

Updates in Primary Care ACP Regional Meeting



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DISCLOSURES

- I have no disclosures related to this presentation.

OUTLINE

- Review recent updates in the literature
- Review cases for application to primary care practice

CASE 1

- 66-year-old male with pmhx HFpEF (EF 57%), CAD, HTN, obesity presents to clinic for annual exam. He reports some shortness of breath walking around his house.

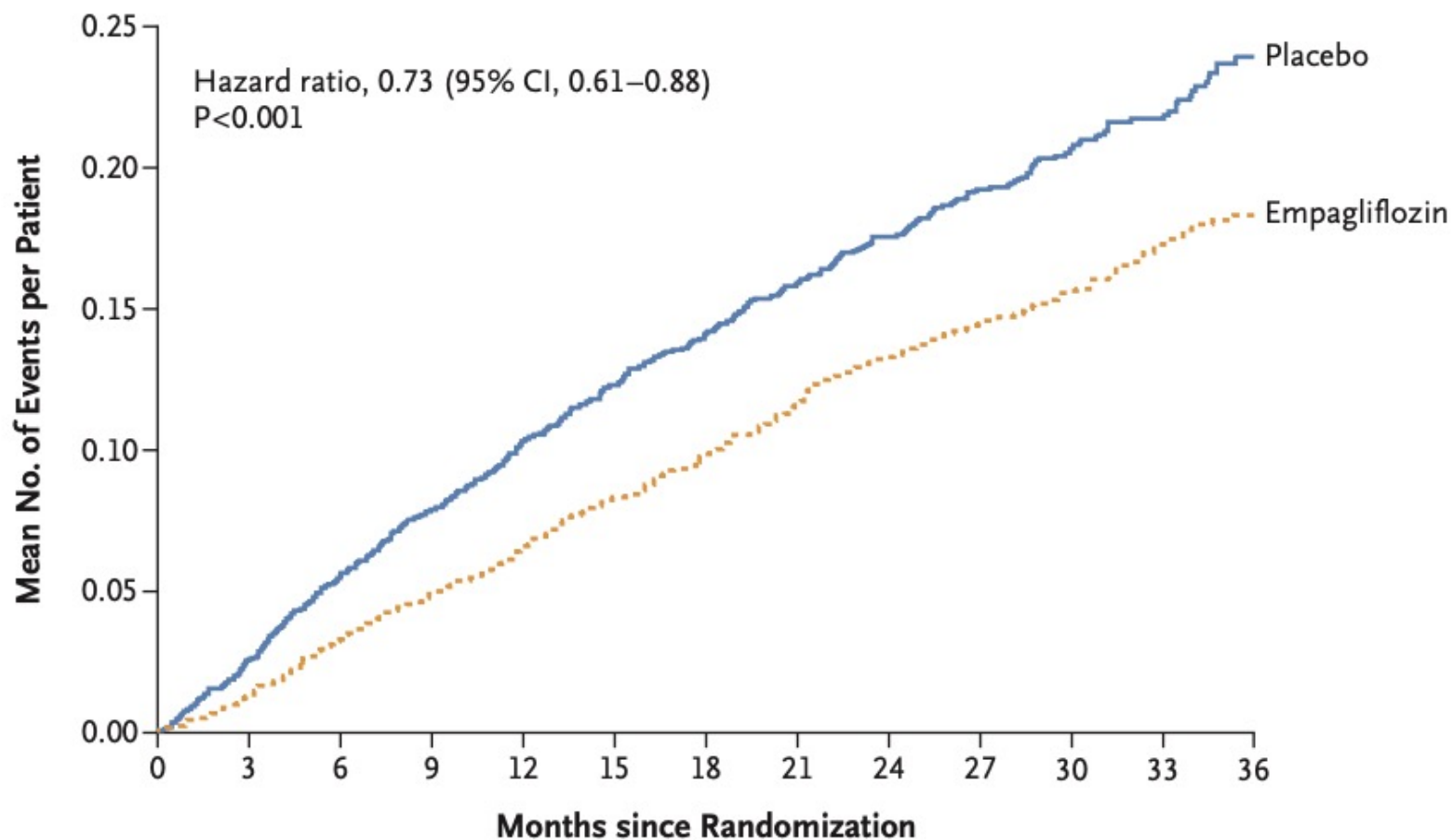
QUESTION CASE 1

- What medication would you add to his regimen for his symptoms?
- A) Spironolactone 50mg daily
 - B) Metoprolol 12.5mg twice daily
 - C) Empagliflozin 10mg daily
 - D) Digoxin 10mg daily

EMPEROR- PRESEVED TRIAL

- **Question:** Will the effects of SGLT2 inhibition with empagliflozin effect major heart failure outcomes in patients with heart failure and a preserved ejection fraction?
- **Design:** randomized, double- blind, parallel- group, placebo-controlled, event- driven trial
- **Intervention:** assigned in a 1:1 ratio to receive placebo or empagliflozin 10 mg per day; enrolled between March 2017- April 2020; 5988 total with empagliflozin (2997 patients), placebo (2991 patients)

- **Criteria of Group:** average age 71, 44% female, 76% white, most Class II symptoms, BMI 29, mean GFR 60
- **Outcome:** composite of cardiovascular death or hospitalization for heart failure
- **Secondary Outcomes:** occurrence of all adjudicated hospitalizations for heart failure, rate of decline in the eGFR



No. at Risk

Placebo	2991	2945	2901	2855	2816	2618	2258	1998	1695	1414	1061	747	448
Empagliflozin	2997	2962	2913	2869	2817	2604	2247	1977	1684	1429	1081	765	446

Figure 3. Hospitalizations for Heart Failure.

The mean number of events per patient for the first secondary outcome (total [first and recurrent] hospitalizations for heart failure) in the two groups is shown.

RESULTS

- Death from cardiovascular causes or hospitalization for heart failure: 13.8% in the empagliflozin group and 17.1% in the placebo group (hazard ratio, 0.79; 95% CI, 0.69 to 0.90; $P < 0.001$)
- Hospitalization for heart failure: 8.6% in the empagliflozin group and 11.8% in the placebo group (hazard ratio, 0.71; 95% CI, 0.60 to 0.83)
- Uncomplicated genital and urinary tract infections and hypotension were reported more frequently with empagliflozin

LIMITATIONS

- Not demographically diverse
- Industry sponsored

SUMMARY

Empagliflozin reduced the risk of cardiovascular death or hospitalization for heart failure in patients with heart failure and a preserved ejection fraction, regardless of the presence or absence of diabetes.

QUESTION CASE 1

- What medication would you add to his regimen for his symptoms?
- A) Spironolactone 50mg daily
- B) Metoprolol 12.5mg twice daily
- C) Empagliflozin 10mg daily
- D) Digoxin 10mg daily

CASE 2

- 47-year-old female with pmhx hypothyroidism, depression presenting to clinic for annual exam. She moved to SLC in the last year and has not seen a physician in the last three years. She wants to get up to date on all her health maintenance. No symptoms or concerns today. Family history only pertinent for mother with type 2DM and father with high cholesterol.

QUESTION CASE 2

She asks about colon cancer screening as her best friend's brother just had a colonoscopy. You recommend:

- A) Start Cologuard at 50
- B) Go see GI
- C) Start colonoscopy at 45
- D) Never do colon cancer screening

Question: To evaluate the benefits and harms of screening for colorectal cancer in adults 40 years or older.

Background: In 2018, 31.2% were not up to date with colon cancer screening

Design: Systemic Review, Comparative Modeling

Population: Asymptomatic adults 45 years or older at average risk of colorectal cancer

- No prior diagnosis of colorectal cancer, adenomatous polyps, or inflammatory bowel disease
- No personal diagnosis or family history of known genetic disorders that predispose them to a high lifetime risk of colorectal cancer

SCREENING MODALITIES

- High-sensitivity gFOBT or FIT every year
- sDNA-FIT every 1 to 3 years
- CT colonography every 5 years
- Flexible sigmoidoscopy every 5 years
- Flexible sigmoidoscopy every 10 years + FIT every year
- Colonoscopy screening every 10 years

CONCLUSION

- Expanded the recommended ages for colorectal cancer screening to 45 to 75 years from 50 to 75 years

Adults aged 50 to 75 years	The USPSTF recommends screening for colorectal cancer in all adults aged 50 to 75 years.	A
Adults aged 45 to 49 years	The USPSTF recommends screening for colorectal cancer in adults aged 45 to 49 years.	B
Adults aged 76 to 85 years	The USPSTF recommends that clinicians selectively offer screening for colorectal cancer in adults aged 76 to 85 years. Evidence indicates that the net benefit of screening all persons in this age group is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the patient's overall health, prior screening history, and preferences.	C

QUESTION CASE 2

She asks about colon cancer screening as her best friend just had a colonoscopy. You recommend:

A) Start Cologuard at 50

B) Go see GI

C) Start colonoscopy at 45

D) Never do colon cancer screening

CASE 3

- The same 47-year-old female with pmhx hypothyroidism, depression presenting to clinic for annual exam. Patient mentions during visit that she would like to taper off her sertraline 100mg because she feels great. She has had two episodes of severe MDD but has been in remission for the last 2.5 years on current regimen.

QUESTION CASE 3

What is the next step in her treatment plan?

- A) Taper and discontinue sertraline
- B) Maintain sertraline 100mg
- C) Convert to alternative SSRI
- D) Refer to psychiatrist for assistance

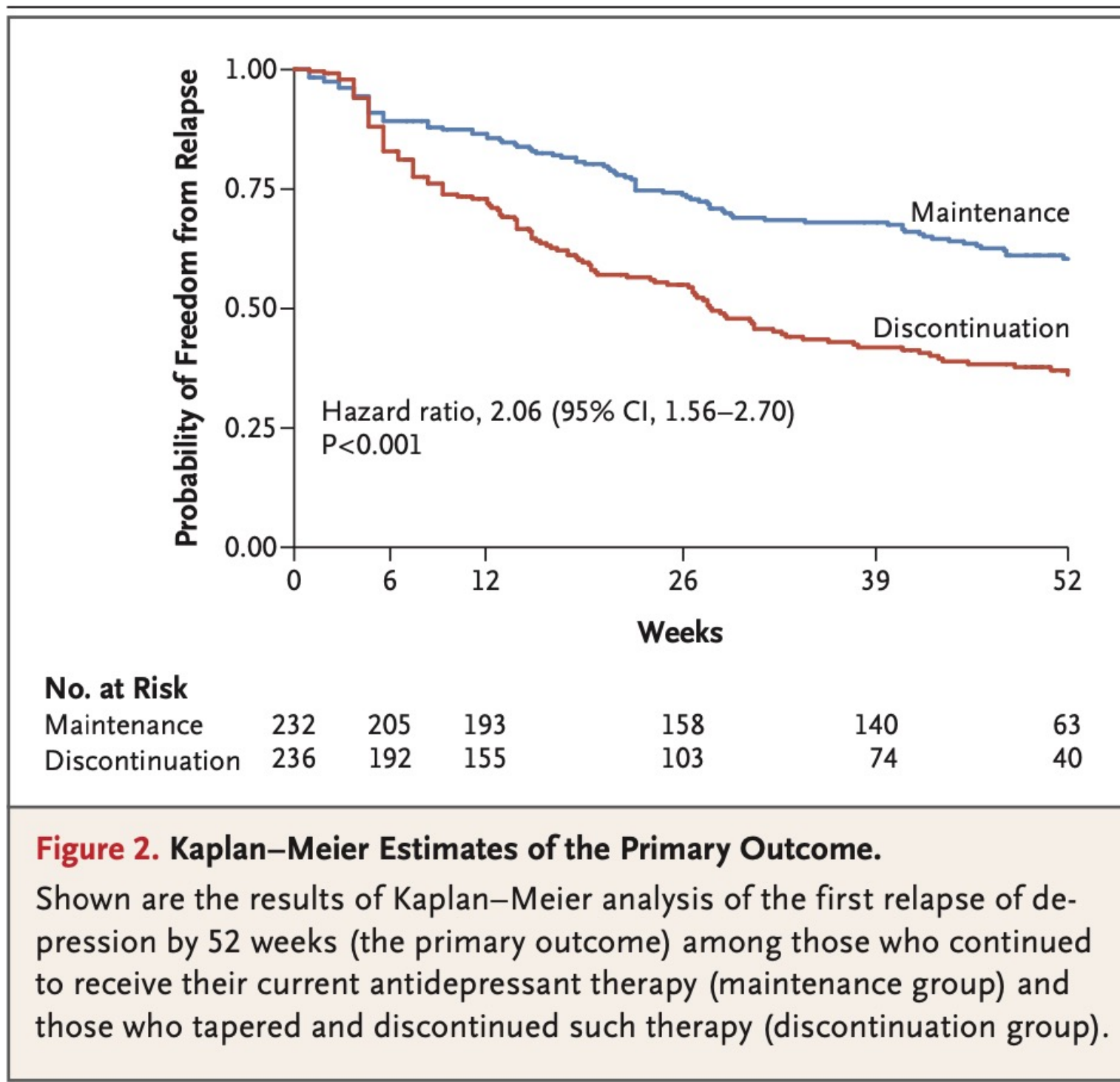
ANTLER TRIAL

ANTIDEPRESSANTS TO PREVENT RELAPSE IN DEPRESSION

- **Question:** In primary care patients with depression in remission, what is the effect of stopping anti-depressants?
- **Design:** randomized, double-blind trial
- **Intervention:** Taper antidepressant or dose of placebo
 - 478 enrolled, 238 assigned to the maintenance group and 240 to the discontinuation group.

ANTLER

- **Criteria of Group:** Adults treated in 150 general practices in UK.
 - 54 was average age (18-74),
 - 73% were women
 - 95% white
- **Outcome:** relapse of depression during the 52-week trial period
- **Secondary Outcomes:** depressive and anxiety symptoms, physical and withdrawal symptoms, quality of life, time to stopping an antidepressant or placebo, and global mood ratings



RESULTS

- Relapse of depression 39% in maintenance group and 56% in discontinuation group during the 52 weeks of the trial (hazard ratio, 2.06; 95% CI, 1.56 to 2.70; $P < 0.001$)
- 70% in the maintenance group adhered to therapy compared to 52% in the discontinuation group

LIMITATIONS

- Trial drugs limited to citalopram, sertraline, fluoxetine and mirtazapine
- Lack of ethnic diversity
- Patients in UK Health System

SUMMARY

- The risk of relapse of depression in primary care patients willing to stop their antidepressant was higher among the patients in the discontinuation group than among those in the maintenance group

QUESTION CASE 3

What is the next step in her treatment?

- A) Taper and discontinue sertraline
- B) Maintain sertraline 100mg
- C) Convert to alternative SSRI
- D) Refer to psychiatrist for assistance

CASE 4

54 year-old male with BMI 33, HTN, CAD, lower back pain presenting for weight loss counseling. He reports he has seen the dietitian, optimized diet and exercise but feels like he is not losing weight. Last A1c 12/2021 was 5.3%.

QUESTION CASE 4

- What do you counsel him for weight loss?
- A) Return to dietitian to discuss
- B) Add Liraglutide 3.0 mg inj daily
- C) Metformin 1000mg PO BID
- D) Add Semaglutide 2.4 mg inj weekly

STEP TRIALS

- STEP trials examine semaglutide at the higher dose of 2.4 mg/week in weight loss, regardless of the presence of type 2 diabetes.
- Semaglutide is a weekly injectable glucagon-like peptide (GLP)-1 receptor agonist
 - Approved for the treatment of people with type 2 diabetes at weekly doses of up to 1.0 mg.
 - Second GLP-1RA approved for weight management after once-daily subcutaneous liraglutide, 3.0 mg

STEP TRIALS

- **STEP 1:** Adults with BMI ≥ 30 without diabetes received 68 weeks of subcutaneous semaglutide or placebo, plus lifestyle intervention- showed 86;4% of semaglutide group lost at least 5% of BW
- **STEP 2** In adults with BMI > 27 and Type 2 diabetes, semaglutide 2.4 mg once a week achieved a superior and clinically meaningful decrease in bodyweight compared with placebo and semaglutide 1.0mg

STEP TRIALS CONT...

- **STEP 3** In adults with overweight or obesity without diabetes, once-weekly subcutaneous semaglutide, 2.4 mg and intensive behavioral therapy resulted in reductions in body weight of 16.0%.
- **STEP 4** Among adults with overweight or obesity who received 20-weeks of subcutaneous semaglutide, 2.4 mg once weekly, maintaining treatment with semaglutide compared with switching to placebo resulted in continued weight loss over the following 48 weeks.

STEP 8

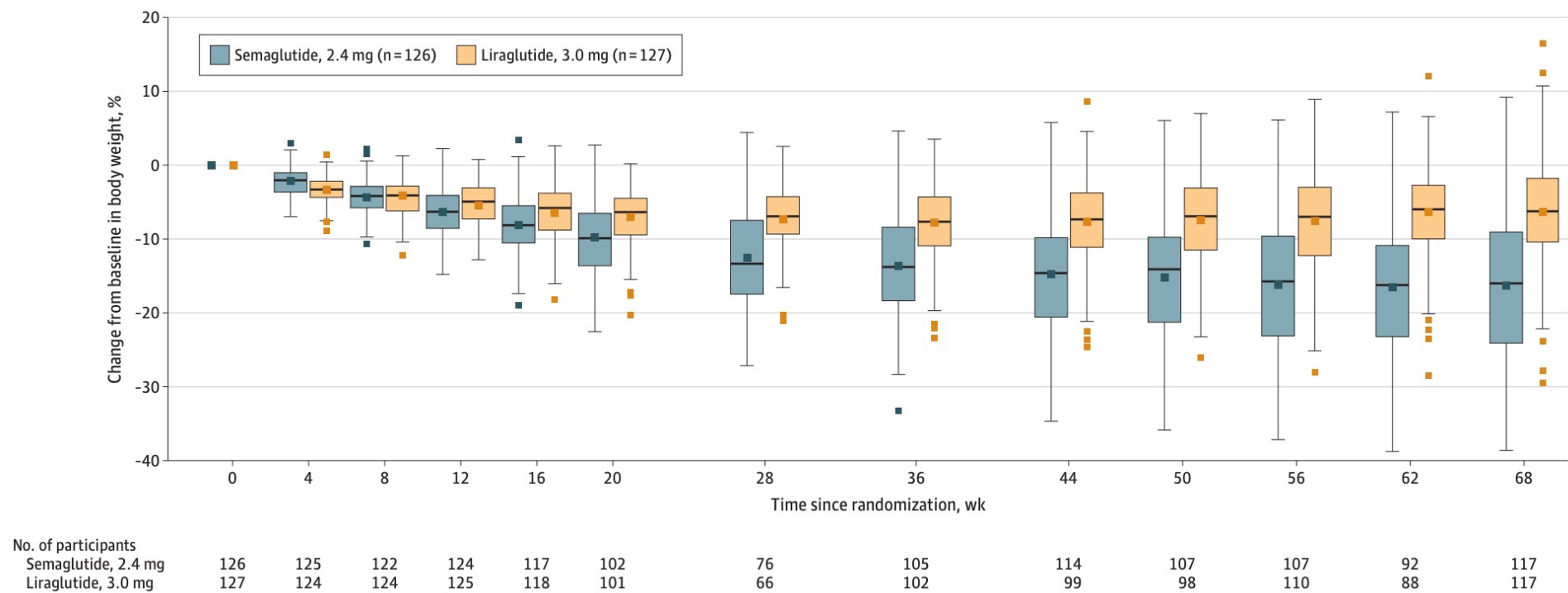
- **Question:** What is the effect of once-weekly subcutaneous semaglutide 2.4 mg vs once-daily subcutaneous liraglutide 3.0 mg, on weight loss when each is added to counseling for diet and physical activity?
- **Design:** Randomized, open-label, 68-week, conducted at 19 US sites from September 2019 to May 2021
- **Intervention:** Assigned to receive once- weekly sq semaglutide 2.4mg or matching placebo, or once-daily sq liraglutide 3.0mg or matching placebo plus diet and physical activity

- **Criteria of Group:** Adults (≥ 18 years old) with 1 or more self-reported unsuccessful dietary weight loss efforts >30 or >27 with 1 or more weight-related comorbidities (hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease)
 - mean age 49, 78.4% female, mean BMI 37.5, 73.7% white, 36.1% with prediabetes
- **Outcome:** percentage change in body weight
- **Secondary Outcomes:** achievement of 10% or more, 15% or more, and 20% or more weight loss at week 68

RESULTS

- Mean weight change from baseline was –15.8% with semaglutide vs –6.4% with liraglutide (difference, –9.4 percentage points [95% CI, –12.0 to –6.8]; $P < .001$)
- The proportions of participants achieving 5% or more weight loss were 87.2% with semaglutide, 58.1% with liraglutide, and 29.5% with placebo
- Proportions of participants discontinuing treatment for any reason were 13.5% with semaglutide and 27.6% with liraglutide.

Figure 2. Percentage Change in Body Weight From Baseline to Week 68 (Observed In-Trial Data; Full Analysis Set)



LIMITATIONS

- Discontinuation policy
 - Participants unable to tolerate 2.4 mg of semaglutide could receive 1.7 mg
 - Participants unable to tolerate 3.0 mg of liraglutide, treatment was discontinued
- Industry sponsored
- Not blinded to dosing differences
 - Participants knew which active treatment they could potentially receive

CONCLUSIONS

- Among adults with overweight or obesity without diabetes, once-weekly subcutaneous semaglutide compared with once-daily subcutaneous liraglutide, added to counseling for diet and physical activity, resulted in significantly greater weight loss at 68 weeks.

QUESTION CASE 4

- What do you counsel him for weight loss?
- A) Return to dietitian to discuss
- B) Add Liraglutide 3.0 mg inj daily
- C) Add metformin 1000mg PO BID
- D) Add Semaglutide 2.4 mg inj weekly

SUMMARY

- Effects of SGLT2 inhibition show benefit in patient with heart failure with preserved ejection fraction
- Initiate colon cancer screening at age 45 for average risk population
- Maintain antidepressants in patients stable on regimen as risk of relapse with discontinuation
- Once-weekly subcutaneous semaglutide when added to diet and physical activity can result in significant weight loss

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