PMR-C 10th Anniversary Symposium

What should GLP-1 based weight loss therapy look like in patients with multimorbidity?

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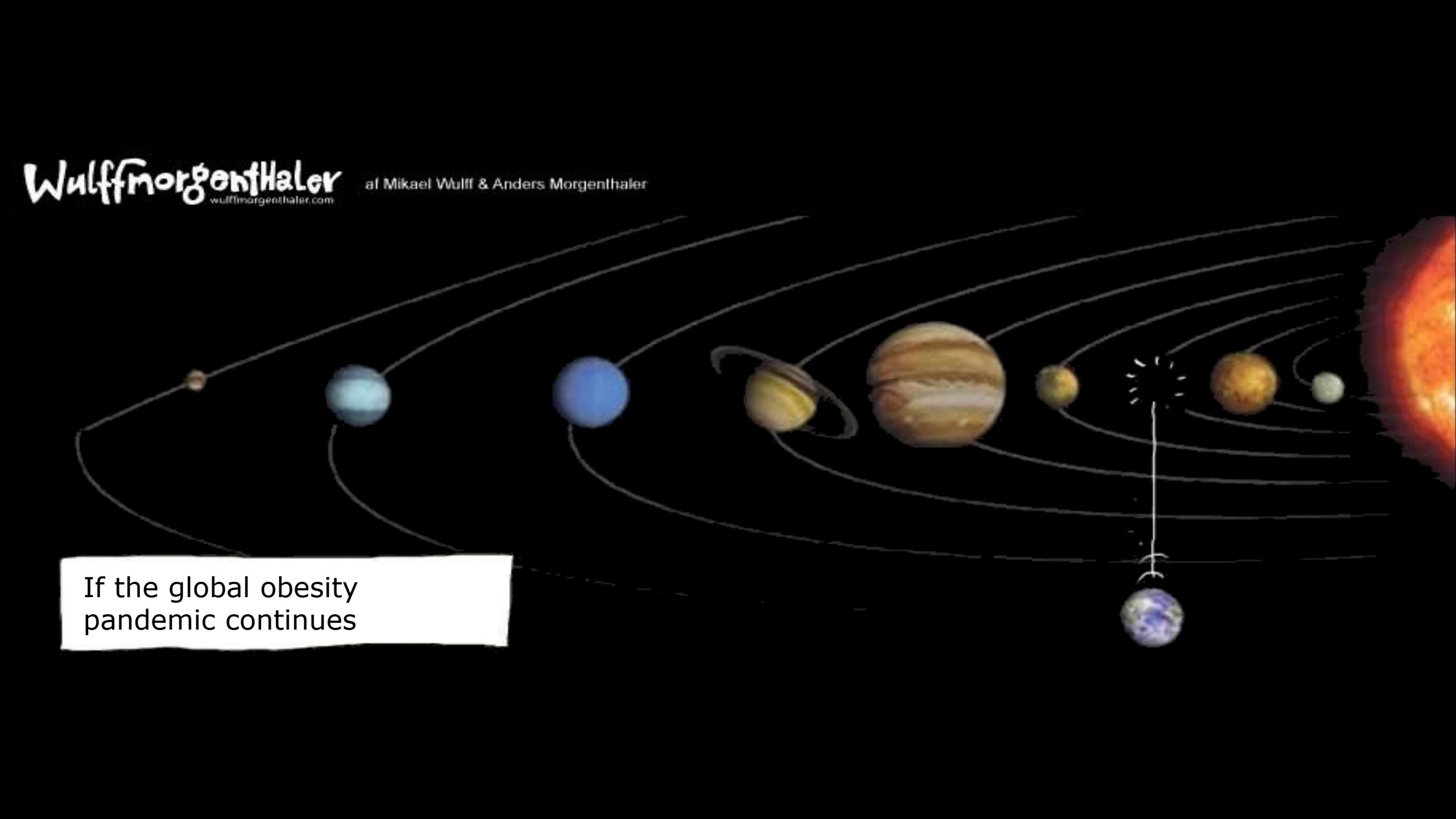
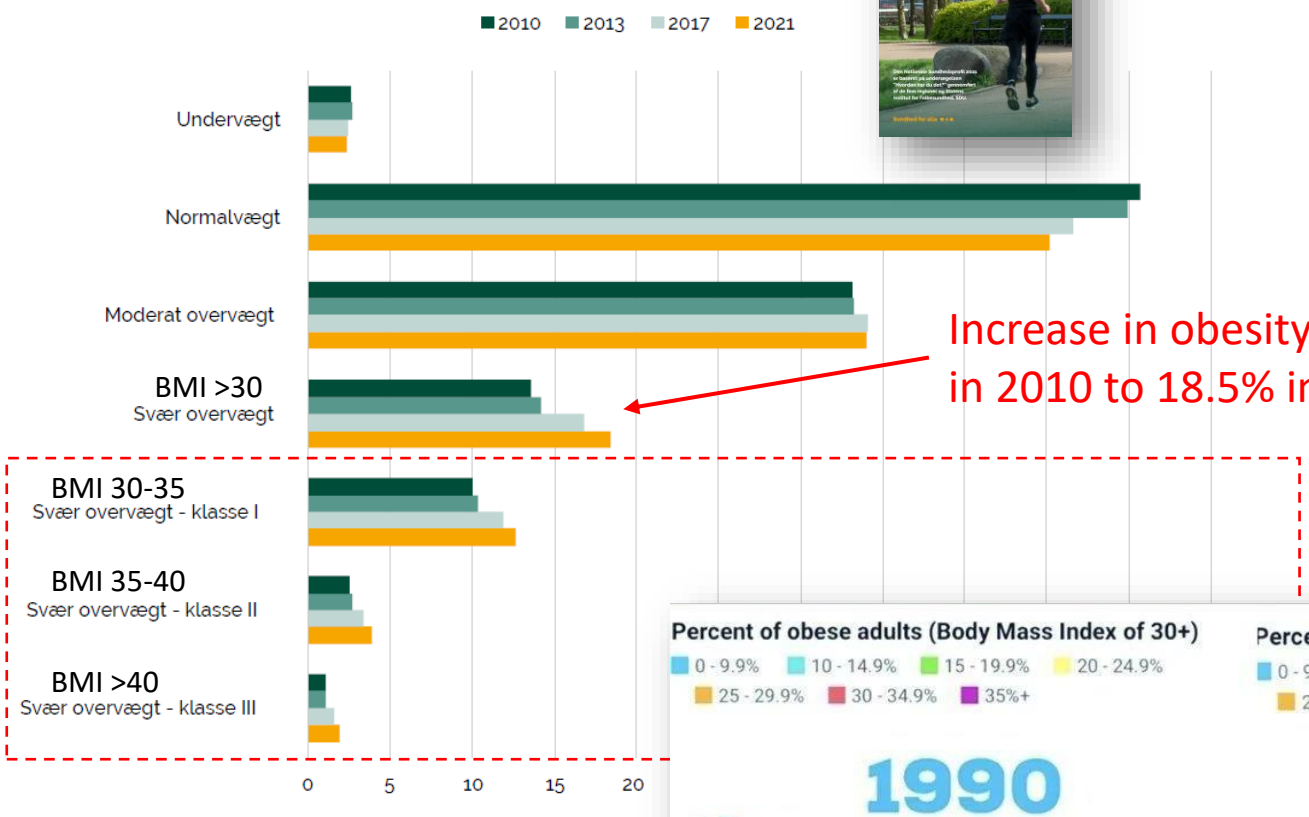
UNIVERSITY OF COPENHAGEN

Conflicts of interest

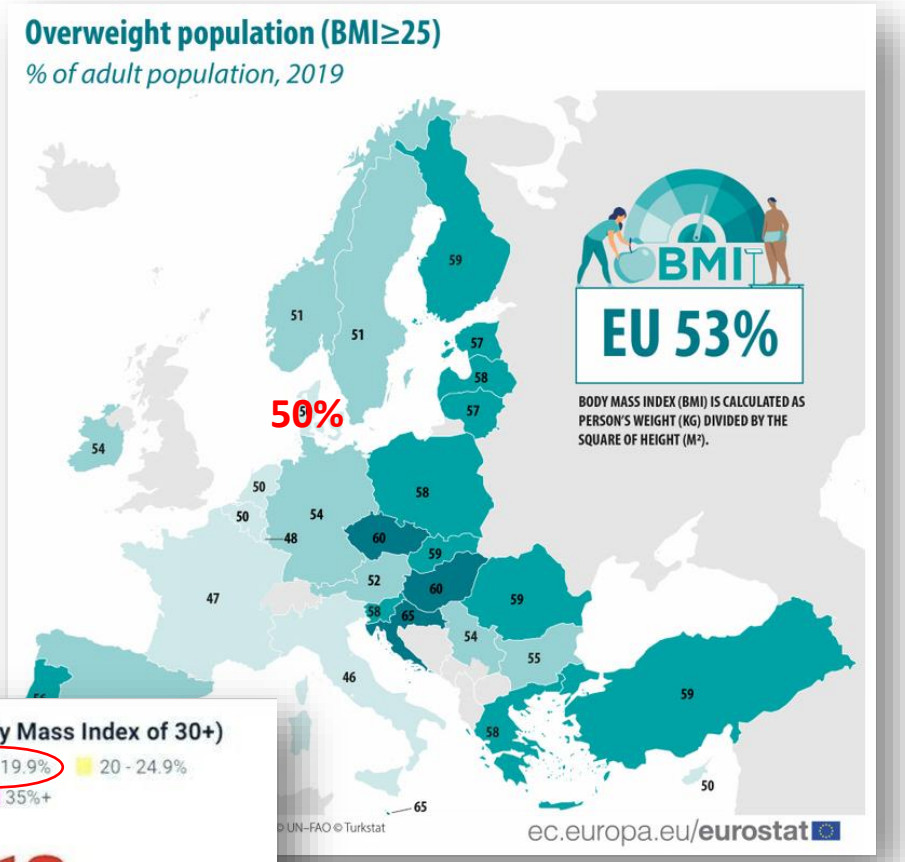
- Served on scientific advisory panels and received lecture fees and/or support for attending meetings from Novo Nordisk Denmark A/S, Boehringer-Ingelheim, and AstraZeneca within the last three years.
- Received research funding from Novo Nordisk Foundation, Danish Diabetes Academy, University of Copenhagen, and Hvidovre Hospital’s Strategic Research Foundation.

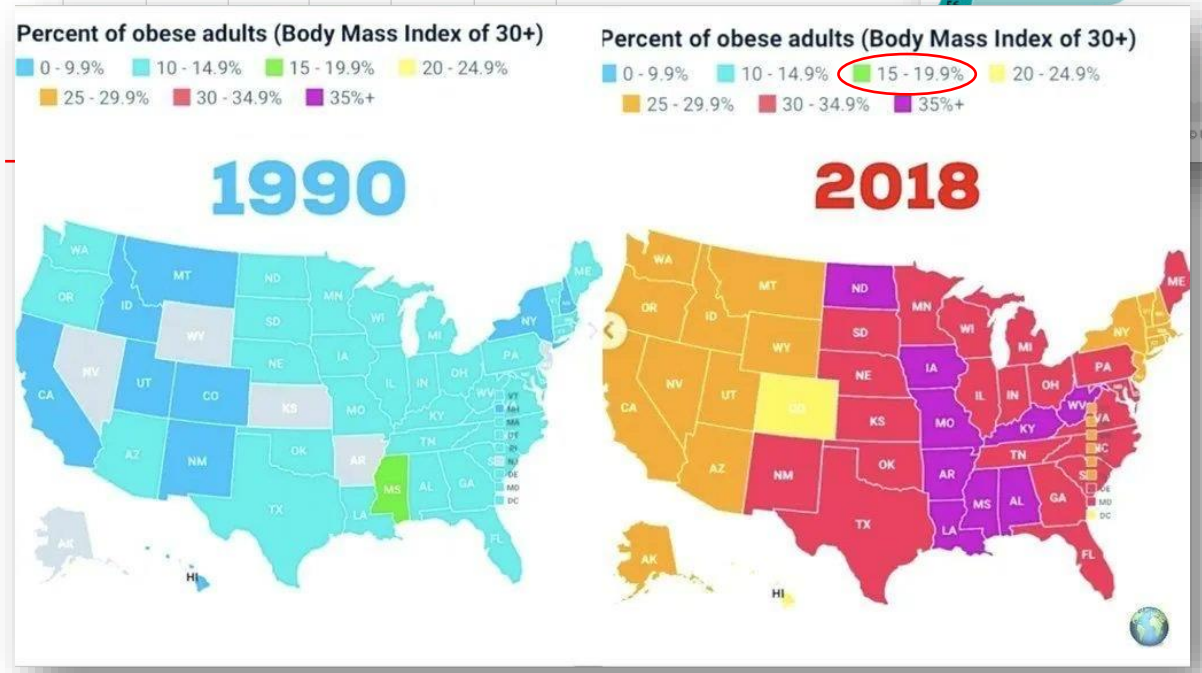

WulffmorgenthaLer
wulffmorgenthaler.com
af Mikael Wulff & Anders Morgenthaler
If the global obesity pandemic continues

Figur 3.5.1 Udvikling i vægtgrupper. 2010, 2013, 2017 og 2021. Procent .



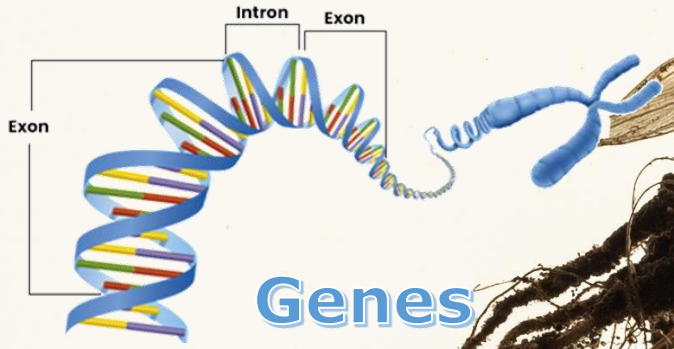
Increase in obesity from 13.6% in 2010 to 18.5% in 2021



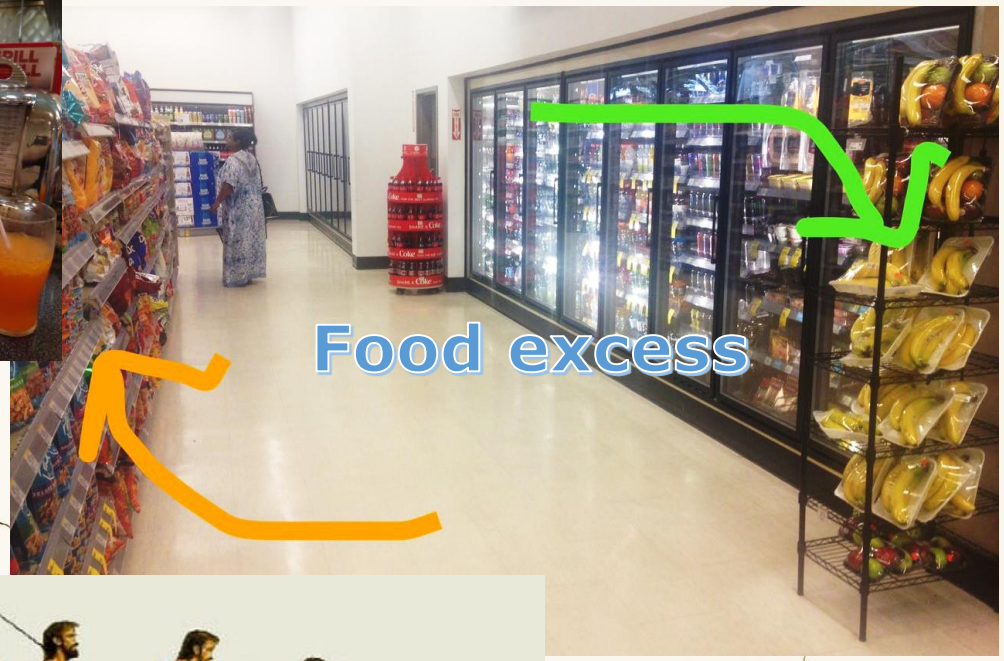


SST/SDU, Eurostat


Venøs tromboembolisme
Hernie
Infertilitet
Proteinuri
PCOS
Fedtlever
Diabetes
Hypertension
Parodentitis
Refluks-sygdom
Apoplexi
Artritis urica
Infektioner
Inflammation
Stigmatisering
Kræft
Angst
Gestationel diabetes
Astma
Artrose
Arbejdsløshed
Dyslipidæmi
Depression
Hirsutisme
Søvnapnø
Hjertesvigt
Lymfødem
Galdesten
Iskæmisk hjertesygdom



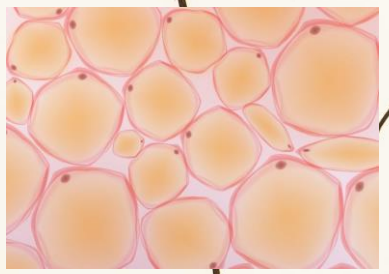
Genes



Food excess

Apetite regulation

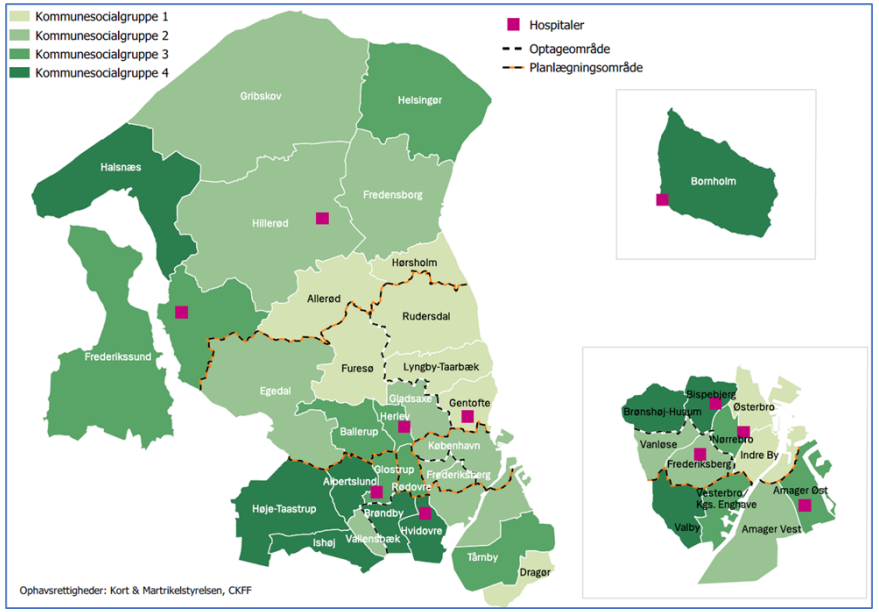
Physical inactivity



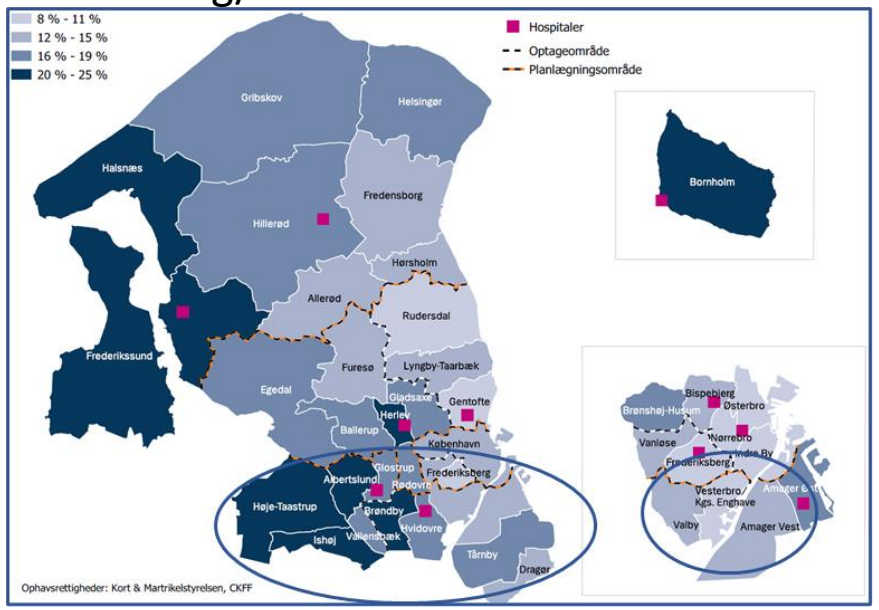
Fat storage capacity

Social inequality

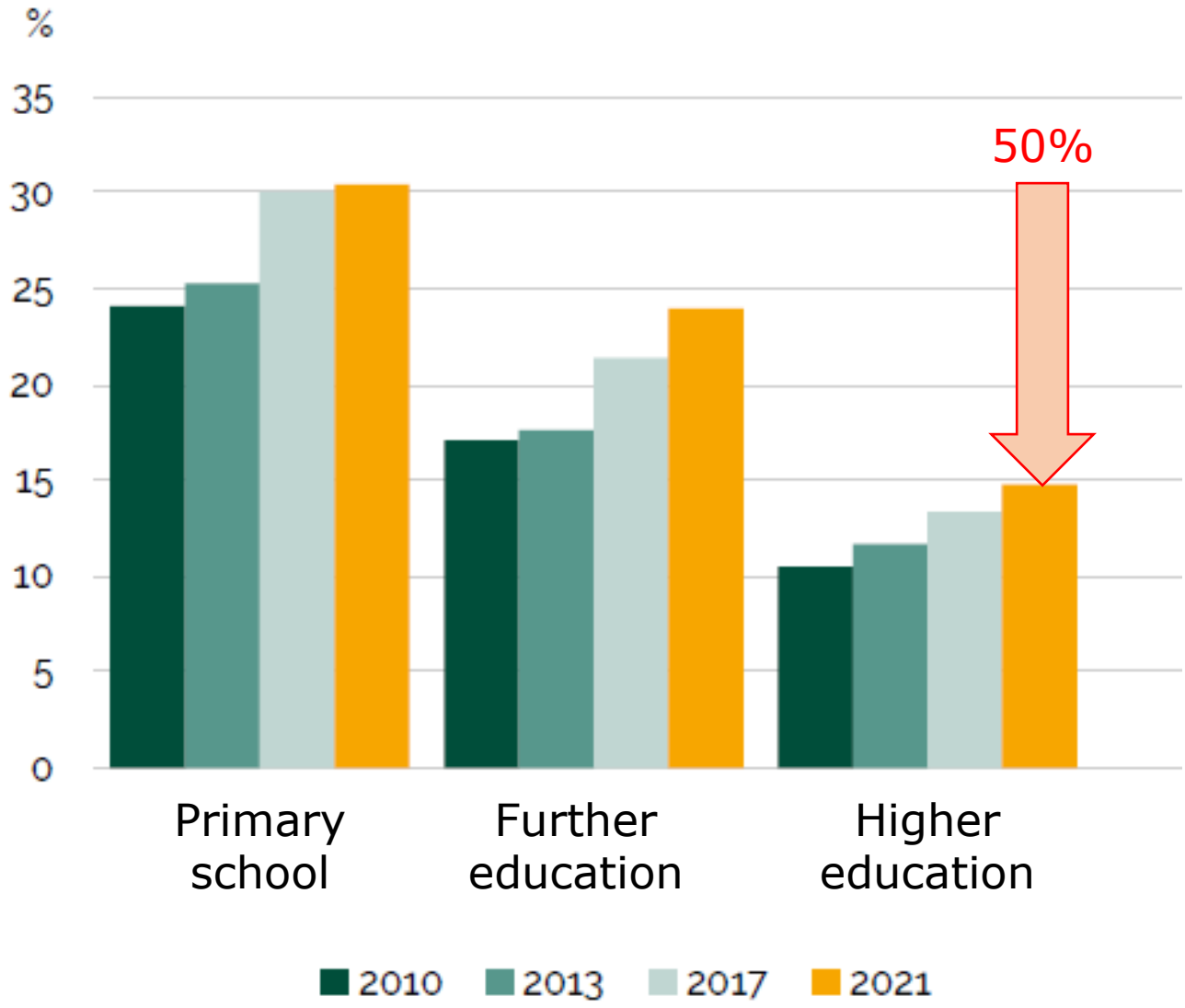
Social class



BMI > 30 kg/m^2



Proportion of Danish men with BMI >30 kg/m^2



Danskernes Sundhed

Obesity stigma

- Misconception that a person's **body weight is purely within their control** and obesity is a choice that can be easily reversed by **eating less and exercising more**.
- Negative stereotypes portraying people with obesity as **lazy, gluttonous and lacking in willpower and intelligence**.
- Weight stigma is associated with **disordered eating**, **sleep disturbance** and **exercise avoidance**, even after controlling for BMI.
- Weight stigma increases the risk of **psychological problems** (depression, anxiety etc.) and experimental weight stigma leads to **physiological stress** (increased cortisol and C-reactive protein).

Batterham 2022 Nat Rev Endo, Halfdan Rasmussen

How can we treat obesity?

RANDOMIZED TRIAL OF DIET AND GASTROPLASTY COMPARED WITH DIET ALONE IN MORBID OBESITY

TEIS ANDERSEN, M.D., OLE G. BACKER, M.D., KNUD H. STOKHOLM, M.D., AND FLEMMING QUAADE, M.D.

Abstract We compared the weight-reducing effect of diet and gastroplasty with that of diet alone in a randomized trial in 60 morbidly obese patients followed for two years. Initial median body weight was 120 kg in patients randomly assigned to gastroplasty plus diet and 115 kg in those assigned to diet alone. Maxim losses did not differ significantly between t (26.1 kg in the gastroplasty group and 22.0 group treated with diet alone; P>0.05). The risk of a Type II error with a true difference larger than 9.5 kg was less than 5 per cent. However, the group treated with diet alone regained significantly more weight after maximum weight loss had been achieved, so that the gas- orable net outcome at Med 1984; 310:352-

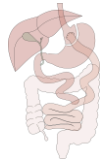
Clinical Trial › Int J Obes Relat Metab Disord. 1992 Apr;16(4):269-77.

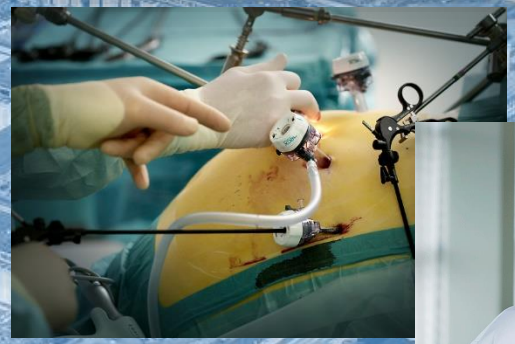
The effect and safety of an ephedrine/caffei compound compared to ephedrine, caffeine placebo in obese subjects on an energy restr diet. A double blind trial

A Astrup [1], L Breum, S Toubro, P Hein, F Quaade

Mechanisms of improved glycaemic control after Roux-en-Y gastric bypass

C. Dirksen · N. B. Jørgensen · K. N. Bojsen-Møller · S. H. Jacobsen · D. L. Hansen · D. Worm · J. J. Holst · S. Madsbad





The NEW ENG

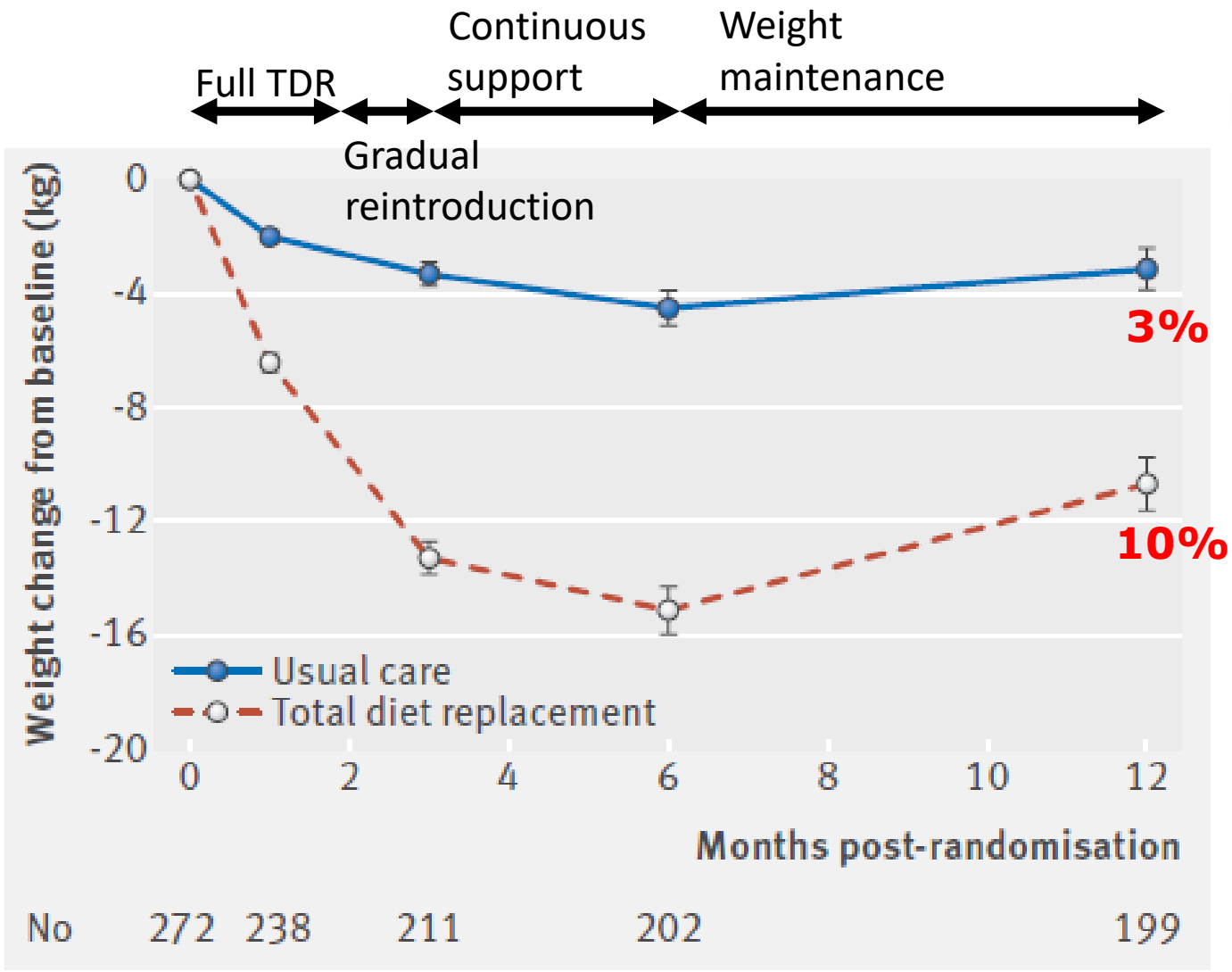
ORIGINAL ARTICLE

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

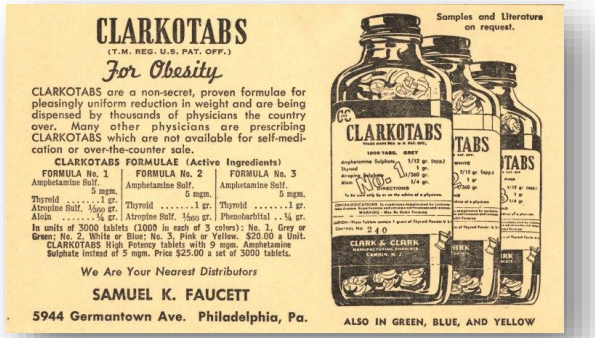
Julie R. Lundgren, M.D., Ph.D., Charlotte Janus, Ph.D., Simon B.K. Jensen, M.Sc., Christian R. Juhl, M.D., Lisa M. Olsen, M.Sc., Rasmus M. Christensen, Maria S. Svane, M.D., Ph.D., Thomas Bandholm, Ph.D., Kirstine N. Bojsen-Møller, M.D., Ph.D., Martin B. Blond, M.D., Bente M. Stallknecht, M.D., D. Sten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

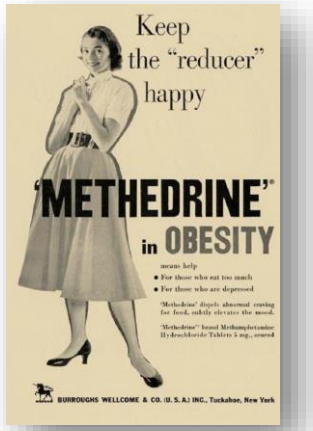
Total dietary replacement – the Droplet trial

278 ptt, BMI 37, T2D 20%, HT 30%. Randomized to 8w TDR (810 kcal/day) or standard weight loss management.



Astbury 2018 BMJ





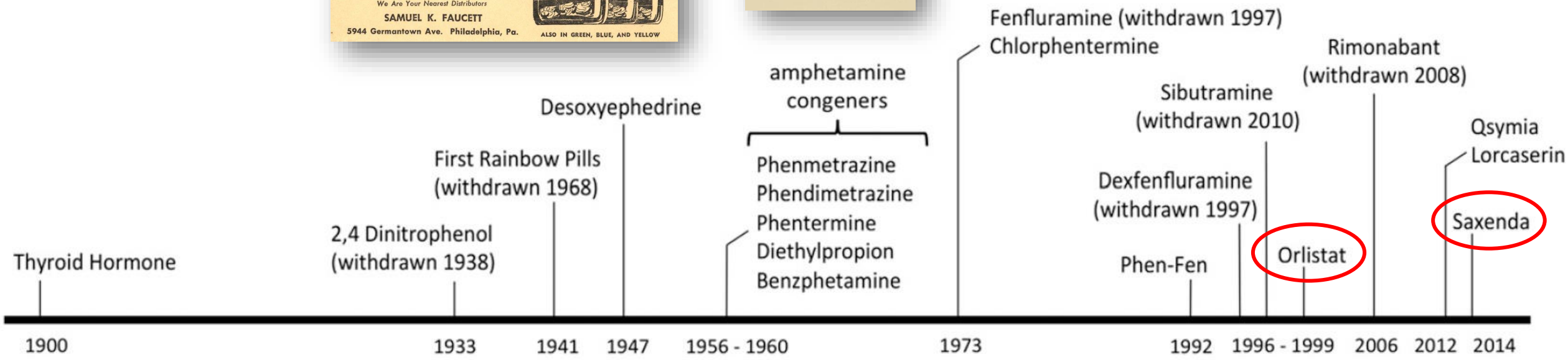


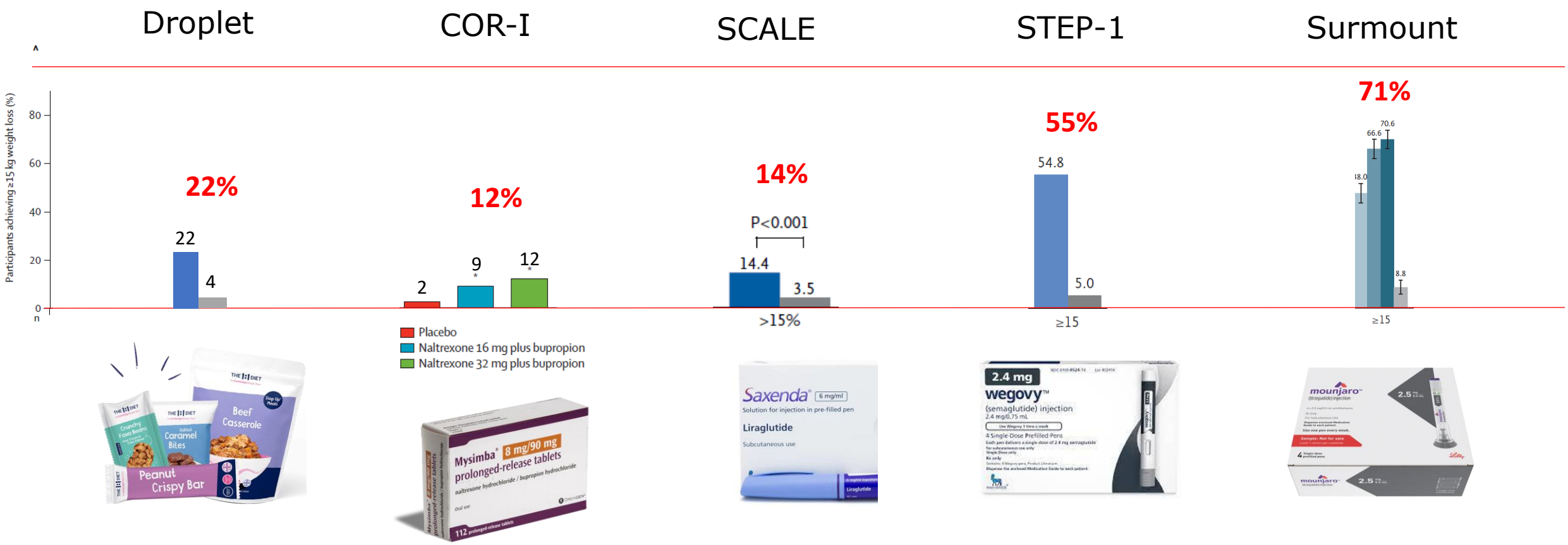
Fig. 1. Time line of pharmacotherapies used to treat obesity from 1900 until today.

2,6 kg (2,2-3,0)

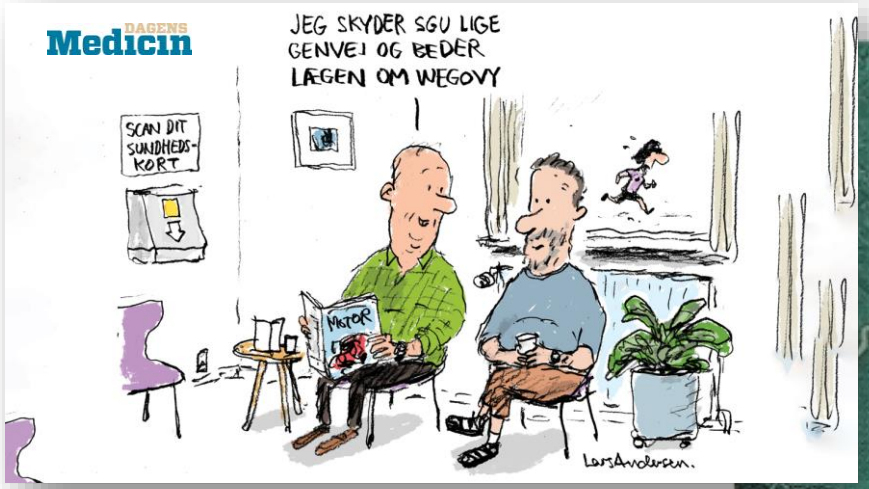
5,3 kg (4,5-6,1)

Müller 2018 Pharma Rev, Khera R 2016 JAMA

Proportion of patients achieving weight loss >15%



Astbury 2018 BMJ, Greenway 2010 Lancet, Pi-Xunier 2015, Wilding 2021 NEJM, Jastreboff 2022 NEJM

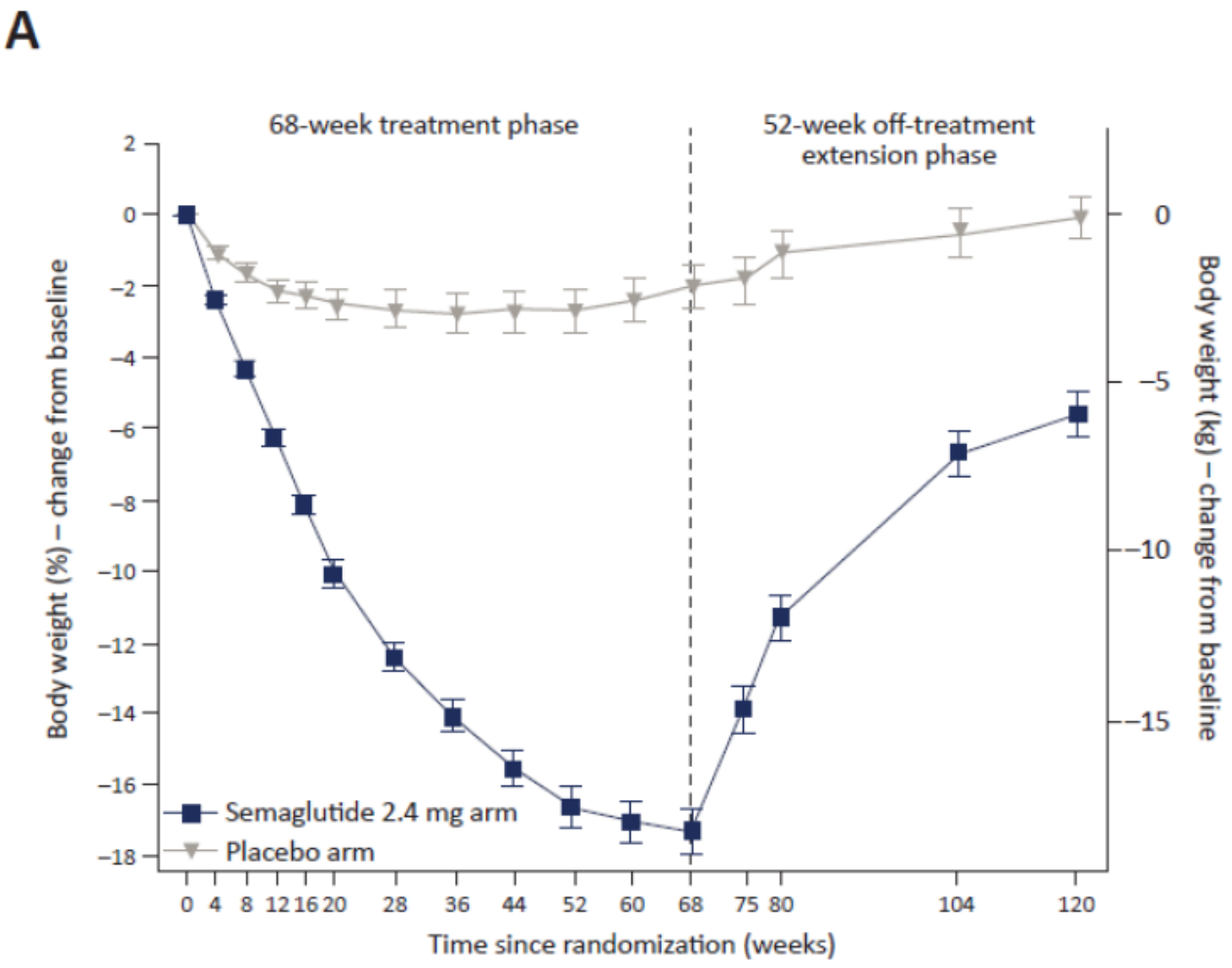


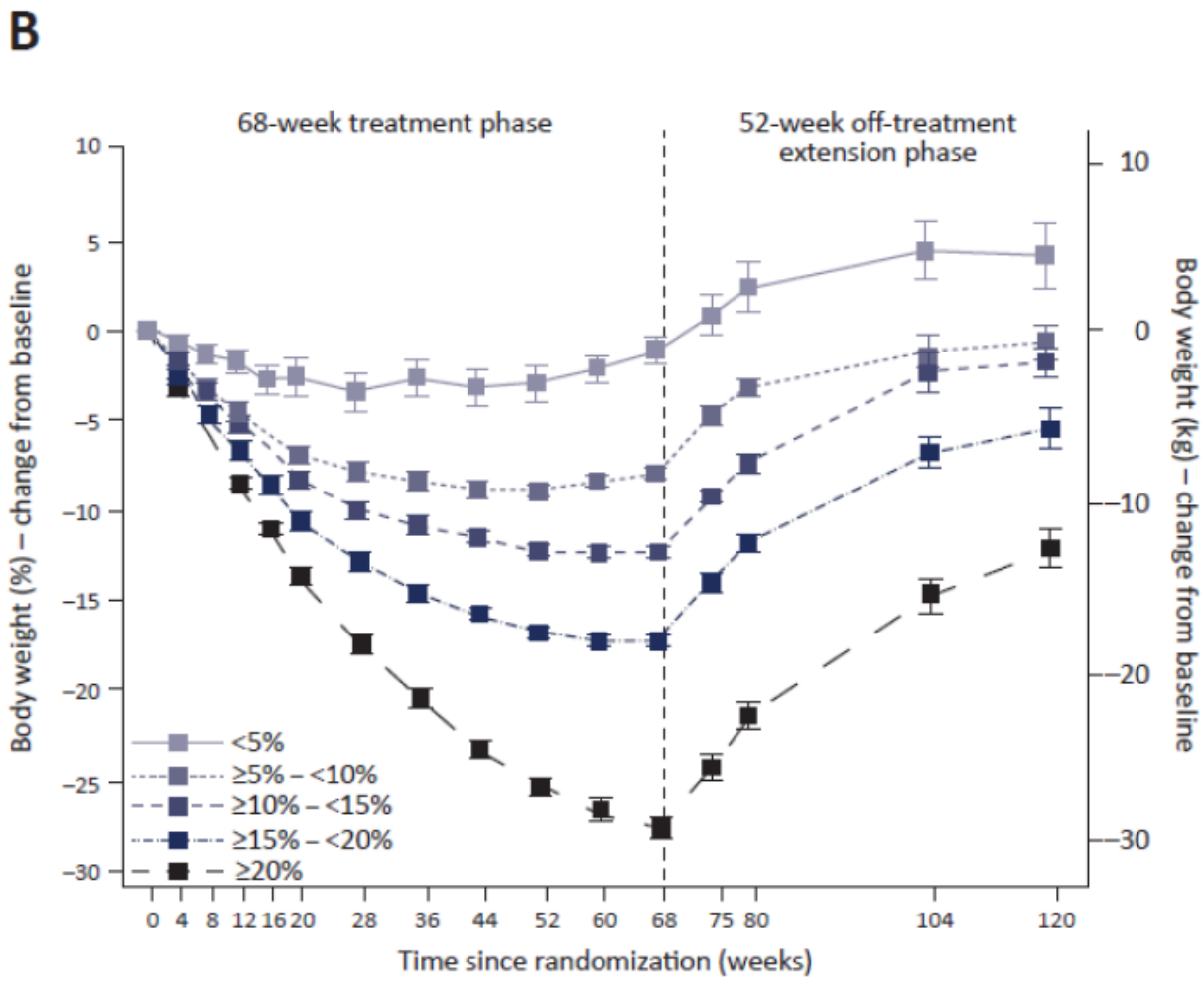
FT Magazine Drugs research + Add to myFT

A new 'miracle' weight-loss drug really works – raising huge questions

Novo Nordisk's Wegovy uses a hormone to regulate hunger. It's wildly effective, but is it misguided?

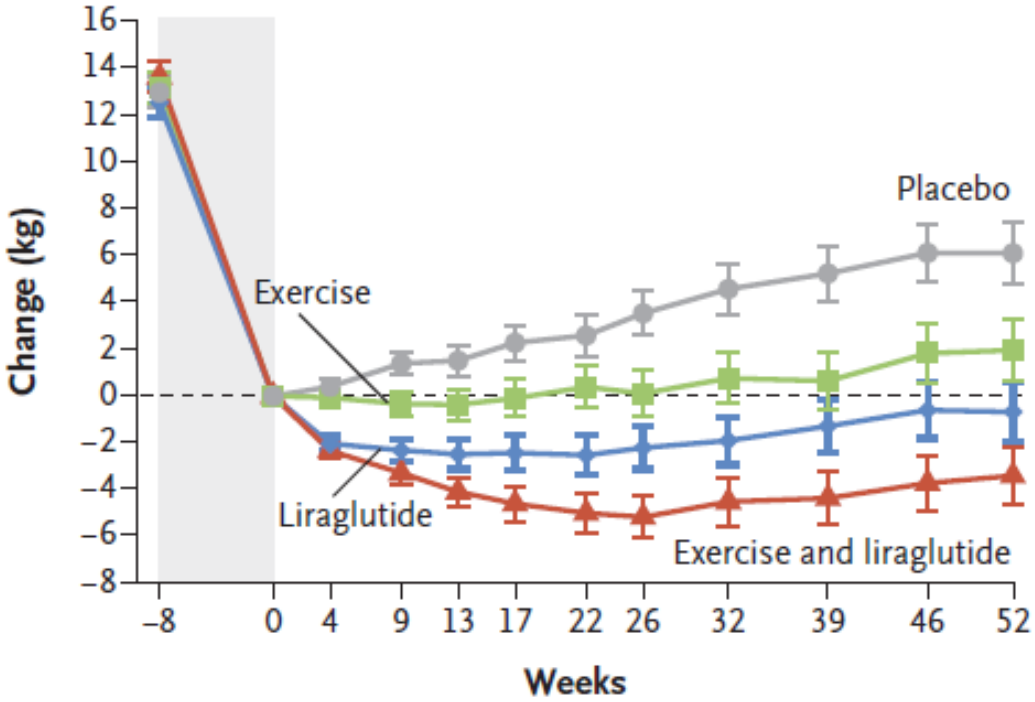
STEP 1 Extention trial

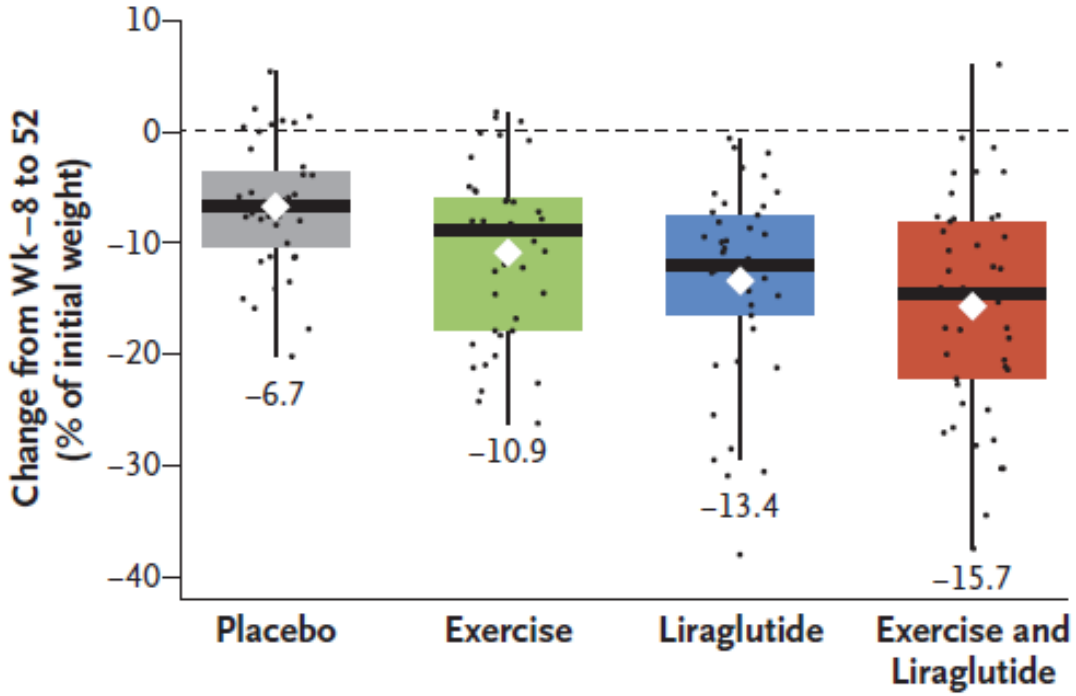




Wilding 2022 DOM

Combining pharmacotherapy and exercise – the S-lite study





S-lite studiet: 200 ptt, BMI 32-43, healthy. Randomized to placebo, liraglutide, exercise or liraglutide and exercise.

Lundgren JR et al NEJM 2021

Clinic for Overweight and Nutrition

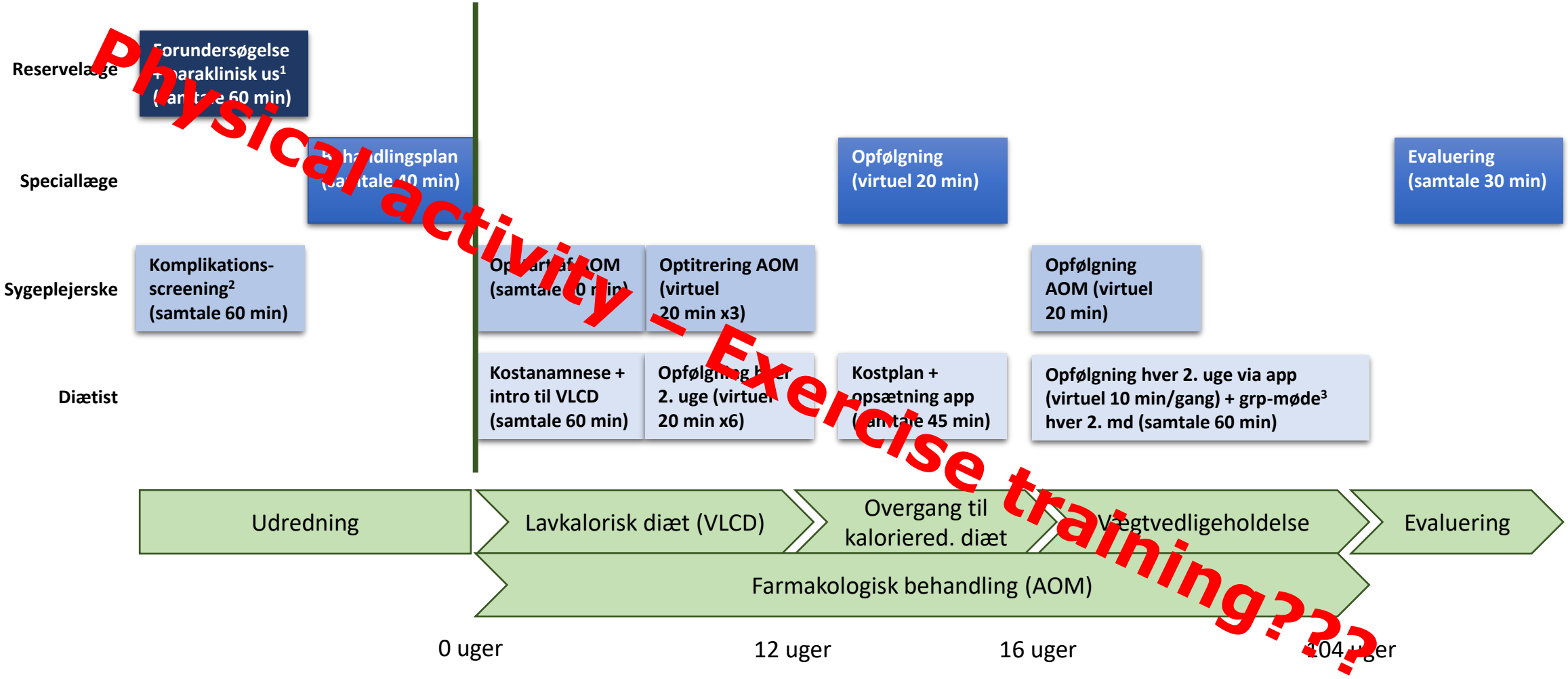
- Joins clinical dieticians, nurses and endocrinologists.
- Provide in-hospital individualized obesity management integrating dietary advice, meal replacements, anti-obesity medications, and obesity surgery (in collaboration with Dept. of Surgical Gastroenterology).
- Collaborate with local primary care providers (GPs and municipalities) to provide obesity management outside the hospital

- **Goal: Use weight loss management to improve health and quality of life for people living with severe obesity and comorbidities**

A new intensive non-surgical weight loss management program

- A treatment option for patient who for medical reasons are ineligible for bariatric surgery.
- Combines low-calorie total diet replacements and GLP-1 receptor agonist treatment.
- Aims for >10% weight loss within 4 months that is sustained for at least 2 years.

Flowchart for højt-specialiseret medicinsk behandling af svær overvægt
Klinik for Svær Overvægt, Endokrinologisk afdeling, Hvidovre Hospital



Physical activity – Exercise training???

AOM = anti-obesity medication; VLCD = very-low calorie diet

[1]Blodprøve, urinprøve, EKG

[2]Hjemme-BT, CRM (søvnapnø-screening)

[3]14 patienter pr. hold

Lighthouse Consortium on Obesity Management (LightCOM)

Rubjerg Knude Fyr
Løkken, Denmark

Vision

To take global leadership within innovative obesity management that benefits people with obesity and society.

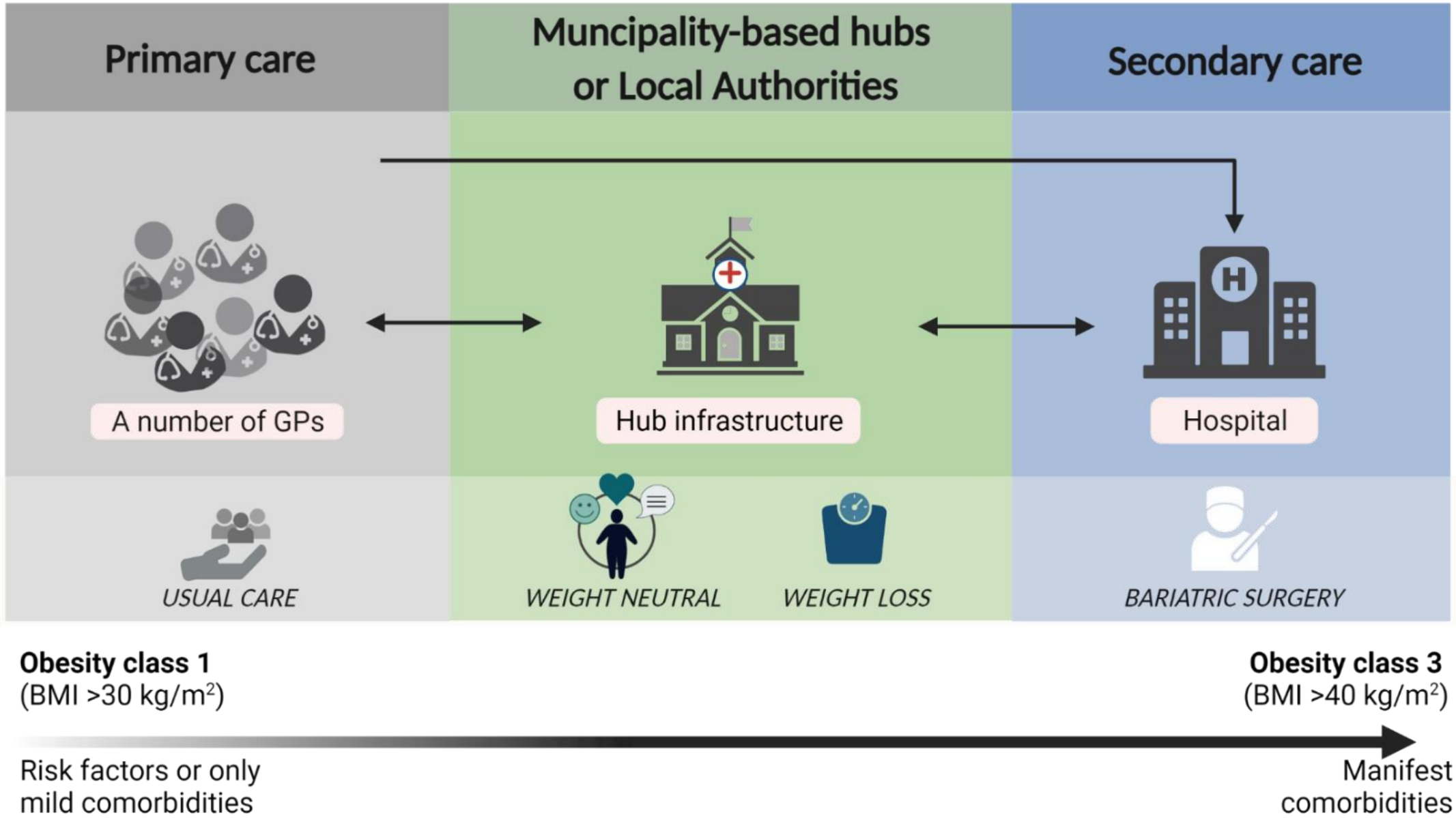
Key objectives

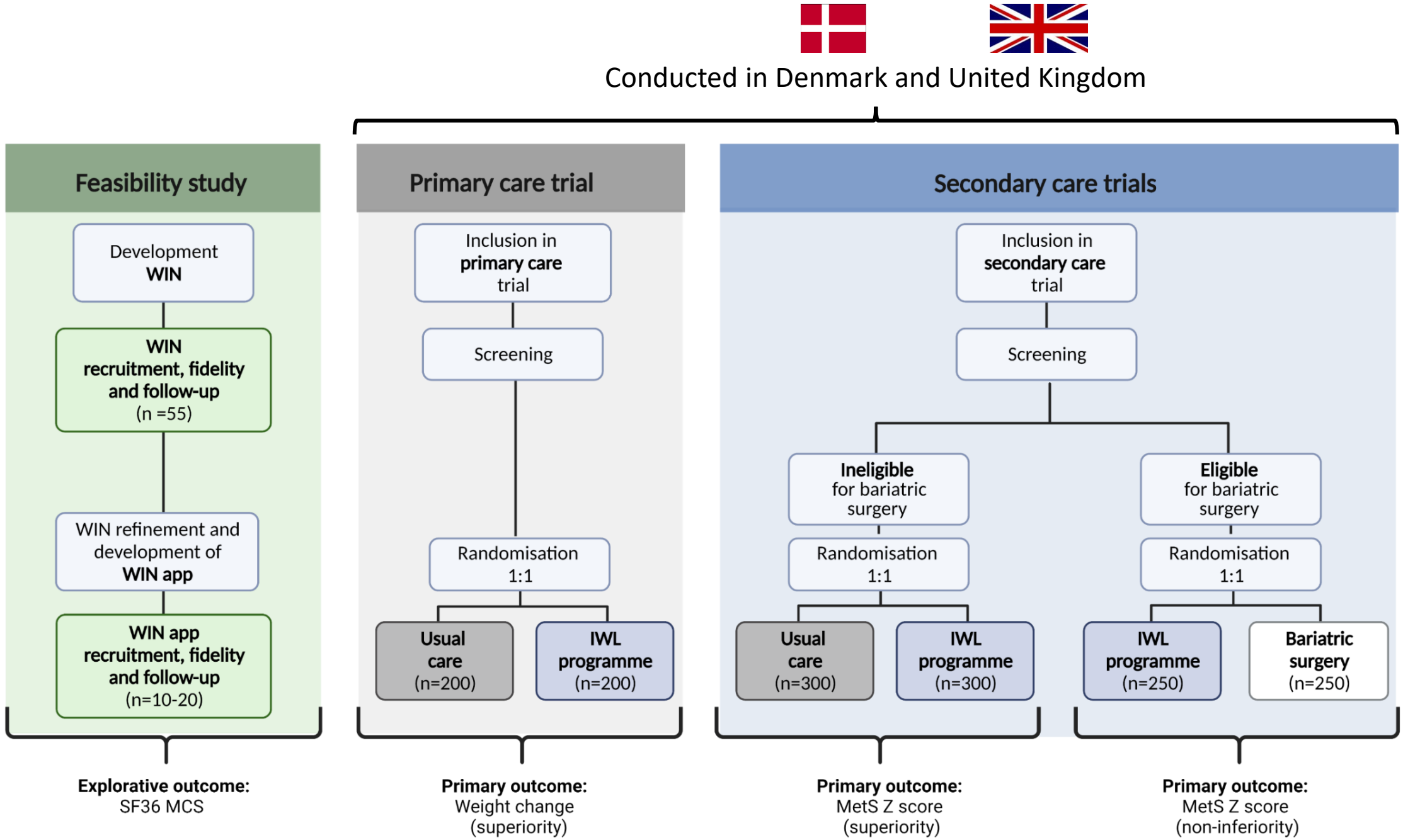
To evaluate a personalised intensive weight loss programme relative to existing obesity management strategies in primary and secondary care using randomised controlled trials.

To develop and commence early phase testing of the feasibility of an intervention that focus on body acceptance, intuitive eating, and physical activity, instead of supporting people with obesity to lose weight.

To join public and private solutions linking innovation and growth in life science and health technology, to improve the delivery of interventions and increase their long-term effectiveness.

Supported by a 180M grant from NNF (NNF22SA0080921)


Primary care
Muncipality-based hubs or Local Authorities
Secondary care
A number of GPs
Hub infrastructure
Hospital
USUAL CARE
WEIGHT NEUTRAL
WEIGHT LOSS
BARIATRIC SURGERY
Obesity class 1
(BMI >30 kg/m²)
Obesity class 3
(BMI >40 kg/m²)
Risk factors or only mild comorbidities
Manifest comorbidities


Conducted in Denmark and United Kingdom
Feasibility study
Development WIN
WIN recruitment, fidelity and follow-up (n =55)
WIN refinement and development of WIN app
WIN app recruitment, fidelity and follow-up (n=10-20)
Explorative outcome: SF36 MCS
Primary care trial
Inclusion in primary care trial
Screening
Randomisation 1:1
Usual care (n=200)
IWL programme (n=200)
Primary outcome: Weight change (superiority)
Secondary care trials
Inclusion in secondary care trial
Screening
Ineligible for bariatric surgery
Randomisation 1:1
Usual care (n=300)
IWL programme (n=300)
Primary outcome: MetS Z score (superiority)
Eligible for bariatric surgery
Randomisation 1:1
IWL programme (n=250)
Bariatric surgery (n=250)
Primary outcome: MetS Z score (non-inferiority)

Thanks for the attention!

Dueodde Fyr, Nexø, Denmark