Obesity Management for the Solo Practitioner McGill Refresher Course

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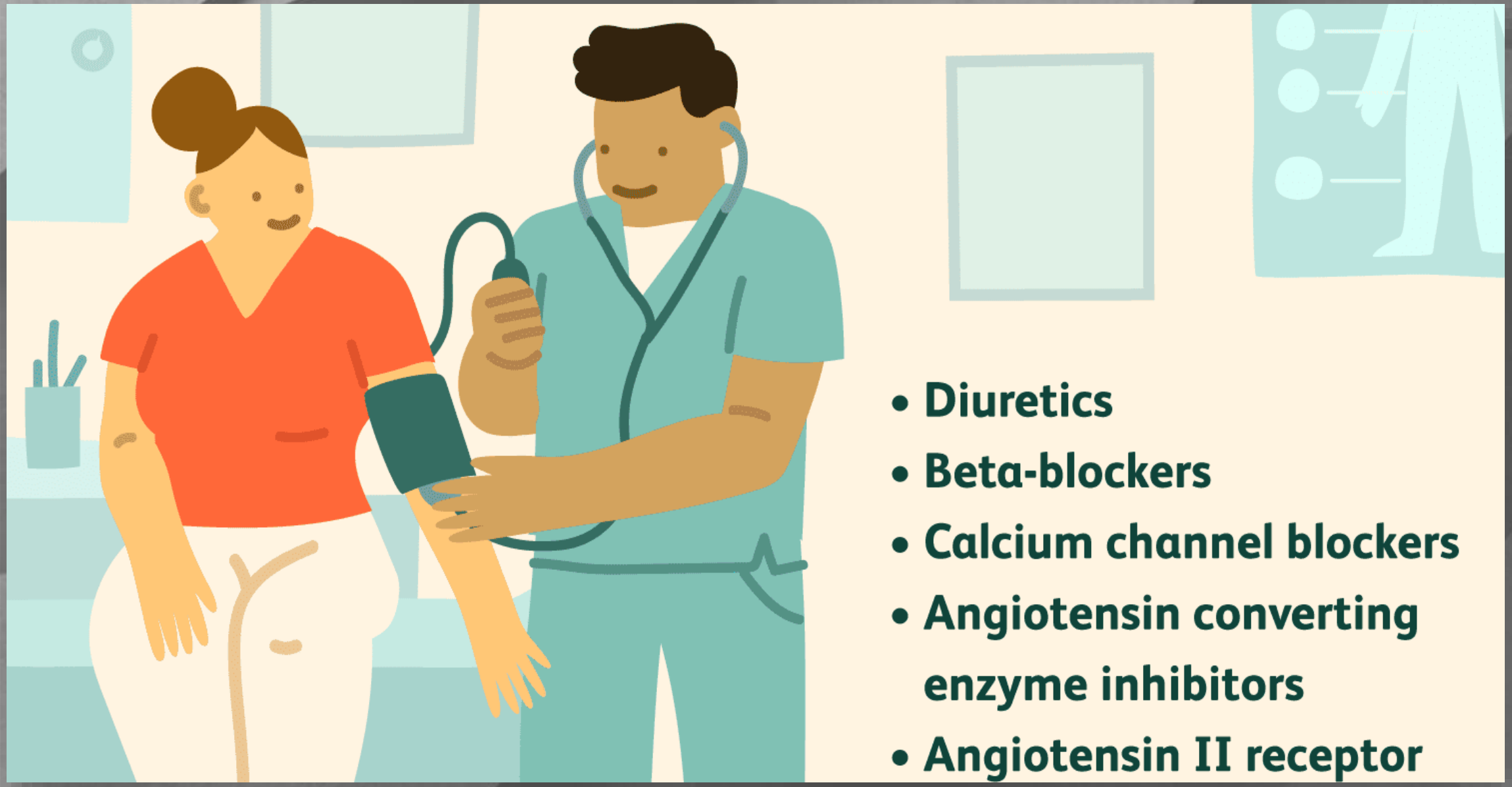
World Health Organization. Obesity and overweight. 2021. Retrieved from https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

The evolution of treatment for chronic diseases

Hypertension treatment pre-pharmacotherapy

Historically…



Armstrong, C. American family physician 2014; 90: 503-504.

Pharmacotherapy has changed the game

Obesity management- multi-disciplinary team

Counsellor

Exercise Specialist

Surgery

Pharmacist

M.D.

Dietitian

Nursing

Forgione, N. et al. Advances in therapy 2018; 35: 191-198.

Obesity management: the solo practitioner

Obesity Canada Guidelines

Canadian Adult Obesity Clinical Practice Guidelines Summary CMAJ 2020

Wharton, S. et al. Canadian Medical Association Journal 2020; 192: E875-891.

GUIDELINE CPD

Obesity in adults: a clinical practice guideline

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This article is available in French at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.191707/-/DC1

CMAJ Podcasts: author interview at https://www.cmaj.ca/lookup/doi/10.1503/cmaj.191707/tab-related-content

Obesity is a complex chronic disease in which abnormal or excess body fat (adiposity) impairs health, increases the risk of long-term medical complications and reduces lifespan.[1] Epidemiologic studies define obesity using the body mass index (BMI; weight/height^2), which can stratify obesity-related health risks at the population level. Obesity is operationally defined as a BMI exceeding 30 kg/m^2 and is subclassified into class 1 (30–34.9), class 2 (35–39.9) and class 3 (≥ 40). At the population level, health complications from excess body fat increase as BMI increases.[2] At the individual level, complications occur because of excess adiposity, location and distribution of adiposity and many other factors, including environmental, genetic, biologic and socioeconomic factors (Box 1).[11]

Over the past 3 decades, the prevalence of obesity has steadily increased throughout the world,[12] and in Canada, it has increased threefold since 1985.[13] Importantly, severe obesity has increased more than fourfold and, in 2016, affected an estimated 1.9 million Canadian adults.[13]

Obesity has become a major public health

KEY POINTS

- Obesity is a prevalent, complex, progressive and relapsing chronic disease, characterized by abnormal or excessive body fat (adiposity), that impairs health.
- People living with obesity face substantial bias and stigma, which contribute to increased morbidity and mortality independent of weight or body mass index.
- This guideline update reflects substantial advances in the epidemiology, determinants, pathophysiology, assessment, prevention and treatment of obesity, and shifts the focus of obesity management toward improving patient-centred health outcomes, rather than weight loss alone.
- Obesity care should be based on evidence-based principles of chronic disease management, must validate patients' lived experiences, move beyond simplistic approaches of "eat less, move more," and address the root drivers of obesity.
- People living with obesity should have access to

Obesity Bias and Stigma

Kirk, S. et al. Canadian Medical Association Journal 2020; 192: E875-891.

Almost everyone has obesity bias

Obesity Canada. Weight bias. 2021. Retrieved from https://obesitycanada.ca/weight-bias/

Obesity bias starts in pre-school

Kornilaki, E. Hellenic Journal of Psychology 2014; 11: 26-46.

HCP are biased and discriminate against PwO

70%

Of people living with obesity report **experiencing stigma from HCPs.**[1]

1. Puhl, R & Brownell, K. Obesity 2006; 14: 1802-1815. 2. Alberga, A. et al. Primary health care research & development 2019: 20.
3. Kirk, S. et al. Canadian Medical Association Journal 2020; 192: E875-891.

Bias and Discrimination

From a family doctor in Canada

- *Losing weight is too hard because the general attitude of patients coming into my clinic in 2020 is that of* ***nonaccountability.***

- *I inquire about their diet and they are incensed when I tell them that* ***perogies*** *are not a good choice. (To help these patients) ….paint billboards with simple common sense info.*

Julie Connolly. Conspiracy theory. Medical Post (2020).

Genetics of obesity

> 140 genetic regions are now known to influence obesity traits

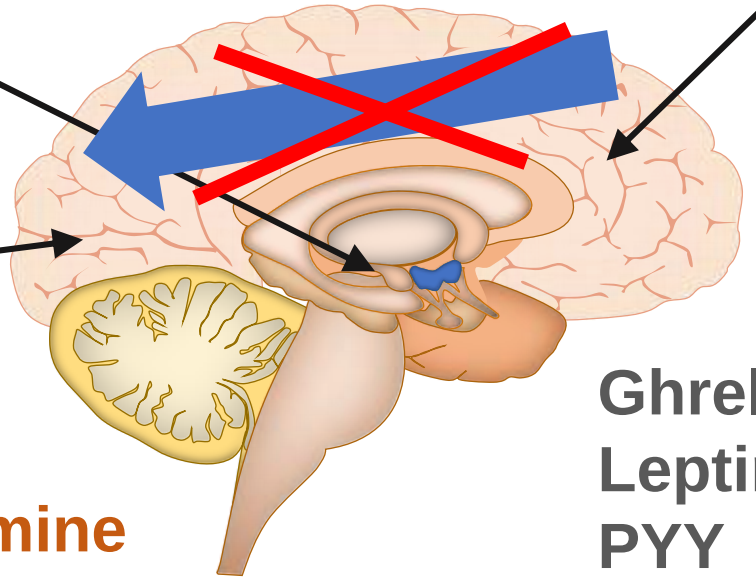
Van Der Klaauw, A & Farooqi, I. Cell 2015;161:119-132.

Neuropathology associated with obesity

Hypothalamic Hunger System

Frontal Lobe Executive Function

Mesolimbic Reward System



Dopamine
Opioid
Cannabinoid
Receptors

Ghrelin
Leptin
PYY
GLP-1
CCK
Amylin

Lau, D & Wharton, S. Canadian Medical Association Journal 2020; 192: E875-891.

Differential mitochondrial gene expression in adipose tissue following weight loss induced by diet or bariatric surgery

MITOCHONDRIA

Dieting – depresses mitochondria function and gene expression

Bariatric surgery – improves the activity and function of mitochondria and gene expression.

van der Kolk, B. et al. The Journal of Clinical Endocrinology & Metabolism 2021;106: 1312-1324.

The three pillars of obesity management that support nutrition and activity

Psychological Intervention

1. Implement multicomponent behaviour modification
2. Manage sleep, time, and stress
3. Cognitive behavioural therapy and/or acceptance and commitment therapy should be provided for patients if appropriate

Pharmacological Therapy

1. Liraglutide
2. Naltrexone/bupropion (in a combination tablet)
3. Orlistat

Criteria
BMI ≥30 kg/m^2 or
BMI ≥27 kg/m^2 with obesity (adiposity) related complications

Bariatric Surgery

Procedure should be decided by surgeon in discussion with patient

1. Sleeve gastrectomy
2. Roux-en-Y gastric bypass
3. Biliopancreatic diversion with/without duodenal switch

Criteria
BMI ≥40 kg/m^2 or
BMI ≥35–40 kg/m^2 with obesity (adiposity) related complications or
BMI ≥30 kg/m^2 with poorly controlled T2D

BMI, bomass index. These medications may not be approved outside of Canada.

Wharton, S. et al. Canadian Medical Association Journal 2020; 192: E875-891.

How much weight loss is needed to improve obesity-related complications?

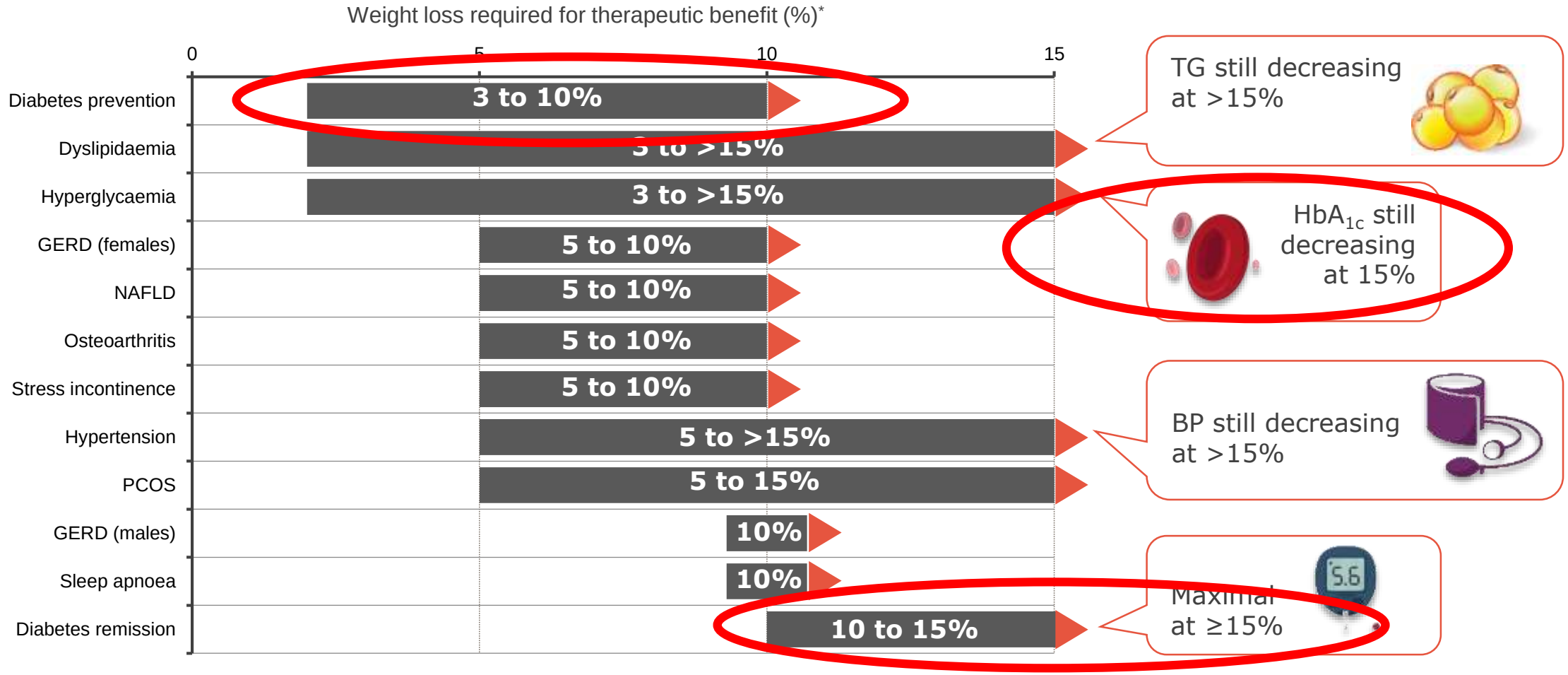


**Figure displays weight loss ranges examined in the studies (impact of >10% weight on NAFLD, and sleep apnea symptoms was not reported).*
BP, blood pressure; GERD, gastroesophageal reflux disease; NAFLD, non-alcoholic fatty liver disease; PCOS, polycystic ovary syndrome; TG, triglycerides.
Adapted from: AACE/ACE Obesity CPG, Endocr Pract. 2016;22(Suppl 3); Cefalu et al. Diabetes Care 2015;38:1567–82; Lean et al. Lancet 2018;391:541–51; Hannah & Harrison. Clin Liver Dis 2016;20:339–50.

WEIGHT LOSS MEDICATIONS THAT FAILED OUR PATIENTS

- Rainbow Pills
  - (Most amphetamines – Cardiac arrythmias)
- Fenfluramine
  - (Heart Valve Defect)
- Rimonabant
  - (Suicides)
- Sibutramine
  - (Heart Attacks)

Current Medications and Beyond

Current Effective Medications

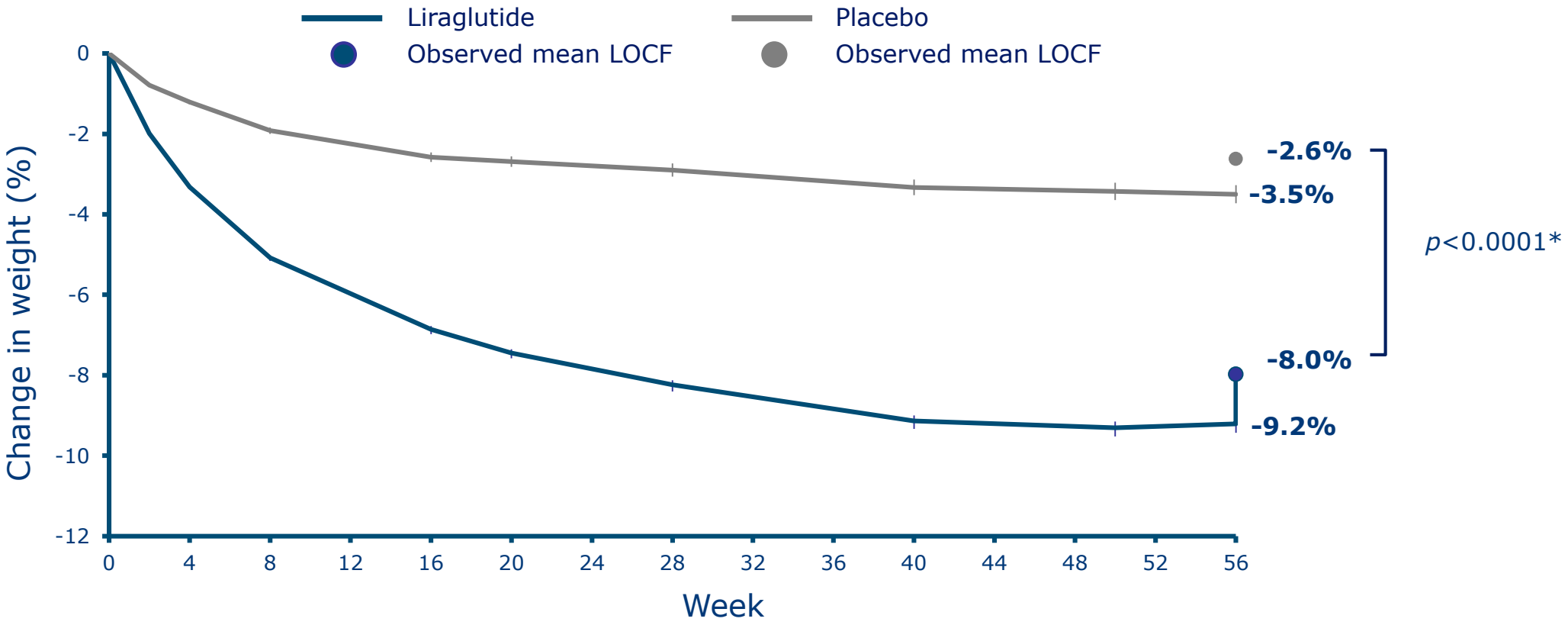
- Naltrexone/Bupropion
  - Combo of 2 older drugs – addictions, cravings
- GLP1 (Liraglutide)
  - Once daily

Emerging Medications

- GLP1 (semaglutide)
  - Once weekly
- Amylin
- Combination Treatments
  - GLP1/Amylin
  - GLP1/GIP
  - GLP1/Glucagon Agonist

SCALE Trial - Liraglutide 3.0mg sc for Obesity

Baseline weight: **106 kg**



Mean waist circumference change: Liraglutide: **-8.2 cm** (baseline: 115 cm) vs.

placebo: -3.9 cm (baseline: 114.5 cm) (*p<0.001*)

FAS, fasting visit data only. Line graphs are observed means (±SE). Circles are observed means LOCF. FAS, full analysis set; LOCF, last observation carried forward; SE, standard error. *Statistical analysis is ANCOVA. Test for no treatment by prediabetes interaction $p=0.5907$

Adapted from Saxenda® (liraglutide), Product Monograph, Novo Nordisk Canada Inc, June 2015

Real World Study in Canada
Liraglutide 3.0 mg n:311 patients

8.1 kg

average weight loss between baseline and 6 months in the ≥6 months cohort

7.1%

average percentage weight loss between baseline and 6 months in the ≥6 months cohort

Improvements in HbA_{1c} and SBP were also observed

Wharton S et al. Obesity, June 2019. https://doi.org/10.1002/oby.22462

Effect of Naltrexone/Bupropion on weight in COR-I

Treatment with NB resulted in significant and sustained weight loss over 56 weeks

COR-I

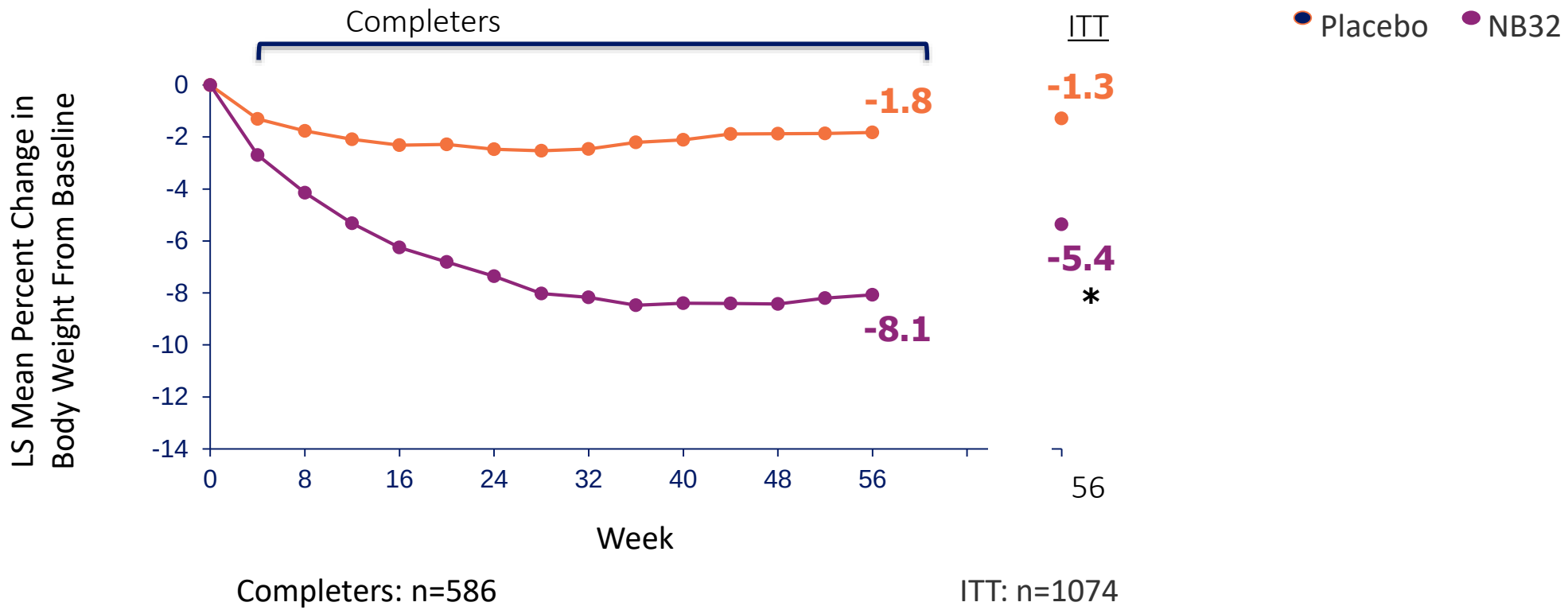


Figure on right republished with permission of the American Diabetes Association, from Hollander P et al,[2] © 2013; permission conveyed through Copyright Clearance Center, Inc.

*P<0.001 vs placebo.

BMOD=behavior modification; DM=diabetes mellitus; ITT=intent-to-treat; LS=least squares.

1. Contrave [prescribing information]. La Jolla, CA: Orexigen Therapeutics, Inc.; 2016. **2.** Greenway FL et al. *Lancet*. 2010;376:595-605. **3.** Wadden TA et al. *Obesity*. 2011;19:110-120. **4.** Hollander P et al. *Diabetes Care*. 2013;36:4022-4029.

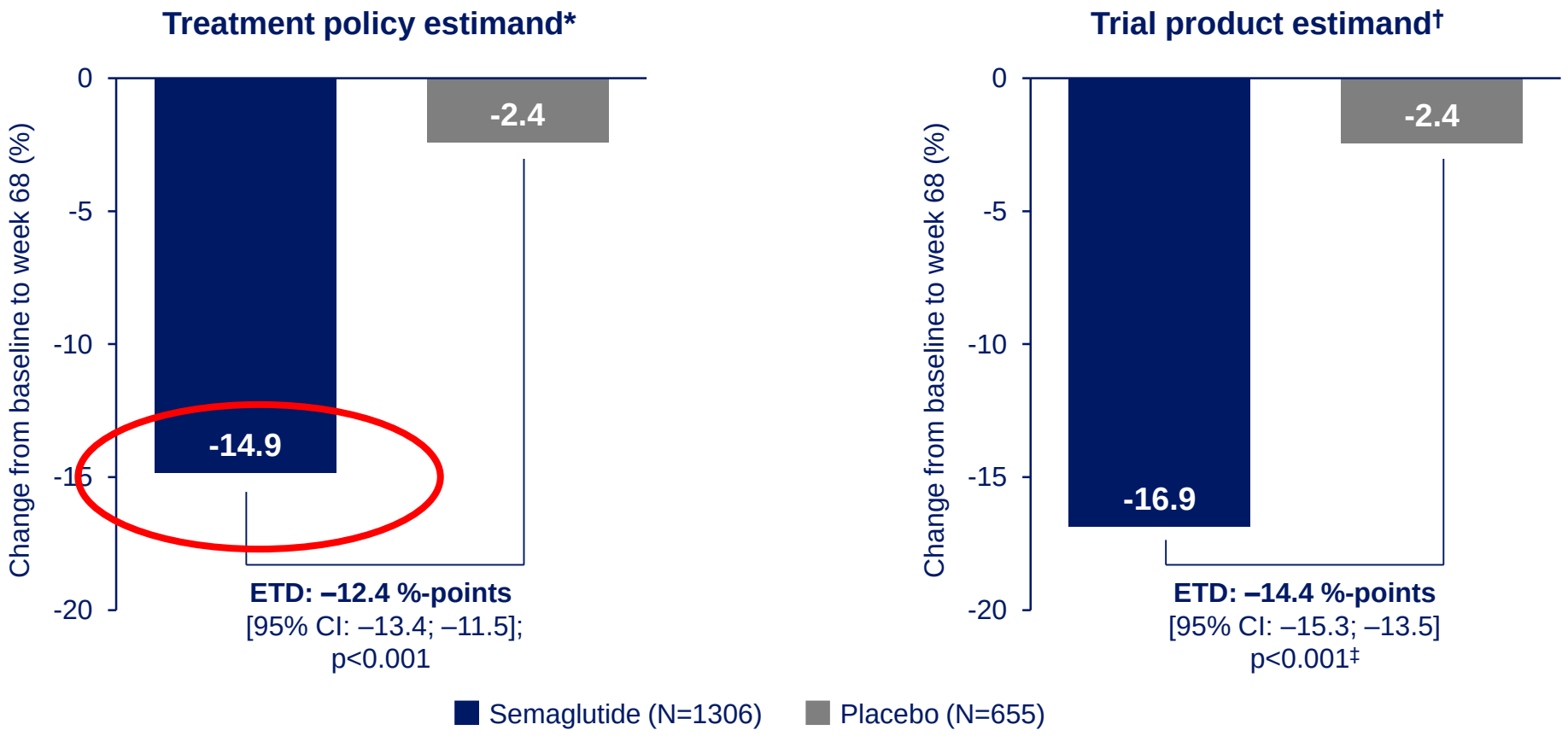
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Once-Weekly Semaglutide in Adults with Overweight or Obesity

John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D., Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D., Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D., Sean Wharton, M.D., Pharm.D., Koutaro Yokote, M.D., Ph.D., Niels Zeuthen, M.Sc., and Robert F. Kushner, M.D., for the STEP 1 Study Group*

Semaglutide 2.4mg
Percentage change in body weight from baseline to week 68



*The treatment policy estimand assesses treatment effect regardless of treatment discontinuation or rescue intervention. Continuous end points were analyzed using analysis of covariance, with randomized treatment as a factor and baseline end point value as a covariate, and a multiple imputation approach for missing data.[1]
†The trial product estimand assesses treatment effect if trial product was taken as intended (i.e. if all participants adhered to treatment and did not receive rescue intervention). End points were analyzed using a mixed model for repeated measurements.
‡Not controlled for multiplicity.

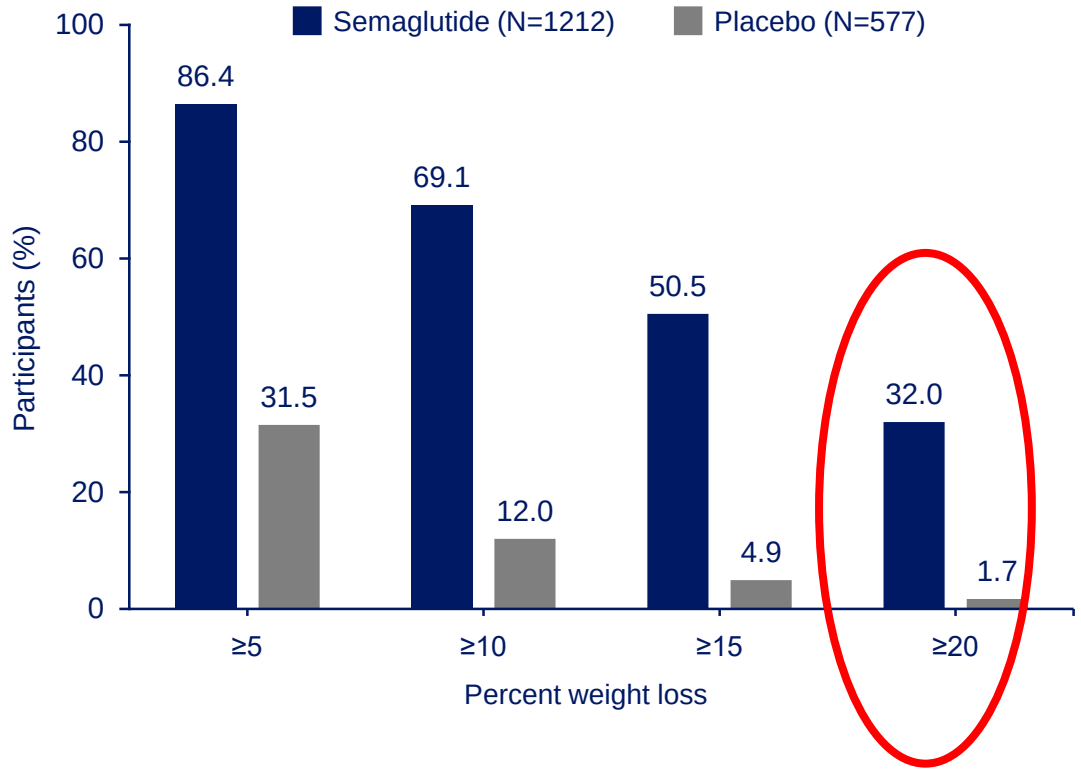
1. Kushner RF, et al. Obesity 2020;6:1050-61. CI, confidence interval; ETD, estimated treatment difference.

Adapted from data presented in Table 2. Coprimary, Confirmatory, and Selected Supportive Secondary and Exploratory End Points for the Treatment Policy Estimand, and Table S2. Co-primary, Confirmatory and Selected Supportive Secondary Endpoints for the Trial Product Estimand.

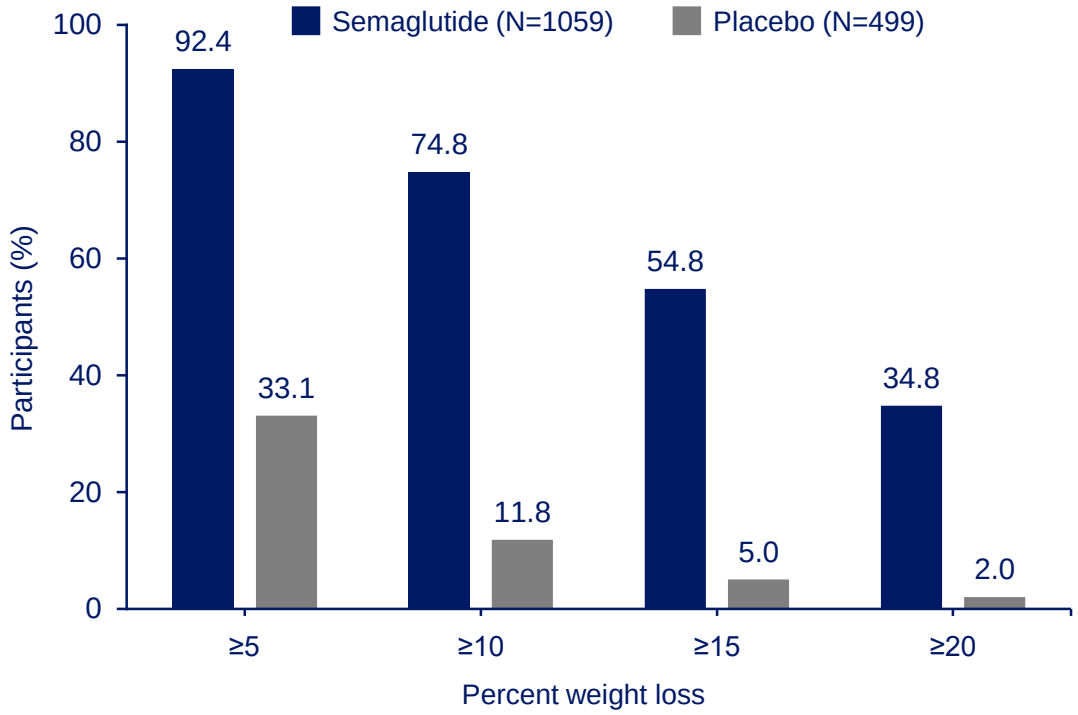
Wilding et al. NEJM 2021; [Full citation to be added once available].

Semaglutide 2.4mg
Achievement of categorical body weight reductions at week 68

In-trial data at week 68



On-treatment data at week 68

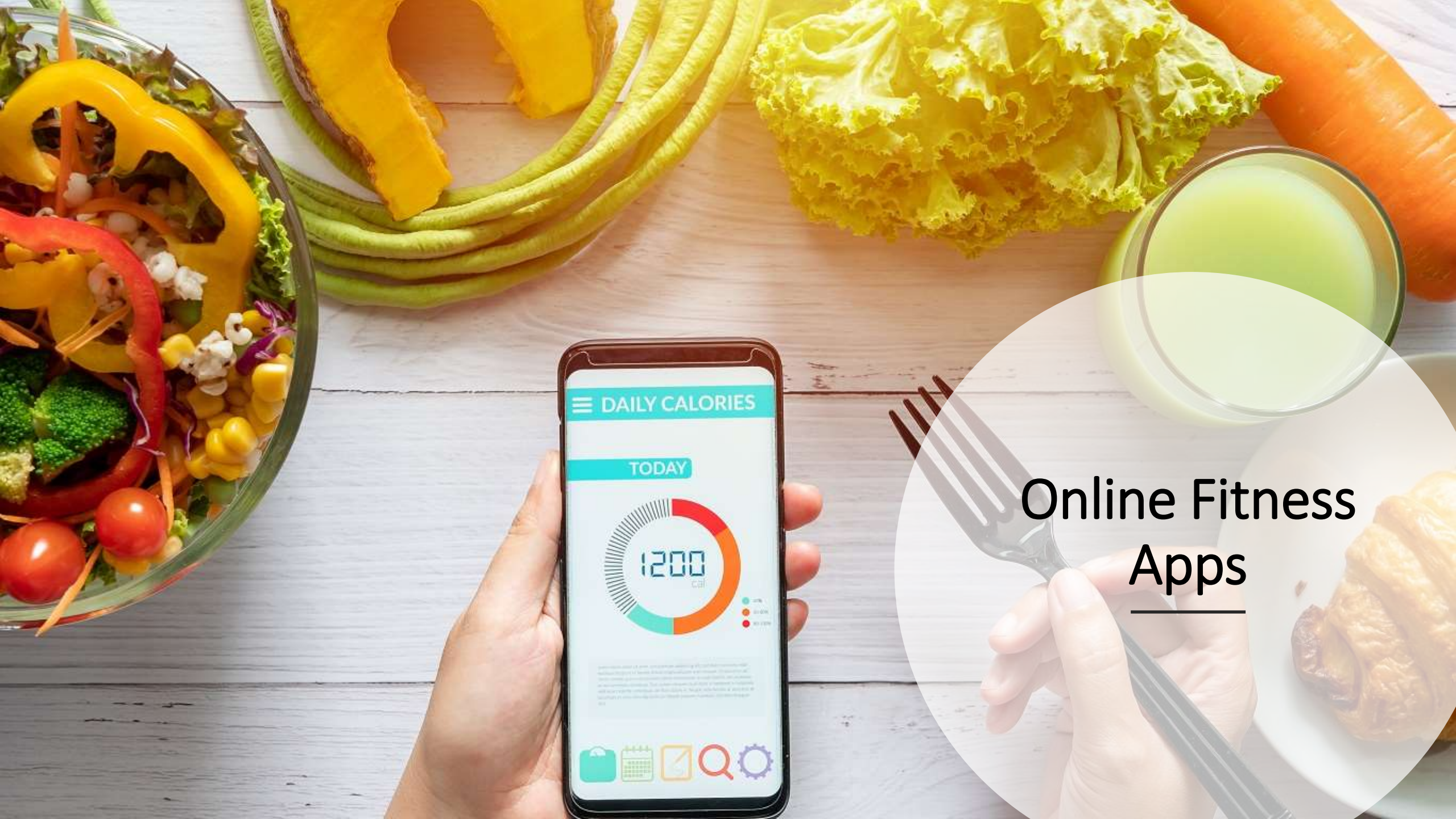


Bar graphs show the percentages of participants with an observation at the week 68 visit in whom body-weight reductions of at least 5%, 10%, 15%, and 20% were achieved from baseline to week 68 during the in-trial observation period and on-treatment observation period.

Adapted from Figure 1C/D. Effect of Once-Weekly Semaglutide, as Compared with Placebo, on Body Weight.

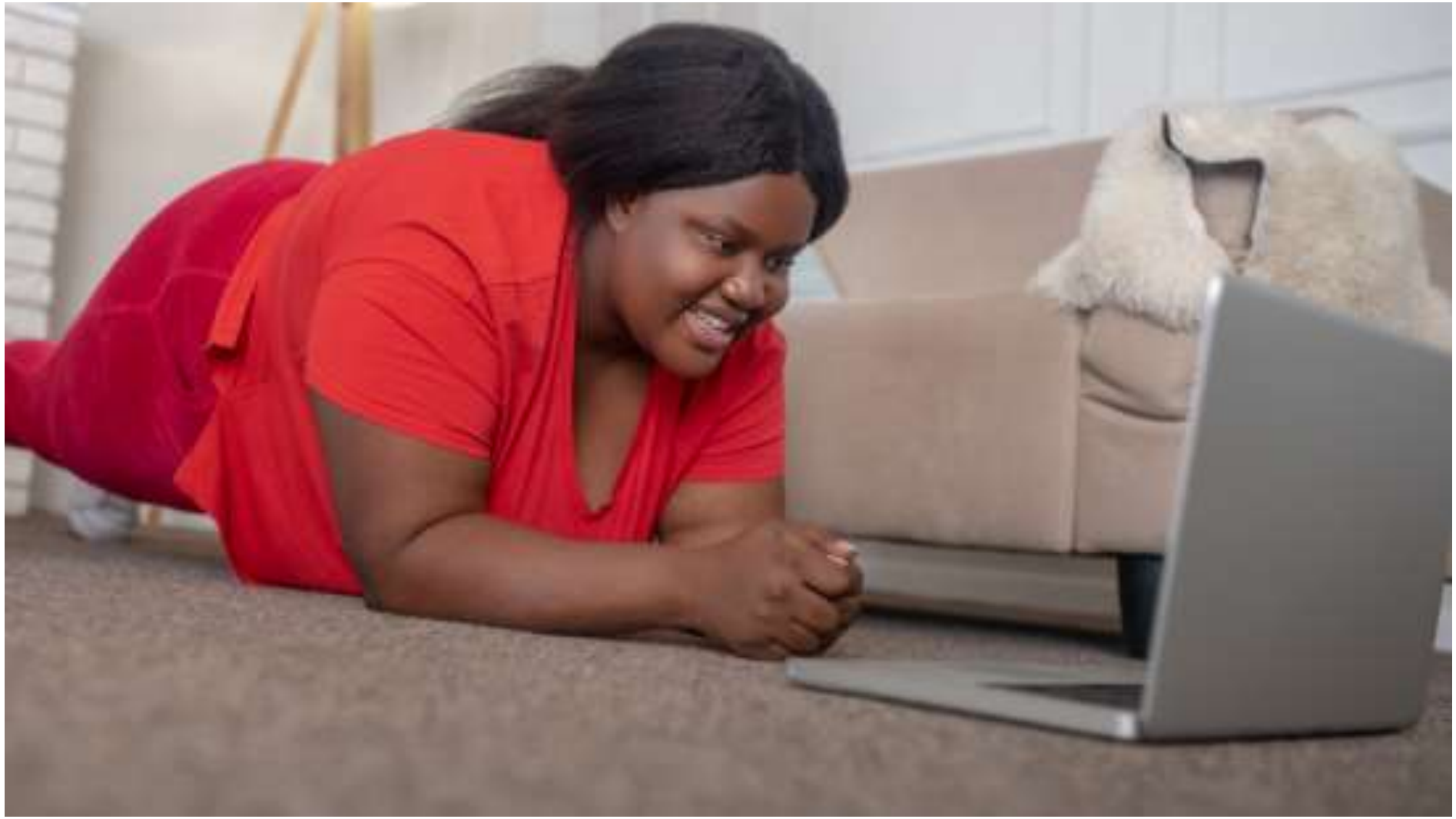
Wilding et al. NEJM 2021; [Full citation to be added once available].

Pharmacotherapy for obesity management



Online Fitness Apps

Self initiated physical activity



Bariatric surgery

Online psychological interventions

Conclusion

All chronic disease management requires a scalable approach - Obesity is no different

The Canadian Obesity Guidelines emphasizes that we need to address bias and stigma in obesity medicine

The pillars of obesity management are psychological intervention, pharmacotherapy and bariatric surgery

Pharmacotherapy is the game changer and along with ONLINE resources, the solo practitioner now has effective tools for weight management