GLP-1 behandling til 12-18 årige børn og unge med overvægt. Indikationer og behandlingsstrategi.

Jens-Christian Holm

Consultant in Paediatrics, PhD, Associate Clinical and Research Professor,
Head of Research and The Children's Obesity Clinic,

European Centre of Management (COM) and

The Danish Childhood Obesity Biobank
Department of Paediatrics
Copenhagen University Hospital Holbæk, Denmark

and

The Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, Denmark

Co-chair of The Childhood Obesity Task Force (EASO)

Årskonference Holbæk modellen

7 September 2021 Hotel Nyborg Strand

ECO ONLINE 2021
28TH EUROPEAN CONGRESS ON OBESITY
10-13 MAY, 2021

EASO

European Association for the Study of Obesity

EASO Collaborating Centres for Obesity Management (COMs)
Paediatric Section

Centre: **The Children's Obesity Clinic, Copenhagen University Hospital Holbæk, Denmark**
Contact: **Jens-Christian Holm**

We would like to take this opportunity to thank you for submitting an application for your centre to become an EASO accredited Collaborating Paediatric Centre for Obesity Management.

Under the EASO COM scheme, paediatric obesity management centres (including university and public clinics) are accredited against a set of carefully developed criteria and in accordance with accepted European and academic guidelines, with applying centres assessed by the EASO Childhood Obesity Task Force (COTF). The COTF has completed its assessment of your centre and we are pleased to confirm that your application was successful – your centre has thus been granted EASO COM status for the three year period **1st May 2019 to 30th April 2022.**

Your centre will therefore be recognised by EASO as a leading paediatric obesity management centre in Europe throughout that period. The EASO COM network brings together accredited centres from across Europe and as a member of this network, your centre will have the opportunity to contribute to a number of important EASO projects. One of the main goals of the COM network is to develop consensus guidelines on a number of management issues, with consensus achieved via the exchange of expertise during specially convened 'Paediatric COM Summit Meetings'.

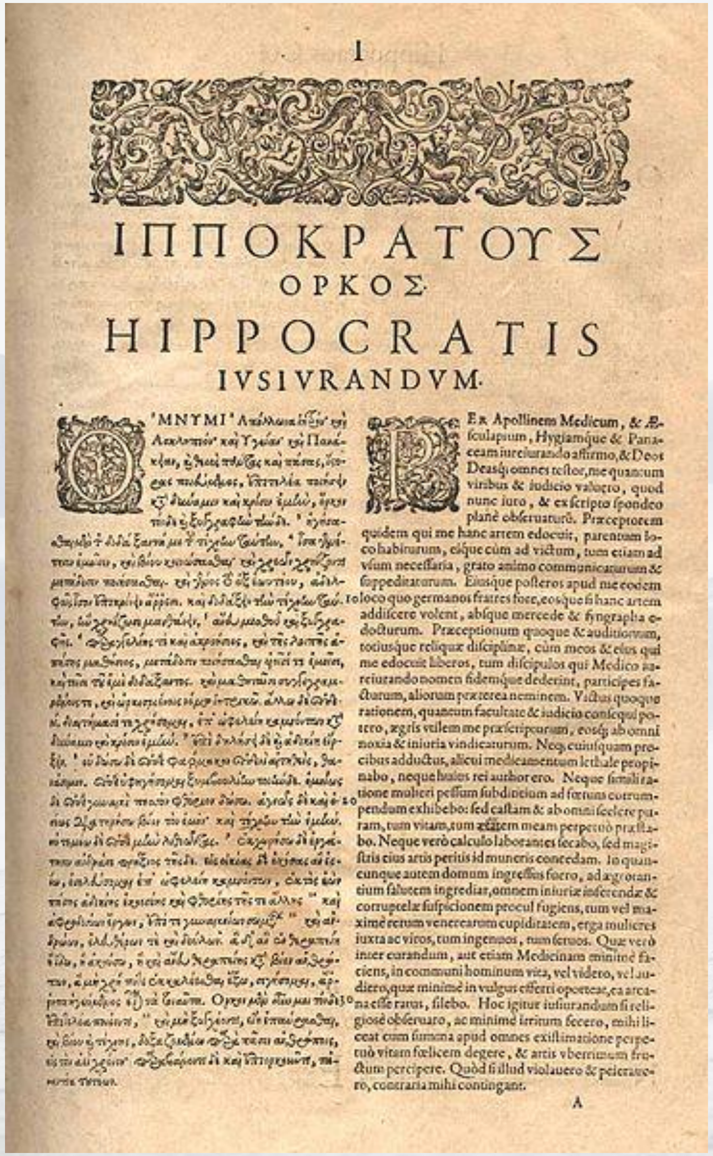
We will send further information in due course and look forward to working with you to develop the EASO Paediatric COM network and its important actions in the coming years.

With kind regards
Yours sincerely

Professor Nathalie Farpour-Lambert
President, EASO

Mr Euan Woodward
Executive Director, EASO

On behalf of the EASO COTF and Executive Committee.



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ΙΠΠΟΚΡΑΤΟΥΣ
ΟΡΚΟΣ
HIPPOCRATIS
IVSIVRANDVM.

Per Apollinem Medicum, & Aesculapium, Hygiamque & Panaceam iureiurando affirmo, & Deos Deasq; omnes testor, me quantum viribus & iudicio valuero, quod nunc iuro, & ex scripto spondeo planè obseruaturũ. Praeceptorem quidem qui me hanc artem edocuit, parentum loco habiturum, eique cùm ad victum, tum etiam ad vsum necessaria, grato animo communicaturum & suppeditaturum. Eiusque posteros apud me eodem loco quo germanos fratres fore, eosque si hanc artem addiscere volent, absque mercede & syngrapha edocturum. Praeceptionum quoque & auditionum, totiusque reliquae disciplinae, cùm meos & eius qui me edocuit liberos, tum discipulos qui Medico iureiurando nomen fidemque dederint, participes facturum, aliorum praeterea neminem. Victus quoque rationem, quantum facultate & iudicio consequi potero, aegris vtilem me praescripturum, eosq; ab omni noxia & iniuria vindicaturum. Neq; cuiusquam precibus adductus, alicui medicamentum lethale propinabo, neque huius rei author ero. Neque simili ratione mulieri pessum subditicium ad foetum corrumpendum exhibebo: sed castam & ab omni scelere puram, tum vitam, tum artem meam perpetuò praestabo. Neque verò calculo laborantes secabo, sed magistris eius artis peritis id muneris concedam. In quamcunque autem domum ingressus fuero, ad aegrotantium salutem ingrediar, omnem iniuriae inferendae & corruptelae suspicionem procul fugiens, tum vel maximè rerum venerearum cupiditatem, erga mulieres iuxta ac viros, tum ingenuos, tum seruos. Quae verò inter curandum, aut etiam Medicinam minimè faciens, in communi hominum vita, vel videro, vel audiero, quae minimè in vulgus efferri oporteat, ea arcana esse ratus, silebo. Hoc igitur iusiurandum si religiosè obseruaro, ac minimè irritum fecero, mihi liceat cum summa apud omnes existimatione perpetuò vitam foelicem degere, & artis vberrimum fructum percipere. Quòd si illud violauero & peierauero, contraria mihi contingant.

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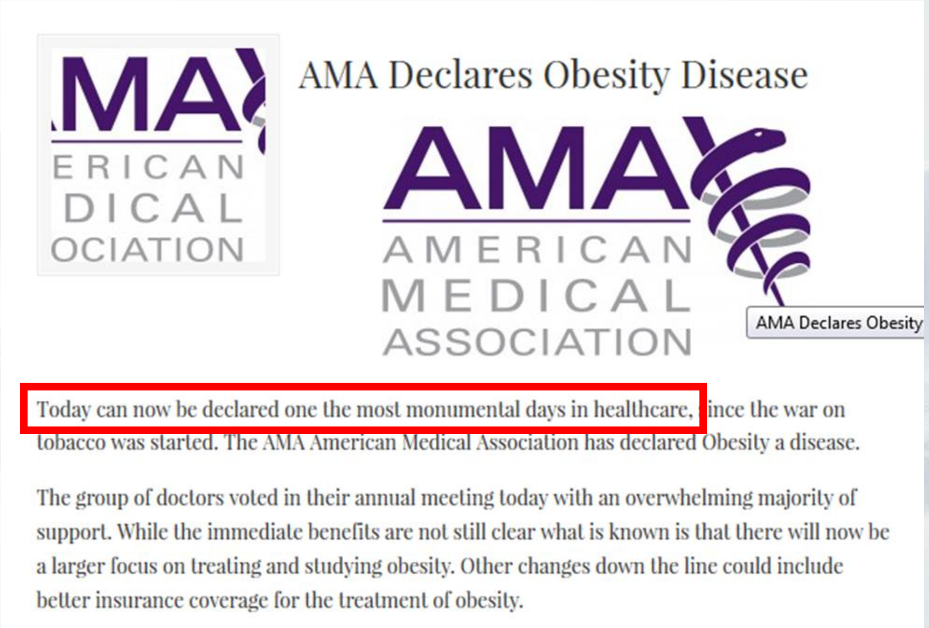

AMA Declares Obesity Disease

Today can now be declared one the most monumental days in healthcare, since the war on tobacco was started. The AMA American Medical Association has declared Obesity a disease.

The group of doctors voted in their annual meeting today with an overwhelming majority of support. While the immediate benefits are not still clear what is known is that there will now be a larger focus on treating and studying obesity. Other changes down the line could include better insurance coverage for the treatment of obesity.

Obesity Facts
The European Journal of Obesity

Obes Facts 2015;8:342–349
DOI: 10.1159/000441483
Received: May 11, 2015
Accepted: September 4, 2015
Published online: October 16, 2015

Clinical Information

Childhood Obesity Is a Chronic Disease Demanding Specific Health Care – a Position Statement from the Childhood Obesity Task Force (COTF) of the European Association for the Study of Obesity (EASO)

Nathalie J. Farpour-Lambert[a] Jennifer L. Baker[b, c] Maria Hassapidou[d] Jens Christian Holm[e] Paulina Nowicka[f] Grace O'Malley[g] Ram Weiss[h]

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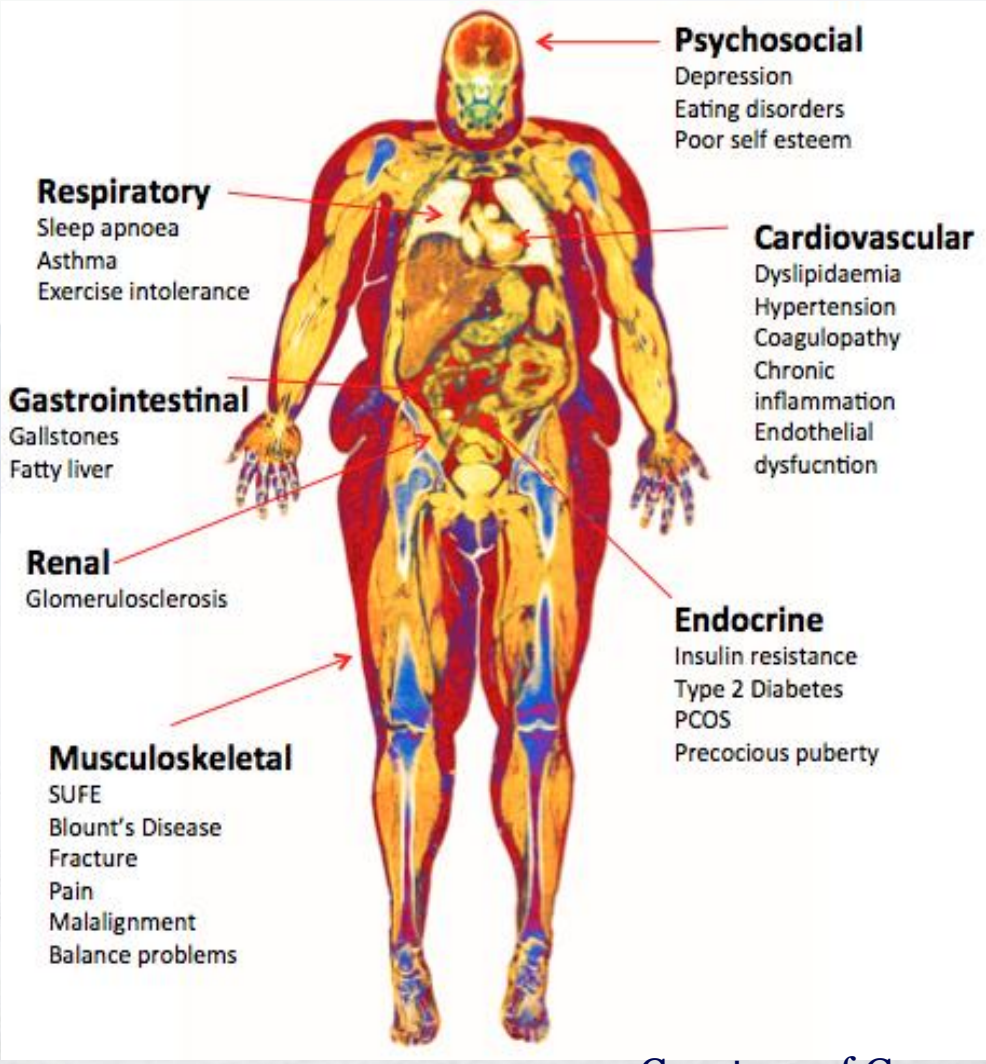
Obesity related Complications



Courtesy of Grace O'Malley, PhD, The Children's University Hospital, Dublin, Ireland

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Change in Overweight from Childhood to Early Adulthood and Risk of Type 2 Diabetes

Lise G. Bjerregaard, Ph.D., Britt W. Jensen, Ph.D., Lars Ängquist, Ph.D., Merete Osler, D.M.Sc., Thorkild I.A. Sørensen, D.M.Sc., and Jennifer L. Baker, Ph.D.

CONCLUSIONS Childhood overweight at 7 years of age was associated with increased risks of adult type 2 diabetes only if it continued until puberty or later ages.

N Engl J Med 2018;378:1302-12.
DOI: 10.1056/NEJMoa1713231

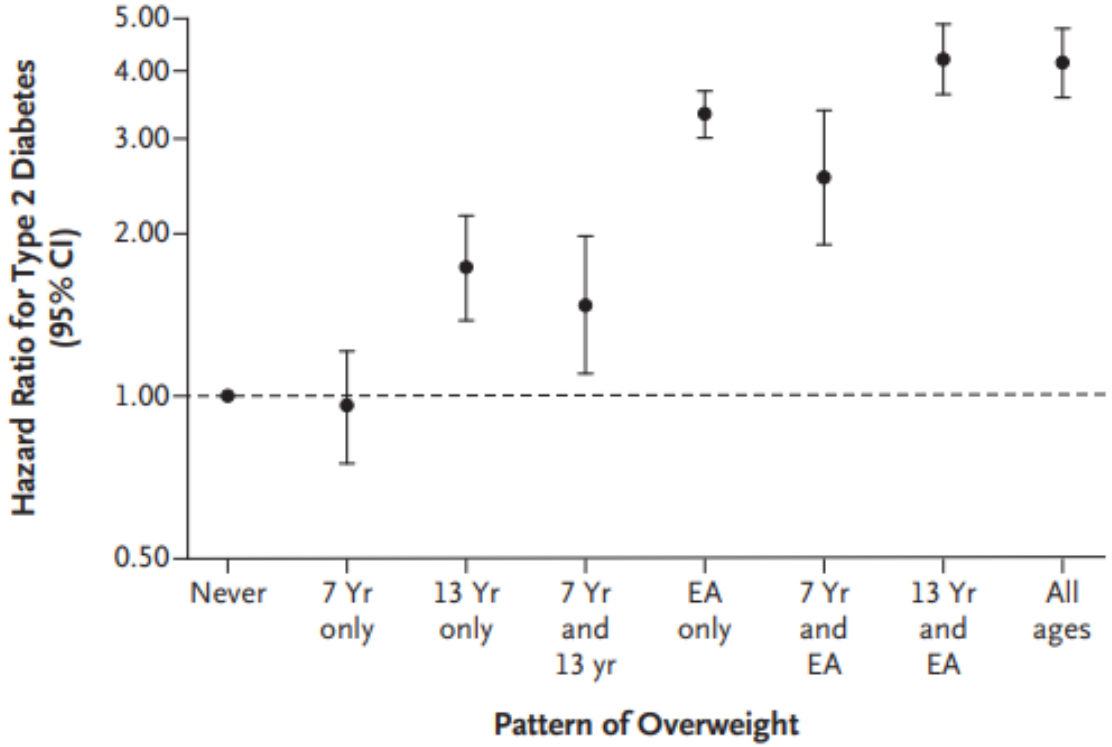
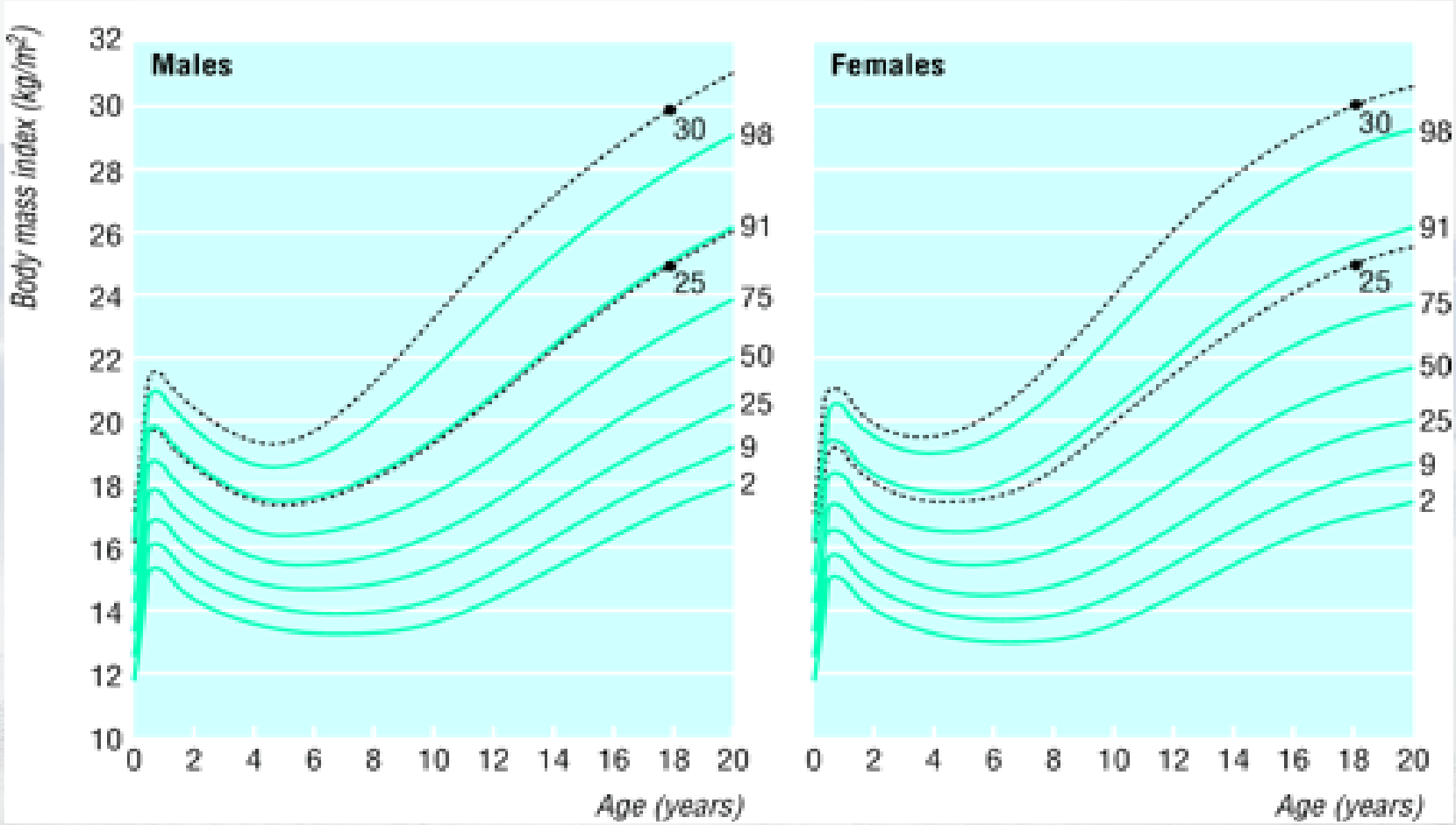


Figure 1. Patterns of Overweight at 7 Years of Age, 13 Years of Age, and Early Adulthood (EA) and the Risk of Type 2 Diabetes at 30 to 60 Years of Age.

In the calculation of hazard ratios for the development of type 2 diabetes, men who had not been overweight at any of the ages examined were used as the reference group. When Bonferroni corrections were applied, overweight only at the ages of 7 and 13 years was no longer significantly associated with an increased risk of type 2 diabetes (unadjusted P=0.01; number of tests, 7; P=0.07 with Bonferroni correction applied [7×0.01]), whereas all other significant associations remained significant. CI denotes confidence interval.

Definition of obesity



Danish clinical guidelines for examination and treatment of overweight and obese children and adolescents in a pediatric setting

Anders Johansen, Jens-Christian Holm, Seija Pearson, Mimi Kjærsgaard, Lone Marie Larsen, Birgitte Højgaard, Dina Cortes

This guideline by the Obesity Committee within The Danish Paediatric Society has also been approved by the Committees for Endocrinology, Gastroenterology, Cardiology, Neonatology and Nephro-urology within The Danish Paediatric Society, Danish Paediatricians Organization, The Danish Society for Diabetes in Childhood and The Danish Association for the Study of Obesity.
The Danish College of General Practitioners supports the referral criteria for pediatric evaluation. November 28, 2014.

Correspondence: Anders Johansen, Department of Growth and Reproduction, Copenhagen University Hospital Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen, Denmark

E-mail: Anders.johansen.01@regionh.dk

Dan Med J 2015;62(5):C5024

ly among the youngest boys (11). Furthermore, recent data shows an approximately 10% prevalence of overweight and obesity among preschool children (12). In the Funen birth cohort from 2001, the prevalence of obesity in children was 1.9% of the children aged 2.5-3.5 years; 2.5% of those aged 3.5-4.5 years; and 2.5% in the group aged 4.5-5.5 years (12). In Copenhagen in 2007, the prevalence of obesity in 5-8 year old girls and boys was 3.7% and 2.6% respectively, whilst in 14-16 year old girls and boys, it was 4.7% and 4.2% respectively (13). In the 2010 "Schoolchildren Study" comprising a random sample of schools in Denmark 2-3% of the children aged 11, 13 and 15 years were obese based on a BMI calculated from the children's self-reported height and weight (14).

It may seem discouraging, that a previous Cochrane review has

Indication for evaluation and treatment of obesity

Iso BMI of 30 (Obesity)

or

Iso BMI of 25 (Overweight) and one of the following complications

Complicated obesity 1

- Suspision of specific medical cause
- Dyscrine features
- Slow height growth
- Late psychomotoric development
- Persistent overeating / ”binge-eating” and search of food
- Rapidly increasing BMI

Complicated obesity 2

- Other complications; hypertension, dyslipidemia, elevated liver enzymes, insulin resistence, prediabetes, T2DM, PCOS, obstructive sleep apnoa.
- Familial disposition for 2 or more of; T2DM, hypertension, dyslipidemia, metabolic syndrome, heart disease, obesity

Symptoms

- Sleep, snoring apnea
- Shorter sleep time, daytime sleepiness
- Headeaches
- Shortness of breath, excercise intolerance, wheezing, cough
- Vague recurrent abdominal pains
- Heartburn, dysphagia, regurgitation, chestpain, epigastric pain
- Abdominal pain, distension, flatulence, fecal soiling, enuresis, encopresis
- Upper right quadrant pain, clicky pains, epigastric pains, vomiting
- Polyuria, polydipsia
- Oligomenorhea, dysfunctional uterine bleeding
- Hip, groin pains, painful or waddling gait
- Knee pain
- Foot pain
- Flat affect or sad mood, loss of interest/pleasure, worries/fears
- Body dissatisfaction, school avoidance, poor selfesteem, social problems, isolation
- Hyperphagia, eating out of control, binge, bulimia
- Striae, rash, irritation, acne, pigmentation

History 1

- Pregnancy, delivery, breast feeding, early growth
- Other diseases, antibiotics, obesity debut, earlier treatment
- Predisposition to obesity, hypertension, dyslipidemia, type 2 diabetes, cardiovascular disease , obesity
- Etnicity / consanguinity with risk of disease
- Headache, ((pseudo)tumor cerebri, hypertension), daily somnolence and snorring (sleep apnoa)
- Stomach pains (constipation, psychogene, gall bladder stones, steatosis)
- Pains in hip/knees/ancles (epifysiolyse, arthrosis, fractures)
- Girls after menarche; irregular menstruation and/or hirsutism (polycystic ovaria syndrome)

History 2

- Nutrition and excercise; quality, frequencies, amounts (specific questioning) including organised/unorganised
- Medications (glucocorticoids, psychopharmaci, thyroid function)
- Addictions (tobacco increase insulin-resistence and risk of cardiovascular disease, alcohol can increase caloric intake)
- Social setting; school attendence, thriving, bullying, family structure and dynamics, school transportation,
- Sleep history. Apnea, sleep duration
- Psychosocial; depression, low self esteem, anxiety, bullying, isolation, inactivity

Examination 1

- Height and weight, calculation of BMI (changes herein)
- Waist circumference (evaluation of treatment response). Between hip and ribs. Important to measure with same technique
- Height and weight according to growth curves
- Calculation of target height according to genetic (parental) potential i.e. Girls; mean of parental height minus 6,5 cm and Boys; mean of parental height minus 6,5 cm
- Is the patient growing according to target height?
- Most children with simple obesity have a height at or above their target percentile for height and normal or advanced boneage

Examination 2

- Low height for age and overweight/obesity raise suspision and medical concern of syndromes, chromosomal, and endocrinological evaluation
- Puberty staging a.m. Tanner, hirsutism
- Blood pressure (appropriate cuff, sitting position with support under the feet, laying down after 10 minutes rest, measurement repeated 3 times (until there is less than 5 mm Hg difference between the 2 latter measurements). If hypertensive; manuel blood pressure measurement recommended and or 24 hour blood pressure surveilance

Examination 3

- Quality of life evaluation
- Adapted neurological examination (pathology in the hypothalamic area)
- Acantosis nigricans with special attention towards the neck, axilla, and inguinal (often associated with insulin resistence)
- Striae, infections, psoriasis, HS

Blood sampling

- Thyroid status; TSH, fT4, fT3
- Sugar status; HbA1c, blood sugar, maybe insulin
- Lipids; total cholesterol and fractions, triglycerides
- Liver enzymes; ALAT, alkaline phosphatase, bilirubin, GGT
- Calcium metabolism; PTH, ionised calcium, phosphate, albumin, and vitamine D
- If blood sampling is not taken in the fasting condition and shows elevated lipids or sugar status, then repeated in the fasting condition

Body composition

- DEXA scan (optimal)
- Alternatively impedance
- Measurement of fat and fat free mass and changes herein
- MRS

Special findings with indication for further evaluation 1

- Syndromatic obesity; Karyotype, Prader Willi syndrome, Bardet Biedel. Suspicion of monogenic obesity; MC4R (melanocortin 4 receptor), leptin and leptin receptor and others demands specific genetic investigations
- Hypertensio arterialis; elaborate as hypertensive patients according to guideline

Special findings with indication for further evaluation 2

- Vitamine D insufficiency; according to guideline
- Prediabetes; HbA1c at 5,7-6,4% (39-47 mmol/mol) or several blood sugars between 5,6–6,9 mmol/l or an OGTT 7,8-11,0 mmol/l should be referred to paediatric diabetologist

Special findings with indication for further evaluation 3

- Pubertas praecox
- Pubertas tarda
- Hirsutism or irregular menses; Blood for 17-OH-Progesterone, testosterone, oestradiol, LH, FSH, and or ultrasonic evaluation of ovaries for PCOS
- Non-alcoholic steatosis; MR-spectroskopy or US
- Astma or other respiratory symtoms; spirometry
- Sleep apnoea; sleep investigation

Special findings with indication for further evaluation 4

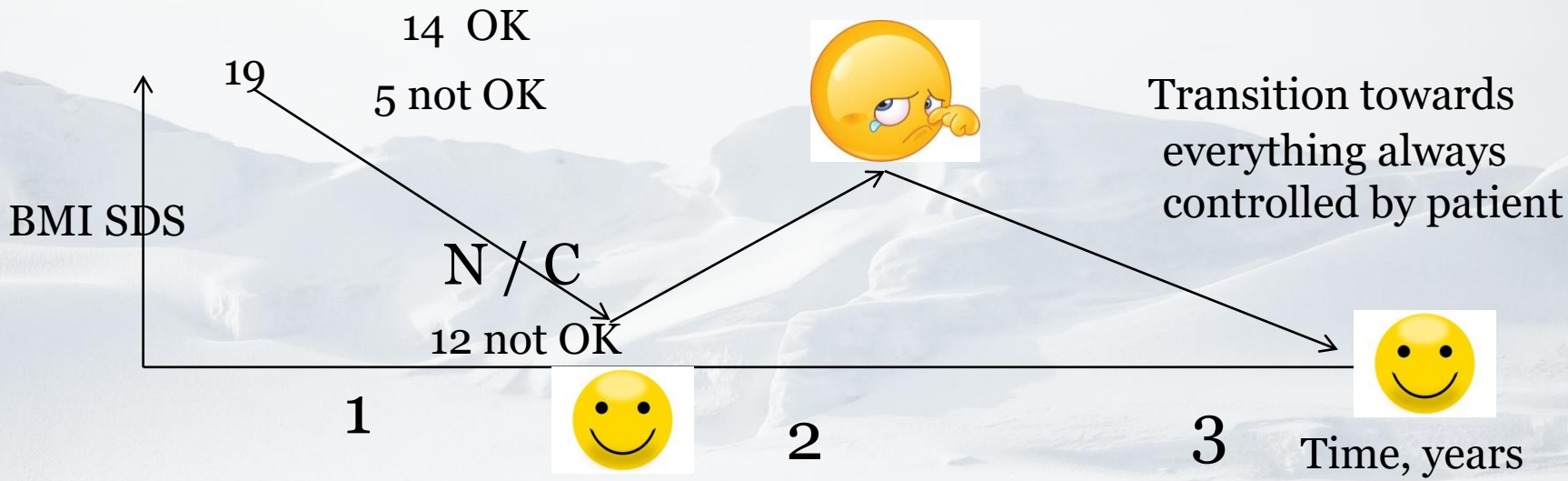
- Lower extremities; pains and limited mobility; X-ray and relevant examination
- Rapidly developing obesity; think prolactin, ACTH, morning-cortisol and urine-cortisol (x 3 if possible), MR-scan of brain
- Low quality of life scoring; think contact to school, psychologist, or social worker
- Social difficulties/challenges; think contact to primary care, social worker, or psychologist

Follow-up assessments - during growth and development

- History, symptoms, physical examination
- Degree of overweight/obesity, body composition
- Obesity related complications
- Quality of life
- Adherence to treatment
- Life functionality
- Genetic testing
- Guidance and care

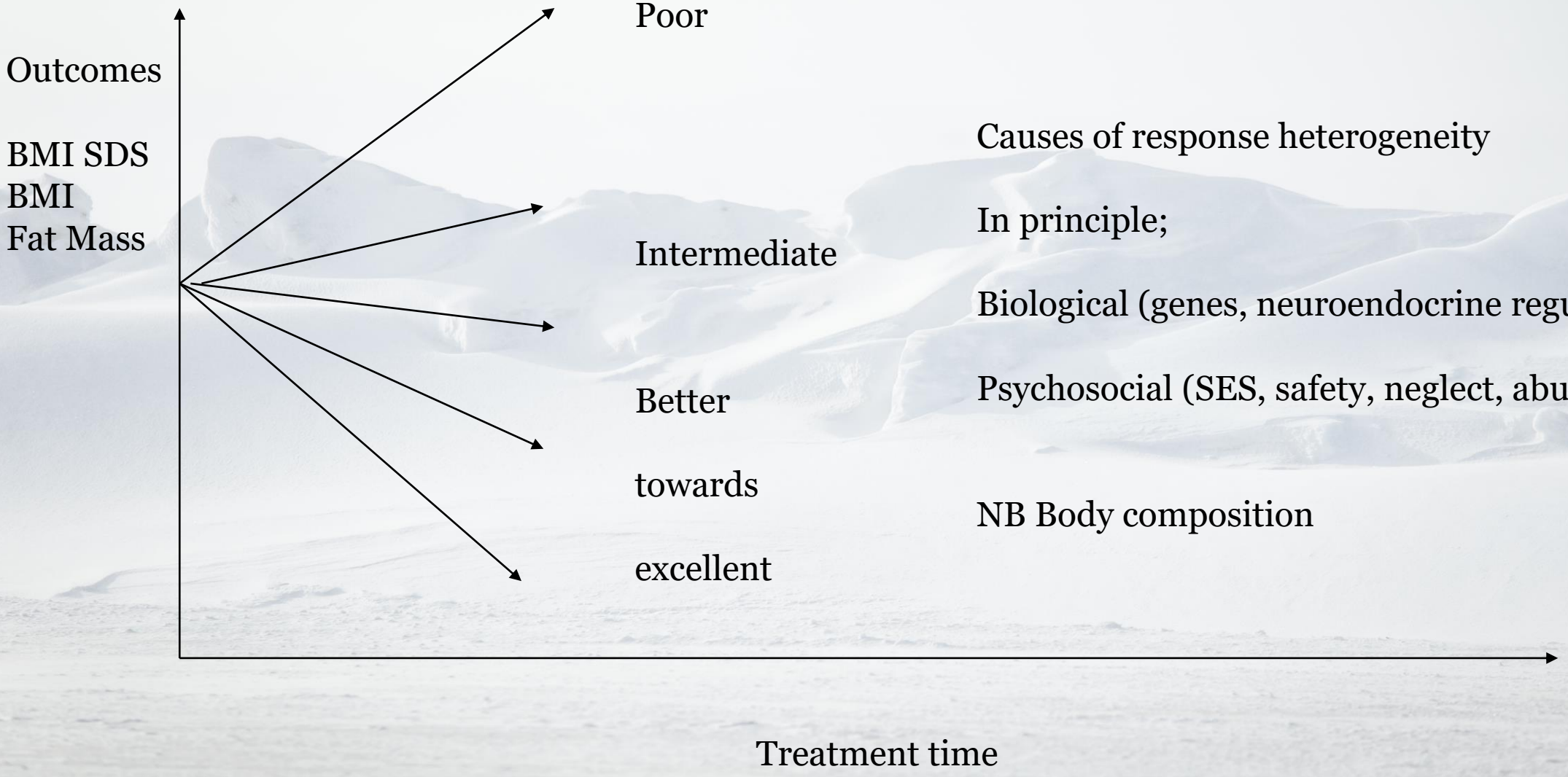
Dynamics of weight loss

Expected treatment outcome, process development



- Phase 1; weight loss by treatment plan
- Phase 2; compliance/ adaptation against weight loss
- Phase 3; realizing your reality and treatment need
- Induce process development within the family

Fat mass regulation
- expected treatment heterogeneity i.e. treatment responses



Causes of response heterogeneity

In principle;

Biological (genes, neuroendocrine regulation etc) or

Psychosocial (SES, safety, neglect, abuse etc)

NB Body composition

Novo Nordisk press release
26 March 2021

- Committee for Medicinal Products for Human Use (CHMP) European Medicines Agency has recommended the use of Saxenda® is expanded for the treatment of obesity in adolescents aged 12-17 years
- CHMP opinion referred to the European Comission
- Decision in may 2021. Approved in Denmark.
- Based on safety and efficacy of Liraglutide 3.0 mg
- Dose escalation over 4-8 weeks
- Sub-cutaneous daily administration
- Adjunct to lifestyle therapy

GLP-1

- Increases postprandial insulin level in a glucose dependent manner
- Reduces glucagon secretion
- Delays gastric emptying
- Reduce appetite and energy intake
- Hypothalamic effects

THE JOURNAL OF PEDIATRICS • www.jpeds.com

Liraglutide in an Adolescent Population with Obesity: A Randomized, Double-Blind, Placebo-Controlled 5-Week Trial to Assess Safety, Tolerability, and Pharmacokinetics of Liraglutide in Adolescents Aged 12-17 Years

Thomas Danne, MD[1], Torben Biester, MD[1], Kerstin Kapitzke, MD[1], Sanja H. Jacobsen, MSc[2], Lisbeth V. Jacobsen, MSc[2], Kristin C. Carlsson Petri, PhD[2], Paula M. Hale, MD[3], and Olga Kordonouri, MD[1]

Conclusions Liraglutide had a similar safety and tolerability profile compared with adults when administered to adolescents with obesity, with no unexpected safety/tolerability issues. Results suggest that the dosing regimen approved for weight management in adults may be appropriate for use in adolescents. (J Pediatr 2016;■■:■■-■■). Trial registration ClinicalTrials.gov: NCT01789086.

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*

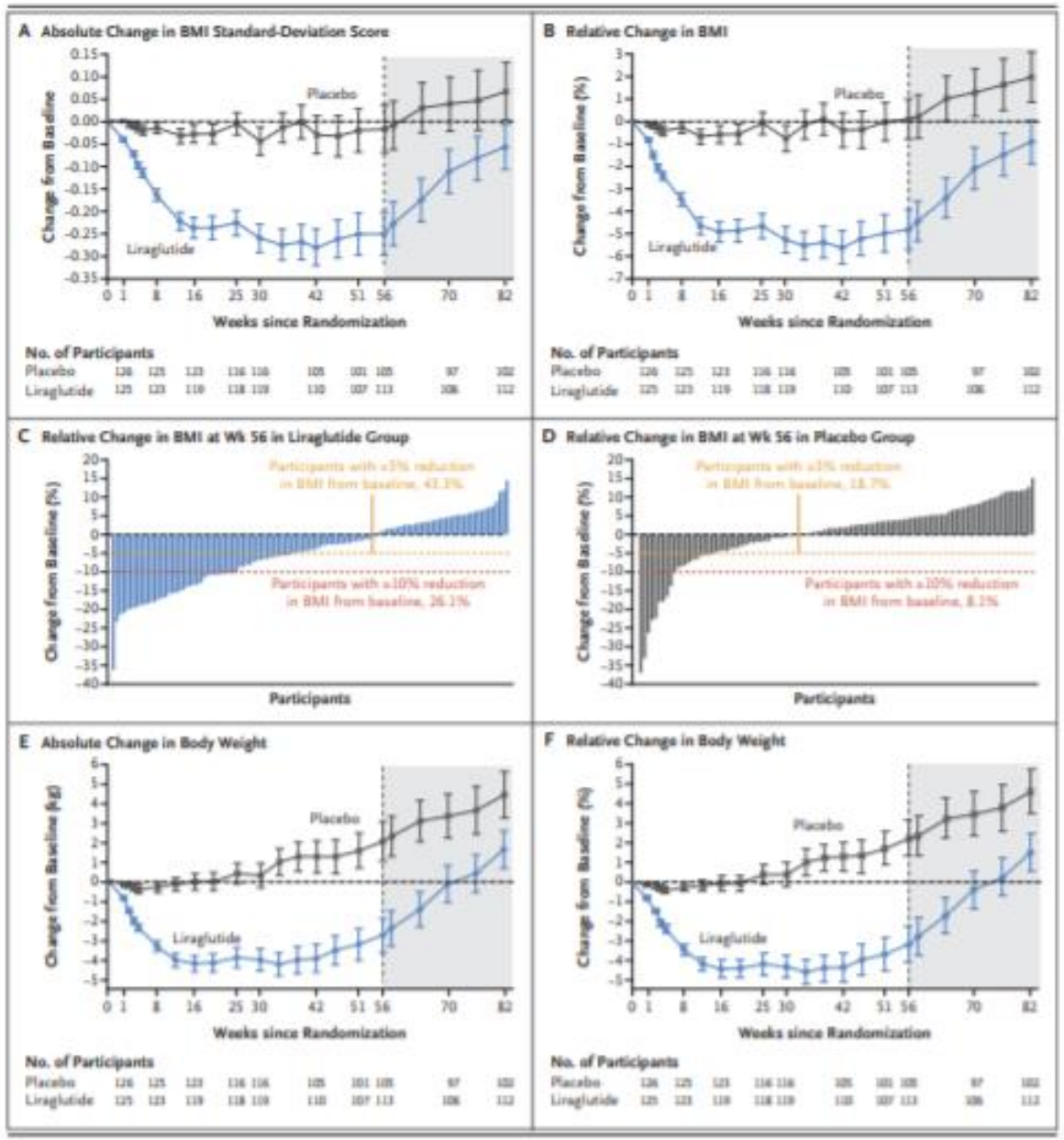
COUNSELING IN HEALTH NUTRITION AND PHYSICAL ACTIVITY

Participants received individualized counseling in healthy nutrition that was performed by a certified dietician and evaluated at every visit using a numerical rating scale.

Participants received individualized counseling in physical activity at every visit that was performed by site staff trained in physical activity counseling. Participants were encouraged to engage in 60 minutes of moderate- to high-intensity physical activity daily.

This article was published on March 31, 2020, at NEJM.org. DOI: 10.1056/NEJMoa1916038

The NEW ENGLAND JOURNAL of MEDICINE



5 participants receiving placebo (six events) dur-

Events related to psychiatric disorders oc-

Table 3. Adverse Events during the Treatment Period.*

Event	Liraglutide (N=125)			Placebo (N=126)			P Value
	no. of participants (%)	*no. of events*	*events/1000 exposure-yr*	*no. of participants (%)*	*no. of events*	*events/1000 exposure-yr*	
Any adverse events	111 (88.8)	777	6187.8	107 (84.9)	627	5018.5	0.07†
Gastrointestinal adverse events	81 (64.8)	319	2540.4	46 (36.5)	121	968.5	0.001†
Serious adverse events‡	3 (2.4)	3	23.9	5 (4.0)	6	48.0	0.72§
Adverse events that led to treatment discontinuation	13 (10.4)	19	151.3	0	0	0	<0.001§
Adverse events that occurred in ≥5% of participants							
Nasopharyngitis	34 (27.2)	68	541.5	38 (30.2)	80	640.3	0.60¶
Nausea	53 (42.4)	101	804.3	18 (14.3)	25	200.1	<0.001¶
Headache	29 (23.2)	43	342.4	35 (27.8)	53	424.2	0.41¶
Vomiting	43 (34.4)	85	676.9	5 (4.0)	8	64.0	<0.001¶
Diarrhea	28 (22.4)	44	350.4	18 (14.3)	29	232.1	0.10¶
Upper abdominal pain	17 (13.6)	25	199.1	17 (13.5)	23	184.1	0.98¶
Oropharyngeal pain	11 (8.8)	11	87.6	15 (11.9)	18	144.1	0.42¶
Influenza	11 (8.8)	11	87.6	12 (9.5)	12	96.0	0.84¶
Gastroenteritis	16 (12.8)	22	175.2	6 (4.8)	9	72.0	0.02¶
Upper respiratory tract infection	11 (8.8)	14	111.5	11 (8.7)	16	128.1	0.98¶
Abdominal pain	10 (8.0)	15	119.5	11 (8.7)	15	120.1	0.83¶
Pyrexia	10 (8.0)	11	87.6	9 (7.1)	11	88.0	0.80¶
Dizziness	13 (10.4)	15	119.5	4 (3.2)	5	40.0	0.02¶
Dysmenorrhea	4 (3.2)	5	39.8	8 (6.3)	16	128.1	0.38§
Arthralgia	3 (2.4)	3	23.9	8 (6.3)	8	64.0	0.22§
Pharyngitis	4 (3.2)	5	39.8	7 (5.6)	7	56.0	0.54§

* Adverse events and serious adverse events that occurred from week 0 through week 56 among adolescents in the safety population are included in the table and presented with their preferred terms. Events were included if the date of onset was between the first day the trial drug was administered and 14 days after the last day the trial drug was administered, at the follow-up visit, or at the last trial visit.

† The P value was calculated with a negative binomial model. The number of events was analyzed with a negative binomial model with log-link function and the logarithm of the exposure time (1000 years) for which an adverse event is considered to be reported during the treatment period as an offset. The model included treatment, sex, region, baseline glycemic category, stratification factor for Tanner stage, and interaction between baseline glycemic category and stratification factor for Tanner stage as fixed effects.

‡ The following serious adverse events were reported in one participant each: postprocedural hemorrhage, myositis, and completed suicide in the liraglutide group; and appendicitis, pneumonia, acute cholecystitis, cholelithiasis, and thrombophlebitis in the placebo group.

§ The P value was calculated by means of Fisher's exact test on the basis of the number of participants.

¶ The P value was calculated by means of Pearson's chi-square test on the basis of the number of participants.

Expected indications

- 12-17 years
- Iso BMI of 30, and or related complications
- Poor response to lifestyle alone
- Adjunct to obesity management!
- Identify those in need!
- Safety and side effects!
- Duration and cost!
- Treatment effect after termination of GLP-1!

Stopping rules

- Considerations from FDA/EMA
- 5 (or 10) % weight loss required to continue!
- Body composition during growth and development!
- Patients difficult to treat are offered suboptimal management solutions?
- Response patterns i.e. genetics GRS/PGRS
- Success criteria, move beyond BMI

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

Article Contents

CORRECTED PROOF

Fasting Plasma GLP-1 Is Associated With Overweight/Obesity and Cardiometabolic Risk Factors in Children and Adolescents

Sara E Stinson, Anna E Jonsson, Morten A V Lund, Christine Frithioff-Bøjsøe, Louise Aas Holm, Oluf Pedersen, Lars Ängquist, Thorkild I A Sørensen, Jens J Holst, Michael Christiansen, Jens-Christian Holm, Bolette Hartmann, Torben Hansen

The Journal of Clinical Endocrinology & Metabolism, dgab098,
https://doi.org/10.1210/clinem/dgab098
Published: 17 February 2021 **Article history** ▾

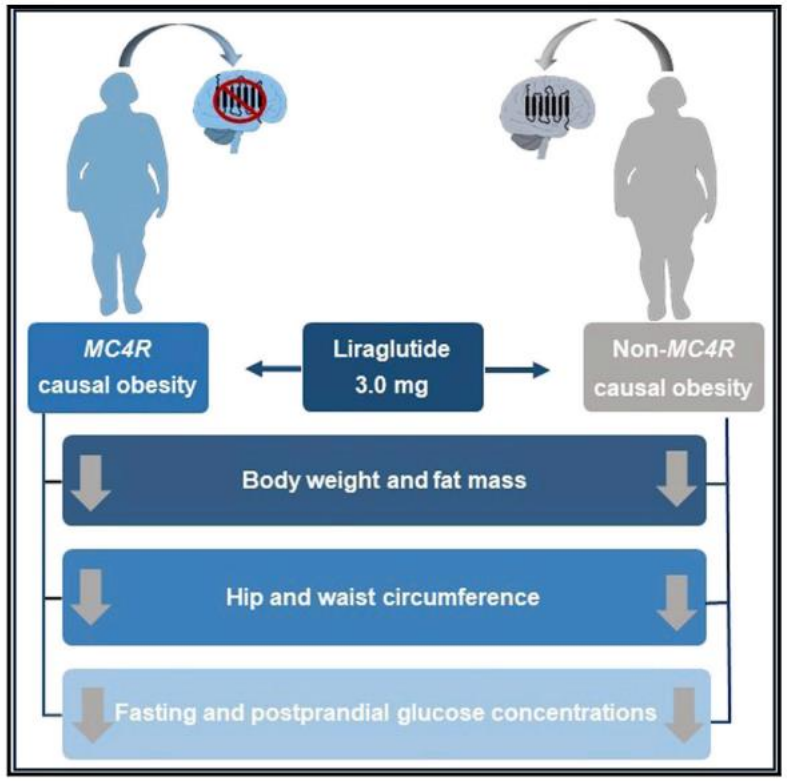
Conclusion

Overweight/obesity in children and adolescents is associated with increased fasting plasma total GLP-1 concentrations, which was predictive of higher CMR factors.

Cell Metabolism

Patients with Obesity Caused by Melanocortin-4 Receptor Mutations Can Be Treated with a Glucagon-like Peptide-1 Receptor Agonist

Graphical Abstract



Authors

Eva W. Iepsen, Jinyi Zhang, Henrik S. Thomsen, ..., Jens J. Holst, Jens-Christian Holm, Signe S. Torekov

Correspondence

epwi@sund.ku.dk (E.W.I.), torekov@sund.ku.dk (S.S.T.)

In Brief

Iepsen et al. show that the diabetes and obesity drug liraglutide, which has appetite-suppressing effects, caused weight loss in obese patients with mutations in the appetite-regulating *melanocortin-4 receptor* (*MC4R*). These results show that the appetite effects of liraglutide are independent of the MC4R pathway and offer therapeutic opportunities for patients with *MC4R* causal obesity.

Highlights

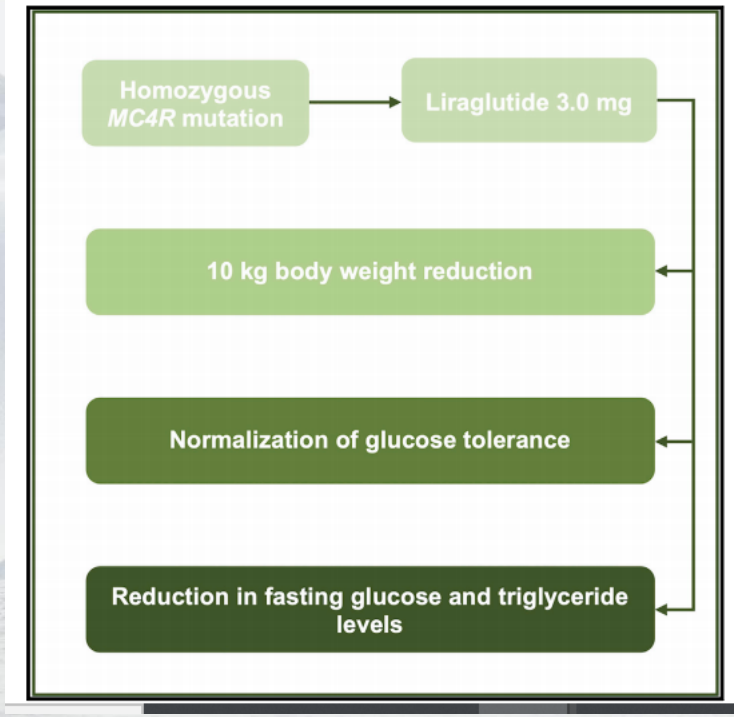
- Fully functional MC4Rs are not required for GLP-1 RA-mediated weight loss
- Liraglutide caused a 6% weight loss in patients with *MC4R* mutations and controls
- Fat mass, waist circumference, and glucose concentrations improved with treatment
- Liraglutide is an effective treatment of the most common form of monogenic obesity

Cell Reports
Medicine

Report

GLP-1 Receptor Agonist Treatment in Morbid Obesity and Type 2 Diabetes Due to Pathogenic Homozygous Melanocortin-4 Receptor Mutation: A Case Report

Graphical Abstract



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In Brief

In this case report, Iepsen et al. show that the GLP-1 RA liraglutide induces a weight loss of 10 kg and normalization of glucose tolerance in a woman homozygous for pathogenic *MC4R* mutation. Thus, the appetite-reducing effects of liraglutide are preserved in *MC4R* causal obesity and independent of the MC4R pathway.

Highlights

- Liraglutide induces weight loss in a woman homozygous for pathogenic *MC4R* mutation
- Glucose tolerance normalized and fasting glucose and triglyceride levels reduced
- MC4R is not required for GLP-1 RA-mediated weight loss
- Liraglutide is an effective treatment for the most common form of monogenic obesity

ORIGINAL ARTICLE

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

Julie R. Lundgren, M.D., Ph.D., Charlotte Janus, Ph.D., Simon B.K. Jensen, M.Sc., Christian R. Juhl, M.D., Lisa M. Olsen, M.Sc., Rasmus M. Christensen, B.Sc.Med., Maria S. Svane, M.D., Ph.D., Thomas Bandholm, Ph.D., Kirstine N. Bojsen-Møller, M.D., Ph.D., Martin B. Blond, M.D., Ph.D., Jens-Erik B. Jensen, M.D., Ph.D., Bente M. Stallknecht, M.D., D.M.Sc., Jens J. Holst, M.D., D.M.Sc., Sten Madsbad, M.D., D.M.Sc., and Signe S. Torekov, Ph.D.

CONCLUSIONS A strategy combining exercise and liraglutide therapy improved healthy weight loss maintenance more than either treatment alone.

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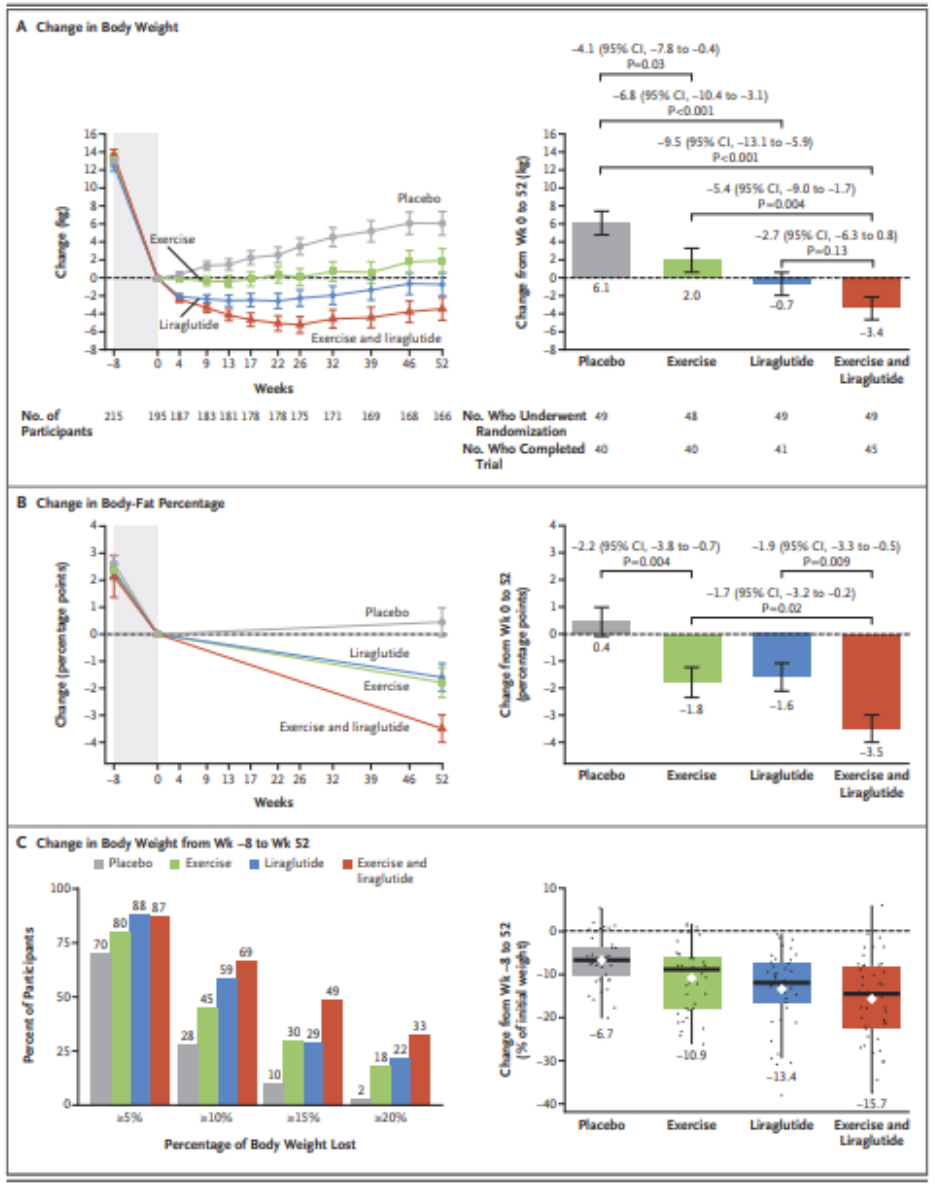

DANISH TREATMENT MODEL WORKS: 3 OF 4 CHILDREN LOSE WEIGHT AND KEEP IT OFF

Disclosures

- Lecture fees and honoraria from Novo Nordisk and Rhythm Pharmaceuticals
- Board member; Danish Association for the Study of Obesity
- Member Obesity Committe; Danish Paediatric Society
- Co-chair; The Childhood Obesity Task Force EASO
- Ex-Officio Executive Committe EASO
- Dr Holm provides training and treatment

Thank you very much for your attention

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