



Have we Found the Cure for Obesity?

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VP & Chief Medical Director

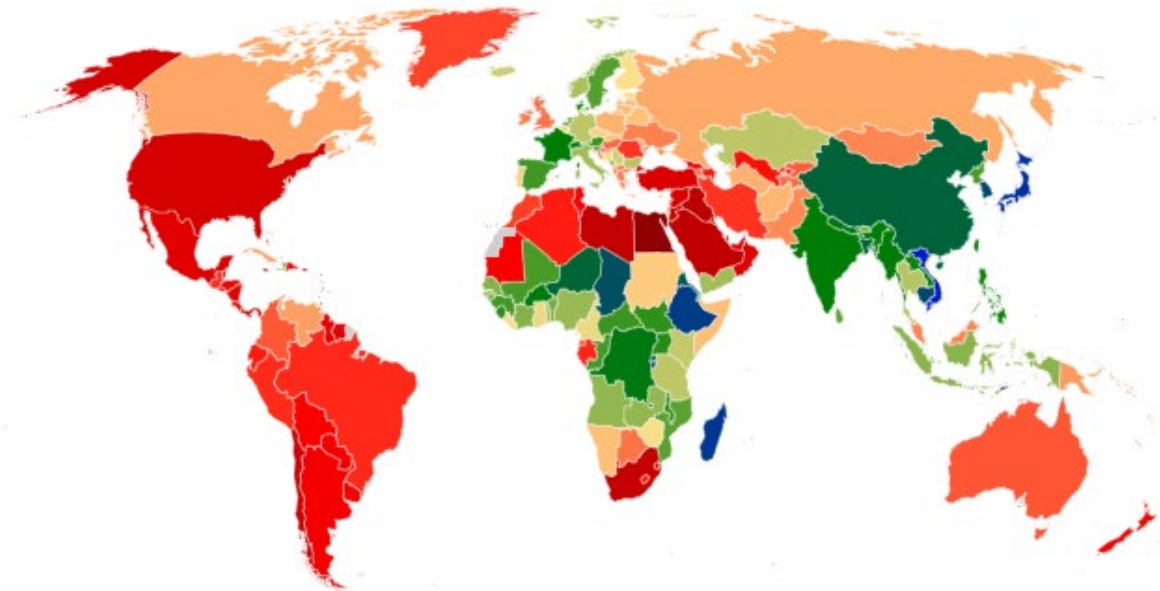
CCIA Claims & Operations Symposium – 14 November 2024

Munich RE ®

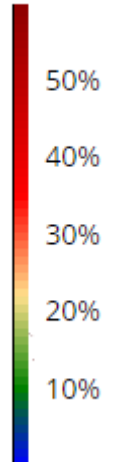
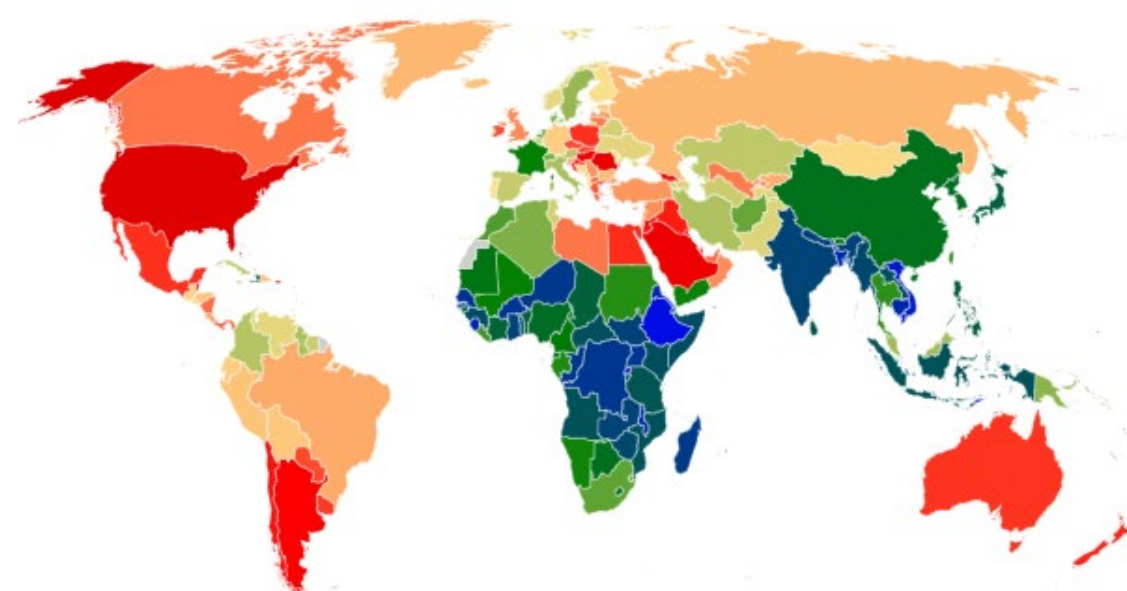
Obesity Trends

Not getting any better!

Female 2022



Male 2022



*Obesity refers to BMI ≥ 30 kg/m².
Age-standardised estimates for adults aged 20 years and older.*

Obesity Forecast



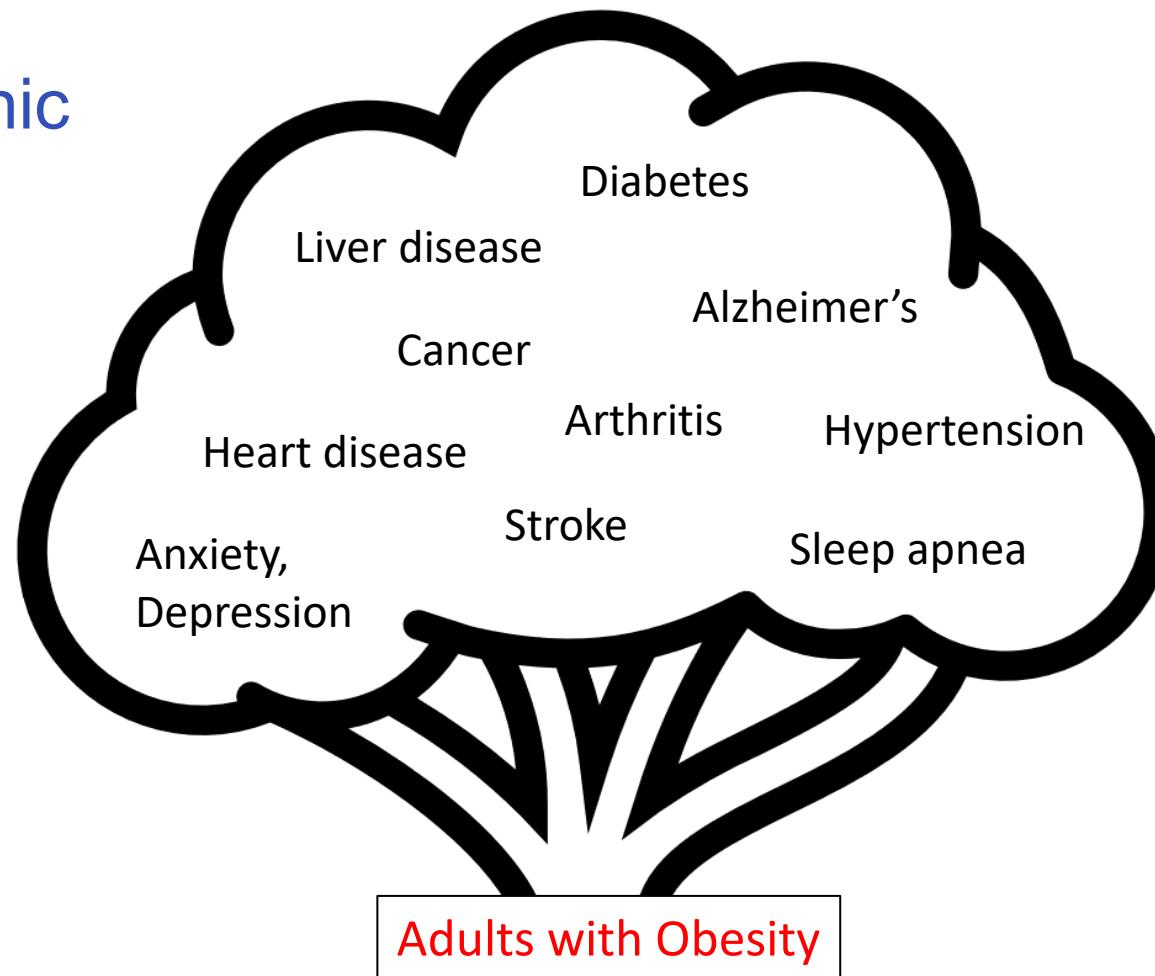
HEALTH

Report: Obesity could cost the world over \$4 trillion a year by 2035

By Julia Belluz March 2, 2023

Childhood obesity levels could more than double by 2035

Associated Chronic Diseases



Adults with Obesity

Root causes:

Genetics
Epigenetics

Poor diet quality

Lack of exercise

Endocrine disrupting chemicals

Barriers to health care

Weight bias and stigmatization

Stress/ Distress

Insufficient economic resources



Body Weight & Cancer Risk

In the United States, the percentage of overweight and obese adults and children has soared over the past several decades. Studies show that with that increased weight comes an increased risk of developing certain types of cancers.

**EXCESS BODY WEIGHT,
POOR NUTRITION, PHYSICAL INACTIVITY,
AND EXCESS ALCOHOL CONSUMPTION**

=

ABOUT

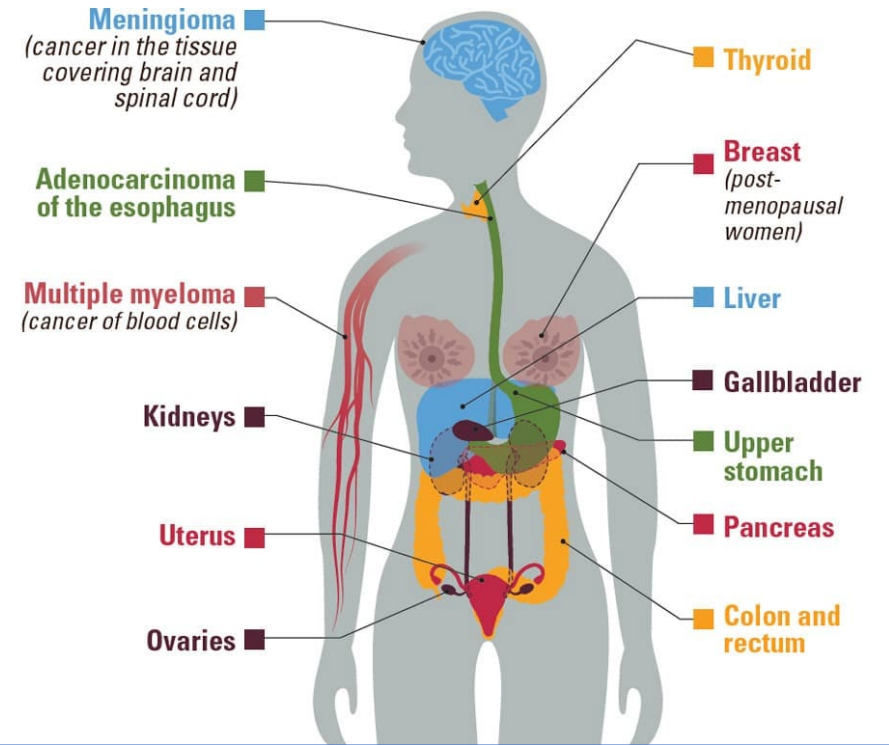
1 IN 5 CANCER CASES



OVERWEIGHT OR OBESITY RAISES A PERSON'S RISK OF GETTING AT LEAST

13 TYPES OF CANCER

13 cancers are associated with overweight and obesity



71%
**OF AMERICAN ADULTS
ARE OVERWEIGHT OR OBESE**

<https://www.cancer.org/cancer/risk-prevention/diet-physical-activity/body-weight-and-cancer-risk/infographic.html>
<https://www.cdc.gov/cancer/obesity/index.htm>

Increasing Cancer in those < 50 years old

Emerging cancer trends among young adults in the USA: analysis of a population-based cancer registry

Hyuna Sung, Rebecca L Siegel, Philip S Rosenberg, Ahmedin Jemal

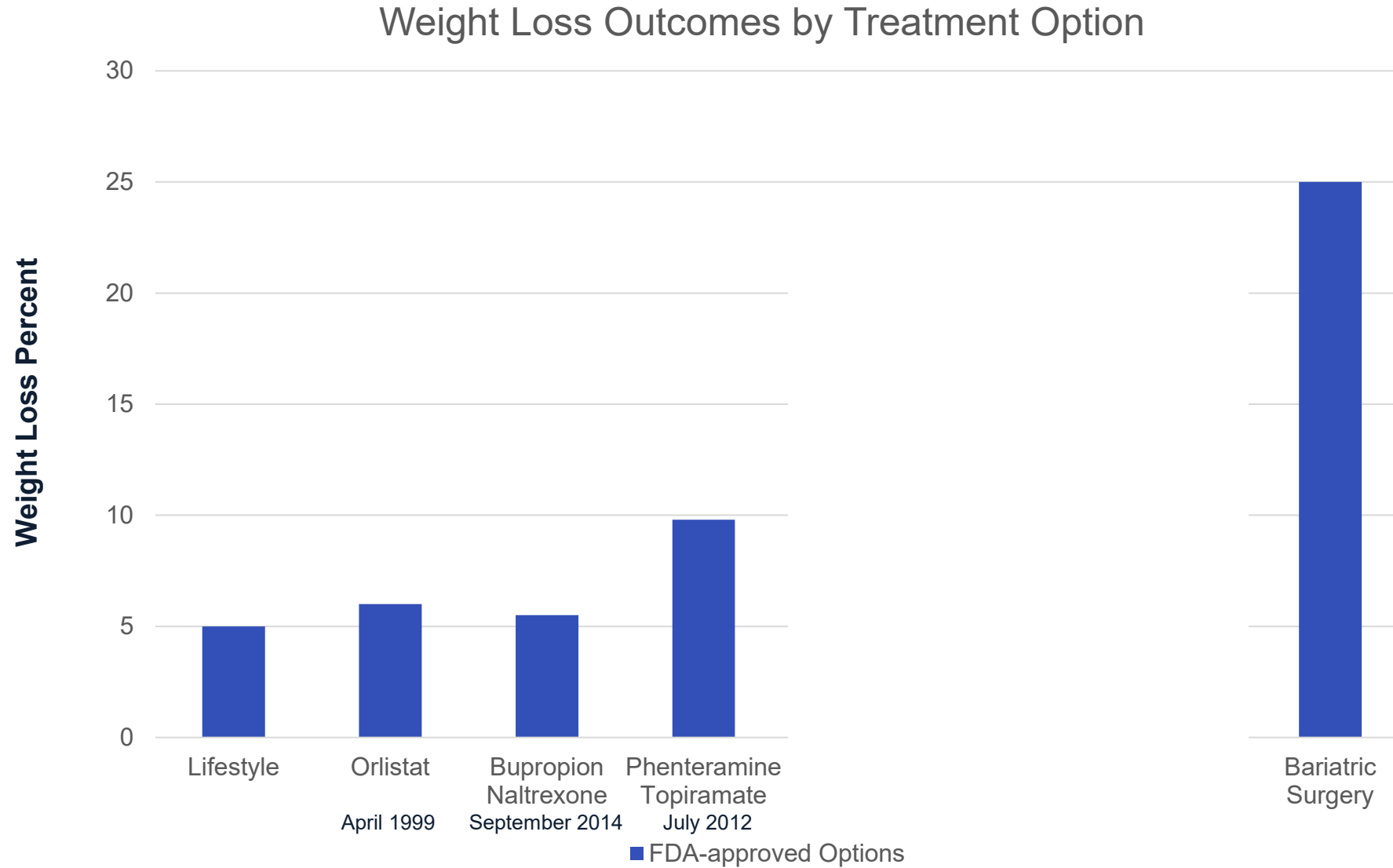


Interpretation The risk of developing an obesity-related cancer seems to be increasing in a stepwise manner in successively younger birth cohorts in the USA. Further studies are needed to elucidate exposures responsible for these emerging trends, including excess bodyweight and other risk factors.

**Mammograms should start at
40 to address rising breast
cancer rates at younger ages**
(April 2024, USPSTF)

**Colonoscopies should start
at age 45**
(May 2021, USPSTF)

Losing Weight is HARD!!!



GLP-1 receptor agonists

Mimics the hormone glucagon-like peptide 1 (GLP-1)

Initially approved for Type 2 Diabetes (2005)

Generally taken as a shot (SQ injection)



Proven weight loss

Added metabolic benefits

GLP-1 receptor agonists

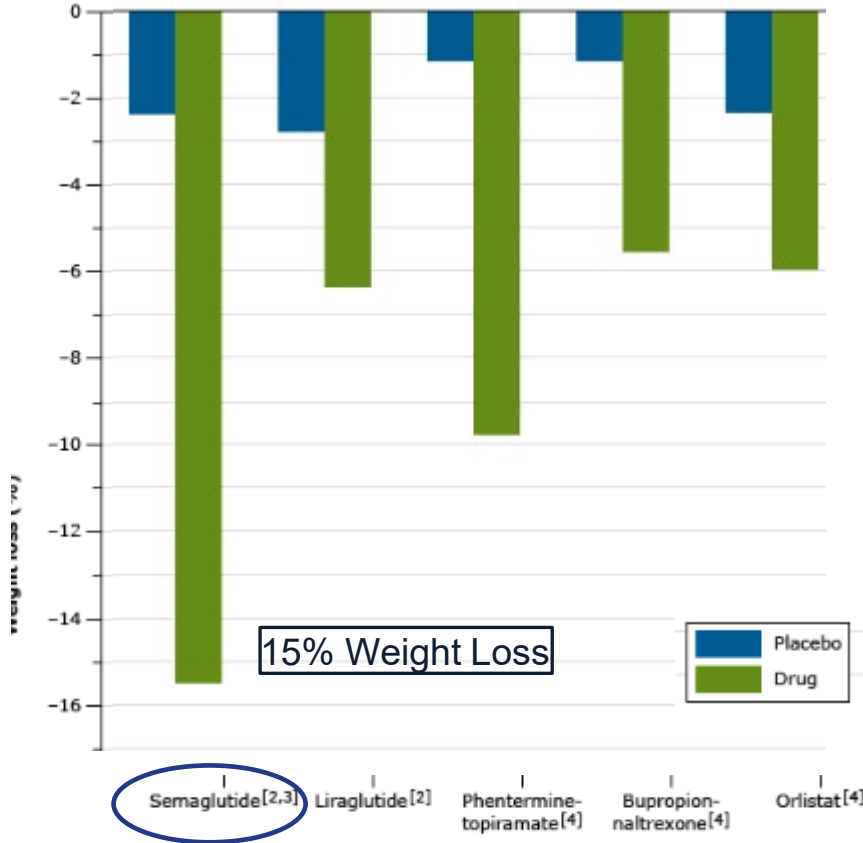
Two are FDA-approved in the US for treatment of long-term weight management

liraglutide 3.0 mg SQ daily (2014)
semaglutide 2.4 mg SQ weekly (2021)



with many more in the pipeline!

Weight loss outcomes with FDA-approved medications



68 weeks (semaglutide, liraglutide)
 52 weeks (other medications)

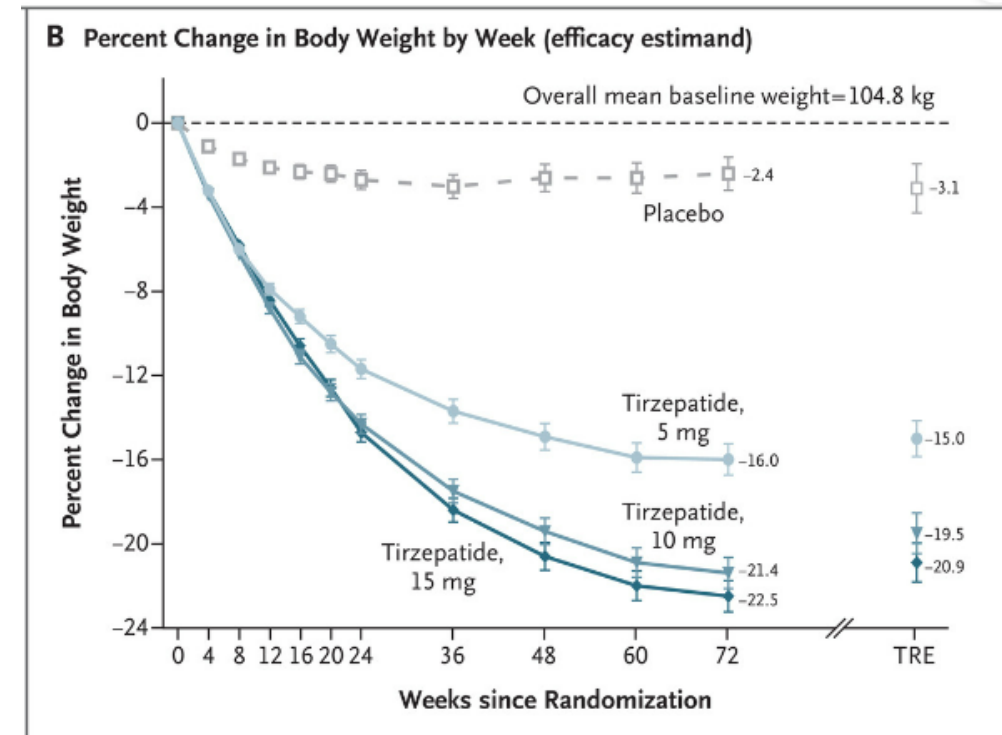
Dual-Acting GLP-1 and GIP receptor agonist

- GLP1 = glucagon-like peptide 1
- GIP = glucose-dependent insulinotropic polypeptide
- FDA-approved for weight loss Nov 2023
- Very effective in weight loss
- tizepatide (Eli Lilly)
 - **Zepbound™** for weight loss
 - **Mounjaro®** for DM (FDA approved May 2022)

ORIGINAL ARTICLE

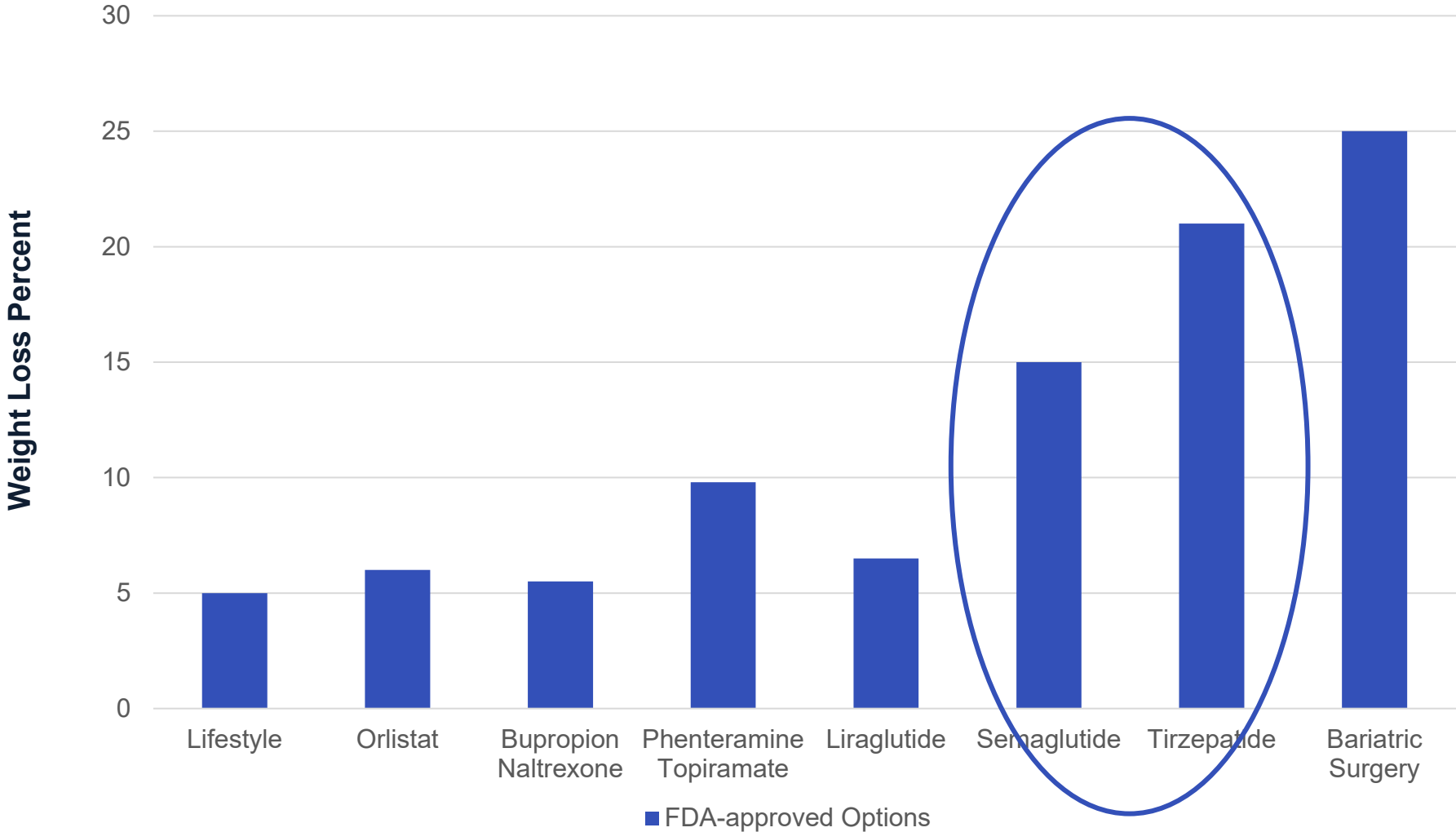
Tirzepatide Once Weekly for the Treatment of Obesity

Ania M. Jastreboff, M.D., Ph.D., Louis J. Aronne, M.D., Nadia N. Ahmad, M.D., M.P.H., Sean Wharton, M.D., Pharm.D., Lisa Connery, M.D., Breno Alves, M.D., Arihiro Kiyosue, M.D., Ph.D., Shuyu Zhang, M.S., Bing Liu, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Adam



GLP-1 RAs and dual GLP-1/GIP RAs

Weight Loss Outcomes by Treatment Option



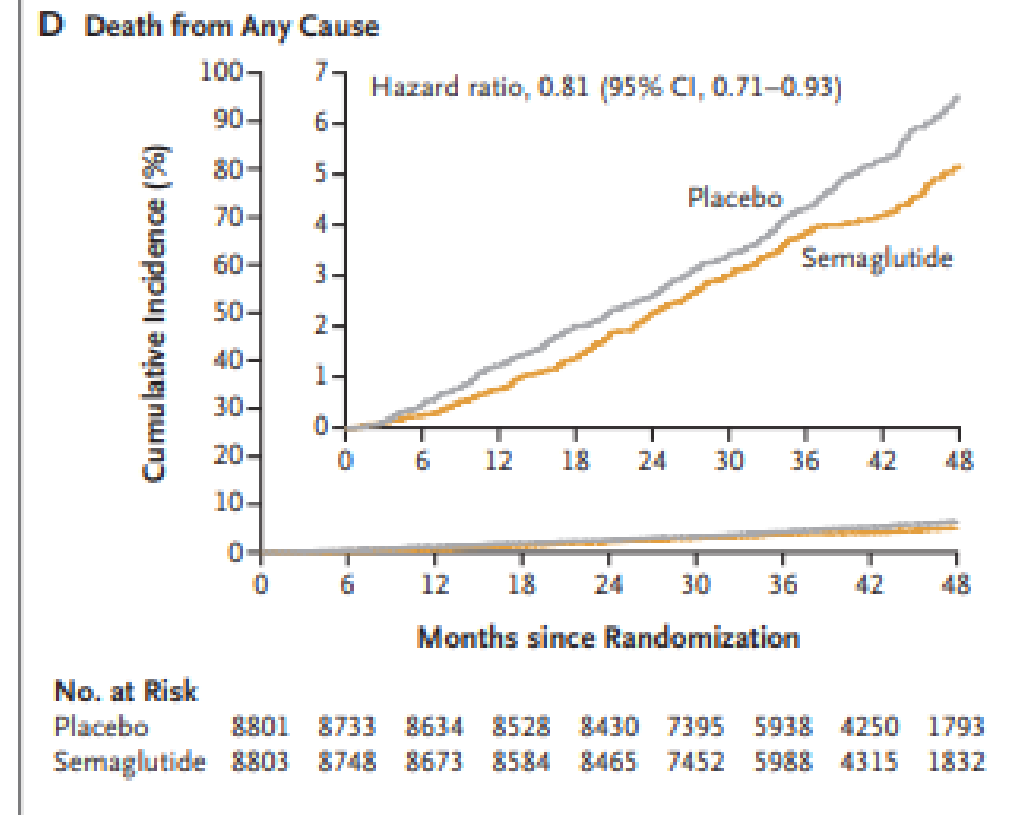
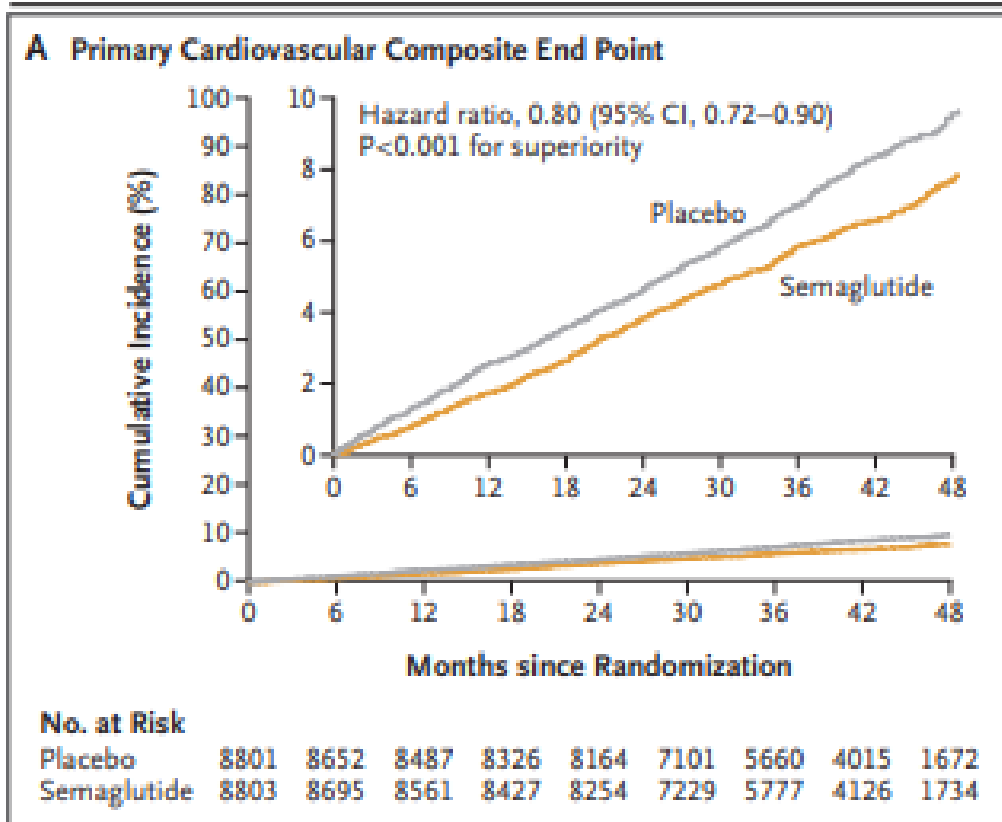
Indications and Dosing Schedules

- Vary by **indication** (diabetes vs. obesity)
- Vary by **dosing schedule** (daily vs. weekly)
- Vary by **dose** (generally dose used for obesity is higher than that used for DM2)
- Manufacturer’s attempt to distinguish by using different brand names for the same drug name

Generic Name	Indication	Brand Name	Dosage	Manufacturer	FDA Approval
liraglutide	Type 2 diabetes	Victoza®	1.2 mg to 1.8 mg SQ daily	Novo Nordisk	Jan 2010
	Obesity (ages 12+)	Saxenda®	3.0 mg SQ daily	Novo Nordisk	Dec 2014
semaglutide	Type 2 diabetes	Ozempic®	Escalating doses up to max 2.0 mg SQ weekly	Novo Nordisk	Dec 2017
	Type 2 diabetes	Rebelsus®	3mg to 14 mg once daily pill	Novo Nordisk	Sep 2019
	Obesity (ages 12+) AND to reduce major cardiovascular events	Wegovy®	Escalating doses up to max 2.4 mg SQ weekly	Novo Nordisk	Jun 2021 Mar 2024 (CV risk)
tirzepatide	Type 2 diabetes	Mounjaro®	2.5 mg to 15 mg SQ weekly	Eli Lilly	May 2022
	Obesity	Zepbound®	2.5 mg to 15mg SQ weekly	Eli Lilly	Nov 2023

Semaglutide and Heart Outcomes in Obesity without Diabetes

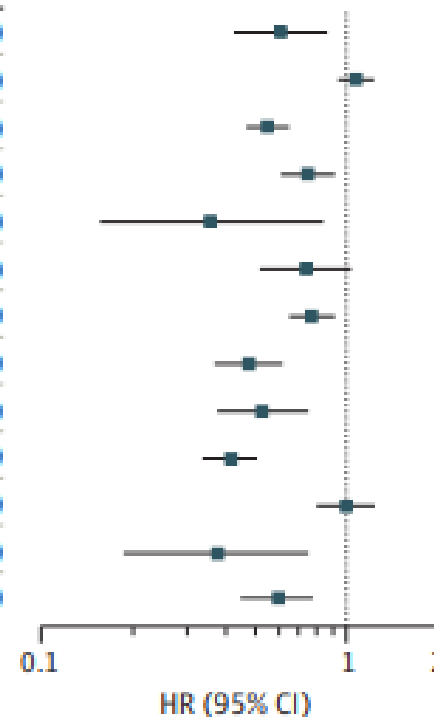
17,000+ patients; 45+ years old with preexisting heart disease and BMI ≥ 27



GLP-1 RAs and 13 Obesity-Associated Cancers in DM Type 2

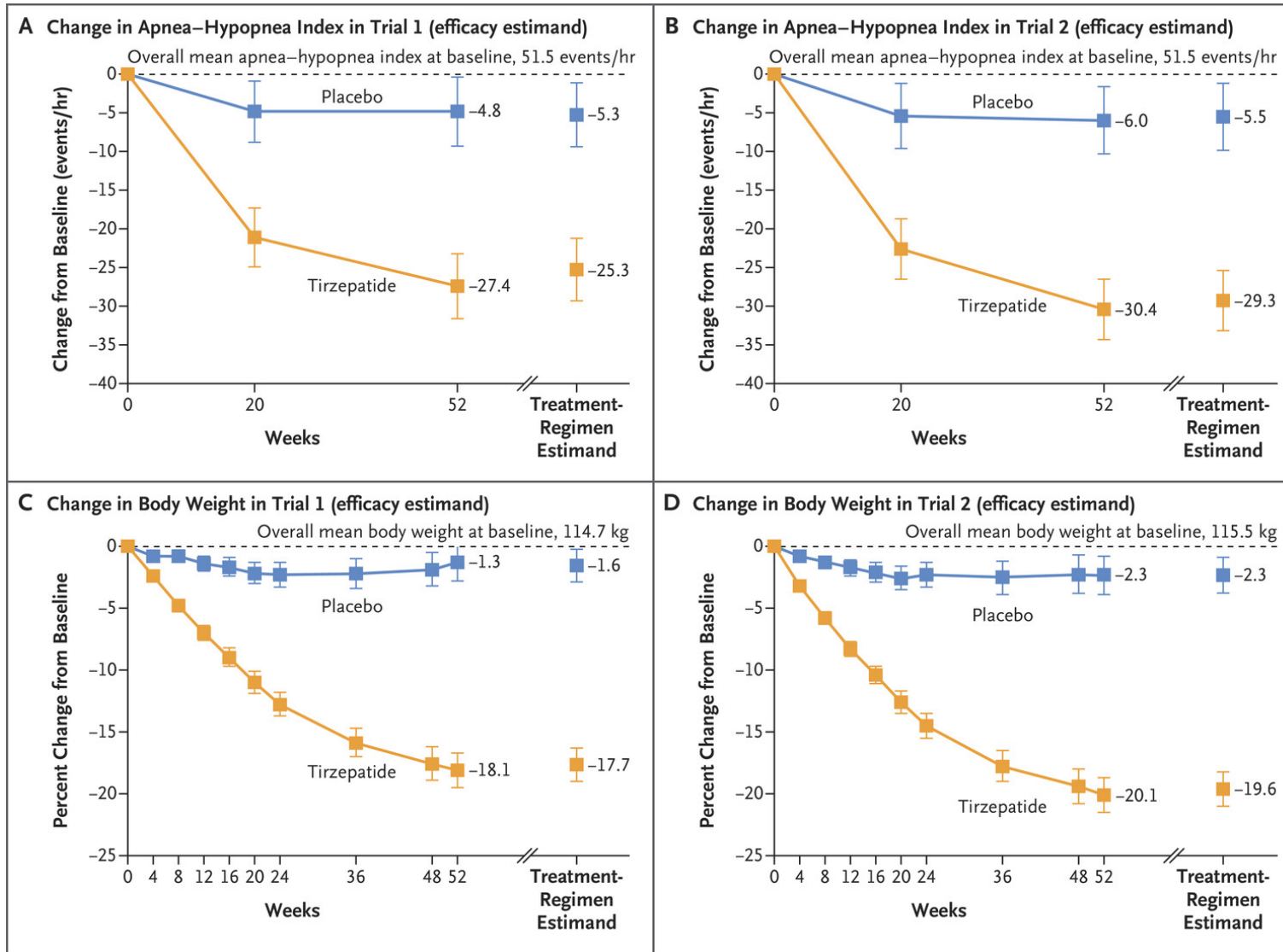
Figure 2. Risk of 13 Obesity-Associated Cancers Among Patients Receiving Glucagon-Like Peptide 1 Receptor Agonists (GLP-1RAs) vs Those Receiving Insulins

Outcome (N= 1 651 452)	Group prescribed GLP-IRAs but not insulin, No (%) (n= 48 983)	Group prescribed insulin but not GLP-IRAs, No (%) (n= 1 044 745)	HR (95% CI)
Esophageal cancer (n= 48 437)	49 (0.10)	77 (0.16)	0.60 (0.42-0.86)
Breast cancer (n= 13 768)	427 (3.08)	379 (2.94)	1.07 (0.93-1.23)
Colorectal cancer (n= 48 443)	223 (0.46)	391 (0.81)	0.54 (0.46-0.64)
Endometrial cancer (n= 25 750)	160 (0.62)	210 (0.82)	0.74 (0.60-0.91)
Gallbladder cancer (n= 48 587)	<10 (<0.02)	19 (0.04)	0.35 (0.15-0.83)
Stomach cancer (n= 48 449)	56 (0.12)	75 (0.16)	0.73 (0.51-1.03)
Kidney cancer (n= 48 322)	223 (0.46)	284 (0.59)	0.76 (0.64-0.91)
Hepatocellular carcinoma (n= 48 397)	79 (0.16)	167 (0.35)	0.47 (0.36-0.61)
Ovarian cancer (n= 25 739)	51 (0.20)	94 (0.37)	0.52 (0.37-0.74)
Pancreatic cancer (n= 48 490)	123 (0.25)	290 (0.60)	0.41 (0.33-0.50)
Thyroid cancer (n= 48 527)	154 (0.32)	149 (0.31)	0.99 (0.79-1.24)
Meningioma (n= 48 518)	11 (0.02)	29 (0.06)	0.37 (0.18-0.74)
Multiple myeloma (n= 48 527)	80 (0.17)	131 (0.27)	0.59 (0.44-0.77)



Retrospective observational cohort study
 Nationwide USA using EHR data
 Over **1.65 million patients** with T2D and
 no prior history of obesity-associated
 cancer
 GLP-1 RAs vs. insulin vs. metformin
 15-year follow-up period
 Mean age 59.8

Tirzepatide for Treatment of OSA and Obesity

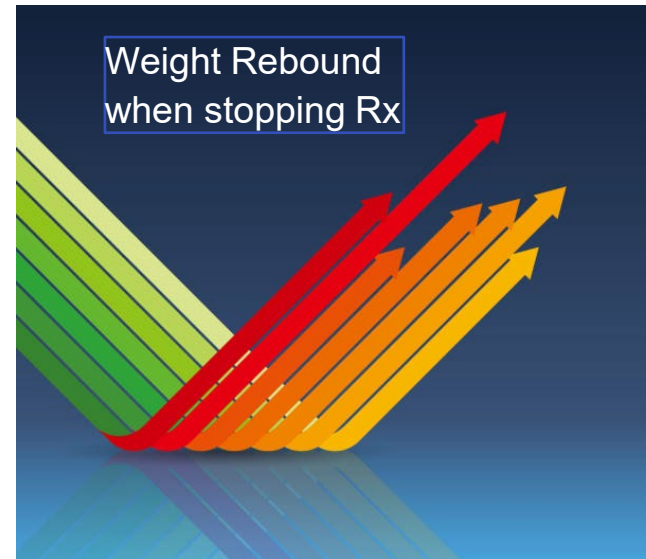
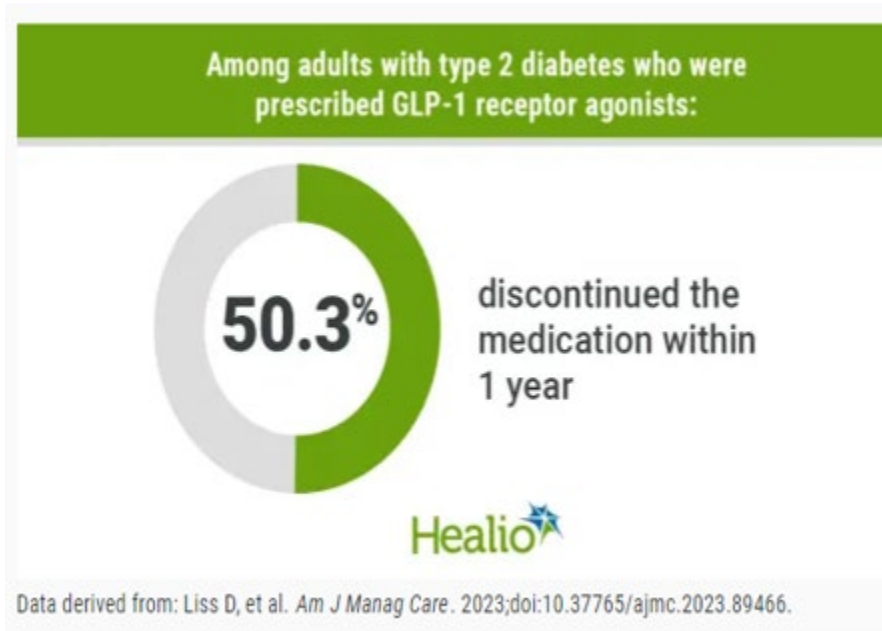


- SURMOUNT-OSA trial
- 60 sites over 9 countries
- Weekly tirzepatide vs. placebo
- 469 adults with moderate-to-severe OSA and obesity (no DM)

Obesity drugs have another superpower: taming inflammation



Cons



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**SUPPLY
& DEMAND**

GLP-1 Agonists for Obesity – A New Recipe for Success?

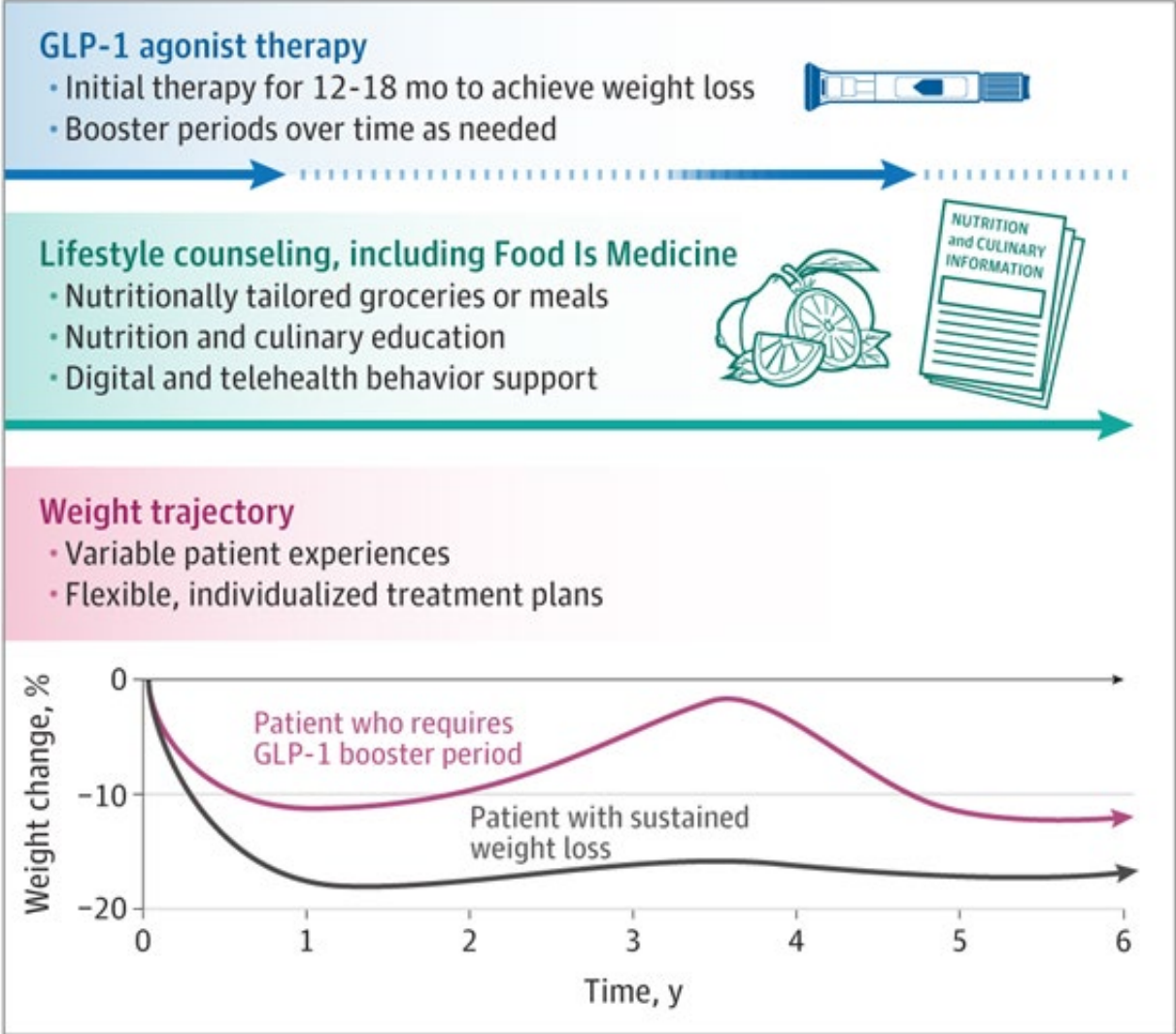
“People are fed by the Food Industry, which pays no attention to health,



and are treated by the Health Industry, which pays no attention to food.”

Wendell Berry

<https://healthandwellbeing4u.wordpress.com/2015/07/10/a-quote-from-wendell-berry/>



JAMA. Published online February 29, 2024. doi:10.1001/jama.2024.2252

Diet is still IMPORTANT!

Mediterranean Diet



[Mediterranean Diet \(clevelandclinic.org\)](https://www.clevelandclinic.org)

Vegetarian or Vegan Diet



[Can the Vegetarian Diet Be Healthy? - American Society for Nutrition](https://www.amsosociety.org)

Physical Activity and Mortality

September 3, 2021

Steps per Day and All-Cause Mortality in Middle-aged Adults in the Coronary Artery Risk Development in Young Adults Study

Amanda E. Paluch, PhD¹; Kelley Pettee Gabriel, PhD²; Janet E. Fulton, PhD³; [et al](#)

7000 steps/day
50-79% lower risk

41-65 years old

March 2022

Daily steps and all-cause mortality: a meta-analysis of 15 international cohorts

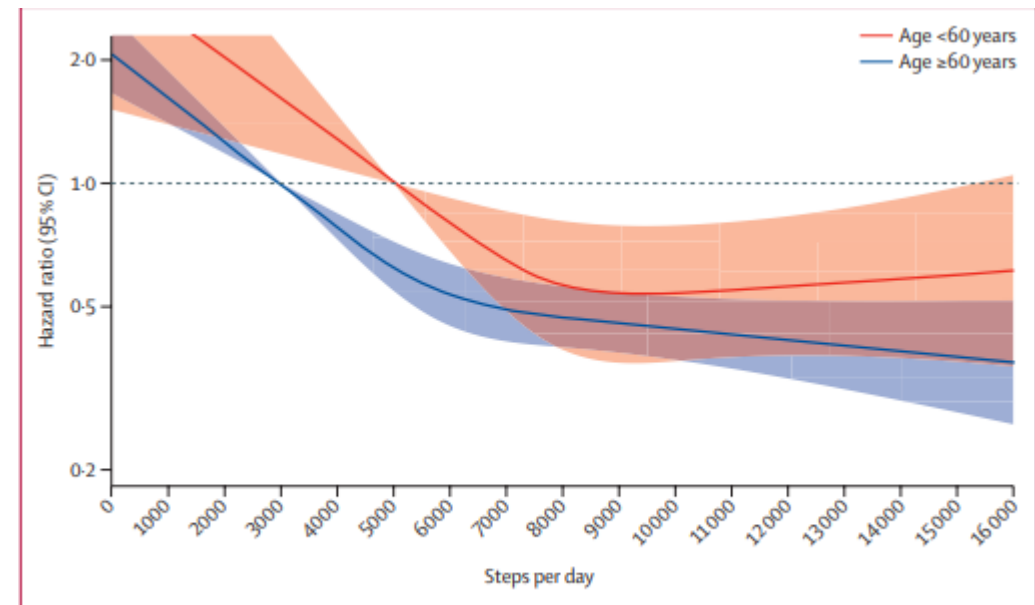
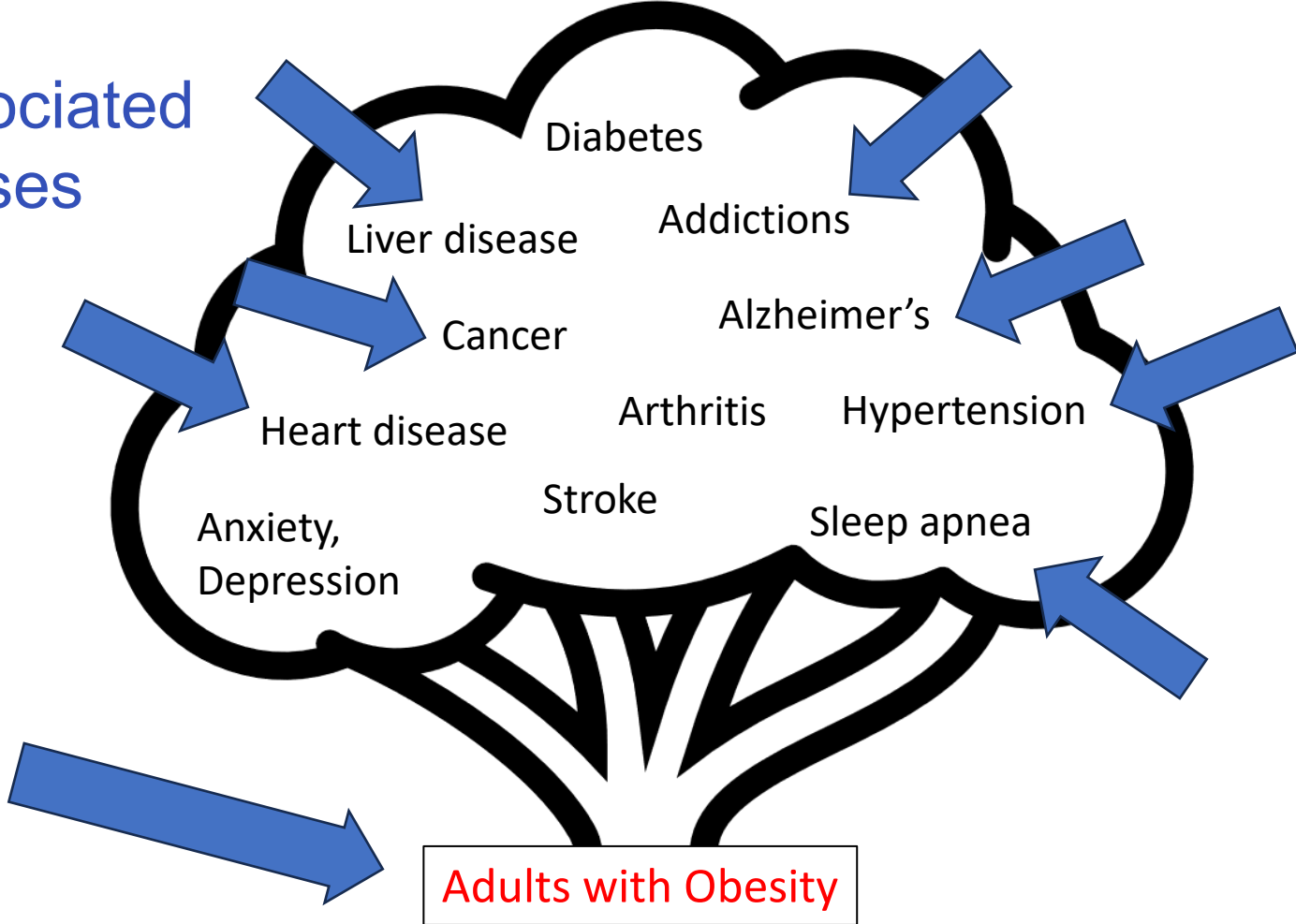


Figure 3: Dose-response association between steps per day and all-cause mortality, by age group

6000-8000 steps/day
40-53% lower risk
Adults 60+ years old

Impact on Associated Chronic Diseases

GLP-1 receptor agonists



Root causes:

- Genetics
- Epigenetics
- Poor diet quality
- Weight bias and stigmatization
- Stress/ Distress
- Lack of exercise
- Endocrine disrupting chemicals
- Barriers to health care
- Insufficient economic resources

THANK YOU!

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