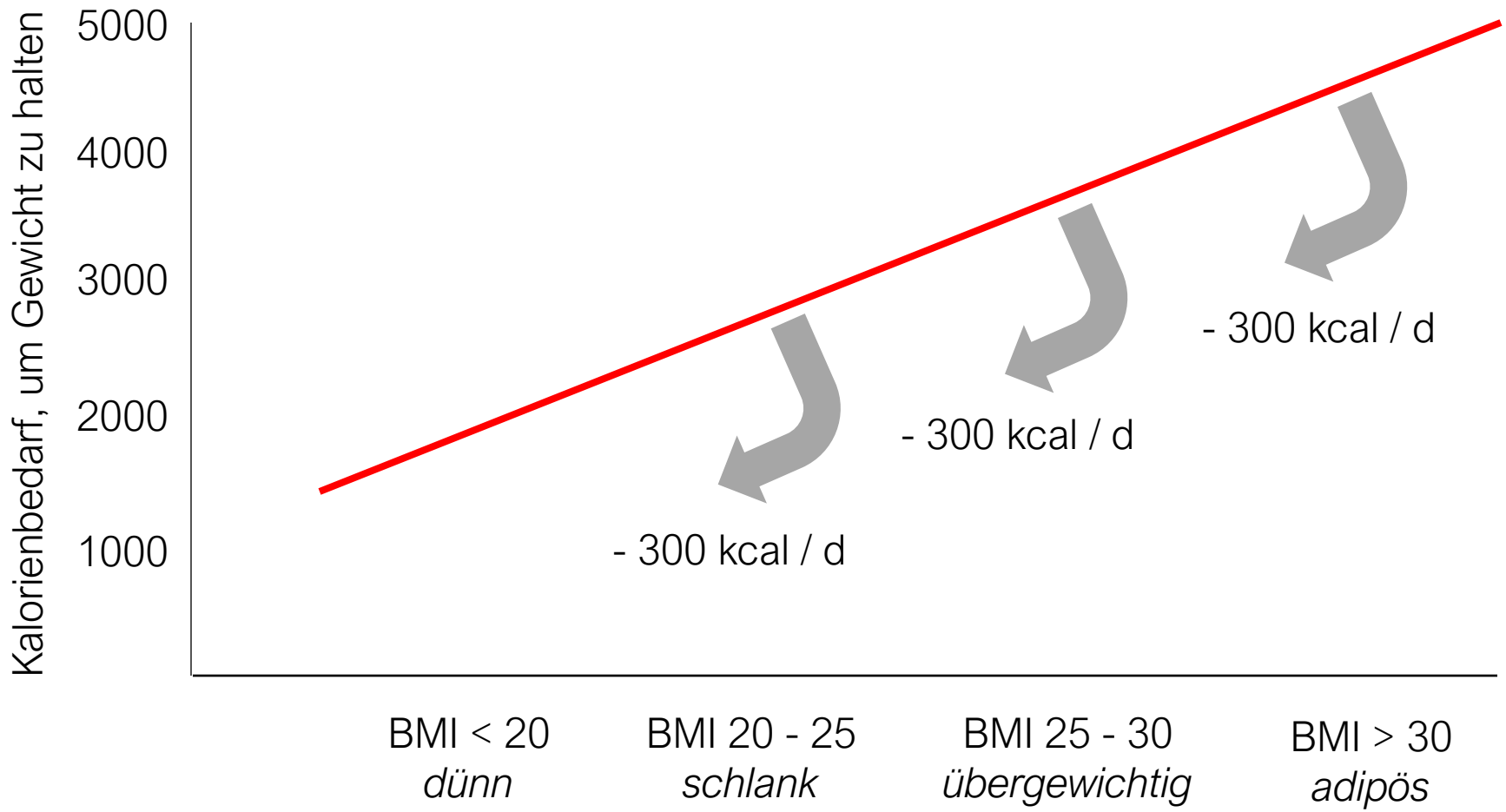


151 $ / W

- Zucker
- Ω 6 / Ω 3
- Ges. Fettsäuren
+ Ballaststoffe

Cell Metab. 2019

Verminderter Umsatz nach Gewichtsabnahme



Rosenbaum et al. American Journal of Physiology 1996, Sumithran et al., NEJM 2011

Hunger, Genuss, Gewohnheit

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Biologie

Hypothalamus

Leptin, GPI, PYY,
GLP 1, Ghrelin, …

Medikamente

Operation

Homöostatisches Essen

«Hunger»

Hedonistisches Essen

«Genuss»

Exekutives Essen

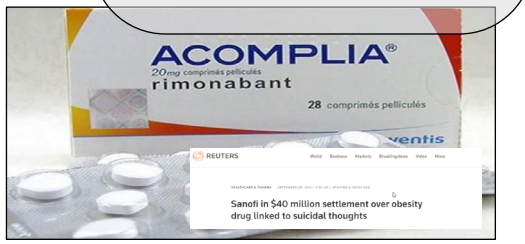
«Entscheiden zu Essen»

Psychologie

Mesolimbisches System

Dopamin-, Opioid,-
Cannabinoid-
rezeptoren

(Medikamente)



Lifestyle **Verhaltenstherapie**

A. Sharma, SGED 2022

Hypothalamus – Ziel der Inkretine

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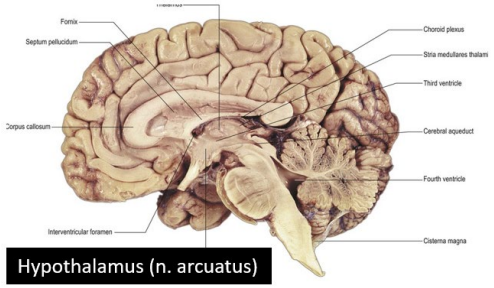

Hypothalamus (n. arcuatus)

Glucagon (Pankreas)

GIP (Duodenum)

N. vagus

Ghrelin (Magen)

Insulin (Pankreas)

GLP-1 (Dünndarm)

PYY (Colon)

CCK (Duodenum)

Leptin (Fettgewebe)

Energieaufnahme

Energieverbrauch

Hypothalamus

NPY

POMC

AgRP

CART

Leptin – erster Vertreter der Inkretine

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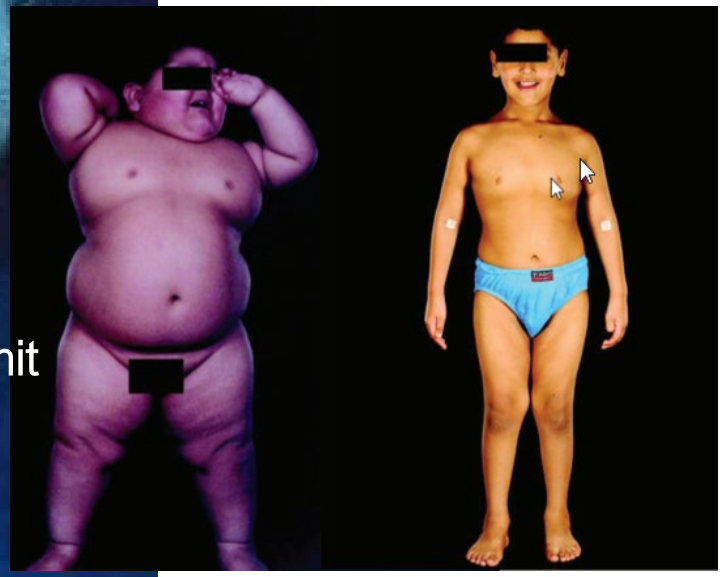
- Spezifische Genmutation führt zu endogenem Leptinmangel und damit Hyperphagie und massiver Gewichtszunahme.
- Exogene Leptingabe macht diesen Effekt reversibel.



Nature 1994,Nature 1990, Endocrinology reviews 2018

Gesundheit, *nicht Ästhetik*

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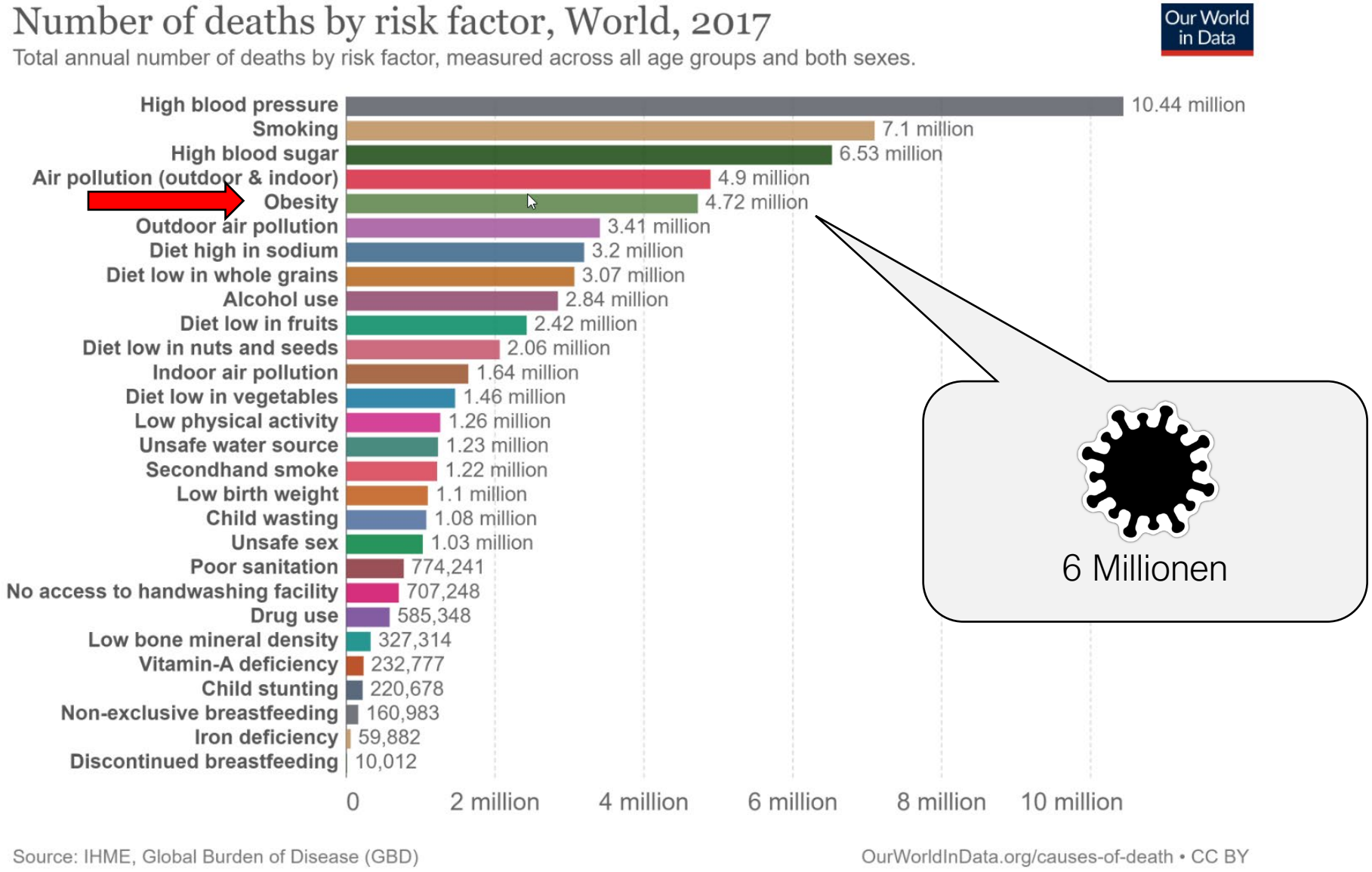
LUZERN SURSEE WOLHUSEN



Sekundärkomplikationen – *metabolisches Syndrom & mehr*

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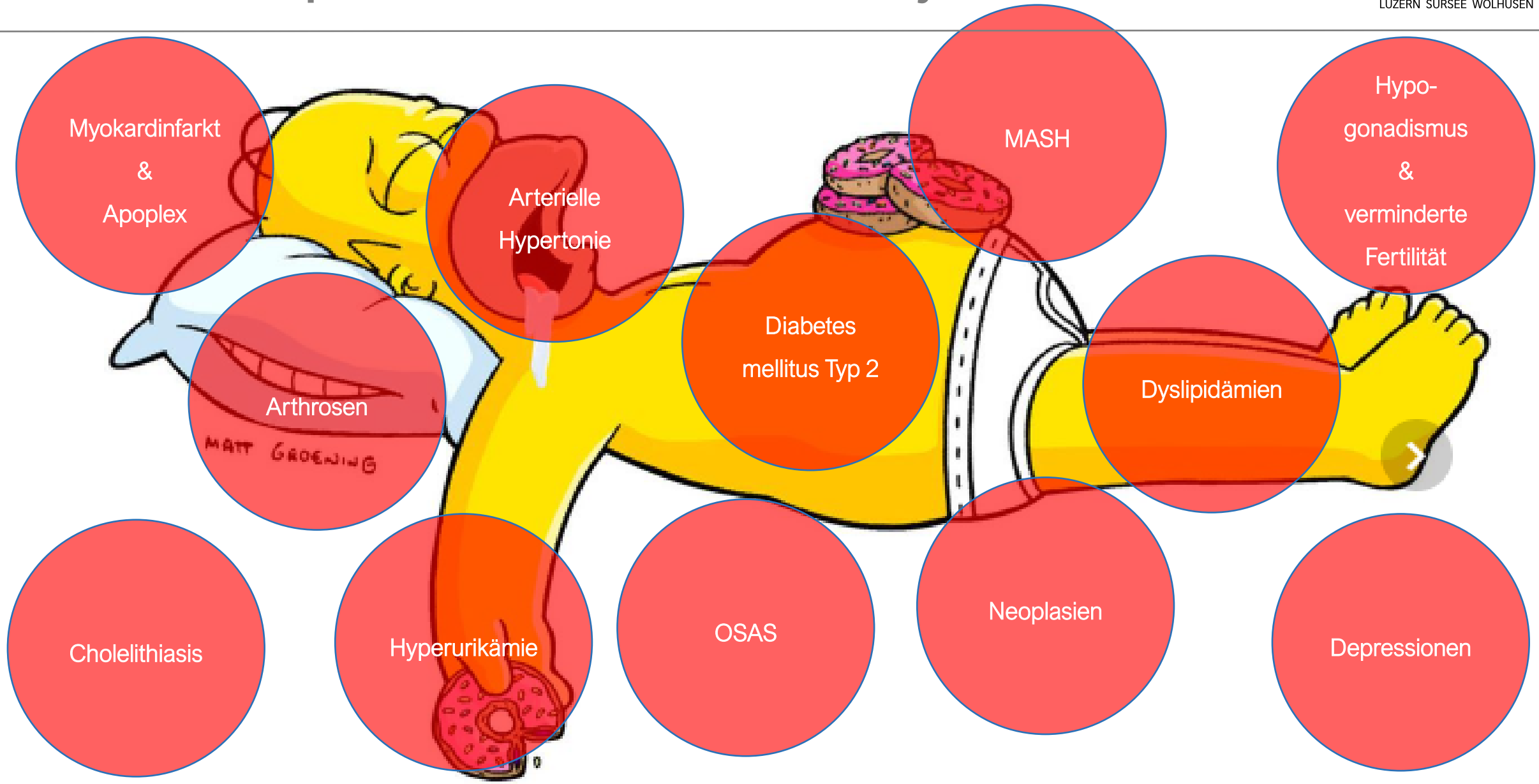
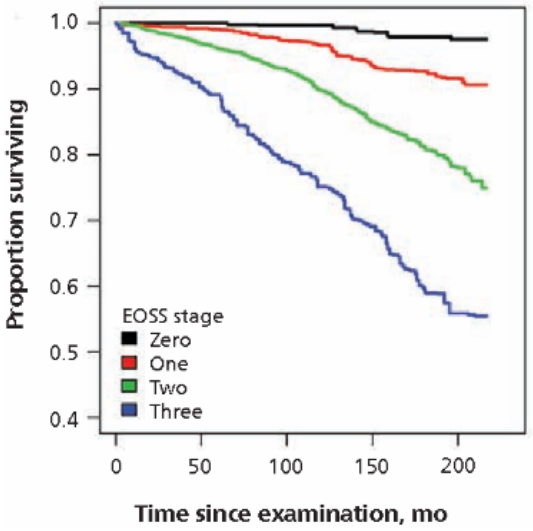
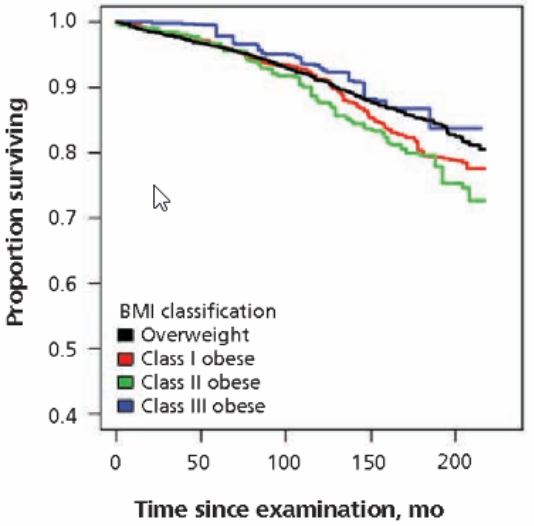


Edmonton Obesity Staging System (EOSS)





STAGE 0

- **NO** sign of obesity-related risk factors
- **NO** physical symptoms
- **NO** psychological symptoms
- **NO** functional limitations

Case Example:
Physically active female with a BMI of 32 kg/m², no risk factors, no physical symptoms, no self-esteem issues, and no functional limitations.

Class I, Stage 0 Obesity

EOSS Score

WHO Obesity Classfication

STAGE 1

- Patient has obesity-related **SUBCLINICAL** risk factors (borderline hypertension, impaired fasting glucose, elevated liver enzymes, etc.)

- OR -

- **MILD** physical symptoms - patient currently not requiring medical treatment for comorbidities (dyspnea on moderate exertion, occasional aches/pains, fatigue, etc.)

- OR -

- **MILD** obesity-related psychological symptoms and/or mild impairment of well-being (quality of life not impacted)

Case Example:
38 year old female with a BMI of 59.2 kg/m², borderline hypertension, mild lower back pain, and knee pain. Patient does not require any medical intervention.

Class III, Stage 1 Obesity

WHO CLASSIFICATION OF WEIGHT STATUS (**BMI kg/m²**)

Obese Class I ..... 30 - 34.9
Obese Class II ..... 35 - 39.9
Obese Class III ..... ≥40

Stage 0 / Stage 1 Obesity

Patient ***does not meet clinical criteria for admission*** at this time.
Please refer to primary care for further preventative treatment options.

STAGE 2

- Patient has **ESTABLISHED** obesity-related comorbidities requiring medical intervention (HTN, Type 2 Diabetes, sleep apnea, PCOS, osteoarthritis, reflux disease)

- OR -

- **MODERATE** obesity-related psychological symptoms (depression, eating disorders, anxiety disorder)

- OR -

- **MODERATE** functional limitations in daily activities (quality of life is beginning to be impacted)

Case Example:
32 year old male with a BMI of 36 kg/m² who has primary hypertension and obstructive sleep apnea.

Class II, Stage 2 Obesity

STAGE 3

- Patient has **significant** obesity-related end-organ damage (myocardial infarction, heart failure, diabetic complications, incapacitating osteoarthritis)

- OR -

- **SIGNIFICANT** obesity-related psychological symptoms (major depression, suicide ideation)

- OR -

- **SIGNIFICANT** functional limitations (eg: unable to work or complete routine activities, reduced mobility)
- **SIGNIFICANT** impairment of well-being (quality of life is significantly impacted)

Case Example:
49 year old female with a BMI of 67 kg/m² diagnosed with sleep apnea, CV disease, GERD, and suffered from stroke. Patient's mobility is significantly limited due to osteoarthritis and gout.

Class III, Stage 3 Obesity

STAGE 4

- **SEVERE** (potential end stage) from obesity-related comorbidities

- OR -

- **SEVERELY** disabling psychological symptoms

- OR -

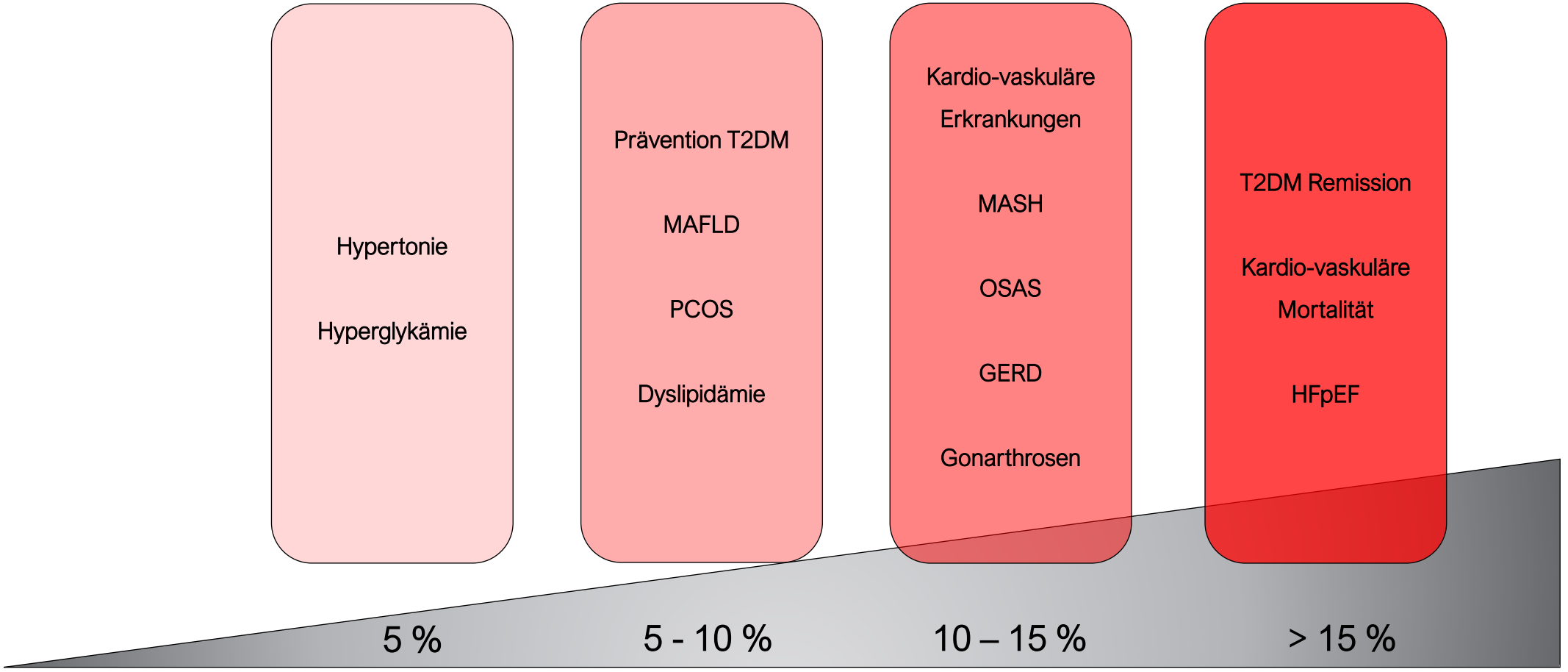
- **SEVERE** functional limitations

Case Example:
45 year old female with a BMI of 54 kg/m² who is in a wheel chair because of disabling arthritis, severe hyperpnea, and anxiety disorder.

Class III, Stage 4 Obesity

Sharma et al., Int. J. Obes. 2009, NHANES III 1988 - 1994

Abnahme von Gewicht und Komorbiditäten



Garvey et al. Endocr. Pract. 2016, Look AHEAD Research Group Lancet Diabetes Endocrinol. 2016, Lean et al. Lancet 2018, Benraoune Curr. Opin. Cardiol. , Sundström J et al. Circulation 2017

49 jähriger Patient mit metabolischem Syndrom

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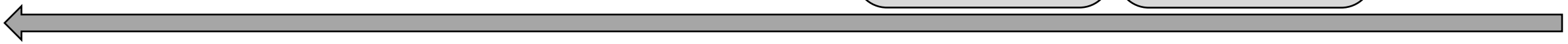
BMI 29 (Monat 10)	BMI 33 (Monat 0)
Liraglutide 3,0 mg	Janumet 50/1000 mg Candesartan 16 mg Atorvastatin 40 mg CPAP



HbA1c (IFCC)	29-42	mmol/molHb	34	40
HbA1c (DCCT)	4.8-5.9	%	5.3	5.7
Creatinin (enzymatisch)	59-104	µmol/L	75	
eGFR	-	ml/min/1.73m²	> 90 *	
Cholesterin gesamt	<5.2	mmol/L	4.07	3.56
Cholesterin-HDL	>1	mmol/L	1.35	1.31 *
Cholesterin-LDL	-	mmol/L	2.63 +	2.51 *
Triglyceride	< 2.0	mmol/L	0.62	0.54
Enzyme				
ALAT/GPT	10-50	U/L	36	
ASAT/GOT	<50	U/L		
Amylase	28-100	U/L	50	
Lipase	13-60	U/L	33	

Vergangenheit

Gegenwart


0.25 mg
0.5 mg
wegovy®
1 mg
wegovy®
1.7 mg
wegovy®
(semaglutide) injection
2.4 mg
wegovy®
(semaglutide) injection
2.4 mg/0.75 mL
Use Wegovy 1 time a week
4 Single-Dose Prefilled Pens
Each pen delivers a single dose of 2.4 mg semaglutide
For subcutaneous use only
Single-Dose only
Rx only
Dispense the enclosed Medication Guide to each patient.
novo nordisk


mounjaro™
(tirzepatide) injection
2.5 mg
0.5 mL
4 x 2.5 mg/0.5 mL prefilled pens
Rx Only
For Subcutaneous Use
Dispense enclosed Medication Guide to each patient.
Use one pen every week.
Sample: Not for sale
Limit 1 carton per customer
4 Single-dose prefilled pens
Lilly

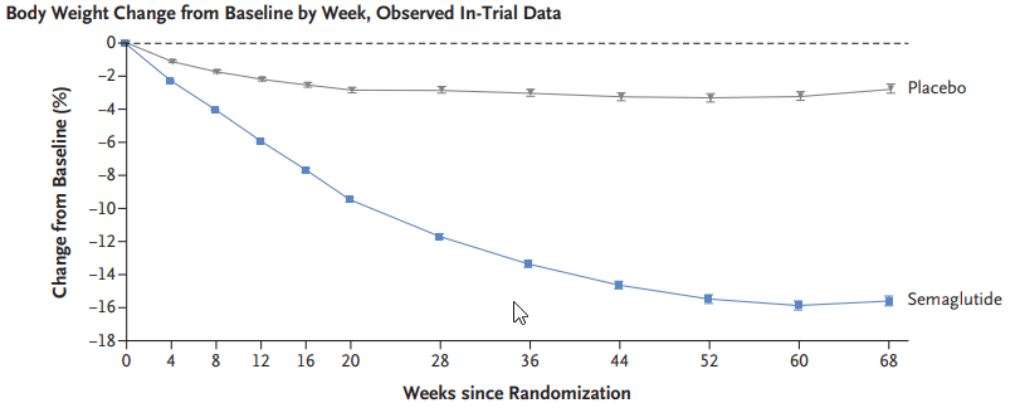

zepbound
2.5
(tirzepatide) injection

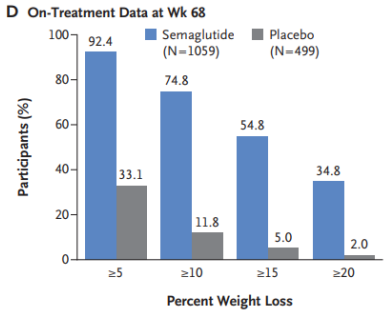
Zweiter GLP-1-Agonist - **Semaglutide**

luzerner kantonsspital
LUZERN SURSEE WOLHUSEN

Once-Weekly Semaglutide in Adults with Overweight or Obesity

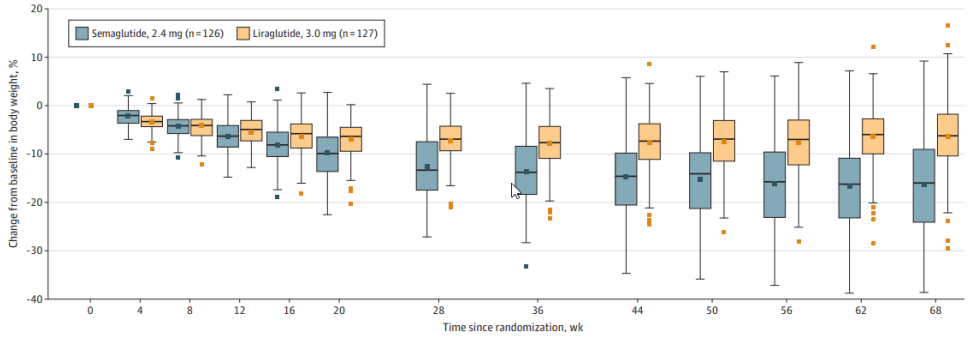
John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D., Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D., Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D., Sean Wharton,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

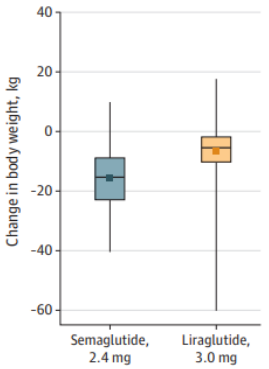




Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes
The STEP 8 Randomized Clinical Trial

Domenica M. Rubino, MD; Frank L. Greenway, MD; Usman Khalid, MD, PhD; Patrick M. O'Neil, PhD; Julio Rosenstock, MD; Rasmus Sørrig, MD, PhD; Thomas A. Wadden, PhD; Alicja Wizert, PhD; W. Timothy Garvey, MD; for the STEP 8 Investigators





Semaglutid 2.4 mg = Wegovy®

NEJM 2021, JAMA 2022

Erster Doppelagonist - GLP-1 & GIP Agonist **Tirzepatid**

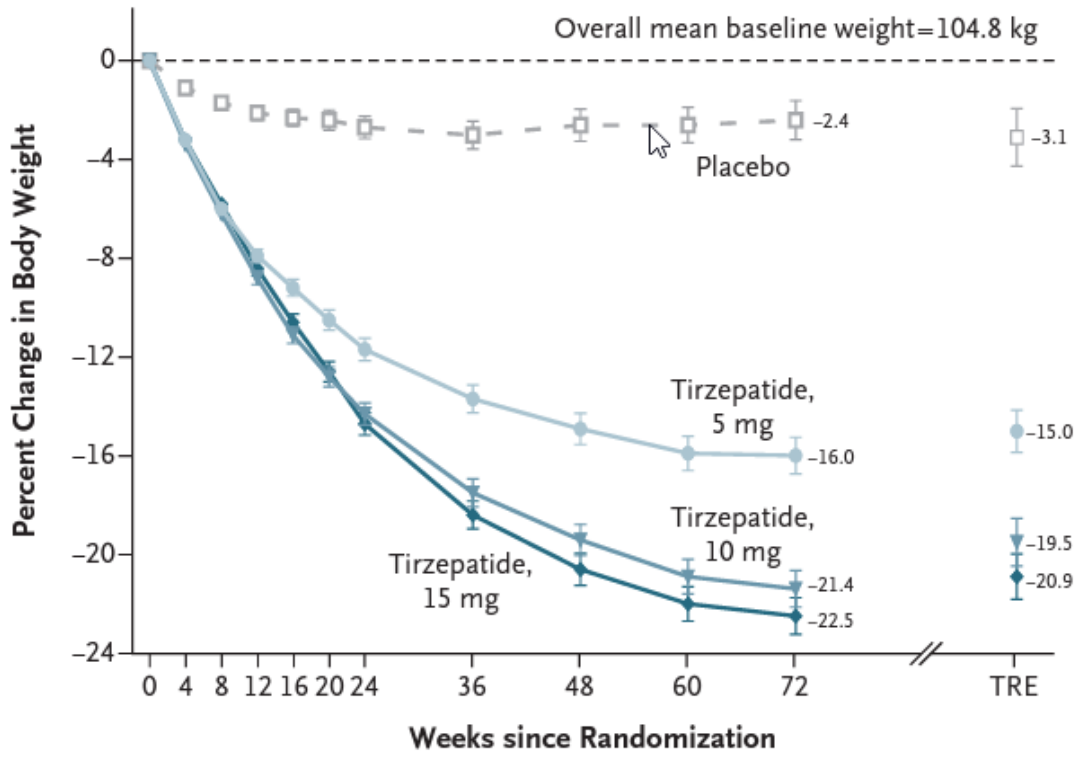
luzerner kantonsspital
LUZERN SURSEE WOLHUSEN

ORIGINAL ARTICLE

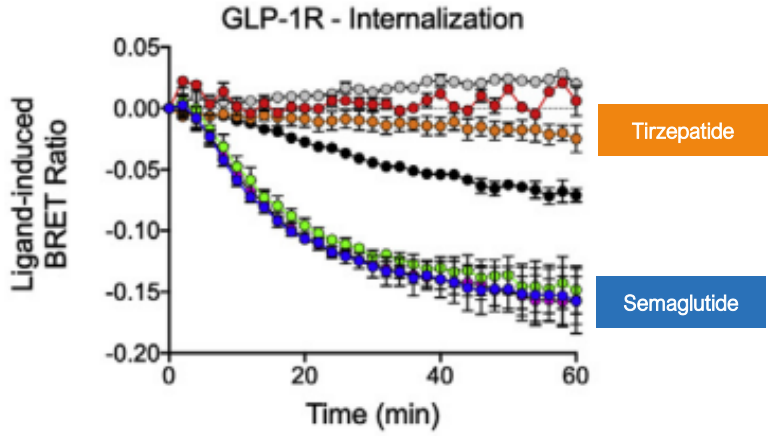
Tirzepatide Once Weekly for the Treatment of Obesity

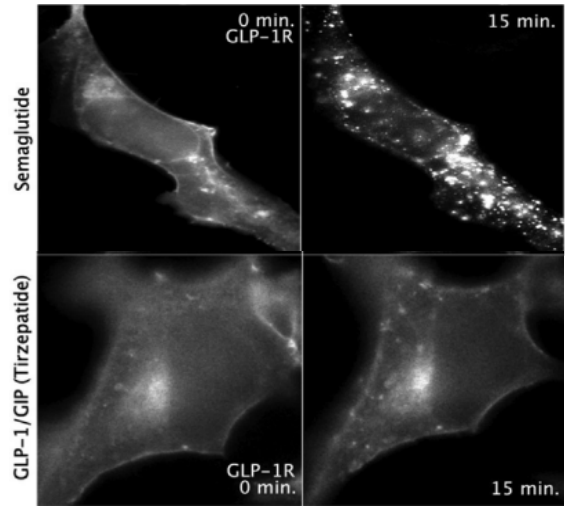
Ania M. Jastreboff, M.D., Ph.D., Louis J. Aronne, M.D., Nadia N. Ahmad, M.D., M.P.H., Sean Wharton, M.D., Pharm.D., Lisa Connery, M.D., Breno Alves, M.D., Arihiro Kiyosue, M.D., Ph.D., Shuyu Zhang, M.S., Bing Liu, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Adam Stefanski, M.D., Ph.D. for the SURMOUNT-1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

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



Tirzepatid 5 – 15 mg = Mounjaro™ (USA)





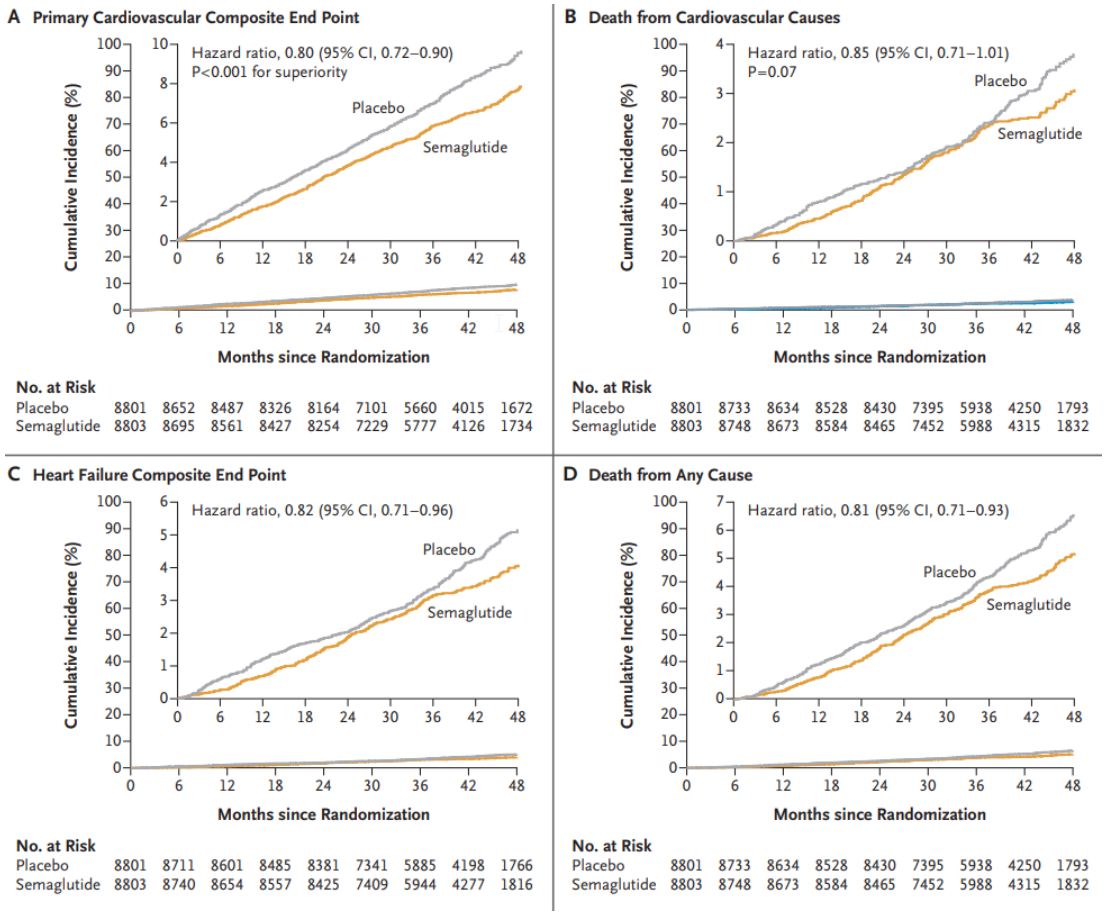
NEJM 06/2022, Novikoff et al. Mol. Metabolism 2021

Kardiovaskuläre Endpunktstudien bei Adipositas

luzerner kantonsspital
LUZERN SURSEE WOLHUSEN

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*



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*

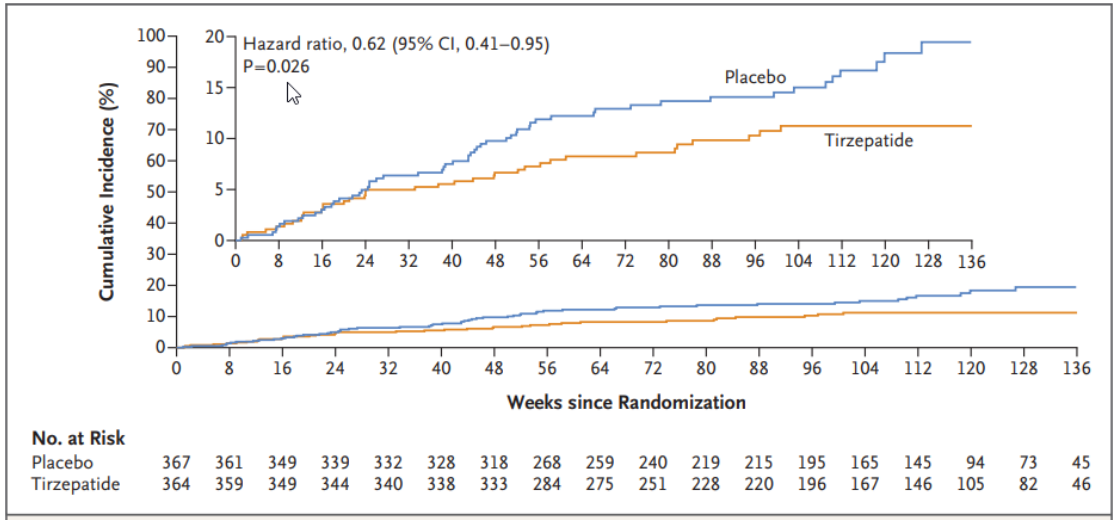


Figure 1. Composite of Death from Cardiovascular Causes or a Worsening Heart-Failure Event.

Shown is the cumulative incidence of death from cardiovascular causes or a worsening heart-failure event (the composite primary end point), assessed in a time-to-first-event analysis, among 364 patients who received tirzepatide and 367 patients who received placebo. The inset shows the same data on an expanded y axis.

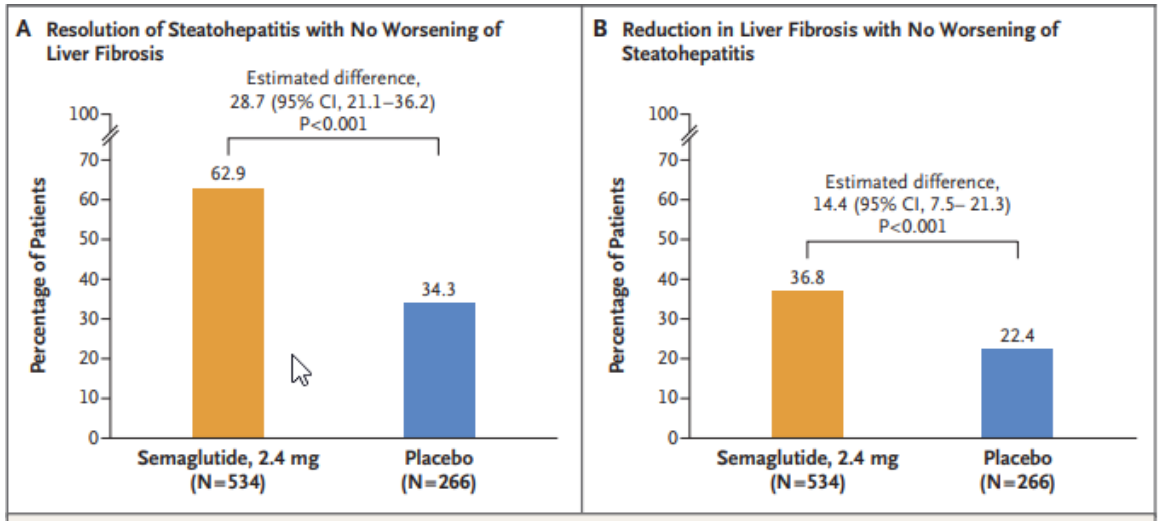
NEJM 12/2023, NEJM 01/2025

MAFLD und MASH-Therapie mit Inkretinen

luzerner kantonsspital
LUZERN SURSEE WOLHUSEN

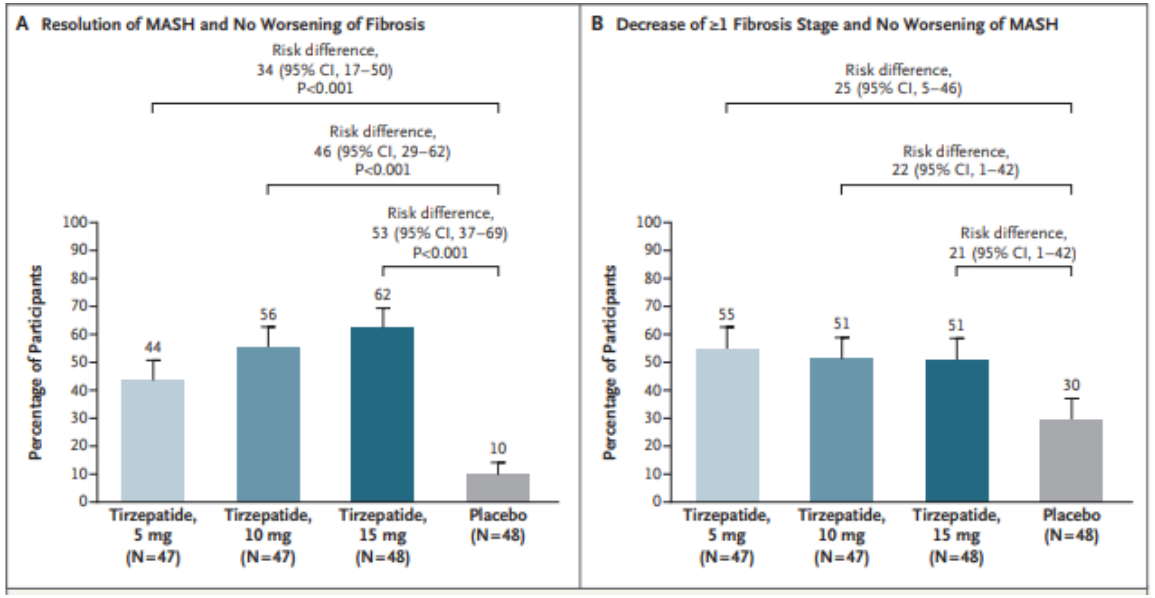
Phase 3 Trial of Semaglutide in Metabolic Dysfunction–Associated Steatohepatitis

Authors: Arun J. Sanyal, M.D., Philip N. Newsome, M.B., Ch.B., Ph.D., Iris Kliers, M.D., Laura Harms Østergaard, M.Sc., Michelle T. Long, M.D., Mette Skalshøi Kjær, M.D., Ph.D., Anna M.G. Cali, M.D., Elisabetta Bugianesi, M.D., Ph.D., Mary E. Rinella, M.D., Michael Roden, M.D., and Vlad Ratziu, M.D., Ph.D., for the ESSENCE Study Group* Author Info



Tirzepatide for Metabolic Dysfunction–Associated Steatohepatitis with Liver Fibrosis

Authors: Rohit Loomba, M.D., Mark L. Hartman, M.D., Eric J. Lawitz, M.D., Raj Vuppalanchi, M.D., Jérôme Boursier, M.D., Ph.D., Elisabetta Bugianesi, M.D., Ph.D., Masato Yoneda, M.D., Ph.D., +9, for the SYNERGY-NASH Investigators* Author Info & Affiliations



NEJM 2025, NEJM 2024

Zukünftiger Dualagonist (GLP-1-Amylin)

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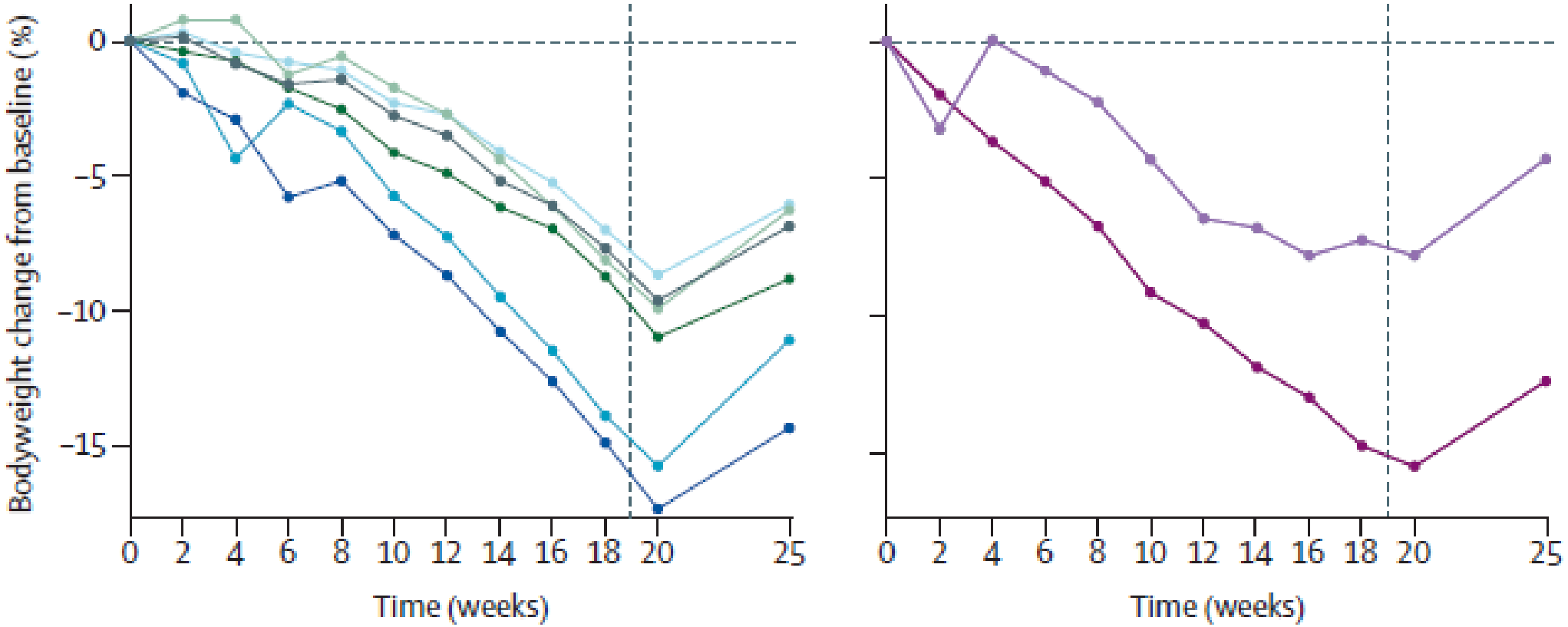
Safety, tolerability, pharmacokinetics, and pharmacodynamics of concomitant administration of multiple doses of cagrilintide with semaglutide 2·4 mg for weight management: a randomised, controlled, phase 1b trial

Lone B Enebo, Kasper K Berthelsen, Martin Kankam, Michael T Lund, Domenica M Rubino, Altynai Satylganova, David C W Lau



Lancet 2021

Zukünftiger Triple-Agonist (GLP-1-GIP-Glucagon)

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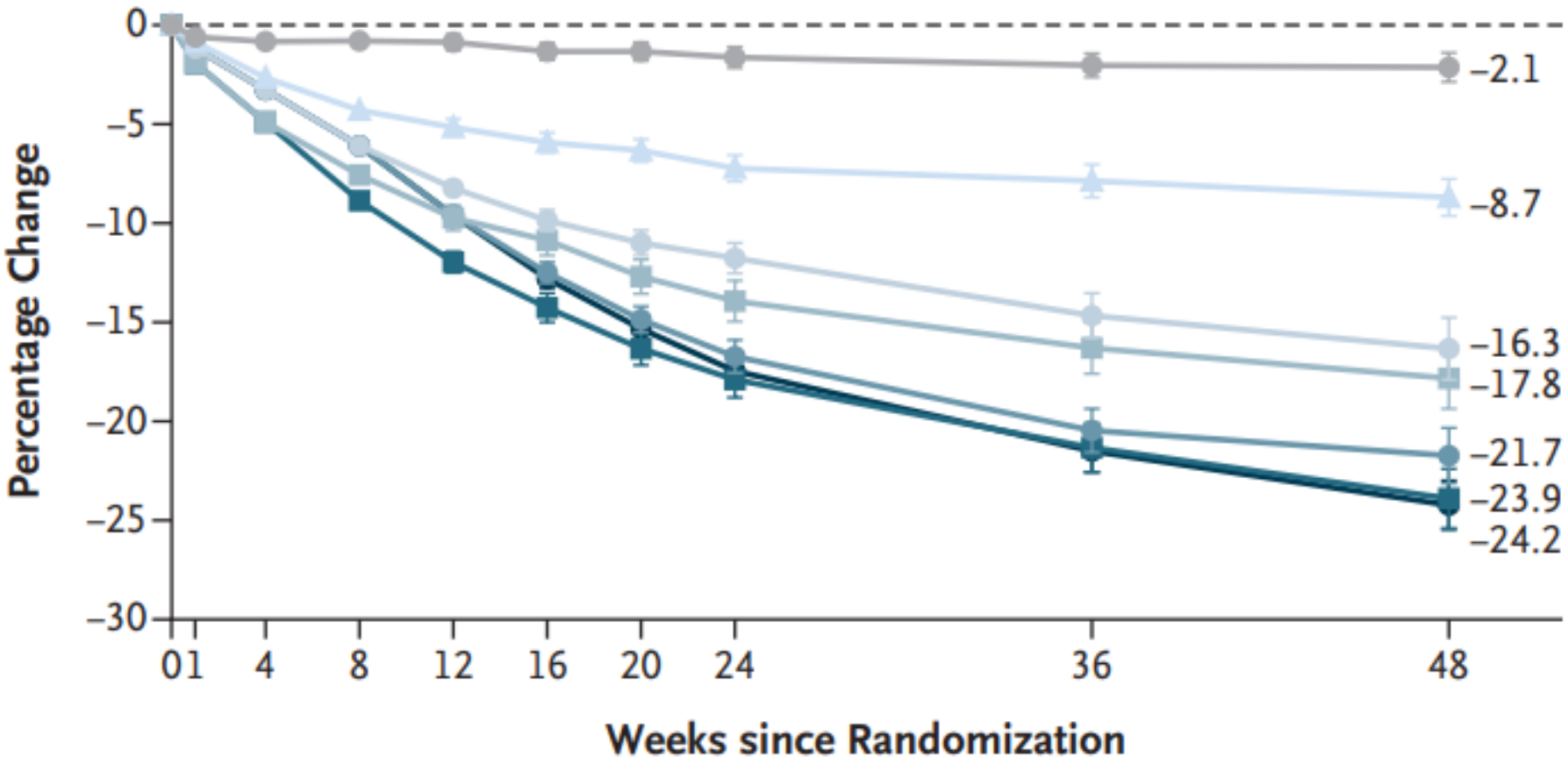
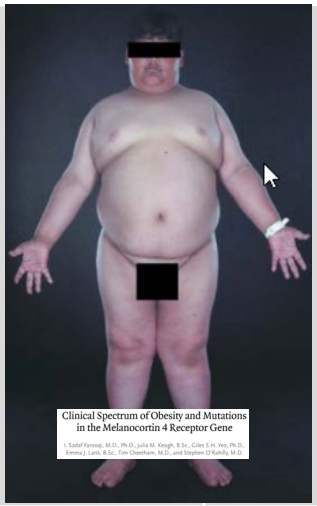
Triple–Hormone-Receptor Agonist Retatrutide for Obesity — A Phase 2 Trial

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*



NEJM 08/2023

Weitere Substanzen

Substanz	Gewichtsabnahme	Besonderheit
Setmelanotide (Imcivree®) Melanocortin-4-Rezeptoragonist MC4R-Mutation bei schwerer Adipositas (0.5 - 1 %)  	- 15 %	Bei **monogenetischen Adipositasformen** (POMC-Mangel, Leptinrezeptor-Mutation, Bardet-Biedl-Syndrom, Prader-Willi-Syndrom, Alström-Syndrom). *FDA und EMA Zulassung* ✓
Cotagutide GLP-1- und Glukagon-Rezeptor-Agonist	- 15 %	Steigerung der Thermogenese Studienfokus u.a. auf **NASH**
Bimagrumab Activin-II-Rezeptor monoklonaler Antikörper	- 21 % (Fettmasse)	Blockade des natürlichen **Muskelabbaus** Steigerung **Thermogenese**

Diabetes Obesity Res. 2020, Arrubia et al., Obesity Week 2021, Heymsfield et all. JAMA Net. Open 2021, Boyle et al., Mol. Metab 2018, Diabetes Obesity Research 2020, NEJM 2003

Verschiedene Realitäten