Läkemedelsbehandling av obesitas hos barn

Mellansvenskt läkemedelsforum

UKK 12 februari 2025

Anders Forslund
Akademiska Barnsjukhuset
Uppsala, Sweden

AKADEMISKA BARNSJUKHUSET

Jävsdeklaration

- Styrelseledamot Svensk förening barnobesitas (2018-2022)
- Styrelseledamot ECOG /European Childhood Obesity Group
- Ledamot i European Childhood Obesity Group (ECOG) (2017-2021)
- Coordinerande Principal Investigator i Combat-JUDO. EU finansierat project där vi studerade Exenatide extended release på barnobesitas (2015-2016)
- Principal investigator Novonordisk studie med Liraglutide på ungdomar (12-18 år) med obesitas (2016-2019)
- Principal investigator Novonordisk studie med Semaglutide på barn (6-12 år) med obesitas (2016-2019)
- Sponsor och Coordinerade Principal Investigator I MINT (Metformin Intervention) studien på barn I åldern 6-18 år med obesitas. Finansierad av Merck
- Har patent I ett läkemedel mot obesitas (Fixed combination, modified relesease av Orlistat och Acarbos) och aktier i företaget Empros Pharma
- Föreläst vid ett rundabord samtal med politiker och ansvariga inom sjukvården, arvoderat av Novonordisk

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

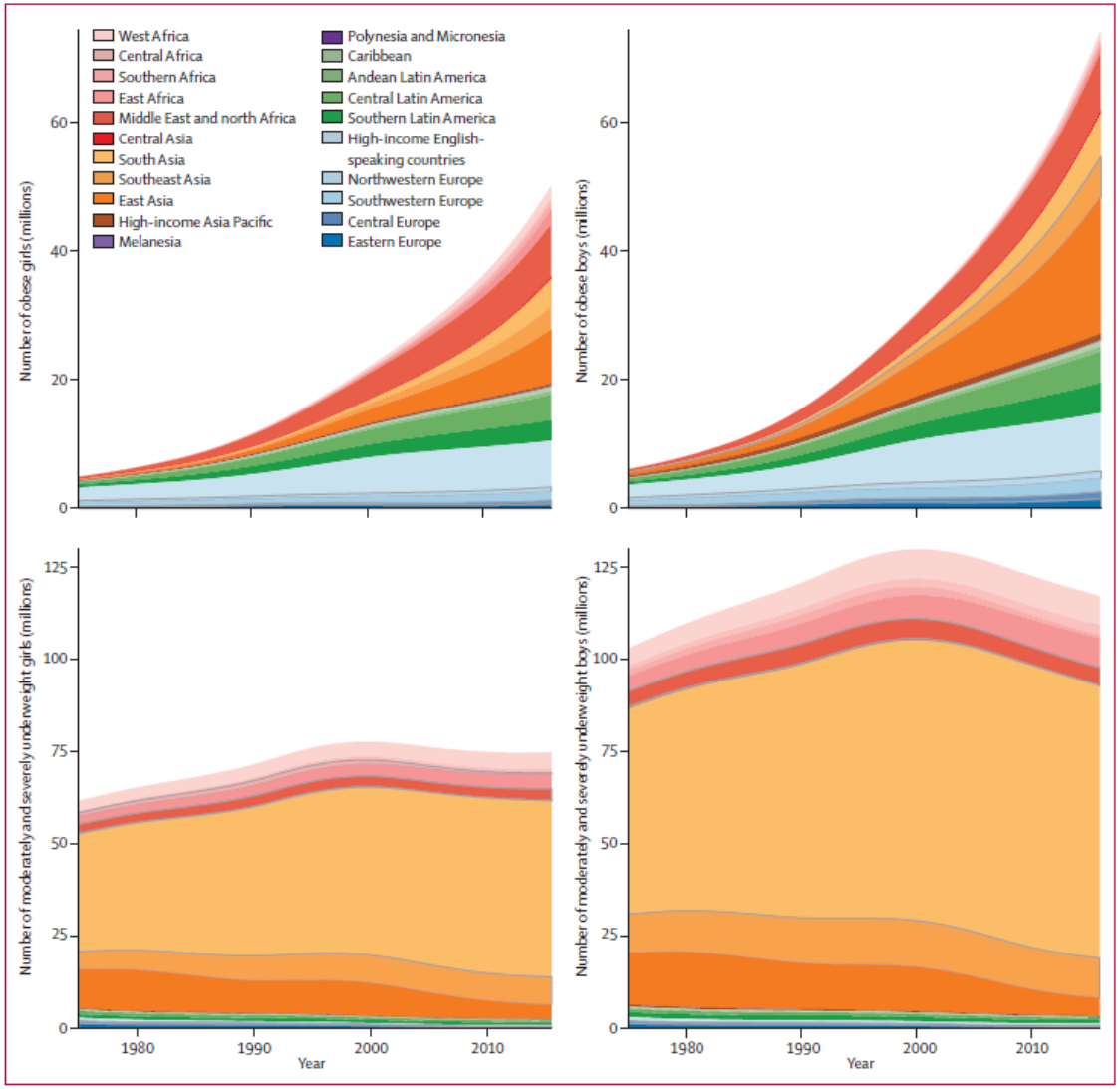
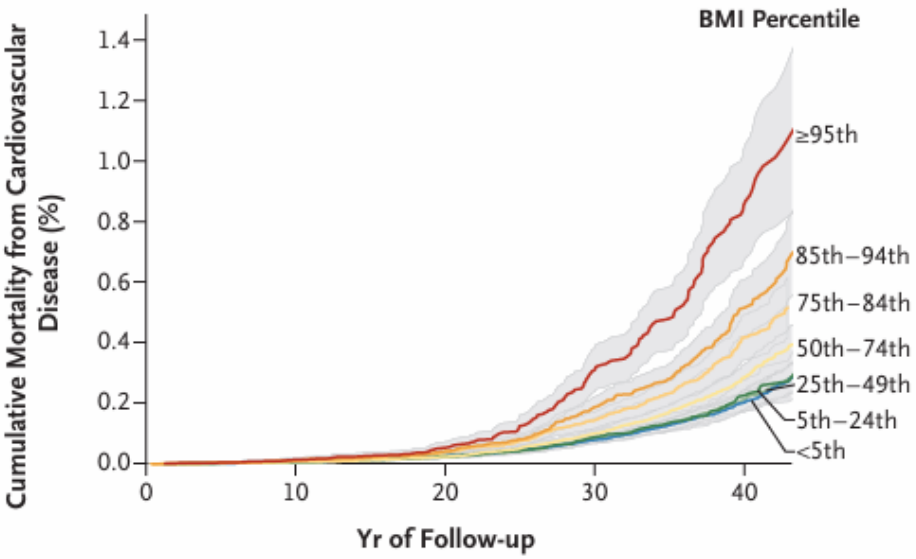


Figure 10: **Trends in the number of children and adolescents with obesity and with moderate and severe underweight by region**
Children and adolescents were aged 5–19 years. See appendix for results for adults. BMI=body-mass index.

ÖVERVIKTSENHETEN för barn & ungdom



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

AKADEMISKA BARNSJUKHUSET

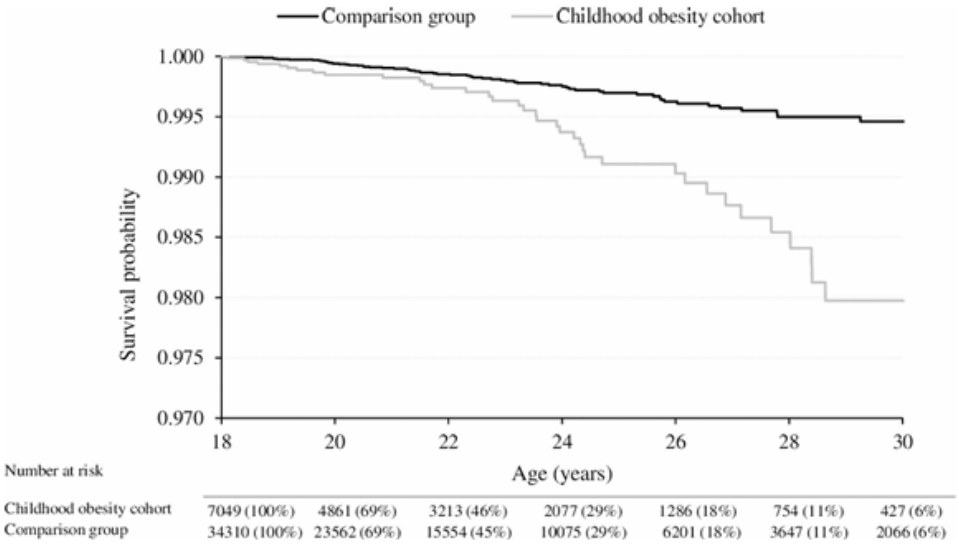
RESEARCH ARTICLE

Association of childhood obesity with risk of early all-cause and cause-specific mortality: A Swedish prospective cohort study

Louise Lindberg[1]*, Pernilla Danielsson[1], Martina Persson[2,3,4], Claude Marcus[1], Emilia Hagman[1]

1 Division of Pediatrics, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden, **2** Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, **3** Department of Diabetes and Endocrinology, Sachsska Children's Hospital, Södersjukhuset, Stockholm, Sweden, **4** Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden

* louise.lindberg@ki.se



Number at risk

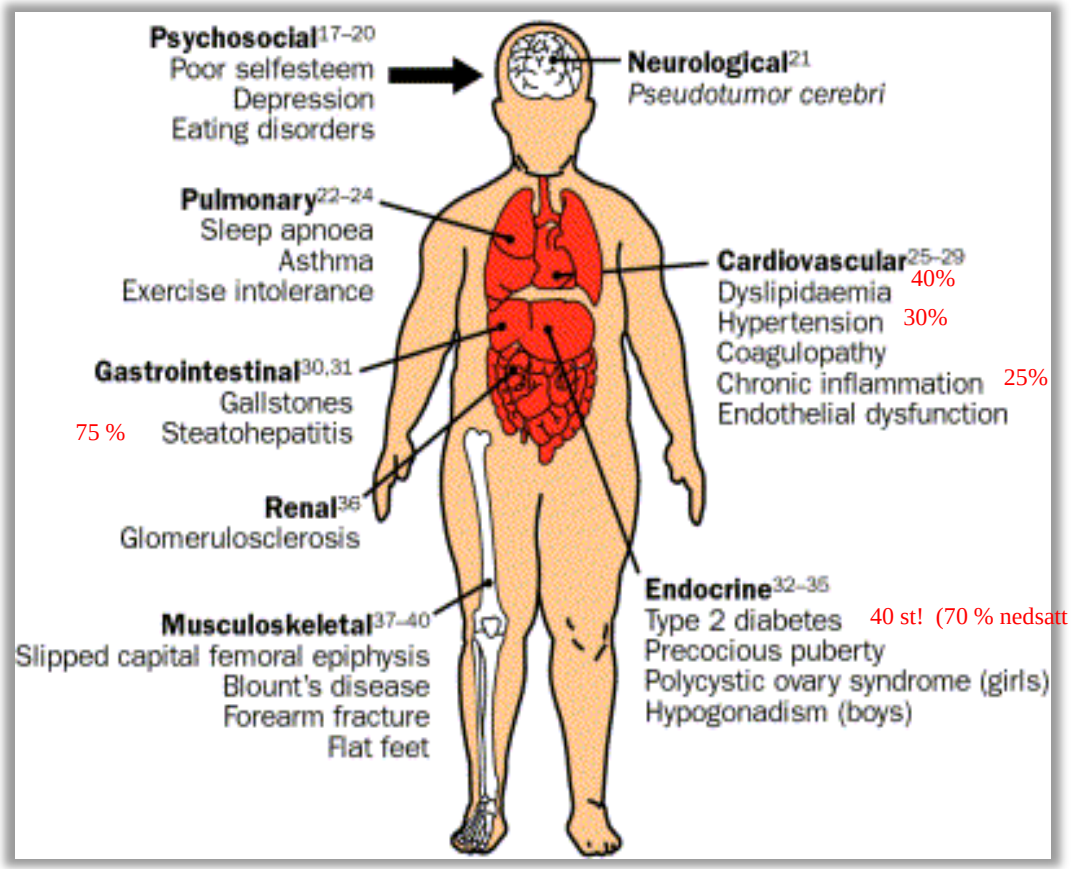
Childhood obesity cohort	7049 (100%)	4861 (69%)	3213 (46%)	2077 (29%)	1286 (18%)	754 (11%)	427 (6%)
Comparison group	34310 (100%)	23562 (69%)	15554 (45%)	10075 (29%)	6201 (18%)	3647 (11%)	2066 (6%)

Fig 1. Survival curves of all-cause mortality in the childhood obesity cohort and the comparison group.

https://doi.org/10.1371/journal.pmed.1003078.g001

ÖVERVIKTSENHETEN för barn & ungdom

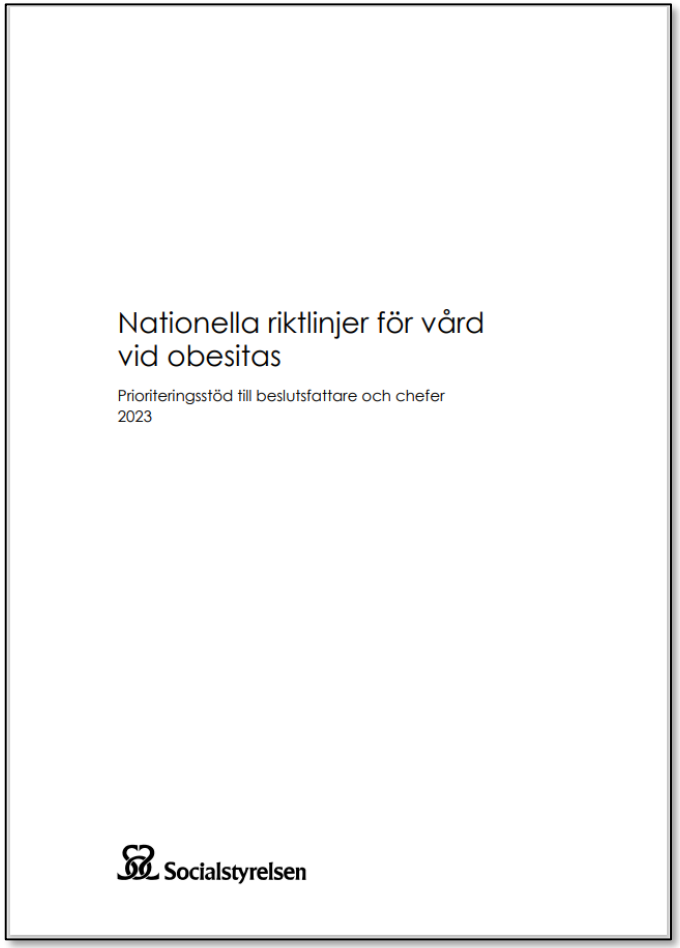
Komplikationer till barnfetma



Svininfluensa! Covid-19!

Lancet 2002, **360:** 473–82

AKADEMISKA BARNSJUKHUSET



ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

Rekommendationer till hälso- och sjukvården: Kirurgi

Id	Erbjud operationen …	till personer med obesitas som är aktuella för operationen och …	Prioritet
18	gastric bypass	• är vuxna • har BMI ≥ 35	2
14		• är barn i åldern 15–17 år • har BMI ≥ 35	3
16		• är vuxna • har BMI 30–35	3
19	sleeve-gastrektomi	• är vuxna • har BMI ≥ 35	3
20	BPD/DS (biliopankreatisk diversion med duodenal switch)	• är vuxna • har BMI ≥ 50	5
Id	**Endast inom ramen för forskning och utveckling: Erbjud operationen …**	**till personer med obesitas som …**	**Prioritet**
15	sleeve-gastrektomi	• är barn i åldern 15–17 år • har BMI ≥ 35	FoU
17		• är vuxna • har BMI 30–35	FoU

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

15 maj 2023

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

Vårdprogrammet lägger tonvikt på

- Respektfullt och icke stigmatiserande bemötande
- Obesitas är en kronisk sjukdom och ska följas upp
- Att obesitas går att behandla
- Tidig identifikation
- Tidig intensiv individanpassad behandling
- Utbildning och kompetens
- Teamarbete
- Samordning mellan olika vårdnivåer

"Tänk inte att behandlingen ger barnet dålig självkänsla utan tänk istället att barnet ges verktyg för ett liv i hälsa med redskap som kan följa dem resten av liv"

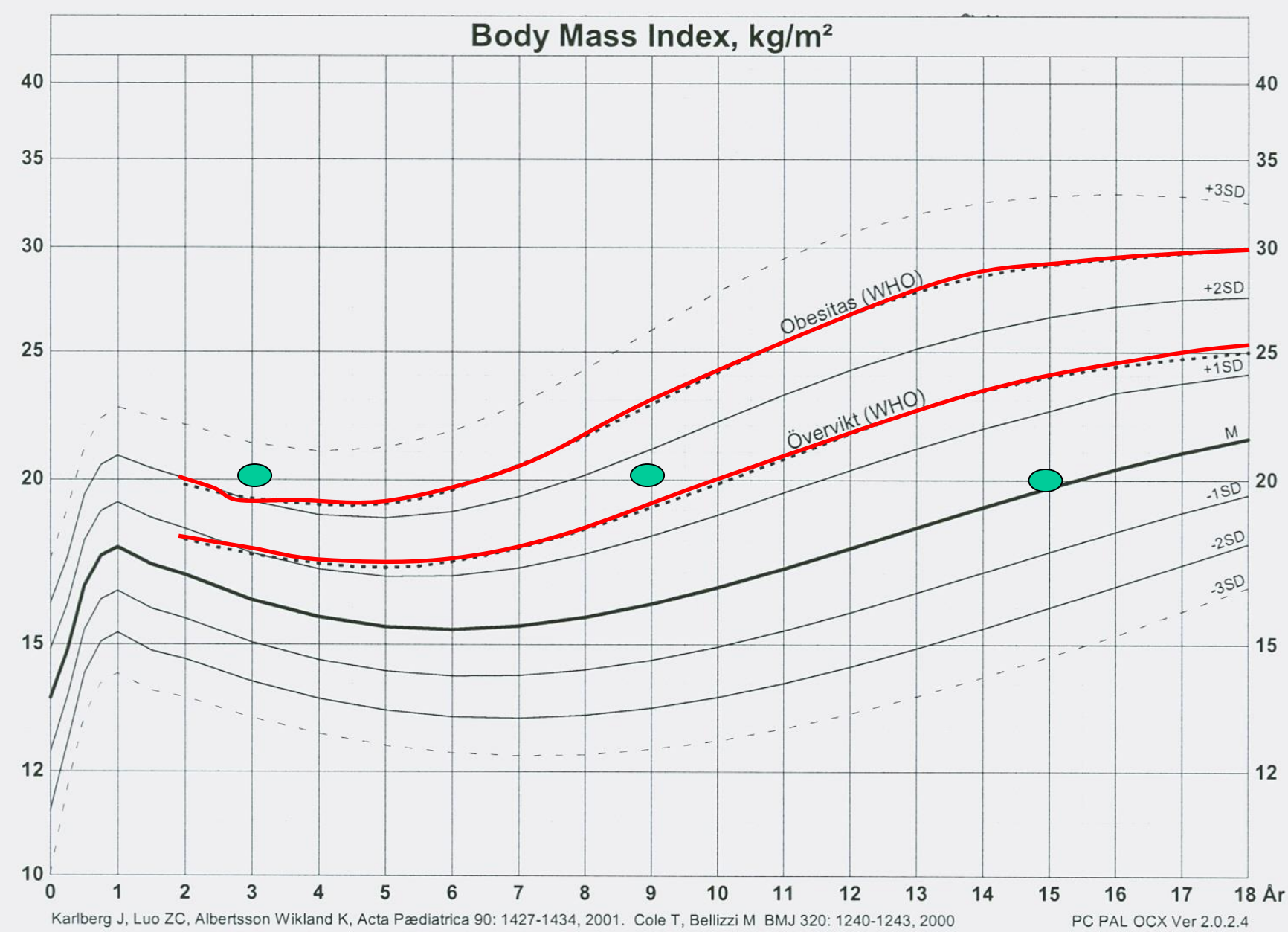
Hälsa oberoende storlek HOBS

ÖVERVIKTSENHETEN för barn & ungdom

Definition av barnövervikt och barnfetma

BMI (Body Mass Index):

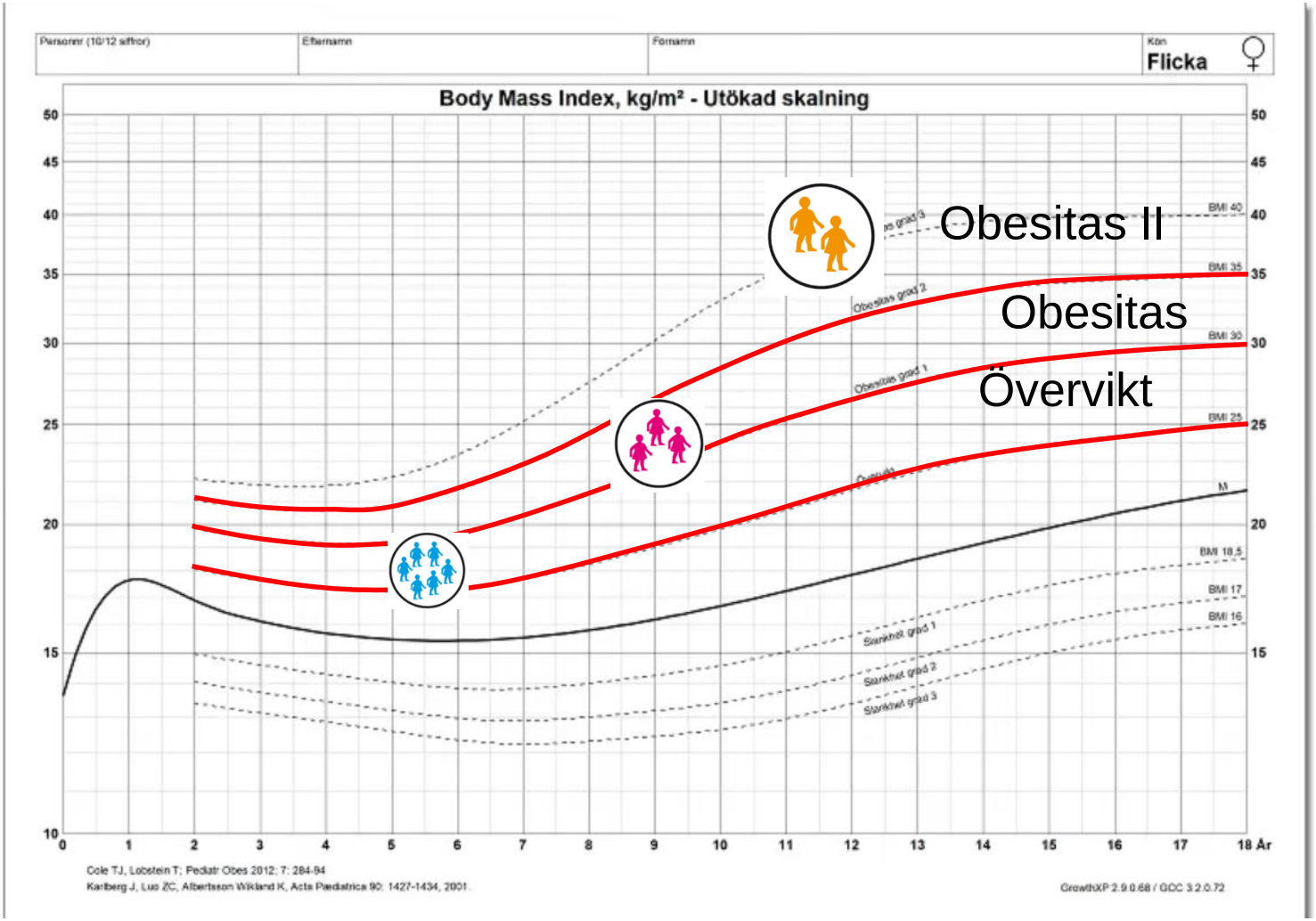
$$\frac{\text{vikt (kg)}}{\text{längd} * \text{längd (m)}} = \frac{39 \text{ kg}}{1{,}40 * 1{,}40 \text{ m}} = 20$$



Karlberg J, Luo ZC, Albertsson Wikland K, Acta Pædiatrica 90: 1427-1434, 2001. Cole T, Bellizzi M BMJ 320: 1240-1243, 2000

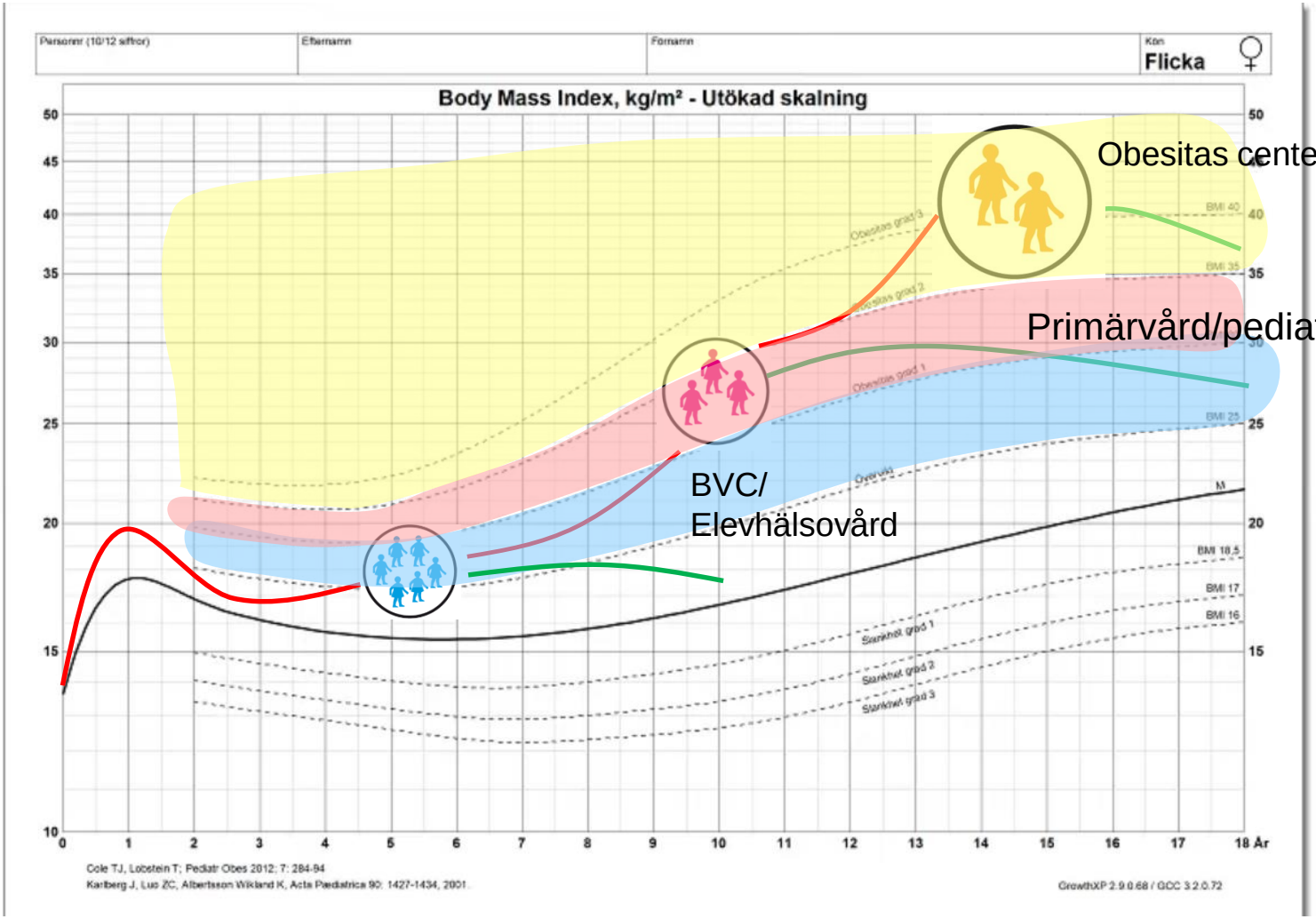
PC PAL OCX Ver 2.0.2.4

AKADEMISKA BARNSJUKHUSET



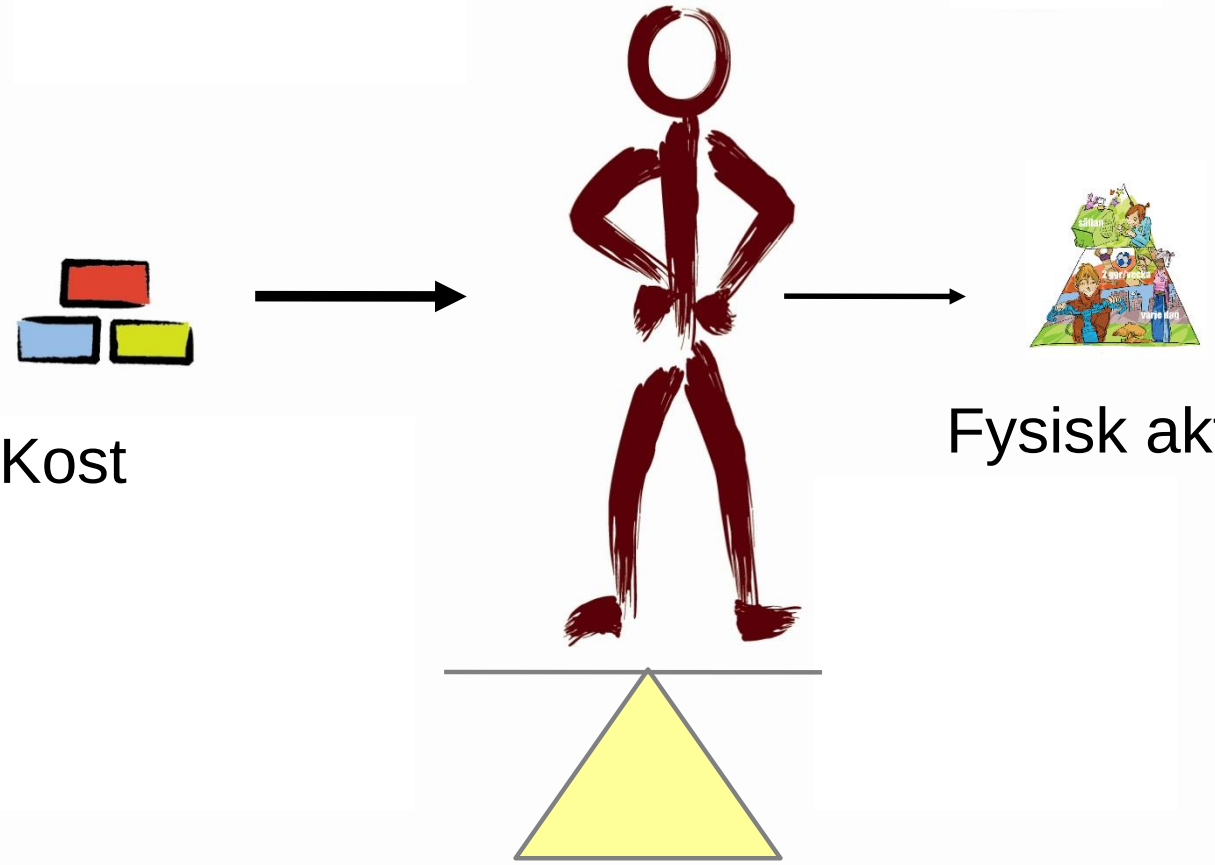
ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET



ÖVERVIKTSENHETEN
för barn & ungdom

Kombinerad **l**evnadsvane**b**ehandling (KLB)



Kost

Fysisk aktivitet

Kost

AKADEMISKA BARNSJUKHUSET

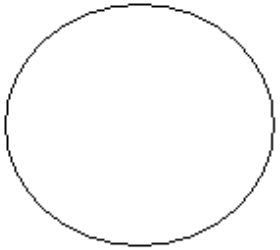
Regelbunda måltider

Portions storlek

Val av dryck

Frukt och grönsaker

Annat

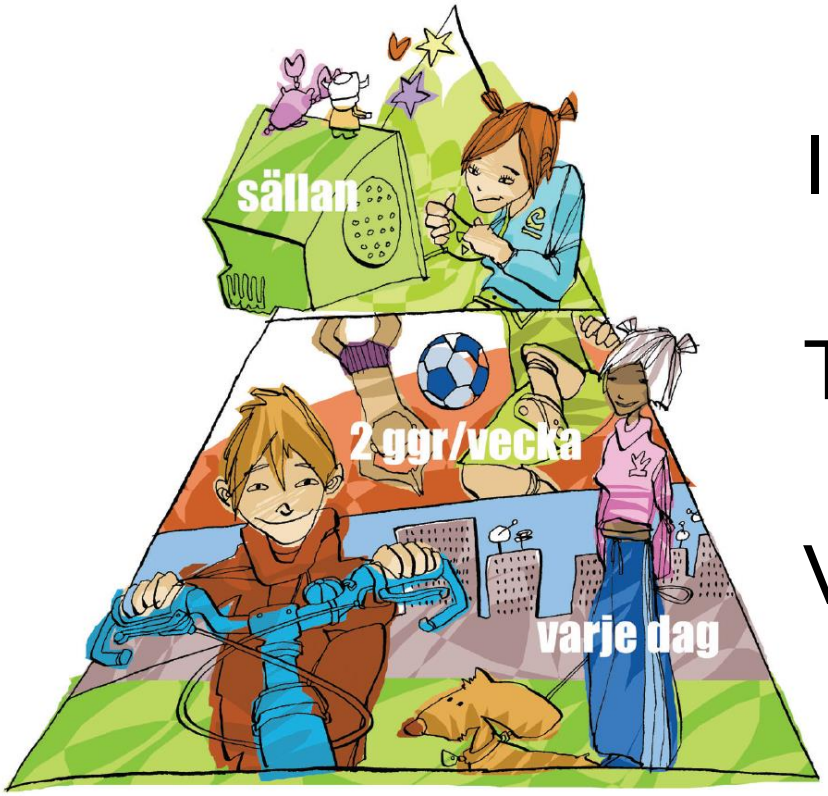


Övrigt

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

Fysisk aktivitet



Inaktivitet

Träning

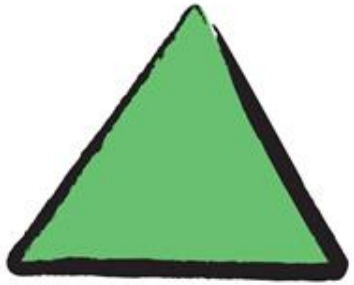
Vardags aktivitet

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

Inaktivitet

Träning

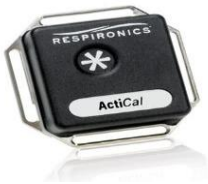


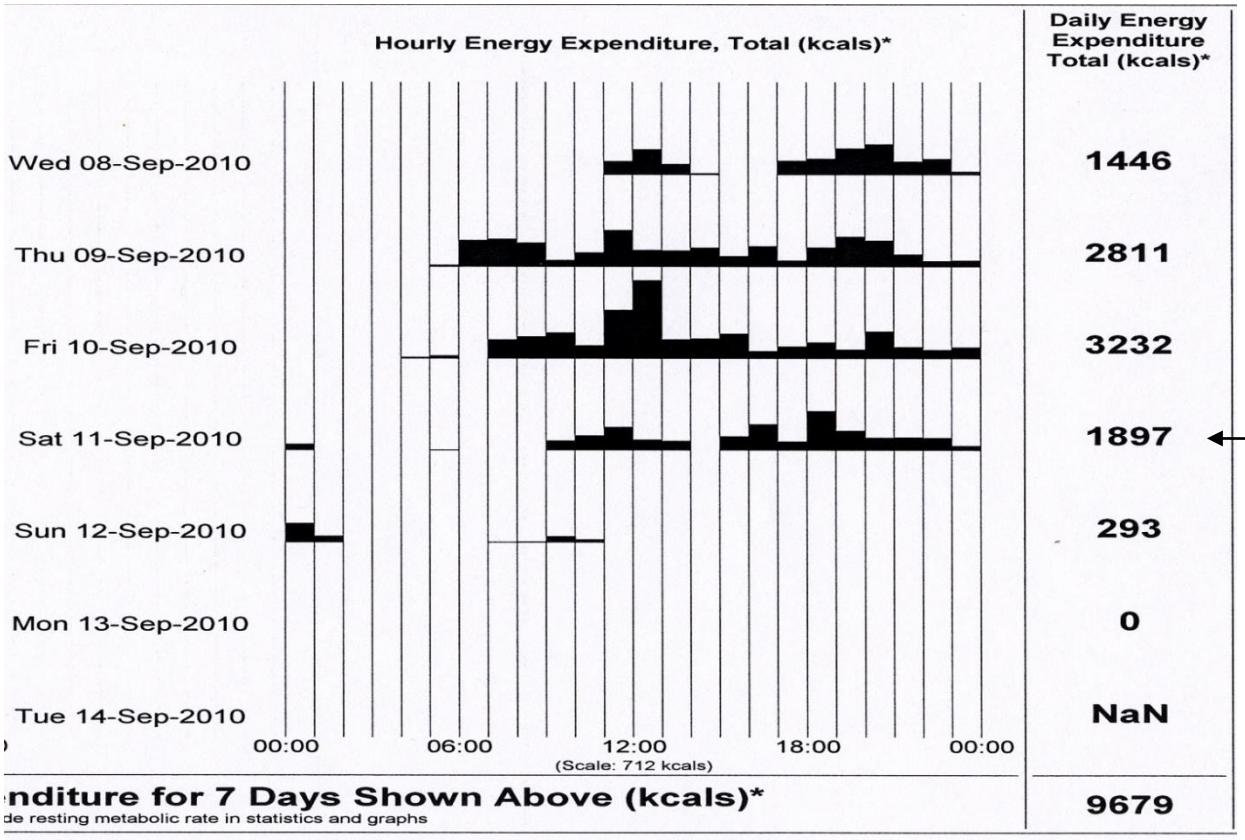
Daglig aktivitet

Annat

AKADEMISKA BARNSJUKHUSET

Daglig aktivitet
(accelerometer)





Skol dag

Helg

ÖVERVIKTSENHETEN för barn & ungdom

Om den initiala livsstilsinterventionen inte är framgångsrik

Är det en brist på kunskap?

Eller hur de ska lyckas med det?

Vad är orsaken?

Behandlingens intensitet?

- Annat?

AKADEMISKA BARNSJUKHUSET

Sömn

Kost

Fysisk aktivitet

Sömn
Sömn duration
Sömn kvalitet
Regelbunden sömn

Melatonin är godkänt för - insomni hos barn och ungdomar 6–17 år med ADHD där sömnhygienåtgärder har varit otillräckliga.

AKADEMISKA BARNSJUKHUSET

REVIEWS

Check for updates

The role of insufficient sleep and circadian misalignment in obesity

Jean-Philippe Chaput[1,2]✉, Andrew W. McHill[3], Rebecca C. Cox[4], Josiane L. Broussard[5,6], Caroline Dutil[1,7], Bruno G. G. da Costa[8], Hugues Sampasa-Kanyinga[1,9] and Kenneth P. Wright Jr[4,6]

Abstract | Traditional risk factors for obesity and the metabolic syndrome, such as excess energy intake and lack of physical activity, cannot fully explain the high prevalence of these conditions. Insufficient sleep and circadian misalignment predispose individuals to poor metabolic health and promote weight gain and have received increased research attention in the past 10 years. Insufficient sleep is defined as sleeping less than recommended for health benefits, whereas circadian misalignment is defined as wakefulness and food intake occurring when the internal circadian system is promoting sleep. This Review discusses the impact of insufficient sleep and circadian misalignment in humans on appetite hormones (focusing on ghrelin, leptin and peptide-YY), energy expenditure, food intake and choice, and risk of obesity. Some potential strategies to reduce the adverse effects of sleep disruption on metabolic health are provided and future research priorities are highlighted. Millions of individuals worldwide do not obtain sufficient sleep for healthy metabolic functions. Furthermore, modern working patterns, lifestyles and technologies are often not conducive to adequate sleep at times when the internal physiological clock is promoting it (for example, late-night screen time, shift work and nocturnal social activities). Efforts are needed to highlight the importance of optimal sleep and circadian health in the maintenance of metabolic health and body weight regulation.

ÖVERVIKTSENHETEN för barn & ungdom

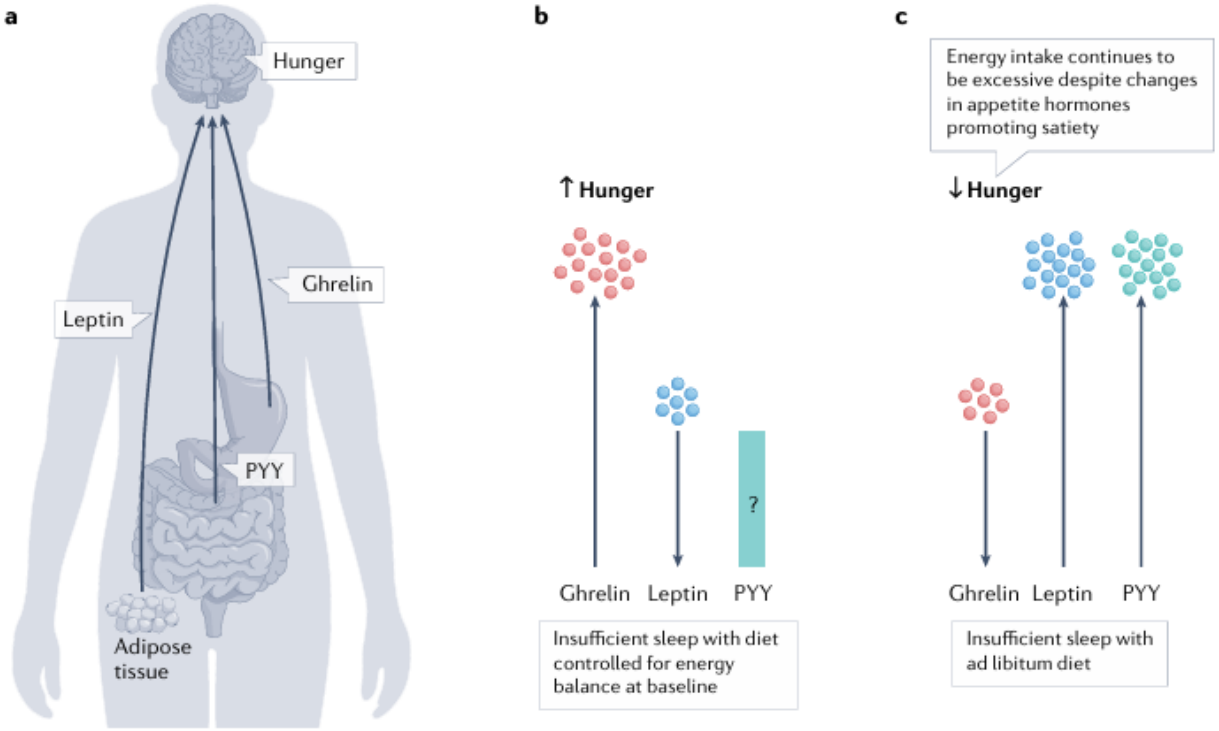


Fig. 3 | **Model of changes in appetite hormones, hunger and energy intake in response to insufficient sleep.** The peripheral appetite-stimulating hormone ghrelin and the satiety hormones leptin and peptide-YY (PYY) feed back to the brain to influence appetite and hunger. When sleep is restricted but diet is controlled for the energy balance needed for a typical day with adequate sleep, the appetite-stimulating hormone ghrelin is increased and the satiety hormone leptin is decreased, resulting in increased hunger levels. By contrast, ghrelin is decreased and leptin and PYY are increased under an ad libitum diet during restricted sleep, reducing hunger levels. Changes in appetite hormones during ad libitum diets are probably due to increased energy intake during sleep restriction. However, energy intake remains excessive despite reductions in hunger, which suggests that other factors promote food intake. It is unknown how PYY might change during sleep restriction under a diet controlled for energy balance for a typical day with adequate sleep.

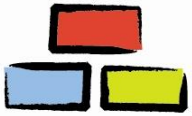
Nature reviews. Endocrinology, 2023-02, Vol.19 (2), p.82-97

Hälsa

Somatisk - psykologisk

Sömn

Kost



Fysisk aktivitet

ÖVERVIKTSENHETEN
för barn & ungdom

AKADEMISKA BARNSJUKHUSET

Hälsa (jaget)

Somatisk:

- Smärta
- Typ 2 diabetes
- NAFLD
- Högt blodtryck
- ..

Psykologiskt

- Själv känsla
- Själv förtroende
- Själv kärlek
- Själv destruktivt
- Depression
- Neuropsykiatri – ADHD/ADD
- Ät störningar

ÖVERVIKTSENHETEN för barn & ungdom

Hälsa

Somatisk - psykologisk

Sömn

Stress

Kost

Fysisk aktivitet

AKADEMISKA BARNSJUKHUSET

Skilsmässa
Föräldrar med drogproblem/alkohol problem
Föräldrar med psykiatriska problem
Övergrepp
Dyslexi
Inlärnings svårigheter
ADHD/ADD (18-58% bland de med obesitas)
Mobbing
Trauma

ÖVERVIKTSENHETEN för barn & ungdom

Yau Y.H.C Stress and Eating Behaviors, 2013 September ; 38(3): 255–267.

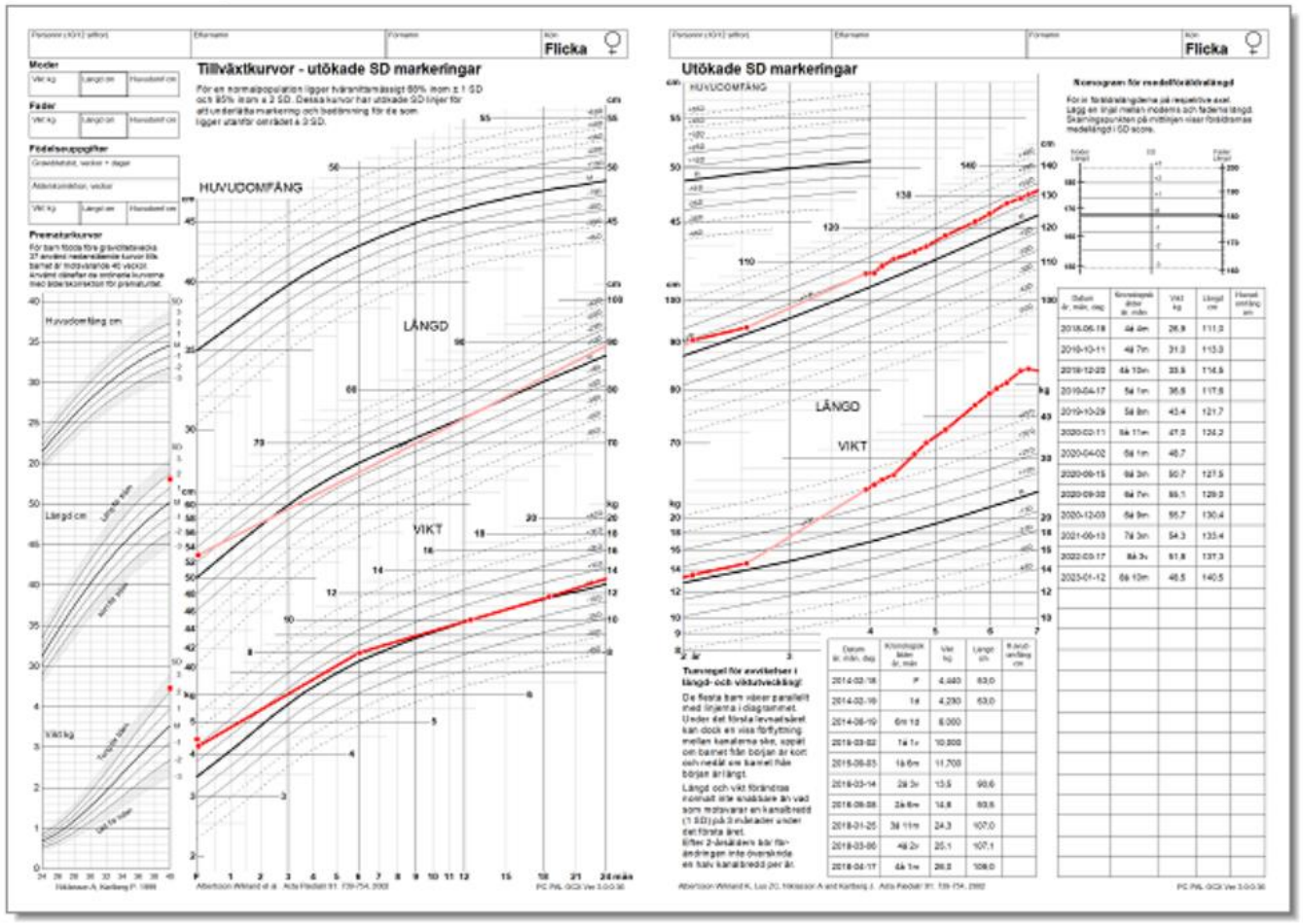
Gundersen C. Linking psychosocial stressors and childhood obesity. obesity reviews (2011) 12, e54–e63

AKADEMISKA BARNSJUKHUSET

Patient exempel

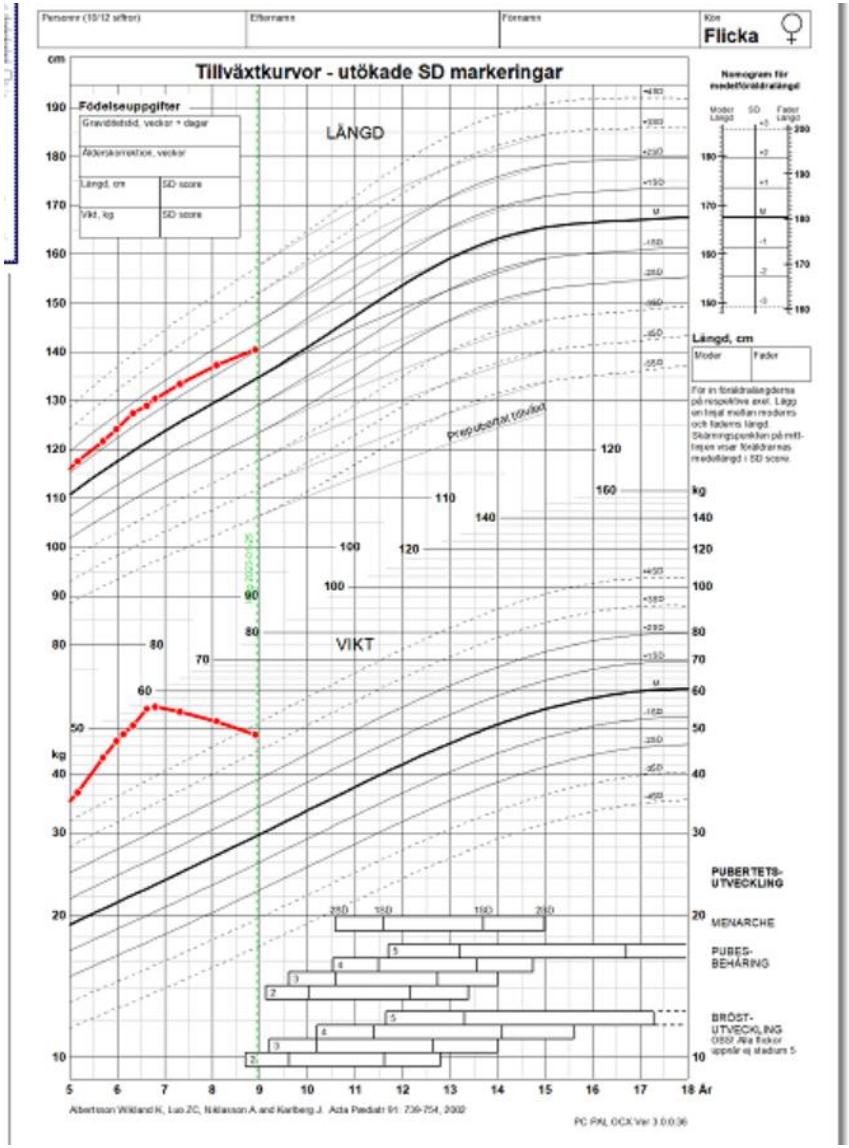
ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET



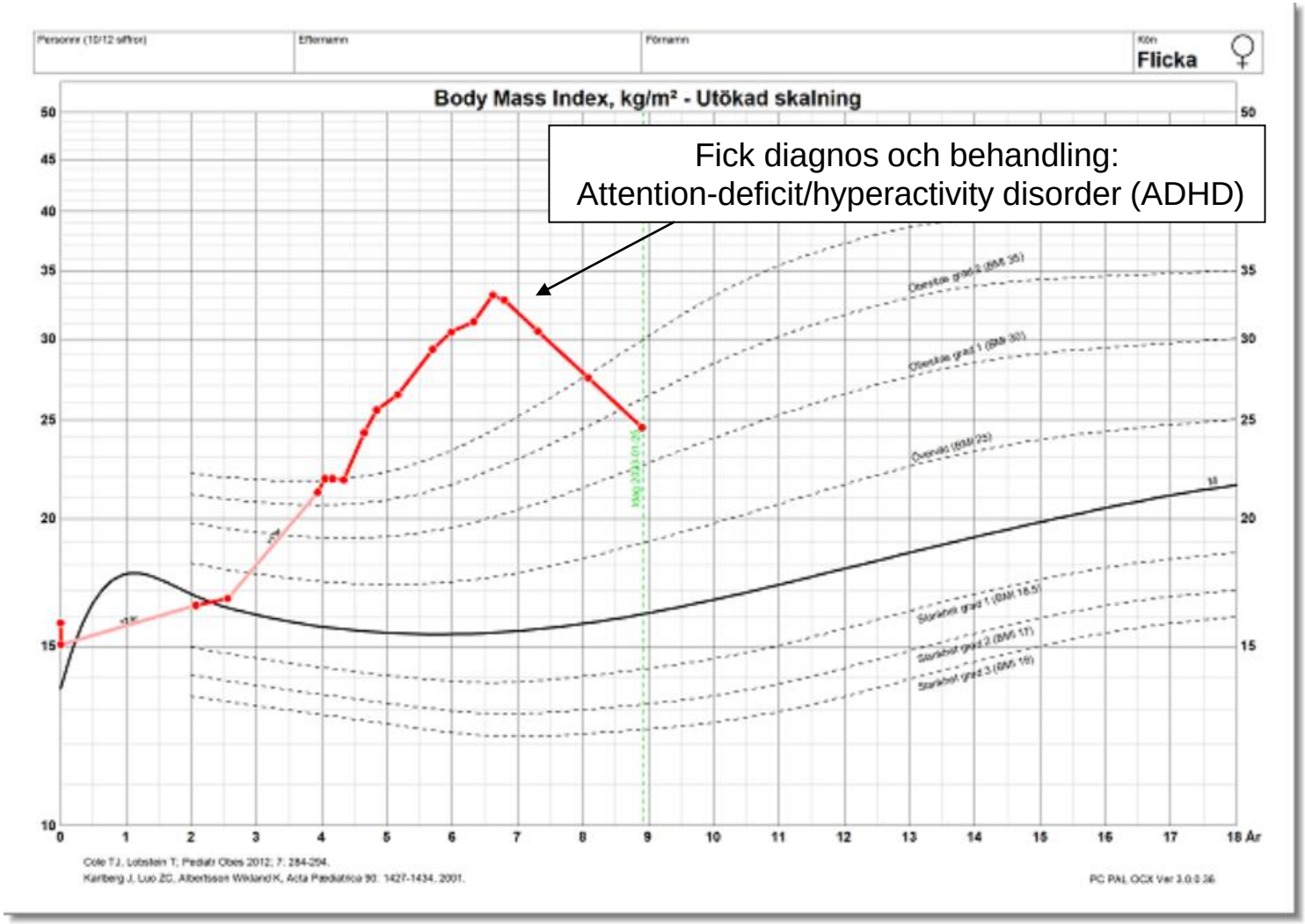
ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA
BARNSJUKHUSET



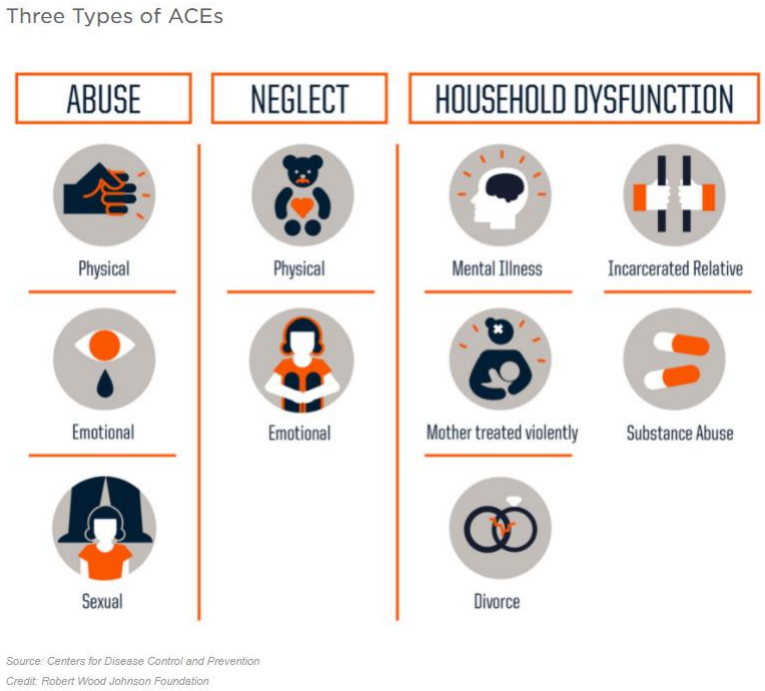
ÖVERVIKTSENHETEN
för barn & ungdom

AKADEMISKA BARNSJUKHUSET



ÖVERVIKTSENHETEN för barn & ungdom

Adverse Childhood Event



Received: 19 November 2020 | Accepted: 13 December 2020
DOI: 10.1111/obr.13204

PEDIATRIC OBESITY/ETIOLOGY

OBESITY Reviews WILEY

The association between adverse childhood experiences and childhood obesity: A systematic review

Krista Schroeder[1] | Brittany R. Schuler[1,2] | Julia M. Kobulsky[1,2] | David B. Sarwer[1,3]

[1]College of Public Health, Temple University, Philadelphia, PA, USA
[2]School of Social Work, Temple University, Philadelphia, PA, USA
[3]Center for Obesity Research and Education, Temple University, Philadelphia, PA, USA

Correspondence
Krista Schroeder, College of Public Health, Temple University, 3307 North Broad Street, Philadelphia, PA 19140, USA.
Email: krista.schroeder@temple.edu

Funding information
Eunice Kennedy Shriver National Institute of Child Health and Human Development, Grant/Award Number: K23HD101554; National Institute of Dental and Craniofacial Research, Grant/Award Number: R01DE026603; National Institute for Diabetes, Digestive, and Kidney Disease, Grant/Award Number: R01DK108628; National Institute on Minority Health and Health Disparities, Grant/Award Number: K01MD015326

Summary
Adverse childhood experiences (ACEs) are associated with numerous physical and mental health issues in children and adults. The effect of ACEs on development of childhood obesity is less understood. This systematic review was undertaken to synthesize the quantitative research examining the relationship between ACEs and childhood obesity. PubMed, PsycInfo, and Web of Science were searched in July 2020; Rayyan was used to screen studies, and the Newcastle-Ottawa Scale was used to assess risk of bias. The search resulted in 6,966 studies screened at title/abstract and 168 at full-text level. Twenty-four studies met inclusion criteria. Study quality was moderate, with greatest risk of bias due to method of assessment of ACEs or sample attrition. Findings suggest ACEs are associated with childhood obesity. Girls may be more sensitive to obesity-related effects of ACEs than boys, sexual abuse appears to have a greater effect on childhood obesity than other ACEs, and co-occurrence of multiple ACEs may be associated with greater childhood obesity risk. Further, the effect of ACEs on development of childhood obesity may take 2–5 years to manifest. Considered collectively, findings suggest a need for greater attention to ACEs in the prevention and treatment of childhood obesity.

KEYWORDS
adverse childhood experiences, obesity, pediatric obesity

Hälsa

Somatisk - psykologisk

Sömn

Stress

Kost

Fysisk aktivitet

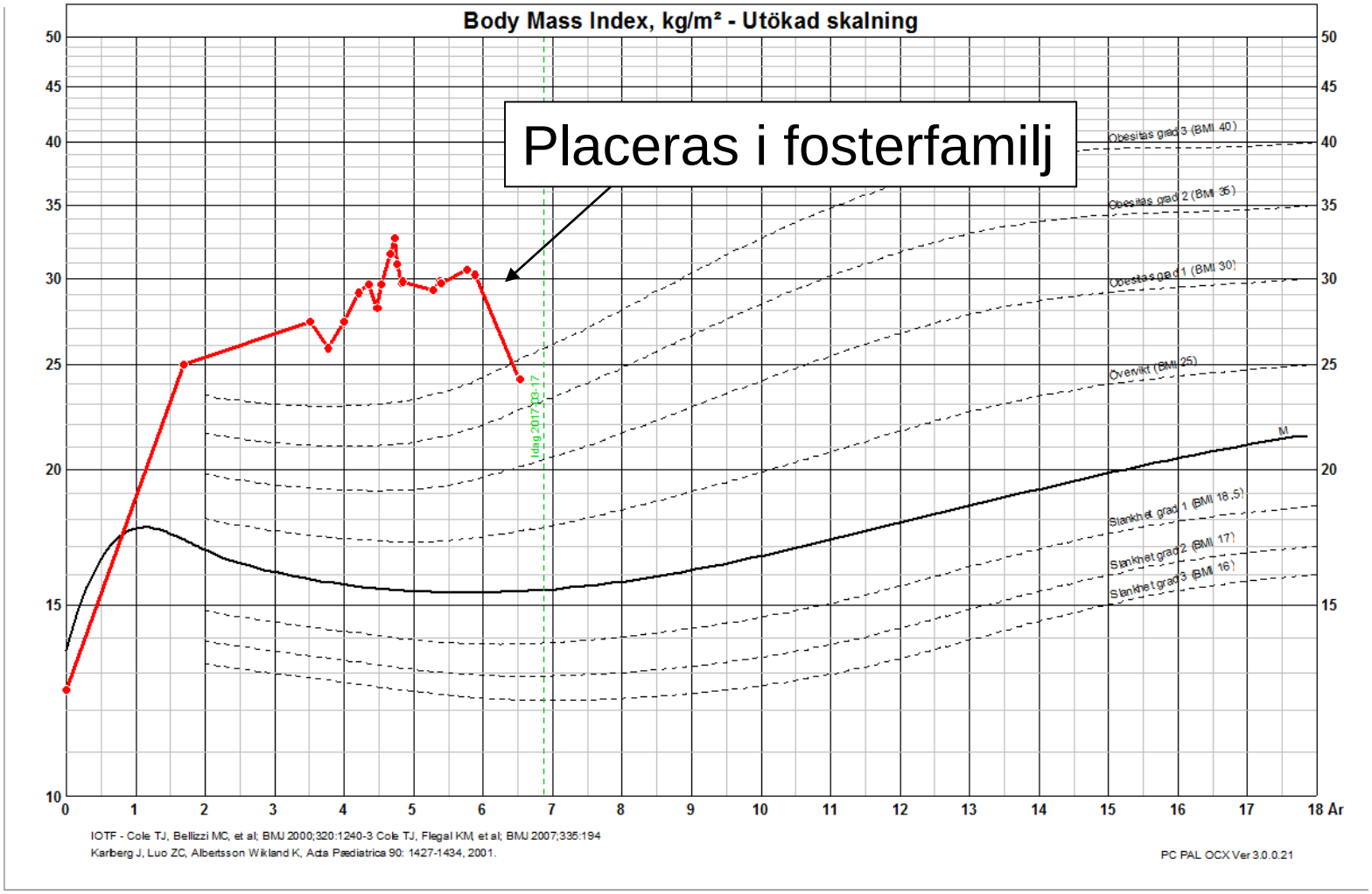
Familj / vänner

AKADEMISKA BARNSJUKHUSET

Familj
Syskon
Släktingar
Vänner
Socialtjänsten
Barnpsykiatrin
Skola
Sjuk och hälsovård
Nätverk

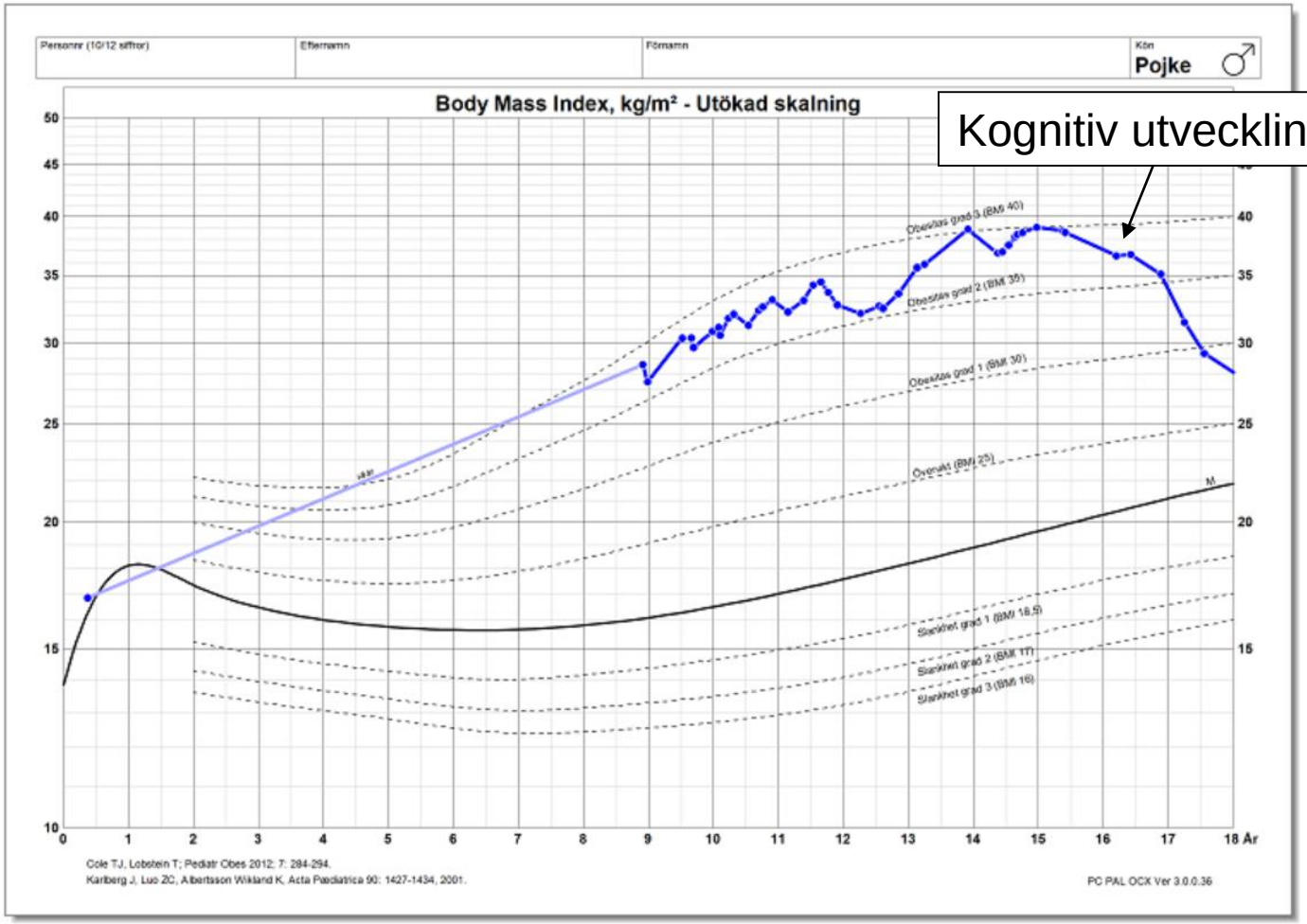
ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET



ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET



ÖVERVIKTSENHETEN för barn & ungdom

Hälsa

Somatisk - psykologisk

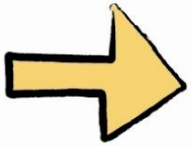
Sömn

Stress

Kost

Fysisk aktivitet

Motivation/mål



Familj / vänner

Motivation / mål

<u>Mål:</u>
Gå ned i vikt – vilken tidsram
Förändra levnadsvanor

<u>Motivation:</u>
Redo att förändra vs tron på att kunna förändra

Mål

- <u>Primär – beteende - dynamisk;</u>
  - Bättre matvanor
  - Aktivitet – mindre inaktivitet, mer fysisk aktivitet
  - Livskvalitet
  - sömn
  - Motivation? Stress?

- <u>Sekundär - resultat- slut mål - statisk;</u>
  - Normala blodfetter, blodtryck, glukos, kroppssammansättning
  - Normalt och bättre BMI

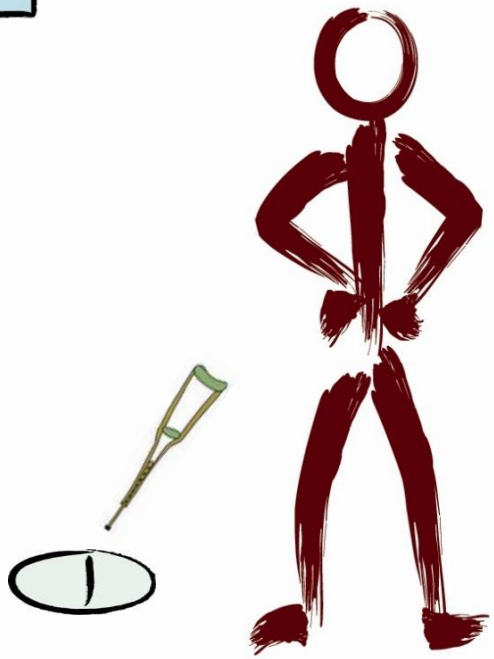
AKADEMISKA BARNSJUKHUSET

Hälsa

Somatisk- psykologisk

sömn

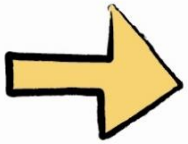
Stress



Kost

Fysisk aktivitet

Motivation/Mål



familj / vänner

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

Läkemedel

Behandla vikten?
och/eller komplikationer?

- Blodtryck
- Blodfetter
- Blodsocker
- Leversteatos

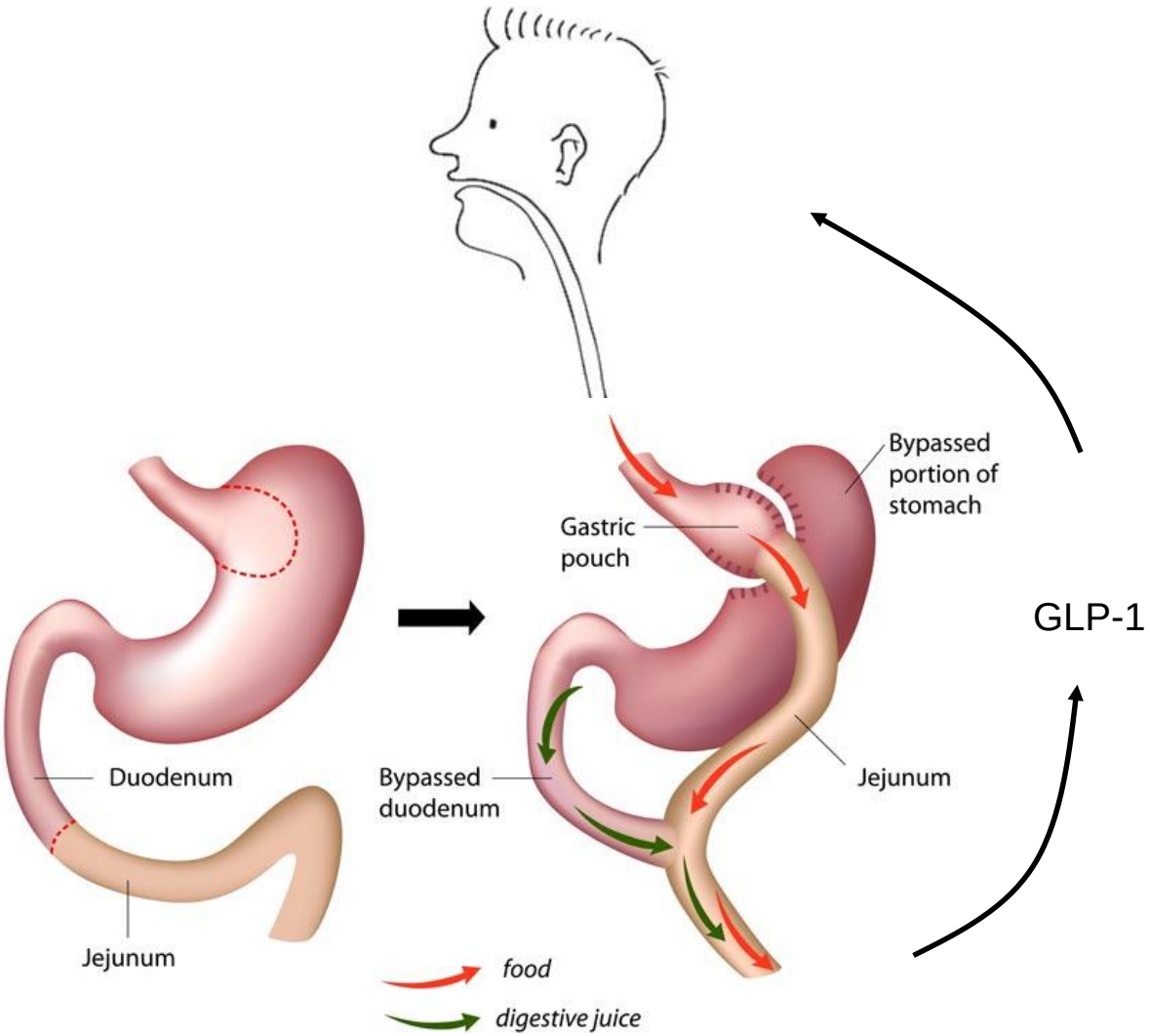
Behandla?

- Neuropsykiatri ADHD/ADD
- Depression
- Ätstörning
- Sömn störning

Det gör livsstilsinterventionen möjlig!

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET



www.ecog-obesity.eu

ÖVERVIKTSENHETEN för barn & ungdom

GLP-1 analoger

AKADEMISKA BARNSJUKHUSET

1 gång per dag

Liraglutide:

0,6 mg 1 gång per dag	vecka 1	
1,2 mg 1 gång per dag	vecka 2	
1,8 mg 1 gång per dag	vecka 3	Victoza® – för typ 2 diabetes, Subventionerat
2,4 mg 1 gång per dag	vecka 4	
3,0 mg 1 gång per dag		Saxenda® – för obesitas, Inte subventionerat godkänt från 12 års ålder

1 gång per vecka

Semaglutide:

0,25 mg 1 gång per vecka	månad 1	
0,5 mg 1 gång per vecka	månad 2	
1,0 mg 1 gång per vecka	månad 3	Ozempic® – för typ 2 diabetes, subventionerat
1,7 mg 1 gång per vecka	månad 4	
2,4 mg 1 gång per vecka	månad 5	Wegovy® – för obesitas, inte subventionerat godkänt från 12 års ålder

Intyg merkostnadsersättning till försäkringskassan

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

The NEW ENGLAND JOURNAL of MEDICINE

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*

ABSTRACT

BACKGROUND

Obesity is a chronic disease with limited treatment options in pediatric patients. Liraglutide may be useful for weight management in adolescents with obesity.

METHODS

In this randomized, double-blind trial, which consisted of a 56-week treatment period and a 26-week follow-up period, we enrolled adolescents (12 to <18 years of age) with obesity and a poor response to lifestyle therapy alone. Participants were randomly assigned (1:1) to receive either liraglutide (3.0 mg) or placebo subcutaneously once daily, in addition to lifestyle therapy. The primary end point was the change from baseline in the body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) standard-deviation score at week 56.

RESULTS

A total of 125 participants were assigned to the liraglutide group and 126 to the placebo group. Liraglutide was superior to placebo with regard to the change from baseline in the BMI standard-deviation score at week 56 (estimated difference, −0.22; 95% confidence interval [CI], −0.37 to −0.08; P=0.002). A reduction in BMI of at least 5% was observed in 51 of 113 participants in the liraglutide group and in 20 of 105 participants in the placebo group (estimated percentage, 43.3% vs. 18.7%), and a reduction in BMI of at least 10% was observed in 33 and 9, respectively (estimated percentage, 26.1% vs. 8.1%). A greater reduction was observed with liraglutide than with placebo for BMI (estimated difference, −4.64 percentage points) and for body weight (estimated difference, −4.50 kg [for absolute change] and −5.01 percentage points [for relative change]). After discontinuation, a greater increase in the BMI standard-deviation score was observed with liraglutide than with placebo (estimated difference, 0.15; 95% CI, 0.07 to 0.23). More participants in the liraglutide group than in the placebo group had gastrointestinal adverse events (81 of 125 [64.8%] vs. 46 of 126 [36.5%]) and adverse events that led to discontinuation of the trial treatment (13 [10.4%] vs. 0). Few participants in either group had serious adverse events (3 [2.4%] vs. 5 [4.0%]). One suicide, which occurred in the liraglutide group, was assessed by the investigator as unlikely to be related to the trial treatment.

CONCLUSIONS

In adolescents with obesity, the use of liraglutide (3.0 mg) plus lifestyle therapy led to a significantly greater reduction in the BMI standard-deviation score than placebo plus lifestyle therapy. (Funded by Novo Nordisk; NN8022-4180 ClinicalTrials.gov number, NCT02918279.)

From the Department of Pediatrics and Center for Pediatric Obesity Medicine, University of Minnesota Medical School, Minneapolis (A.S.K.); Novo Nordisk, Søborg, Denmark (P.A.); Pediatric Endocrinology, Hospital Ángeles Puebla, Puebla City, Mexico (M.B.-P.); the Department of Pediatrics, Division of Pediatric Endocrinology, Universitair Ziekenhuis Brussel, Brussels (I.G.); Novo Nordisk, Plainsboro, NJ (P.M.H.); the Division of Pediatrics, Department of Clinical Science Intervention and Technology, Karolinska Institutet, Stockholm (C.M.); the Division of Pediatric Endocrinology and Diabetes, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY (L.D.M.); Novo Nordisk, Bengaluru, India (N.P.); and the Center for Pediatric Research in Obesity and Metabolism, Division of Pediatric Endocrinology, Metabolism, and Diabetes Mellitus, University of Pittsburgh Medical Center Children's Hospital of Pittsburgh, University of Pittsburgh School of Medicine, Pittsburgh (S.A.). Address reprint requests to Dr. Kelly at the Center for Pediatric Obesity Medicine, University of Minnesota, 717 Delaware St. SE, Rm. 370E, Minneapolis, MN 55414, or at kelly105@umn.edu.

*A complete list of the NN8022-4180 trial investigators is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on March 31, 2020, at NEJM.org.

N Engl J Med 2020;382:2117-28.
DOI: 10.1056/NEJMoa1916038

Liraglutide

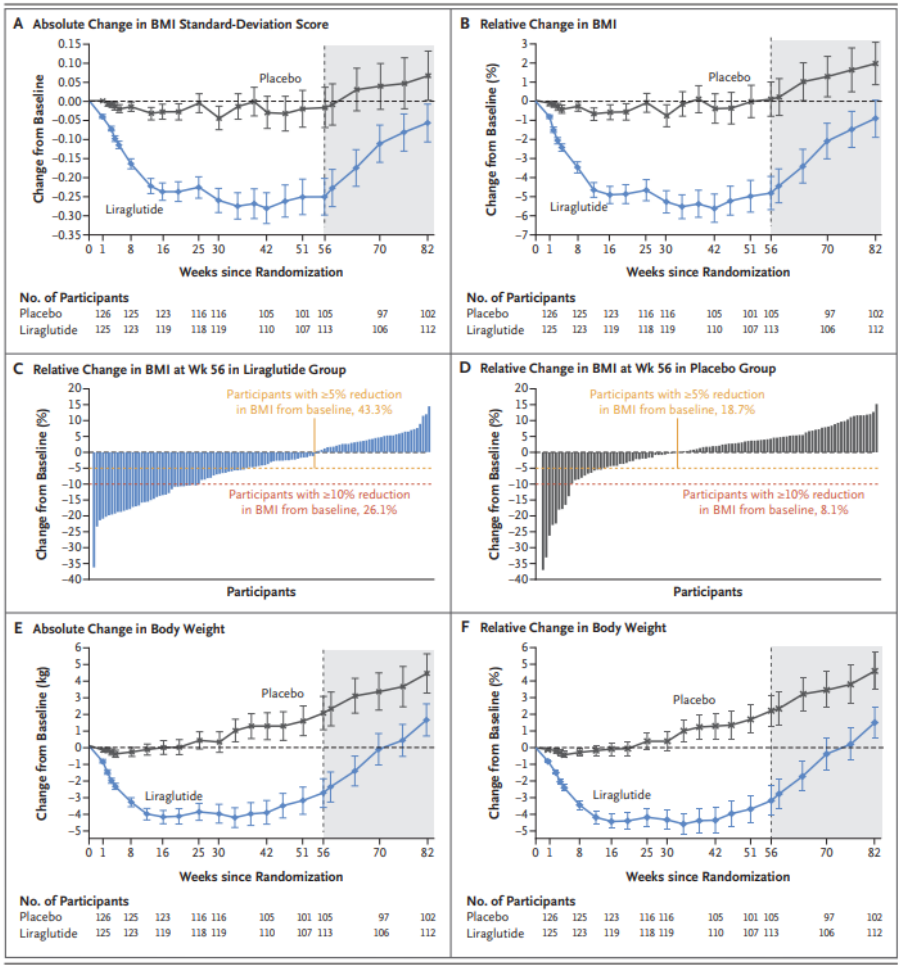
- GLP-1 analog
- Ges subcutant 1 g/d

Publicerades 2020
Godkänd indikation för att behandla Obesitas hos ungdomar 2021

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

The NEW ENGLAND JOURNAL of MEDICINE



Liraglutide 3.0 mg (Saxenda)
ges 1 gång/dag subcutant

Är nu godkänt från 12 år mot obesitas
Är dock inte subventionerat

Vissa individer svarar bra,
En del inte alls

När de har slutat, så går de snabbare Upp i vikt än de som har fått placebo!

- Är det en kronisk behandling?
- Skapar behandlingen problem

ÖVERVIKTSENHETEN för barn & ungdom

ORIGINAL ARTICLE

Once-Weekly Semaglutide in Adolescents with Obesity

Daniel Weghuber, M.D., Timothy Barrett, Ph.D., Margarita Barrientos-Pérez, M.D., Inge Gies, Ph.D., Dan Hesse, Ph.D., Ole K. Jeppesen, M.Sc., Aaron S. Kelly, Ph.D., Lucy D. Mastrandrea, M.D., Rasmus Sørrig, Ph.D., and Silva Arslanian, M.D., for the STEP TEENS Investigators*

ABSTRACT

BACKGROUND

A once-weekly, 2.4-mg dose of subcutaneous semaglutide, a glucagon-like peptide-1 receptor agonist, is used to treat obesity in adults, but assessment of the drug in adolescents has been lacking.

METHODS

In this double-blind, parallel-group, randomized, placebo-controlled trial, we enrolled adolescents (12 to <18 years of age) with obesity (a body-mass index [BMI] in the 95th percentile or higher) or with overweight (a BMI in the 85th percentile or higher) and at least one weight-related coexisting condition. Participants were randomly assigned in a 2:1 ratio to receive once-weekly subcutaneous semaglutide (at a dose of 2.4 mg) or placebo for 68 weeks, plus lifestyle intervention. The primary end point was the percentage change in BMI from baseline to week 68; the secondary confirmatory end point was weight loss of at least 5% at week 68.

RESULTS

A total of 201 participants underwent randomization, and 180 (90%) completed treatment. All but one of the participants had obesity. The mean change in BMI from baseline to week 68 was −16.1% with semaglutide and 0.6% with placebo (estimated difference, −16.7 percentage points; 95% confidence interval [CI], −20.3 to −13.2; P<0.001). At week 68, a total of 95 of 131 participants (73%) in the semaglutide group had weight loss of 5% or more, as compared with 11 of 62 participants (18%) in the placebo group (estimated odds ratio, 14.0; 95% CI, 6.3 to 31.0; P<0.001). Reductions in body weight and improvement with respect to cardiometabolic risk factors (waist circumference and levels of glycated hemoglobin, lipids [except high-density lipoprotein cholesterol], and alanine aminotransferase) were greater with semaglutide than with placebo. The incidence of gastrointestinal adverse events was greater with semaglutide than with placebo (62% vs. 42%). Five participants (4%) in the semaglutide group and no participants in the placebo group had cholelithiasis. Serious adverse events were reported in 15 of 133 participants (11%) in the semaglutide group and in 6 of 67 participants (9%) in the placebo group.

CONCLUSIONS

Among adolescents with obesity, once-weekly treatment with a 2.4-mg dose of semaglutide plus lifestyle intervention resulted in a greater reduction in BMI than lifestyle intervention alone. (Funded by Novo Nordisk; STEP TEENS ClinicalTrials.gov number, NCT04102189.)

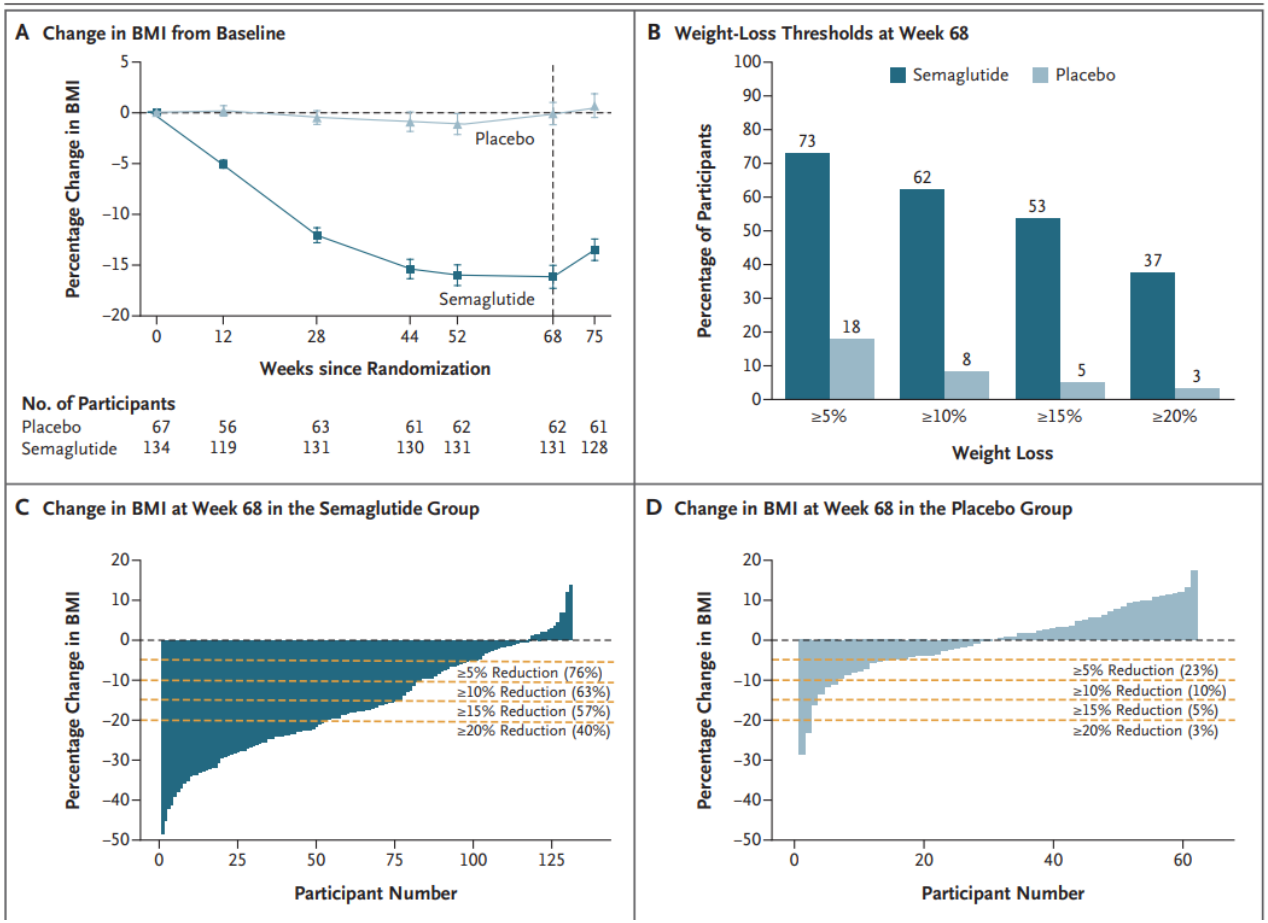
From the Department of Pediatrics, Paracelsus Medical University, Salzburg, Austria (D.W.); the Institute of Cancer and Genomic Sciences, University of Birmingham, Birmingham, United Kingdom (T.B.); the Division of Pediatric Endocrinology, Hospital Angeles Puebla, Puebla City, Mexico (M.B.-P.); the Department of Pediatrics, Division of Pediatric Endocrinology, Universitair Ziekenhuis Brussel, Brussels (I.G.); Novo Nordisk, Søborg, Denmark (D.H., O.K.J., R.S.); the Department of Pediatrics and the Center for Pediatric Obesity Medicine, University of Minnesota Medical School, Minneapolis (A.S.K.); the Division of Pediatric Endocrinology and Diabetes, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY (L.D.M.); and the Center for Pediatric Research in Obesity and Metabolism, Division of Pediatric Endocrinology, Diabetes, and Metabolism, University of Pittsburgh School of Medicine, and UPMC Children's Hospital of Pittsburgh, Pittsburgh (S.A.). Dr. Weghuber can be contacted at d.weghuber@salk.at or at the Department of Pediatrics, Paracelsus Medical University, Müllner Hauptstrasse 48, 5020 Salzburg, Austria.

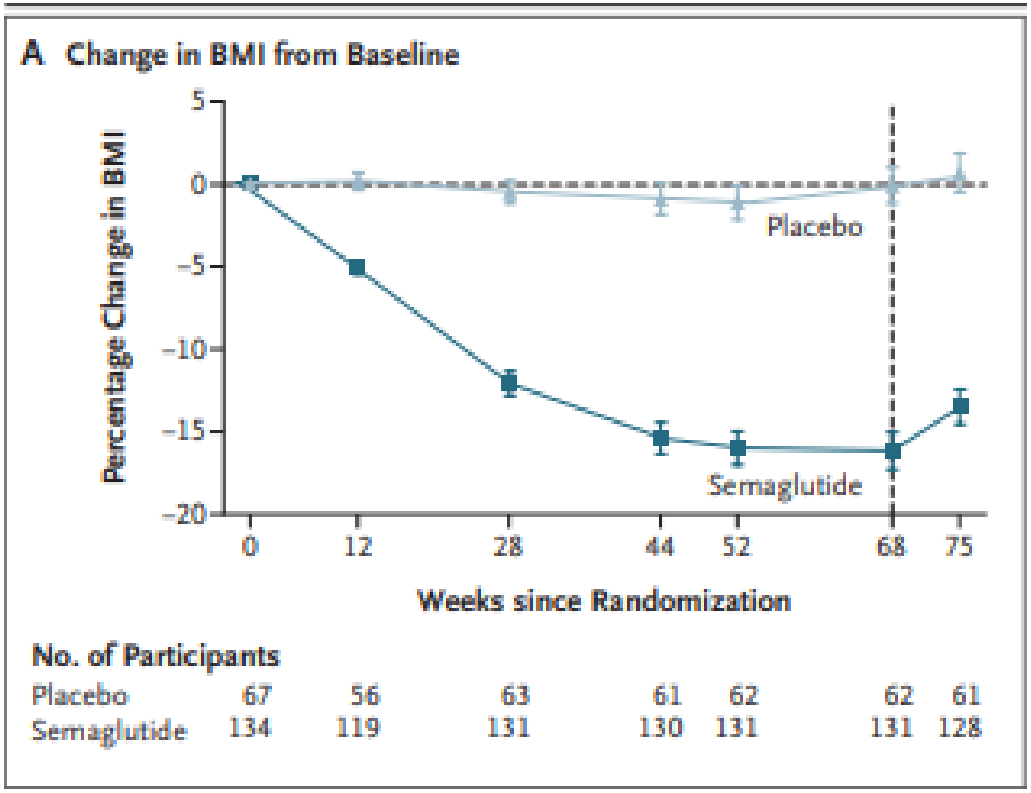
*A complete list of investigators in the STEP TEENS trial is provided in the Supplementary Appendix, available at NEJM.org.

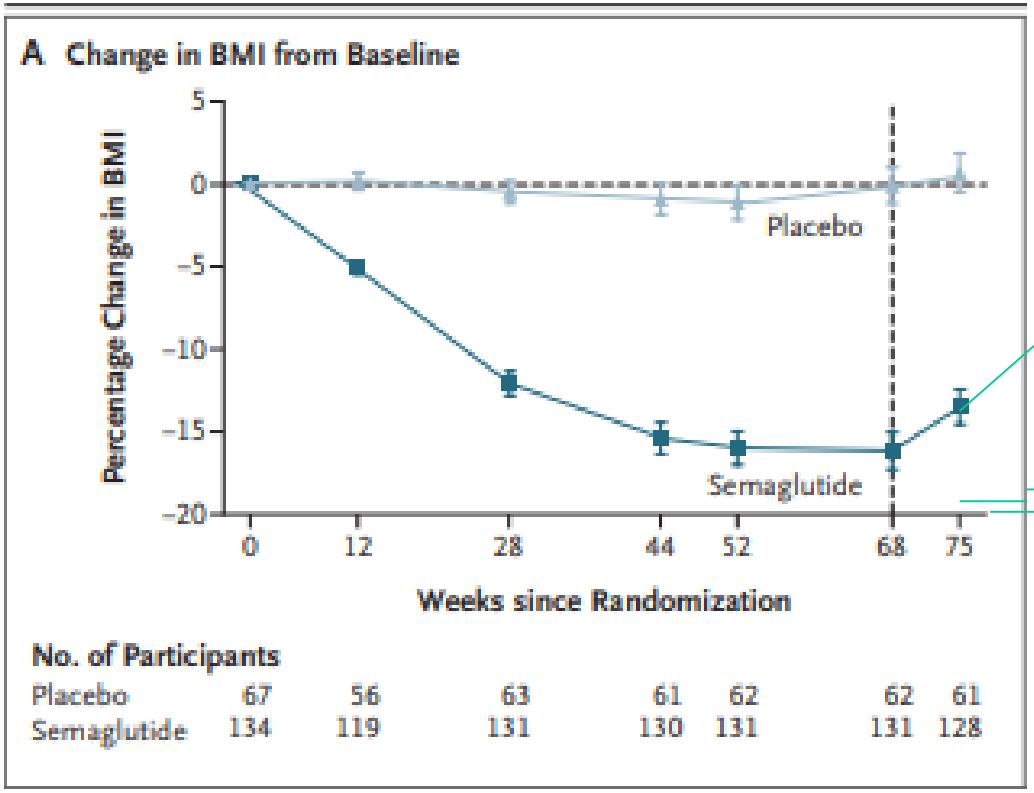
This article was published on November 2, 2022, and updated on November 17, 2022, at NEJM.org.

N Engl J Med 2022;387:2245-57.
DOI: 10.1056/NEJMoa2208601

CME at NEJM.org


A Change in BMI from Baseline
Percentage Change in BMI
5
0
−5
−10
−15
−20
Placebo
Semaglutide
0
12
28
44
52
68
75
Weeks since Randomization
No. of Participants
Placebo 67 56 63 61 62 62 61
Semaglutide 134 119 131 130 131 131 128
B Weight-Loss Thresholds at Week 68
Semaglutide
Placebo
Percentage of Participants
100
90
80
70
60
50
40
30
20
10
0
73
18
62
8
53
5
37
3
≥5%
≥10%
≥15%
≥20%
Weight Loss
C Change in BMI at Week 68 in the Semaglutide Group
Percentage Change in BMI
20
10
0
−10
−20
−30
−40
−50
≥5% Reduction (76%)
≥10% Reduction (63%)
≥15% Reduction (57%)
≥20% Reduction (40%)
0
25
50
75
100
125
Participant Number
D Change in BMI at Week 68 in the Placebo Group
Percentage Change in BMI
20
10
0
−10
−20
−30
−40
−50
≥5% Reduction (23%)
≥10% Reduction (10%)
≥15% Reduction (5%)
≥20% Reduction (3%)
0
20
40
60
Participant Number


A Change in BMI from Baseline
Percentage Change in BMI
5
0
−5
−10
−15
−20
Placebo
Semaglutide
0
12
28
44
52
68
75
Weeks since Randomization
No. of Participants
Placebo 67 56 63 61 62 62 61
Semaglutide 134 119 131 130 131 131 128


A Change in BMI from Baseline
Percentage Change in BMI
5
0
−5
−10
−15
−20
Placebo
Semaglutide
0
12
28
44
52
68
75
Weeks since Randomization
No. of Participants
Placebo 67 56 63 61 62 62 61
Semaglutide 134 119 131 130 131 131 128

AKADEMISKA BARNSJUKHUSET

Approved anti-obesity medications

FDA

Phentermine approved for ≥16 years[1]

Orlistat approved for ≥12 years[2]

Liraglutide 3.0 mg approved for ≥12 years[3]

Phentermine/topiramate approved for ≥12 years[4]

Semaglutide 2.4 mg approved for ≥12 years[5]

EMA MHRA

Liraglutide 3.0 mg approved for ≥12 years[6]

Semaglutide 2.4 mg approved for ≥12 years[7]

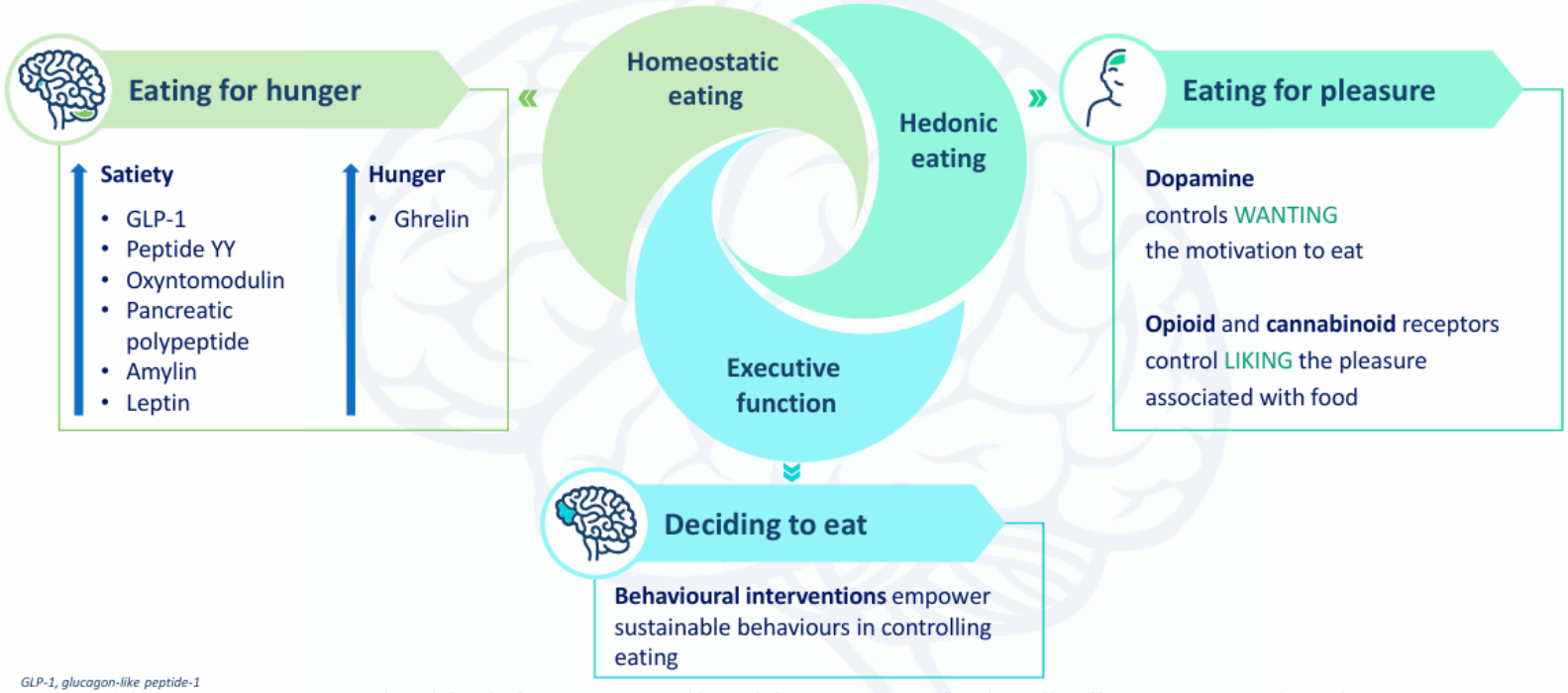
FDA, The US Food and Drug Administration; EMA, The European Medicines Agency; MHRA, The Medicines and Healthcare products Regulatory Agency
1. Suprenza (phentermine) Prescribing Information; 2. Xenical (orlistat) Prescribing Information; 3. Saxenda (liraglutide) Prescribing Information; 4. Qsymia (phentermine/topiramate) Prescribing Information; 5. Wegovy (semaglutide 2.4 mg) Prescribing Information; 6. Saxenda (liraglutide) Summary of product characteristics; 7. Wegovy (semaglutide 2.4 mg) Summary of product characteristics

ÖVERVIKTSENHETEN för barn & ungdom

With permission and acknowledge from D. Weghubers presentation ECOG 2024

AKADEMISKA BARNSJUKHUSET

The role of the brain in regulating appetite



GLP-1, glucagon-like peptide-1

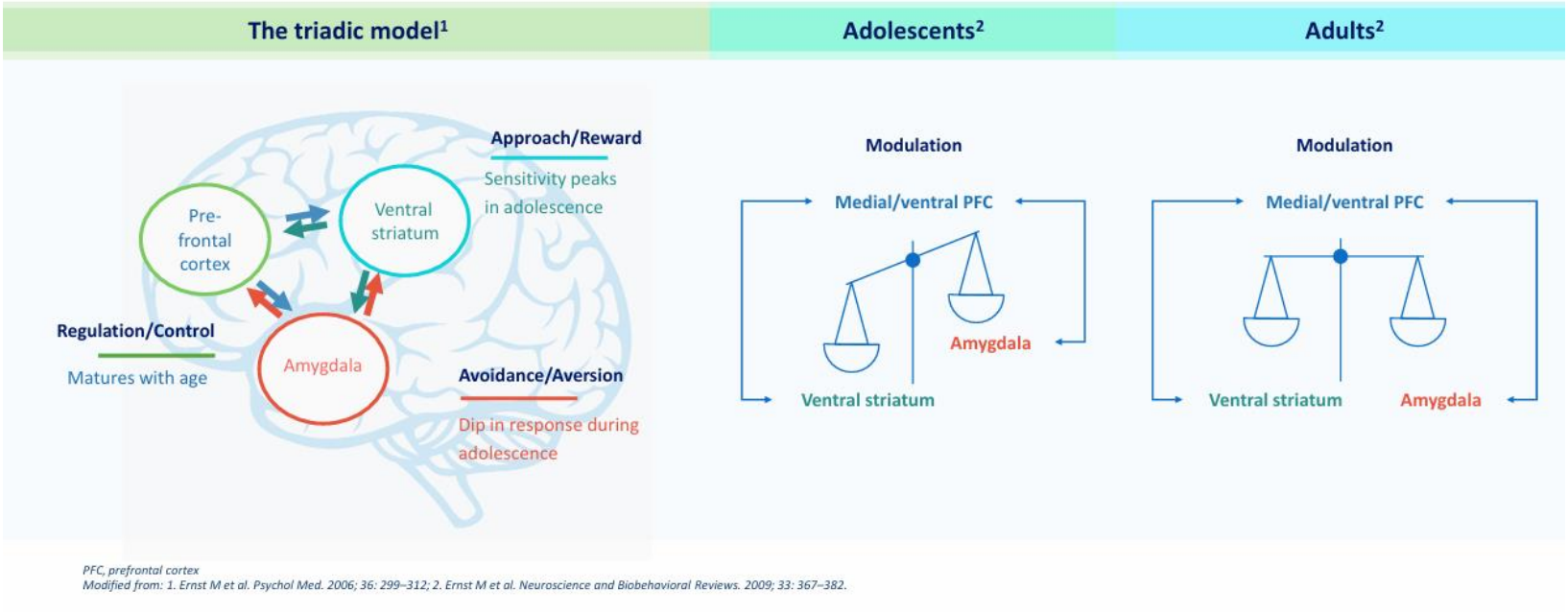
1. Badman MK & Flier JS. Science. 2005;307:1909–14; 2. van Bloemendaal L et al. Diabetes. 2014;63:4186–96; 3. Klok MD et al. Obes Rev. 2007;8:21–34; 4. Hall K et al. Am J Public Health. 2014;104:1169–75; 5. Berridge KC et al. Brain Res. 2010;1350:43–64; 6. Vallis M. Clin Obes. 2019;9:e12299; 7. Lau D et al. Canadian Adult Obesity Clinical Practice Guidelines: The Science of Obesity. Available from https://obesitycanada.ca/guidelines/science.

ÖVERVIKTSENHETEN för barn & ungdom

With permission and acknowledge from D. Weghubers presentation ECOG 2024

AKADEMISKA BARNSJUKHUSET

The balance of control and reward is skewed in adolescents



PFC, prefrontal cortex
Modified from: 1. Ernst M et al. Psychol Med. 2006; 36: 299–312; 2. Ernst M et al. Neuroscience and Biobehavioral Reviews. 2009; 33: 367–382.

ÖVERVIKTSENHETEN för barn & ungdom

With permission and acknowledge from D. Weghubers presentation ECOG 2024

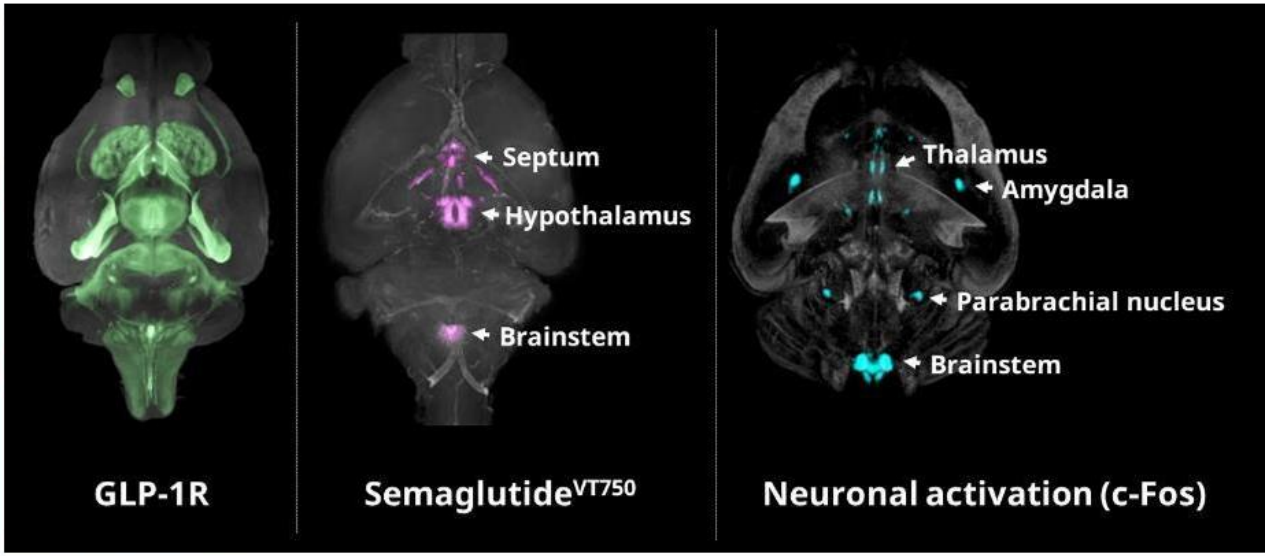
AKADEMISKA BARNSJUKHUSET

GLP-1RAs targets and activates brain regions associated with hedonic and homeostatic control of energy intake

Several GLP-1Rs in the brain

GLP-1R targeting in septum, hypothalamus, and hindbrain

Secondary activation in regions associated with control of food intake and reward



CVO, circumventricular organ; GLP-1R, glucagon-like peptide 1 receptor; NTS, nucleus of the solitary tract
Gabery et al. JCI Insight. 2020; 5: e133429

ÖVERVIKTSENHETEN för barn & ungdom

With permission and acknowledge from D. Weghubers presentation ECOG 2024

AKADEMISKA BARNSJUKHUSET

MINT

METFORMIN INTERVENTION STUDY

Metformin INTervention in children with obesity. A parallel, three arms, randomized, 6 months, multi-center study with metformin extended release (XR) plus lifestyle or metformin immediate release (IR) plus lifestyle or lifestyle alone

EudraCT number: 2019-003940-61

Site Initiation Visit (SIV) Falun 28 okt 2021

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKI

MINT

METFORMIN INTERVENTION STUDY

Fig. 1 *Galega officinalis*. *G. officinalis*, the herbal lineage of metformin, is also known as goat's rue, French lilac, Italian fitch, Spanish sainfoin or professor weed. This plant was used as a traditional medicine in medieval Europe; it is now classed as a noxious weed in many states of the USA. Copyright Malcolm Storey, www.bioimages.org.uk (photograph taken in Berkshire, UK, 1 July 2000)

Table 1 Landmark events in the history of metformin for the management of type 2 diabetes

Year	Landmark	Reference
1772	*Galega officinalis* used to treat symptoms of diabetes (Hill)	[3]
1844–1861	Identification and synthesis of guanidine (Strecker)	[6]
1878–1879	Synthesis of biguanide (Rathke)	[6]
1918	Guanidine lowers blood glucose in animals (Watanabe)	[7]
1922	Synthesis of dimethylbiguanide (Werner and Bell)	[17]
1926–1928	Galegine and synthalin lower blood glucose in animals and humans	[8–13]
1929	Metformin and other biguanides lower blood glucose in animals (Hesse and Taubmann; Slotta and Tschesche)	[18, 19]
1930s	Use of guanidine derivatives to treat diabetes initially grows then declines due to toxicity and also availability of insulin	[6]
1944–1947	Guanidine-based antimalarial agent, proguanil (Paludrine), lowers blood glucose in animals	[20, 21]
1949–1950	Dimethylbiguanide (flumamine) tested as potential antimalarial agent and used to treat influenza in Philippines. Also found to potentially lower blood glucose (Garcia)	[22]
1956	Jan Aron encourages Jean Sterne and Denise Duval to study guanidine-based glucose-lowering agents	[6]
1957	Jean Sterne publishes use of metformin to treat diabetes	[24]
1957–1959	Phenformin and buformin reported as treatments for diabetes	[32, 33, 37, 38]
1958	Metformin introduced to treat diabetes in the UK and other European countries	[6]
1958–1964	Sterne and colleagues (especially Azerad) further evaluate metformin in individuals with diabetes	[25–28, 36]
1968	First large prospective comparator trial of metformin (Edinburgh, UK; notably Duncan, Clarke and Campbell)	[42]
1977–1980	Phenformin and buformin withdrawn in most countries because of risk of lactic acidosis	[49]
1980–1994	Substantial new scientific and clinical evidence (e.g. Hermann, Noel, Wiernsperger and Bailey), strategic input by Lipha pharmaceuticals (e.g. Howlett, Meynaud, Daniel, Goodman) and discussions with the FDA (Reaven, DeFronzo, Bailey, Turner, Garber)	[6, 41, 44, 56–62]
1994–1995	Metformin approved (1994) and introduced (1995) in the USA	[6]
1995–1996	Key publications confirm favourable benefit:risk ratio of metformin in management of T2D	[63, 64]
1995–2000	Extensive diabetes education programme by Bristol-Myers Squibb (e.g. Cryer)	[6]
1998	UKPDS reports long-term metabolic effects of metformin and reduced cardiovascular risk with use	[69]
2000–2002	Extended-release formulation and fixed-dose combination drugs with metformin as the primary active ingredient are approved in the USA	[65, 67]
2002	Metformin reduced progression of 'prediabetes' (IGT and/or IFG) to T2D in the DPP	[82]
2005	The IDF recommends metformin as an initial glucose-lowering pharmacotherapy for T2D. Other guidelines adopt metformin as an initial glucose-lowering agent	[75]
2008	UKPDS follow-up: continued reduction of cardiovascular risk with use of metformin (Holman)	[74]
2011	Metformin included in WHO's essential medicines list	[79]

DPP, Diabetes Prevention Program; IDF, International Diabetes Federation; T2D, type 2 diabetes; WHO, World Health Organization

ÖVERVIKTSENHETEN för barn & ungdom

AKADEMISKA BARNSJUKHUSET

Reviews/Commentaries/ADA Statements

META-ANALYSIS

Metformin … Adolescents

Min Hae Park, msc[1]
Sanjay Kinra, md, phd[1]
Kirsten J. Ward, phd[2]

OBJECTIVE — To summarize the … bolic risk in obese children and adole…

RESEARCH DESIGN AND M… meta-analysis of randomized controll… tion in obese subjects age ≤19 years … interest include changes in BMI and …

RESULTS — Five trials met inclusi… metformin reduced BMI by 1.42 kg/m… insulin of resistance (HOMA-IR) scor…

CONCLUSIONS — Metformin ap… lin resistance in hyperinsulinemic obes… term studies in different populations a… children.

Metformin has been shown to… weight gain, hyperinsuliner… hyperglycemia in adults wit… diabetes (1,2) and to reduce prog… from impaired glucose tolerance to … in those without diabetes (3). These … have led to an increase in the use … formin in obese children with hyper… emia. However, obesity is not a l… indication for metformin in the U.K…

HORMONE RESEARCH IN PÆDIATRICS

Mini Review

Horm Res Paediatr 2013;80:78–85
DOI: 10.1159/000353760

Received: December 7, 2012
Accepted: June 17, 2013
Published online: July 26, 2013

Systematic Review c… Use in Obese Nondi… and Adolescents

Claudia Brufani[a] Antonino Crinò[a] Da…
Marco Cappa[a] Melania Manco[b]

[a]Endocrinology and Diabetes Unit, and [b]Scientific Direc…
Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

Key Words
Metformin · Obesity · Children · Insulin resistance

Abstract

Objective: Childhood obesity has become epider… been accompanied by an increase in prevalenc… diabetes (T2DM) in youth. Addressing obesity an… sistance by drug treatment represents a rational … the prevention of T2DM. A systematic review was … to evaluate the effectiveness of metformin i… weight and ameliorating insulin resistance in ob… betic children. ***Methods:*** A PubMed database … conducted, using 'metformin', 'obesity', 'insulin… 'children', 'adolescents' as search terms. ***Results:*** … were included in the present review. Metformin … istered for 6–12 months at a dosage of 1,000–2,0… ly, decreasing BMI by 1.1–2.7 compared with plac… style intervention alone. Concomitantly, fasting i… tance improved after metformin therapy. Pos… follow-up was performed in one study, showin… 1 year of discontinuation of therapy the decrease… appears. ***Conclusions:*** Short-term metformin tre… pears to moderately affect weight reduction … obese children and adolescents, with a conco… provement in fasting insulin sensitivity. Further s…

Clinical Review & Education

Review | COMPARATIVE EFFECTIVENESS RESEARCH

Systematic Review of the Benefits and Risks of Metformin in Treating Obesity in Children Aged 18 Years and Younger

Marian S. McDonagh, PharmD; Shelley Selph, MD; Alp Ozpinar, BS; Carolyn Foley, BA

IMPORTANCE Childhood obesity is an important public health problem with increasing prevalence. Because treatment often has limited success, new approaches must be identified.

OBJECTIVE To evaluate the effectiveness and safety of metformin for treating obesity in children aged 18 years and younger without a diagnosis of diabetes mellitus.

EVIDENCE REVIEW We included randomized clinical trials identified through searches of MEDLINE, the Cochrane Library, and ClinicalTrials.gov. Our primary outcome measure was change in body mass index (BMI, calculated as weight in kilograms divided by height in meters squared). We assessed study quality, pooled data using a random-effects model, and performed subgroup and sensitivity analyses.

FINDINGS Fourteen randomized clinical trials were eligible. For BMI, moderate-strength evidence indicated a reduction of −1.38 (95% CI, −1.93 to −0.82) from baseline compared with control at 6 months. A similar, if less dramatic, effect was observed in studies less than 6 months, but the pooled estimate from studies of 1 year of treatment was not statistically significant. Subgroup analyses indicated smaller, but significant, effects for those with baseline BMI below 35, those of Hispanic ethnicity, those with acanthosis nigricans, those who had tried and failed diet and exercise programs, and in studies with more girls or higher mean age (adolescents). Moderate-strength evidence indicated that with metformin, 26% reported a gastrointestinal event compared with 13% in control groups (relative risk, 2.05; 95% CI, 1.19-3.54), although there was no difference in discontinuations due to adverse events. No serious adverse events were reported.

CONCLUSIONS AND RELEVANCE Metformin provides a statistically significant, but very modest reduction in BMI when combined with lifestyle interventions over the short term. A large trial is needed to determine the benefits to subgroups or impacts of confounders. In the context of other options for treating childhood obesity, metformin has not been shown to be clinically superior.

JAMA Pediatr. 2014;168(2):178-184. doi:10.1001/jamapediatrics.2013.4200
Published online December 16, 2013.

Supplemental content at jamapediatrics.com

Author Affiliations: Department of Medical Informatics and Clinical Epidemiology, School of Medicine, Oregon Health & Science University, Portland, Oregon (McDonagh, Selph); School of Medicine, Oregon Health & Science University, Portland, Oregon (Ozpinar, Foley).

Corresponding Author: Marian S. McDonagh, PharmD, Department of Medical Informatics and Clinical Epidemiology, School of Medicine, Oregon Health & Science University, 3181 SW Sam Jackson Park Road, Mail Stop BICC, Portland, OR 97239 (mcdonagh@ohsu.edu).

ÖVERVIKTSENHETEN för barn & ungdom

Drug Design, Development and Therapy

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Effects of metformin extended release compared to immediate release formula on glycemic control and glycemic variability in patients with type 2 diabetes

This article was published in the following Dove Press journal:
Drug Design, Development and Therapy
16 May 2017
Number of times this article has been viewed

Giuseppe Derosa[1–4]
Angela D'Angelo[1,4]
Davide Romano[1]
Pamela Maffioli[1,5]

[1]Department of Internal Medicine and Therapeutics, Centre of Diabetes and Metabolic Diseases, [2]Centre for the Study of Endocrine-Metabolic Pathophysiology and Clinical Research, [3]Centre for Prevention, Surveillance, Diagnosis and Treatment of Rare Diseases, Fondazione IRCCS Policlinico San Matteo, [4]Laboratory of Molecular Medicine, [5]PhD School in Experimental Medicine, University of Pavia, Pavia, Italy

Purpose: The purpose of this study is to evaluate, in a randomized clinical trial, the effects of metformin immediate release (IR) compared with metformin extended release (XR) on the gastrointestinal tolerability and glycemic control.

Materials and methods: We enrolled 253 Caucasian patients with type 2 diabetes not well controlled by diet (glycated hemoglobin [HbA_{1c}] >7.0% and <8.5%). Patients were randomized to metformin IR or metformin XR for a period of 6 months at the maximum tolerated dose. The average dose of metformin IR used was 2,000±1,000 mg/day, while that of metformin XR was 1,000±500 mg/day. We evaluated body weight, HbA_{1c}, fasting and postprandial glucose, fasting plasma insulin (FPI) and homeostasis model assessment insulin resistance (HOMA-IR), lipid profile, and levels of some adipocytokines, including tumor necrosis factor-α (TNF-α), high-sensitivity C-reactive protein (hs-CRP), visfatin, and vaspin. Moreover, at the baseline and after 6 months, we administered patients some validated questionnaires to assess patients' satisfaction toward treatments.

Results: After 6 months, both formulations gave a similar reduction in body weight and body mass index (BMI); however, metformin XR gave a greater improvement in glycemic control, FPI, and HOMA-IR, compared with both baseline and metformin IR. A reduction in total cholesterol (TC) and low-density lipoprotein (LDL) cholesterol was observed with metformin XR compared with IR. Levels of TNF-α, hs-CRP, and vaspin were reduced by metformin XR but not by the IR formulation. Metformin XR also raised the levels of visfatin.

Conclusion: Metformin XR formulation seems to be more effective than metformin IR in improving glyco-metabolic control, lipid profile, and levels of some adipocytokines in patients with type 2 diabetes mellitus.

Keywords: glycemic control, insulin resistance, metformin immediate release, metformin extended release

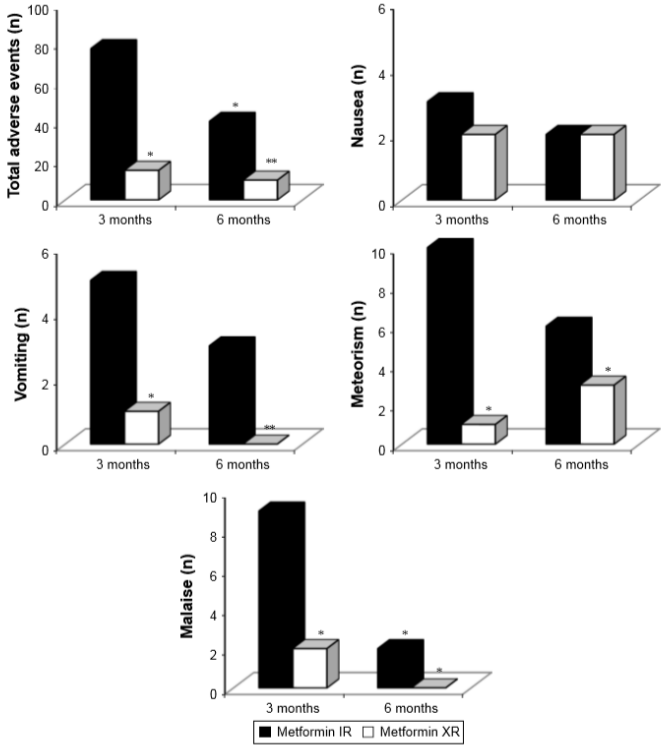


Figure 3 Adverse events with metformin immediate release and metformin extended release.
Notes: Metformin IR dosage: 2,000±1,000 mg/day; metformin XR dosage: 1,000±500 mg/day. *P<0.05 vs 3 months with IR. **P<0.01 vs 3 months with IR.
Abbreviations: IR, immediate release; XR, extended release.

Published in final edited form as:
Diabetes Obes Metab. 2015 April ; 17(4): 363–370. doi:10.1111/dom.12426.

Effects of Metformin on Energy Intake and Satiety in Obese Children

Mopelola A. Adeyemo, MPH[1], **Jennifer R. McDuffie, PhD, RD**[1], **Merel Kozlosky, MS, RD**[2], **Jonathan Krakoff, MD**[3], **Karim A. Calis, PharmD, MPH**[1], **Sheila M. Brady, MSN, CFNP**[1], and **Jack A. Yanovski, MD, PhD**[1]

[1]Program in Developmental Endocrinology and Genetics, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health

[2]Nutrition Department, Clinical Center, National Institutes of Health

[3]Phoenix Epidemiology and Clinical Research Branch, National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)

Abstract

Aims—Metformin's ability to promote weight loss is believed to be at least partly attributable to decreased energy consumption. There are few data regarding the effects of metformin on energy intake in children. We therefore investigated metformin's effects on appetite and energy intake in obese hyperinsulinemic children.

Materials and Methods—We conducted a 6-month randomized, double-blind, placebo-controlled trial to evaluate the effects of metformin 1000mg BID on body weight and energy balance in 100 obese hyperinsulinemic children aged 6–12y. Subjects ate *ad libitum* from standardized food arrays on two separate occasions before, and then again after, 6 months of study medication. The first test meal was consumed after an overnight fast. The second was preceded by a pre-meal load. For each test meal, energy intake was recorded, and subjects completed scales of hunger, fullness, and desire to eat.

Results—Data from the meal studies at baseline and after treatment with study medication were available for 84 children (45 metformin-treated and 39 placebo-treated). Compared with placebo, metformin treatment elicited significant reductions from baseline in adjusted mean energy intake after the pre-meal load (metformin: −104.7±83.8 kcal vs. placebo: +144.2±96.9 kcal; p=0.034) independent of changes in body composition. Metformin also significantly decreased ratings of hunger (−1.5±5.6 vs. +18.6±6.3; p=0.013) and increased ratings of fullness (+10.1±6.2 vs. −12.8±7.0; p=0.01) following the pre-meal load.

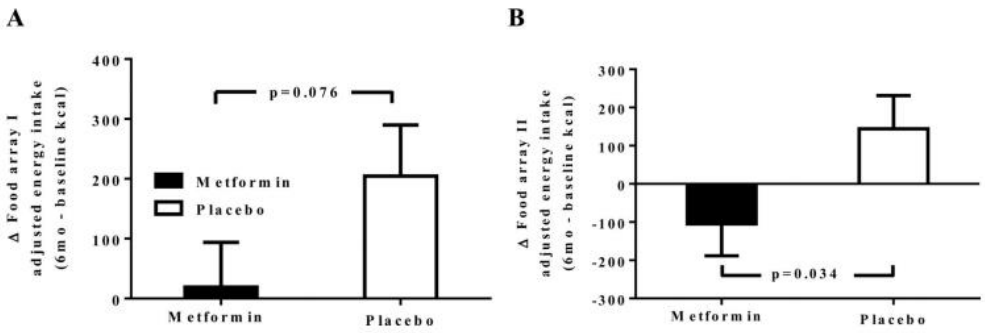


Figure 1.
Change in energy intake from baseline to 6 months of treatment adjusted for changes in body composition for Food Array I (Fig 1A, after an overnight fast) and Food Array II (Fig 1B, after a pre-load shake-like beverage). Mean ± SEM of the change in food intake is shown.

New mechanisms of metformin action: Focusing on mitochondria and the gut

Kyu Yeon Hur, Myung-Shik Lee*

Division of Endocrinology & Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Keywords
Autophagy, Gut, Mitochondria

***Correspondence**
Myung-Shik Lee
Tel.: +82-2-3410-3436
Fax: +82-2-3410-6491
E-mail address: mslee0923@skku.edu

J Diabetes Investig 2015; 6: 600–609

doi: 10.1111/jdi.12328

ABSTRACT

The most well-known mechanism of metformin action, one of the most commonly prescribed antidiabetic drugs, is adenosine monophosphate-activated protein kinase activation; however, recent investigations have shown that adenosine monophosphate-activated protein kinase-independent pathways can explain some of metformin's beneficial metabolic effects as well as undesirable side-effects. Such novel pathways include induction of mitochondrial stress, inhibition of mitochondrial shuttles, alteration of intestinal microbiota, suppression of glucagon signaling, activation of autophagy, attenuation of inflammasome activation, induction of incretin receptors and reduction of terminal endoplasmic reticulum stress. Together, these studies have broadened our understanding of the mechanisms of antidiabetic agents as well as the pathogenic mechanism of diabetes itself. The results of such investigations might help to identify new target molecules and pathways for treatment of diabetes and metabolic syndrome, and could also have broad implications in diseases other than diabetes. Accordingly, new antidiabetic drugs with better efficacy and fewer adverse effects will likely result from these studies.

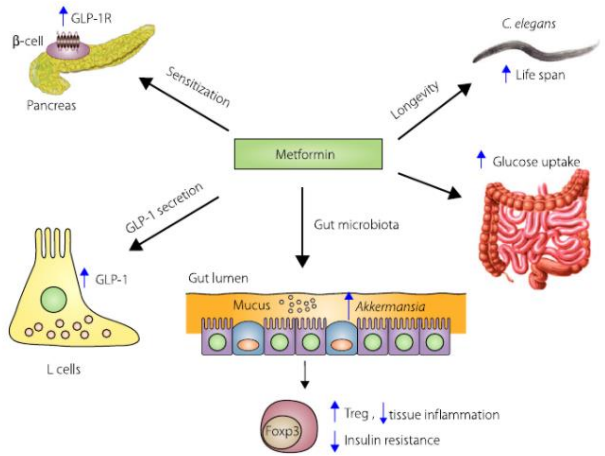
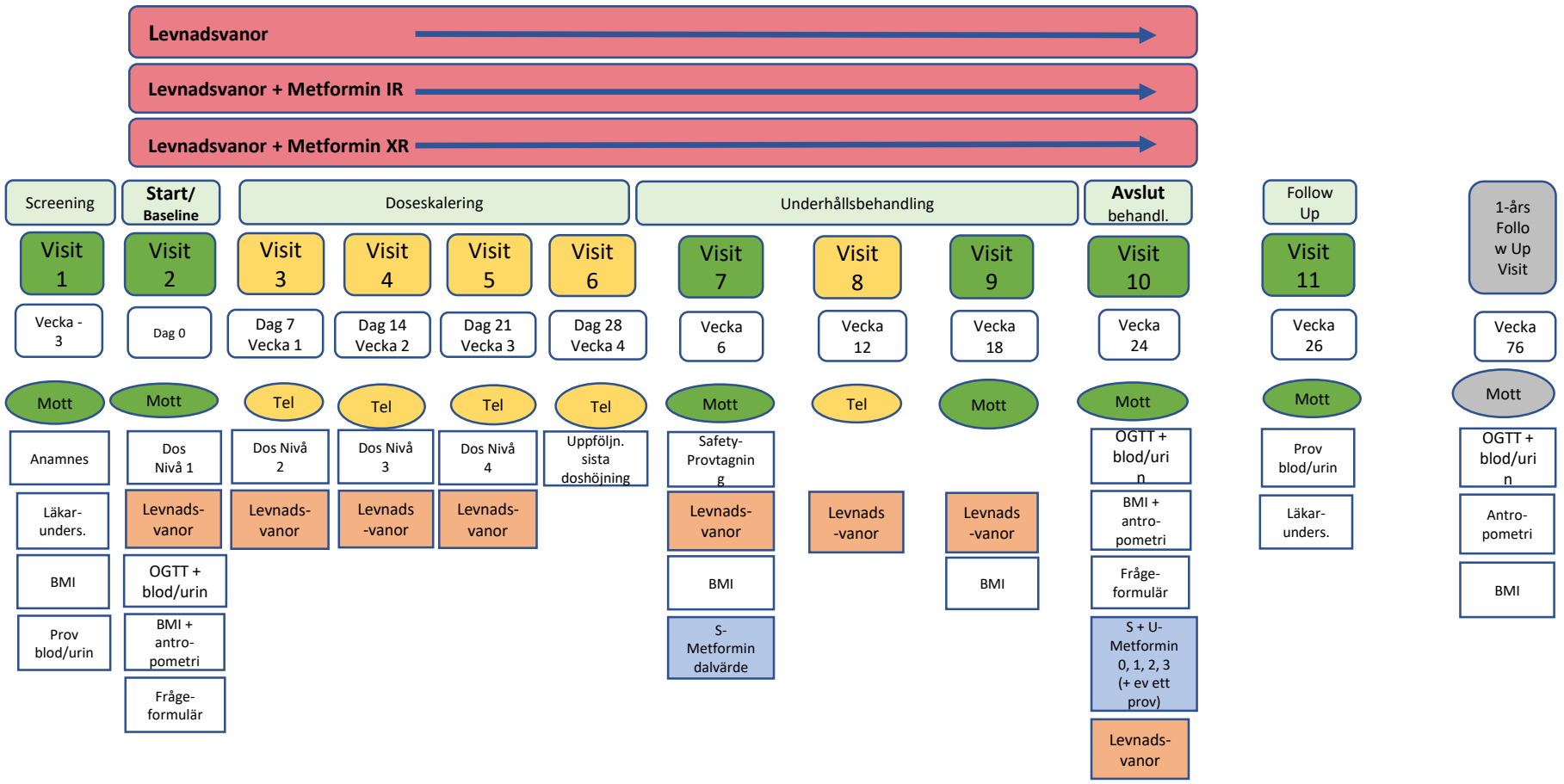
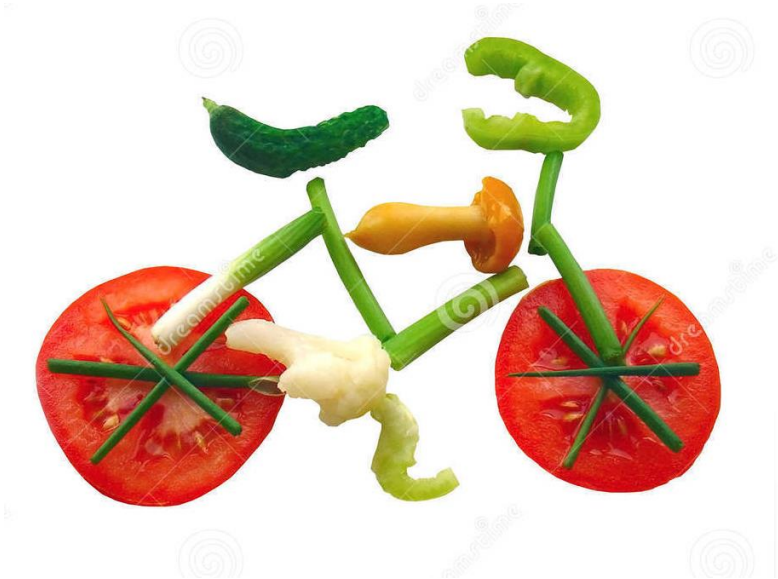


Figure 2 | Effects of metformin on the gut. Metformin induces glucagon-like peptide 1 (GLP-1) release from intestinal L cells, and also GLP-1 receptor expression on pancreatic β-cells. Metformin increases the abundance of *Akkermansia*, a mucus-degrading Gram-negative bacteria, in the gut, which is associated with restoration of reduced regulatory T (Treg) cells and amelioration of low-grade tissue inflammation in the adipose tissue of obese animals. Increased life span of *Caenorhabditis elegans* by metformin has also been attributed to changes in intestinal microbiota. The intestine is a major organ responsible for uptake and utilization of glucose after metformin administration.

Studieupplägg ”MINT”



Levnadsvanor

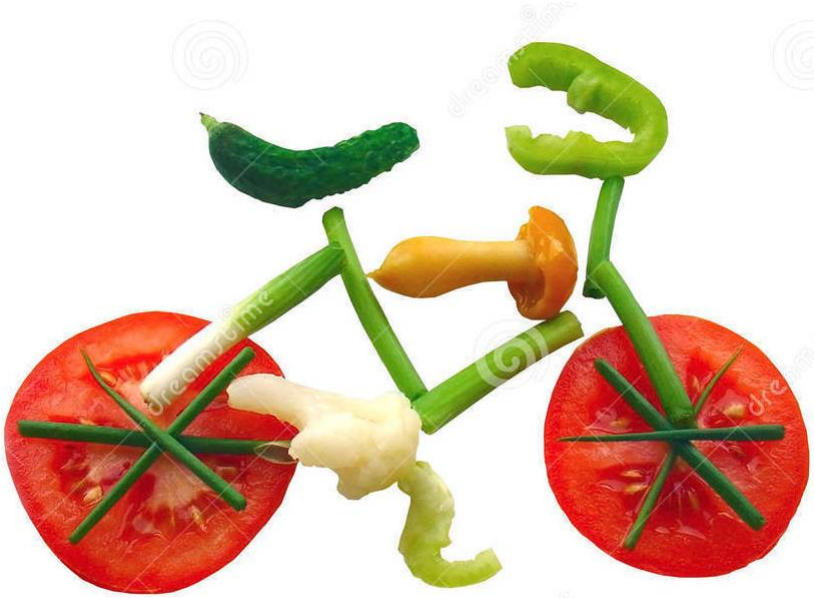


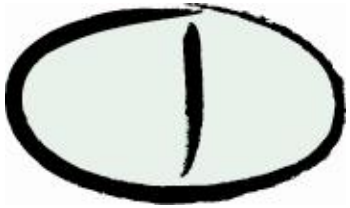
Motiverande samtal

KBT

Lösningsfokuserad familjeterapi

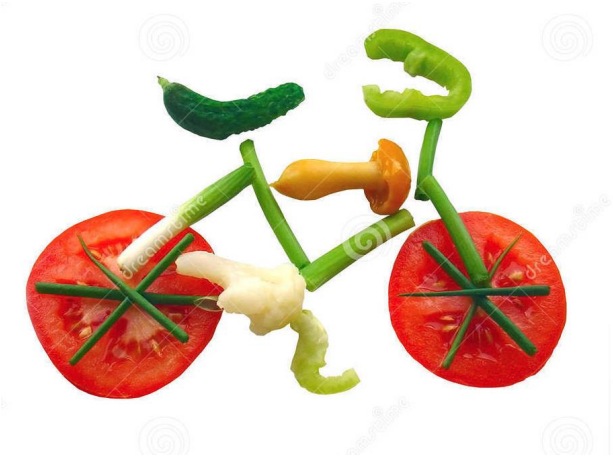
Levnadsvanor + läkemedel

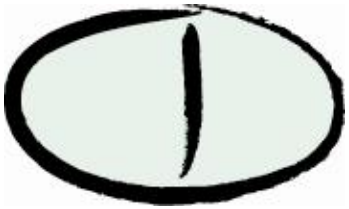




AKADEMISKA BARNSJUKHUSET

Levnadsvanor + läkemedel + operation





ÖVERVIKTSENHETEN för barn & ungdom

Sammanfattning

- Obesitas är en kronisk sjukdom
- Undersök orsaker/svårighet/möjligheter till att förändra levnadsvanor
- Undersök faktorer som,
  - Psykologisk
  - Stress
  - Familj
- Rätt läkemedel till rätt person gör det möjligt att genomföra levnadsvane förändringen
- Teamarbete (läkare, dietist, fysioterapeut, psykolog)

AKADEMISKA BARNSJUKHUSET

Tack!

ÖVERVIKTSENHETEN
för barn & ungdom

Obesitas mottagningen
För barn och ungdomar

ÖVERVIKTSENHETEN
för barn & ungdom