



Massachusetts General Hospital

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# Managing Obesity

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HARVARD  
MEDICAL SCHOOL

*TEACHING AFFILIATE*

**CONTINUING MEDICAL EDUCATION  
DEPARTMENT OF MEDICINE**

# Chika V. Anekwe, MD, MPH, PNS

Instructor in Medicine (HMS)

Obesity Medicine Physician (MGH Weight Center)



- **MD:** University of Connecticut School of Medicine
- **Internship:** Pediatrics, NYU/Bellevue
- **Residency:** Preventive Medicine and Public Health, SUNY Stony Brook University
- **MPH:** Columbia University
- **Boards:** Preventive Medicine, Obesity Medicine, Nation Board of Physician Nutrition Specialists



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# DISCLOSURES

None



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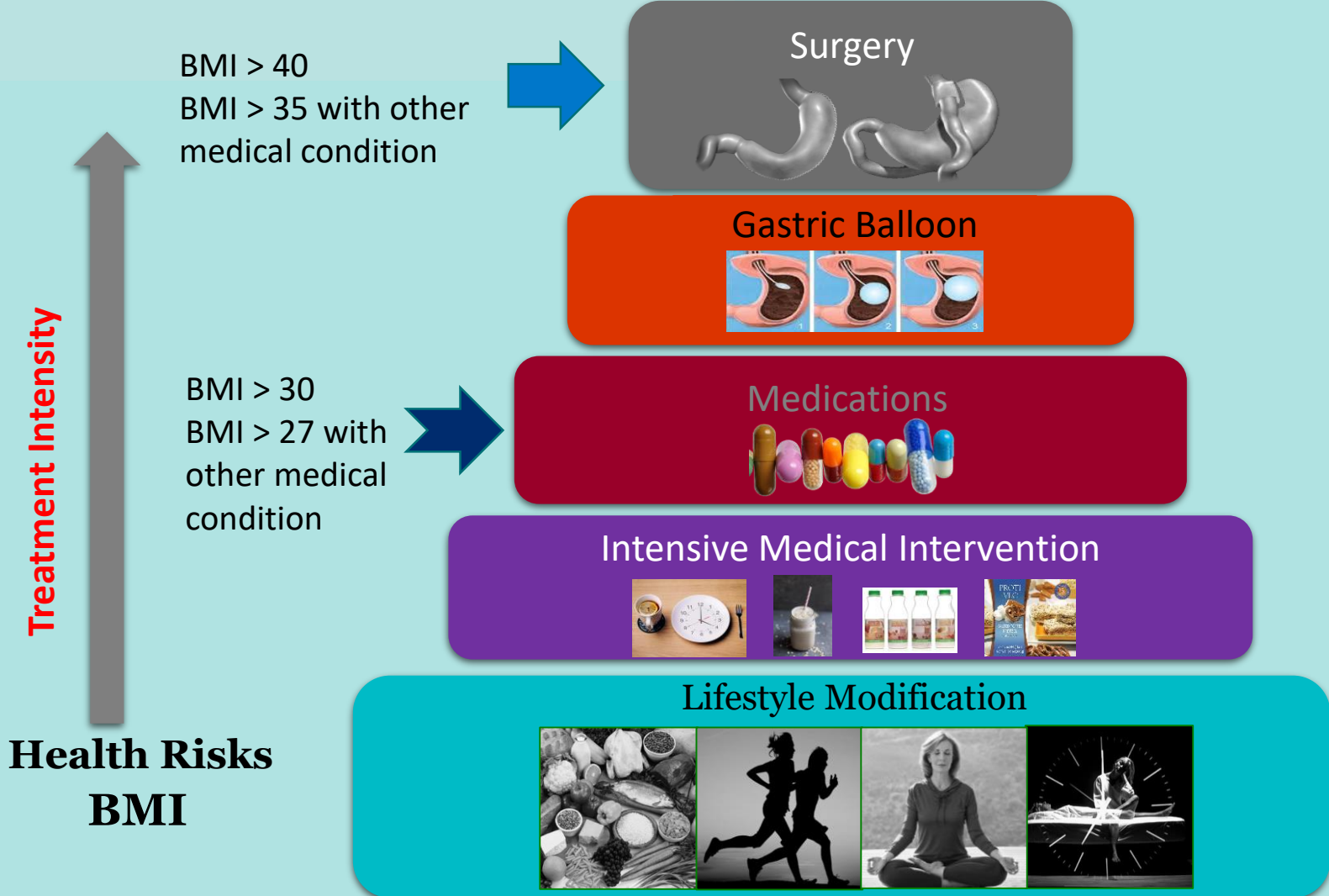
# OBJECTIVES

1. Become familiar with new and upcoming pharmacotherapeutics for the treatment of obesity.
2. Recognize weight stigma as an important source of adverse health outcomes and maladaptive health behaviors.

# Seminal Papers

Date	Journal	Paper
2023	Nature Food	<b>Ad libitum meal energy intake is positively influenced by energy density, eating rate and hyper-palatable food across four dietary patterns</b>
2024	JACC	<b>Sex Differences in Association of Physical Activity with All-Cause and Cardiovascular Mortality</b>
2023	NEJM	<b>Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity</b>
2023	NEJM	<b>Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes</b>
2023	Obesity	<b>Long term Cancer Outcomes After Bariatric Surgery</b>

# Obesity: Multidisciplinary Treatment Approach



# Ad libitum meal energy intake is positively influenced by energy density, eating rate and hyper-palatable food across four dietary patterns

[Tera L. Fazzino](#), [Amber B. Courville](#), [Juen Guo](#) & [Kevin D. Hall](#) 

- Goal: Estimate how energy density, hyper-palatability, protein content and eating rate affected ad libitum energy intake of 2,733 meals from 4 different diets consumed by 35 patients
  - **low fat, low carb, ultra-processed, and unprocessed diet**

# Background on Dietary Approach to Obesity

- Original feeding studies:
  - ultra-processed diet: 500 kcal/day greater mean daily intake compared with unprocessed diet
  - low-carb diet: 700 kcal/day greater mean daily intake than the low-fat diet.
- Meals with greater energy density, more hyper-palatability and higher protein content that are eaten more rapidly were associated with greater energy intake within an eating occasion.
- Hyper-palatable foods were significantly and independently associated with meal energy intake even when considered in combination with non-beverage energy density.

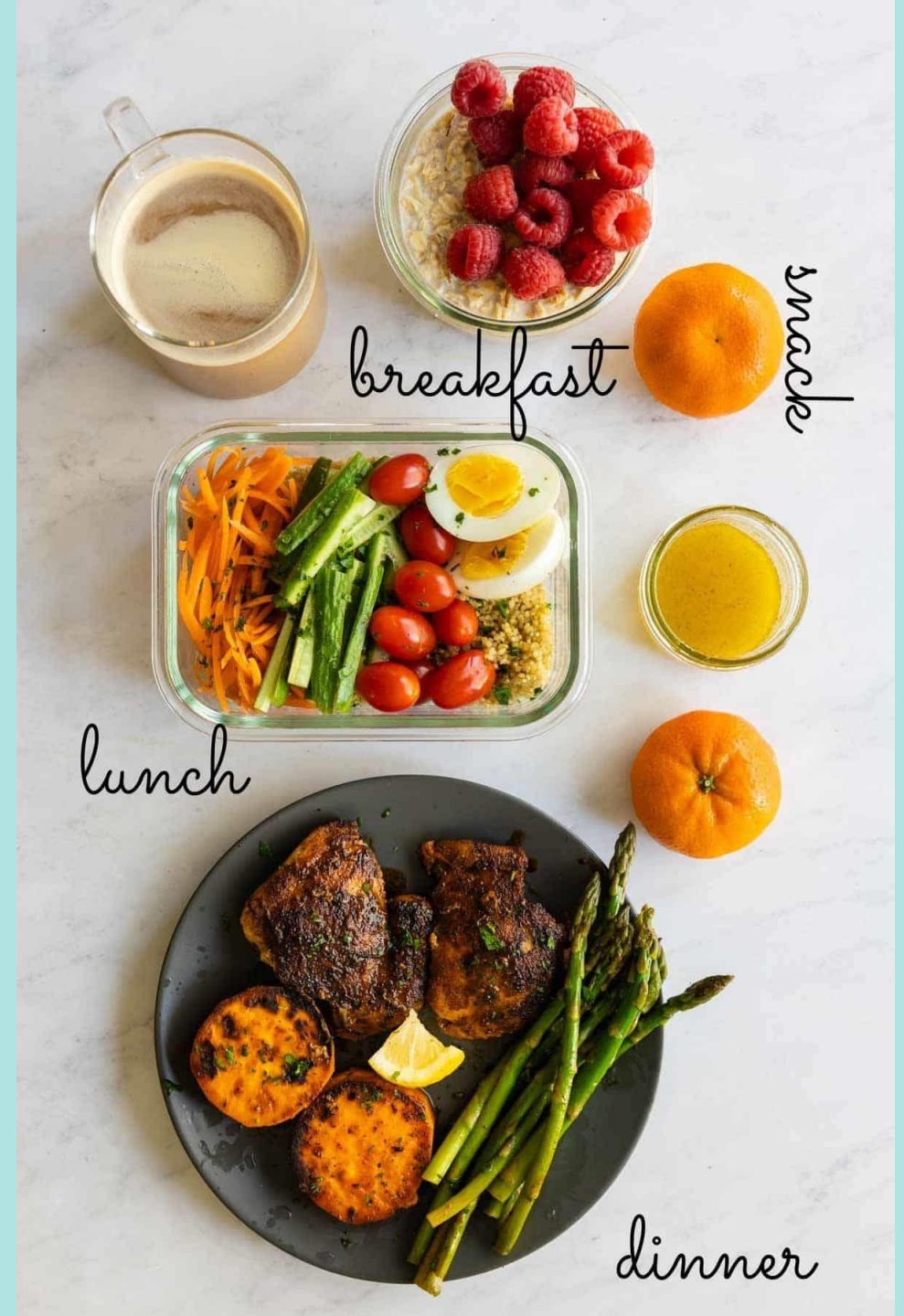
→ These results contribute to a growing body of literature indicating that **hyper-palatable food may be an important contributor to food choice and intake behavior as well as weight gain.**





# Results





- Energy density, eating rate and hyper-palatable foods were consistently positively related to meal energy intake across all diets
- Protein content was positively related to meal energy intake in ultra-processed and unprocessed diets but was not significantly related to energy intake of minimally processed low-fat or low-carbohydrate meals.





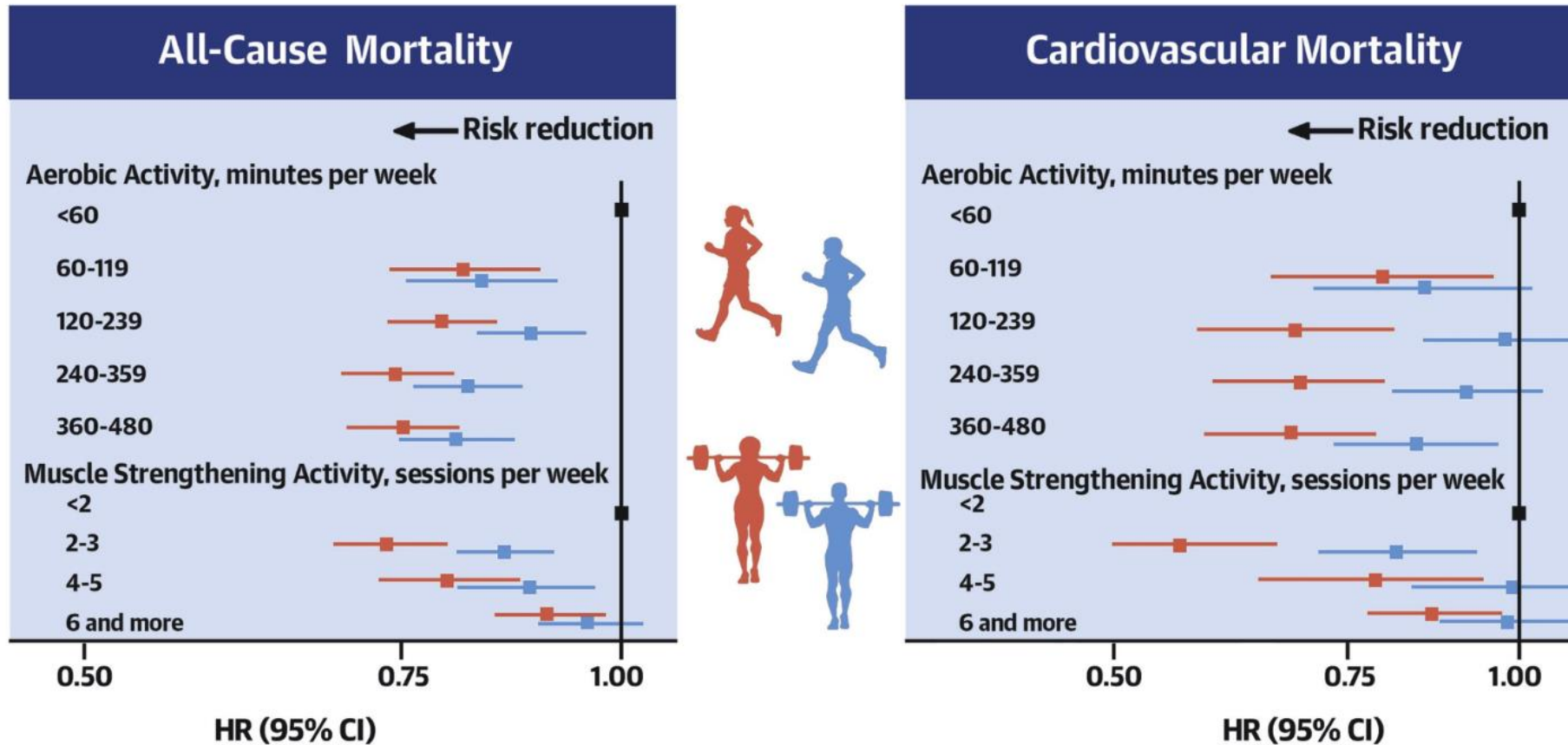
Original Research

# Sex Differences in Association of Physical Activity With All-Cause and Cardiovascular Mortality

Hongwei Ji MD<sup>a\*</sup>  , Martha Gulati MD, MS<sup>b\*</sup>, Tzu Yu Huang MSc<sup>b</sup>, Alan C. Kwan MD<sup>b</sup>,  
David Ouyang MD<sup>b</sup>, Joseph E. Ebinger MD, MS<sup>b</sup>, Kaitlin Casaletto PhD<sup>c</sup>, Kerrie L. Moreau PhD<sup>d e</sup>,  
Hicham Skali MD, MSc<sup>f</sup>, Susan Cheng MD, MMSc, MPH<sup>b</sup>  

- Prospective study of 412,413 U.S. adults (55% female, age 44 ± 17 years)
- Sex-specific multivariable-adjusted associations of physical activity measures (frequency, duration, intensity, type) with all-cause and cardiovascular mortality from 1997 through 2019
- **Goal: Evaluate whether physical activity derived health benefits may differ by sex**

## CENTRAL ILLUSTRATION: Sex Differences in Physical Activity-Associated Mortality Risk Reduction



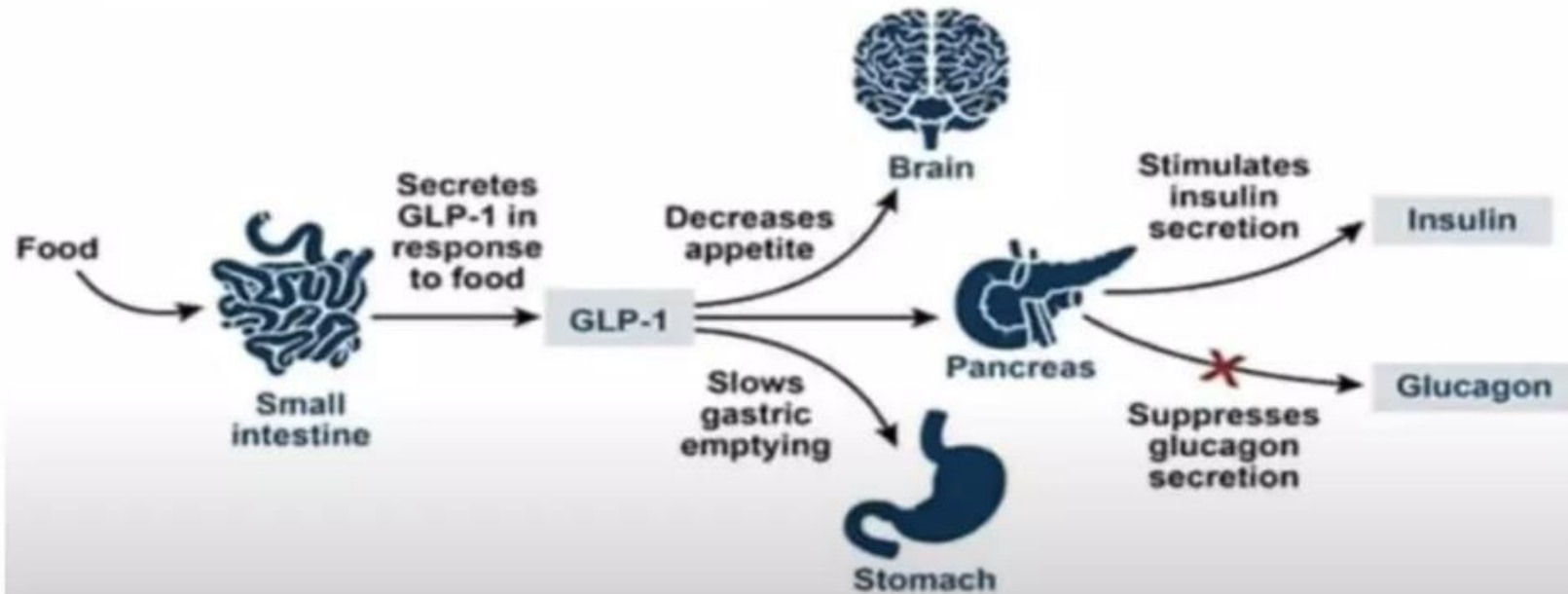
Ji H, et al. J Am Coll Cardiol. 2024;83(8):783-793.

# Results

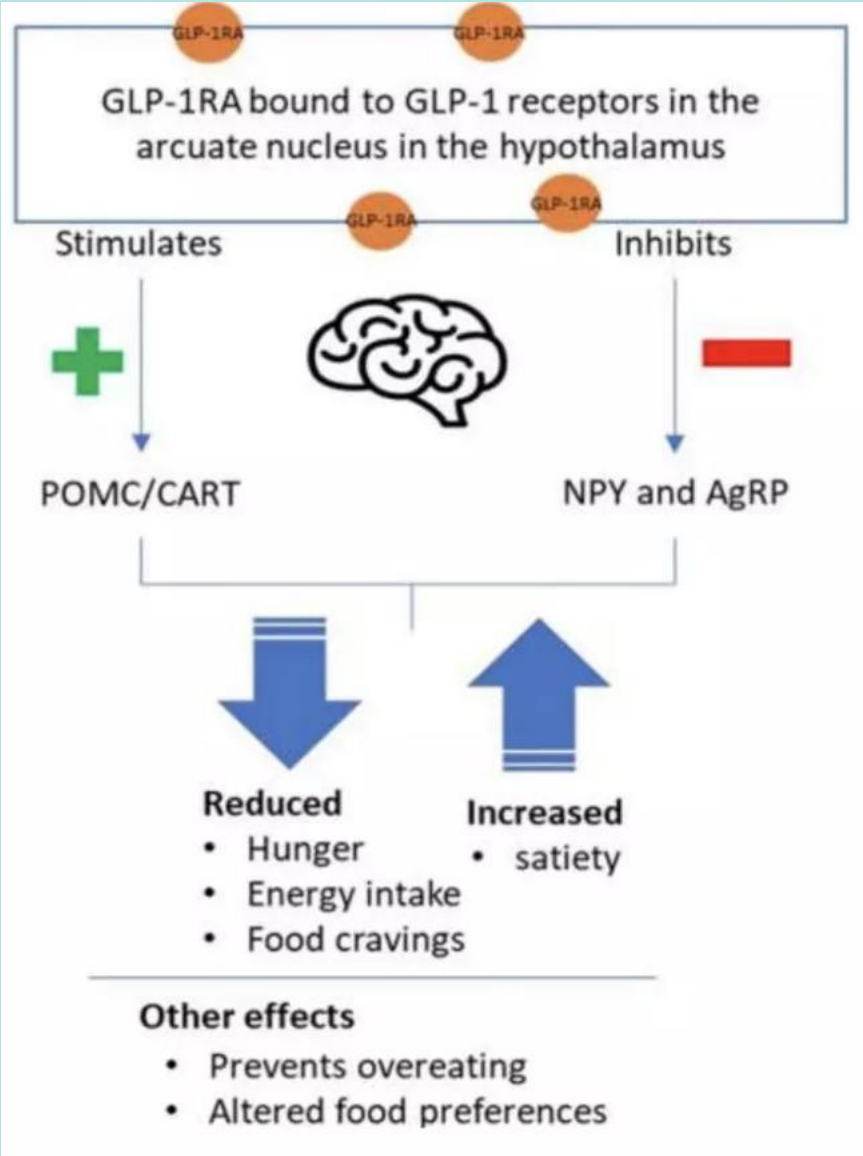
- Women compared with men derived greater gains in all-cause and cardiovascular mortality risk reduction from equivalent doses of leisure-time PA.
- Physiological responses to various types and intensity of PA differ between men and women, as does the associated health benefit. Although women tend to engage in less PA, the survival benefit gained from exercise is greater for women than for men.
- Awareness of this gender gap and motivating women to engage regularly in leisure-time PA could increase their longevity.
- Recognizing the limitations of a one-size-fits-all approach, increasing attention to sex differences in PA-related risks and benefits could augment precision medicine efforts to improve health outcomes.



## GLP-1 RAs *Mechanism of Action*





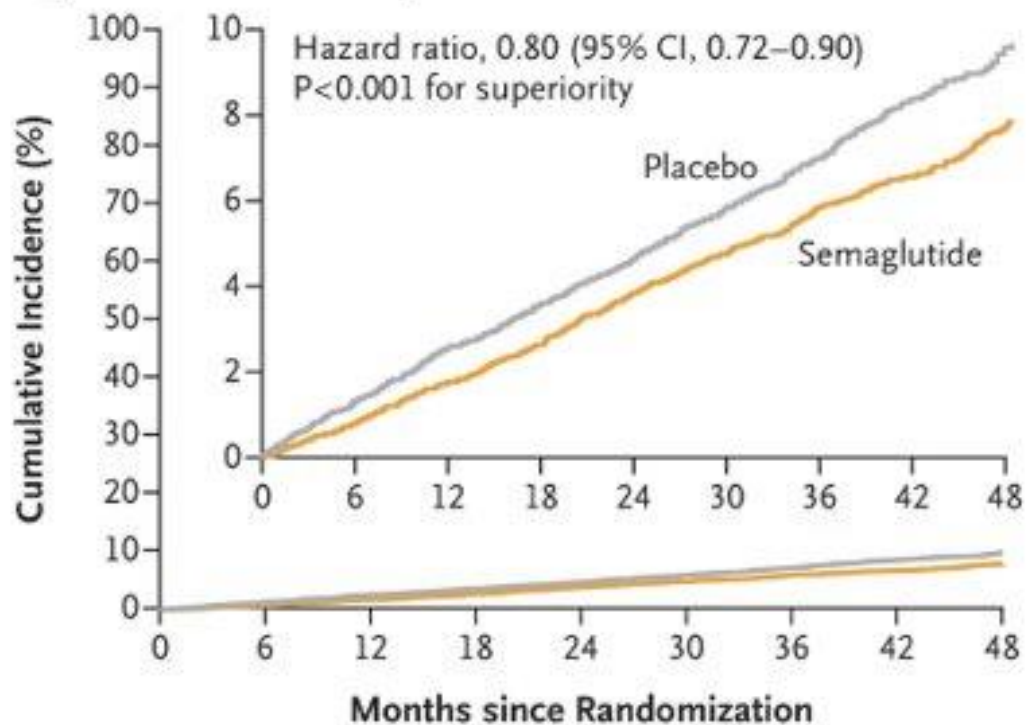


# Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

A. Michael Lincoff, M.D., Kirstine Brown-Frandsen, M.D., Helen M. Colhoun, M.D., John Deanfield, M.D., Scott S. Emerson, M.D., Ph.D., Sille Esbjerg, M.Sc., Søren Hardt-Lindberg, M.D., Ph.D., G. Kees Hovingh, M.D., Ph.D., Steven E. Kahn, M.B., Ch.B., Robert F. Kushner, M.D., Ildiko Lingvay, M.D., M.P.H., Tugce K. Oral, M.D., et al., for the SELECT Trial Investigators\*

- Multicenter, double-blind, randomized, placebo-controlled, event-driven superiority trial conducted over 3 years
- Inclusion criteria: Patients 45 years old or older, history of cardiovascular disease, BMI  $\geq 27$
- Exclusion criteria: history of diabetes, severe heart failure, end-stage kidney disease
- Patients received Semaglutide 2.4mg weekly, 77% patients in treatment arm received this dose

### A Primary Cardiovascular Composite End Point



#### No. at Risk

Placebo	8801	8652	8487	8326	8164	7101	5660	4015	1672
Semaglutide	8803	8695	8561	8427	8254	7229	5777	4126	1734

- Semaglutide 2.4mg weekly over 33 months reduced risk of death from cardiovascular causes (secondary prevention) by 20%
- Effects of Semaglutide occurred early after treatment initiation



# Semaglutide 2.4mg now approved for Medicare patients

01:42 8 March 2024

 Announcement

**Wegovy® approved in the US for cardiovascular risk reduction in people with overweight or obesity and established cardiovascular disease**

# Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

Kosiborod MN et al. DOI: 10.1056/NEJMoa2306963

## CLINICAL PROBLEM

Patients with heart failure with preserved ejection fraction often have obesity, a condition that is associated with a greater burden of heart failure–related symptoms, worse functional capacity, and more impaired quality of life. Whether therapies that target obesity in such patients can alleviate symptoms and physical limitations is unknown.



Heart failure  
with preserved  
ejection fraction  
+ BMI  $\geq 30$

Semaglutide  
(N=263)



Placebo  
(N=266)



## CLINICAL TRIAL

**Design:** A multinational, double-blind, randomized, placebo-controlled trial evaluated whether treatment with semaglutide — a glucagon-like peptide 1 receptor agonist approved for long-term weight management — would reduce heart failure–related symptoms and improve physical function, in addition to inducing weight loss, in adults with heart failure with preserved ejection fraction and obesity.

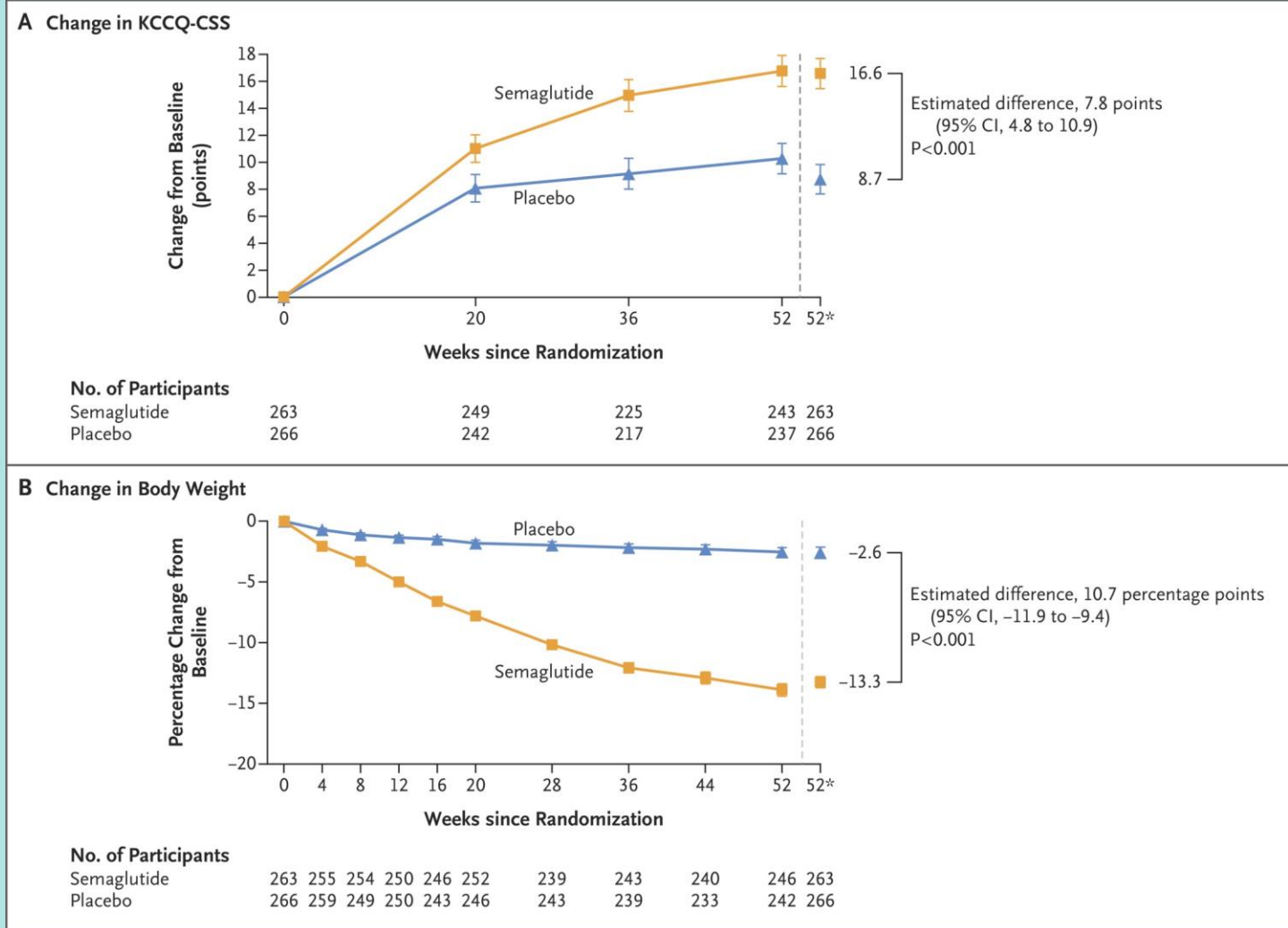
**Intervention:** 529 patients with a body-mass index of  $\geq 30$  were assigned to receive subcutaneous semaglutide (2.4 mg) or placebo once weekly for 52 weeks. The dual primary end points were the change in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS), which quantifies heart failure–related symptoms and physical function, and the change in body weight from baseline to week 52.

# Kansas City Cardiomyopathy Questionnaire Clinical Score Summary (KCCQ-CSS)

- KCCQ scores are scaled from 0 to 100
- Scores are summarized in 25-point ranges, representing health status as follows:
  - 0 to 24: very poor to poor
  - 25 to 49: poor to fair
  - 50 to 74: fair to good
  - 75 to 100: good to excellent

# Results

## Changes from Baseline to Week 52 in the Dual Primary End Points



# Results

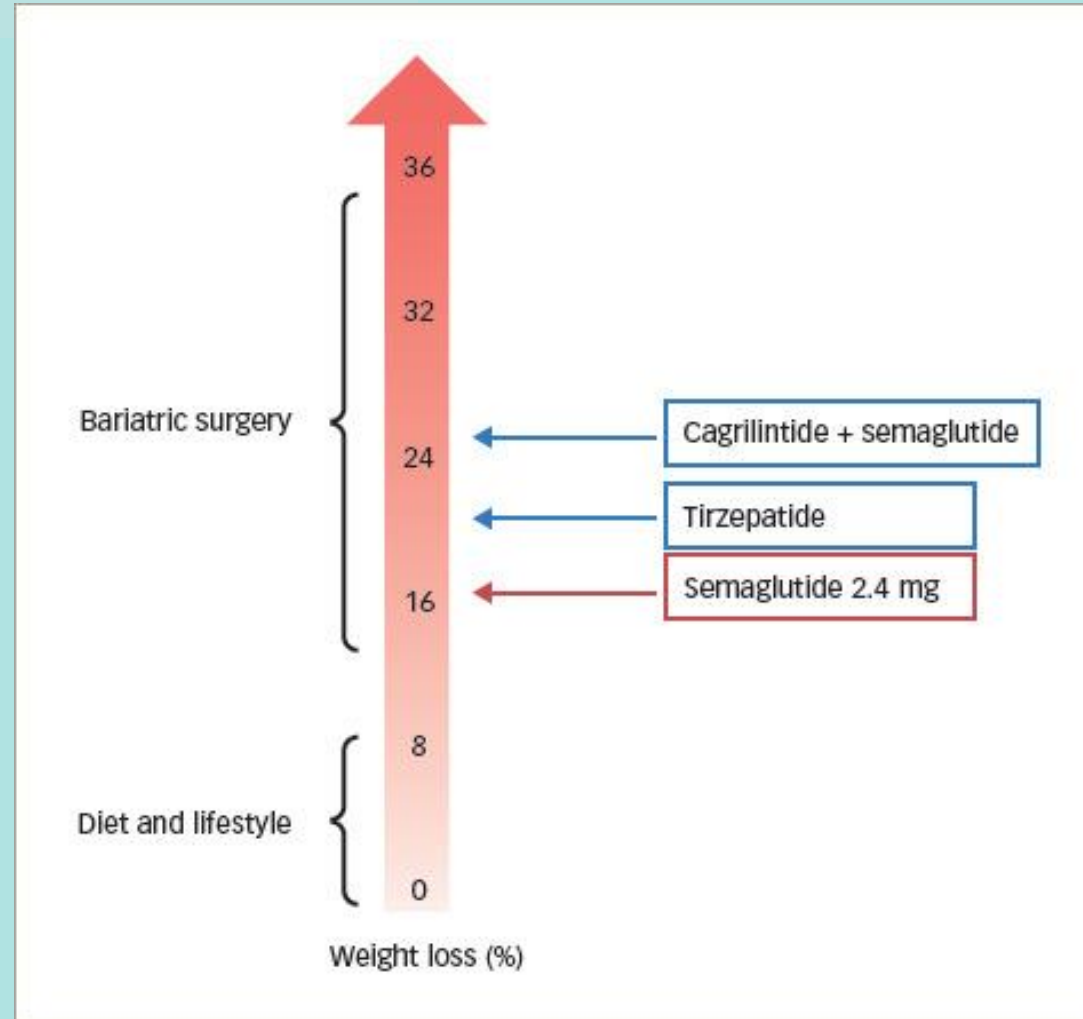
## RESULTS


**Efficacy:** The mean change in KCCQ-CSS and the mean percentage change in body weight were significantly greater with semaglutide than with placebo.

**Safety:** Serious adverse events occurred less often with semaglutide than with placebo, primarily because fewer cardiac disorders occurred in the semaglutide group. Adverse events leading to treatment discontinuation were more common with semaglutide.


→ In patients with heart failure with preserved ejection fraction and obesity, treatment with semaglutide (2.4 mg) led to larger reductions in symptoms and physical limitations, greater improvements in exercise function, and greater weight loss than placebo over 52 weeks

# Anti-obesity pharmacotherapy approaching weight loss results from bariatric surgery



ORIGINAL ARTICLE |  Free Access

## Long-term cancer outcomes after bariatric surgery

Ted D. Adams , Huong Meeks, Alison Fraser, Lance E. Davidson, John Holmen, Michael Newman, Anna R. Ibele, Mary Playdon, Sheetal Hardikar, Nathan Richards, Steven C. Hunt, Jaewhan Kim

First published: 22 August 2023 | <https://doi.org/10.1002/oby.23812>

- Retrospectively (1982-2019), 21,837 bariatric surgery patients (surgery, 1982-2018) were matched 1:1 by age, sex, and BMI with a nonsurgical comparison group.
- Procedures included gastric bypass, gastric banding, sleeve gastrectomy, and duodenal switch.
- Primary outcomes included cancer incidence and mortality, stratified by obesity- and non-obesity-related cancers, sex, cancer stage, and procedure

# Results

- Metabolic surgery patients had a 25% lower risk of any cancer development
- Female surgery patients had a 41% lower risk of obesity related cancers (breast, ovarian, uterine, colon)

Conclusion: Surgery should be recommended to patients as a safe and effective treatment option to lower future cancer risk.



# Question 1:

In the NEJM's "Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity" the difference in the KCCQ-CSS between the semaglutide and placebo groups was:

- A. 4.8
- B. 5.1
- C. 7.8
- D. 10.9



## Question 2:

**Which of the following actions promotes weight stigma?**

- A. Using first person language to refer to patients who have obesity.
- B. Replacing the term morbid obesity with severe or class III obesity in the medical record.
- C. Asking a new patient establishing care with you for permission to discuss their weight.
- D. Referring to a patient who has had difficulty losing weight as noncompliant.



# TAKE HOME MESSAGES

- Comprehensive obesity treatment includes nutritional, behavioral, pharmacotherapeutic and surgical approaches.
- New and upcoming pharmacotherapeutics for the treatment of obesity promise unprecedented weight loss results approaching the weight loss seen with bariatric surgery.
- The growing prevalence of obesity in the US makes addressing weight stigma not only a pressing public health issue, but also a critical step towards advancing the prevention and treatment of obesity.



# References

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- Colin, IM, Gerard, *touchREVIEWS in Endocrinology*. 2022;18(1):35–42

# THANK YOU

Questions, Comments?

