EASO

European Association for the Study of Obesity

EASO Summer School: Masterclass in the Prevention and Management of Obesity

Les Pensières at Fondation Mérieux, Annecy, France
11 to 15 July 2022

Treatment options

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 HOLBAEK Study (formerly; 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)

Strategies

- Multidisciplinary
- Medications
- Surgery
- Digital

Volume 120, Issue Supplement_4

December 2007

SUPPLEMENT ARTICLES | DECEMBER 01 2007

Expert Committee Recommendations Regarding the Prevention, Assessment, and Treatment of Child and Adolescent Overweight and Obesity: Summary Report

Sarah E. Barlow, MD, MPH; and the Expert Committee

Address correspondence to Sarah E. Barlow, MD, MPH, Division of Gastroenterology, Baylor College of Medicine, Te
Children's Hospital, 6701 Fannin St, Suite 1010, Houston, TX 77030. E-mail: sbarlow@bcm.tmc.edu

Pediatrics (2007) 120 (Supplement_4): S164–S192.

https://doi.org/10.1542/peds.2007-2329C **Article history**

SUPPLEMENT ARTICLE

Recommendations for Treatment of Child and Adolescent Overweight and Obesity

Bonnie A. Spear, PhD, RD[a], Sarah E. Barlow, MD, MPH[b], Chris Ervin, MD, FACEP[c], David S. Ludwig, MD, PhD[d], Brian E. Saelens, PhD[e], Karen E. Schetzina, MD, MPH[f], Elsie M. Taveras, MD, MPH[g,h]

[a]Department of Pediatrics, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama; [b]Department of Pediatrics, Saint Louis University, St Louis, Missouri; [c]Georgia Diabetes Coalition, Atlanta, Georgia; [d]Obesity Program, Division of Endocrinology, Children's Hospital Boston, Harvard Medical School, Boston, Massachusetts; [e]Departments of Pediatrics and Psychiatry and Behavioral Sciences, University of Washington–Child Health Institute, Seattle, Washington; [f]Department of Pediatrics, James H. Quillen College of Medicine, East Tennessee State University, Johnson City, Tennessee; [g]Obesity Prevention Program, Department of Ambulatory Care and Prevention, Harvard Pilgrim Health Care and Harvard Medical School, Boston, Massachusetts; [h]Division of General Pediatrics, Children's Hospital Boston, Boston, Massachusetts

The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

In this article, we review evidence about the treatment of obesity that may have applications in primary care, community, and tertiary care settings. We examine current information about eating behaviors, physical activity behaviors, and sedentary behaviors that may affect weight in children and adolescents. We also review studies of multidisciplinary behavior-based obesity treatment programs and information about more aggressive forms of treatment. The writing group has drawn from the available evidence to propose a comprehensive 4-step or staged-care approach for weight management that includes the following stages: (1) Prevention Plus; (2) structured weight management; (3) comprehensive multidisciplinary intervention; and (4) tertiary care intervention. We suggest that providers encourage healthy behaviors while using techniques to motivate patients and families, and interventions should be tailored to the individual child and family. Although more intense treatment stages will generally occur outside the typical office setting, offices can implement less intense intervention strategies. We not ony address specific patient behavior goals but also encourage practices to modify office systems to streamline office-based care and to prepare to coordinate with professionals and programs outside the office for more intensive interventions.

www.pediatrics.org/cgi/doi/10.1542/peds.2007-2329F

doi:10.1542/peds.2007-2329F

Key Words
obesity, treatment

Abbreviations
GI—glycemic index
PSMF—protein-sparing modified fast
CDC—Centers for Disease Control and Prevention
FDA—Food and Drug Administration
CE—consistent evidence
ME—mixed evidence

Accepted for publication Aug 31, 2007

Dr Barlow's current affiliation is Department of Pediatrics, Baylor College of Medicine, Houston, TX.

Address correspondence to Bonnie A. Spear, PhD, RD, Department of Pediatrics, University of Alabama at Birmingham, 1600 7th Ave S, MTC 201, Birmingham, AL 35233. E-mail: bspear@peds.uab.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Obesity in Children and Adolescents
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Based on year 2000 Centers for Disease Control and Prevention growth charts, approximately 17% of children and adolescents aged 2 to 19 years in the United States have obesity, and almost 32% of children and adolescents are overweight or have obesity. Obesity in children and adolescents is associated with morbidity such as mental health and psychological issues, asthma, obstructive sleep apnea, orthopedic problems, and adverse cardiovascular and metabolic outcomes (eg, high blood pressure, abnormal lipid levels, and insulin resistance). Children and adolescents may also experience teasing and bullying behaviors based on their weight. Obesity in childhood and adolescence may continue into adulthood and lead to adverse cardiovascular outcomes or other obesity-related morbidity, such as type 2 diabetes.

SUBPOPULATION CONSIDERATIONS Although the overall rate of child and adolescent obesity has stabilized over the last decade after increasing steadily for 3 decades, obesity rates continue to increase in certain populations, such as African American girls and Hispanic boys. These racial/ethnic differences in obesity prevalence are likely a result of both genetic and nongenetic factors (eg, socioeconomic status, intake of sugar-sweetened beverages and fast food, and having a television in the bedroom).

OBJECTIVE To update the 2010 US Preventive Services Task Force (USPSTF) recommendation on screening for obesity in children 6 years and older.

EVIDENCE REVIEW The USPSTF reviewed the evidence on screening for obesity in children and adolescents and the benefits and harms of weight management interventions.

FINDINGS Comprehensive, intensive behavioral interventions (≥26 contact hours) in children and adolescents 6 years and older who have obesity can result in improvements in weight status for up to 12 months; there is inadequate evidence regarding the effectiveness of less intensive interventions. The harms of behavioral interventions can be bounded as small to none, and the harms of screening are minimal. Therefore, the USPSTF concluded with moderate certainty that screening for obesity in children and adolescents 6 years and older is of moderate net benefit.

CONCLUSIONS AND RECOMMENDATION The USPSTF recommends that clinicians screen for obesity in children and adolescents 6 years and older and offer or refer them to comprehensive, intensive behavioral interventions to promote improvements in weight status. (B recommendation)

Editorial page 2378

Author Audio Interview

Related article page 2427 and JAMA Patient Page page 2460

CME Quiz at jamanetwork.com/learning

Related articles at jamapediatrics.com jamainternalmedicine.com

Author/Group Information: The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.

Corresponding Author: David C. Grossman, MD, MPH (chair@uspstf.net).

JAMA. 2017;317(23):2417-2426. doi:10.1001/jama.2017.6803

Pediatric Obesity—Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline

Dennis M. Styne,[1] Silva A. Arslanian,[2] Ellen L. Connor,[3] Ismaa Sadaf Farooqi,[4] M. Hassan Murad,[5] Janet H. Silverstein,[6] and Jack A. Yanovski[7]

[1]University of California Davis, Sacramento, California 95817; [2]University of Pittsburgh, Pittsburgh, Pennsylvania 15224; [3]University of Wisconsin, Madison, Wisconsin 53792; [4]University of Cambridge, Cambridge CB2 0QQ, United Kingdom; [5]Mayo Clinic, Rochester, Minnesota 55905; [6]University of Florida, Gainesville, Florida 32607; and [7]National Institutes of Health, Bethesda, Maryland 20892

Cosponsoring Associations: The European Society of Endocrinology and the Pediatric Endocrine Society. This guideline was funded by the Endocrine Society.

Objective: To formulate clinical practice guidelines for the assessment, treatment, and prevention of pediatric obesity.

Participants: The participants include an Endocrine Society–appointed Task Force of 6 experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation approach to describe the strength of recommendations and the quality of evidence. The Task Force commissioned 2 systematic reviews and used the best available evidence from other published systematic reviews and individual studies.

Consensus Process: One group meeting, several conference calls, and e-mail communications enabled consensus. Endocrine Society committees and members and co-sponsoring organizations reviewed and commented on preliminary drafts of this guideline.

Conclusion: Pediatric obesity remains an ongoing serious international health concern affecting ~17% of US children and adolescents, threatening their adult health and longevity. Pediatric obesity has its basis in genetic susceptibilities influenced by a permissive environment starting *in utero* and extending through childhood and adolescence. Endocrine etiologies for obesity are rare and usually are accompanied by attenuated growth patterns. Pediatric comorbidities are common and long-term health complications often result; screening for comorbidities of obesity should be applied in a hierarchal, logical manner for early identification before more serious complications result. Genetic screening for rare syndromes is indicated only in the presence of specific historical or physical features. The psychological toll of pediatric obesity on the individual and family necessitates screening for mental health issues and counseling as indicated. The prevention of pediatric obesity by promoting healthful diet, activity, and environment should be a primary goal, as achieving effective, long-lasting results with lifestyle modification once obesity occurs is difficult. Although some behavioral and pharmacotherapy studies report modest success, additional research into accessible and effective methods for preventing and treating pediatric obesity is needed. The use of weight loss medications during childhood and adolescence should be restricted to clinical trials. Increasing evidence

ISSN Print 0021-972X ISSN Online 1945-7197
Printed in USA

Received 30 June 2016. Accepted 10 November 2016.
First Published Online 31 January 2017

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CVD, cardiovascular disease; FDA, Food and Drug Administration; GH, growth hormone; HbA1c, hemoglobin A1c; LAGB, laparoscopic adjustable gastric banding; NAFLD, nonalcoholic fatty liver disease; PCOS, polycystic ovary syndrome; QOL, quality of life; RCT, randomized controlled trial; RYGB, Roux-en-Y gastric bypass; T2DM, type 2 diabetes mellitus; VSG, vertical sleeve gastrectomy; WHO, World Health Organization.

International Journal of Obesity (2018) 42:1823–1833
https://doi.org/10.1038/s41366-018-0230-y

REVIEW ARTICLE

Interventions for treating children and adolescents with overweight and obesity: an overview of Cochrane reviews

Louisa J. Ells[1] · Karen Rees[2] · Tamara Brown[1] · Emma Mead[1,3] · Lena Al-Khudairy[2] · Liane Azevedo[1] · Grant J. McGeechan[1] · Louise Baur[4] · Emma Loveman[5] · Heather Clements[1] · Pura Rayco-Solon[6] · Nathalie Farpour-Lambert[7] · Alessandro Demaio[6]

Received: 19 September 2017 / Revised: 17 May 2018 / Accepted: 15 June 2018 / Published online: 9 October 2018

Abstract

Children and adolescents with overweight and obesity are a global health concern. This is an integrative overview of six Cochrane systematic reviews, providing an up-to-date synthesis of the evidence examining interventions for the treatment of children and adolescents with overweight or obesity. The data extraction and quality assessments for each review were conducted by one author and checked by a second. The six high quality reviews provide evidence on the effectiveness of behaviour changing interventions conducted in children <6 years (7 trials), 6–11 years (70 trials), adolescents 12–17 years (44 trials) and interventions that target only parents of children aged 5–11 years (20 trials); in addition to interventions examining surgery (1 trial) and drugs (21 trials). Most of the evidence was derived from high-income countries and published in the last two decades. Collectively, the evidence suggests that multi-component behaviour changing interventions may be beneficial in achieving small reductions in body weight status in children of all ages, with low adverse event occurrence were reported. More research is required to understand which specific intervention components are most effective and in whom, and how best to maintain intervention effects. Evidence from surgical and drug interventions was too limited to make inferences about use and safety, and adverse events were a serious consideration.

Overview

- An integrative overview of six Cochrane Systematic Reviews
  - **Bariatric surgery** (Ells LJ et al. 2015)
  - **Drug interventions** (Mead et. al 2016)
  - **Parent-only interventions** (Loveman et. al 2015)
  - **Lifestyle intervention up to 6 years** (Colquitt et al 2016)
  - **Lifestyle intervention up to 6 to 11 years** (Mead E et al. 2017)
  - **Lifestyle intervention up to 12 to 17 years** (Al-Khudairy 2016)

Methods

- **Aim**: To update the Oude Luttikhuis (2009) review.
- Data was extracted using a standardised data collection form.
- Revised Assessment of Multiple Systematic Reviews (R-AMSTAR) measurement tool for review quality.
- **The primary outcomes**: Changes in BMI or BMI z-score.
- Cochrane ‘risk of bias’ assessment
- Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment

Included studies

- All reviews were published between 2015 and 2017
- Includes RCTs with a minimum of six months data from baseline
- Total of 163 studies (19,756 participants)
- Trials conducted between 1968 and 2016, from 30 countries.
  - USA (n = 73, 45%)
  - Europe (n = 44, 27%),
  - Upper-middle-income countries (n= 16, 10%)
- Trial samples sizes within reviews ranged from 10 to 686 participants.

Included participants and intervention

- Exclusion: Children with critical illness or syndromic forms of obesity
- Children with overweight or obesity
- **Median BMI z-score** across the lifestyle reviews: Between 2.2 and 2.3
- The median proportion of females ranged from 54% to 65%
- Limited reporting of socioeconomic status and ethnicity

- Interventions could be undertaken in any setting,
- More than half of the trials (n=85) were undertaken in **either primary or secondary care**.

Outcome measures

- **Primary outcomes**
  - BMI or BMI z-score
  - Body weight
  - Adverse events
- **Secondary outcomes**
  - Health-related quality of life
  - Self-esteem
  - All-cause mortality
  - Morbidity
  - Body fat distribution
  - Behaviour change
  - Participants' views of the intervention
  - Socioeconomic effects

Lifestyle intervention up to 6 to 11 years
Mead E *et al*. 2017

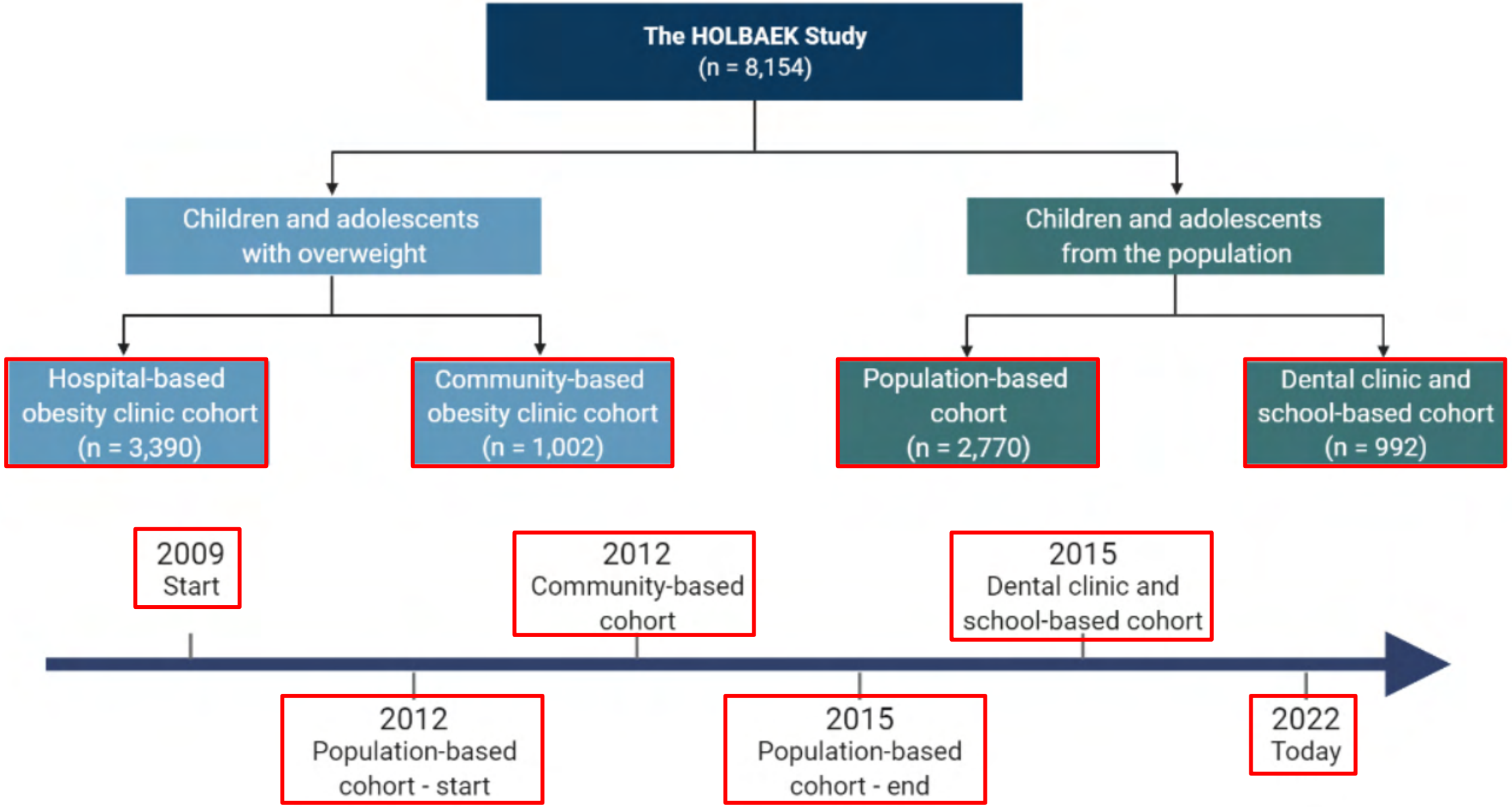
- 70 trials (8,461 participants)
- Four cluster trials and 20 ongoing trials in 2016
- 65 trials included both the child and parent/caregiver
- 49 trials included both a dietary, physical activity and behavioural component
- Delivery and content of the interventions varied considerably
- Sample sizes ranged from 16 to 686 participants
- Median of the mean BMI z-score at baseline was 2.2 (range1.3 to 5.6)
- Duration of the interventions: Range 0.25–24 months
- Follow-up from baseline: Range 5.5–36 months.
- 37 trials reported **BMI z-score** suitable for metaanalysis => change in favour of intervention of −0.06 units, (95% CI: −0.10 to −0.02); 4019 participants).

Lifestyle intervention up to 12 to 17 years
Al-Khudairy 2016

- 44 trials (4781 participants) and 50 ongoing studies in 2016
- Duration of interventions: Ranged from 6 weeks to 2 years
- Follow-up from baseline: Range from 24 weeks to 2 years
- Five trials focusing on physical activity, five on diet only, and 34 multi-component interventions.
- Setting and content of the interventions varied considerably.
- Sample size ranged from 10 to 521 participants.
- Overall mean difference in BMI z-score was −0.13 units (95% CI: −0.21 to −0.05) (2399 participants; 20 trials).
- This reduction remained in long term follow-up studies (18–24 months) with BMI z-score −0.34 units (95% CI: −0.66 to −0.02) (602 participants; five trials).

Cochrane Reviews
Conclusions

- Summary of 6 CSR from 2015-2017 based on 163 studies (19.756 individuals) carried out from 1968 to 2016 in 30 countries.
- Investigated effects of behavioral based treatment (121 studies), treatment of parents (20 studies), drug therapy (21 studies) and bariatric surgery (1 study).
- Main conclusions: Interventions are different in design, form and execution.
- A ”multi-component” behavioral based treatment may lead to a positive result in terms of change in body weight.
- Largest reductions in BMI SDS were seen in the group of 2-5 yrs (-0.3), while lesser were seen in the group of 6-11 yrs (-0.06).
- The degree of drop-out was not documented, but has traditionally been high.

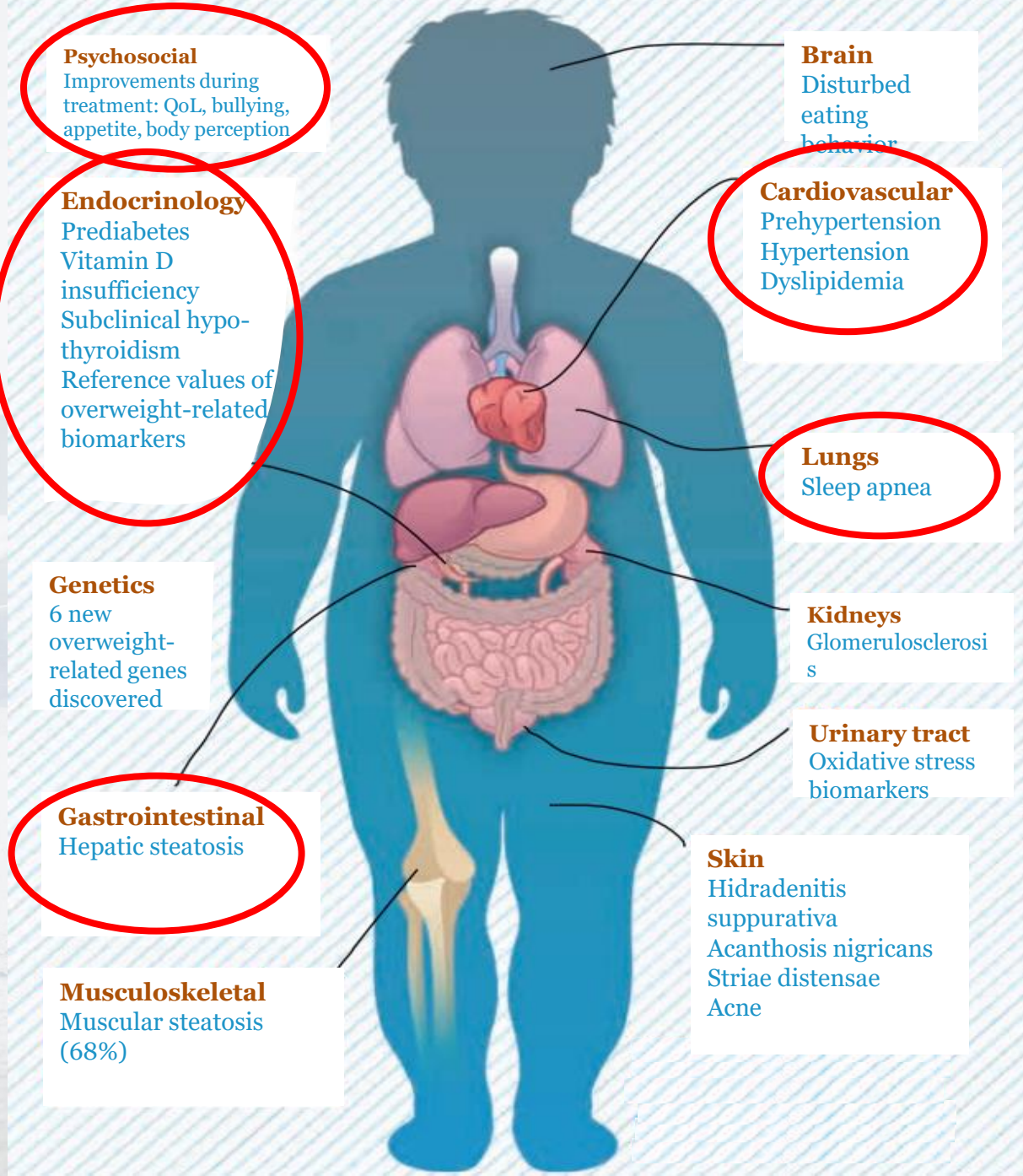

The HOLBAEK Study
(n = 8,154)
Children and adolescents with overweight
Children and adolescents from the population
Hospital-based obesity clinic cohort
(n = 3,390)
Community-based obesity clinic cohort
(n = 1,002)
Population-based cohort
(n = 2,770)
Dental clinic and school-based cohort
(n = 992)
2009
Start
2012
Community-based cohort
2015
Dental clinic and school-based cohort
2012
Population-based cohort - start
2015
Population-based cohort - end
2022
Today

Complications to overweight

- 75% with low self-esteem, self-confidence or quality of life
- 82% with disturbed eating
- 50% with hypertension or prehypertension
- 28% with dyslipidemia
- 60% with vitamin-D insufficiency
- 14% with prediabetes
- 45% with sleep apnea
- 31% with hepatic steatosis

- Fogh, J Paediatr Child Health. 2020; 56(4):542-549
- Mollerup, J Hum Hypertens. 2017;31(10):640-646
- Nielsen, BMC Pediatr. 2017 Apr 28;17(1):116
- Plesner, J Pediatr Endocrinol Metab. 2018;26;31(1):53-61
- Kloppenborg, Pediatr Diabetes. 2018 May;19(3):356-365
- Andersen, Eur Arch Otorhinolaryngol. 2019 Mar;276(3):871-878
- Fonvig, PLoS One. 2015 Aug 7;10(8):e0135018

(Courtesy of Dr Holm)



The Children`s Obesity Clinic

BMI above 99% percentile
for age and gender

Age between 3-22 years

No selection criteria

Holm JC *et al* IJPO. 2011 Aug;6(3-4):188-96.

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.

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

Tobacco and alcohol

- Stop smoking. Provide help and courses to stop smoking
- Passive smoking
- Alcohol not recommended before the age of 18 years and allways less than 5 drinks per 24 hours according to the National Health Board
- Parental abuse

Follow-up assessments
- during growth, development, challenges and life

- Treatment development, symptoms, physical examination
- Degree of overweight/obesity, body composition
- Obesity related complications
- Quality of life
- Adherence to treatment
- Tobacco, alcohol and drugs
- Life functionality, physical and mental
- Genetic testing
- Guidance and care

Referrals

- Depending on who you are and where you are
- Primary, secondary or tertiary clinic
- Depending on medical networks and availability of diverse competences. Nearly all Departments; Child Psychiatry, Social, Sleep, Orthopedia, Cardiovascular, Neurology, etc
- Geography
- Cost
- Balance act; who will remain responsible of treatment?
- Guidance?

Original Article

Longitudinal evaluation of an mHealth overweight and obesity management tool

Ida Olivia Juhl Langkjær[1]^, Cilius Esmann Fonvig[2,3]^, Louise Aas Holm[2]^, Andreas Friis Pihl[4,5]^, Jens-Christian Holm[1,2,3]^

[1]University of Copenhagen, Faculty of Health and Medical Sciences, Copenhagen, Denmark; [2]Faculty of Health and Medical Sciences, Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, Copenhagen, Denmark; [3]Dr Holm App Aps., Holbæk, Denmark; [4]Research Unit of General Practice, University of Southern Denmark, Odense, Denmark; [5]Roche Diagnostics Denmark, Hvidovre, Denmark

Contributions: (I) Conception and design: CE Fonvig, JC Holm; (II) Administrative support: None; (III) Provision of study materials or patients: CE Fonvig, JC Holm; (IV) Collection and assembly of data: CE Fonvig; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Jens-Christian Holm. Kalundborgvej 114, 4300 Holbæk, Denmark. Email: jch@drholm.com.

THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

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*

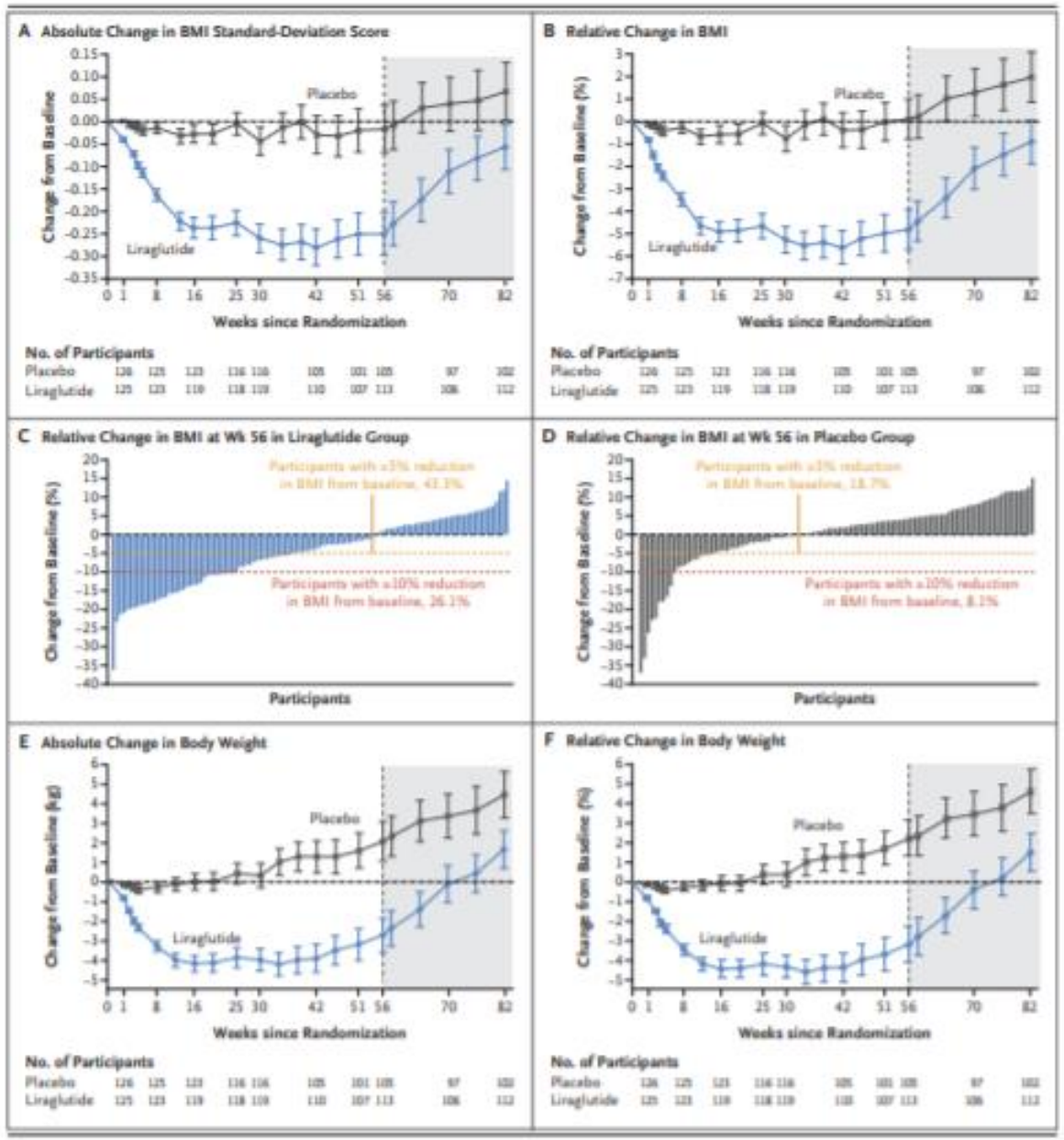
COUNSELING IN HEALTH NUTRITION AND PHYSICAL ACTIVITY

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.

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!

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** ▾

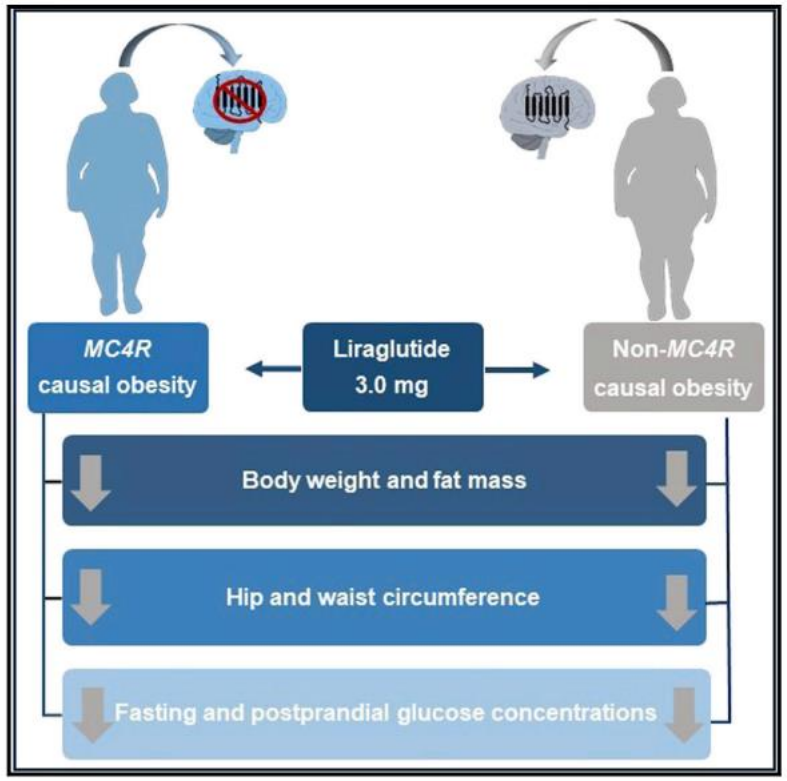
Conclusion

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

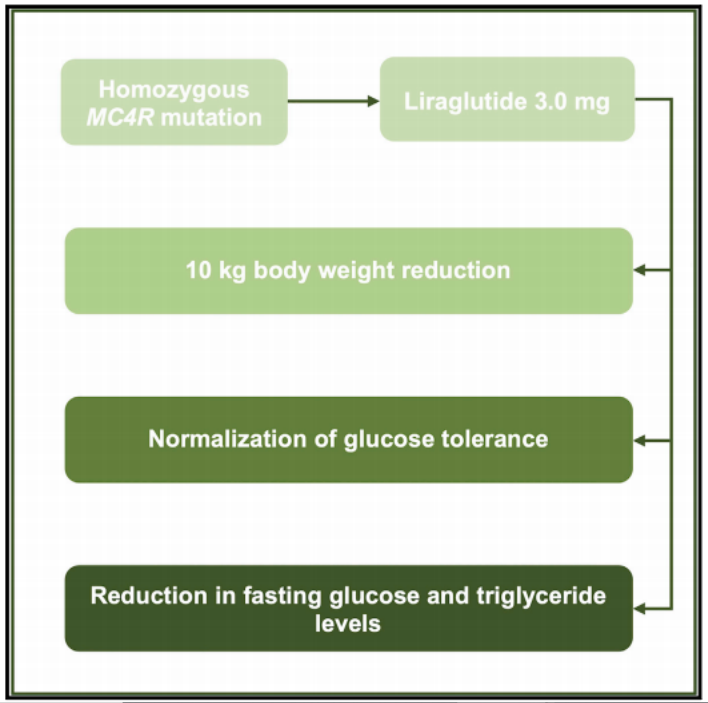
- Fully functional MC4Rs are not required for GLP-1 RA-mediated weight loss
- Liraglutide caused a 6% weight loss in patients with *MC4R* mutations and controls
- Fat mass, waist circumference, and glucose concentrations improved with treatment
- Liraglutide is an effective treatment of the most common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



Authors

Eva W. Iepsen, Christian T. Have, Simon Veedfald, ..., Jens-Christian Holm, Torben Hansen, Signe S. Torekov

Correspondence

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

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

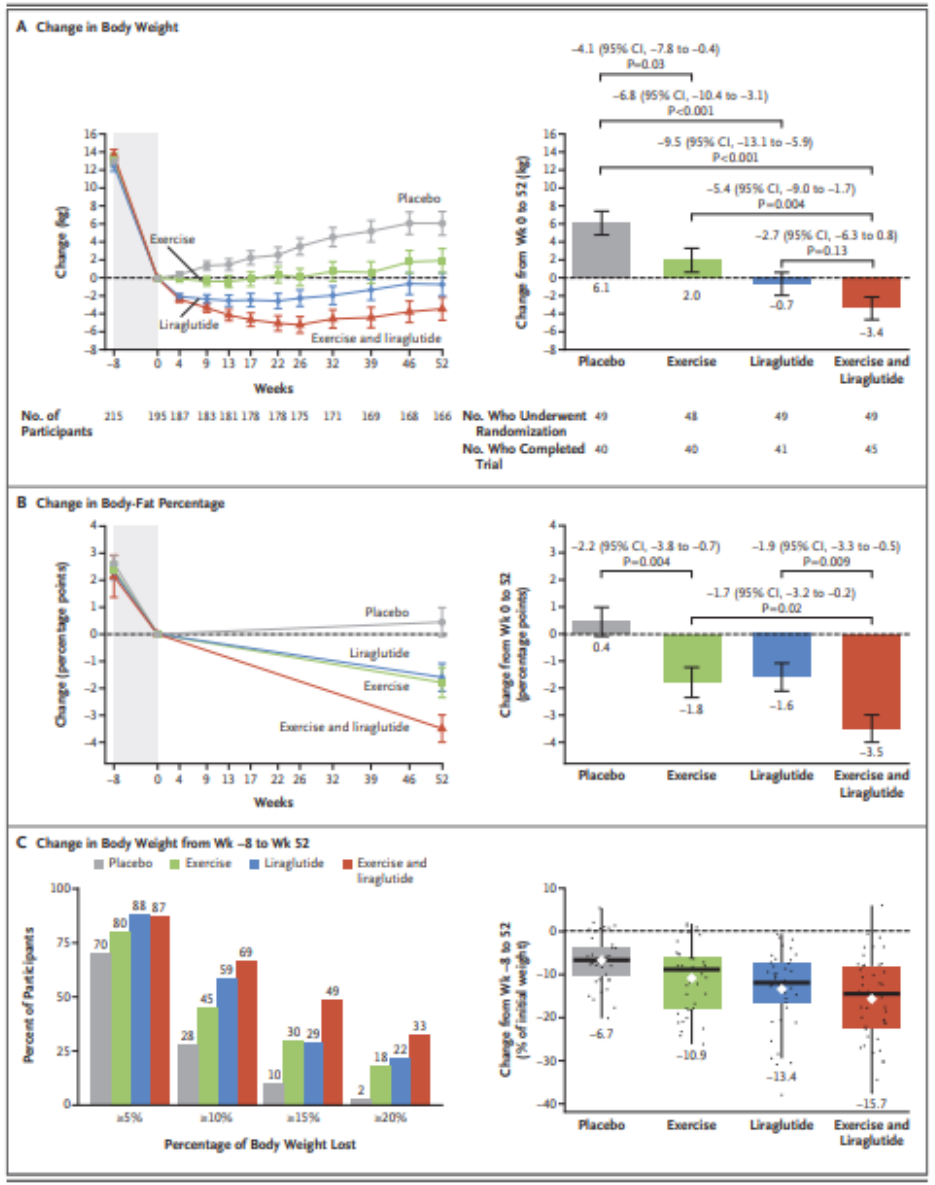
Healthy Weight Loss Maintenance with Exercise, Liraglutide, or Both Combined

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.

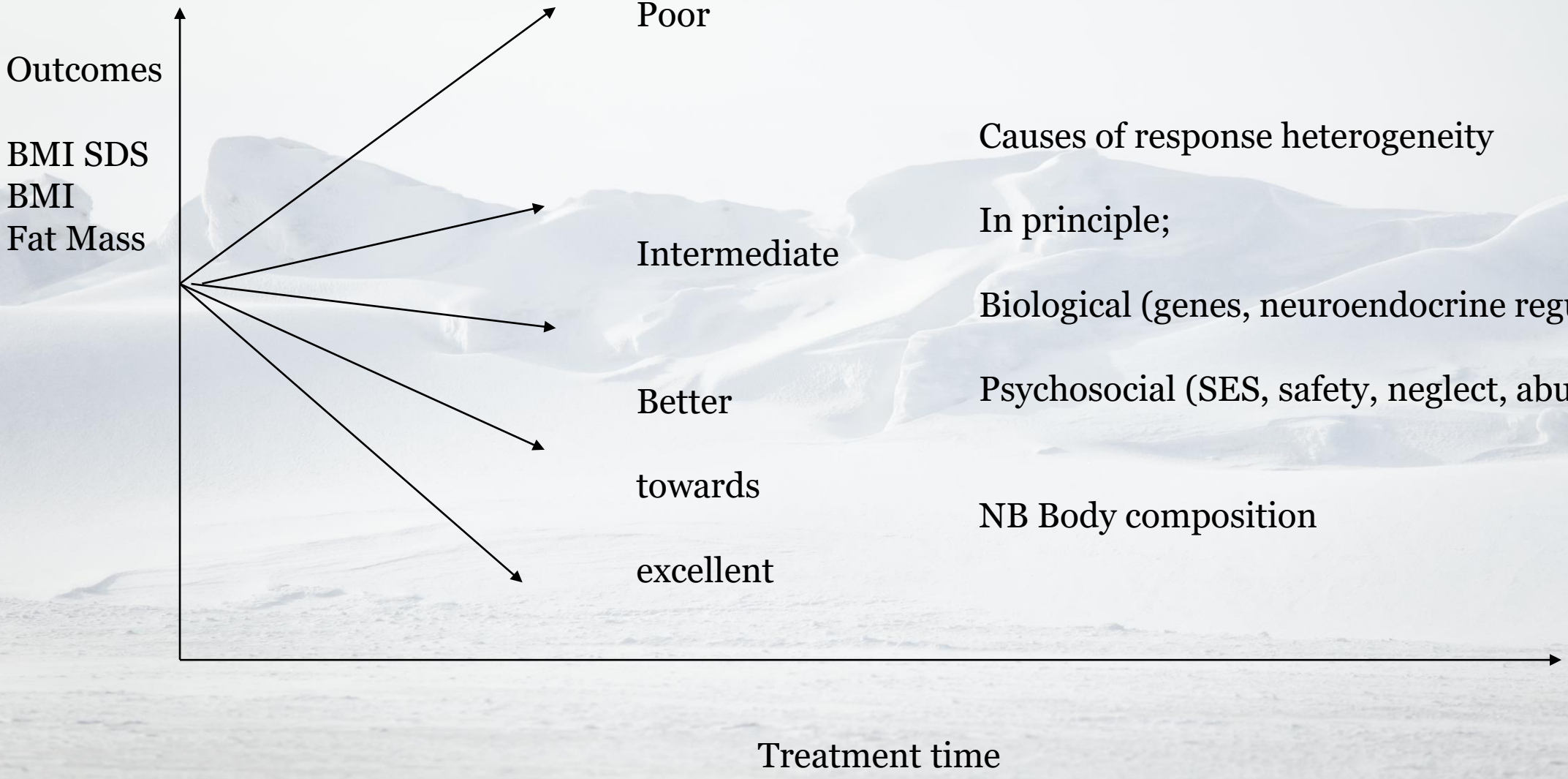
CONCLUSIONS A strategy combining exercise and liraglutide therapy improved healthy weight loss maintenance more than either treatment alone.

N Engl J Med 2021;384:1719-30.
DOI: 10.1056/NEJMoa2028198

The NEW ENGLAND JOURNAL of MEDICINE



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



Causes of response heterogeneity

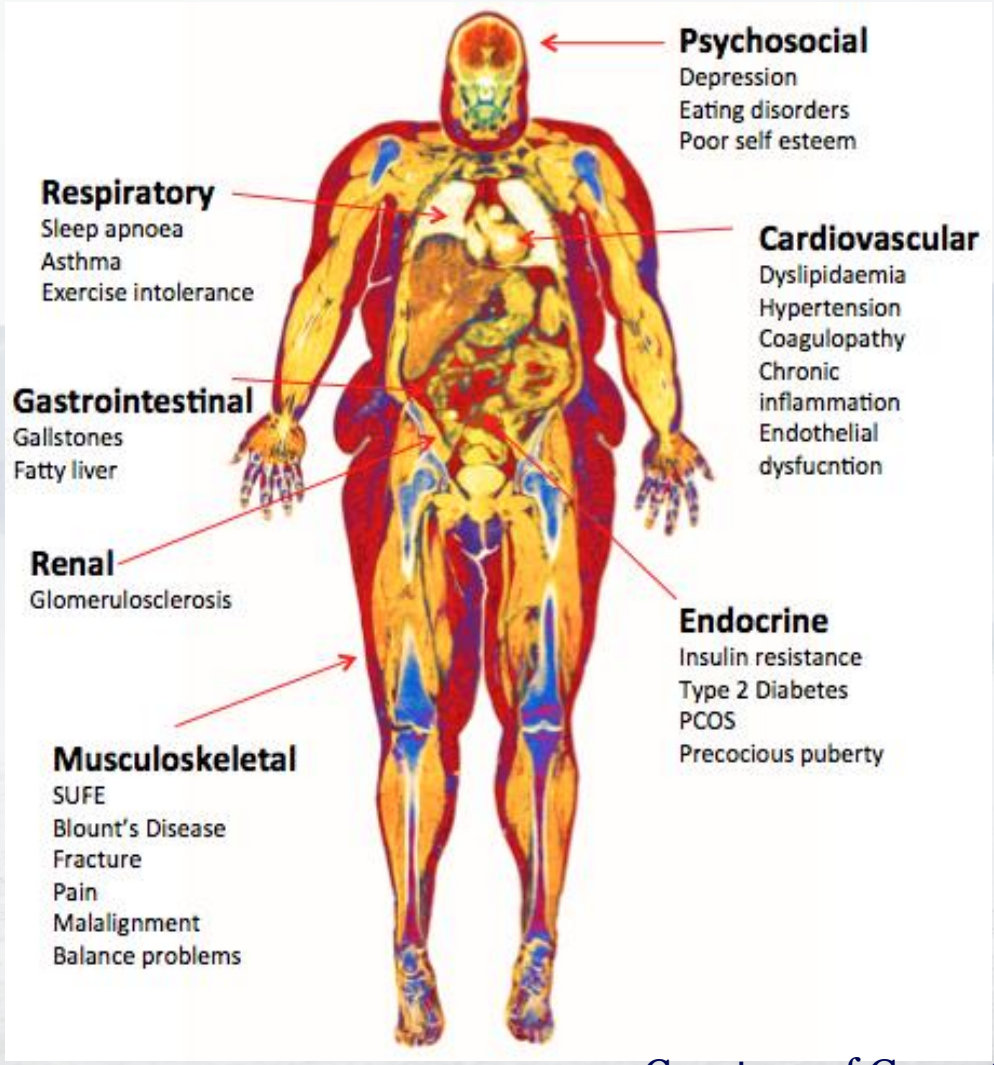
In principle;

Biological (genes, neuroendocrine regulation etc) or

Psychosocial (SES, safety, neglect, abuse etc)

NB Body composition

Obesity related Complications

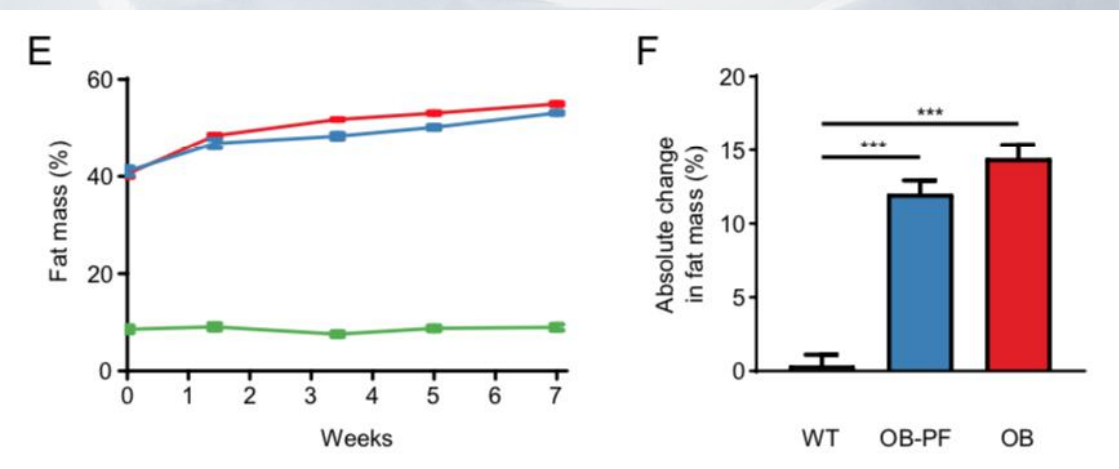


Courtesy of Grace O'Malley, PhD, The Children's University Hospital, Dublin, Ireland

Li X *et al.* Obesity 2010; 18(3):456-62.

Impaired glucose metabolism and altered gut microbiome despite calorie restriction of ob/ob mice

- Pair-fed ob/ob mice exhibited even more compromised glucose metabolism and maintained strikingly similar high body fat percentage at the cost of lean body mass.



A Kashani, AD Brejnrod, C Jin, T Kern, AN Madsen, LA Holm, GK Gerber, JC Holm, T Hansen, B Holst, M Arumugam Animal Microbiome; 2019

Negative energy balance?

- *Induces* comprehensive neuroendocrinological adaptations
- Energy balance is not just a passive balance, but instead an *active asymmetric* biological function to ensure and secure sufficient energy to demands in the future
- Fat and energy regulation is able of being ”*energy efficient*”
- *Be careful* about expectations/predujice since you really dont know what is going on in the individual patient


BBC World News (ENG)
Se senere
Se på YouTube

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

Many thanks for the attention

Mail jhom@regionsjaelland.dk and jch@drholm.com

LinkedIn Jens-Christian Holm

Orcid 0000-0003-4653-342X

Facebook Jens-Christian Holm

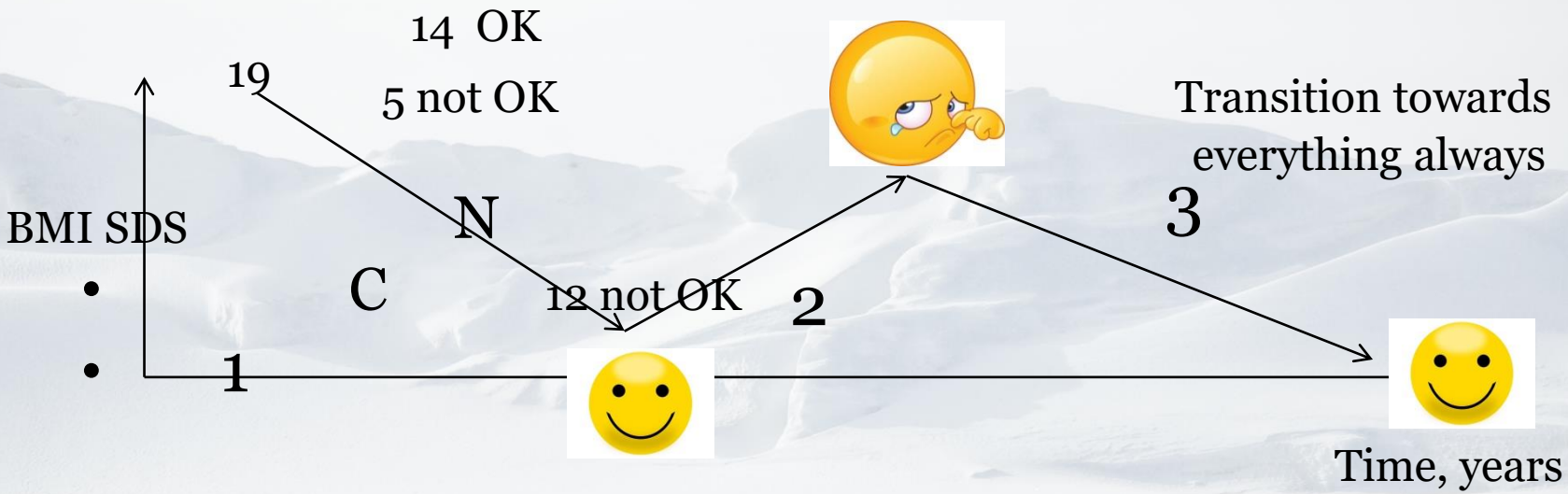
Instagram JensChristianHolm

Twitter JC_Holm

Homepage www.jenschristianholm.dk/uk/

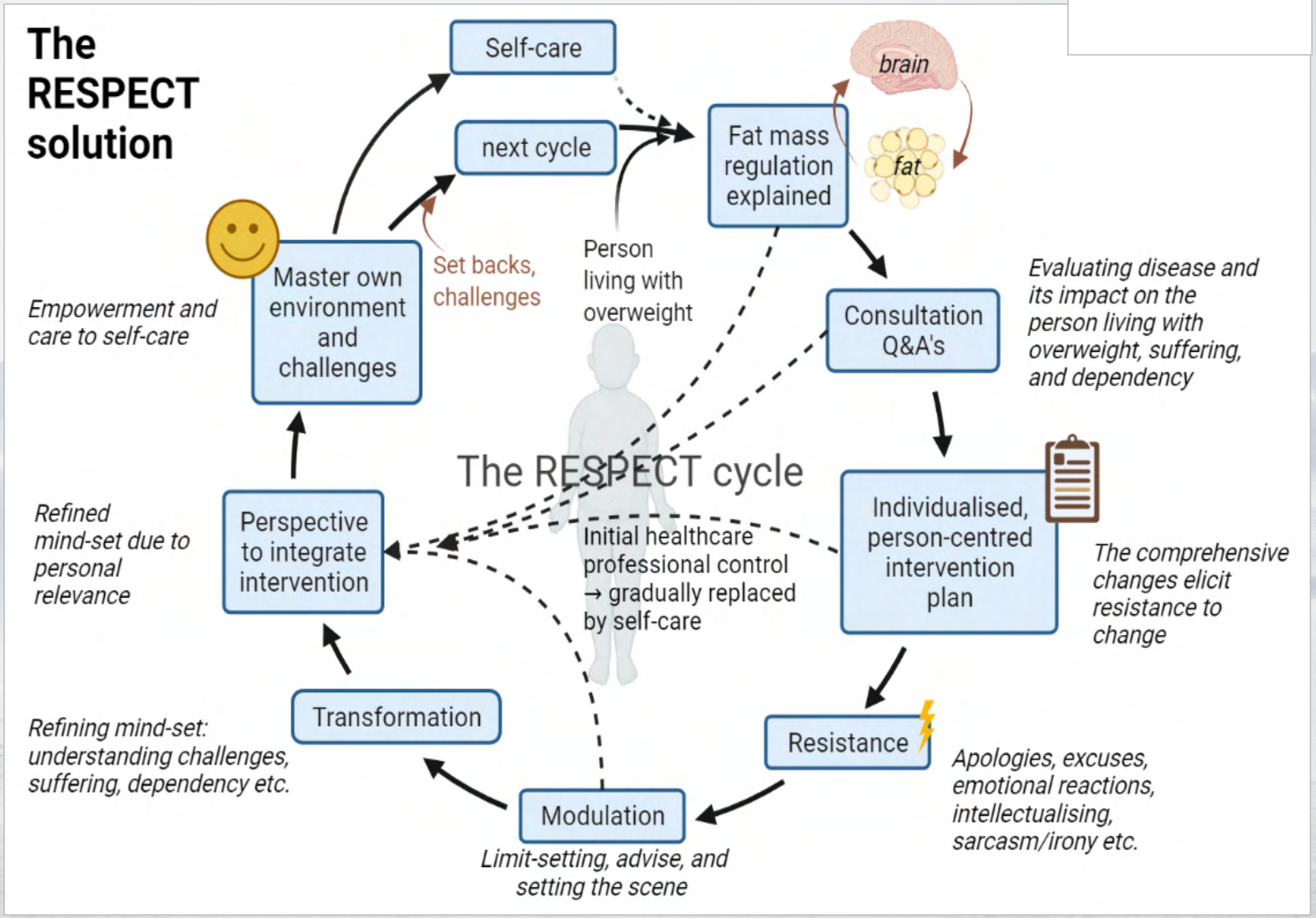
The dynamics of weight loss

- 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

Figure 2.


The RESPECT solution
Self-care
next cycle
brain
fat
Fat mass regulation explained
Person living with overweight
Set backs, challenges
Master own environment and challenges
Empowerment and care to self-care
Consultation Q&A's
Evaluating disease and its impact on the person living with overweight, suffering, and dependency
The RESPECT cycle
Individualised, person-centred intervention plan
The comprehensive changes elicit resistance to change
Initial healthcare professional control → gradually replaced by self-care
Perspective to integrate intervention
Refined mind-set due to personal relevance
Resistance
Apologies, excuses, emotional reactions, intellectualising, sarcasm/irony etc.
Transformation
Refining mind-set: understanding challenges, suffering, dependency etc.
Modulation
Limit-setting, advise, and setting the scene

nature genetics

Article | Published: 01 May 2019

Maternal and fetal genetic effects on birth weight and their relevance to cardio-metabolic risk factors

Nicole M. Warrington, Robin N. Beaumont, […] Rachel M. Freathy

Nature Genetics **51**, 804–814 (2019) | Download Citation

Abstract

Birth weight variation is influenced by fetal and maternal genetic and non-genetic factors, and has been reproducibly associated with future cardio-metabolic health outcomes. In expanded genome-wide association analyses of own birth weight (n = 321,223) and offspring birth

OXFORD

Human Molecular Genetics, 2016, Vol. 25, No. 2 389–403

doi: 10.1093/hmg/ddv472
Advance Access Publication Date: 24 November 2015
Association Studies Article

ASSOCIATION STUDIES ARTICLE

Genome-wide association analysis identifies three new susceptibility loci for childhood body mass index

Abstract

A large number of genetic loci are associated with adult body mass index. However, the genetics of childhood body mass index are largely unknown. We performed a meta-analysis of genome-wide association studies of childhood body mass index, using sex- and age-adjusted standard deviation scores. We included 35 668 children from 20 studies in the discovery phase and 11 873 children from 13 studies in the replication phase. In total, 15 loci reached genome-wide significance (P-value $< 5 \times 10^{-8}$) in the joint discovery and replication analysis, of which 12 are previously identified loci in or close to *ADCY3*, *GNPDA2*, *TMEM18*, *SEC16B*, *FAIM2*, *FTO*, *TFAP2B*, *TNNI3K*, *MC4R*, *GPR61*, *LMX1B* and *OLFM4* associated with adult body mass index or childhood obesity. We identified three novel loci: rs13253111 near *ELP3*, rs8092503 near *RAB27B* and rs13387838 near *ADAM23*. Per additional risk allele, body mass index increased 0.04 Standard Deviation Score (SDS) [Standard Error (SE) 0.007], 0.05 SDS (SE 0.008) and 0.14 SDS (SE 0.025), for rs13253111, rs8092503 and rs13387838, respectively. A genetic risk score combining all 15 SNPs showed that each additional average risk allele was associated with a 0.073 SDS (SE 0.011, P-value $= 3.12 \times 10^{-10}$) increase in childhood body mass index in a population of 1955 children. This risk score explained 2% of the variance in childhood body mass index. This study highlights the shared genetic background between childhood and adult body mass index and adds three novel loci. These loci likely represent age-related differences in strength of the associations with body mass index.

LETTER

doi:10.1038/nature19806

Genome-wide associations for birth weight and correlations with adult disease

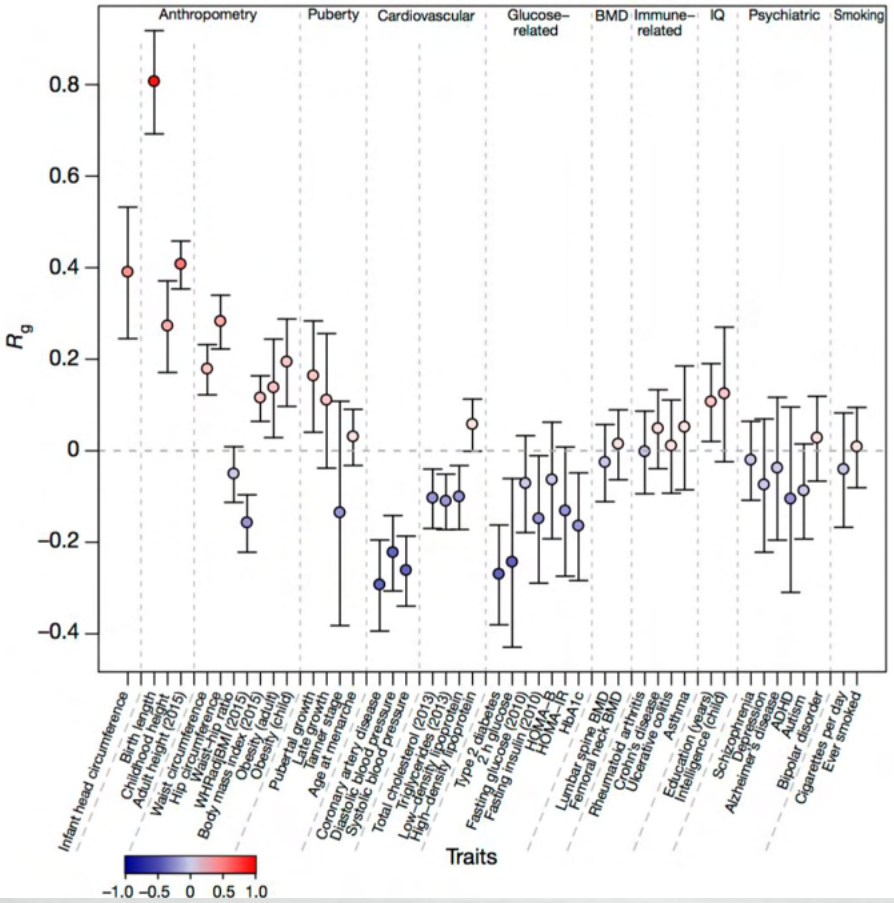


Figure 1 | Genome-wide genetic correlation between BW and a range of traits and diseases in later life. Genetic correlation (R_g) and corresponding s.e. (error bars) between BW and the traits displayed on the *x* axis were estimated using linkage-disequilibrium score regression (ref. 8). The genetic correlation estimates (R_g) are colour coded according to their intensity and direction (red for positive and blue for inverse correlation). WHRadjBMI, waist–hip ratio adjusted for body mass index; HOMA-B/IR, homeostasis model assessment of beta-cell function/insulin resistance; HbA1c, haemoglobin A1c; BMD, bone mineral density; ADHD, attention deficit hyperactivity disorder. See Supplementary Table 12 for references for each of the traits and diseases displayed.

Nature. 2016 Sep 28;538(7624):248-252. doi: 10.1038/nature19806.