

Endokrinologie/Diabetologie-Kolloquium  
15.03.2023

# **Management der Adipositas:**

## **Lifestyle – Medikamente - Chirurgie**

Stefan Aczél, Claudine Falconnier, Patrick Folie

# **Obesity: a chronic relapsing progressive disease process.**

A position statement of the World Obesity Federation

**„Obesogenic Environment“:** komplexe Interaktionen Lebensstil (hochkalorische Nahrung, Bewegungsmangel) – Umwelt – (epi-)genetische Faktoren; Funktion des neuroendokrinen Systems gestört

# Definition und Klassifikation der Adipositas

Definition: = Fettleibigkeit = Vermehrung des Körperfett

Klassifikation: BMI, Taillenumfang

Weitere Abklärungen: Anamnese / Status / Labor  
Co-Morbiditäten?

# Therapieziele

- Nicht nur Gewichtsreduktion!
- Gewicht / BMI nicht so wichtig wie Bauchumfang / body composition:  
Erhaltung der fettfreien Masse, Reduktion der Fettmasse

Cave: "sarkopene Adipositas"

- Komplikationen verhindern
- Verbesserung von Co-Morbiditäten
- Verbesserung der Lebensqualität und des Wohlbefindens
- Weitere Gewichtszunahme / -wiederzunahme verhindern

Geringe Gewichtsreduktionen (5%) führen zu  
relevanten Verbesserungen

Stärkere Gewichtsreduktionen führen zu  
stärkeren Verbesserungen

# **Konservative Adipositastherapie: 3 Säulen**

## **- Lebenstilintervention**

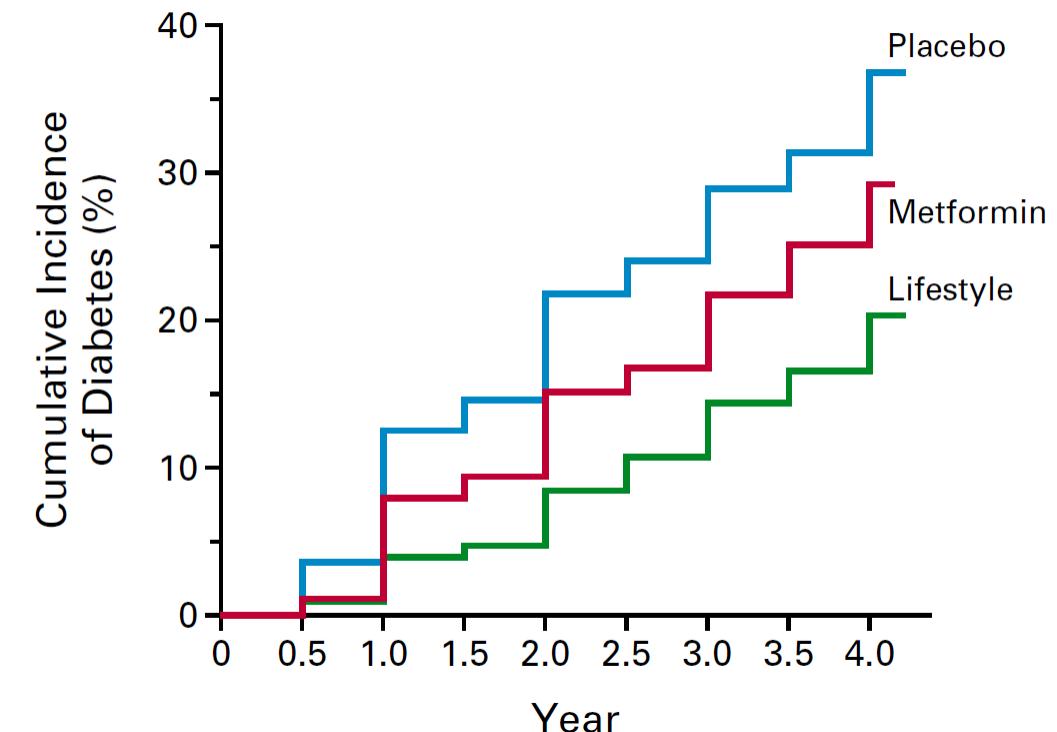
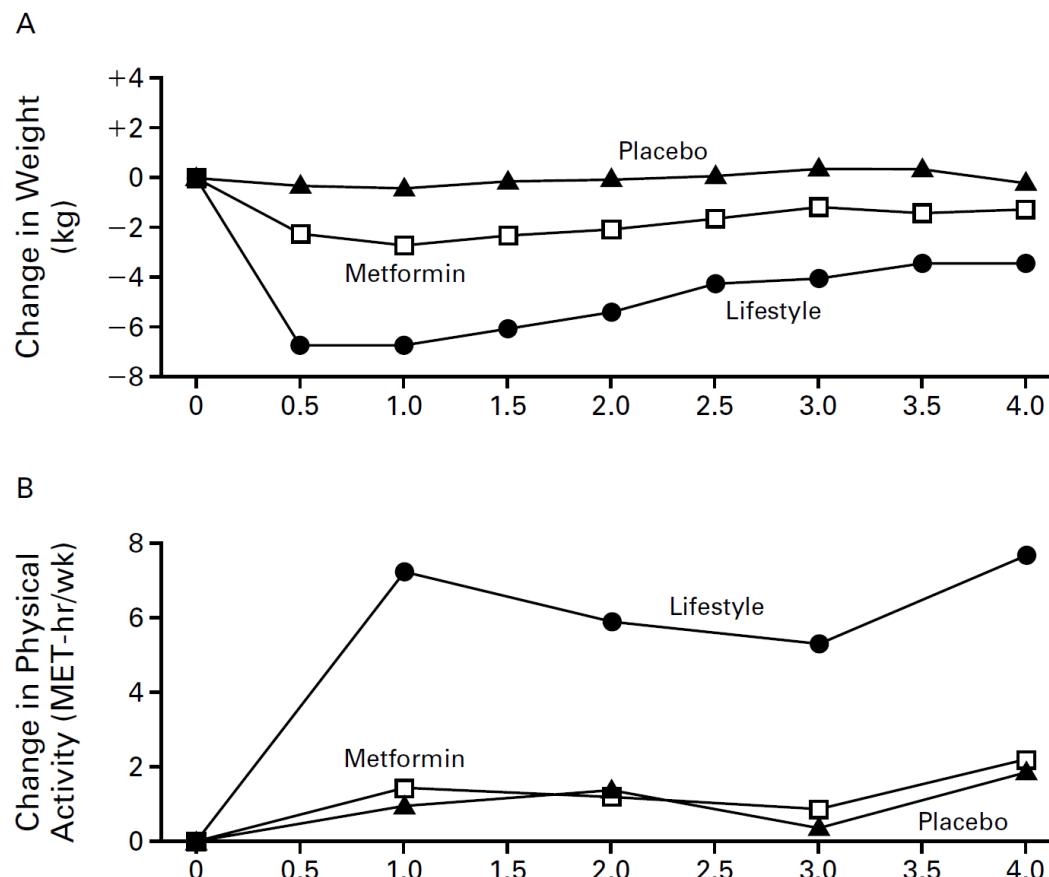


## Lifestyle-Intervention

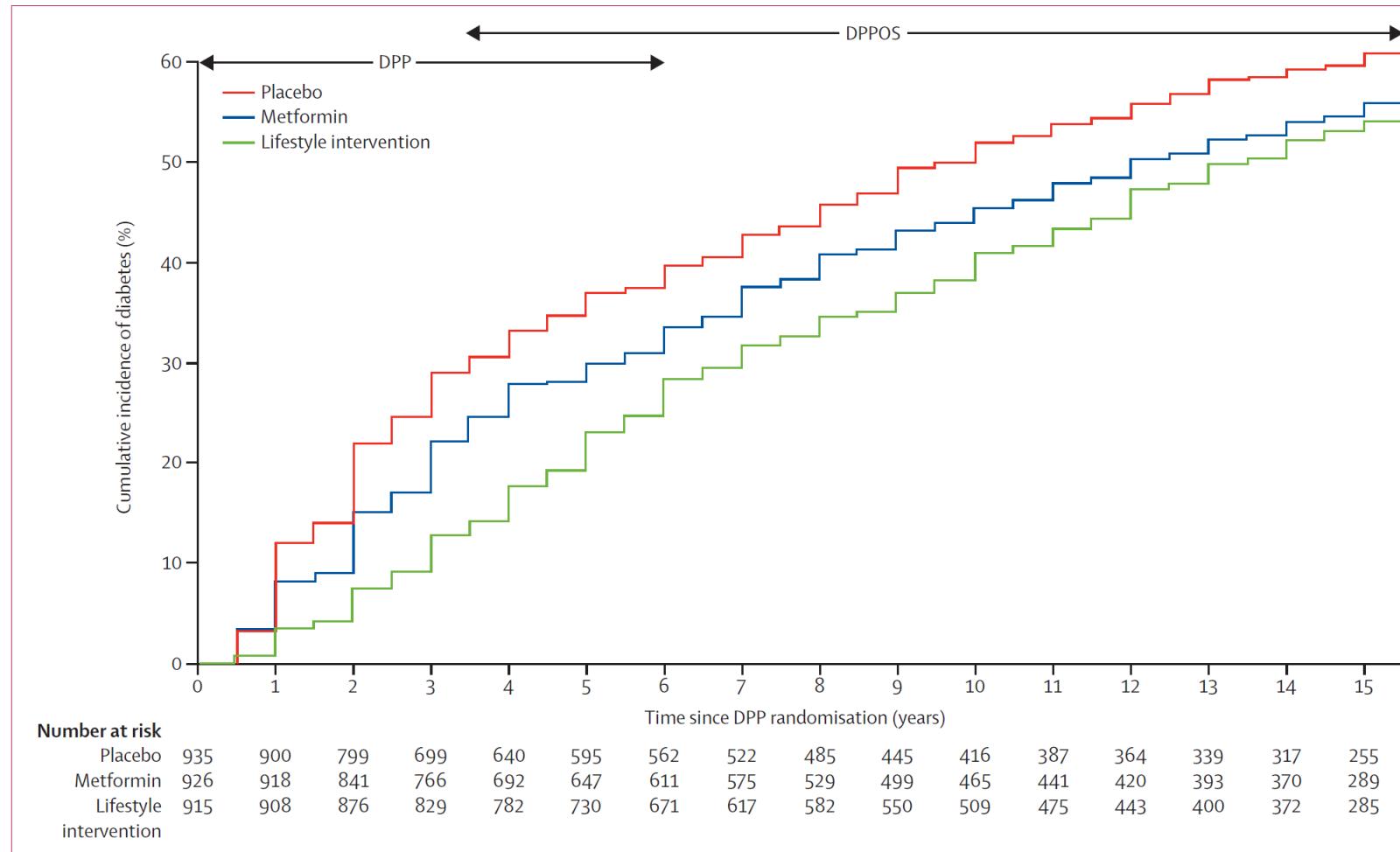
- **Kalorienreduzierte Diät**
  - Energiedefizit  $\geq 500\text{kcal/d}$ ; oft 1200-1500 kcal/d für Frauen, 1500-1800 kcal/d für Männer
- **Gesteigerte körperliche Aktivität**
  - z.B. forciertes Gehen  $\geq 150\text{min/Woche}$ ; 200-300min/Woche um das Gewicht zu halten bzw. um sek. Zunahme zu minimieren ( $> 1 \text{ Jahr}$ )
- **Verhaltenstherapie**
  - Strukturiertes Verhaltenstherapieprogramm
  - Regelmässige Selbstbeobachtung der Nahrungsaufnahme, der körperlichen Aktivität und des Gewichts - Achtsamkeit

# REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE INTERVENTION OR METFORMIN

DIABETES PREVENTION PROGRAM RESEARCH GROUP\*



# Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study



# Preventing weight gain in adults: systematic review and meta-analysis of RCTs

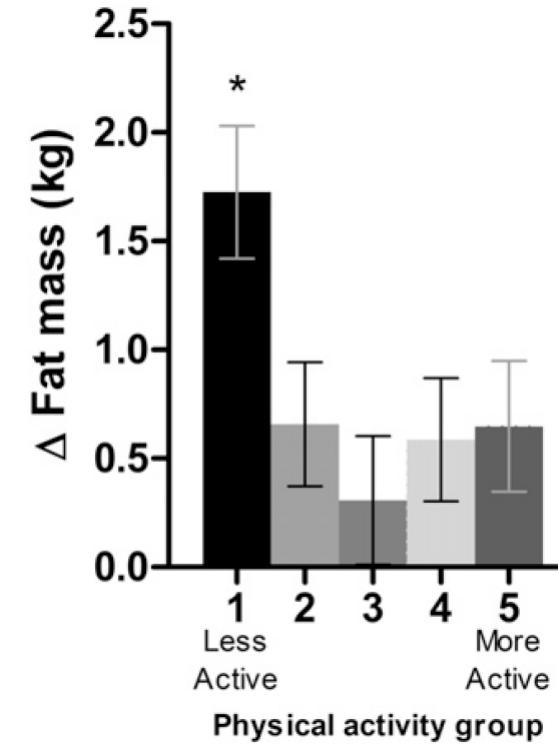
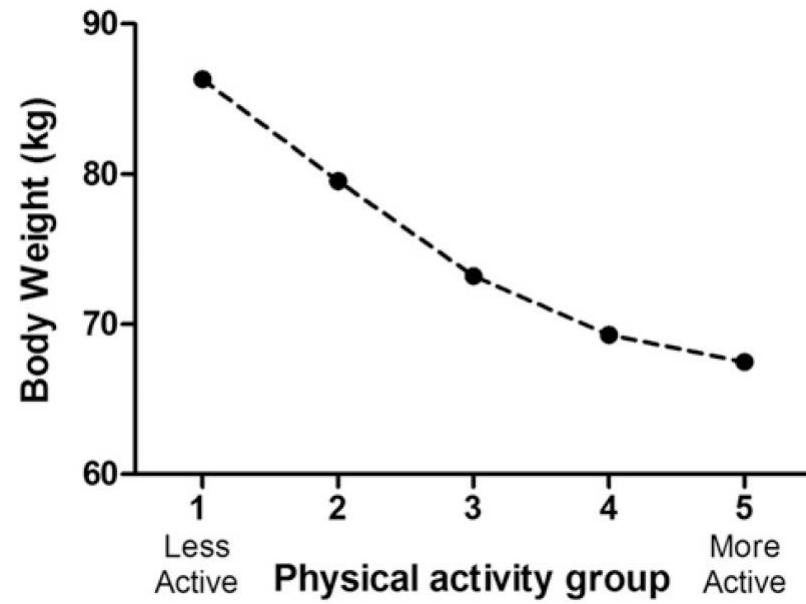
Study or Subgroup	Intervention			Control			Weight	Mean Difference IV, Random, 95% CI [kg]	Mean Difference IV, Random, 95% CI [kg]
	Mean [kg]	SD [kg]	Total	Mean [kg]	SD [kg]	Total			
<b>2.1.1 Weight change (all participants)</b>									
Bennett 2013	-1	4.77	91	0.5	4.85	94	4.4%	-1.50 [-2.89, -0.11]	
Bertz 2015	-0.47	3.66	67	1.08	4.38	68	4.5%	-1.55 [-2.91, -0.19]	
Chang 2010	85.18	5.84	12	85.35	5.54	26	0.8%	-0.17 [-4.01, 3.87]	
Chang 2017	85.49	4.95	219	85.51	4.93	124	6.0%	-0.02 [-1.11, 1.07]	
Donnelly 2003	81.97	12.76	41	87.71	11.56	33	0.4%	-5.74 [-11.29, -0.19]	
Eiben 2006	-1.9	6.78	18	2.6	6.57	22	0.7%	-4.50 [-8.67, -0.33]	
Forster 1988	-0.95	2.74	103	-0.14	2.81	108	8.7%	-0.81 [-1.56, -0.06]	
Gow 2010	0.31	1.43	119	0.47	1.56	40	10.7%	-0.16 [-0.71, 0.39]	
Hivert 2007	-0.6	3.46	48	0.7	4.16	48	3.8%	-1.30 [-2.83, 0.23]	
Jeffery 1999	1.55	7.01	395	1.8	6.1	414	7.4%	-0.25 [-1.16, 0.66]	
Katterman 2014	-1.5	2.75	26	0.48	1.9	25	4.9%	-1.98 [-3.27, -0.69]	
Klem 2000	-1.36	2.02	34	-0.2	1.3	21	7.6%	-1.16 [-2.04, -0.28]	
Leermakers 1998	-1.63	2.52	44	0.22	1.9	18	5.6%	-1.85 [-3.00, -0.70]	
Lemon 2014	78.3	18.9	354	79.9	18.1	286	1.3%	-1.60 [-4.48, 1.28]	
Levine 2007	-0.18	4.57	147	0.8	5.8	75	3.9%	-0.98 [-2.49, 0.53]	
Lombard 2010	72.14	13.63	109	75.51	15.24	106	0.8%	-3.37 [-7.24, 0.50]	
Lombard 2016	77.51	18.06	259	76.6	18.85	233	1.1%	0.91 [-2.36, 4.18]	
Lytle 2017	73.8	11.72	187	74.4	11.55	179	1.9%	-0.60 [-2.98, 1.78]	
Mason 2018	79.95	18.96	132	80.16	18.77	134	0.6%	-0.21 [-4.74, 4.32]	
Matvienko 2001	67.7	13.6	18	68.9	18.4	15	0.1%	-1.20 [-12.43, 10.03]	
Medina 2018	73.16	19.63	28	70.62	11.01	22	0.2%	2.54 [-6.06, 11.14]	
Metzgar 2016	75.15	8.3	55	77.2	11	25	0.5%	-2.05 [-6.89, 2.79]	
Middleton 2014	66.81	11.65	47	70.39	11.92	48	0.5%	-3.58 [-8.32, 1.16]	
Nikolaou 2015	65.5	13.01	3867	66.9	13.2	2134	9.3%	-1.40 [-2.09, -0.71]	
Partridge 2016	76	10.7	115	78.8	12.6	125	1.3%	-2.80 [-5.75, 0.15]	
Verweij 2012	84.9	16.1	233	87	16.1	223	1.3%	-2.10 [-5.06, 0.86]	
Williams 2014	65.6	8.5	22	67.4	6.7	18	0.5%	-1.80 [-6.51, 2.91]	
Williams 2019	66.4	8.7	16	68.3	7.2	14	0.4%	-1.90 [-7.59, 3.79]	
Wing 2016	-1.47	2.62	251	0.26	2.59	139	10.8%	-1.73 [-2.27, -1.19]	
<b>Subtotal (95% CI)</b>			<b>7057</b>			<b>4817</b>	<b>100.0%</b>	<b>-1.15 [-1.50, -0.80]</b>	<b>♦</b>

Heterogeneity:  $\tau^2 = 0.22$ ;  $\text{Chi}^2 = 41.67$ ,  $df = 28$  ( $P = 0.05$ );  $I^2 = 33\%$

Test for overall effect:  $Z = 6.44$  ( $P < 0.00001$ )



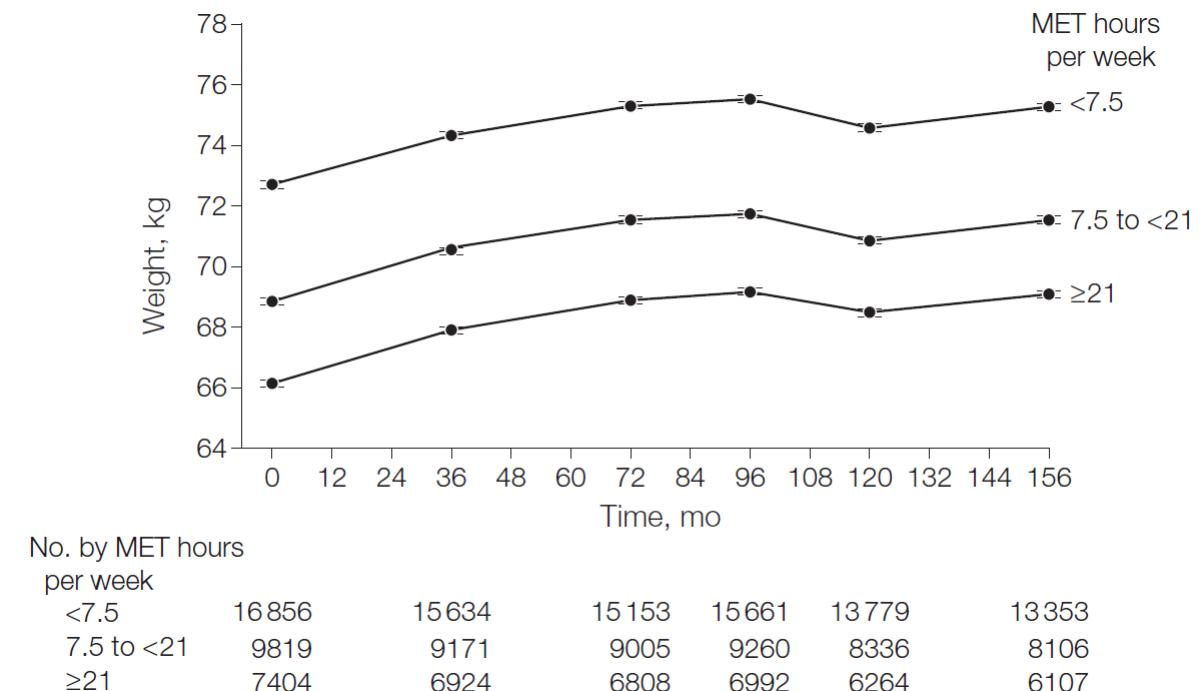
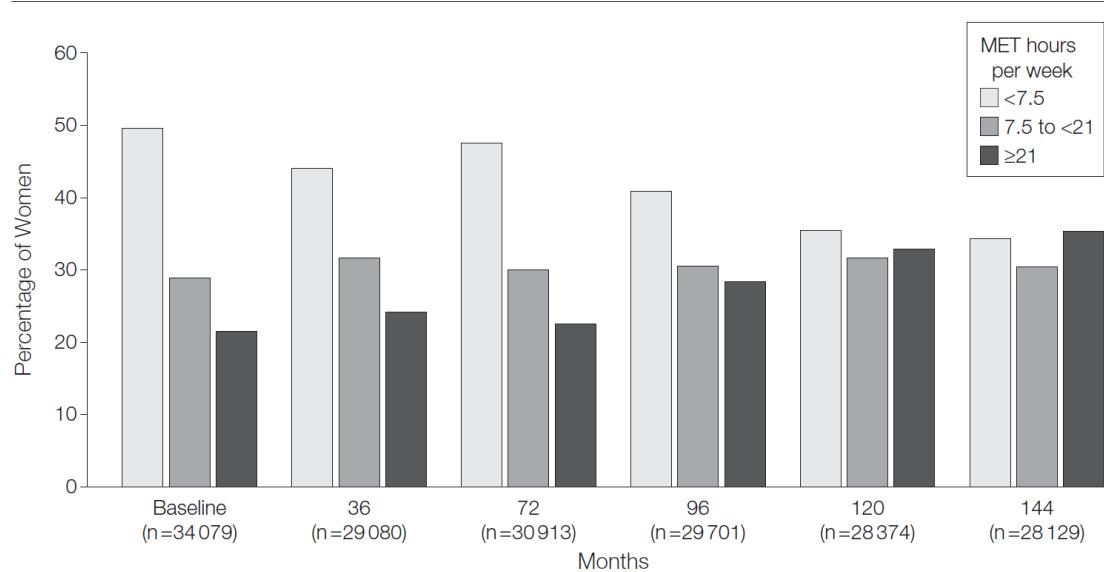
# Low levels of physical activity are associated with dysregulation of energy intake and fat mass gain over 1 year



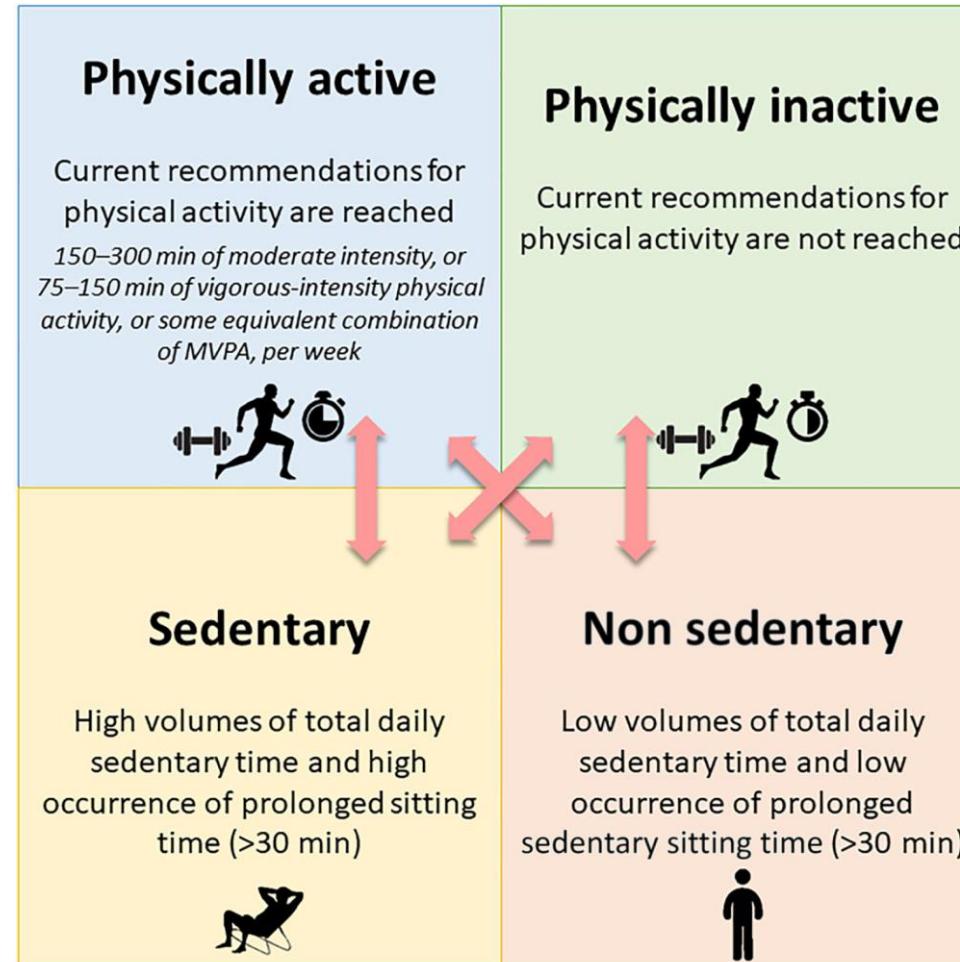
# Physical Activity and Weight Gain Prevention

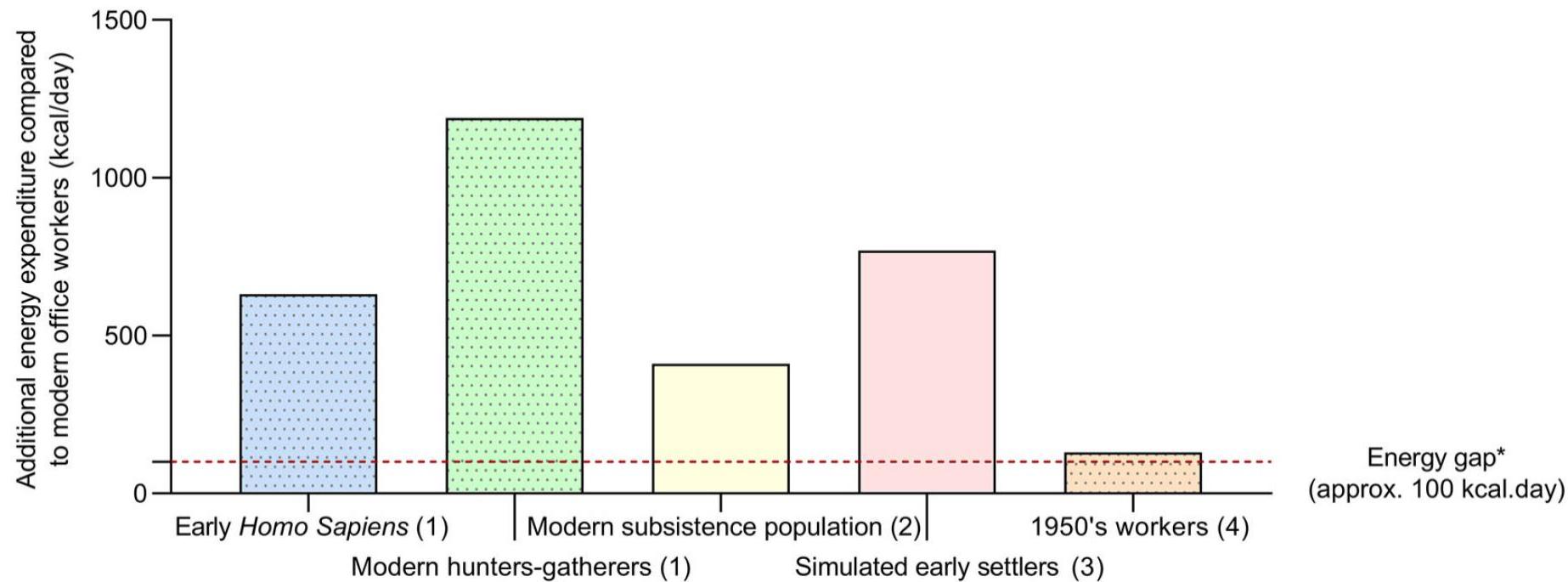
Women's Health Study: 34 079 healthy US women (mean age, 54.2 years) from 1992-2007

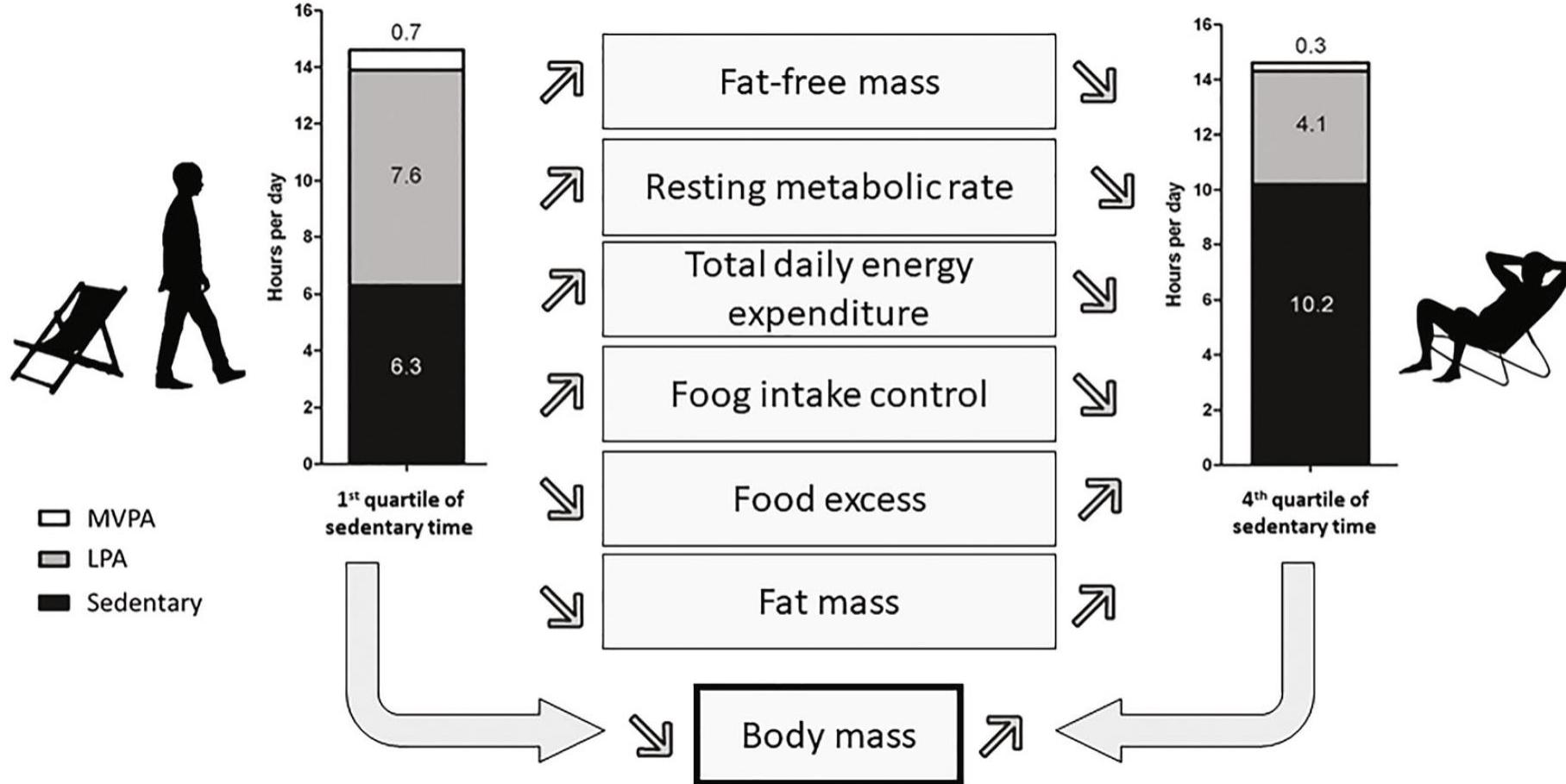
**Figure 1.** Physical Activity Levels Throughout Women's Health Study



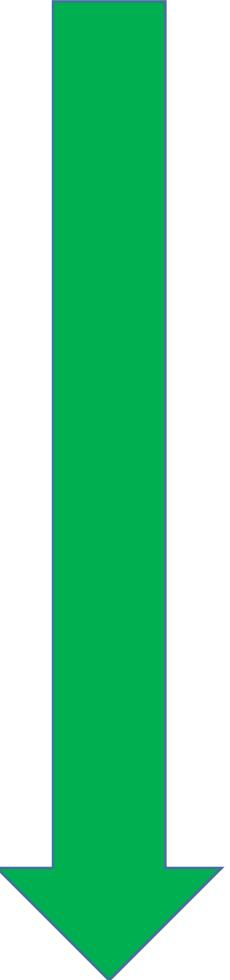
# The role of physical activity in the regulation of body weight: The overlooked contribution of light physical activity and sedentary behaviors

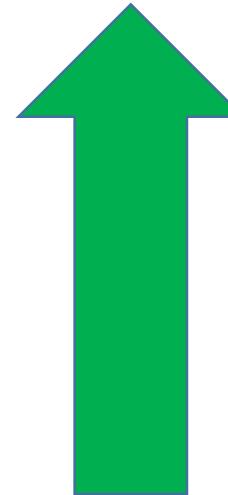






# Regelmässige körperliche Aktivität.....

- 
- Gesamt mortalität
  - Kardiovaskuläre Mortalität
  - Kardiovaskuläre Erkrankungen
  - Hypertonie
  - T2DM
  - Dyslipidämie
  - Diverse Malignome
  - Demenz
  - Angst, Depression
  - Gewichtszunahme
  - Stürze / Sturzverletzungen
  - Schwangerschaft: Gewichtsexzess, GDM, postpartale Depression



- Lebensqualität
- Schlaf
- Kognitive Leistungen
- Gewichtsabnahme
- Gewichtsstabilität
- Knochengesundheit

# Körperliche Aktivität zur Therapie der Adipositas

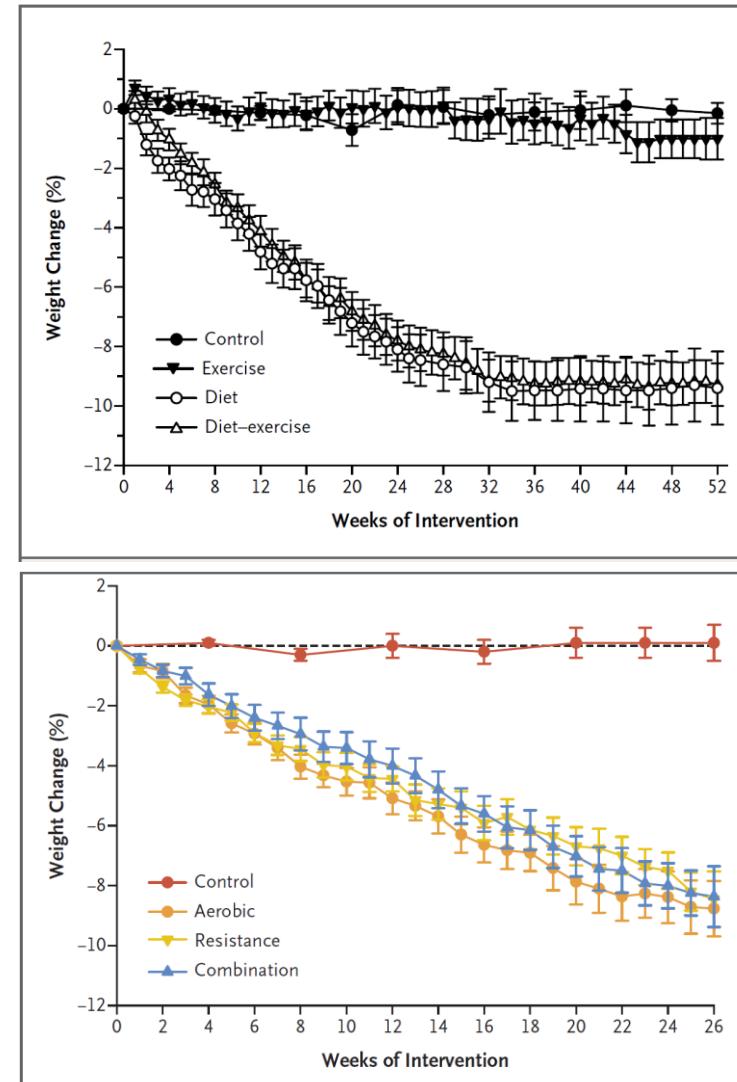
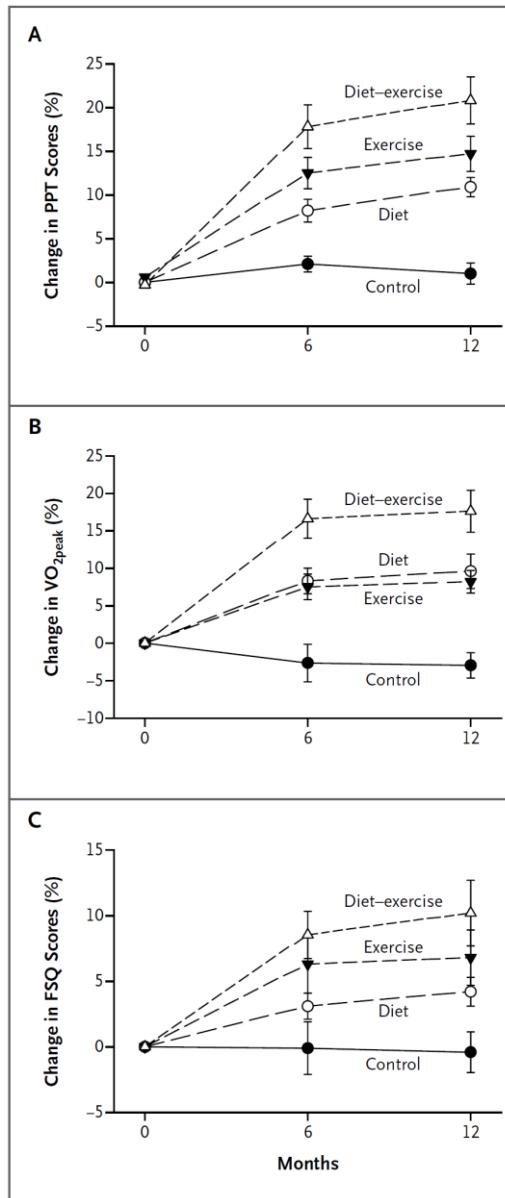
moderater Nutzen in Metaanalysen: **minus 1.6 kg**;

hohe vs niedrige Intensität: Differenz **1.5 kg**

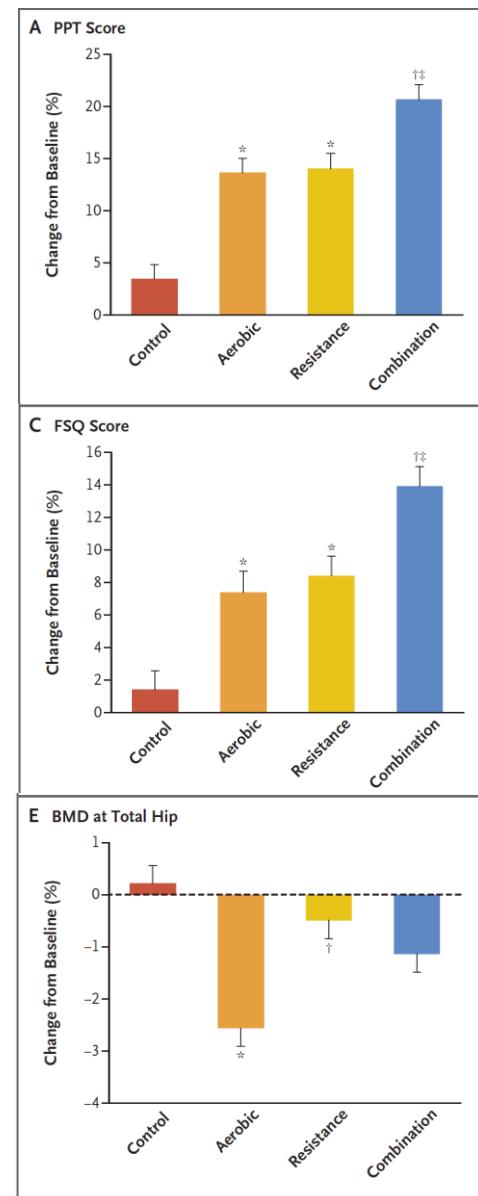
Moderate Reduktion von **Taillenumfang und Blutdruck**

Vergleich mit Diät alleine: Bessere Reduktion der **Körperfettmasse**, gleiche Reduktion von abdominalem / viszeralem Fett und Insulinresistenz

# Diät oder Training (Kraft-?, Ausdauer-?) bei älteren Patienten?



PPT....Physical Performance Test; FSQ.... Functional Status Questionnaire



## Körperliches Training

Wahrscheinlich Kombination Ausdauer- und Krafttraining ideal

andere Studie: höhere Intensität bessere Resultate im oGTT

für viele Patienten: (forciertes) Gehen am Besten

*Arch Intern Med 2009; 169:122; CMAJ Open 2014; 2:E306; JAMA 1999; 281:335*

**Any exercise program should be designed to fit into the health and physical conditions of the participant.**

Empfehlungen:

zusätzlich 1000 – 1200 kcal / Woche bzw > 150 kcal / Tag

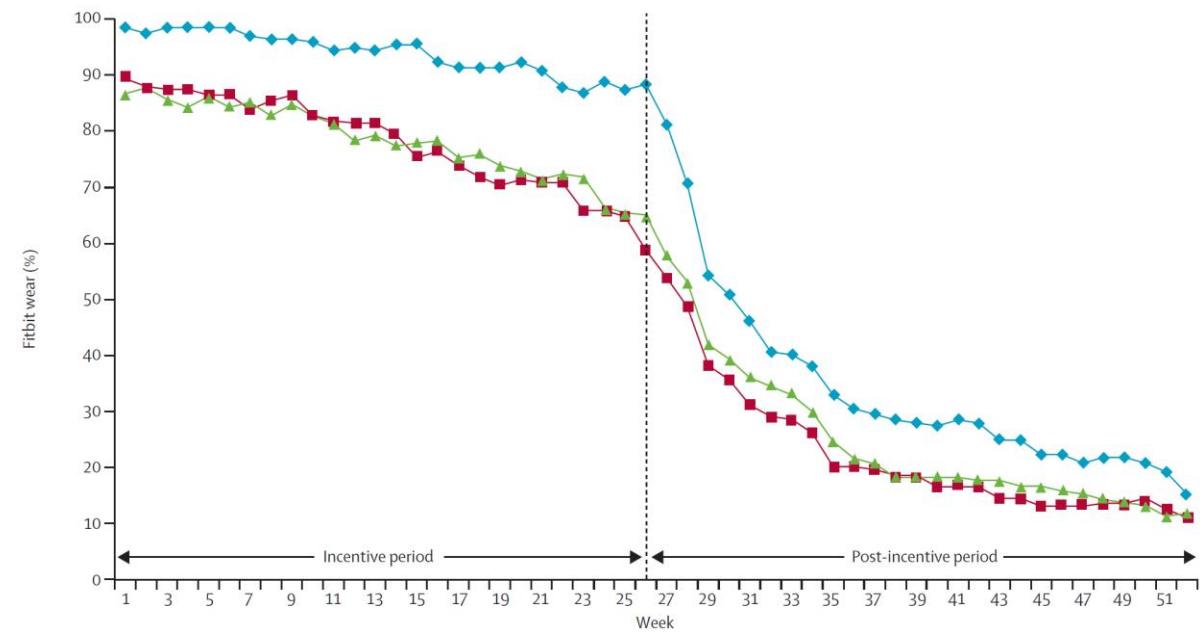
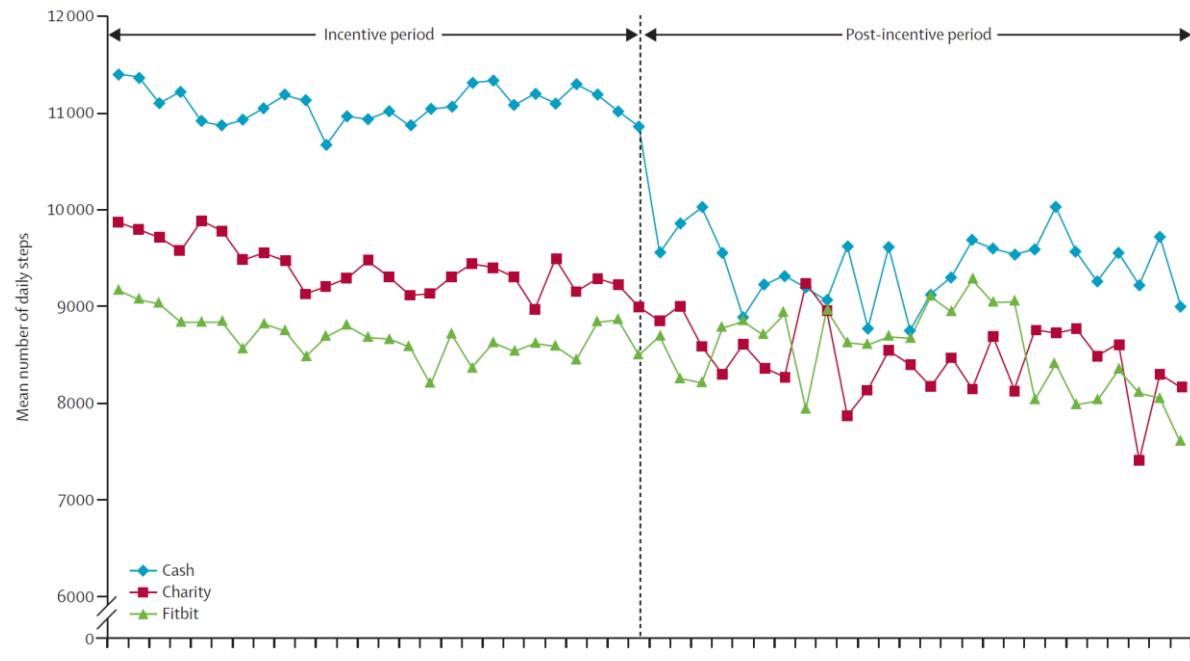
Gewichtserhaltung: meist > 60 min täglich moderate Intensität



## „Activity tracker“ - Fitnessarmband

	<b>Standard intervention</b>	<b>Enhanced intervention</b>
Weight, mean (95% CI), kg		
Baseline	95.2 (93.0-97.3)	96.3 (94.2-98.5)
24 mo	89.3 (87.1-91.5)	92.8 (90.6-95.0)
Estimated weight loss, mean (95% CI), kg	5.9 (5.0-6.8)	3.5 (2.6-4.5)
Difference: 2.4 kg (95% CI 1.0-3.7), p=0.002		

# „Activity tracker“ - Fitnessarmband



# Ernährung

(Protein-)Modifiziertes Fasten (Very Low Caloric Diet, VLCD)	Max. 400-500(-800) kcal/Tag (Protein, Kohlenhydrate, Fette)	Gewichtsreduktion
Heilfasten nach Buchinger	Gemüsebrühe, Obst- und Gemüsesäfte und Honig (30 g); reichlich Getränke ärztlich betreut, stationär	Gewichtsreduktion; psychische Veränderungen, Bewusstseinsveränderungen
Kontinuierliche Energie-Reduktion  Intermittierendes Fasten: Alternate-Day Fasting, ADF	Täglich (500-)800-1000 kcal unter dem Energieumsatz  Abwechselnd 1 Tag keine Energiezufuhr (oder 25% des Energieumsatzes) und 1 Tag <i>Ad-libitum</i> -Ernährung	Ziel: Gewichtsabnahme; Verlängerung der Lebenszeit; verzögerte degenerative Prozesse; Reduktion von kardiovaskulären Risikofaktoren
Whole-Day Fasting (WDF)  Time-Restricted Feeding	Abwechselnd Tage mit Nulldiät und nicht limitierter Energieaufnahme (2/5)  Tageszeitlich begrenztes Fasten (20 h «undereating», 4 h «overeating»; nur 1 Mahlzeit/Tag)	
Totales Fasten (Nulldiät; Crash-Diät)	mehrere Tage keine/geringe Energie-aufnahme (max. 25% des Umsatzes); energiefreie Getränke erlaubt	Schnelle Gewichtsabnahme

Low-carbohydrate Diät	60-130 g KH (245-530 kcal) / Tag
Very-low carbohydrate Diät (ketogene Diät)	0-60 g KH
High-protein Diät	Mindestens 20 % der Kalorien von Protein
Mediterrane Diät	Viele ungesättigte Fettsäuren; moderat Alkohol; viel Gemüse, Früchte, Hülsenfrüchte, Nüsse, Getreide; moderat Milchprodukte, wenig Fleisch
Formula-Diäten	Mahlzeitenersatz durch kalorienreduzierten Shake/Pulver
Low-fat Diät	Fett < 30 %
High-monounsaturated-fatty-acid Diät	Öl mit 60 % MUFA
Vegetarische Diät	
Diäten mit niedrigem glykämischen Index	
Very low calorie diet	200-800 kcal / Tag
“Hunger-Diät”	< 200 kcal / Tag

# Intervallfasten

16:8

20:4

23:1

5:2 (WDF)

ADF

WDF: Abnahme des Körpergewichts und der Fettmasse im Vergleich zu den jeweiligen Ausgangswerten beziehungsweise im Vergleich zu einer nicht fastenden Kontrollgruppe.

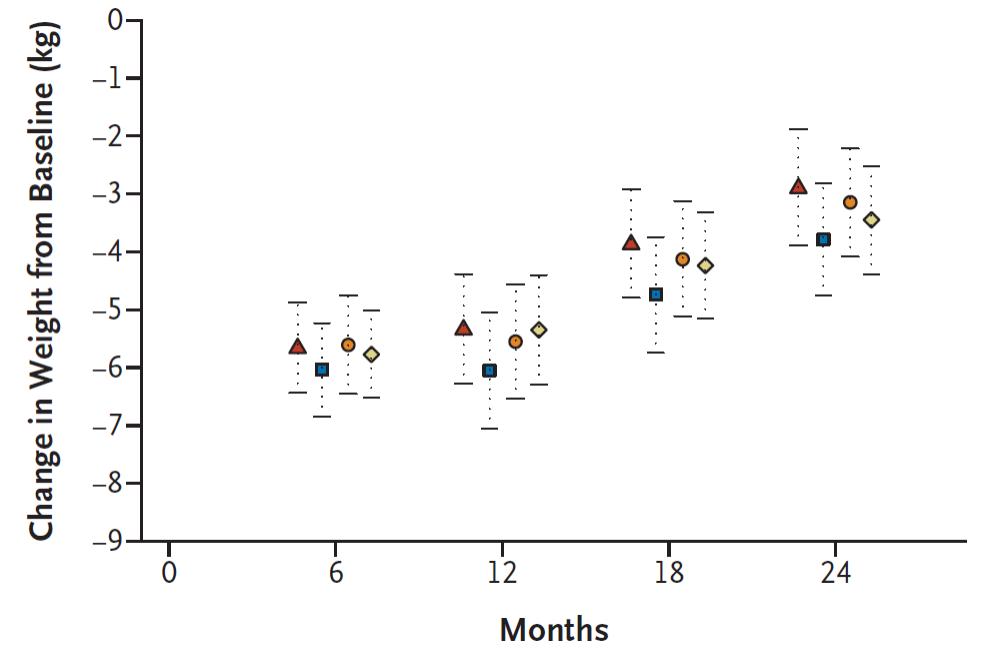
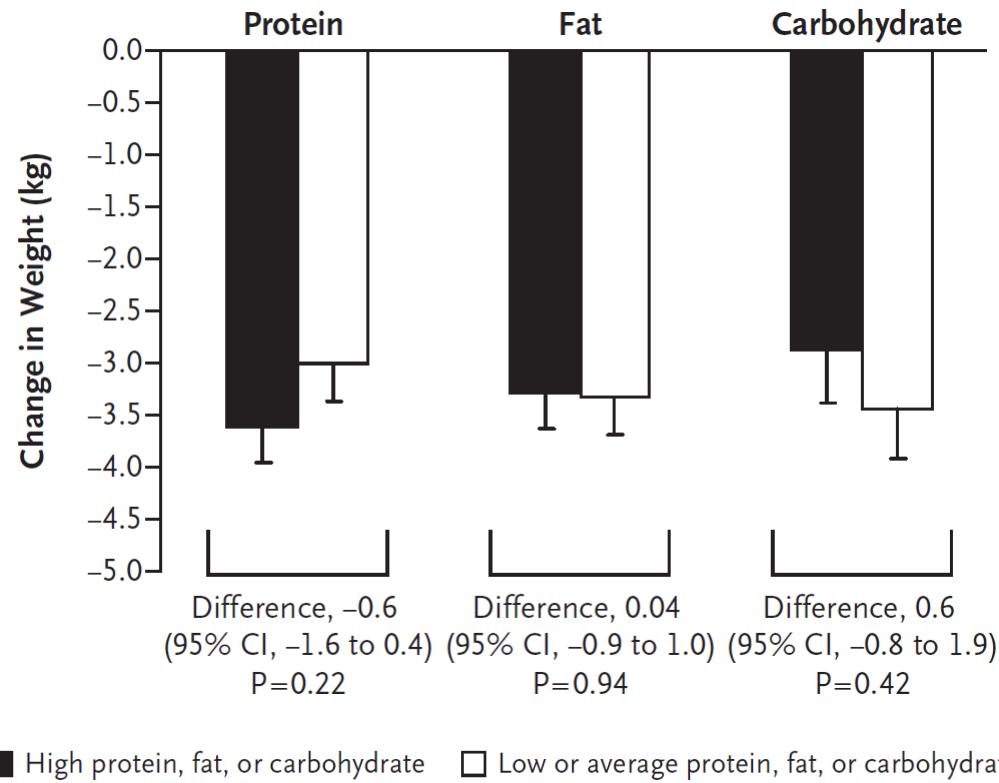
ADF vs WDF keine methodisch bedingten Unterschiede: Gewichtsabnahme nur beeinflusst vom Ausmass der Energiereduktion

*NutrRev 2015 – 73 – 661-74*

Time Restricted Feeding: im cross-over Design leichte Abnahme der Energieaufnahme (–65 kcal/Tag), nach 8 Wochen messbare Abnahme des Körpergewichts und der Körperfettmasse

*AJCN 2007 – 85 – 981-8*

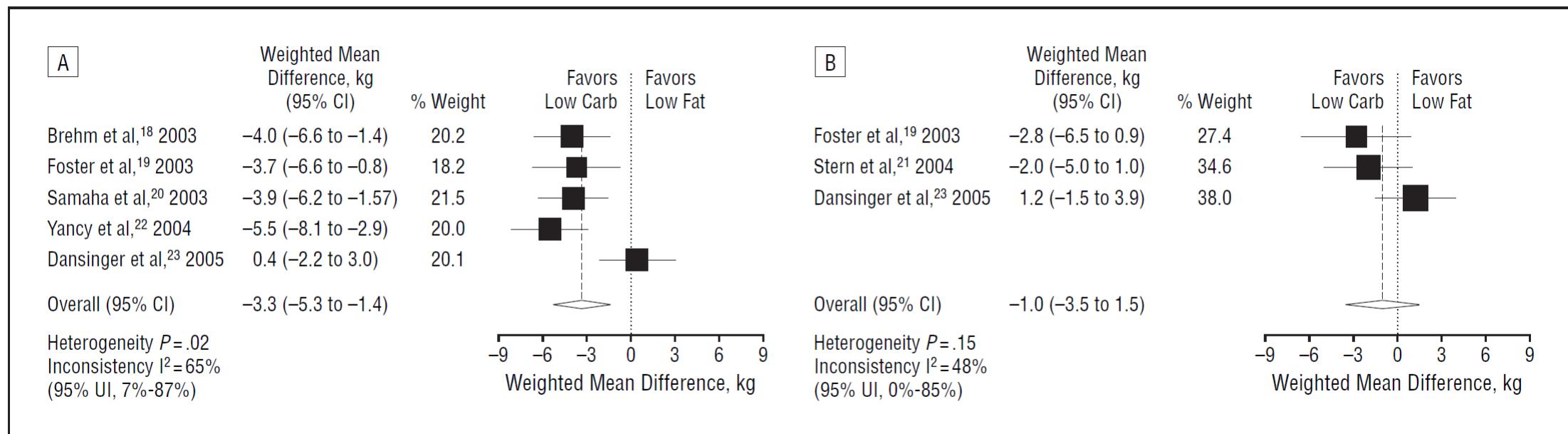
# Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein, and Carbohydrates



Conclusions: Reduced-calorie diets result in clinically meaningful weight loss **regardless of which macronutrients they emphasize.**

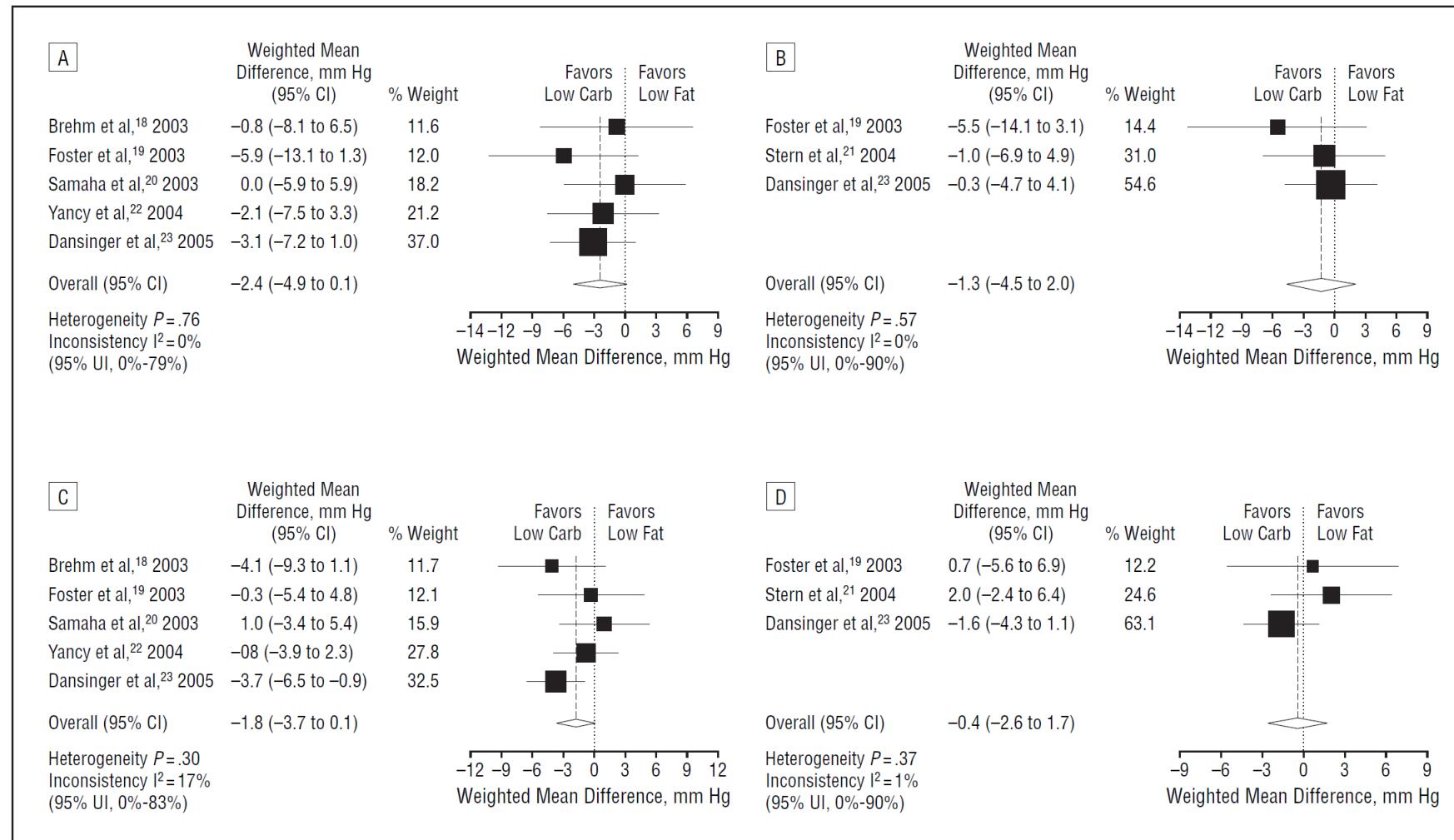
# Effects of Low-Carbohydrate vs Low-Fat Diets on Weight Loss and Cardiovascular Risk Factors

Weighted mean differences in weight loss after 6 (A) and 12 (B) months of follow-up



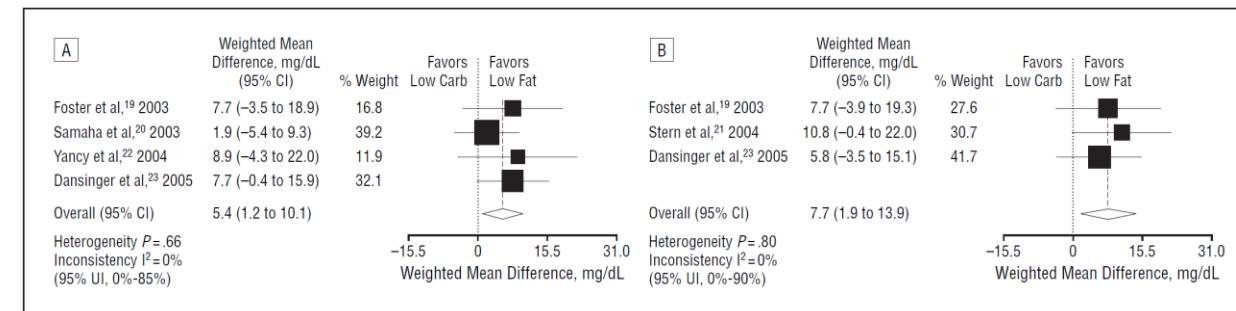
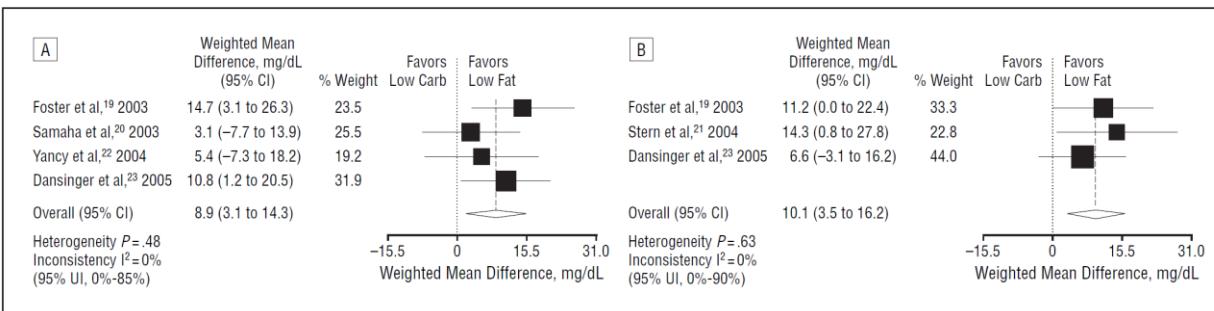
# Effects of Low-Carbohydrate vs Low-Fat Diets on Weight Loss and Cardiovascular Risk Factors

Weighted mean differences in systolic and diastolic blood pressure (BP) after 6 and 12 months of follow-up.

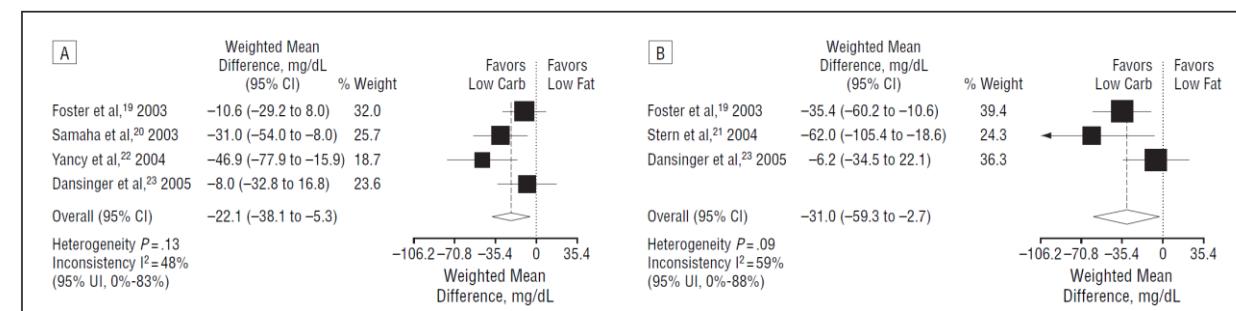
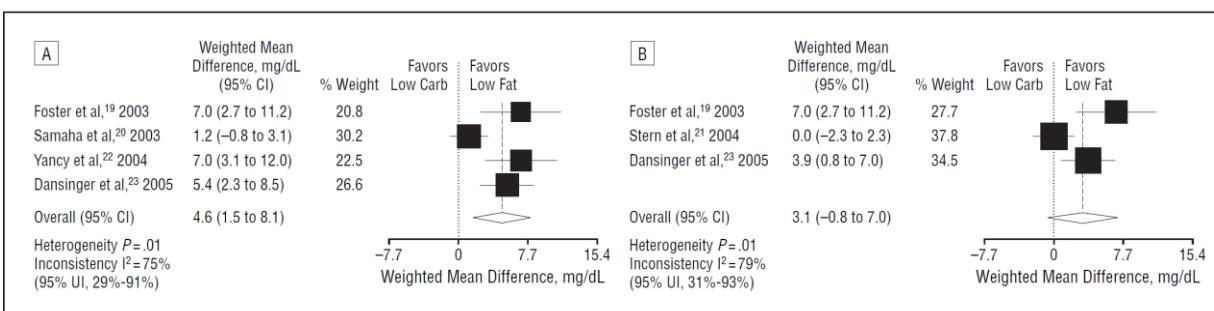


# Effects of Low-Carbohydrate vs Low-Fat Diets on Weight Loss and Cardiovascular Risk Factors

Weighted mean differences in total and LDL cholesterol level after 6 (A) and 12 (B) months of follow-up.

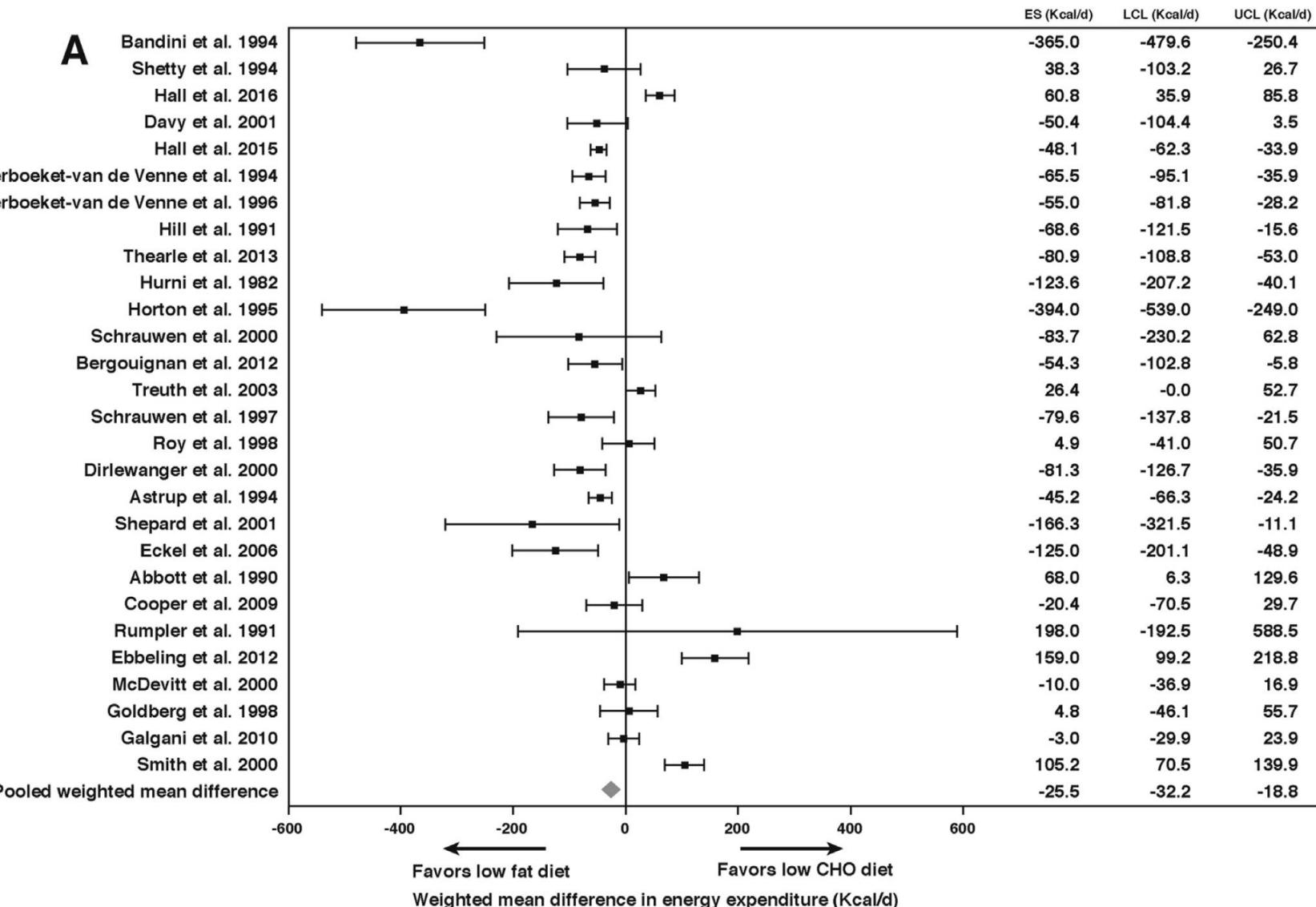


Weighted mean differences in HDL cholesterol and triglyceride level after 6 (A) and 12 (B) months of follow-up.



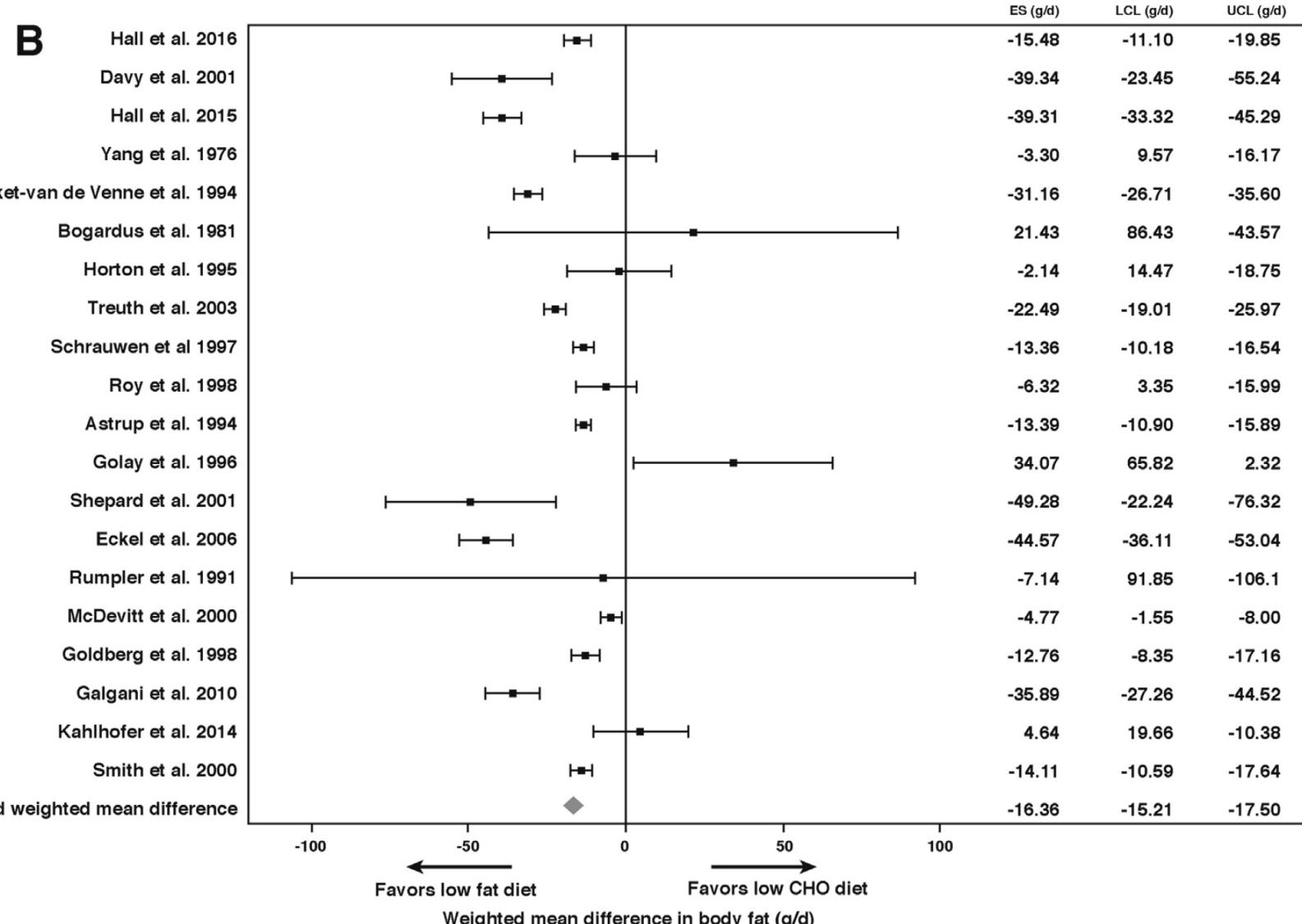
# Obesity Energetics: Body Weight Regulation and the Effects of Diet Composition

## Energy expenditure



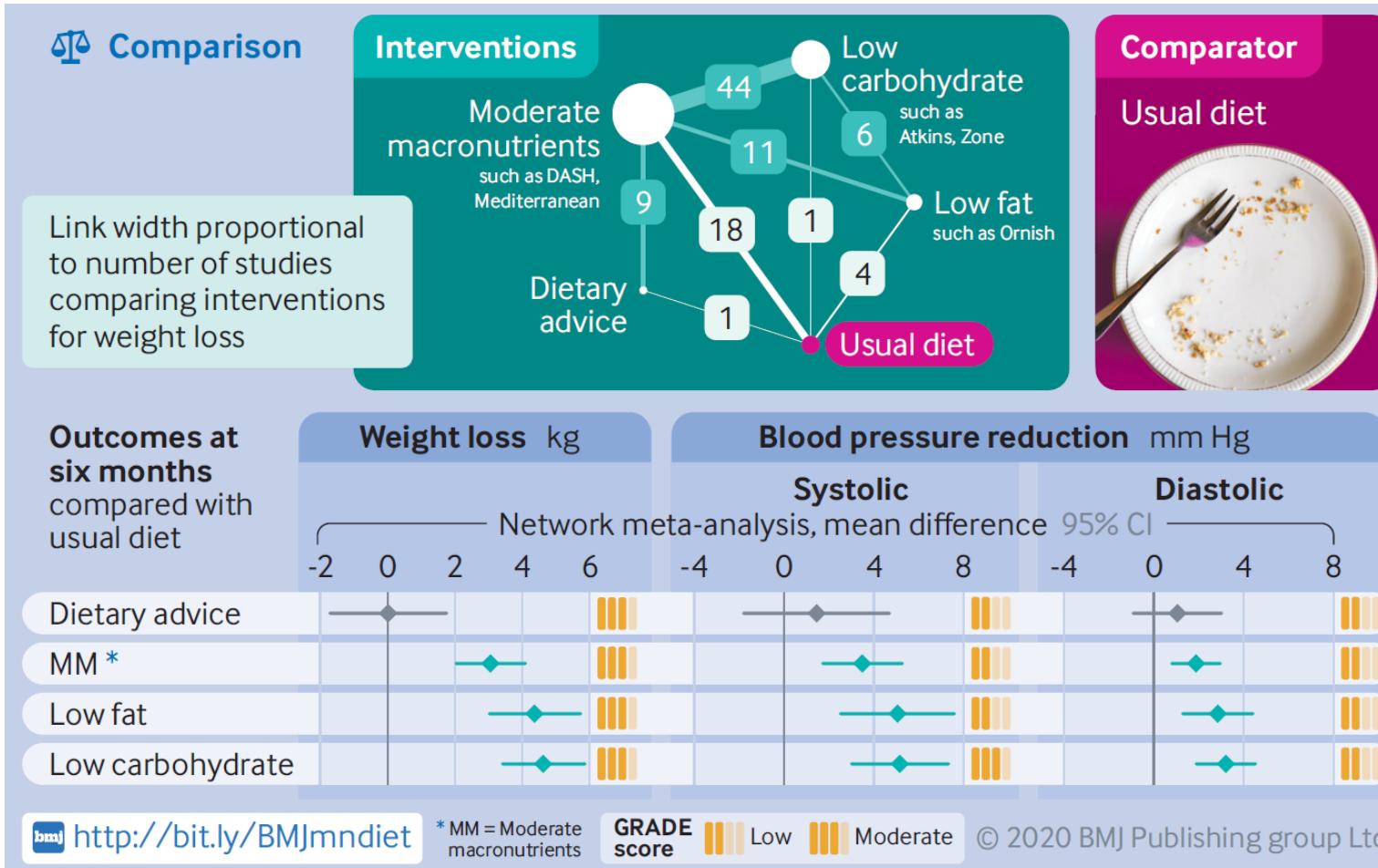
# Obesity Energetics: Body Weight Regulation and the Effects of Diet Composition

## Body fat



# Comparison of dietary macronutrient patterns of 14 popular named dietary programmes for weight and cardiovascular risk factor reduction in adults: systematic review and network meta-analysis of randomised trials

BMJ 2020;369:m696



121 RCTs, 21 942 pts

12 month follow-up: Weight reduction diminished; aside from the Mediterranean diet for LDL reduction, improvements in cardiovascular risk factors largely disappeared.

**Differences between diets were typically small to trivial and often based on low certainty evidence**

# Low-Carbohydrate Diets and All-Cause and Cause-Specific Mortality

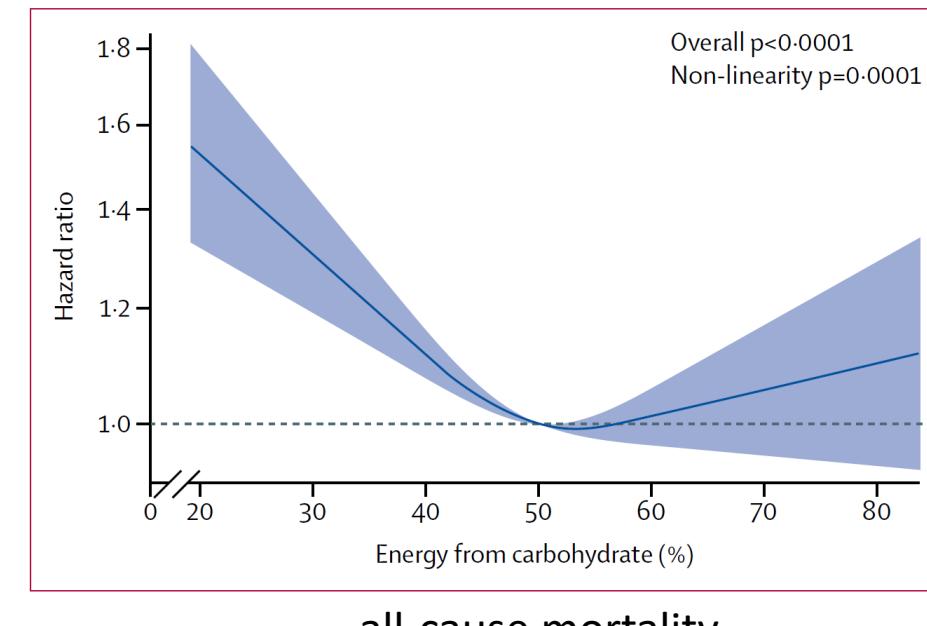
Nurses' Health Study and Health Professionals' Follow-up Study

.....modest **increase** in overall **mortality** in a pooled analysis (hazard ratio [HR] comparing extreme deciles, 1.12 [95% CI, 1.01 to 1.24];  $P$  for trend 0.136).

.... **animal** low-carbohydrate score – **higher** mortality....

.... **vegetable** low-carbohydrate score – **lower** mortality....

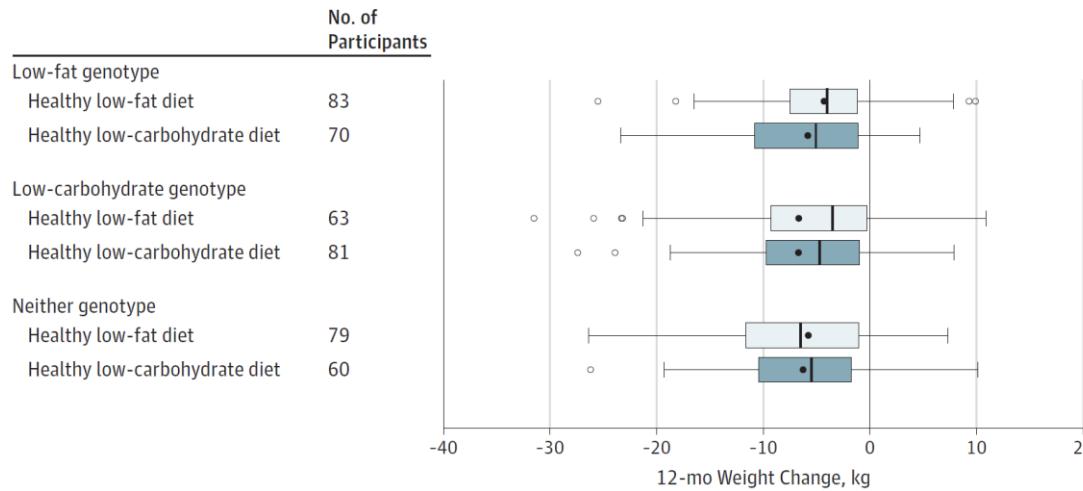
Long-term risks of low-CHO ketogenic diet:  
Atherosclerosis Risk in Communities (ARIC) study:



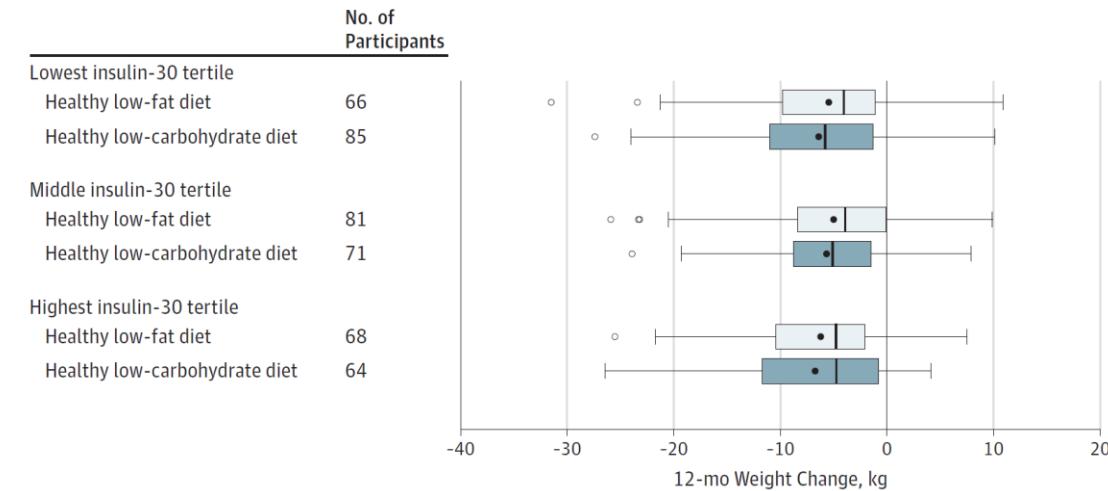
# Effect of Low-Fat vs Low-Carbohydrate Diet on 12-Month Weight Loss in Overweight Adults and the Association With Genotype Pattern or Insulin Secretion

## The DIETFITS Randomized Clinical Trial

A 12-mo Weight loss by diet and genotype



B 12-mo Weight loss by diet and insulin-30 tertile at baseline

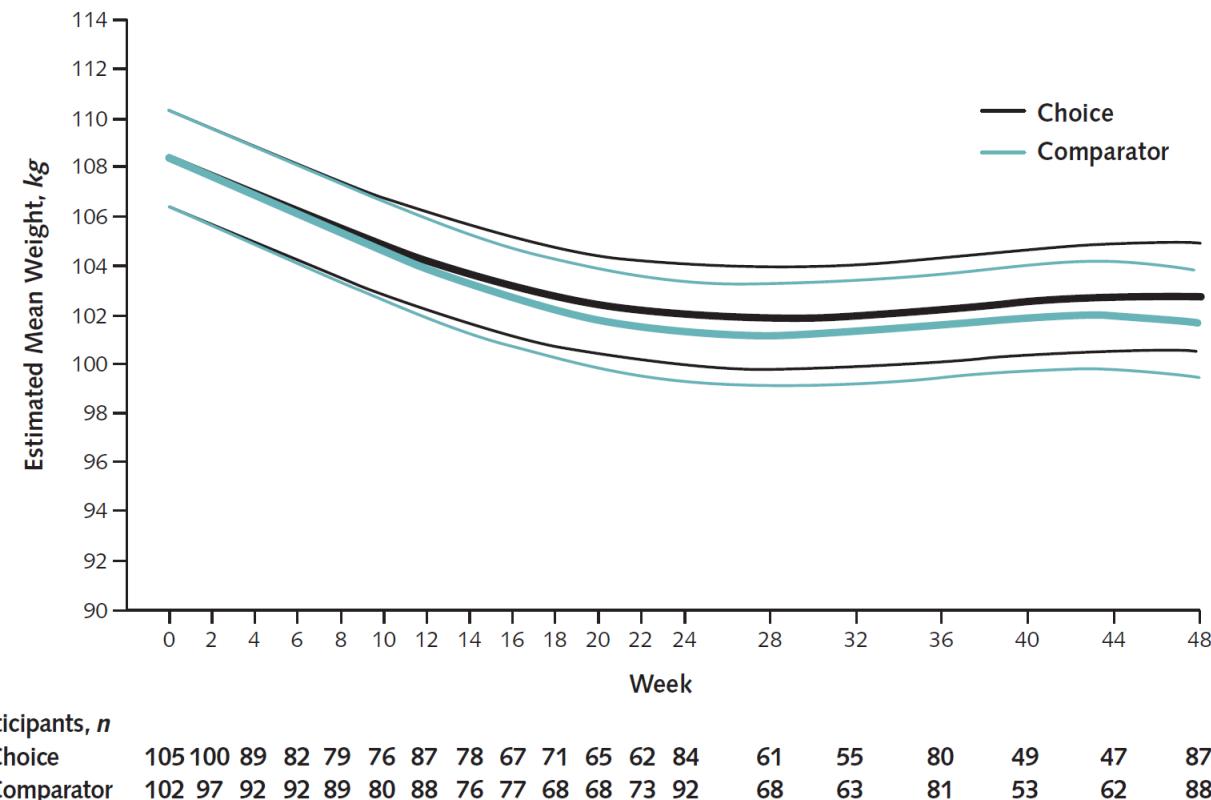


SNPs from 3 genes (*PPARG*, *ADRB2*, and *FABP2*)

# Effect of Allowing Choice of Diet on Weight Loss

Doppel-Randomisierung: A) Wahl zwischen 2 Diäten, B) low-carb vs low-fat

Mean weight trajectories and 95% CIs over 48 wk.

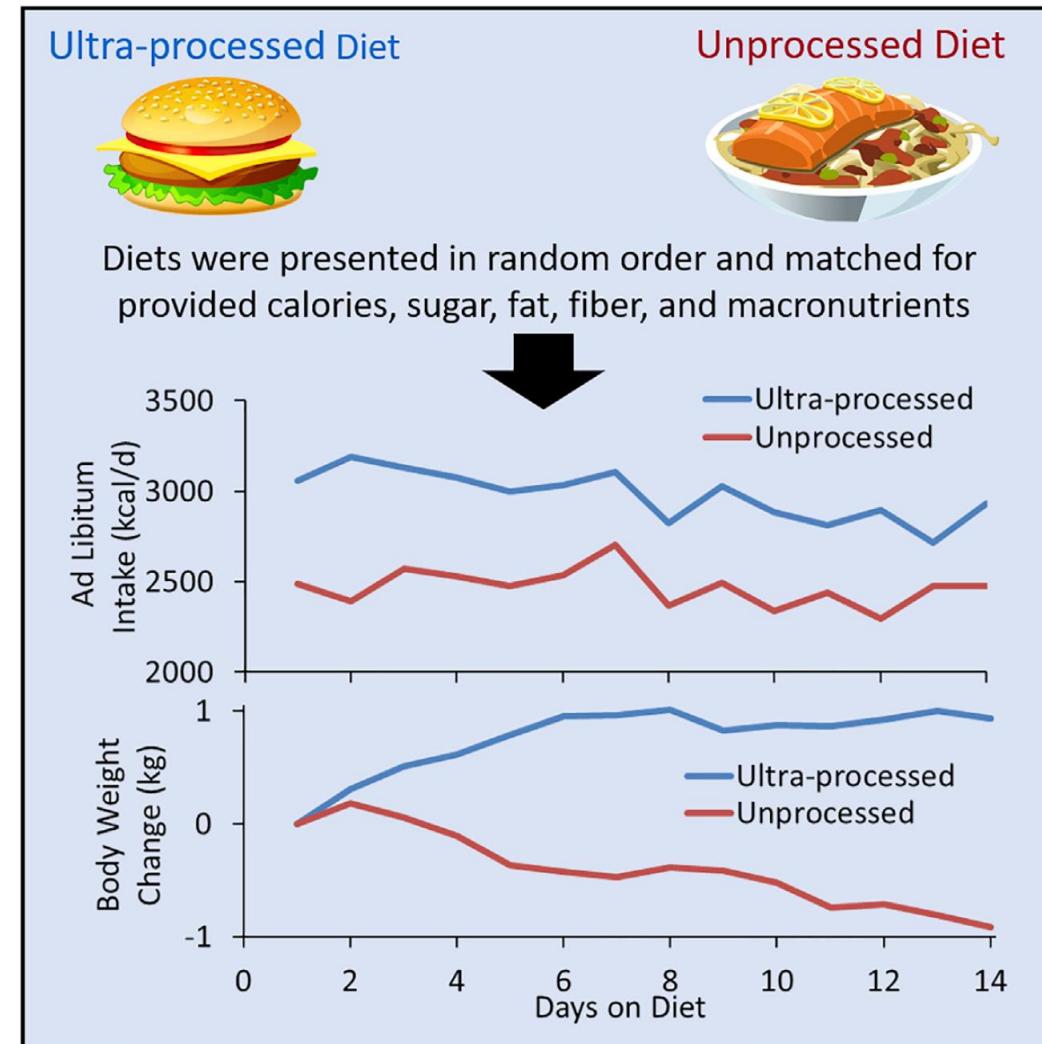


estimated mean weight loss:  
choice: 5.7 kg (95% CI, 4.3 to 7.0 kg)  
comparator: 6.7 kg (CI, 5.4 to 8.0 kg)  
(mean diff. 1.1 kg [CI, 2.9 to 0.8 kg];  $P=0.26$ )

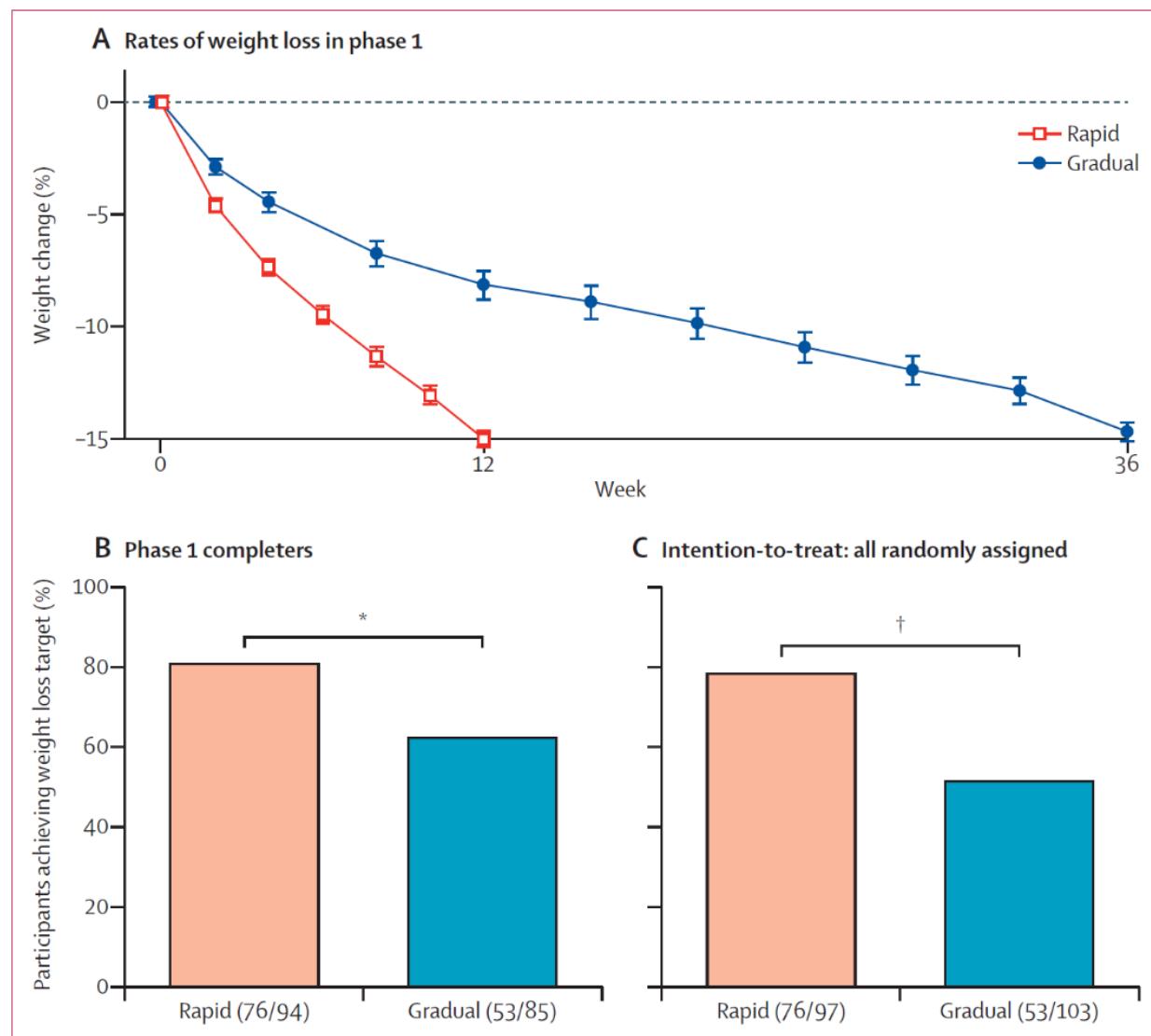
# Ernährung: Empfehlungen

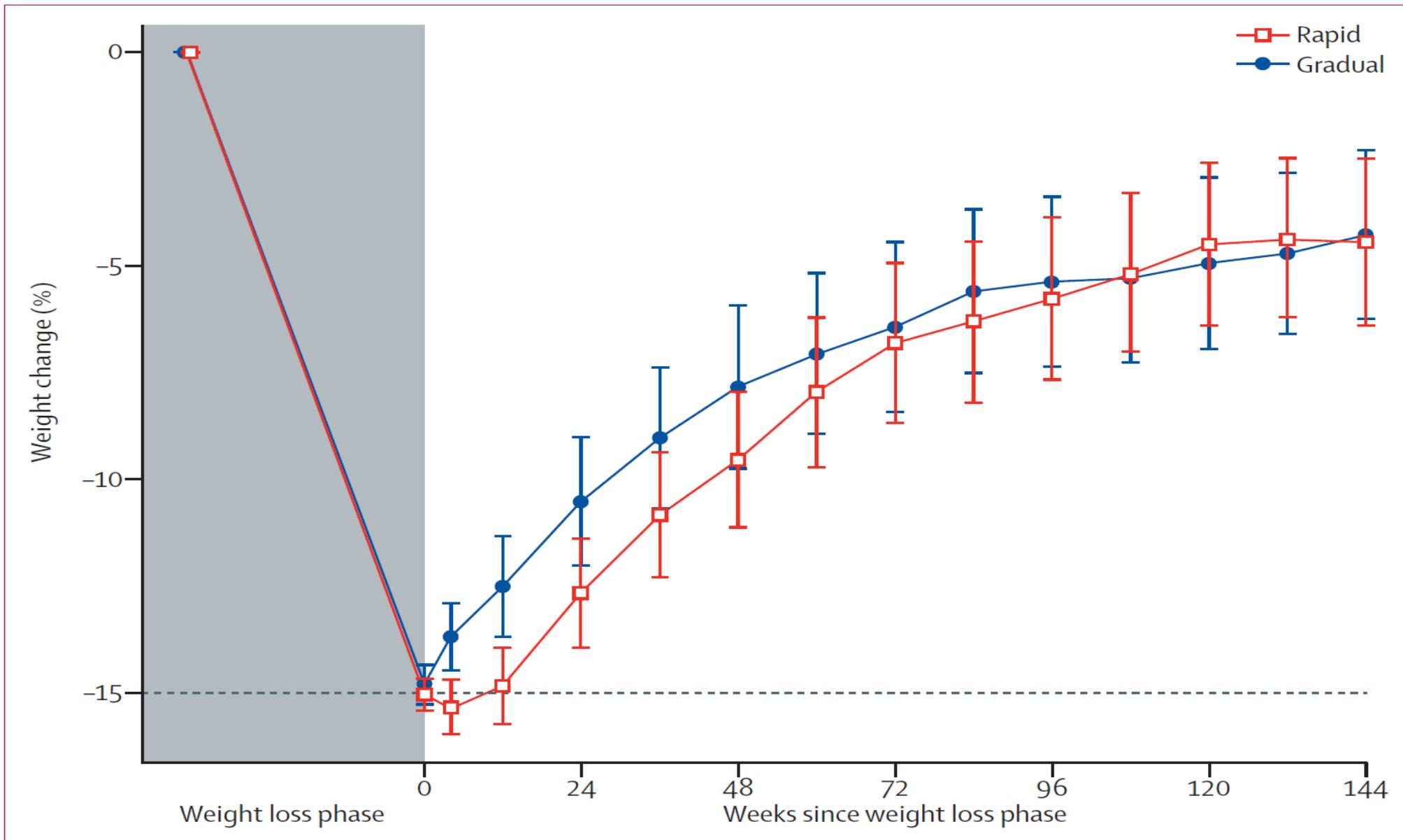
- Kalorienhaltige Getränke (ungewollte Kalorien) und (stark) verarbeitete Lebensmittel meiden
- Kontrolle der Portionen
- Selbstbeobachtung
- Gesundheitsbewusster, langfristiger Zugang zum Essen

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

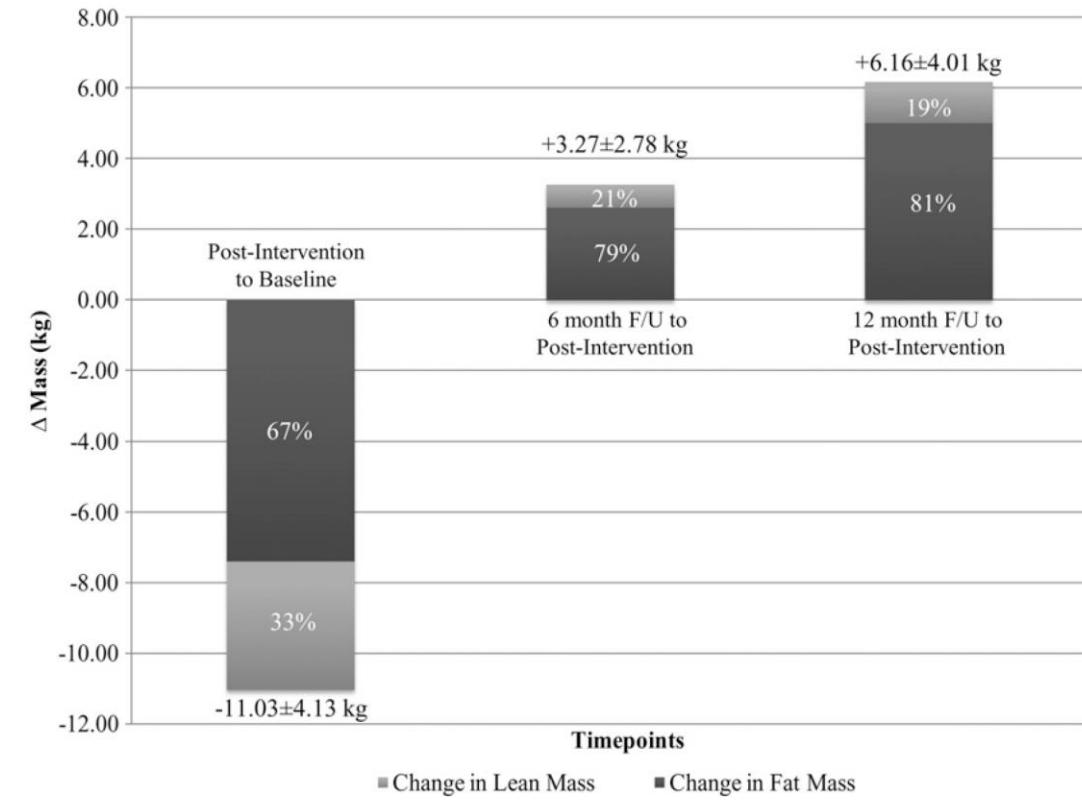
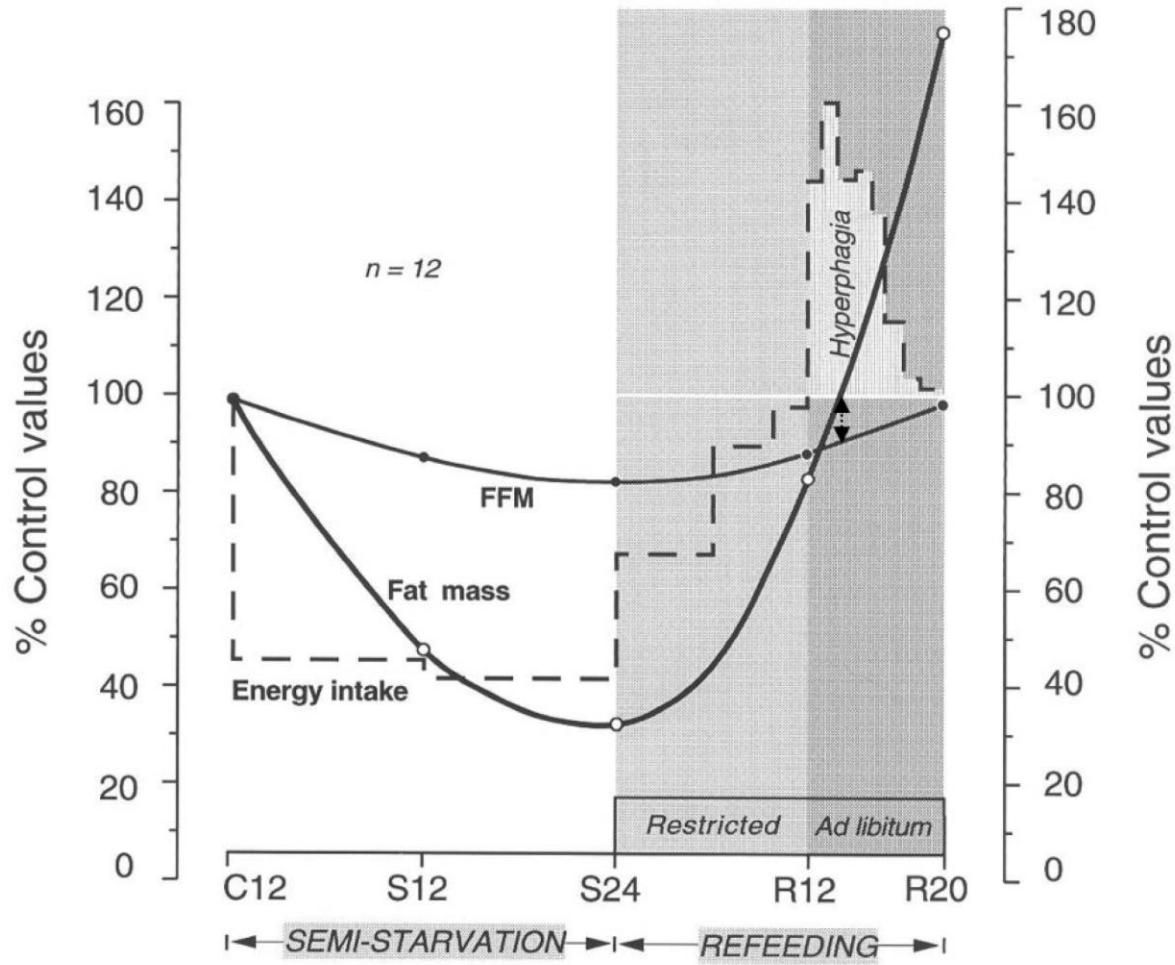


# Rasche Gewichtsreduktion führt zu rascher Wiederzunahme?

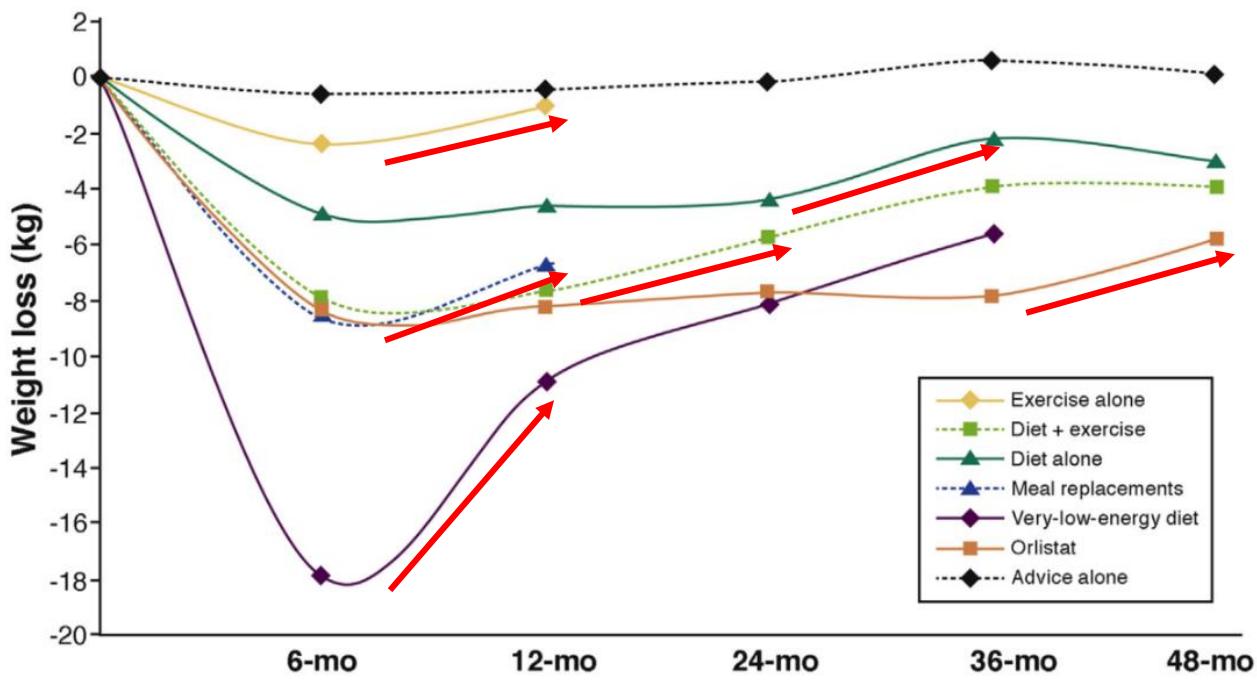




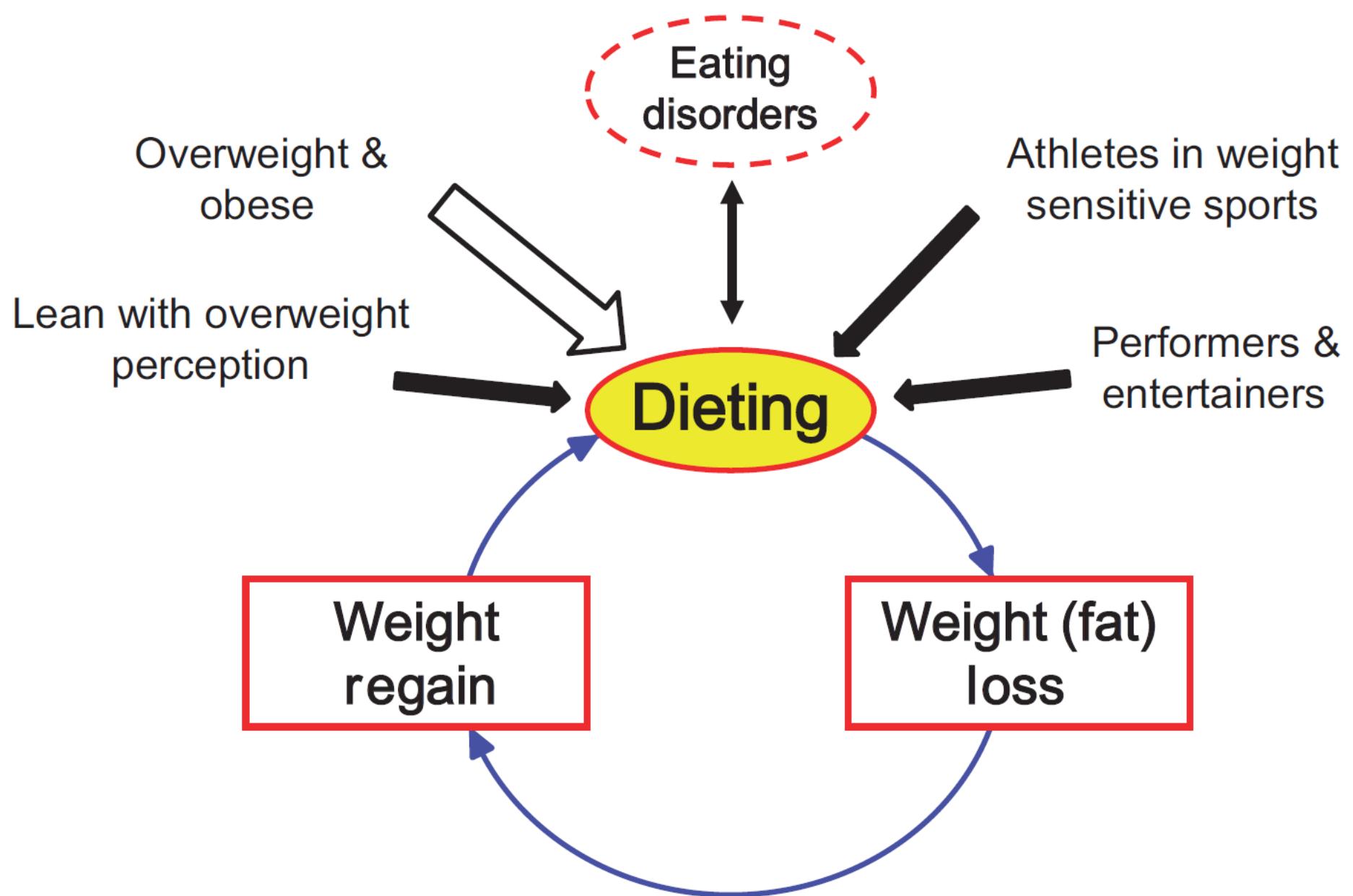
**Figure 3:** Mean weight change (% change, 95% CI) during phase 2 for study completers (n=61 in rapid weight loss and n=43 in gradual weight loss group)



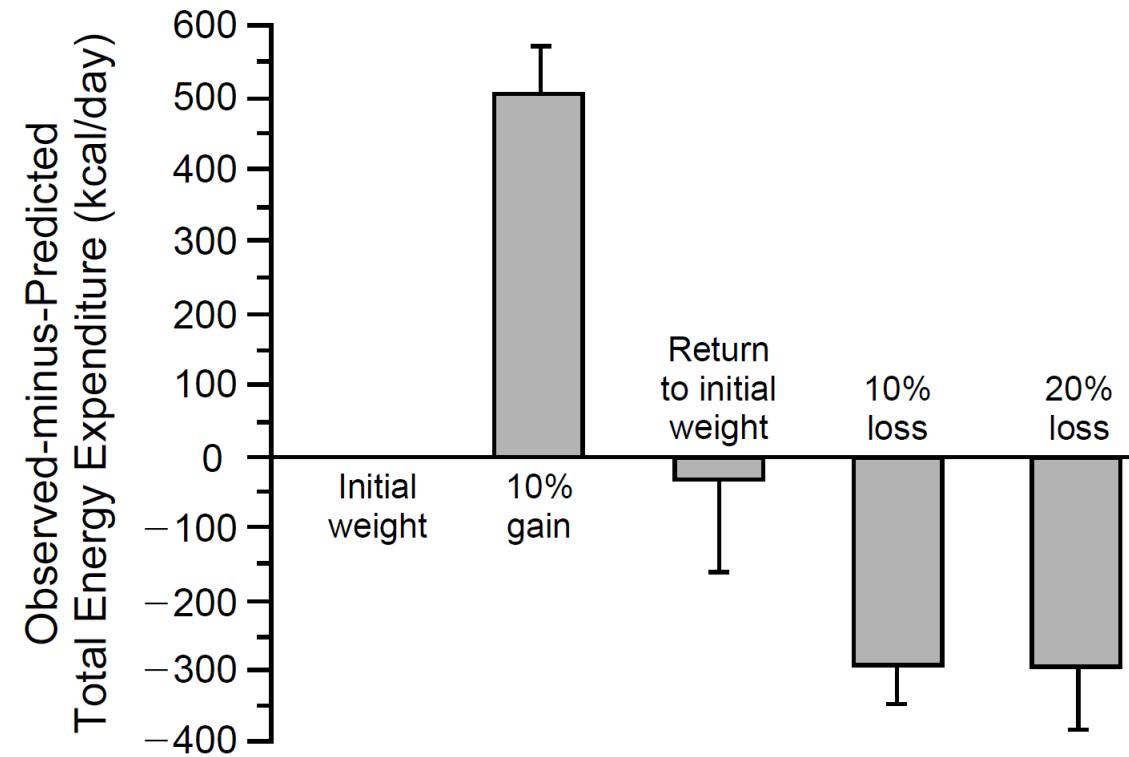
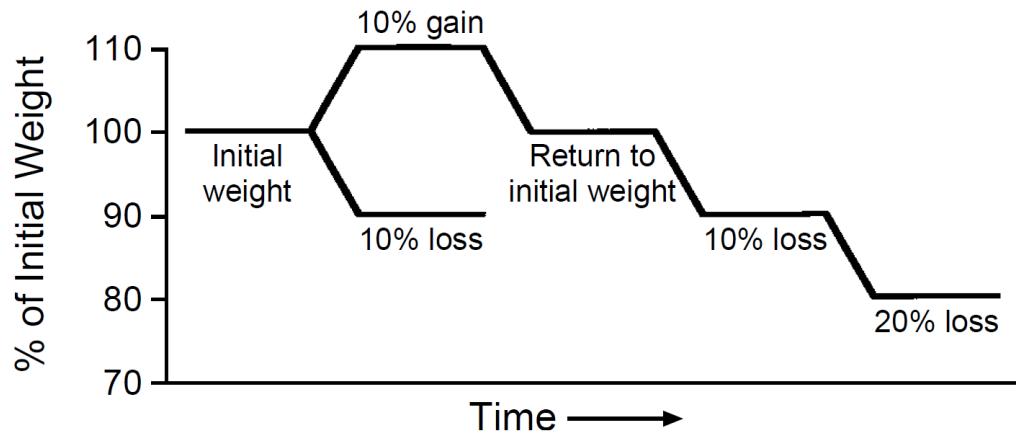
# Gewichtsverlauf über die Zeit.....



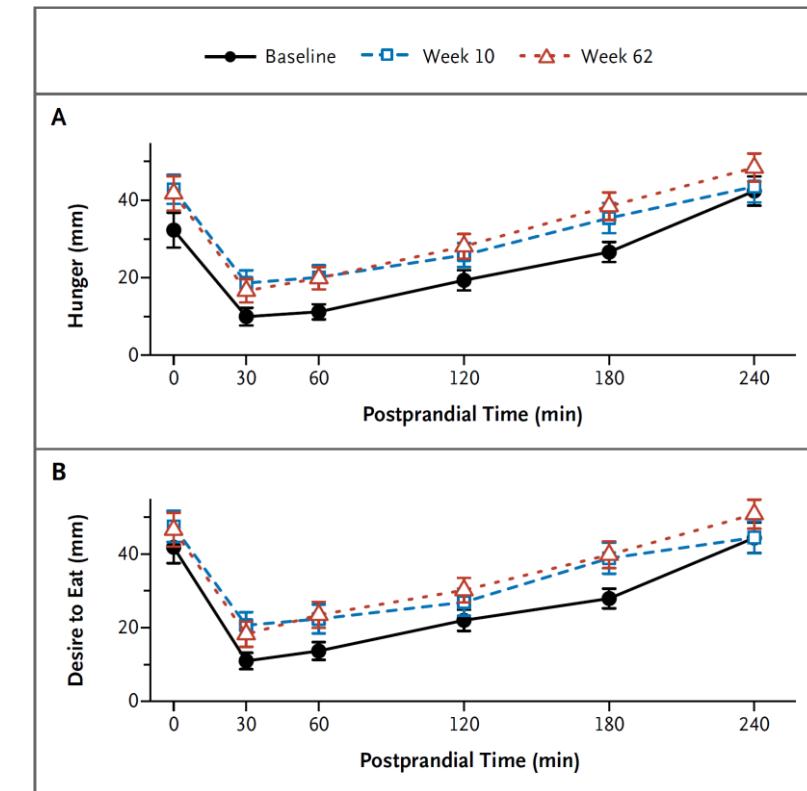
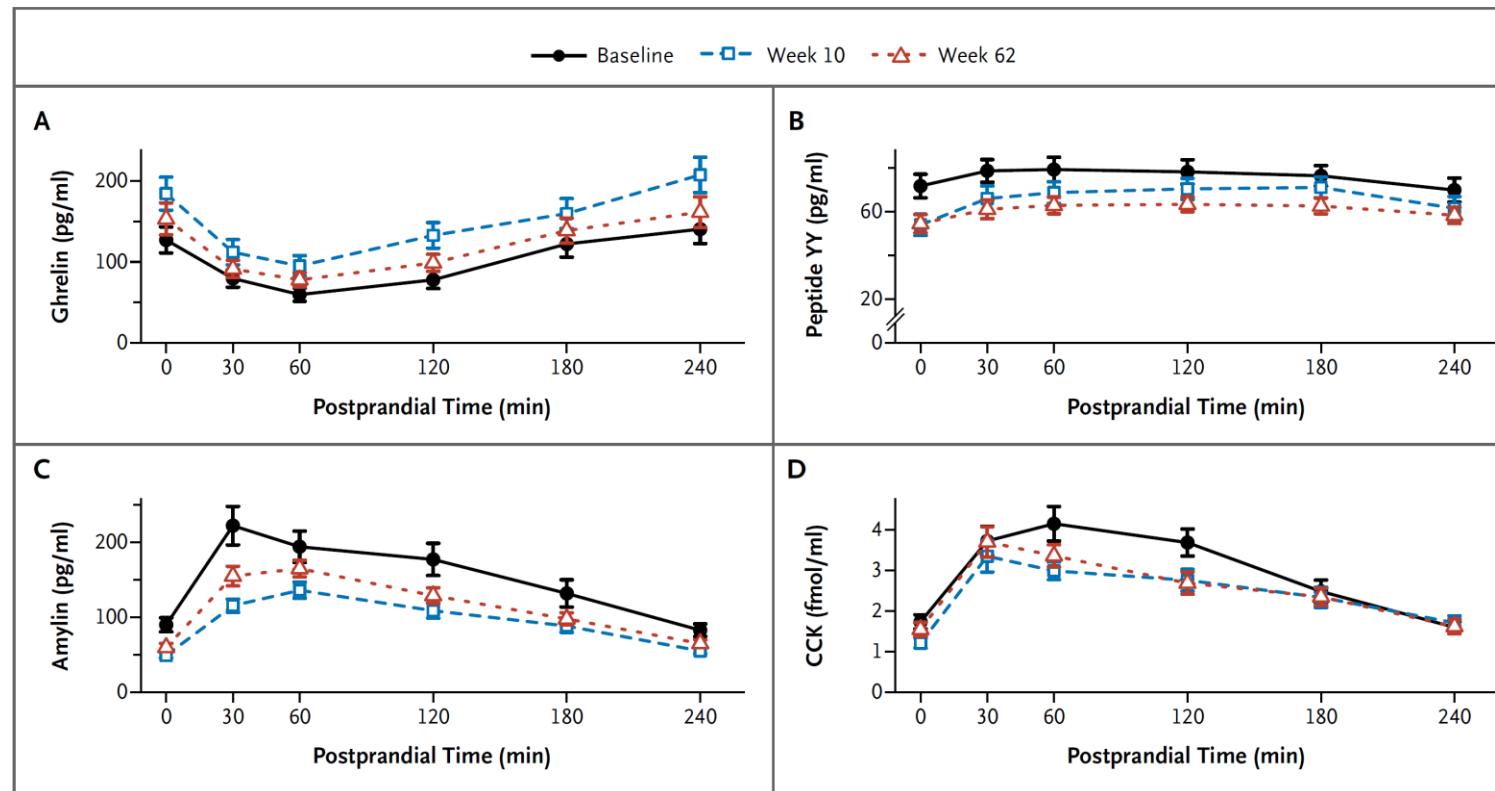
**Figure 2.** Average weight loss of subjects completing a minimum 1-year weight-management intervention based on review of 80 studies ( $n=26,455$ ; 18,199 completers [69%]). (Reprinted with permission.<sup>69</sup>) (Data from sibutramine has been removed.)



## Changes in energy expenditure resulting from altered body weight



# Long-Term Persistence of Hormonal Adaptations to Weight Loss

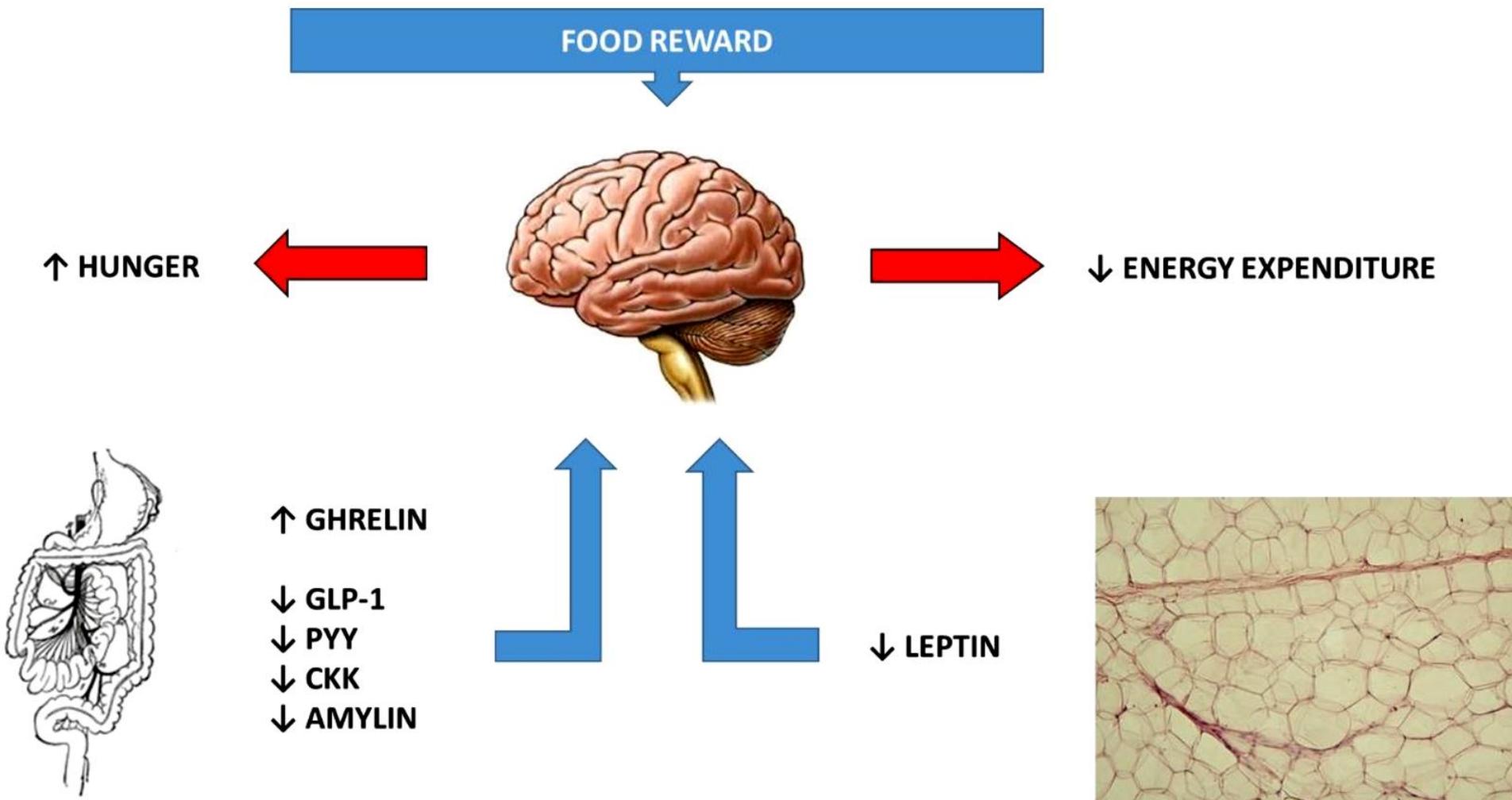


# Persistent Metabolic Adaptation 6 Years After “The Biggest Loser” Competition

				P		
	Baseline	End of competition at 30 weeks	Follow-up at 6 years	Baseline vs. 30 weeks	Baseline vs. 6 years	30 weeks vs. 6 years
Age (years)	34.9 ± 10.3	35.4 ± 10.3	41.3 ± 10.3	<0.0001	<0.0001	<0.0001
Weight (kg)	148.9 ± 40.5	90.6 ± 24.5	131.6 ± 45.3	<0.0001	0.0294	0.0002
BMI ( $\text{kg}/\text{m}^2$ )	49.5 ± 10.1	30.2 ± 6.7	43.8 ± 13.4	<0.0001	0.0243	0.0002
% Body fat	49.3 ± 5.2	28.1 ± 8.9	44.7 ± 10	<0.0001	0.0894	0.0003
FM (kg)	73.4 ± 22.6	26.2 ± 13.6	61.4 ± 30	<0.0001	0.0448	0.0001
FFM (kg)	75.5 ± 21.1	64.4 ± 15.5	70.2 ± 18.3	<0.0001	0.0354	0.0101
RQ	0.77 ± 0.05	0.75 ± 0.03	0.81 ± 0.02	0.272	0.0312	<0.0001
RMR measured (kcal/d)	2,607 ± 649	1,996 ± 358	1,903 ± 466	0.0004	<0.0001	0.3481
RMR predicted (kcal/d)	2,577 ± 574	2,272 ± 435	2,403 ± 507	<0.0001	0.0058	0.0168
Metabolic adaptation (kcal/d)	29 ± 206	-275 ± 207	-499 ± 207	0.0061	<0.0001	0.0075
TEE (kcal/d)	3,804 ± 926	3,002 ± 573	3,429 ± 581	0.0014	0.0189	0.0034
Physical activity (kcal/kg/d)	5.6 ± 1.8	10.0 ± 4.6	10.1 ± 4.0	0.0027	0.001	0.8219

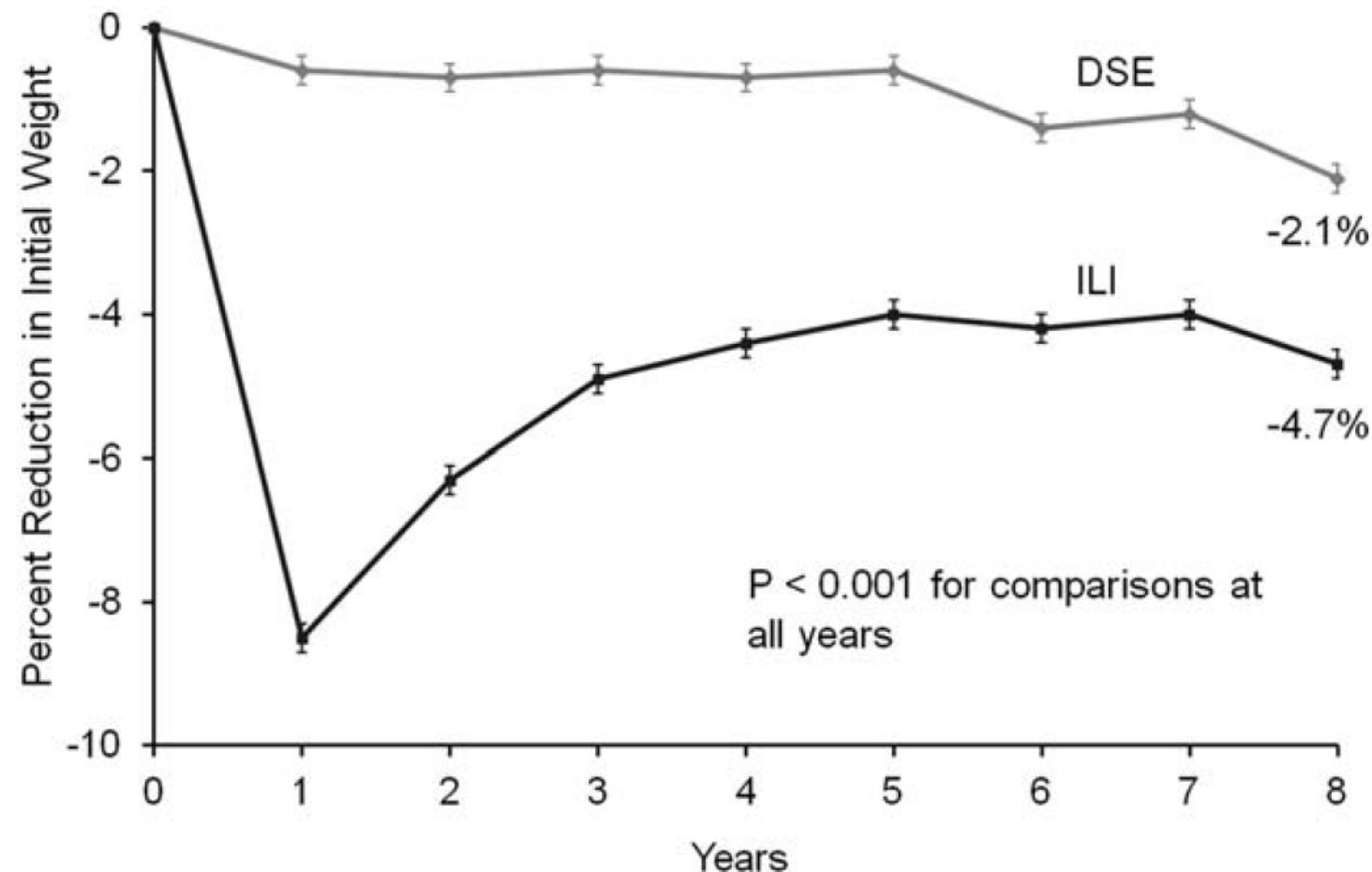
The predicted RMR was obtained using a linear regression equation developed using baseline data on body composition, age, and sex in the full 16-subject cohort. The P values were not adjusted for multiple comparisons.

BMI, body mass index; FM, fat mass; FFM, fat-free mass; RMR, resting metabolic rate; RQ, respiratory quotient; TEE, total energy expenditure.



**Cave: sarkopene Adipositas**

# Eight-Year Weight Losses with an Intensive Lifestyle Intervention: The Look AHEAD Study (Action for Health in Diabetes)



ILI...Intensive Lifestyle Intervention, DSE...Diabetes Support and Education

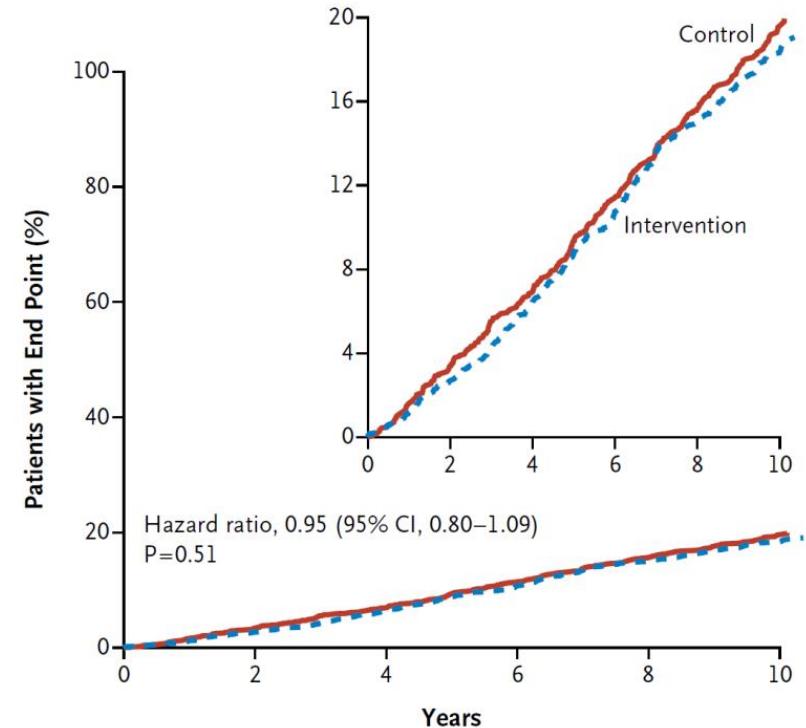
Obesity 2014;22:5-13

# Look AHEAD

Weniger Antihypertensiva, Statine, Insulin

Verbesserung von:

- OSAS
- Inkontinenz
- NAFLD
- Nierenerkrankung
- Depression
- Lebensqualität
- Sexualität
- Mobilität
- Körperliche Funktionen



No. at Risk	Control	2575	2425	2296	2156	2019	688
Intervention	2570	2447	2326	2192	2049	505	

Endpunkt: Kardiovask. Tod, MI, Schlaganfall, Ang.pect.-Hosp

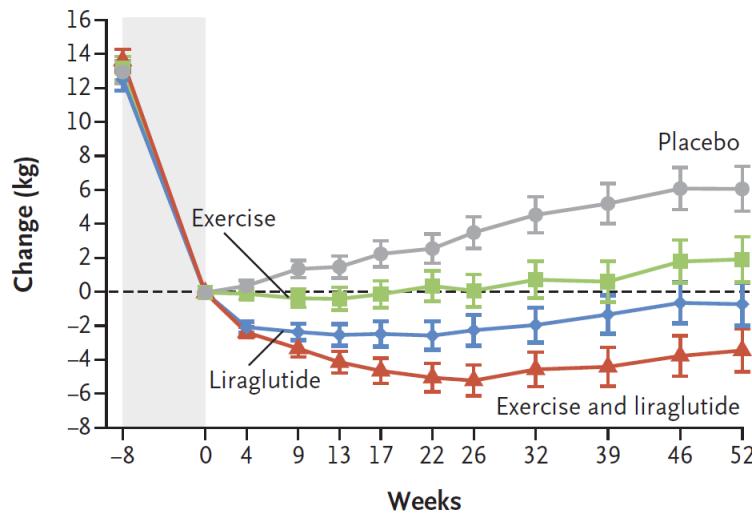
# **Association of the magnitude of weight loss and changes in physical fitness with long-term cardiovascular disease outcomes in overweight or obese people with type 2 diabetes: a post-hoc analysis of the Look AHEAD randomized clinical trial**

Gewichtsreduktion  $\geq 10\%$  im ersten Jahr (n = 1013, 21%):

- Primärer Endpunkt (kardiovask. Tod, nicht-tödl. MI, Schlaganfall, Hospitalisation wegen AP): minus 21 % (HR 0.79, 95%CI 0.64–0.98; p=0.034)
- Sekundärer Endpunkt (prim. plus CABG, Carotid-Endarterektomie, PCI, Hosp. wg. HI, PAVK, Gesamt mortalität): minus 24 % (HR 0.76, 95% CI 0.63-0.91, p=0.003)

# Healthy Weight Loss Maintenance with Exercise, Liraglutide, or Both Combined

**A Change in Body Weight**



-4.1 (95% CI, -7.8 to -0.4)  
P=0.03

-6.8 (95% CI, -10.4 to -3.1)  
P<0.001

-9.5 (95% CI, -13.1 to -5.9)  
P<0.001

-5.4 (95% CI, -9.0 to -1.7)  
P=0.004

-2.7 (95% CI, -6.3 to 0.8)  
P=0.13

6.1  
2.0  
-0.7  
-3.4

Change from Wk 0 to 52 (kg)

No. Who Underwent Randomization  
No. Who Completed Trial

No. of Participants

215 195 187 183 181 178 178 175 171 169 168 166

49

48

49

49

183 181 178 178 175 171 169 168 166

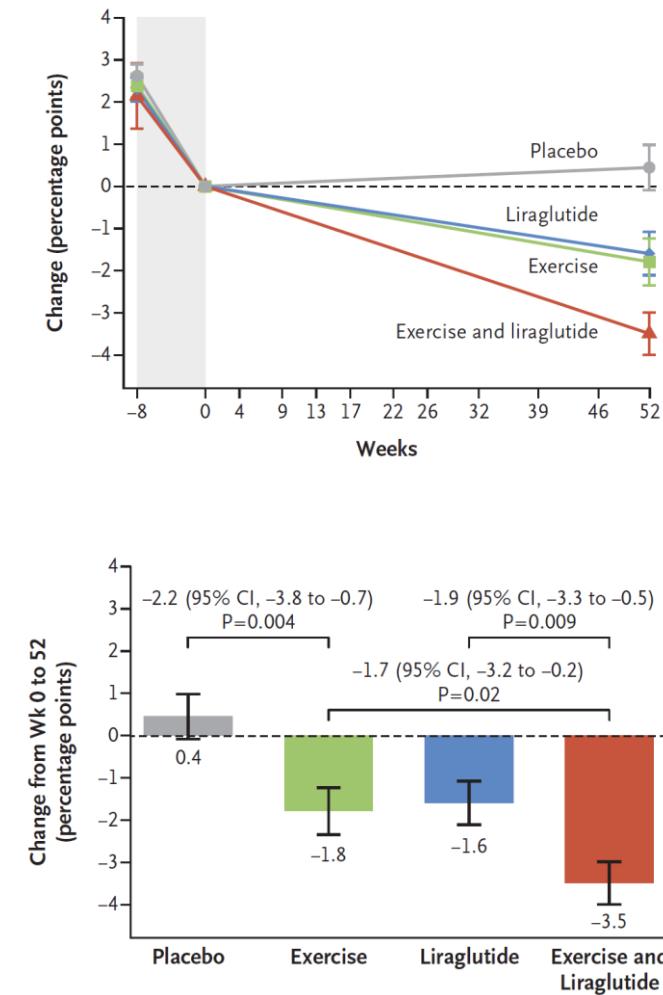
40

40

41

45

**B Change in Body-Fat Percentage**



## Take home messages

- Adipositas: chronische, wiederkehrende, progressive Erkrankung.
- Risiko abklären: BMI, Taillenumfang, Co-Morbiditäten – Therapieziele festlegen.
- Aktivität: je aktiver desto besser.
- Kombination Kraft- und Ausdauertraining wahrscheinlich am Besten.
- Ernährung / Diät: keine Diät ist einer anderen prinzipiell überlegen.
- Keine Diät passt für alle zu jeder Zeit - „one size fits all“ gibt es nicht.
- Rotieren der verschiedenen Diätformen ist empfehlenswert.
- An Genetik angepasste Diät bisher nicht wirksam. Technische Hilfsmittel?
- Langzeitresultate?
- Sarkopene Adipositas vermeiden.
- Tendenz zu sekundärer Gewichtszunahme: Gewichtserhaltung ist schwierig (noch schwieriger).