

Adipositas und Metabolisches Syndrom

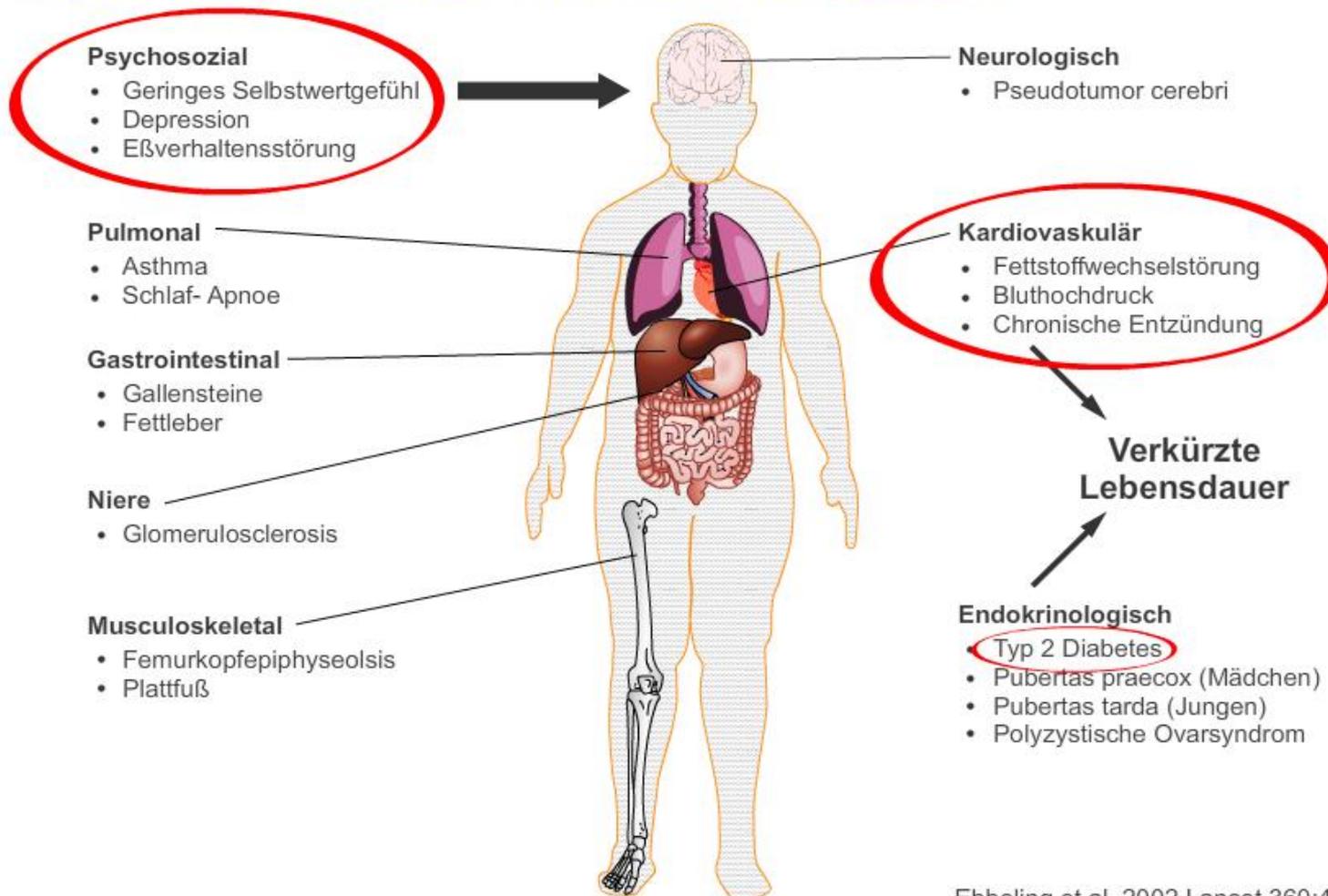
Folgeerkrankungen, Prävention und Therapie



T. Reinehr

Abteilung für Pädiatrische Endokrinologie,
Diabetologie und Ernährungsmedizin
Vestische Kinder- und Jugendklinik Datteln
Universität Witten/Herdecke

Folgeerkrankungen der Adipositas im Kindesalter



Lebensqualität bei kindlicher Adipositas

- Kinder sind lieber mit behinderten Kindern befreundet als mit adipösen Kindern
- Lebensqualität adipöser Kinder geringer als krebskranker Kinder

Einfluss des BMI im Kindesalter auf die Lebenserwartung

Baker JL, et al *N.Engl.J.Med.* 2007:

- 25 Jahres follow-up Studie bei 276,835 dänischen Kindern
- **kindlicher BMI prädiktiv für koronare Herzerkrankung im Alter \geq 25 Jahre**

Franks PW et al *N.Engl.J.Med.* 2010:

- 55 Jahres follow-up Studie bei 4857 PIMA Indianer
- **kindlicher BMI war signifikant mit Tod $<$ 55 Lebensjahr assoziiert**

Definition

Metabolischen Syndrom im Kindes- und Jugendalter

- Pathologische Glucosetoleranz + mindestens 2 der Kriterien:
 - Bluthochdruck
 - Dyslipidämie: Hypertriglyceridämie oder HDL-cholesterinerniedrigung
 - Bauchumfang > 95 cm oder BMI > 97 .Percentile

Body-Mass Index in 2.3 Million Adolescents and Cardiovascular Death in Adulthood

Gilad Twig, M.D., Ph.D., Gal Yaniv, M.D., Ph.D., Hagai Levine, M.D., M.P.H., Adi Leiba, M.D., M.H.A., Nehama Goldberger, M.Sc., Estela Derazne, M.Sc., Dana Ben-Ami Shor, M.D., Dorit Tzur, M.B.A., Arnon Afek, M.D., M.H.A., Ari Shamiss, M.D., M.P.H., Ziona Haklai, M.A., and Jeremy D. Kark, M.D., Ph.D.

ABSTRACT

BACKGROUND

In light of the worldwide increase in childhood obesity, we examined the association between body-mass index (BMI) in late adolescence and death from cardiovascular causes in adulthood.

METHODS

We grouped data on BMI, as measured from 1967 through 2010 in 2.3 million Israeli adolescents (mean age, 17.3±0.4 years), according to age- and sex-specific percentiles from the U.S. Centers for Disease Control and Prevention. Primary outcomes were the number of deaths attributed to coronary heart disease, stroke, sudden death from an unknown cause, or a combination of all three categories (total cardiovascular causes) by mid-2011. Cox proportional-hazards models were used.

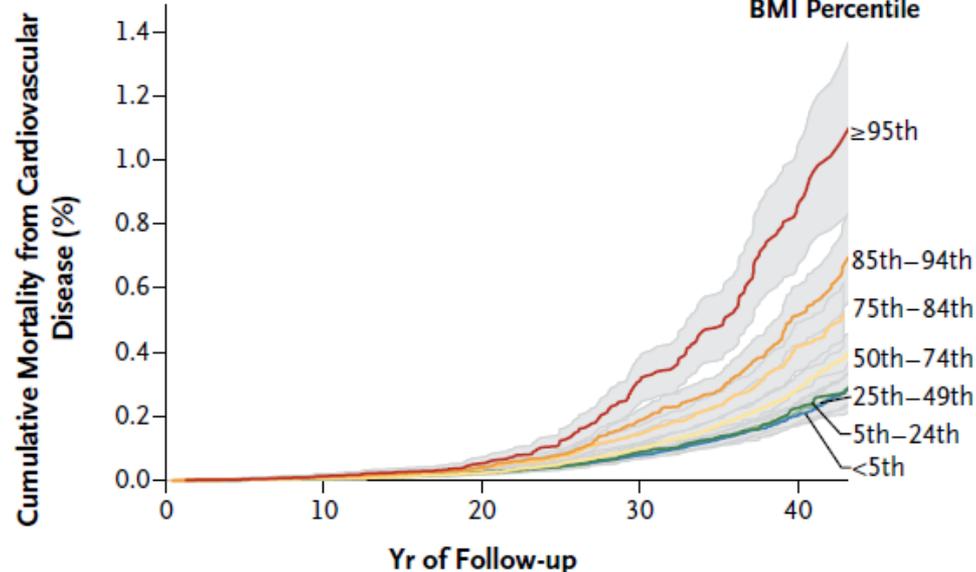
RESULTS

During 42,297,007 person-years of follow-up, 2918 of 32,127 deaths (9.1%) were from cardiovascular causes, including 1497 from coronary heart disease, 528 from stroke, and 893 from sudden death. On multivariable analysis, there was a graded increase in the risk of death from cardiovascular causes and all causes that started among participants in the group that was in the 50th to 74th percentiles of BMI (i.e., within the accepted normal range). Hazard ratios in the obese group (≥95th percentile for BMI), as compared with the reference group in the 5th to 24th percentiles, were 4.9 (95% confidence interval [CI], 3.9 to 6.1) for death from coronary heart disease, 2.6 (95% CI, 1.7 to 4.1) for death from stroke, 2.1 (95% CI, 1.5 to 2.9) for sudden death, and 3.5 (95% CI, 2.9 to 4.1) for death from total cardiovascular causes, after adjustment for sex, age, birth year, sociodemographic charac-

From the Department of Medicine (G.T., A.L., D.B.A.S., A.S.) and the Dr. Pinchas Bornstein Talpajot Medical Leadership Program (G.T., G.Y.), Sheba Medical Center, Tel Hashomer, the Israel Defense Forces Medical Corps (G.T., G.Y., A.L., E.D., D.I.), Sackler School of Medicine, Tel Aviv University, Tel Aviv (G.T., A.L., E.D., D.B.A.S., A.A., A.S.), and Hebrew University–Hadassah School of Public Health and Community Medicine (H.L., J.D.K.) and the Israel Ministry of Health (N.G., A.A., Z.H.), Jerusalem—all in Israel; and the Department of Medicine, Mount Auburn Hospital, Harvard Medical School, Cambridge, MA (A.L.). Address reprint requests to Dr. Twig at the Department of Medicine B, Sheba Medical Center, Tel Hashomer, Ramat Gan 52621, Israel, or at gilad.twig@gmail.com.

This article was published on April 13, 2016, at nejm.org.

DOI: 10.1056/NEJMoa1503840
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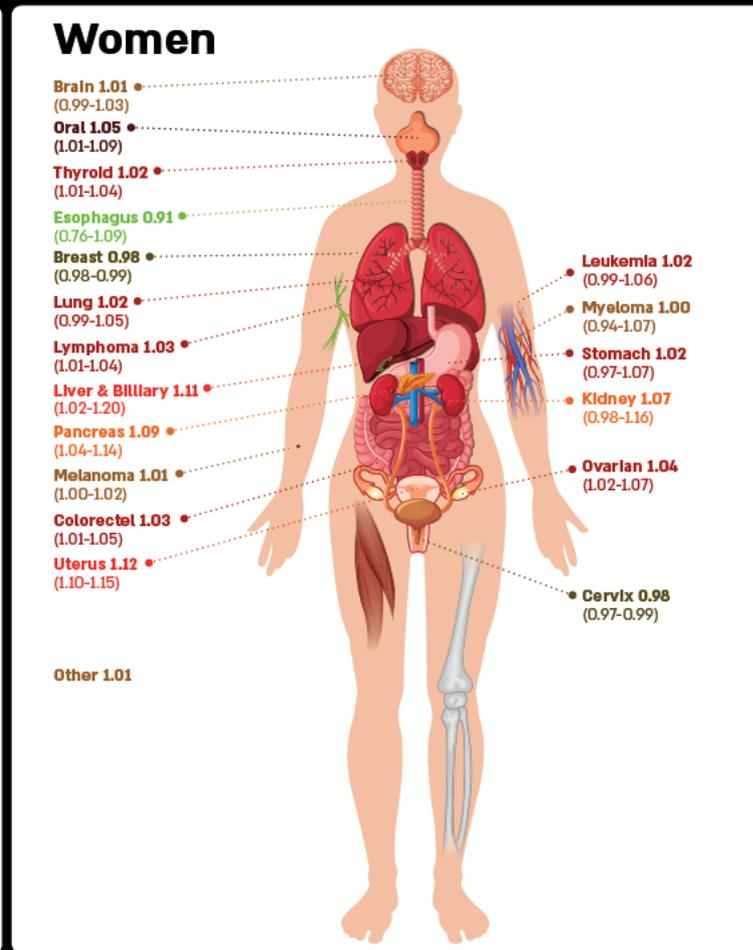
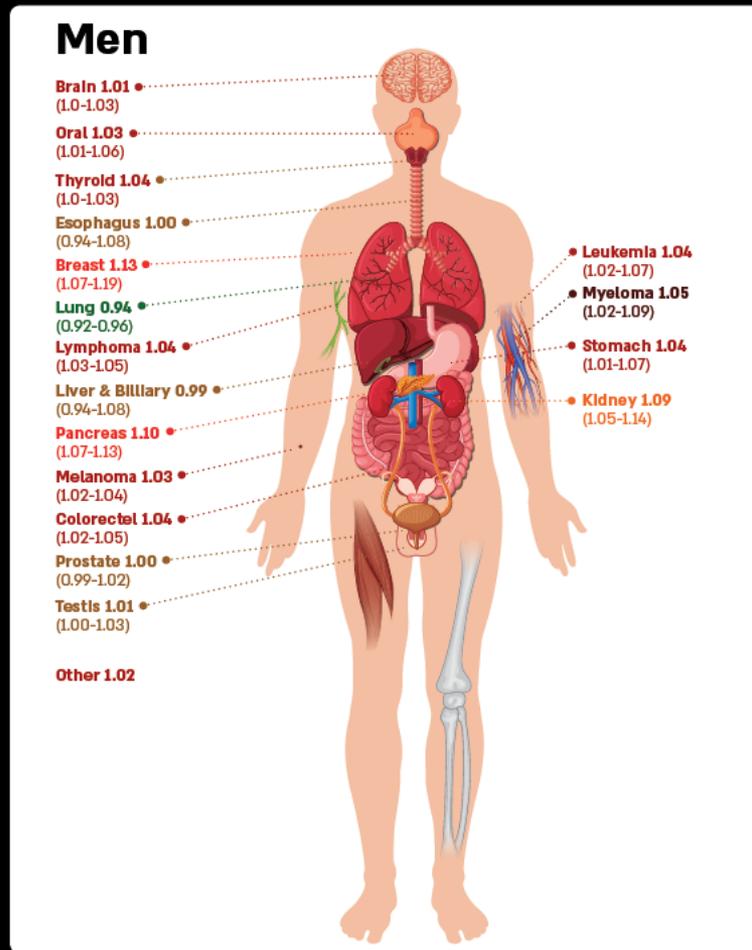
No. at Risk

Participants at risk	1,712,018	1,042,018	540,636	160,145
Cumulative person-yr	17,201,301	30,718,320	38,472,521	41,926,636
Cumulative cardiovascular deaths	185	609	1,577	2,676

Figure 2. Body-Mass Index (BMI) during Adolescence and Subsequent Cardiovascular Mortality.

Shown are rates of death from cardiovascular causes during up to 44 years of follow-up according to the percentile of BMI during adolescence, among 2,298,130 participants who were assessed between the ages of 16 and 19 years. Included in the 2918 deaths from cardiovascular causes were deaths from coronary artery disease and stroke and sudden deaths of unknown cause. Gray shading denotes 95% confidence intervals. The model was adjusted for sex, age at examination, birth year, education, residential socioeconomic status, country of origin, and height. Also shown are the numbers of participants at risk, cumulative person-years, and the cumulative numbers of deaths from cardiovascular causes through 40 years of follow-up. An additional 242 deaths from cardiovascular causes occurred between 40 years and the study cutoff of 44 years.

Cancer Incidence 30 years later based on BMI at 17 years



Unadjusted hazard ratio per BMI unit



Risk increases above the 75th BMI percentile

Twig et al
Lancet Endo
Diabetes
2020

Screening Folgeerkrankungen

HbA1c als
Diabetes-
screening

BRD: HbA1c keine
Erwähnung

Table 2. Screening for Comorbidities of Pediatric Overweight or Obesity

Comorbidity	Tests and Interpretation	Source
Prediabetes HbA1c	5.7% to <6.5% (39 to <48 mmol/mol) (note the unpredictability of this test in pediatrics in the text) ^a Fasting plasma glucose of ≥ 100 but <126 mg/dL (≥ 5.6 but <7.0 mmol/L)	American Diabetes Association (59)
IFG (verify fasting status) IGT (if OGTT is used)	Two-hour glucose of ≥ 140 but <200 mg/dL (≥ 7.8 but <11.1 mmol/L)	
Diabetes mellitus	HbA1c $\geq 6.5\%$ (≥ 48 mmol/mol) ^{a,b} Fasting plasma glucose of ≥ 126 mg/dL (≥ 7.0 mmol/L) (fasting is defined as no caloric intake for 8 h) ^b Two-hour plasma glucose of ≥ 200 mg/dL (≥ 11.1 mmol/L) during an OGTT ^b In a patient with classic symptoms of hyperglycemia, a random plasma glucose of ≥ 200 mg/dL	American Diabetes Association (59)
Dyslipidemia	Fasting lipids Triglycerides (mg/dL) (multiply by 0.0113 to convert to mmol/L): 0–9 y < 75 (acceptable), 75–99 (borderline high), ≥ 100 (high); 10–19 y < 90 (acceptable), 90–129 (borderline high), ≥ 130 (high) LDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): < 110 (acceptable), 110–129 (borderline high), ≥ 130 (high) Total cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): < 170 (acceptable), 170–199 (borderline high), ≥ 200 (high) HDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): < 40 (low), 40–45 (borderline low), > 45 (acceptable) Non-HDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L) (can be nonfasting) < 120 (acceptable), 120–144 (borderline high), ≥ 145 (high)	Expert Panel Summary Report (58)
Prehypertension and hypertension	3–11 y: (standardized according to sex, age, and height percentile) BP > 90th percentile to <95th percentile = prehypertension BP \geq 95th percentile to <99th percentile + 5 mm Hg = stage 1 HTN BP \geq 99th percentile + 5 mm Hg = stage 2 HTN 12–17 y: (standardized according to sex, age, and height percentile) BP of >90th percentile to <95th percentile or > 120/80 = prehypertension BP \geq 95th percentile to <99th percentile + 5 mm Hg = stage 1 HTN BP \geq 99th percentile + 5 mm Hg = stage 2 HTN 18 to 21 y: BP \geq 120/80 to 139/89 mm Hg = prehypertension BP \geq 140/90 to 159/99 mm Hg = stage 1 HTN BP \geq 160/100 to 179/109 mm Hg = stage 2 HTN BP > 180/110 mm Hg = stage 3 HTN	Expert Panel Summary Report (58); Mancía et al., 2013 (61)
NAFLD	ALT > 25 U/L (boys) and >22 U/L (girls)	Schwimmer et al., 2010 (62)
PCOS	Free and total testosterone and SHBG, per Endocrine Society PCOS guidelines ^c	Legro et al., 2013 (63)
Obstructive sleep apnea	If positive history, refer to pulmonary for nocturnal polysomnography and if not available overnight oximetry	Wise et al., 2011 (48)
Psychiatric	If positive history, refer to mental health specialist	Zamethkin et al., 2004 (51)

Summary of Recommendations

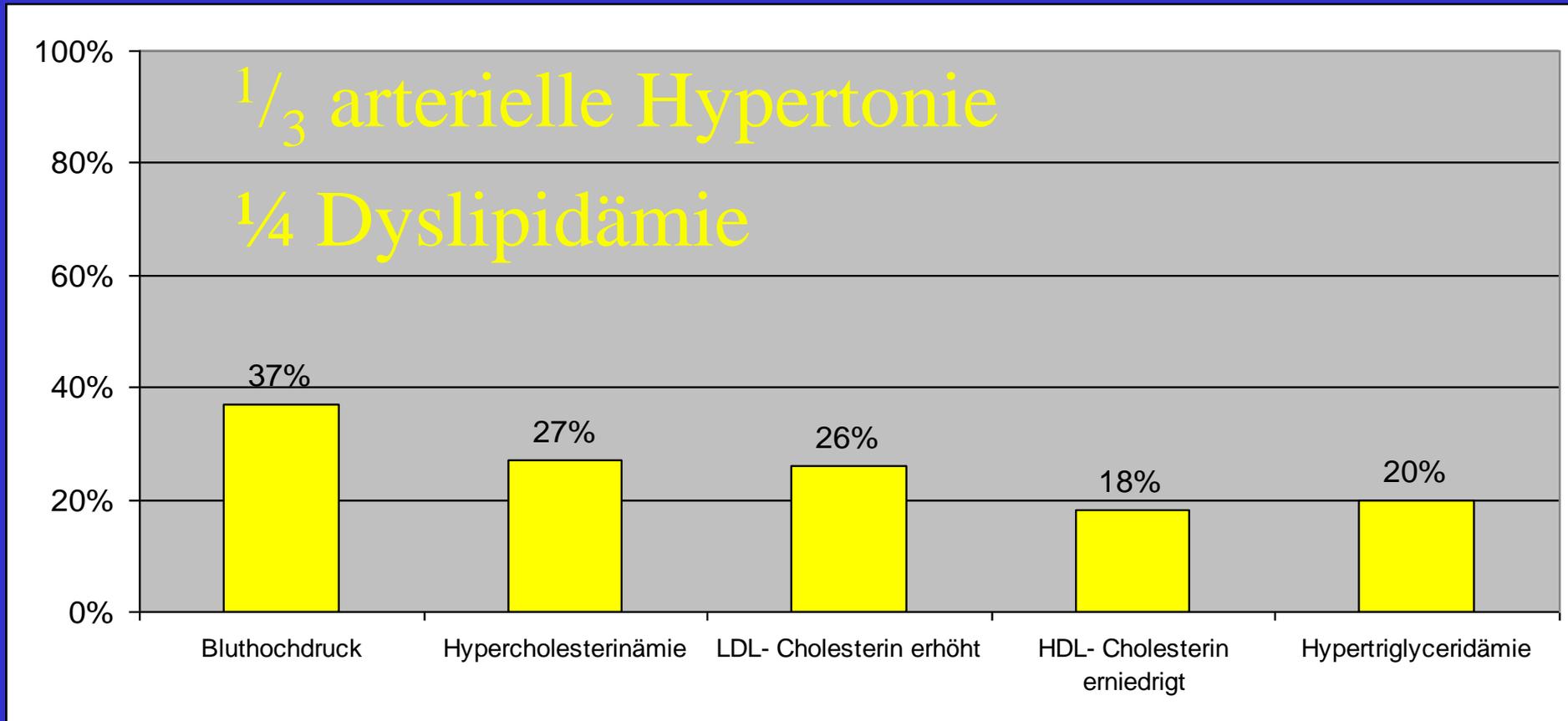
1.0 Diagnosing overweight and obesity

- 1.1 We recommend using body mass index (BMI) and the Centers for Disease Control and Prevention (CDC) normative BMI percentiles to diagnose overweight or obesity in children and adolescents ≥ 2 years of age. (1 $\oplus\oplus\oplus\circ$)
- 1.2 We recommend diagnosing a child or adolescent >2 years of age as overweight if the BMI is ≥ 85 th percentile but <95 th percentile for age and sex, as obese if the BMI is ≥ 95 th percentile, and as extremely obese if the BMI is $\geq 120\%$ of the 95th percentile or ≥ 35 kg/m² (1 $\oplus\oplus\circ\circ$). We suggest that clinicians take into account that variations in BMI correlate differently to comorbidities according to race/ethnicity and that increased muscle mass increases BMI. (2 $\oplus\circ\circ\circ$)
- 1.3 We suggest calculating, plotting, and reviewing a child's or adolescent's BMI percentile at least annually during well-child and/or sick-child visits. (Ungraded Good Practice Statement)
- 1.4 We suggest that a child <2 years of age be diagnosed as obese if the sex-specific weight for recumbent length is ≥ 97.7 th percentile on the World Health Organization (WHO) charts, as US and international pediatric groups accept this method as valid. (2 $\oplus\circ\circ\circ$)
- 1.5 We recommend against routine laboratory evaluations for endocrine etiologies of pediatric obesity unless the patient's stature and/or height velocity are attenuated (assessed in relationship to genetic/familial potential and pubertal stage). (1 $\oplus\oplus\oplus\circ$)
- 1.6 We recommend that children or adolescents with a BMI of ≥ 85 th percentile be evaluated for potential comorbidities (see Table 2 and Fig. 1). (1 $\oplus\oplus\oplus\circ$)

1.7 We recommend against measuring insulin concentrations when evaluating children or adolescents for obesity. (1 $\oplus\oplus\oplus\circ$)

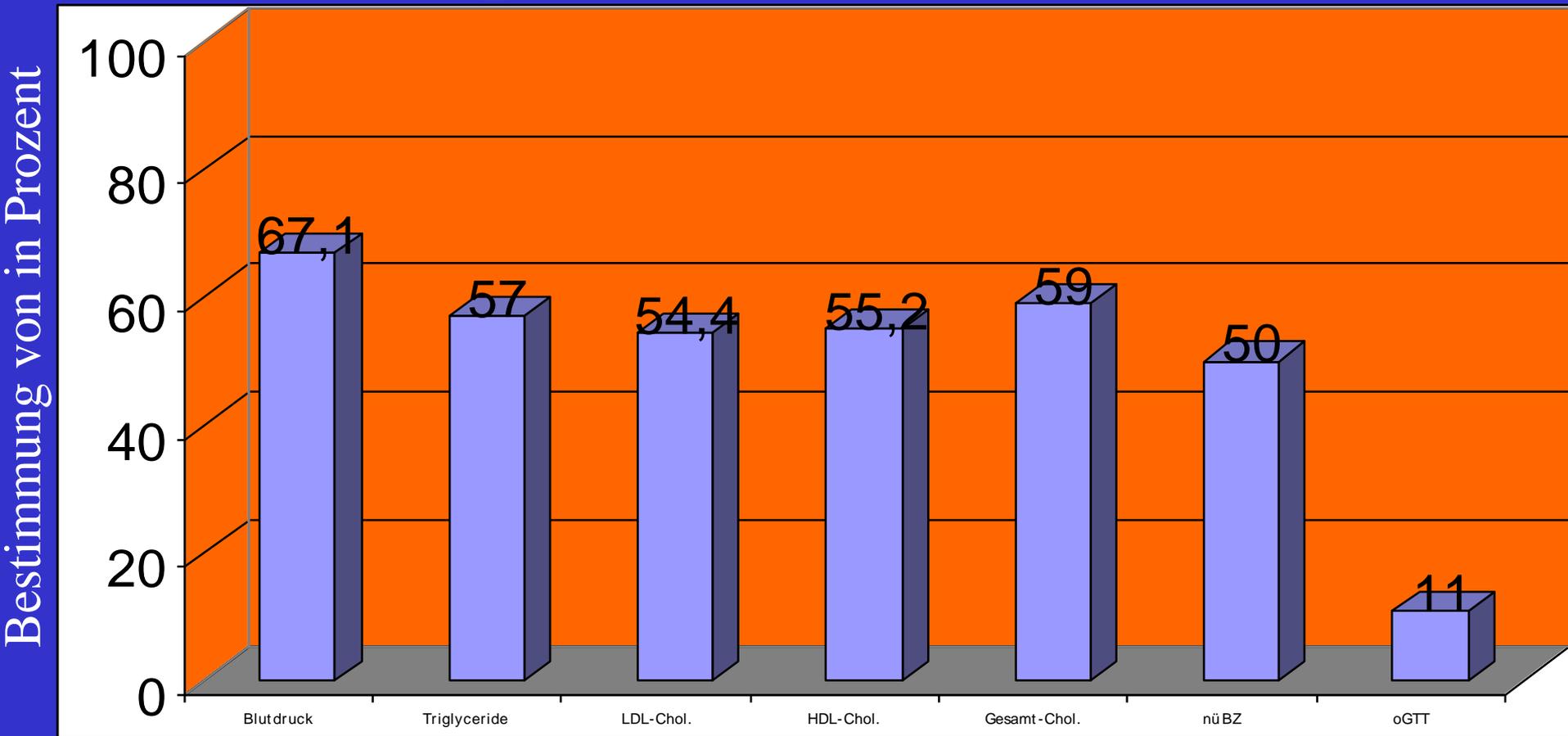
Häufigkeit Komorbidität bei 1004 deutschen adipösen Kindern

(Alter 4-18 Jahre, Median 12)



Reinehr et al. Cardiovascular risk factors in overweight European children and adolescents: relation to gender, age and degree of overweight. Nutr Metab Cardiovasc Dis 2005; 15:181-187

Untersuchung kardiovaskuläres Risikoprofil in deutschen Therapiezentren (n=1807 Kinder)



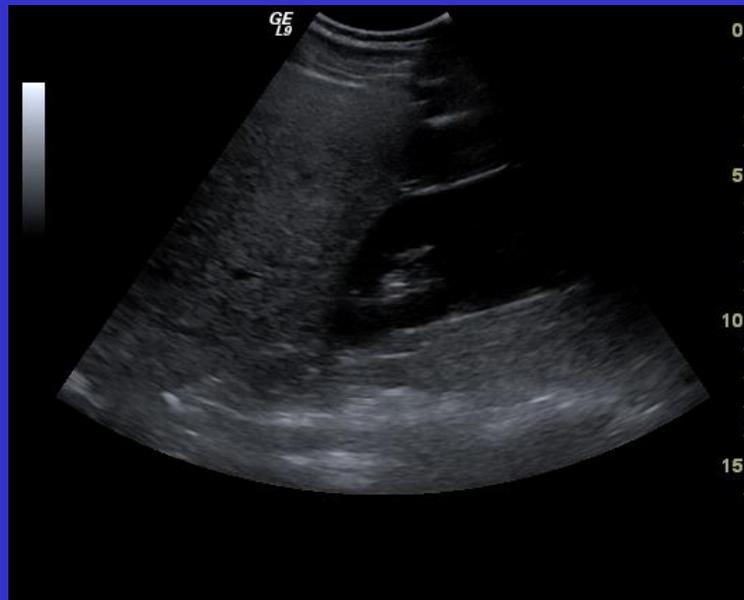
Quelle: BZgA Studie

Häufigkeit Typ 2 Diabetes bei Kindern und Jugendlichen in BRD

- In Deutschland ~1.000 Kinder und Jugendliche mit Typ 2 Diabetes mellitus bekannt (apv, dpv)
 - Etwa 330.000 adipöse Jugendliche (Alter 12 - 18 Jahre)
 - 1 % Dm2 Ergebnis aller Dm2-Screeningstudien in BRD bei Kindern ab 12 Jahren (Wabitsch 2005, Reinehr 2006, Wiegand 2008)
 - 3.300 Jugendliche mit Dm2 zu erwarten
- ➔ **Nur jeder 3. (!) bekannt**

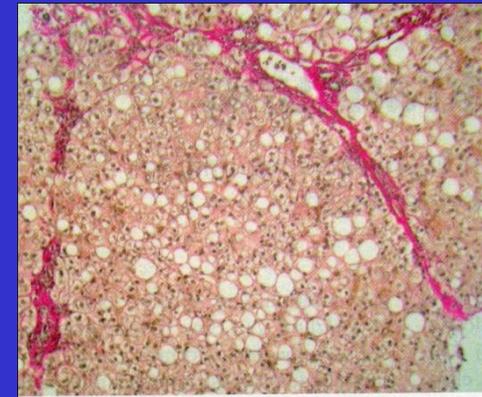
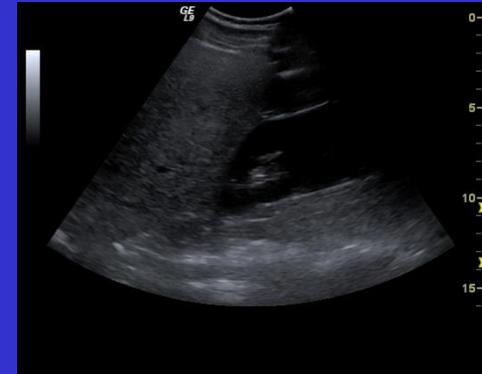
Nichtalkoholische Fettleberkrankheit

- Klinik: asymptomatisch
- Labor:
 - Transaminasenerhöhung (< 100 U/l)
 - **ALT > AST**
- Sono: Verfettung der Leber



Nichtalkoholische Fettleberkrankheit

- Klinik: asymptomatisch
- Labor:
 - Transaminasenerhöhung (< 100 U/l)
 - **ALT > AST**
- Sono: Verfettung der Leber
- Histologie:
 - Steatosis (Ballonierung, Verfettung, Nekrose)
 - Steatohepatitis (begleitende entzündliche Zellinfiltrate)
- Prognose:
 - meist gut
 - aber auch Übergang in Lebercirrhose !
- DD: Hepatitis, Stoffwechselerkrankungen, M. Wilson



Polyzystische Ovarsyndrom (PCOS)

- Definition:
 - **Zyklusstörung / Amenorrhoe**
 - **Hyperandrogenämie**
- Leitsymptome:
 - Zyklusstörung (Cave Regelunregelmäßigkeit ersten 2 Jahre nach Menarche physiologisch)
 - Hirsutismus
 - Acanthosis nigricans
- Diagnostik:
 - Ausschluß NNRtumor und late onset AGS
 - **Testosteron erhöht, SHBG erniedrigt, LH/FSH > 1**
 - Polyzystische Ovarien nur z.T. nachweisbar!
- Komplikationen:
 - Infertilität
 - Mamma-/Endometriumcarcinom durch hohe Östrogene

Schlaf- Apnoe Syndrom

- V.a. extreme adipöse Jugendliche
- Durch Verengung Kehlkopfbereich durch Fettmassen
- Klinik:
 - Tagesmüdigkeit
 - Antriebsarmut
 - Schnarchen
- Im Gegensatz zum Erwachsenenalter reversibel bei Gewichtsabnahme
- Diagnose: Schlaflaboruntersuchung

Folgeerscheinung der Adipositas, die meist keiner weiteren Abklärung bedürfen

- Striae distensae= „Schwangerschaftstreifen“
- (Pseudo)gynäkomastie Jungen
- „Hypogenitalismus“ Jungen: Fettschürze über Genitale
- relativer Großwuchs (akzeleriertes Knochenalter)

Sinnvolle Diagnostik bei Adipositas -Grunderkrankungen-

- Bei Wachstumsstörung:
 - Schilddrüsenwerte
 - E`lyte inklusive Phosphat
 - Dexamethasonhemmttest
 - Wachstumshormondiagnostik: Stimulationstests
- Bei syndromalen Stigmata:
 - Evtl humangenet. oder neuropädiatrische Vorstellung
- Bei BMI $> 25 \text{ kg/m}^2$ im Alter von 2 Jahre:
genetisches Panel

Sinnvolle Diagnostik bei Adipositas -Folgeerkrankungen-

- Bauchumfang
- Blutdruck
 - ggf 24h Blutdruckmessung
- Nüchtern BE:
 - HDL/LDL- Cholesterin, Triglyceride,
 - Bei Familienanamnese Diabetes: HbA1c
 - *Transaminasen: Konsequenz?*
- Ggf. Schlaflabor bei Tagesmüdigkeit, Schnarchen und extremer Adipositas
- Ggf orthopäd Konsil: Knicksenkfuß, X/O- Beinstellung
- Bei Regelstörung/Hirsutismus: endokrinol. Vorstellung

siehe auch Leitlinien AGA: www.a-g-a.de

Prävention

Prävention der Adipositas

Aufklärungskampagnen in Kindergärten oder Schulen

- Cochrane Library:

Präventionsprogramme in Schulen oder Kindergärten ohne Erfolg auf Gewichtsstatus, aber Verbesserung Gesundheitswissen

(Campbell 2003 Cochrane Library)

- Beispiele aus Deutschland ohne Einfluss auf BMI / Prävalenz Übergewicht
 - Tiger Kids Kindergarten (Clin Nutr. 2009;28:122-8)
 - Urmel ICE Schule (Obes Facts. 2012;5(1):1-11)

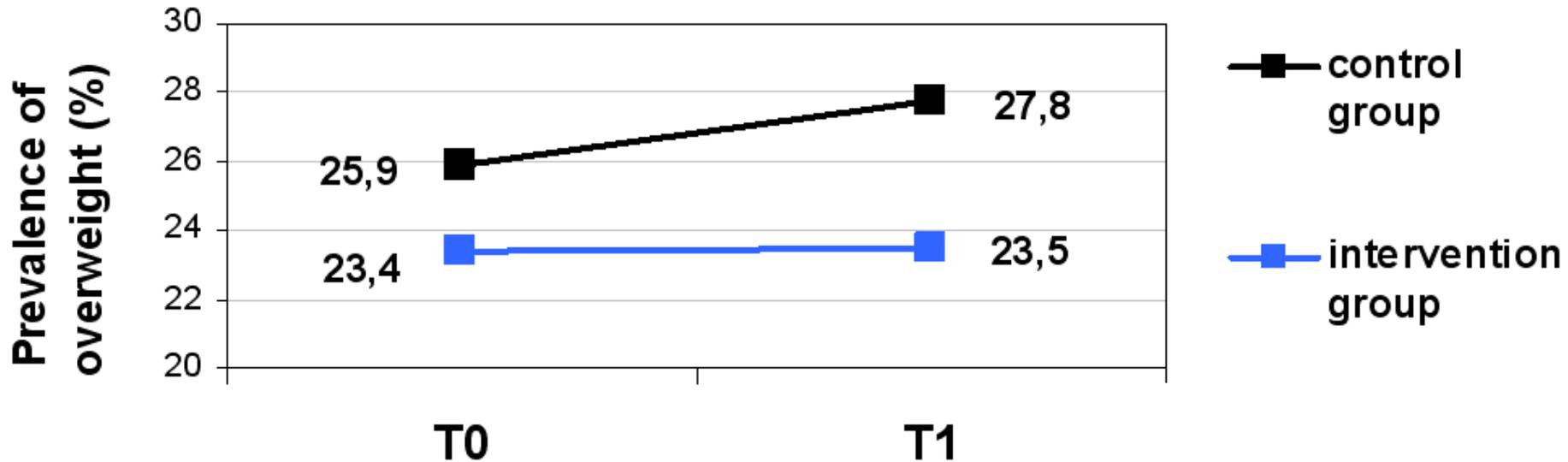
Prävention der Adipositas

- Placentainsuffizienz verhindern
 - Diabetes in Schwangerschaft konsequent behandeln
- } Gynäkologe
- Stillen fördern (??)
 - Rasche Gewichtszunahme nach Geburt verhindern
(insbesondere bei SGA)
 - Proteinarme Milchen
- } Neonatologe
- Keine Kinderlebensmittel
 - Gesüßte Getränke und fast food einschränken
 - Fernseh-/Medienkonsum einschränken
- } Pädiater
- Kinderlebensmittelwerbungverbot
 - Verbot gesüßte Getränke an Schulen
 - Verhältnisprävention statt Verhaltensprävention
- } Politik

Interventionsstudie

- 40 Schulen in Essen und Dortmund
(n=3000 Kinder)
- randomisiert Intervention oder Kontrollgruppe
- Intervention über 9 Monate:
 - Getränkeautomat Wasser, farbige Flaschen
 - Keine gesüßten Getränke

Prevalence of overweight



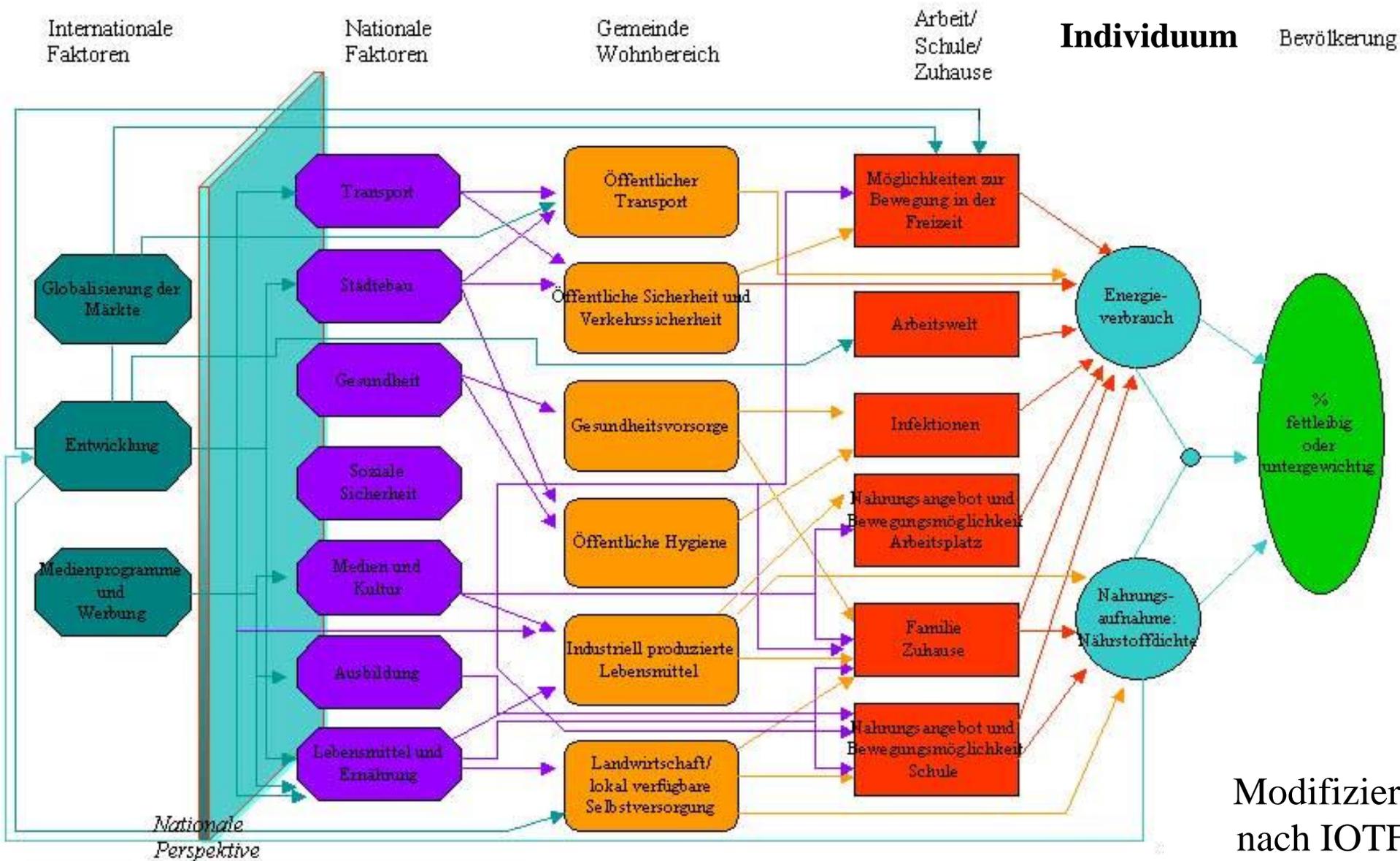
At follow-up in the IG compared to CG:

OR = 0,69 p=0,041

- Muckelbauer, Kersting, Toschke, Reinehr,
•Pediatrics 2009 & Obesity Facts 2009

Die globale Perspektive

Netzwerk kausaler Faktoren der Adipositas



Modifiziert
nach IOTF

Therapieoptionen bei Adipositas im Kindes- und Jugendalter

- Lebensstilintervention
- Medikamente
- Bariatrische Chirurgie

Interventions for treating obesity in children (Review)

Oude Luttikhuis H, Baur L, Jansen H, Shrewsbury VA, O'Malley C, Stolk RP, Summerbell CD

64 randomisiert kontrollierte Studien mit 5230 Teilnehmern

Schlussfolgerung: kombinierte Lifestyle Intervention führt im Gegensatz zur Selbstbehandlung oder "Standardcare" zu einer klinisch relevanter Reduktion des Übergewichts insbesondere, wenn die Eltern eingebunden sind.

Treatment of Pediatric Obesity: An Umbrella Systematic Review

Tamim Rajjo,^{1,2} Khaled Mohammed,^{1,3} Mouaz Alsawas,^{1,3} Ahmed T. Ahmed,¹ Wigdan Farah,^{1,3} Noor Asi,^{1,3} Jehad Almasri,^{1,3} Larry J. Prokop,⁴ and Mohammad Hassan Murad^{1,3}

¹Evidence-Based Practice Center, Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, ²Department of Family Medicine, ³Division of Preventive, Occupational and Aerospace Medicine, and ⁴Library Public Services, Mayo Clinic, Rochester, Minnesota 55905

Objective: Multiple interventions are available to reduce excess body weight in children. We appraised the quality of evidence supporting each intervention and assessed the effectiveness on different obesity-related outcomes.

Methods: We conducted a systematic search for systematic reviews of randomized controlled trials evaluating pediatric obesity interventions applied for ≥ 6 months. We assessed the quality of evidence for each intervention using GRADE (Grading of Recommendation, Assessment, Development, and Evaluation) approach.

Results: From 16 systematic reviews, we identified 133 eligible randomized controlled trials. Physical activity interventions reduced systolic blood pressure and fasting glucose (low to moderate quality of evidence). Dietary interventions with low-carbohydrate diets had a similar effect to low-fat diets in terms of body mass index (BMI) reduction (moderate quality of evidence). Educational interventions reduced waist circumference, BMI, and diastolic blood pressure (low quality of evidence). Pharmacological interventions reduced BMI (metformin, sibutramine, orlistat) and waist circumference (sibutramine, orlistat) and increased high-density lipoprotein cholesterol (sibutramine) but also raised systolic and diastolic blood pressure (sibutramine). Surgical interventions (laparoscopic adjustable gastric banding, Roux-en-Y gastric bypass, sleeve gastrectomy) resulted in the largest BMI reduction (moderate quality of evidence). Combined interventions consisting of dietary modification, physical activity, behavioral therapy, and education significantly reduced systolic and diastolic blood pressure, BMI, and triglycerides. Combined parent-child interventions and parent-only interventions had similar effects on BMI (low quality of evidence).

Conclusions: Several childhood obesity interventions are effective in improving metabolic and anthropometric measures. A comprehensive multicomponent intervention, however, appears to have the best overall outcomes. (*J Clin Endocrinol Metab* 102: 763–775, 2017)

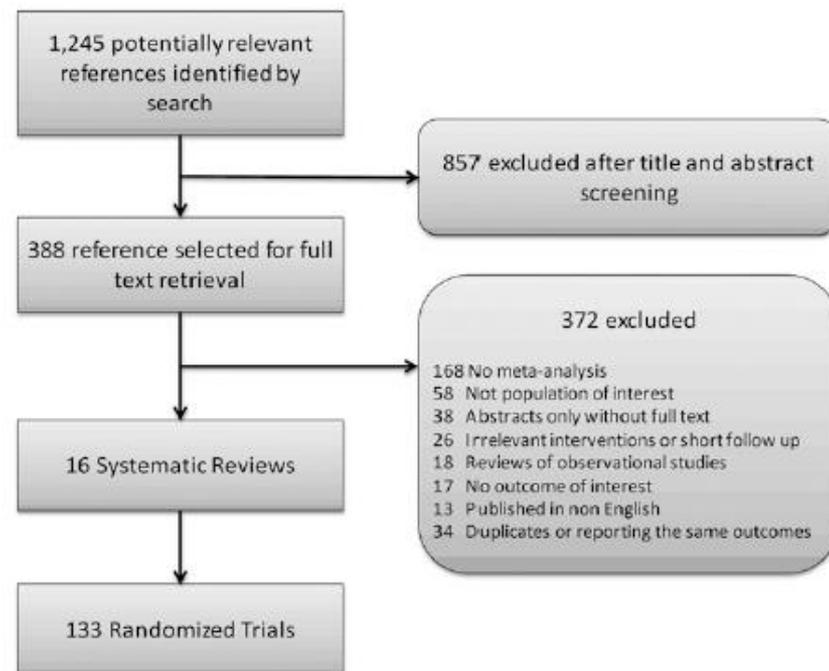
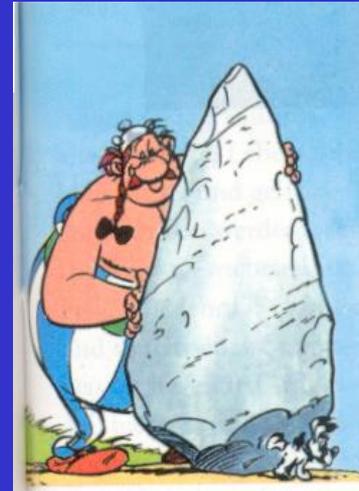
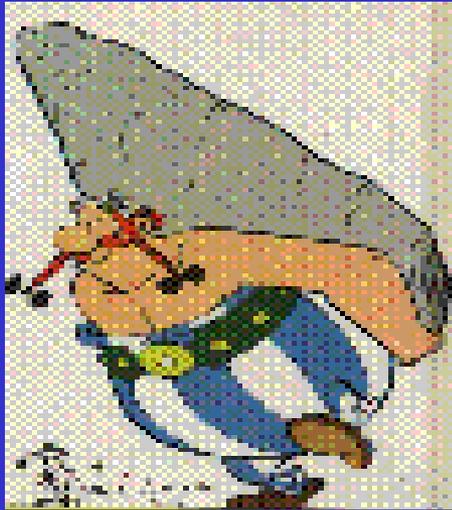


Figure 1. The process of study selection.

Schlußfolgerung

- Nur Bewegungstherapie: keine Gewichtsabnahme, jedoch Verbesserung Blutdruck
- Art der Diät unerheblich
- Kombination aus Bewegungs-, Ernährungs- und Verhaltenstherapie unter Einschluss der Eltern führt zu Gewichtsreduktion, die das kardiovaskuläre Profil verbessert

Adipositasprogramm “Obeldicks“



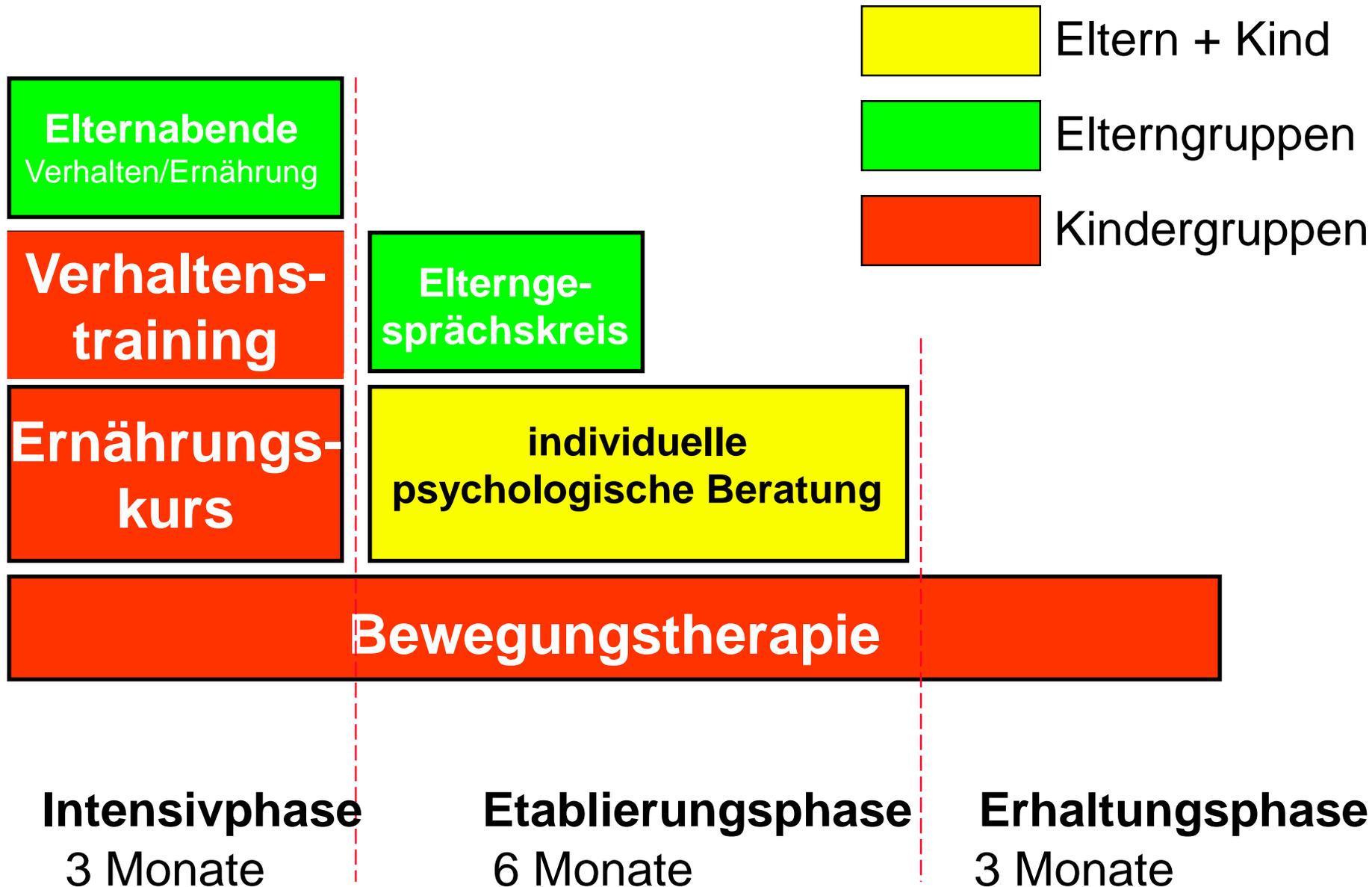
Reinehr¹, Schaefer², Kersting², Damschen¹, Dobe¹, Rose¹,
von Köding¹, Hoffmann¹, W. Andler¹

¹: Vestische Kinder- und Jugendklinik, Universität Witten- Herdecke

²: Forschungsinstitut für Kinderernährung Dortmund

ausgezeichnet mit dem 1.Preis des Gesundheitspreises NRW 2000 und dem
Gesundheitspreis der Stiftung Rufzeichen Gesundheit! 2007

Ambulantes Adipositasprogramm „Obeldicks“ für adipöse Kinder



Lebensmittel



fette Käse- + Wurstsorten
Butter, Margarine,
Pommes, Chips, Nüsse



fettarme Käse-+ Wurst
Geflügel, Halbfettmargarine
Weingummi, Wassereis



fettarmer Fisch
Kartoffeln
Gemüse, Obst



Getränke

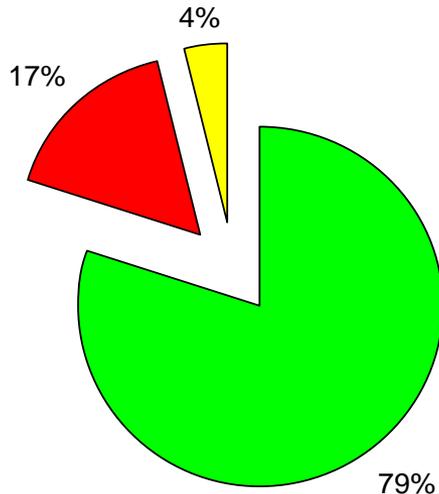


Cola, Fanta
Malzbier
Vollmilch

Obstsäfte
Kakao aus
fettarmer Milch

Mineralwasser
Früchtetee

Ergebnisse der Therapie bei 2500 adipösen Teilnehmern



Reduktion >0.2 SDS-BMI: 69%

Reduktion >0.5 SDS-BMI: 52%

Kinder mit Gewichtsreduktion in
Lifestyle Intervention:

- reduzierten Blutdruck
- reduzierten Triglyceride
- reduzierten LDL- Cholesterin
- zeigten ansteigendes HDL- Chol.
- reduzierten Insulinresistenz (HOMA)

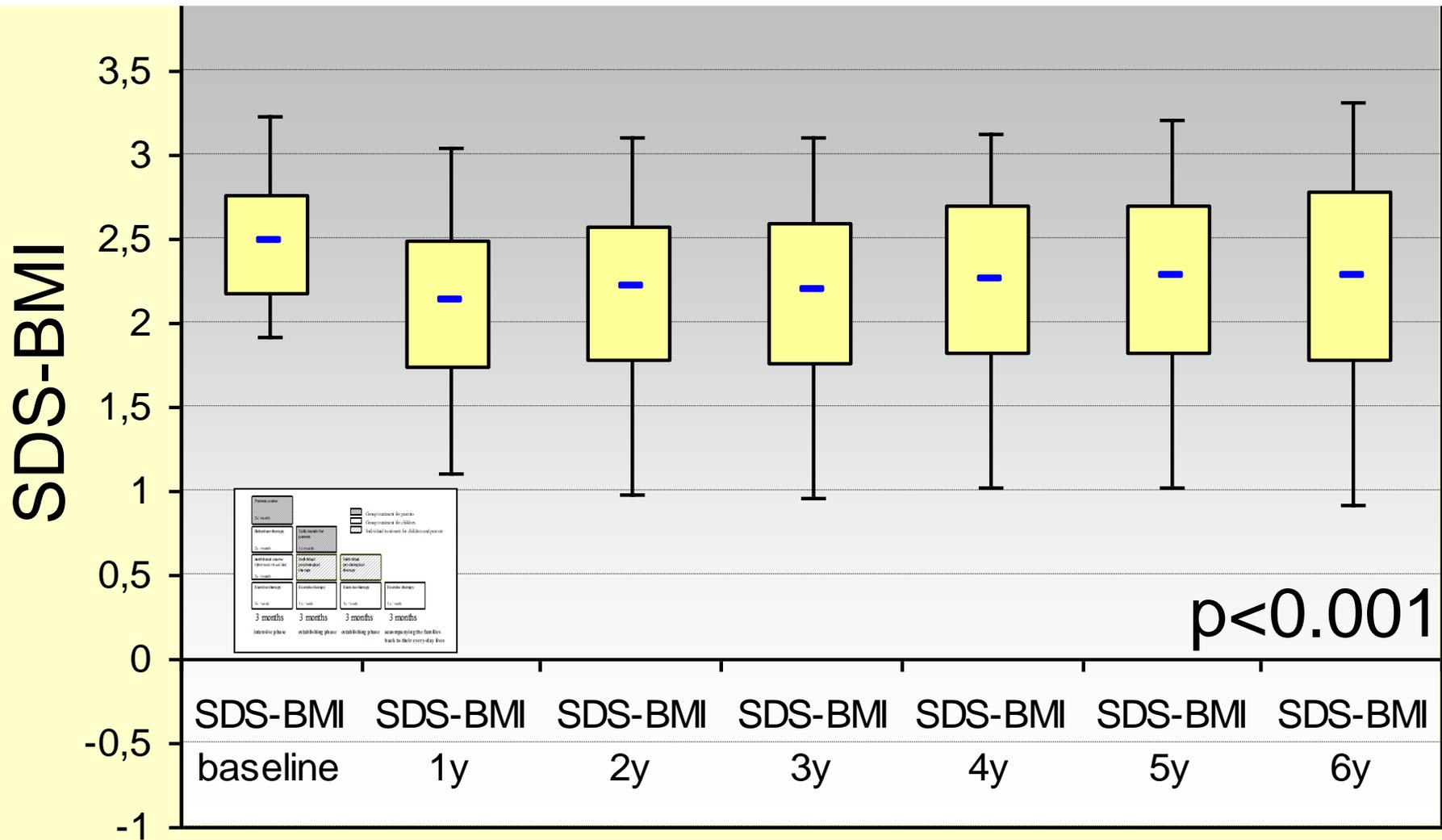
am Ende der Intervention und 1 Jahr
nach Ende der Intervention im Gegensatz
zu einer unbehandelten Kontrollgruppe

Veränderung SDS-BMI* im Mittel:
-0,40 (SD 0,35)

Reinehr et al. Int J Obes 2003;89:419-422 & JPGN 2003;37:72-74 &
Pediatrics 2004;114:1569-1573 & Arch Dis Child 2004;89:419-422 &
Klin Päd 2005; 217: 1-8 & Kinder- und Jugendmedizin 2001;82:33-36 & 2005;5:79-84

Intention- to- treat analysis

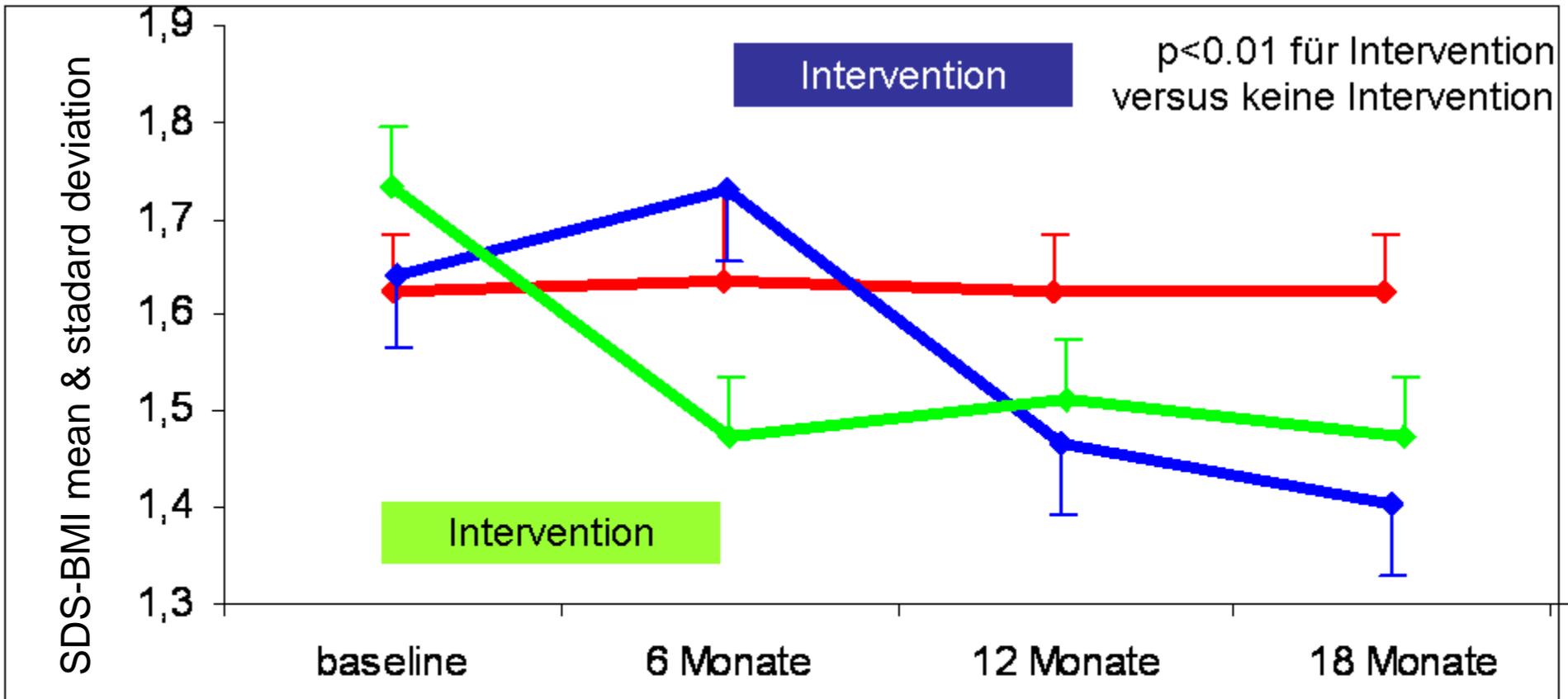
n=263



Reinehr et al Int J Obes 2009

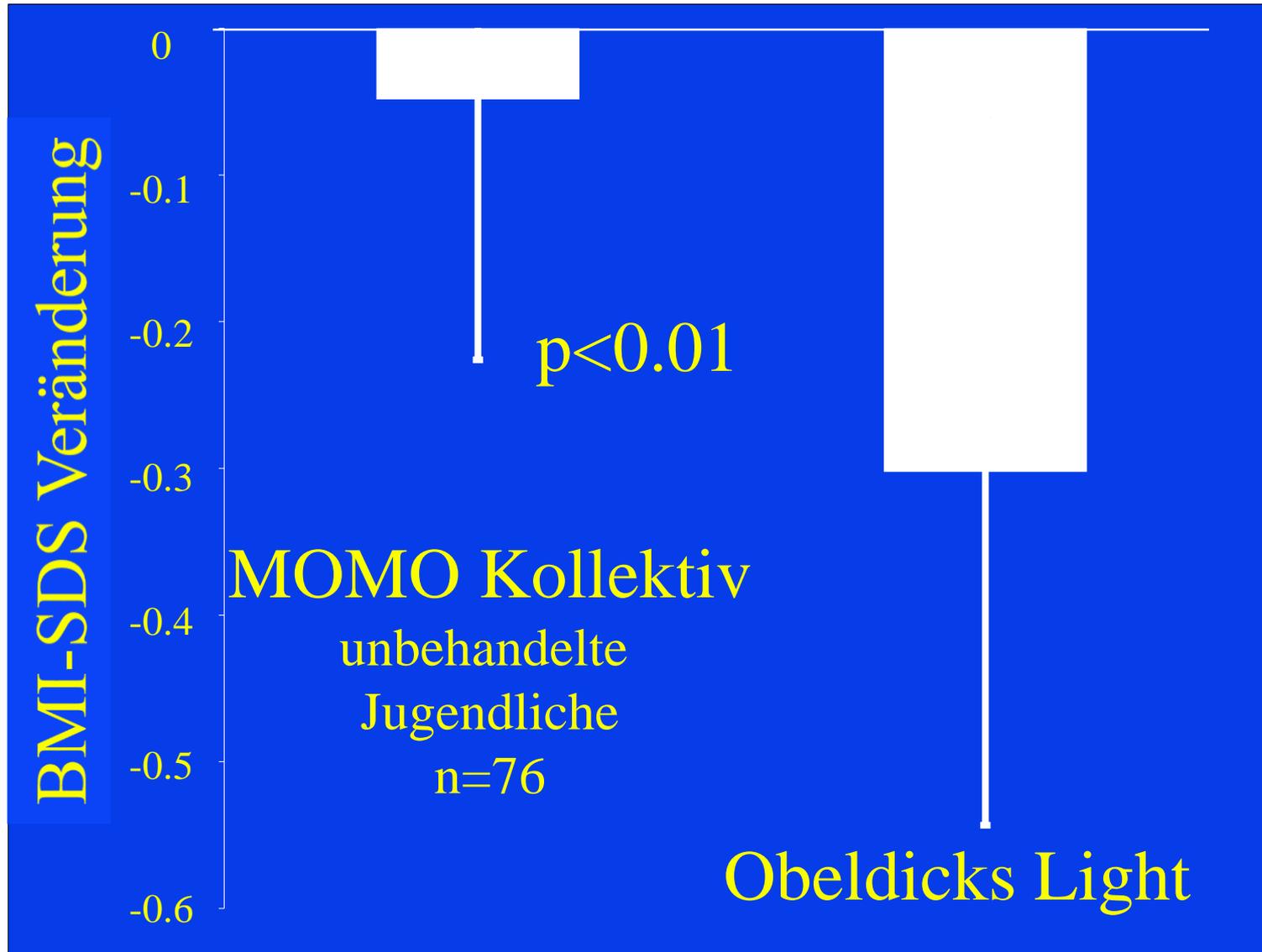
Randomized controlled trial

Reinehr et al. Clin Nutr 2010 & 2011



- Intervention baseline – 6 Monate, $p < 0,01$ baseline versus 6, 12 und 18 Monaten
- Intervention 6 Monate – 12 Monate, $p < 0,01$ 6 Monate versus 12 und 18 Monaten
- Keine Intervention, keine Signifikanz im Vergleich innerhalb dieser Gruppe

6 Jahres follow up



gefördert durch BMBF 01EL619

Thomas Reinehr · Michael Dobe
Mathilde Kersting

Therapie der Adipositas im Kindes- und Jugendalter

Die Schulungsprogramme
OBELDICKS Light und OBELDICKS
für übergewichtige und adipöse
Kinder und Jugendliche

2., korrigierte und erweiterte Auflage



mit CD-ROM

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Pädiatrische Ernährungsmedizin

Grundlagen und praktische Anwendung

Schattauer

Thomas Reinehr

Therapie der Adipositas im Vorschulalter

Das Schulungsprogramm OBELDICKS
Mini



mit CD-ROM

HOGREFE



Thomas Reinehr / Michael Dobe
Mathilde Kersting

Abnehmen mit Obeldicks und Optimix

Ein Ratgeber
für Eltern übergewichtiger Kinder

2., überarbeitete Auflage

HOGREFE

Thomas Reinehr · Michael Dobe · Mathilde Kersting

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Ein Ratgeber für Eltern übergewichtiger Kinder

2., überarbeitete Auflage 2009,
ca. 200 Seiten, ca. € 16,95 / sFr. 28,40
ISBN 978-3-8017-2271-5

Aus dem Inhalt:

Probleme der Verhaltenstherapie

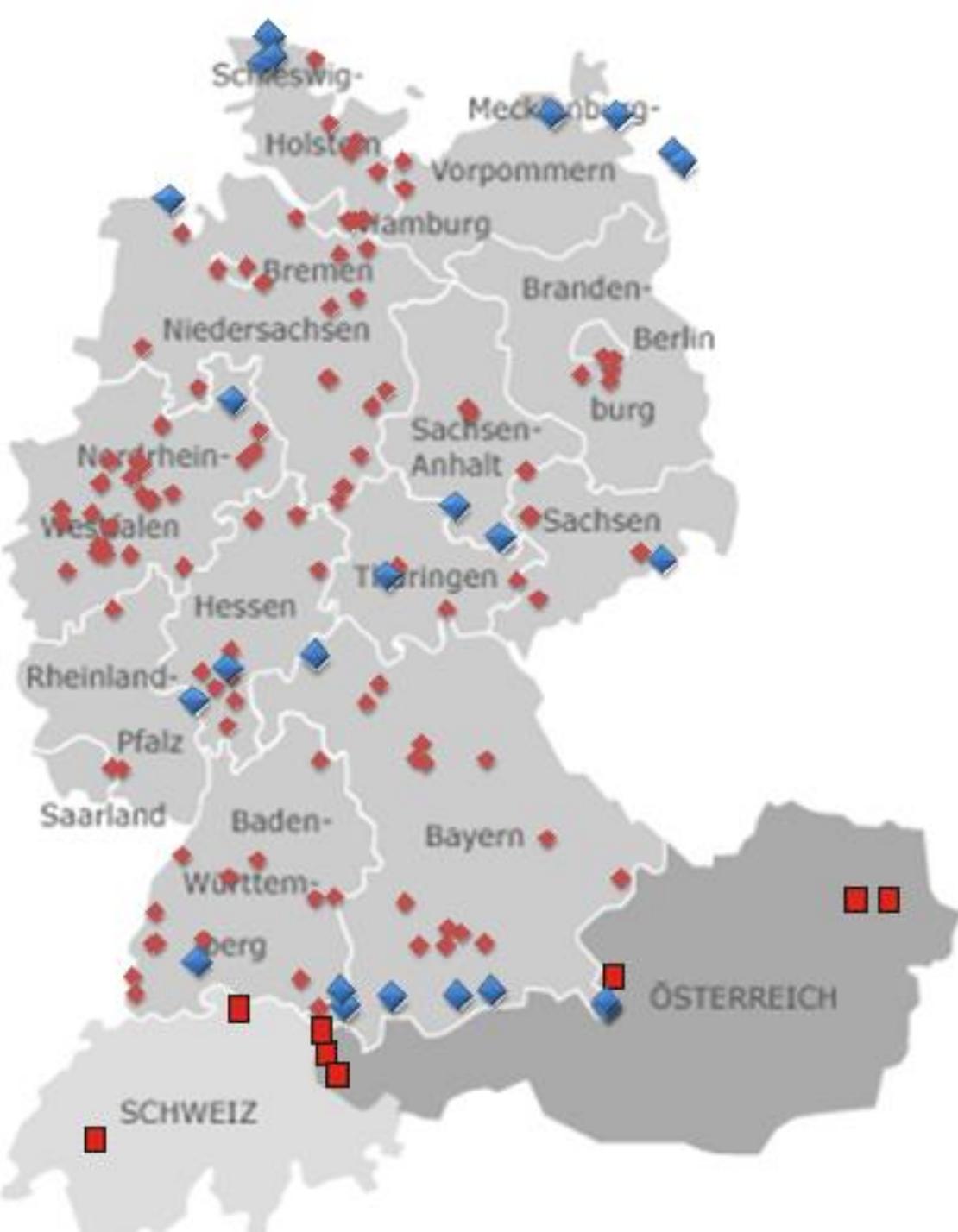
- verhaltenstherapeutische Interventionen nur bei Motivierten erfolgversprechend
- hoher Zeitwand für Familien in Schulungsprogrammen
- meist Mittelschicht mit Schulungsprogrammen erreicht
- wahrscheinlich Mehrzahl der adipösen Kinder und Jugendlichen mit Schulungsprogrammen nicht behandelbar

APV- Participants

62 842 patients

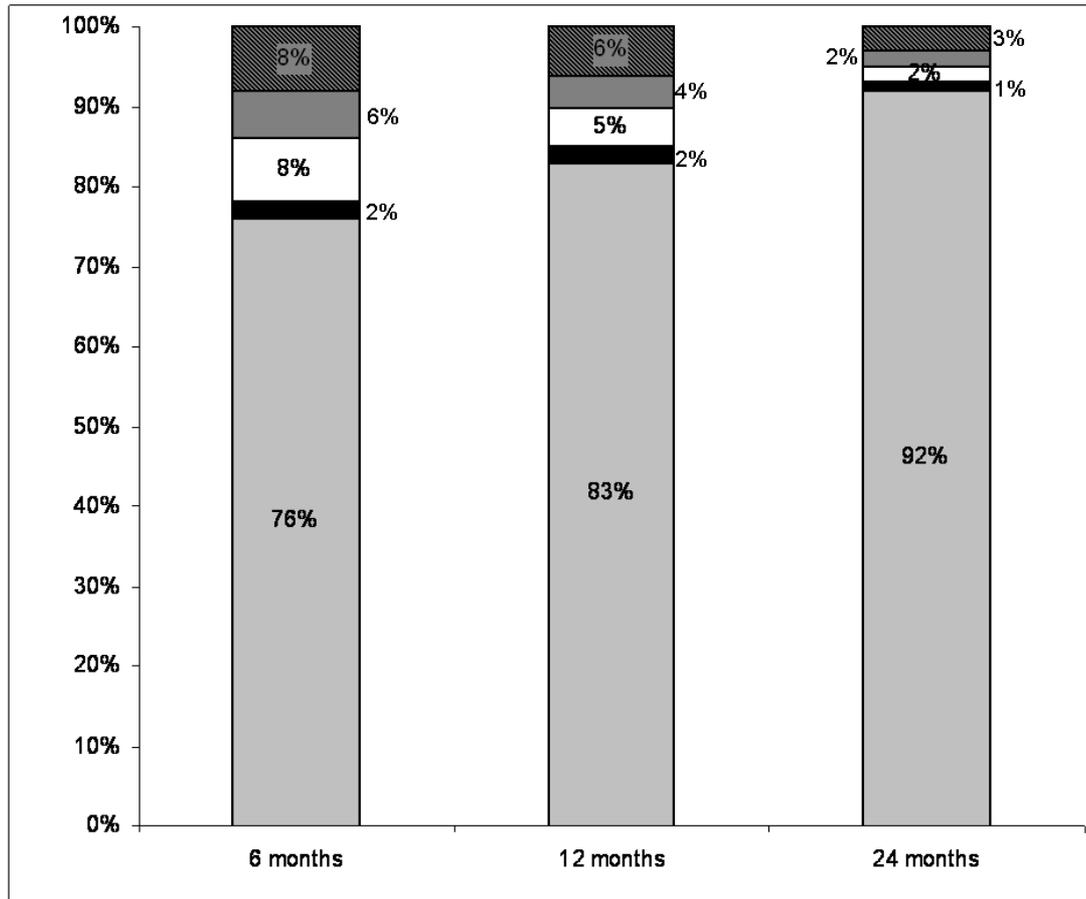
201 361 Visits

163 centers



outpatient centres
Inpatients centres

2-year follow-up in 21,784 overweight, obese and extremely obese children and adolescents treated with lifestyle Interventions under real life conditions



- Reduction SDS-BMI >0,5
- Reduction SDS-BMI >0,2-0,5
- Reduction SDS-BMI <=0,2
- increase SDS-BMI
- No follow-up

Extrem adipöse Jugendliche sprechen nicht auf eine Lebensstilintervention an

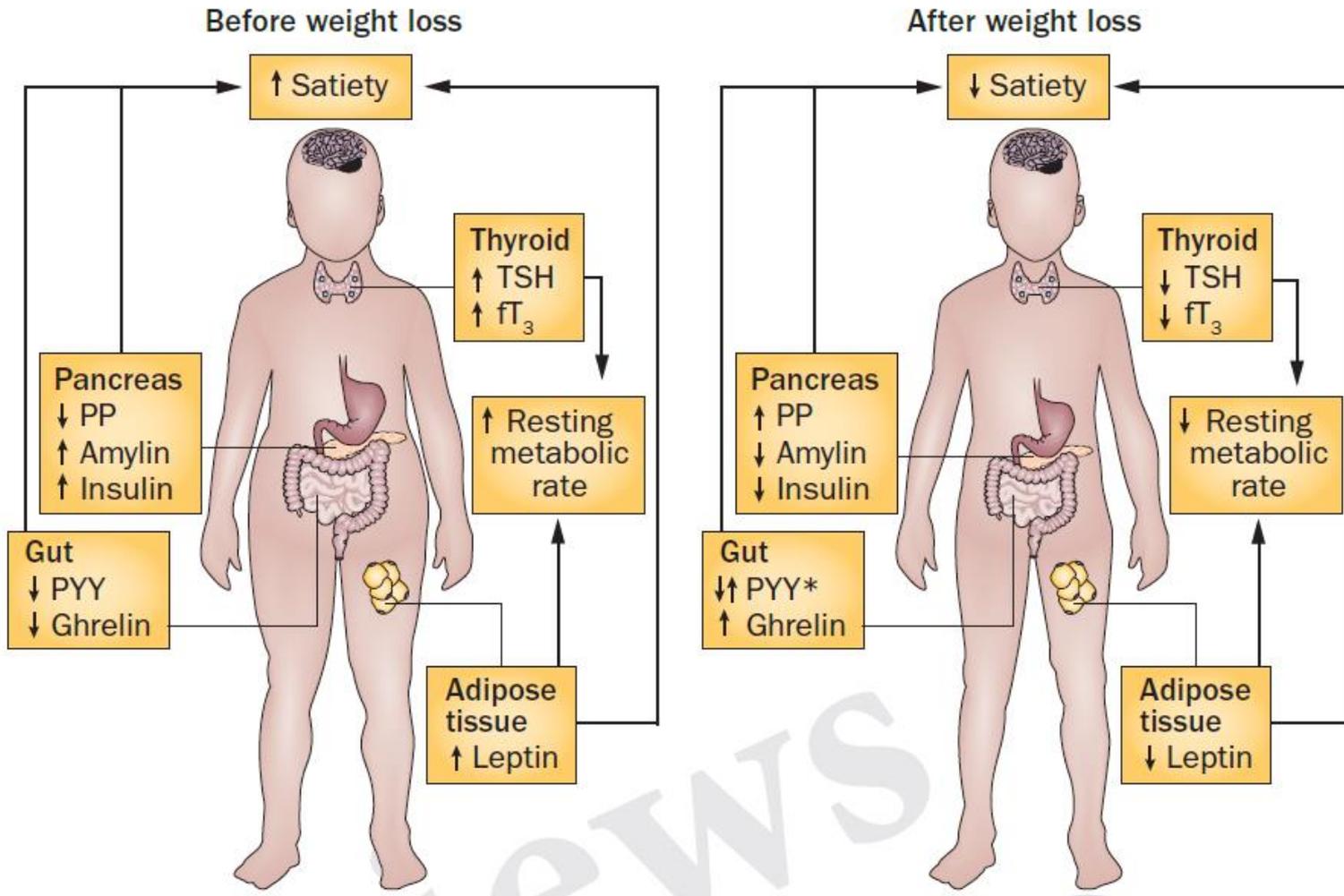
Danielsson P, Kowalski J, Ekblom Ö, Marcus C.
Response of severely obese children and adolescents
to behavioral treatment. Arch Pediatr Adolesc Med.
2012;166:1103-8.

Knop C, Singer V, Uysal Y, Schaefer A, Wolters B,
Reinehr T. Extremely obese children respond better
than extremely obese adolescents to lifestyle
interventions. Pediatr Obes. 2015 Feb;10(1):7-14

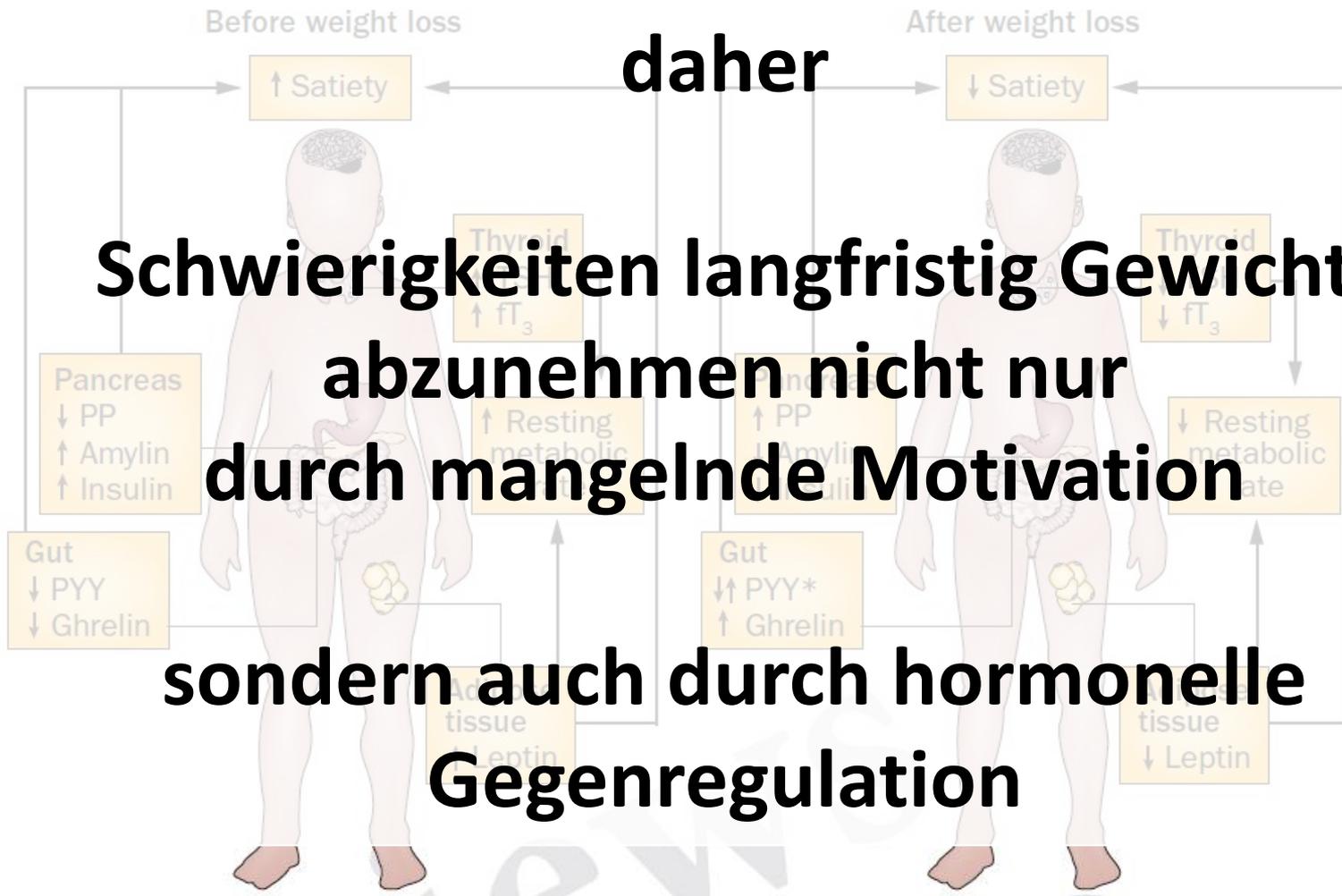
Gegenregulationsmechanismen

- Adipöse, die Gewicht abnehmen, benötigen im Vergleich zu einer Person, die schon immer dieses Gewicht hatte, 10-15% weniger Kalorien, um das reduzierte Gewicht zu halten
 - Anstieg der orexigenen Hormone bei Diät
 - durch Reduktion Grundumsatz

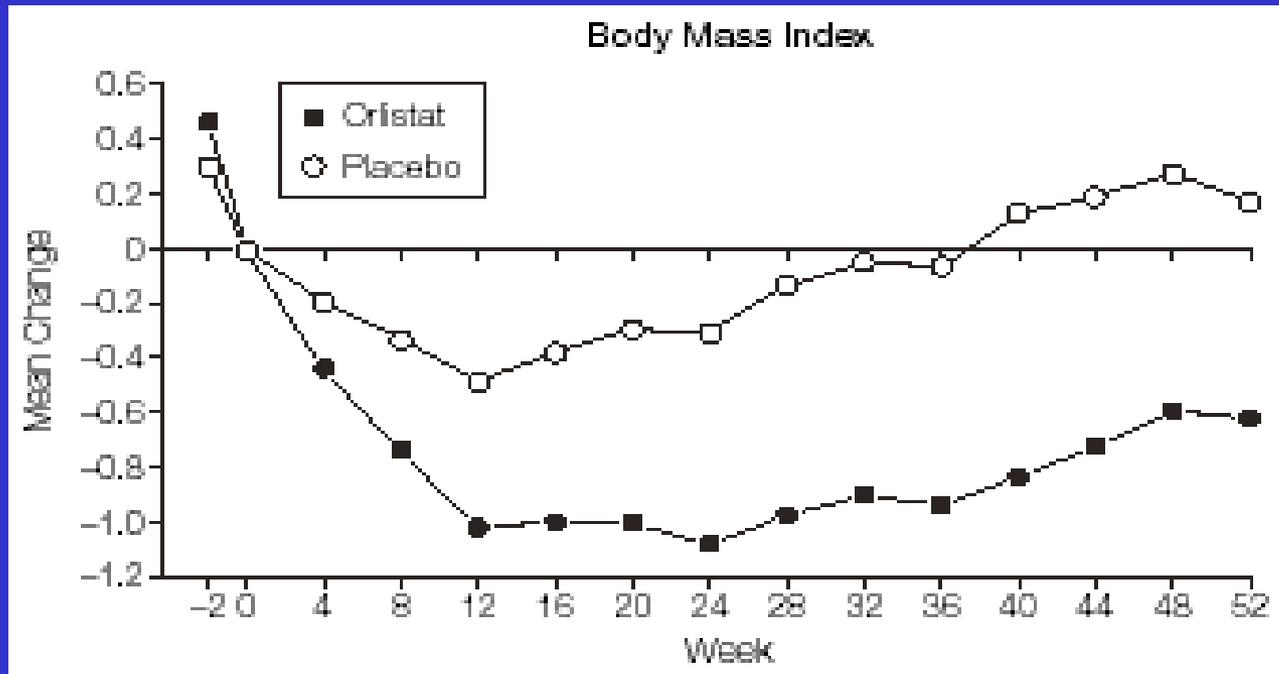
Hormonelle Gegenregulation bei Gewichtsveränderung



Hormonelle Gegenregulation bei Gewichtsveränderung



Xenical



Plazebo 34.6 kg/m²; Xenical 35.2 kg/m²

*p=0.001 vs. Plazebo

Chanoine et al. (2005) JAMA 293, 2873-2883

Sicherheit und Verträglichkeit von Xenical

- Nebenwirkungsprofil entsprach dem von Erwachsenen
- Gastrointestinale Wirkungen waren häufiger bei Xenical-behandelten Patienten, aber generell nur mild ausgeprägt
- Der Grad der fettlöslichen Vitamine (A, D and E) unterschied sich nicht signifikant zwischen den beiden Gruppen
- Das Verhältnis der Patienten mit schwerwiegenden Ereignissen unterschied sich nicht zwischen Xenical und Plazebo (3 %)

ORIGINAL ARTICLE

A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity

Aaron S. Kelly, Ph.D., Pernille Auerbach, M.D., Ph.D., Margarita Barrientos-Perez, M.D., Inge Gies, M.D., Ph.D., Paula M. Hale, M.D., Claude Marcus, M.D., Ph.D., Lucy D. Mastrandrea, M.D., Ph.D., Nandana Prabhu, M.Sc., and Silva Arslanian, M.D., for the NN8022-4180 Trial Investigators*

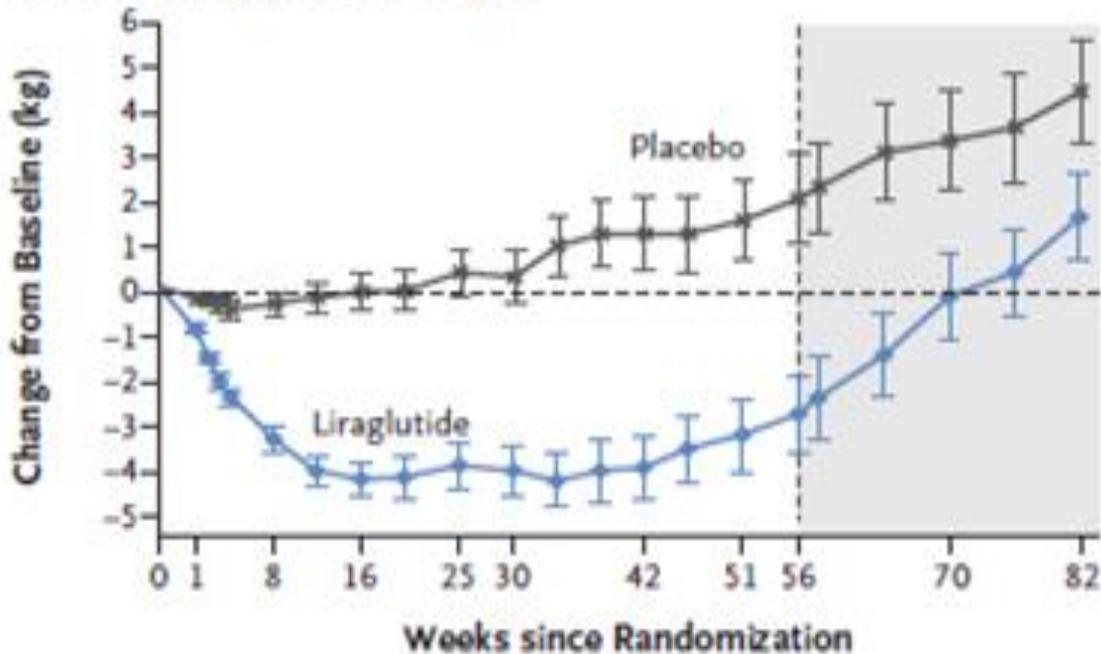
NEJM 2020

ABSTRACT

BACKGROUND

Obesity is a chronic disease with limited treatment options in pediatric patients.

E Absolute Change in Body Weight



No. of Participants

Placebo	126	125	123	116	116	105	101	105	97	102
Liraglutide	125	123	119	118	119	110	107	113	106	112

But:
Weight loss was in maximum 5kg
and after end of treatment there was no effect

BRIEF REPORT

Proopiomelanocortin Deficiency Treated with a Melanocortin-4 Receptor Agonist

Peter Kühnen, M.D., Karine Clément, M.D., Ph.D., Susanna Wiegand, M.D., Oliver Blankenstein, M.D., Keith Gottesdiener, M.D., Lea L. Martini, M.D., Knut Mai, M.D., Ulrike Blume-Peytavi, M.D., Annette Grüters, M.D., and Heiko Krude, M.D.

SUMMARY

Patients with rare defects in the gene encoding proopiomelanocortin (*POMC*) have extreme early-onset obesity, hyperphagia, hypopigmentation, and hypocortisolism, resulting from the lack of the proopiomelanocortin-derived peptides melanocyte-stimulating hormone and corticotropin. In such patients, adrenal insufficiency must be treated with hydrocortisone early in life. No effective pharmacologic treatments have been available for the hyperphagia and obesity that characterize the condition. In this investigator-initiated, open-label study, two patients with proopiomelanocortin deficiency were treated with setmelanotide, a new melanocortin-4 receptor agonist. The patients had a sustainable reduction in hunger and substantial weight loss (51.0 kg after 42 weeks in Patient 1 and 20.5 kg after 12 weeks in Patient 2).

Setmelanotide: MC4R Agonist

-bei POMC Mutation
-bei Leptinresistenz

Regelkreis Hypothalamus

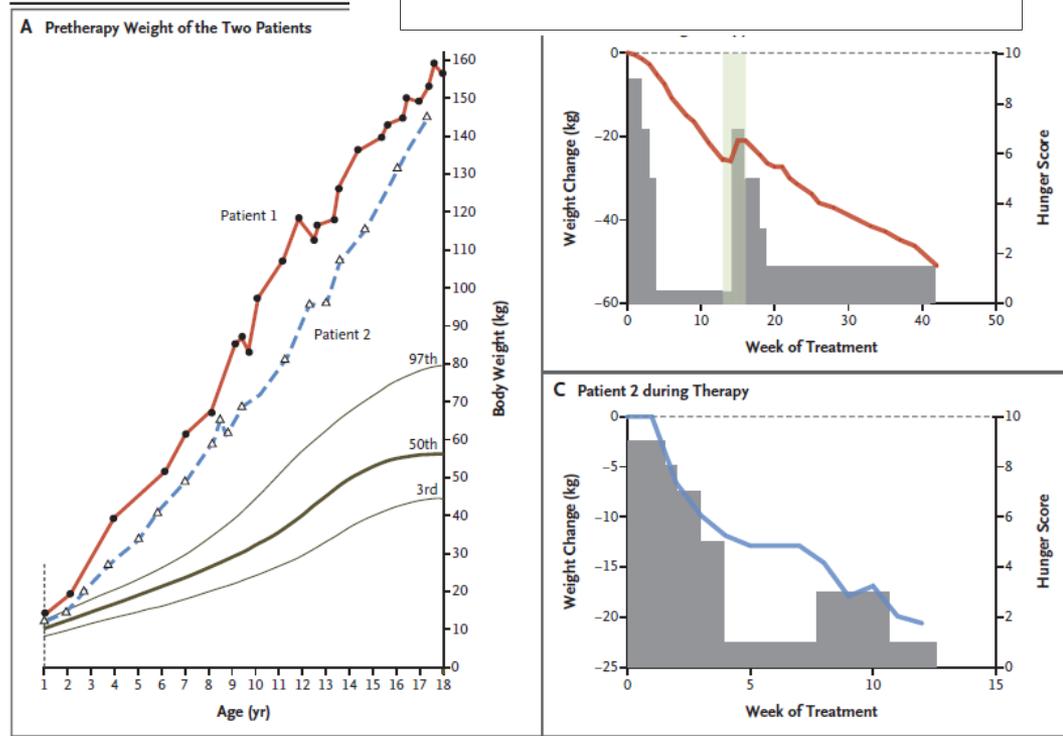
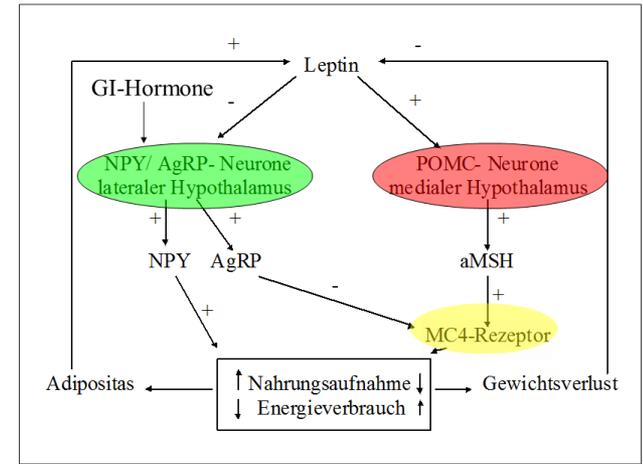


Figure 1. Pretherapy Weight and Changes in Weight and Hunger Scores during Therapy. Panel A shows the body weight of Patient 1 and Patient 2 in the first 18 and 17 years of life, respectively, as compared with normal percentiles for girls of their age.⁸ Panel B shows weight change (left scale and red line) and hunger scores (on a scale of 0 [no hunger] to 10 [extreme hunger]; right scale and gray bars) in Patient 1 during therapy. After the initial 13 weeks of treatment, Patient 1 entered a 3-week off-treatment phase (marked in green), before treatment was restarted. Data are shown to 42 weeks. Panel C shows weight change (blue line) and hunger scores (gray bars) in Patient 2 during the initial 12 weeks of therapy.

Morbide Adipositas bei Jugendlichen

pharmakologische Therapien

- Kritisch betrachtet werden muss die möglicherweise lebenslange Medikation.
- Mittelfristiges Ziel muss daher die Verfestigung erlernter neuer Verhaltensweisen sein.
- **“Überbrückung“ von besonderen Schwierigkeiten der Adipositastherapie in der Adoleszenz**
(Gewichtszunahme, Compliance, Kontrolle, Insulinresistenz, u.a.)
durch eine medikamentöse Therapie.
- Zugelassen aber keine Kostenübernahme durch die Krankenkasse(ab 12 J.):
 - Orlistat
 - Liraglutide

Therapie arterielle Hypertonie bei Adipositas

- ACE- Hemmer
- oder CaAntagonist
- Keine b- Blocker !

Therapie Hypertriglyceridämie bei Adipositas

- ab Triglyceride $> 500\text{mg/dl}$
 - Eicosapen® 1x3 – 2x3 Kps
 - NW: Brechreiz, Thromboaggregation gehemmt
 - Alternative: Fibrate (aber keine Zulassung im Kindesalter)
 - Meist Triglyceride $< 500\text{ mg/dl}$ daher
Medikamente nicht erforderlich

Therapie Hypercholesterinämie bei Adipositas

- Ab LDL-C. >190 oder LDL-C >160mg/dl +Familienanamnese
- Medikamente erst ab (7)-10.Lj
- Ziel < 170mg/dl LDL-Chol
- Ernährung: Sitosterin: in becel pro Aktiv
- [Colestyramin (Quantalan[®]): wird meist nicht genommen
 - 0,2-0,3g/kg (1 Btl Quantalan^R =4g) als Enddosis in 2-3 ED
 - NW: Völlegefühl, Obstipation, Steatorrhoe, schlechte Compliance]
- HMG-CoA-Reduktasehemmer: ab 8 Lebensjahre
 - NW: Transaminasenerhöhung, CK-Erhöhung, Pankreatitis
 - sehr wirksam
 - Zugelassen:
 - Pravastatin ab 8. Lebensjahr: max 20mg / Tag 1 ED abends (EMEA)
 - Simvastatin (Zocor[®]), Lovastatin und Atorvastatin ab 10. LJ (USA)

RCT bariatrische Chirurgie versus Lebensstil Intervention bei extrem adipösen Jugendlichen

- N= 50 ;14 bis 18 Lebensjahre

Ergebnis:

- >50% Gewichtsverlust nach 2 Jahren follow-up
 - 21 (84%) Jugendlichen in Gastric Banding Gruppe
 - 3 (12%) Jugendliche in Lifestyle Intervention
- Mittlere Gewichtsveränderung nach 2 Jahren
 - Gastric banding Gruppe: **-34.6 kg** (95% CI, 30.2-39.0),
 - Lifestyle Gruppe: **-3.0 kg** (95% CI, 2.1-8.1), p<0.001
- **Bariatrische Chirurgie viel wirksamer als Lebensstil-Intervention bei extrem adipösen Jugendlichen**

O'Brien PE et al.: Laparoscopic adjustable gastric banding in severely obese adolescents: a randomized trial. JAMA. 2010;303:519-26.

Operationsindikation für Kinder und Jugendliche

- BMI > 40kg/m² oder BMI > 35 kg/m² + Komorbidität
- Mindestens 6 Monate Teilnahme Therapieprogramm an spezialisiertem Zentrum
- Chirurgie an Standort mit pädiatrischem know-how
- Ausschluß bei nicht suffizient behandelten psychotischen, depressiven Erkrankungen und Persönlichkeitsstörungen

Laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity (AMOS): a prospective, 5-year, Swedish nationwide study



Torsten Olbers, Andrew J Beamish, Eva Gronowitz, Carl-Erik Flodmark, Jovanna Dahlgren, Gustaf Bruze, Kerstin Ekborn, Peter Friberg, Gunnar Göthberg, Kajsa Järholm, Jan Karlsson, Staffan Mårild, Martin Neovius, Markku Peltonen, Claude Marcus

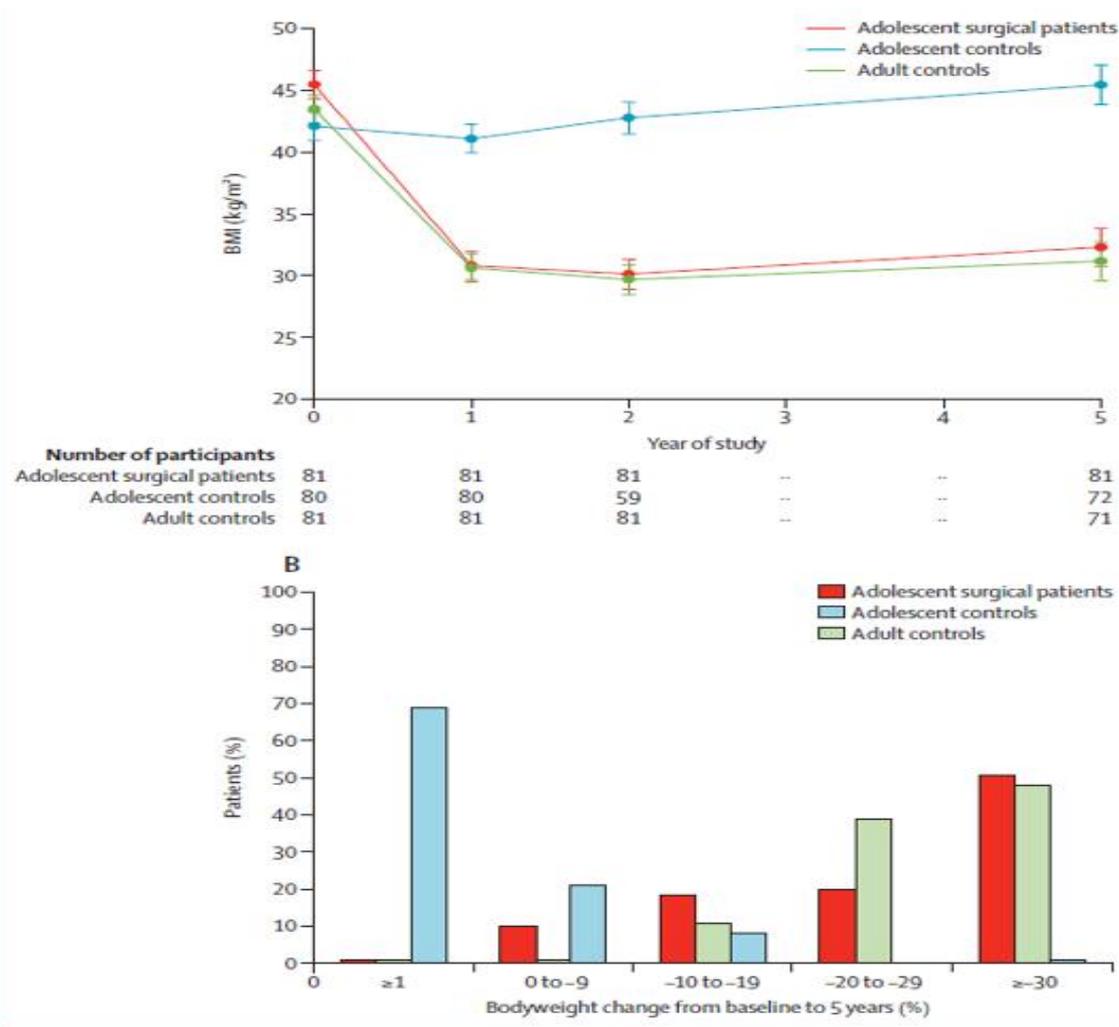


Figure 2: Change in BMI (A) and bodyweight (B) from baseline to 5 years
Data for adolescent controls are presented using the last-observation-before-surgery-carried-forward assumption for crossovers who underwent surgery within the follow-up period. Data points in (A) are the mean value and error bars show the 95% CI.

Lancet Diabetes Endocrinol 2017

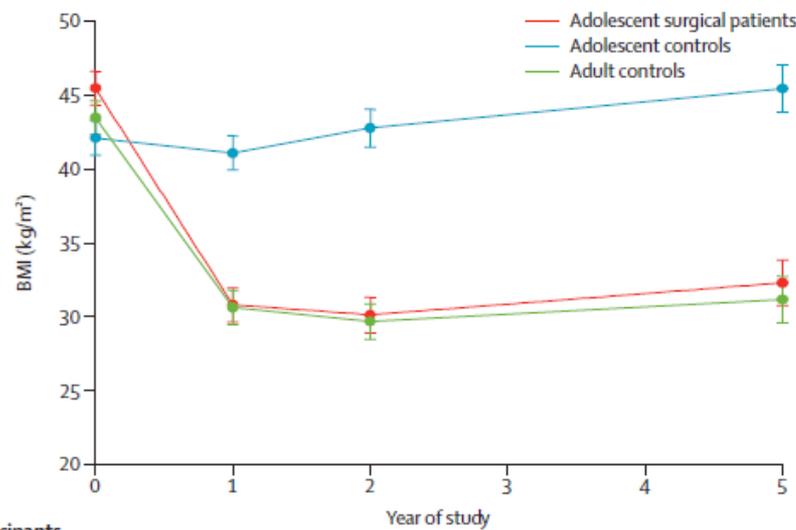
Published Online
January 5, 2017
[http://dx.doi.org/10.1016/S2213-8587\(16\)30424-7](http://dx.doi.org/10.1016/S2213-8587(16)30424-7)

See Online/Articles
[http://dx.doi.org/10.1016/S2213-8587\(16\)30315-1](http://dx.doi.org/10.1016/S2213-8587(16)30315-1)

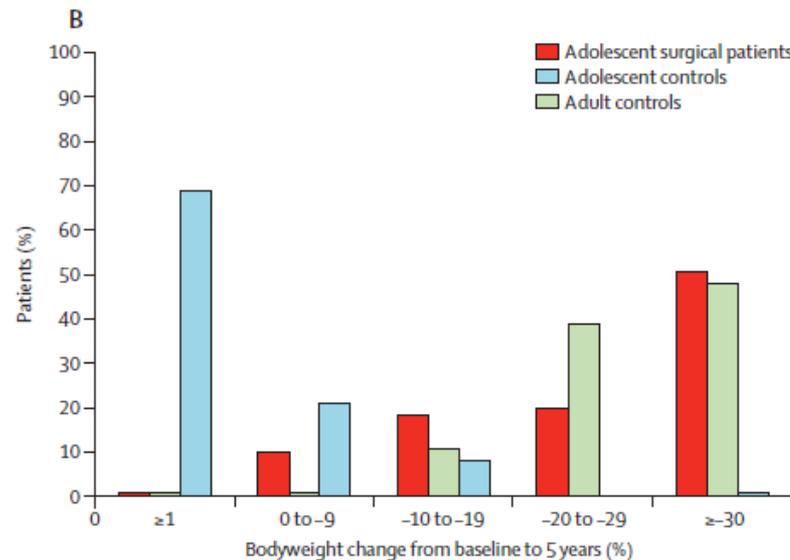
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[http://dx.doi.org/10.1016/S2213-8587\(16\)30425-9](http://dx.doi.org/10.1016/S2213-8587(16)30425-9)

Department of Gastrointestinal Research (T Olbers PhD, A J Beamish MD, E Gronowitz PhD), Department of Paediatrics (J Dahlgren PhD, E Gronowitz), Department of Health and Care Sciences (S Mårild PhD), and Department of Paediatric Surgery, Queen Silvia Children's Hospital (G Göthberg PhD), Sahlgrenska University Hospital, Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden; Department of Research, Royal College of Surgeons of England, London, UK (A J Beamish); Childhood Obesity Unit, Skåne University Hospital, Malmö, Sweden (C-E Flodmark PhD, K Järholm PhD); Clinical Epidemiology Unit, Department of Medicine, Solna, Karolinska University Hospital, Stockholm, Sweden (G Bruze PhD, M Neovius PhD); Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet, Stockholm, Sweden (K Ekborn PhD, C Marcus PhD); Department of Molecular and

Nebenwirkungen



Number of participants	Year of study					
Adolescent surgical patients	81	81	81	81
Adolescent controls	80	80	59	72
Adult controls	81	81	81	71



Number of patients (%)

Serious adverse events

All surgery	20/81* (25%)
Laparoscopy (small bowel obstruction)†	11/81 (14%)
Cholecystectomy (gallstones)	9/81 (11%)
Laparotomy (severe abdominal pain)	1/81 (1%)
Blood or iron transfusion (severe anaemia)‡	2/81 (2%)
Observation and investigation only (abdominal pain)	9/81 (11%)
Psychiatric assessment (drug abuse)§	6/81 (7%)

Other adverse outcomes

Anaemia	25/77 (32%)
Vitamin D deficiency	20/73 (30%)
Low vitamin B12	16/73 (22%)
Low ferritin or iron	51/77 (66%)
Assessment by eating disorder team¶	1/81 (1%)

Serious adverse events entailed admission to hospital. Other adverse events did not need admission. Definitions and thresholds are provided in the appendix (pp 6, 7). *21 procedures in 20 patients; †Obstruction caused by internal herniation or adhesions. ‡Anaemia requiring admission for iron therapy or blood transfusion. §Narcotic abuse requiring medical referral or intervention. ¶Individual was referred for assessment but was never diagnosed with an eating disorder.

Table 4: Adverse outcomes in adolescents after Roux-en-Y gastric bypass during the 5-year study period

Figure 2: Change in BMI (A) and bodyweight (B) from baseline to 5 years

Data for adolescent controls are presented using the last-observation-before-surgery-carried-forward assumption for crossovers who underwent surgery within the follow-up period. Data points in (A) are the mean value and error bars show the 95% CI.

5-year mental health and eating pattern outcomes following bariatric surgery in adolescents: a prospective cohort study

Kajsa Järnholm, Gustaf Bruze, Mariku Peltonen, Claude Marcus, Carl-Erik Flodmark, Pia Herfridsson, Andrew J Beamish, Eva Gronowitz, Jovanna Dahligen, Jan Karlsson*, Torsten Olbers*

Summary

Background Mental health problems are prevalent among adolescents with severe obesity, but long-term mental health outcomes after adolescent bariatric surgery are not well known. We aimed to assess mental health outcomes over 5 years of follow-up after Roux-en-Y gastric bypass surgery in adolescents who participated in the Adolescent Morbid Obesity Surgery (AMOS) study.

Methods This was a non-randomised matched-control study in adolescents aged 13–18 years who had a BMI of 40 kg/m² or higher, or 35 kg/m² or higher in addition to obesity-related comorbidity; who had previously undergone failed comprehensive conservative treatment; and were of pubertal Tanner stage III or higher, with height growth velocity beyond peak. A contemporary control group, matched for BMI, age, and sex, who underwent conventional obesity treatment, was obtained from the Swedish Childhood Obesity Treatment Register. Data on dispensed psychiatric drugs and specialist treatment for mental disorders were retrieved from national registers with complete coverage. In the surgical group only, questionnaires were used to assess self-esteem (Rosenberg Self-Esteem [RSE] score), mood (Mood Adjective Checklist [MACL]), and eating patterns (Binge Eating Scale [BES] and Three-Factor Eating Questionnaire-R21 [TFEQ]). This study is registered with ClinicalTrials.gov (NCT00289705).

Findings Between April 10, 2006, and May 20, 2009, 81 adolescents (53 [65%] female) underwent Roux-en-Y gastric bypass surgery, and 80 control participants received conventional treatment. The proportion of participants prescribed psychiatric drugs did not differ between groups in the years before study inclusion (pre-baseline; absolute risk difference 5% [95% CI -7 to 16], $p=0.4263$) or after intervention (10% [-6 to 24], $p=0.2175$). Treatment for mental and behavioural disorders did not differ between groups before baseline (2% [-10 to 14], $p=0.7135$); however, adolescents in the surgical group had more specialised psychiatric treatment in the 5 years after obesity treatment than did the control group (15% [1 to 28], $p=0.0410$). There were few patients who discontinued psychiatric treatment post-surgery (three [4%] receiving psychiatric drug treatment and six [7%] receiving specialised care for a mental disorder before surgery). In the surgical group, self-esteem (RSE score) was improved after 5 years (mixed model mean 21.6 [95% CI 19.9 to 23.4]) relative to baseline (18.9 [17.4 to 20.4], $p=0.0059$), but overall mood (MACL score) was not (2.8 [2.7 to 2.9] at 5 years vs 2.7 [2.6 to 2.8] at baseline, $p=0.0737$). Binge eating was improved at 5 years (0.2 [7.4 to 11.3] relative to baseline [15.0 [12.5 to 16.5], $p=0.0001$). Relative changes in BMI were not associated

Implications of all the available evidence

Metabolic and bariatric surgery improves many aspects of physical health and quality of life in adolescents with severe obesity. However, long-term alleviation of mental health problems should not be expected, and adolescents and their caregivers should be given realistic expectations in advance of embarking on a surgical pathway. A multidisciplinary team should offer long-term mental health support after adolescent bariatric surgery.



Lancet Child Adolesc Health 2020

Published Online
January 21, 2020
[https://doi.org/10.1016/S2352-4642\(19\)30433-X](https://doi.org/10.1016/S2352-4642(19)30433-X)

See Online/Comment
[https://doi.org/10.1016/S2352-4642\(19\)30433-X](https://doi.org/10.1016/S2352-4642(19)30433-X)

*Joint senior authors

Childhood Obesity Unit, Skåne University Hospital, Malmö, Sweden (K Järnholm PhD); Department of Pediatrics, Institute of Clinical Sciences (K Järnholm, A J Beamish MD, E Gronowitz PhD), Prof J Dahligen PhD, Prof T Olbers PhD) and

Department of Internal Medicine and Clinical Nutrition (P Herfridsson MD), Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; Department of Medicine, Soina, Clinical Epidemiology Division (G Bruze PhD) and Department of Clinical Science,

Intervention, and Technology (Prof C Marcus PhD), Karolinska Institutet, Stockholm, Sweden; National Institute for Health and Welfare, Helsinki, Finland (Prof M Peltonen PhD);

Department of Clinical Sciences in Malmö, Lund University, and, Sweden (C-E Flodmark PhD);

Department of Research, Royal College of Surgeons in England, London, UK (A J Beamish); Işgözü Vizeira Göcaland, Sahlgrenska University Hospital, Regional Obesity Centre, Gothenburg, Sweden (Prof J Dahligen); University

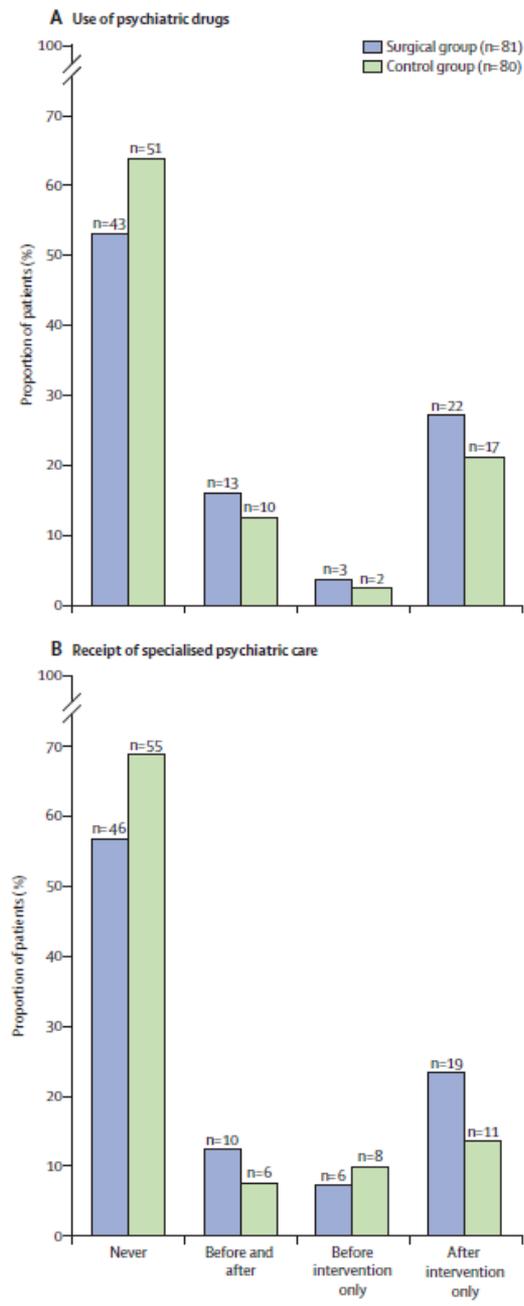


Figure 2: Prevalence of psychiatric drug treatment (A) or specialised care with a psychiatric diagnosis as the main diagnosis (B) before and after Roux-en-Y gastric bypass (surgical group) or conservative management (control group) for obesity during 5 years of follow-up

Nachteil der Adipositaschirurgie

- Operativer Eingriff mit Mortalitätsrisiko
- Chirurgischer Eingriff bleibt lebenslang
- Essverhalten muss bei einem Teil der Verfahren verändert werden
- Langfristige Morbidität und Mortalität bei Jugendlichen nicht bekannt
- Häufig lebenslange Vitaminsubstitution erforderlich (Therapieadhärenz!)
- Ethisches Problem bei Jugendlichen bzgl. Aufklärung

Behandlung extrem adipöser Jugendlichen an der Vestischen Kinder- und Jugendklinik Datteln

- Dreistufiges Vorgehen

1. Lebensstilintervention

Falls gewünscht

2. OP Vorbereitungskurs:

- Besprechung der OP Verfahren
- Aufklärung über Nebenwirkungen

3. Psycholog. / Psychiatrisches Gutachten:

- Motivation, Ausschluss psychiatrische Erkrankung als KI

Outcome (Jahre 2012 bis 2016) an der VKJK Datteln

- n= 283 extreme adipöse Jugendliche 14 - 18 Jahre
 - 56% Junge
 - Medianes Alter 16.2 (95%CI: 15.8-16.6) Jahre
 - Medianer BMI 41.4 (95%CI 39.5-43.3) kg/m²
 - 76 (26.8%) begannen Lebensstilintervention
 - 37 (48.6%) beendeten Lebensstilintervention
 - 10 (3.5%) nahmen am OP Vorbereitungskurs teil
 - 2 (20%) lehnten danach OP ab
 - 2 (20%) aufgrund psychiatrischer Erkrankungen ausgeschlossen
 - 5 (50%) operiert
 - 1 (10%) Krankenkasse verweigerte Kostenübernahme
 - **6 (2.1%) von 283 extrem adipösen Jugendlichen wollen OP und sind für OP geeignet**

Aufgabe des Kinder- und Jugendarztes bei Adipositas im Kindes- und Jugendalter

- *Übergewicht und Adipositas erkennen*
- *Grunderkrankungen ausschließen*
- *Erfassung von Folgeerkrankungen*
- *sinnvolle Therapiemaßnahmen einleiten*
- *Therapie der Folgeerkrankungen bei mangelnder Gewichtsreduktion*