



# EVERYTHING YOU NEED TO KNOW ABOUT GLUCAGON-LIKE PEPTIDE 1 THERAPIES

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# DISCLOSURES

- None



# EDUCATIONAL NEED / PRACTICE GAP

- Practice Gap
  - Research in the field of Glucagon-like Peptide 1 therapies (GLP-1s) has been happening at a rapid pace making it difficult for physicians to keep up.
  - Questions from patients regarding the class of medications have accelerated due to traditional media, social media and word-of-mouth.
- Educational Need
  - Providers need to be familiar with GLP-1s, to discuss their risks and benefits with patient and recommend tailored therapy based on underlying health conditions and patient goals.

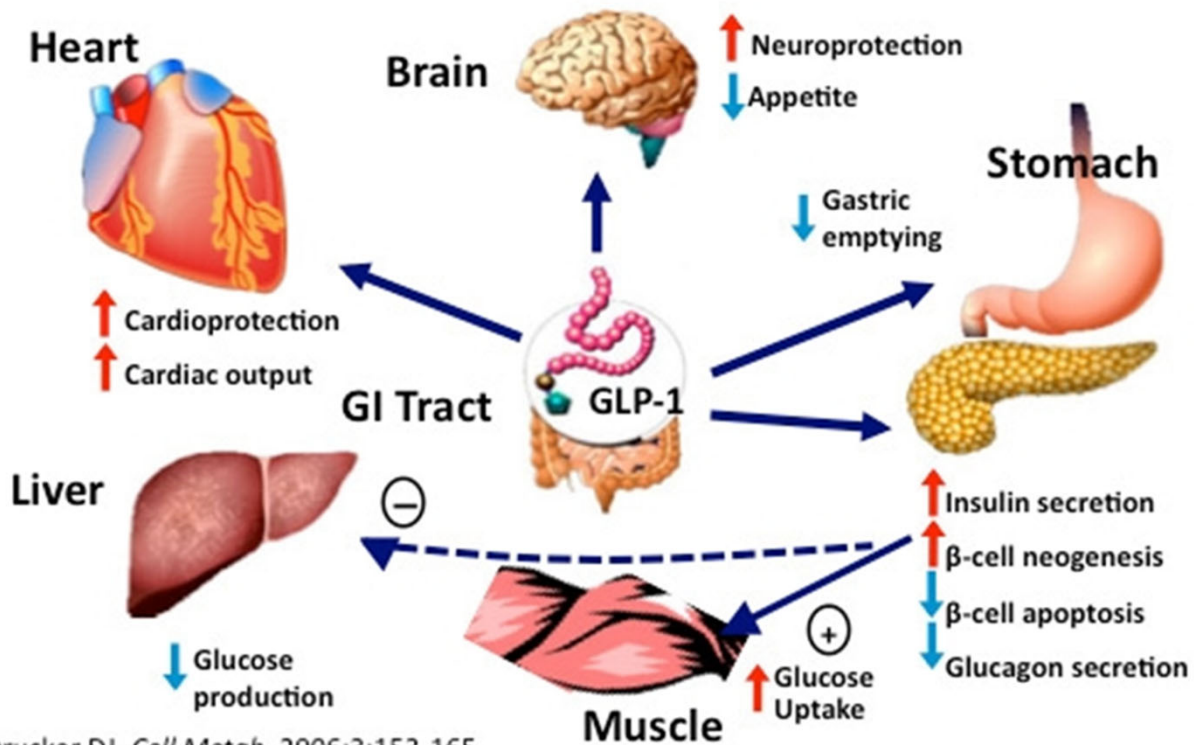


## OBJECTIVES

- Participants will be able to describe the mechanism of action of GLP-1 therapies
- Participants will be able to compare the benefits of different GLP-1 therapies
- Participants will be able to solve common problems related to GLP-1 usage

# WHAT IS GLUCAGON-LIKE PEPTIDE 1 (GLP-1)?

## GLP-1 Actions in Peripheral Tissue



Drucker DJ. *Cell Metab.* 2006;3:153-165.

# GLP-1 THERAPIES

Exenatide (Byetta ®) – Subcutaneous BID dosing

Extended release exenatide (Bydureon ®) – subcutaneous once weekly dosing

Liraglutide (Victoza ®) – subcutaneous once daily dosing

Dulaglutide (Trulicity ®) – subcutaneous once weekly dosing

Lixisenatide (Adlyxin ®, Soliqua®) – subcutaneous once daily dosing

Tirzepatide (Mounjaro ®, Zepbound ®) – subcutaneous once weekly dosing (includes GIP)

Retatrutide – subcutaneous once weekly (includes GIP and GRA)

Semaglutide (Ozempic ®, Wegovy ®, Rybelsus ®)

- Ozempic ®, Wegovy ® -- subcutaneous once weekly dosing
- Rybelsus ® -- oral once daily dosing
- CagriSema ® -- subcutaneous once weekly dosing (Includes GIP)

# GLYCEMIC CONTROL



## **KAHOOT.IT QUESTION 1 & 2**

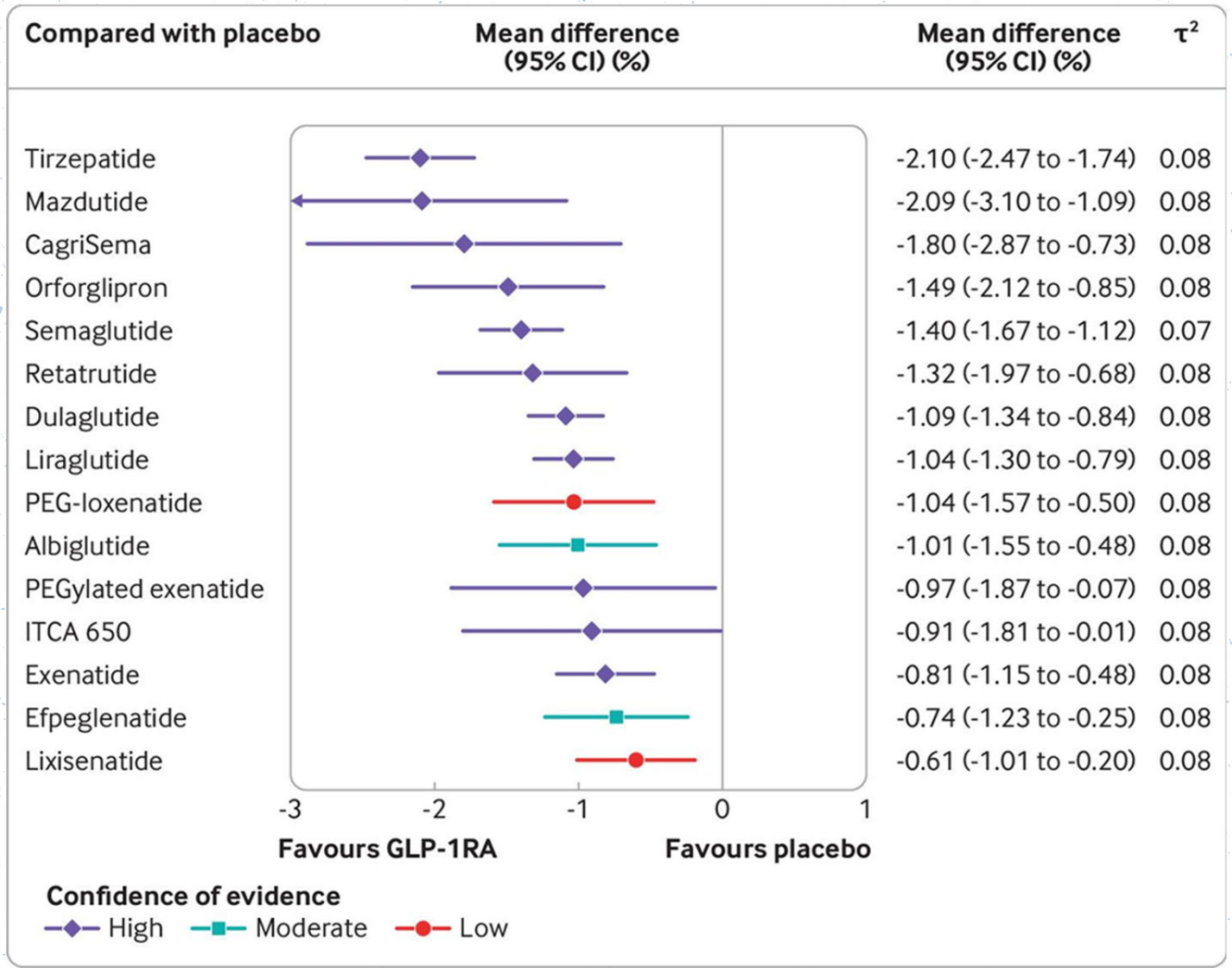
- Go to Kahoot.it
- Enter the game code shown
- Put in a nickname
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- No points taken away for incorrect answers
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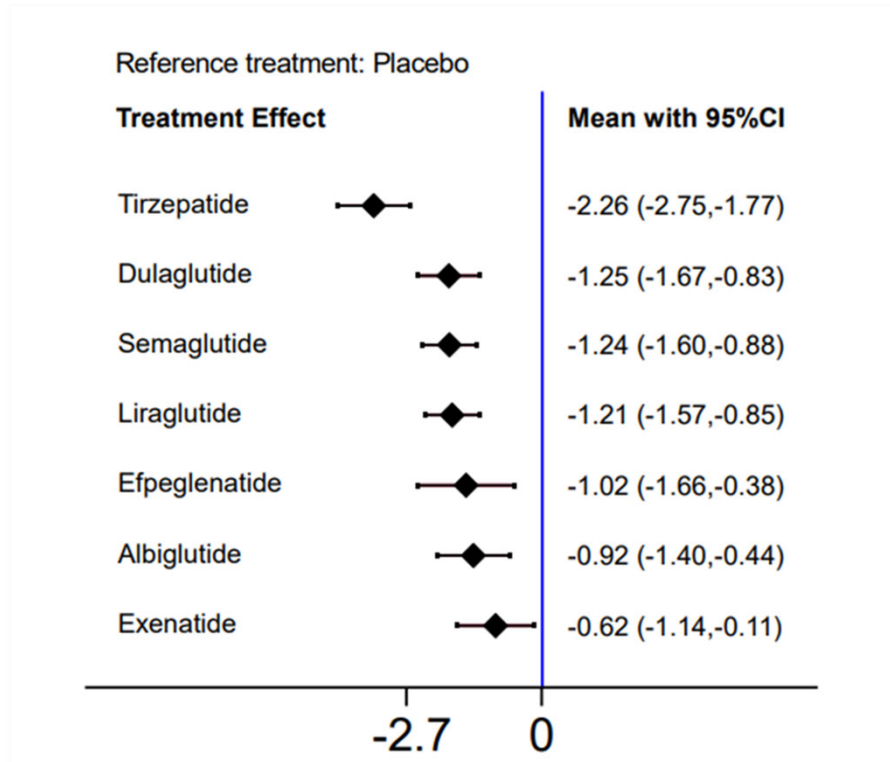
# **YAO H, ZHANG A, LI D, WU Y, WANG C, WAN J ET AL. COMPARATIVE EFFECTIVENESS OF GLP-1 RECEPTOR AGONISTS ON GLYCAEMIC CONTROL, BODY WEIGHT, AND LIPID PROFILE FOR TYPE 2 DIABETES: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS *BMJ* 2024; 384:E076410**

- Metanalysis of 76 trials involving 15 GLP-1s and 39,246 patients across 56 countries with type 2 diabetes.
- Had to include a placebo arm and be at least 12 weeks in duration.
- Study duration length varied from 12 to 78 weeks with mean age of 56.79 years, mean HbA1C of 8.13% and mean BMI of 31.73.
- Study compared A1C lowering, weight loss and other metabolic indicators among GLP-1s as well as adverse effects.



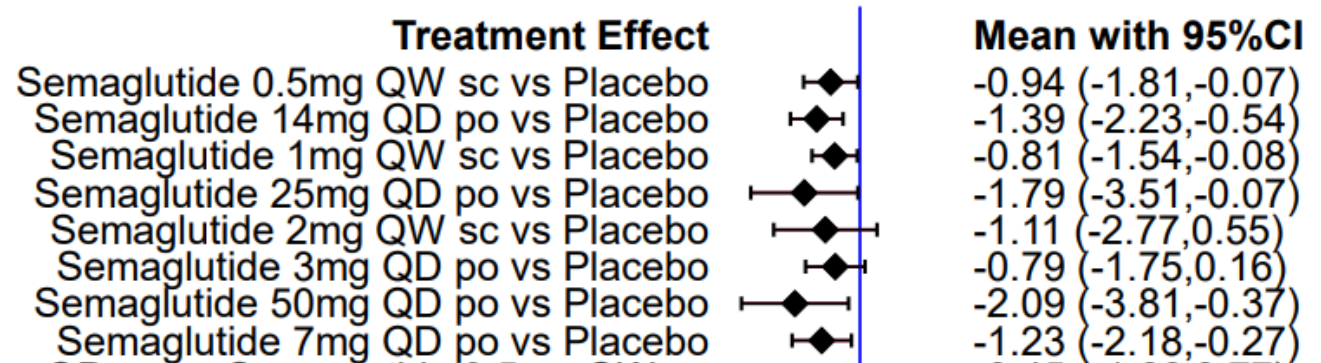
**Figure S15.3:** The effects of GLP-IRAs in long-term intervention (>12 months).

(A) Forest plot of HbA1c




Yao H, Zhang A, Li D, Wu Y, Wang C, Wan J et al. Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis *BMJ* 2024; 384:e076410

## (A2) Forest plot of HbA1c

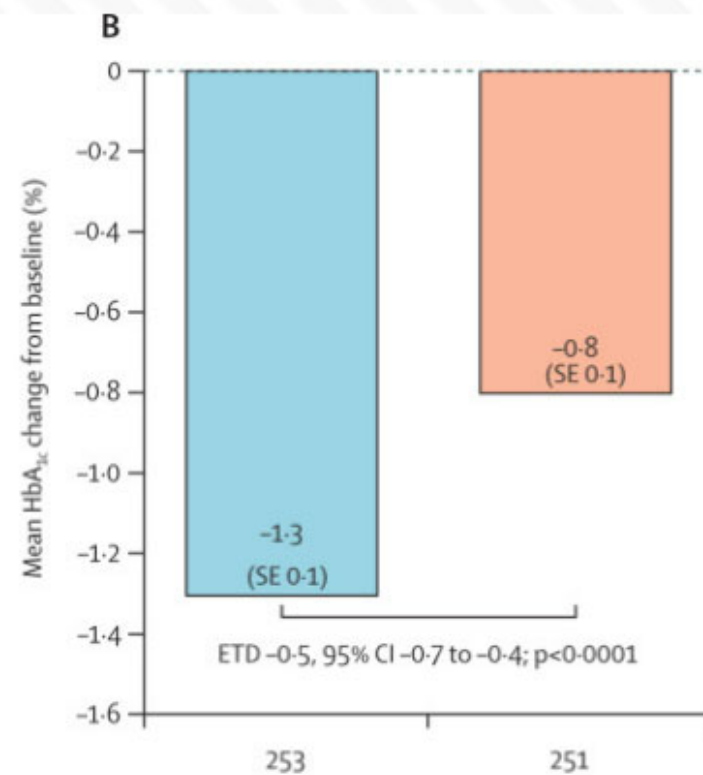
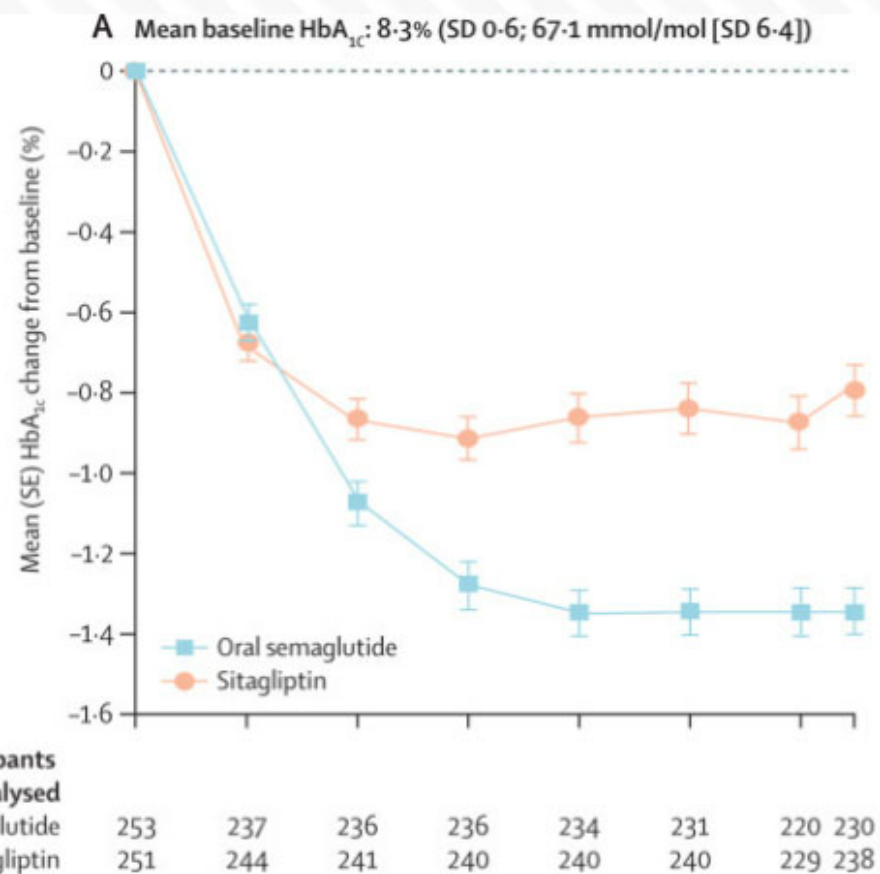


Yao H, Zhang A, Li D, Wu Y, Wang C, Wan J et al. Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis *BMJ* 2024; 384:e076410





**PIEBER TR ET AL. EFFICACY AND SAFETY OF ORAL SEMAGLUTIDE WITH FLEXIBLE DOSE ADJUSTMENT VERSUS SITAGLIPTIN IN TYPE 2 DIABETES (PIONEER 7). LANCET DIABETES ENDOCRINOL. 2019 JUL;7(7):528-539.**

- 504 patients with Type 2 diabetes from 81 countries.
- Given oral semaglutide or sitagliptin and monitored for 52 weeks.
- Primary outcomes was % of patients with A1C < 7%. Secondary outcomes included weight loss and reduction in A1C.

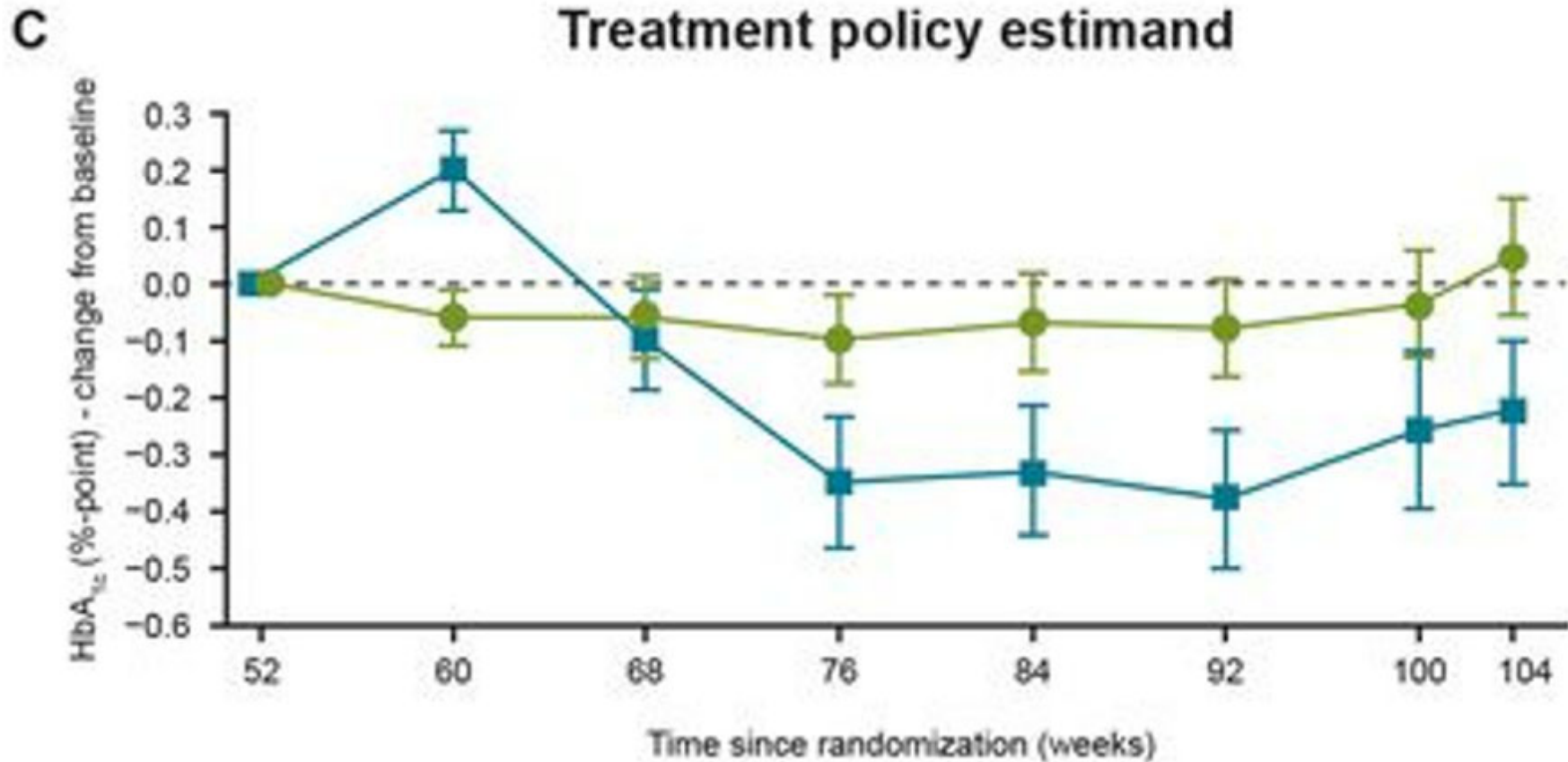


Buse JB et al. Long-term efficacy and safety of oral semaglutide and the effect of switching from sitagliptin to oral semaglutide in patients with type 2 diabetes. *BMJ Open Diabetes Res Care*. 2020 Dec;8(2):e001649.



## **BUSE JB ET AL. LONG-TERM EFFICACY AND SAFETY OF ORAL SEMAGLUTIDE AND THE EFFECT OF SWITCHING FROM SITAGLIPTIN TO ORAL SEMAGLUTIDE IN PATIENTS WITH TYPE 2 DIABETES. BMJ OPEN DIABETES RES CARE. 2020 DEC;8(2):E001649.**

- 198 patients with Type 2 diabetes from 81 countries who had been on sitagliptin for 52 weeks.
- Half were switched to oral semaglutide and half were continued on sitagliptin and monitored for 52 weeks.
- Primary outcome was reduction in A1C from baseline.



Buse JB et al. Long-term efficacy and safety of oral semaglutide and the effect of switching from sitagliptin to oral semaglutide in patients with type 2 diabetes. *BMJ Open Diabetes Res Care.* 2020 Dec;8(2):e001649.



# OBESITY IN PATIENTS WITH DM II



## **KAHOOT.IT QUESTION 3**

- Go to Kahoot.it
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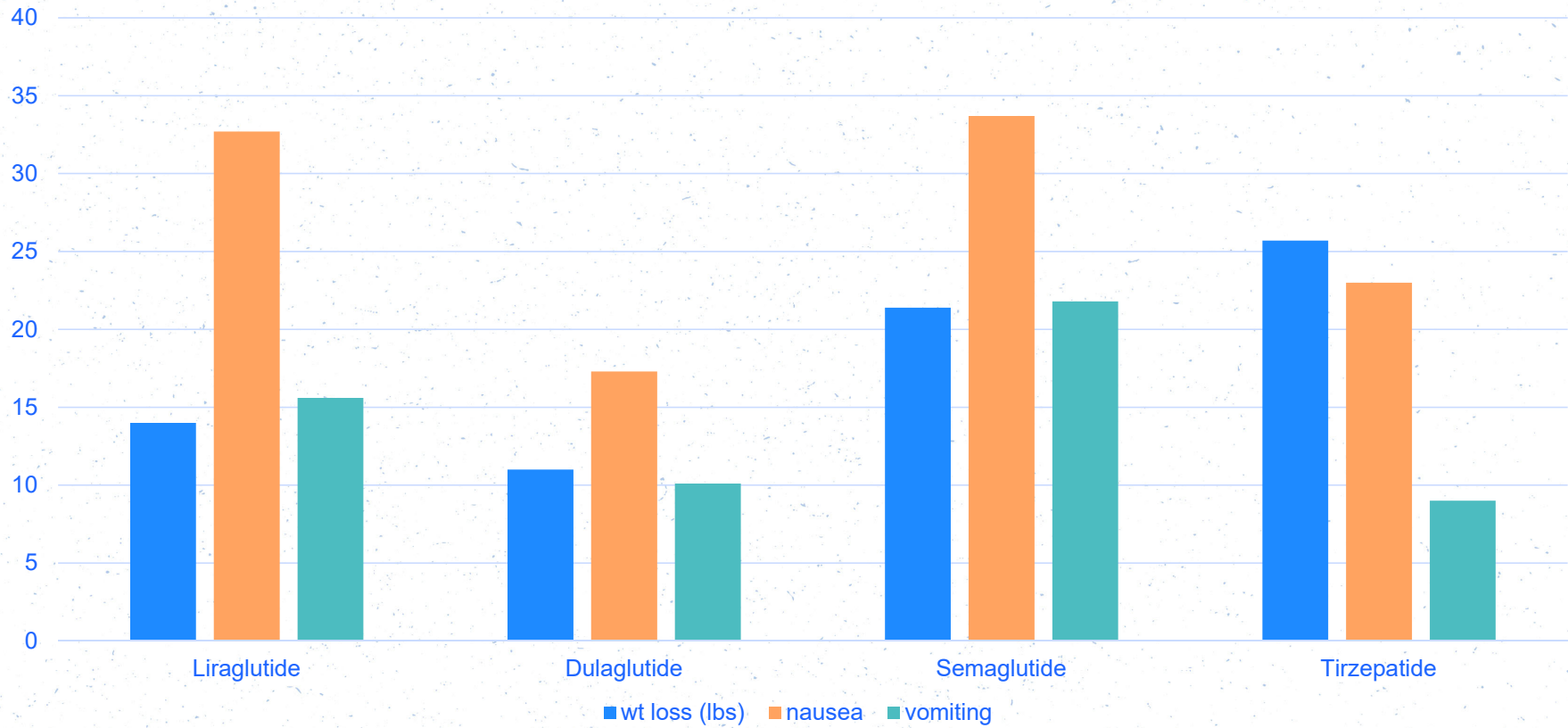
# GLP-1 TRIALS AND WEIGHT LOSS IN PATIENTS WITH DIABETES

- AWARD-11: Dulaglutide at doses of 1.5, 3 and 4.5 mg in patients on metformin with BMI > 25 (mean BMI 34.2) at 52 weeks.
- SCALE Diabetes: Liraglutide at dose of 1.8 and 3 mg in patients w/ BMI > 27 (mean BMI 37) at 52 weeks.
- STEP-2: Semaglutide at dose of 1 mg and 2.4 mg in patients w/ BMI > 27 (mean BMI 35.7) at 52 weeks.
- SURPASS-4: Tirzepatide at doses of 5, 10 and 15 mg in patients with BMI > 25 (mean BMI 32.6) at 52 weeks.

# GLP-1 TRIALS AND WEIGHT LOSS IN PATIENTS WITH DIABETES

- Dulaglutide 1.5 = 3.5 kg (N/V/D = 14.2/6.4/7.7), 3.0 = 4.3 kg (N/V/D = 16.1/9.1/12), 4.5 = 5 kg (N/V/D = 17.3/10.1/11.6)
- Liraglutide 1.8 mg = 5 kg (N/V/D = 31.4/10.0/17.6) and 3.0 mg = 6.4 kg (N/V/D = 32.7/15.6/25.6)
- Semaglutide 1.0 mg = 6.9 kg (N/V/D = 32.1/13.4/22.1) and 2.4 mg 9.7 kg = (N/V/D = 33.7/21.8/21.3)
- Tirzepatide 5 = 7.1 kg (N/V/D = 12/5/13), 10 = 9.5 kg (N/V/D = 16/8/20), 15 = 11.7 kg (N/V/D = 23/9/22)

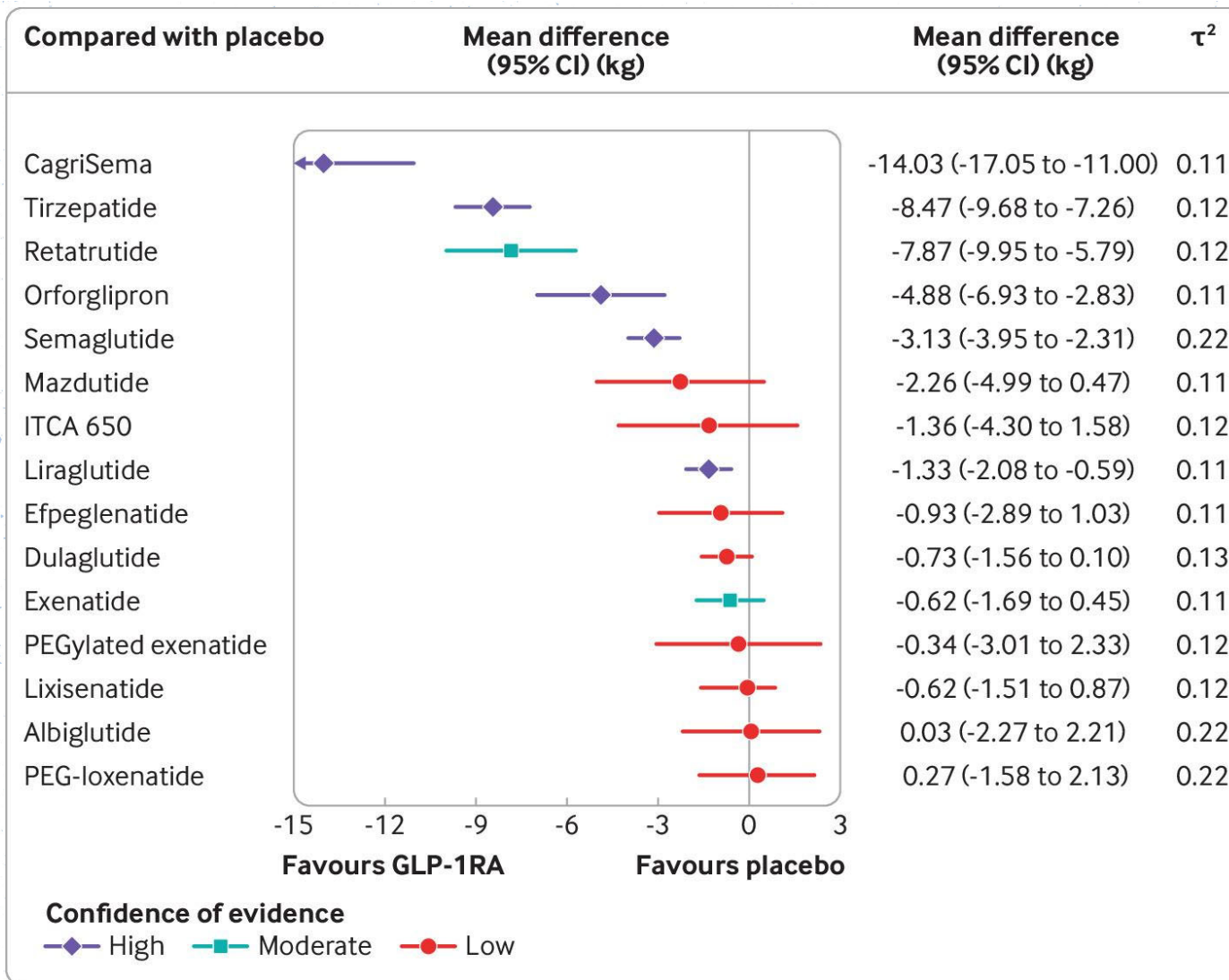
## Comparison of GLP-1 Efficacy and Side Effects at Max Doses



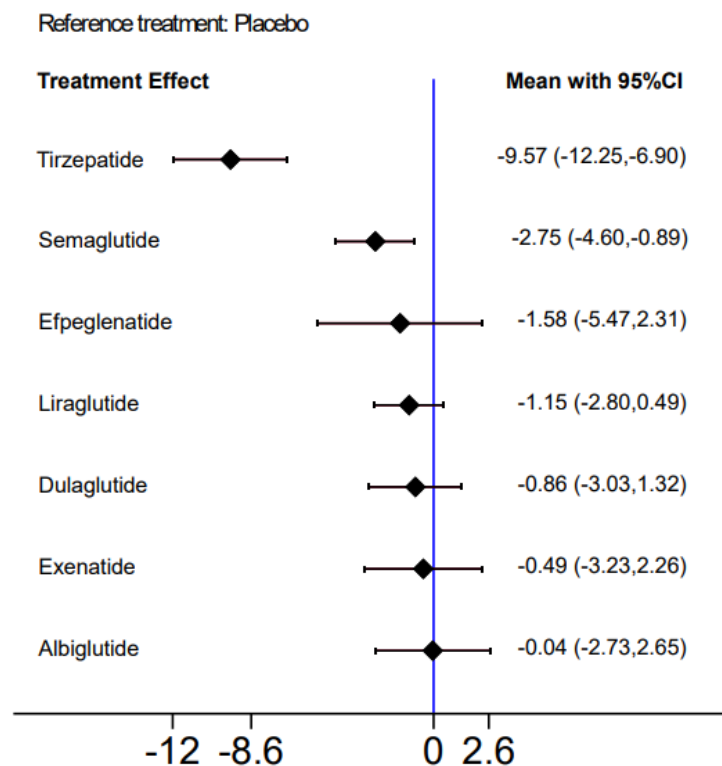


# **YAO H, ZHANG A, LI D, WU Y, WANG C, WAN J ET AL. COMPARATIVE EFFECTIVENESS OF GLP-1 RECEPTOR AGONISTS ON GLYCAEMIC CONTROL, BODY WEIGHT, AND LIPID PROFILE FOR TYPE 2 DIABETES: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS *BMJ* 2024; 384:E076410**

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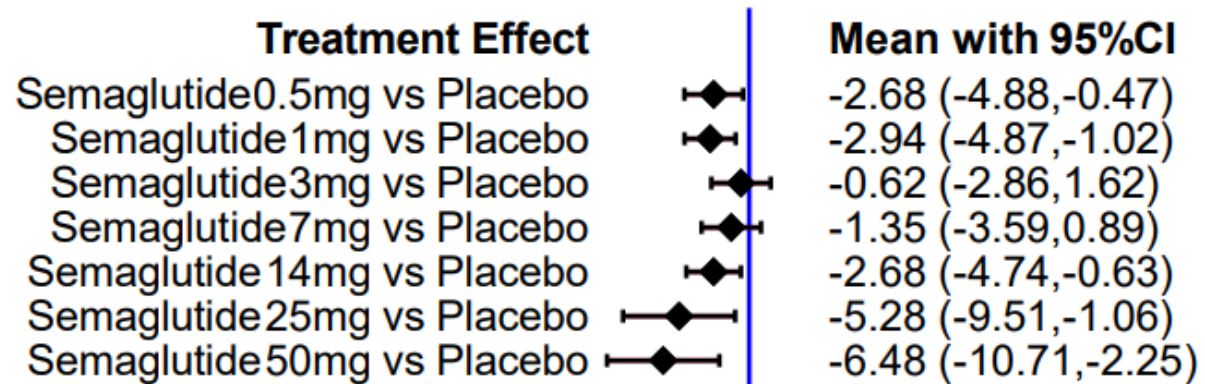
(C) weight loss



Yao H, Zhang A, Li D, Wu Y, Wang C, Wan J et al. Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis *BMJ* 2024; 384:e076410



## (C2) Forest plot of weight loss



Yao H, Zhang A, Li D, Wu Y, Wang C, Wan J et al. Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis *BMJ* 2024; 384:e076410

# OBESITY IN PATIENTS WITHOUT DM II



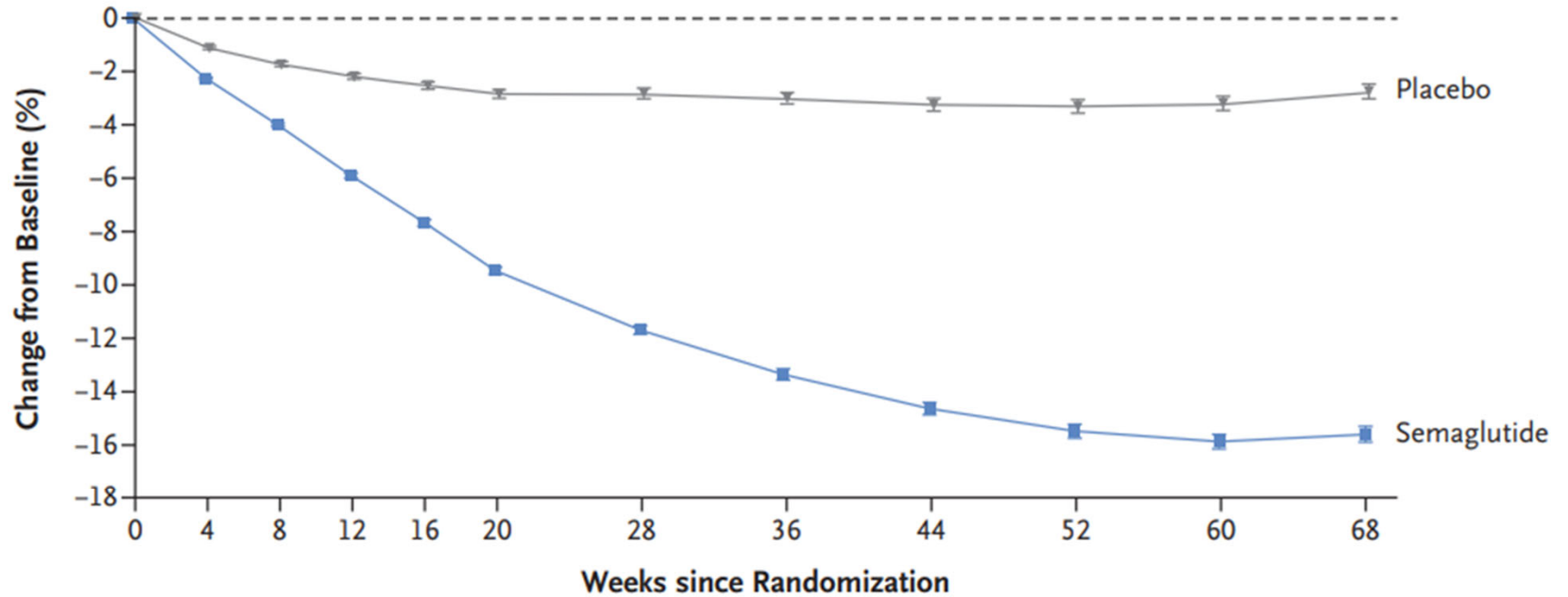
## **KAHOOT.IT QUESTIONS 4-7**

- Go to Kahoot.it
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## **STEP-1: WILDING ET AL. ONCE-WEEKLY SEMAGLUTIDE IN ADULTS WITH OVERWEIGHT OR OBESITY. N ENGL J MED. 2021 FEB;384(11):989-1002.**

- 1,961 adult patients with BMI > 30 (or BMI > 27 with comorbidity) without type 2 diabetes. Average BMI was 38.
- Placebo vs. 2.4 mg semaglutide with 16 week dose escalation period and then observed for 52 weeks.
- Primary outcome was % change in weight from baseline.


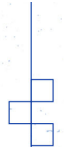
**A Body Weight Change from Baseline by Week, Observed In-Trial Data**



**No. at Risk**

Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

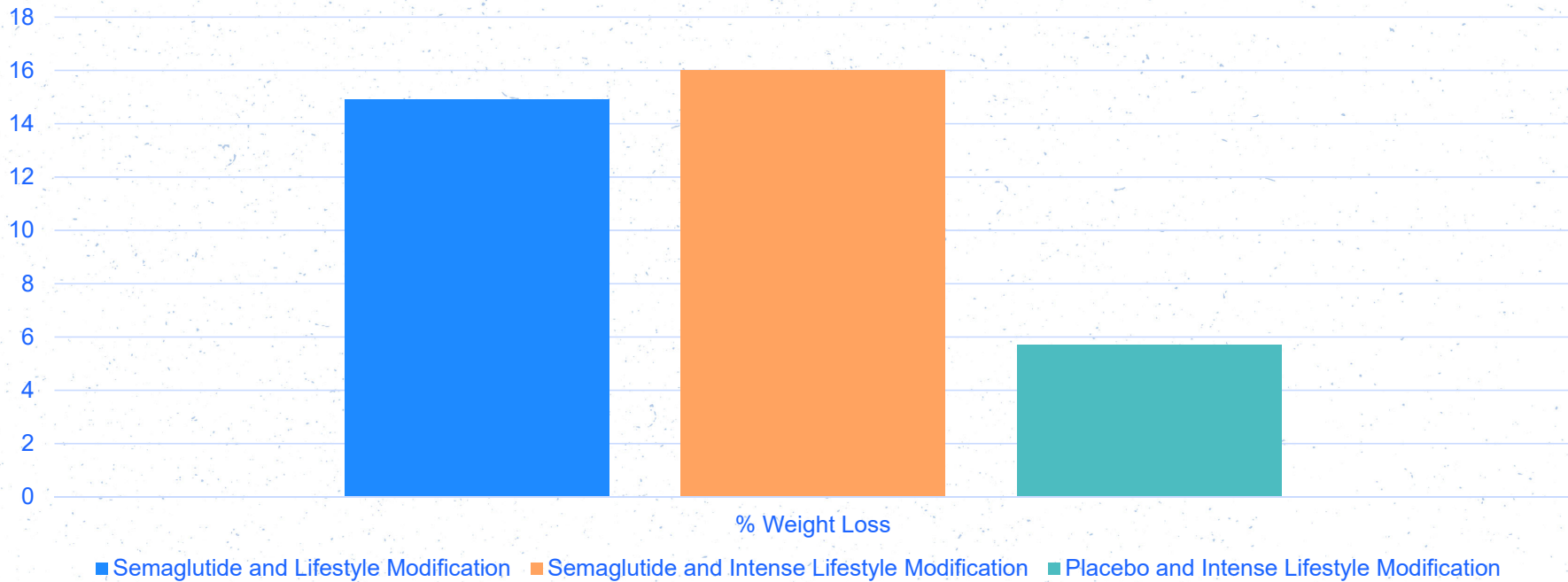
Wilding et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. *N Engl J Med.* 2021 Feb;384(11):989-1002.



## **STEP 3: WADDEN ET AL. EFFECT OF SUBCUTANEOUS SEMAGLUTIDE VS PLACEBO AS AN ADJUNCT TO INTENSIVE BEHAVIORAL THERAPY ON BODY WEIGHT IN ADULTS WITH OVERWEIGHT OR OBESITY. *JAMA*. 2021;325(14):1403–1413.**

- 611 adult patients with BMI > 30 (or BMI > 27 with comorbidity) without type 2 diabetes. Average BMI was 38.
- Placebo and intense lifestyle modification vs. 2.4 mg semaglutide with 16 week dose escalation period and then observed for 52 weeks.
- Primary outcome was % change in weight from baseline.

## Semaglutide With and Without Intense Lifestyle Modification



STEP 3: Wadden et al. Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity. *JAMA*. 2021;325(14):1403–1413.

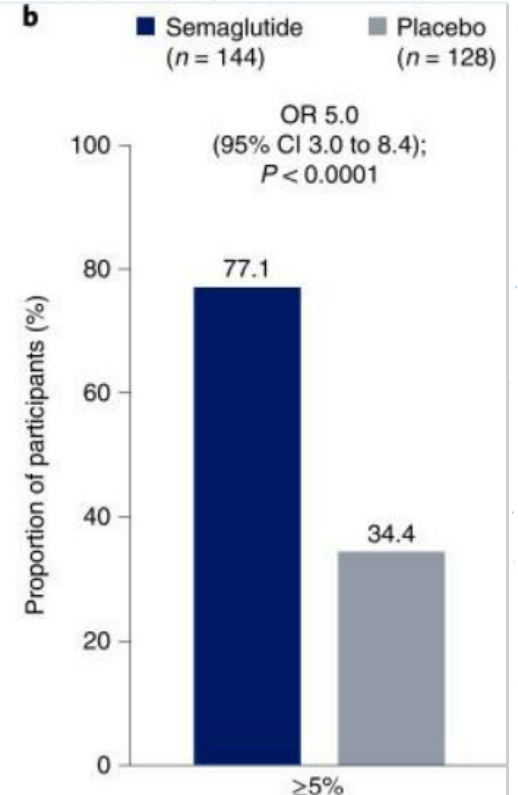
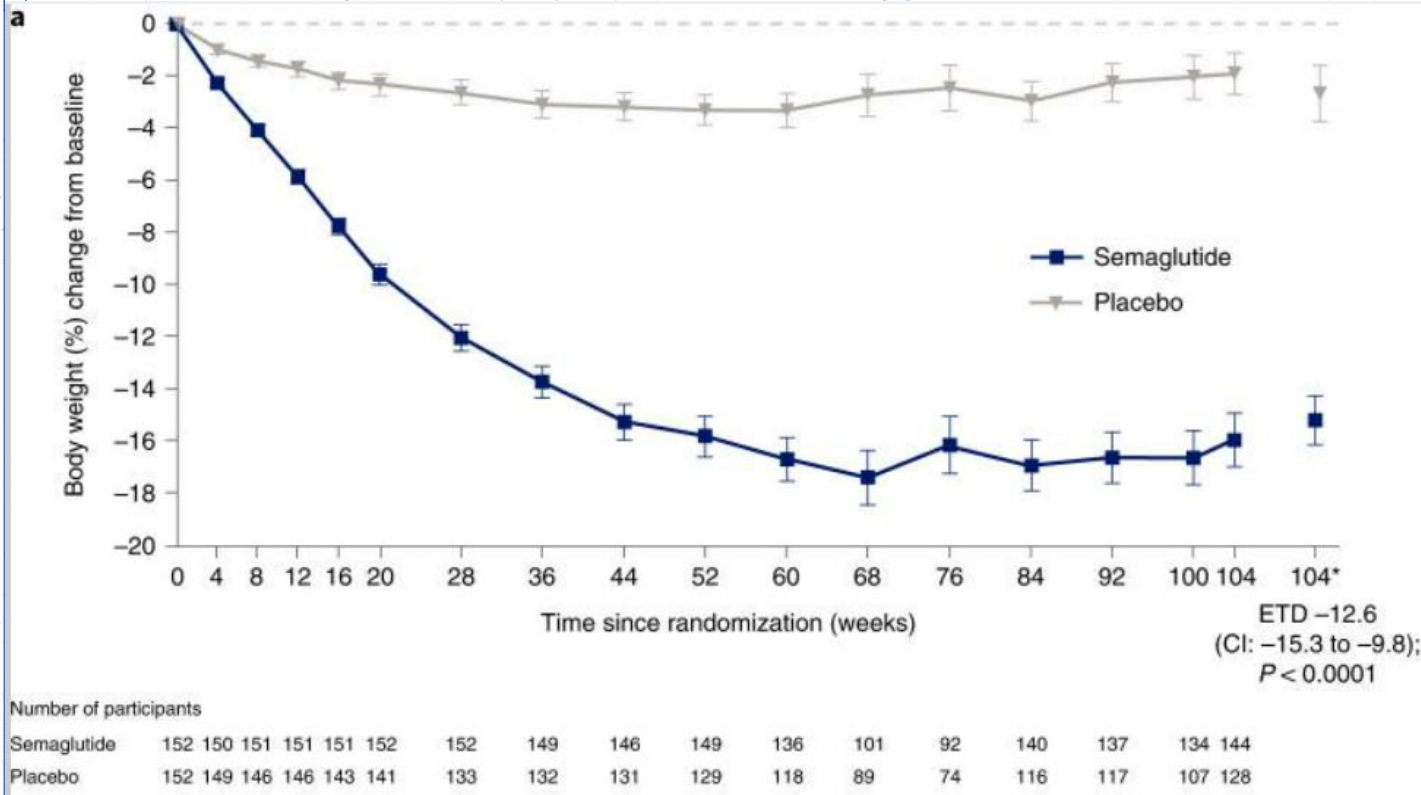
VS STEP 1



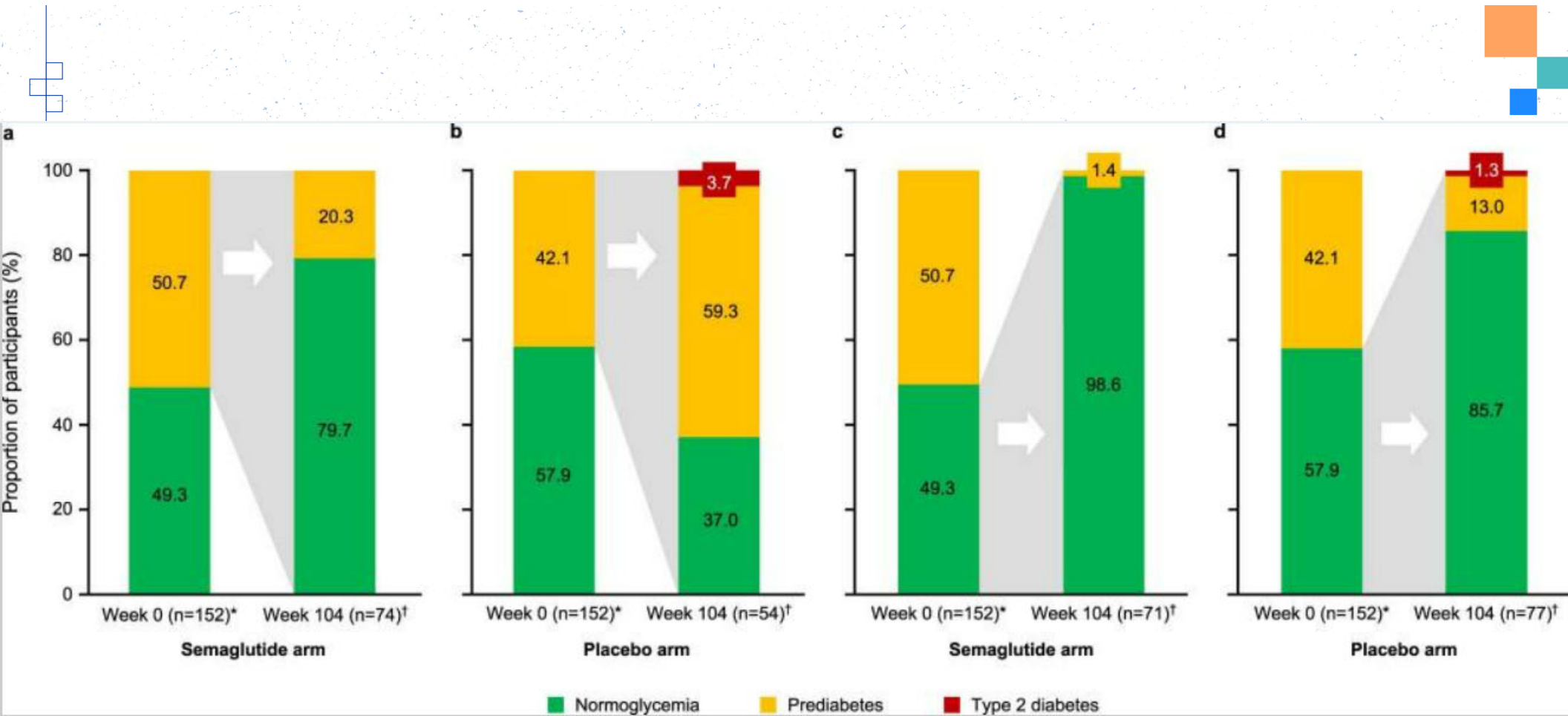
## **STEP 5: GARVEY WT ET AL. TWO-YEAR EFFECTS OF SEMAGLUTIDE IN ADULTS WITH OVERWEIGHT OR OBESITY. NAT MED. 2022 OCT;28(10):2083-2091.**

- 304 adult patients with BMI > 30 (or BMI > 27 with comorbidity) without type 2 diabetes. Average BMI was 38.
- Placebo vs. 2.4 mg semaglutide observed for 104 weeks.
- Primary outcome was % change in weight from baseline.





STEP 5: Garvey WT et al. Two-year effects of semaglutide in adults with overweight or obesity. Nat Med. 2022 Oct;28(10):2083-2091.



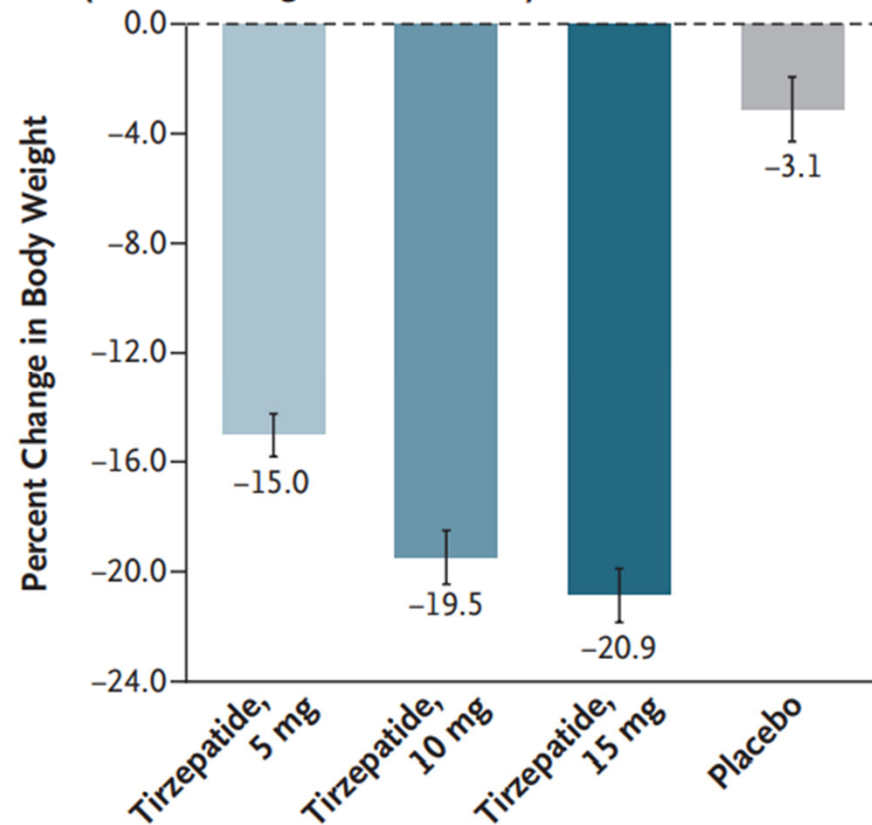
STEP 5: Garvey WT et al. Two-year effects of semaglutide in adults with overweight or obesity. Nat Med. 2022 Oct;28(10):2083-2091.





## **SURMOUNT-1: JASTREBOOF ET AL. TIRZEPATIDE ONCE WEEKLY FOR THE TREATMENT OF OBESITY. N ENGL J MED. 2022 JUN 4;387(3):205-216.**

- 2,539 patients with BMI > 30 (or BMI > 27 with comorbidity) without type 2 diabetes. Average BMI was 38.
- Placebo vs. 5, 10 and 15 mg tirzepatide with 20 wk dose escalation period and then observed for 52 weeks.
- Primary outcome was % change in weight from baseline.

**A Overall Percent Change in Body Weight from Baseline  
(treatment-regimen estimand)**



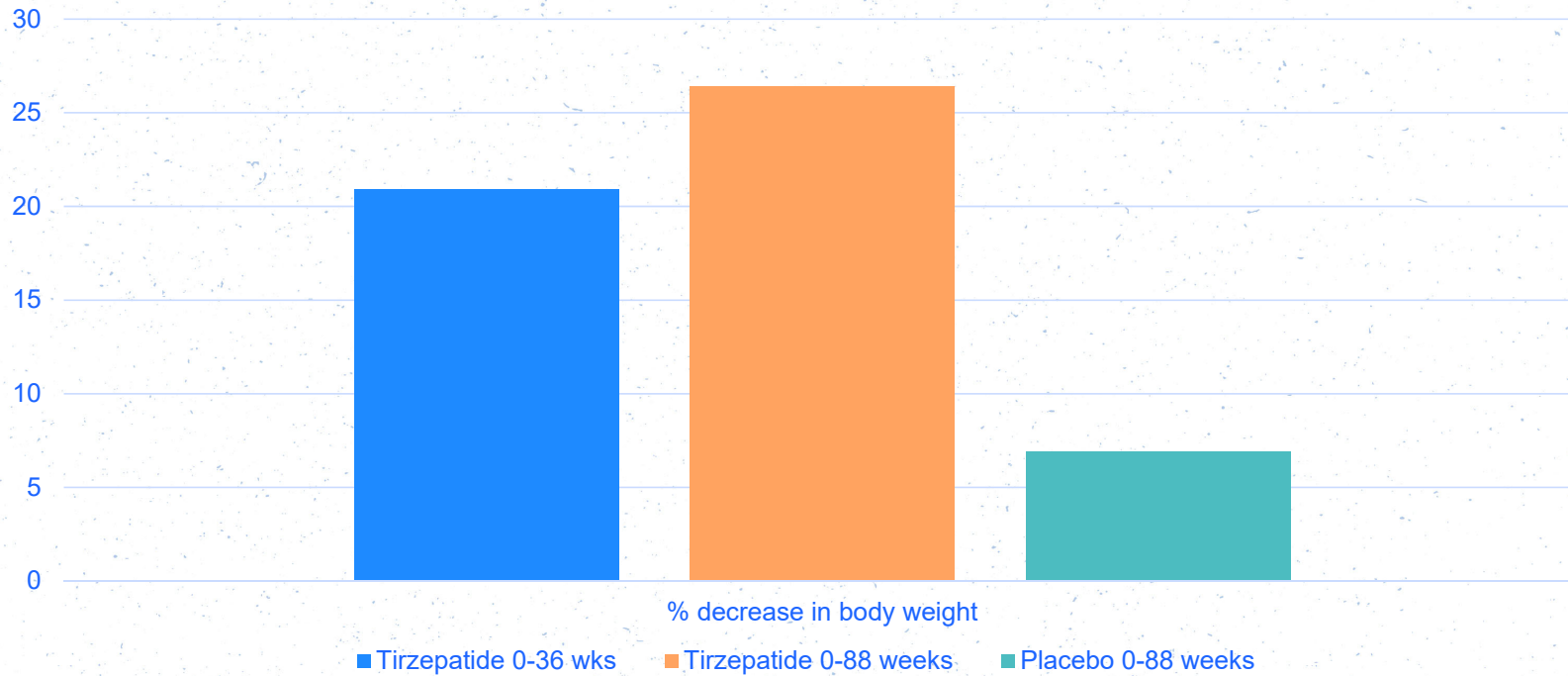
SURMOUNT-1: Jastreboof et al. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022 Jun 4;387(3):205-216.



# **ARONNE LJ, SATTAR N, ET. AL. CONTINUED TREATMENT WITH TIRZEPATIDE FOR MAINTENANCE OF WEIGHT REDUCTION IN ADULTS WITH OBESITY: THE SURMOUNT-4 RANDOMIZED CLINICAL TRIAL. JAMA. 2024 JAN 2;331(1):38-48.**

- 670 patients with BMI > 30 (or BMI > 27 with comorbidity) without type 2 diabetes.
- Participants given 36 weeks of tirzepatide 10 or 15 mg (92.7%) and then half were taken off the medication and the other half were continued on medications for an additional 52 weeks.
- Primary outcome was % change in weight from 36 weeks to week 88.

## Surmount-4 Long Term Tirzepatide vs Lifestyle Modification Only



Aronne LJ, Sattar N, Et. Al. Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial. JAMA. 2024 Jan 2;331(1):38-48.

# CARDIOVASCULAR OUTCOMES



## **KAHOOT.IT QUESTIONS 8 & 9**

- Go to Kahoot.it
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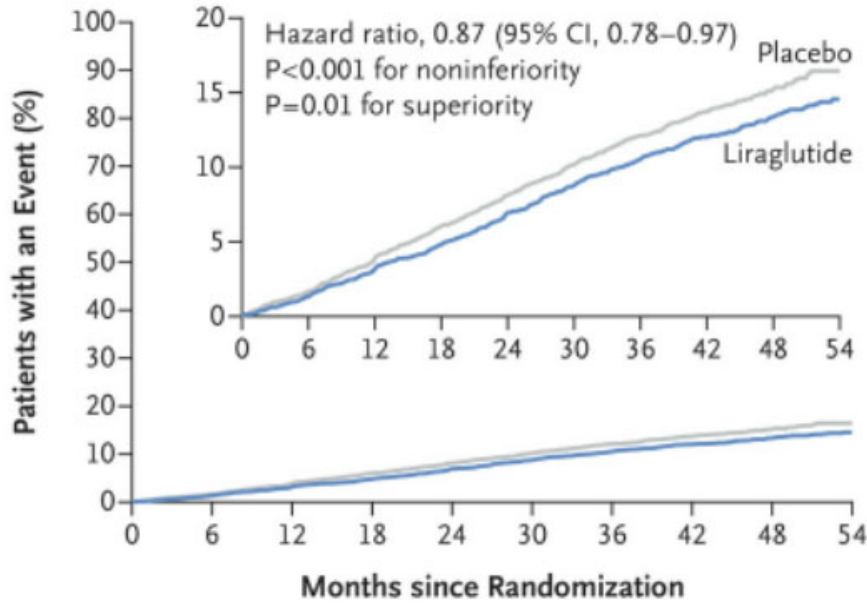


## **LEADER TRIAL: MARSO ET AL. LIRAGLUTIDE AND CARDIOVASCULAR OUTCOMES IN TYPE 2 DIABETES. N ENGL J MED. 2016 JUL 28;375(4):311-22.**

- 9,340 patients with type 2 diabetes at high risk of cardiovascular disease (81.3% were > 50 y/o and had known cardiovascular disease).
- Treated with liraglutide or placebo.
- A1C > 7.0%.
- Primary endpoint was death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.



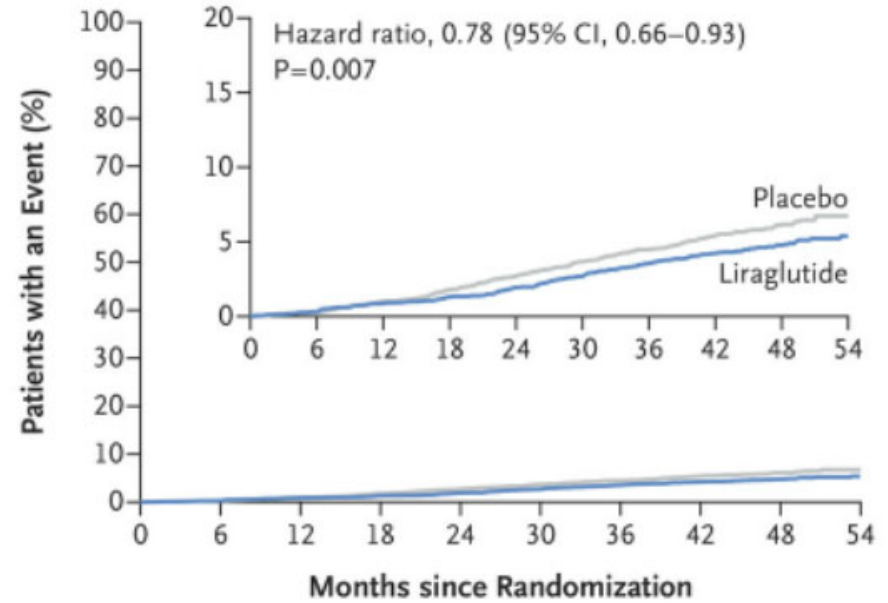
### A Primary Outcome



#### No. at Risk

Liraglutide	4668	4593	4496	4400	4280	4172	4072	3982	1562	424
Placebo	4672	4588	4473	4352	4237	4123	4010	3914	1543	407

### B Death from Cardiovascular Causes



#### No. at Risk

Liraglutide	4668	4641	4599	4558	4505	4445	4382	4322	1723	484
Placebo	4672	4648	4601	4546	4479	4407	4338	4267	1709	465

Marso et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med.* 2016 Jul 28;375(4):311-22.



Risk of CVD						
≥50 yr of age and established CVD	7598	536/3831 (14.0)	629/3767 (16.7)		0.83 (0.74–0.93)	0.04
≥60 yr of age and risk factors for CVD	1742	72/837 (8.6)	65/905 (7.2)		1.20 (0.86–1.67)	

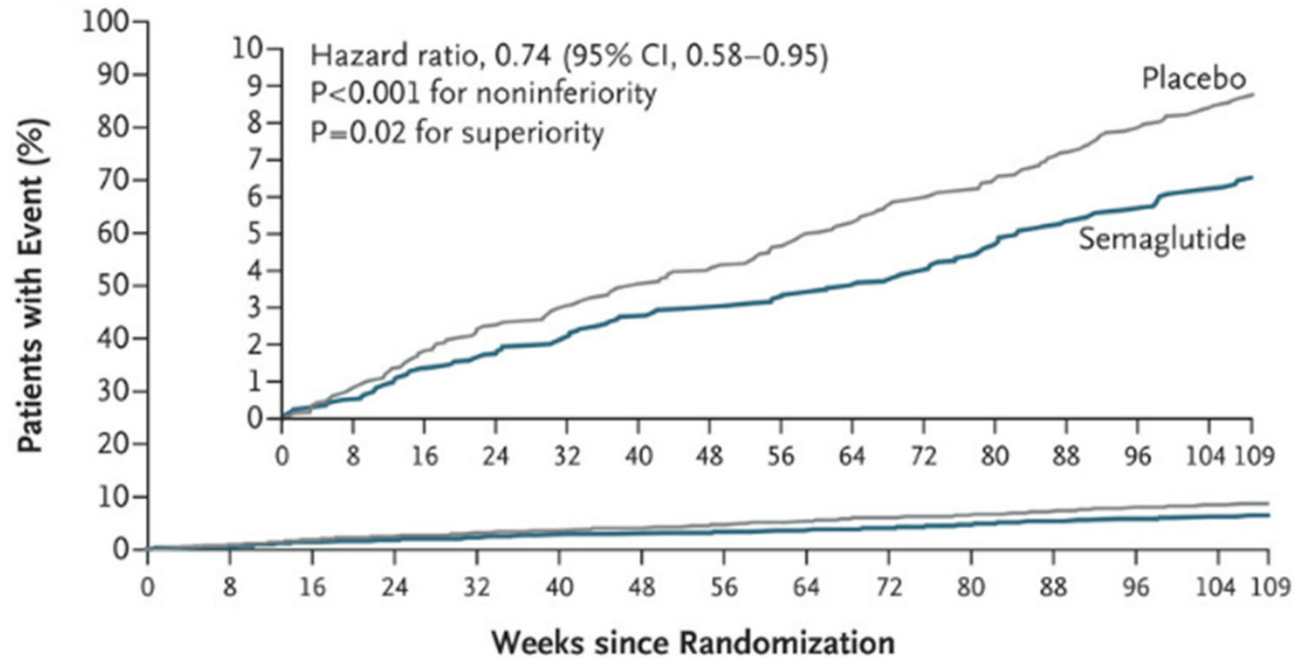
Marso et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med.* 2016 Jul 28;375(4):311-22.



## **SUSTAIN-6: MARSO ET AL. SEMAGLUTIDE AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES. N ENGL J MED. 2016 NOV 10;375(19):1834-1844.**

- 3,297 patients with type 2 diabetes at high risk for cardiovascular events (83% had CVD).
- SQ semaglutide vs. placebo.
- A1C > 7.0%.
- Primary endpoint was composite of cardiovascular death, nonfatal MI, and stroke.

### A Primary Outcome



#### No. at Risk

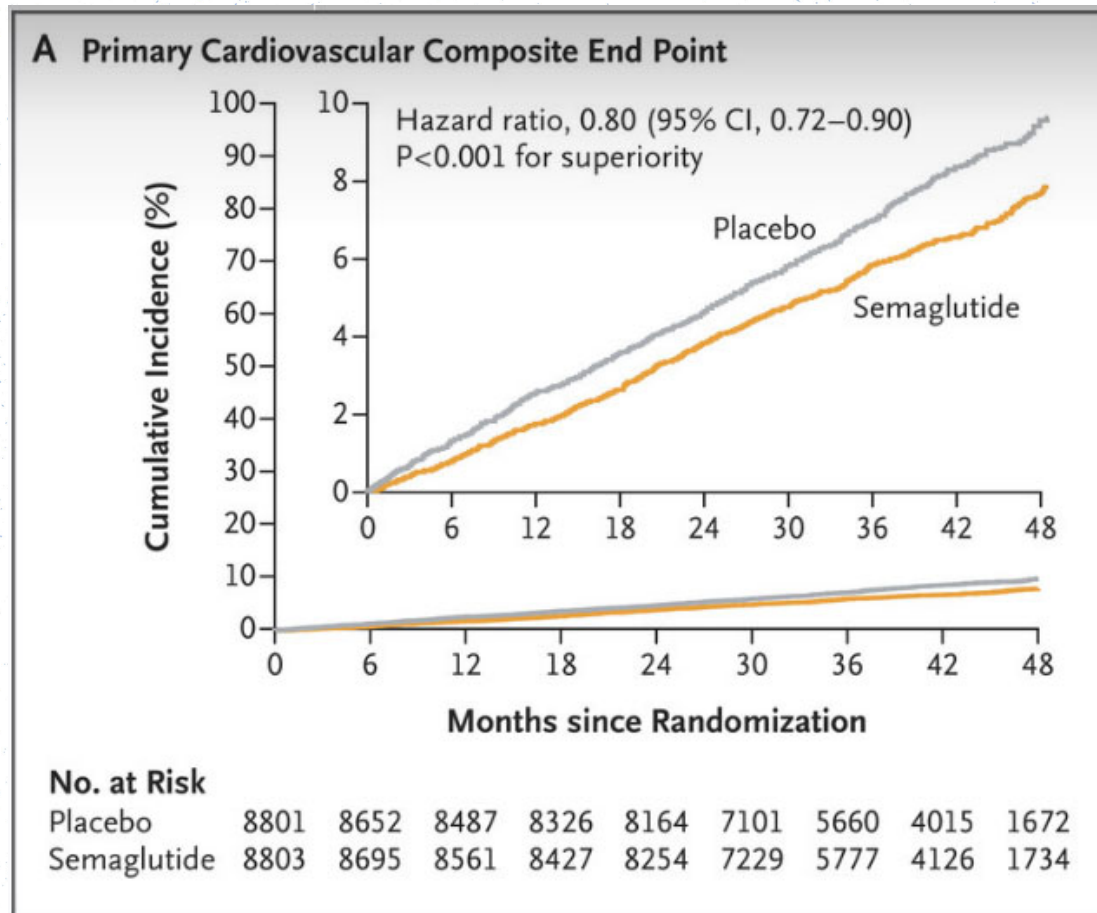
Placebo	1649	1616	1586	1567	1534	1508	1479
Semaglutide	1648	1619	1601	1584	1568	1543	1524

Marso et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. *N Engl J Med.* 2016 Nov 10;375(19):1834-1844.

28

# **LINCOFF ET AL. SEMAGLUTIDE AND CARDIOVASCULAR OUTCOMES IN OBESITY WITHOUT DIABETES. N ENGL J MED. 2023 NOV 11;389(24):2221-2232.**

- 17,604 patients with BMI > 21, 45 years of age or older, with pre-existing cardiovascular disease and no diabetes.
- SQ semaglutide 2.4 mg vs. placebo.
- Primary endpoint was composite of cardiovascular death, nonfatal MI, and stroke.



Lincoff et al. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. *N Engl J Med.* 2023 Nov 11;389(24):2221-2232.



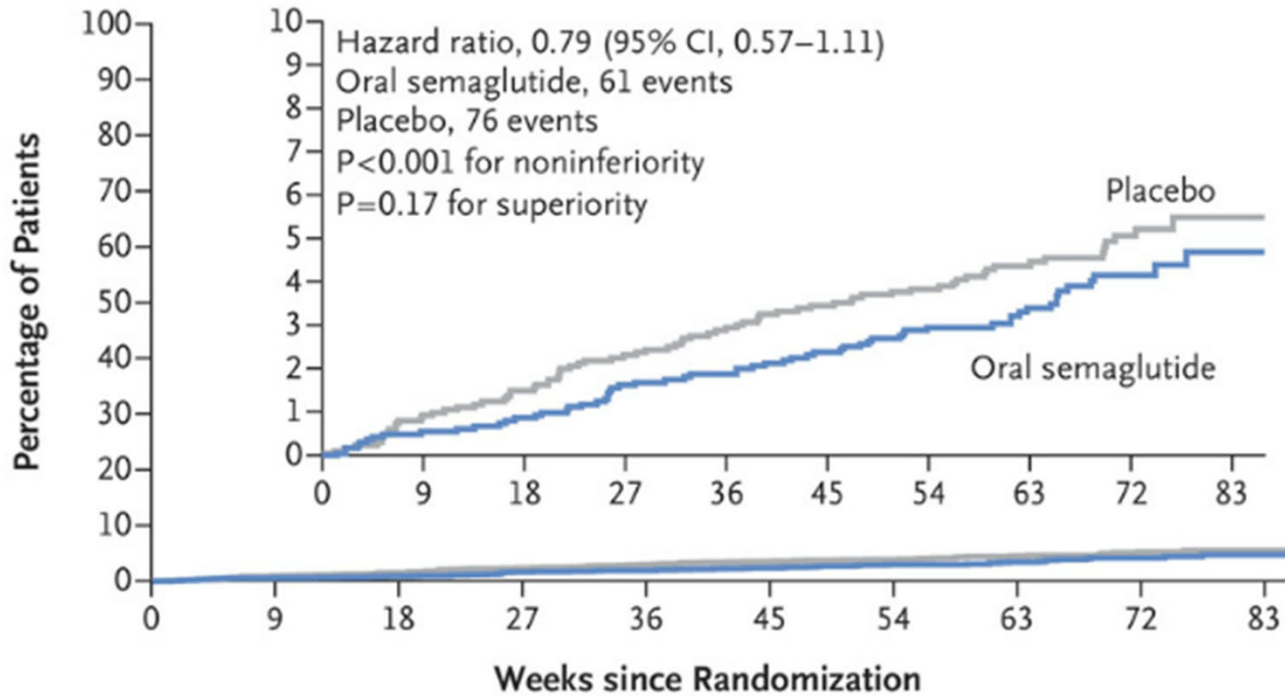
## **PIONEER 6: HUSAIN ET AL. ORAL SEMAGLUTIDE AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES. N ENGL J MED. 2019 AUG 29;381(9):841-85.**

- 3,183 patients with type 2 diabetes at high risk of cardiovascular disease (84.7% had known CVD).
- Placebo vs. oral semaglutide.
- Primary outcome was time to a composite of death from cardiovascular causes, nonfatal MI, and nonfatal stroke.





### A Composite Primary Outcome



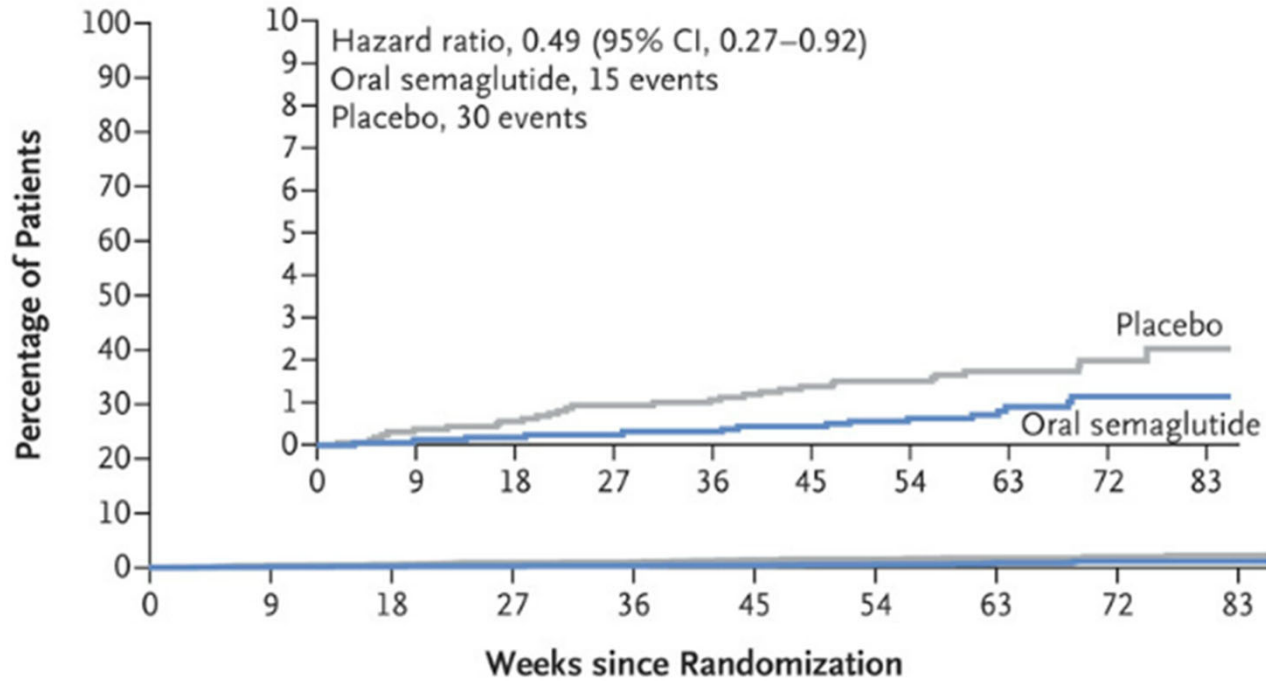
#### No. at Risk

Oral semaglutide	1591	1583	1575	1564	1557	1547	1512	1062	735	16
Placebo	1592	1577	1565	1551	1538	1528	1489	1032	713	11

Husain et al. Oral Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. *N Engl J Med.* 2019 Aug 29;381(9):841-85.




### D Death from Cardiovascular Causes



#### No. at Risk

Oral semaglutide	1591	1590	1586	1585	1582	1578	1548	1091	757	18
Placebo	1592	1586	1580	1572	1568	1561	1525	1063	739	11

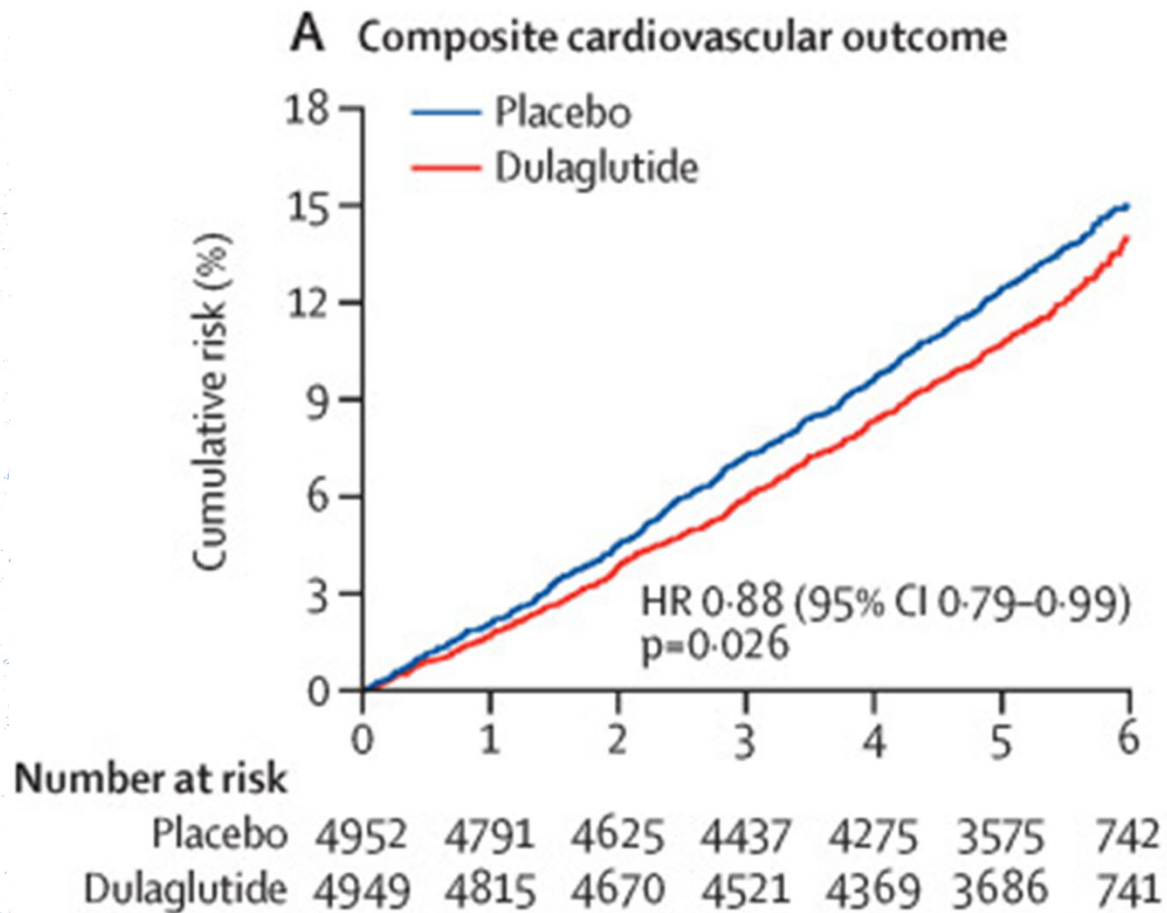
Husain et al. Oral Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. *N Engl J Med.* 2019 Aug 29;381(9):841-85.



# **REWIND: GERSTEIN ET AL. DULAGLUTIDE AND CARDIOVASCULAR OUTCOMES IN TYPE 2 DIABETES (REWIND): A DOUBLE-BLIND, RANDOMIZED PLACEBO-CONTROLLED TRIAL. LANCET. 2019 JUL 13;394(10193):121-130.**





- 9,901 patients with type 2 diabetes at high risk of cardiovascular disease (31.5% had known CVD).
- Placebo vs. 1.5 mg dulaglutide.
- Primary outcome was time to a composite of death from cardiovascular causes, nonfatal MI, and nonfatal stroke.



Gerstein et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. *Lancet*. 2019 Jul 13;394(10193):121-130.



**History of cardiovascular disease\***

Yes	280/1560 (17.9%)	3.7	315/1554 (20.3%)	4.2		0.87 (0.74-1.02)
No	277/3093 (8.9%)	1.7	317/3128 (10.1%)	2.0		0.87 (0.74-1.02)

Gerstein et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. Lancet. 2019 Jul 13;394(10193):121-130.

# RENAL OUTCOMES



## **KAHOOT.IT QUESTION 10**

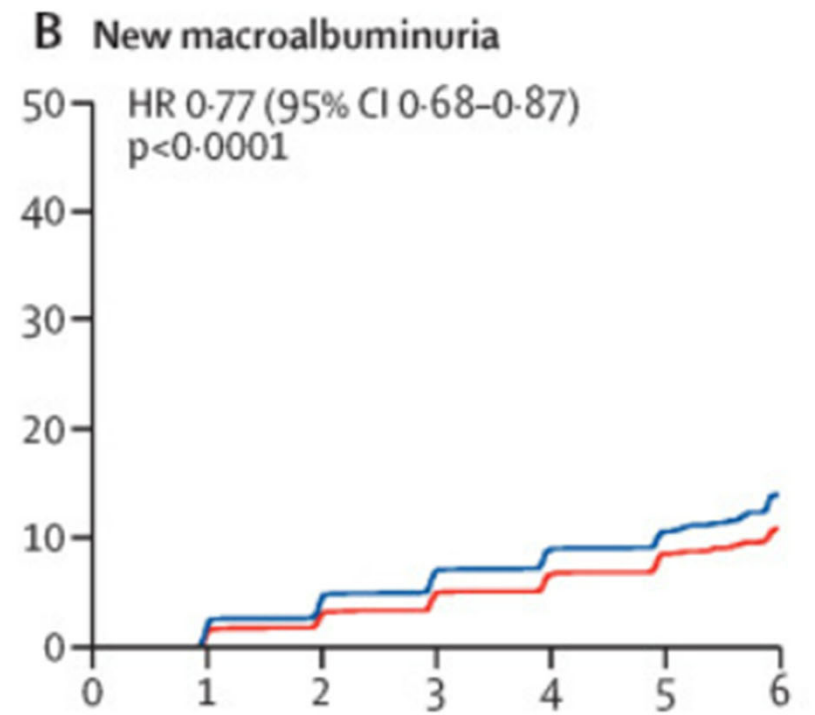
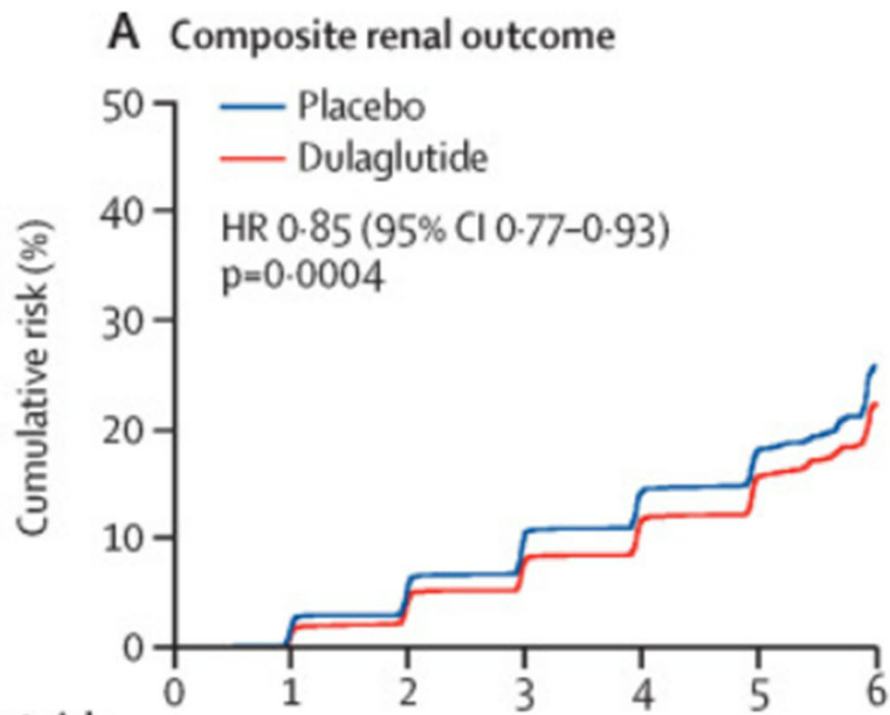
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Microvascular event	355 (7.6)	2.0	416 (8.9)	2.3	0.84 (0.73–0.97)	0.02
Retinopathy	106 (2.3)	0.6	92 (2.0)	0.5	1.15 (0.87–1.52)	0.33
Nephropathy	268 (5.7)	1.5	337 (7.2)	1.9	0.78 (0.67–0.92)	0.003

Marso et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2016 Jul 28;375(4):311-22.





**Number at risk**

Placebo	4952	4756	4475	4145	3887	3169	641
Dulaglutide	4949	4798	4571	4303	4045	3320	667

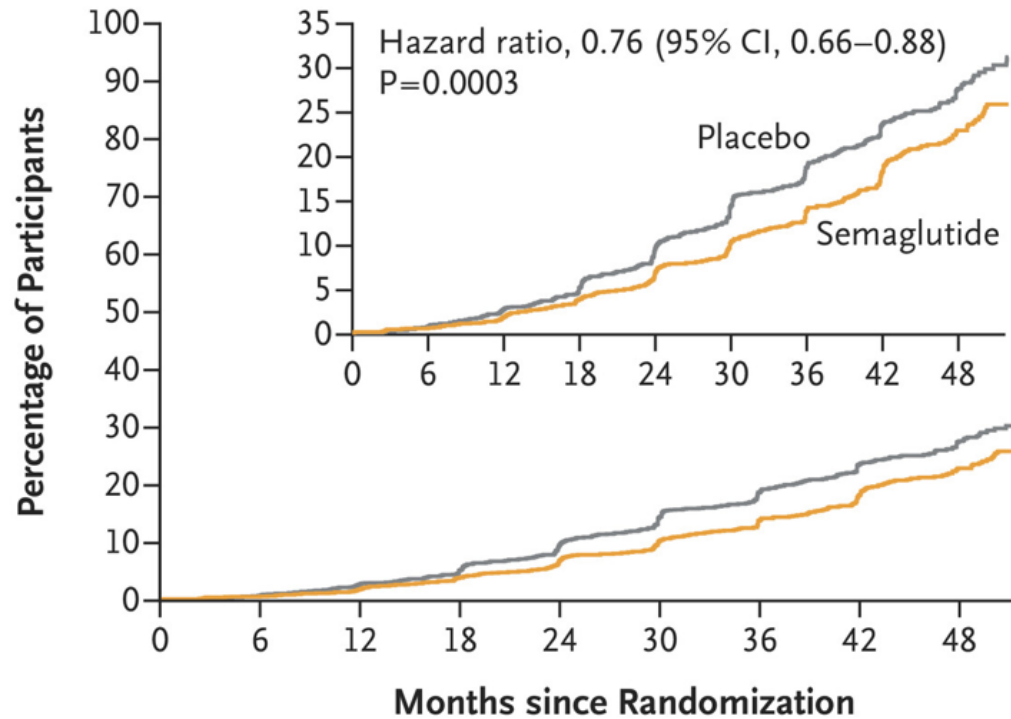
Gerstein et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomized placebo-controlled trial. *Lancet*. 2019 Jul 13;394(10193):121-130.



# **PERKOVIC ET AL. EFFECTS OF SEMAGLUTIDE ON CHRONIC KIDNEY DISEASE IN PATIENTS WITH TYPE 2 DIABETES. N ENGL J MED. 2024 JUL 11;391(2):109-121.**

- 3,533 patients with type 2 diabetes and CKD (defined as either eGFR of 50-75 with urinary albumin-to-creatinine ratio of  $> 300$  or eGFR 20-50 with urinary albumin-to-creatinine ratio of  $> 300$ ).
- Placebo vs. 1.0 mg semaglutide.
- Primary outcome was major kidney disease events – a composite of onset of kidney failure, at least a 50% reduction in eGFR from baseline, or death from kidney related cardiovascular causes.

### A First Major Kidney Disease Event

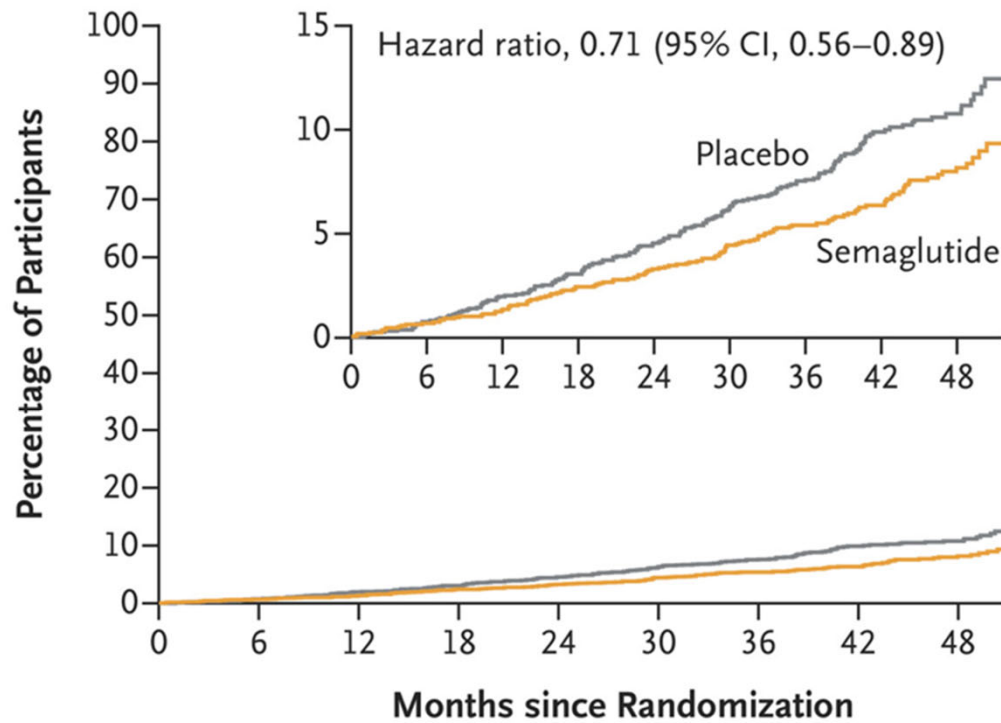


#### No. at Risk

Placebo	1766	1736	1682	1605	1516	1408	1048	660	354
Semaglutide	1767	1738	1693	1640	1572	1489	1131	742	392

Perkovic Et Al. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. N Engl J Med. 2024 Jul 11;391(2):109-121.

### C Death from Cardiovascular Causes

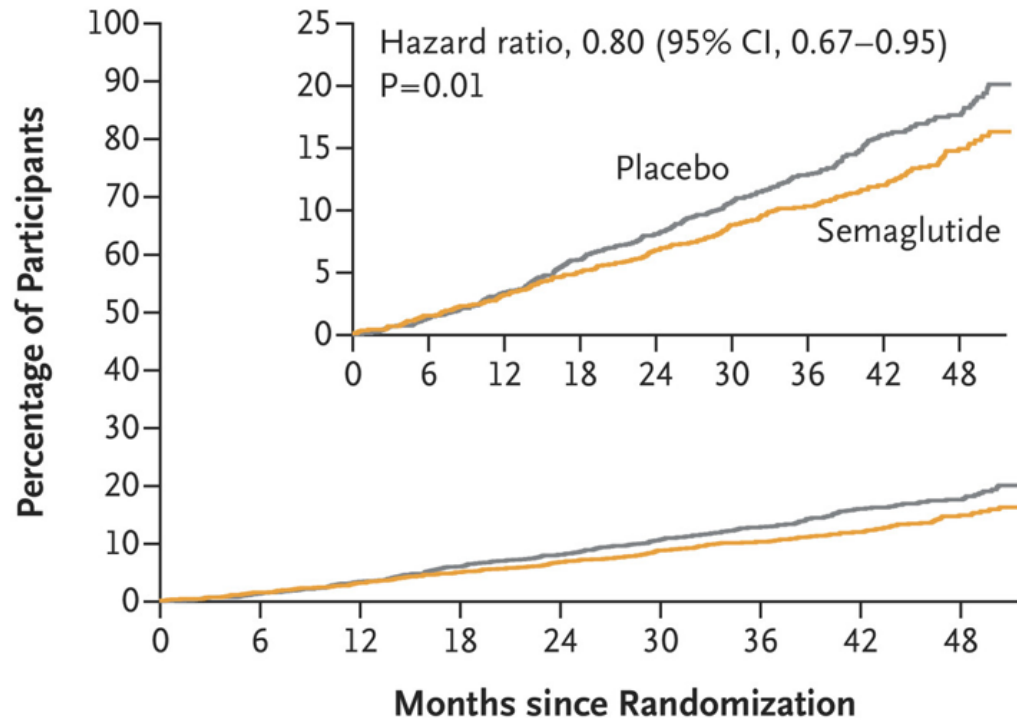


#### No. at Risk

Placebo	1766	1737	1697	1641	1601	1544	1185	772	437
Semaglutide	1767	1739	1703	1665	1627	1583	1234	838	460

Perkovic Et Al. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. N Engl J Med. 2024 Jul 11;391(2):109-121.

## F Death from Any Cause



### No. at Risk

Placebo	1766	1737	1697	1641	1601	1544	1185	772	437
Semaglutide	1767	1739	1703	1665	1627	1583	1234	838	460

Perkovic Et Al. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. N Engl J Med. 2024 Jul 11;391(2):109-121.

# SIDE EFFECTS



## **KAHOOT.IT QUESTION 11**

- Go to Kahoot.it
- Enter the game code shown
- Put in a nickname
- Points are given for correct answers.
- The faster the correct answer is given, the more points that are awarded
- No points taken away for incorrect answers
- Be first. Be right.



## CONTRAINDICATIONS

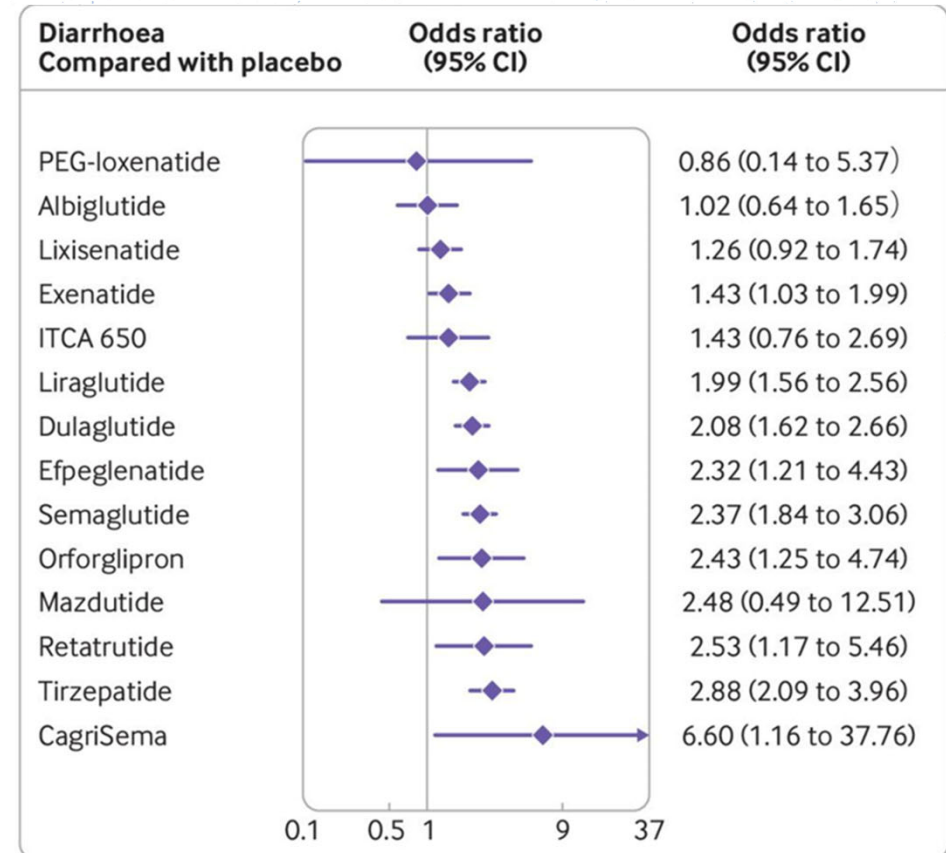
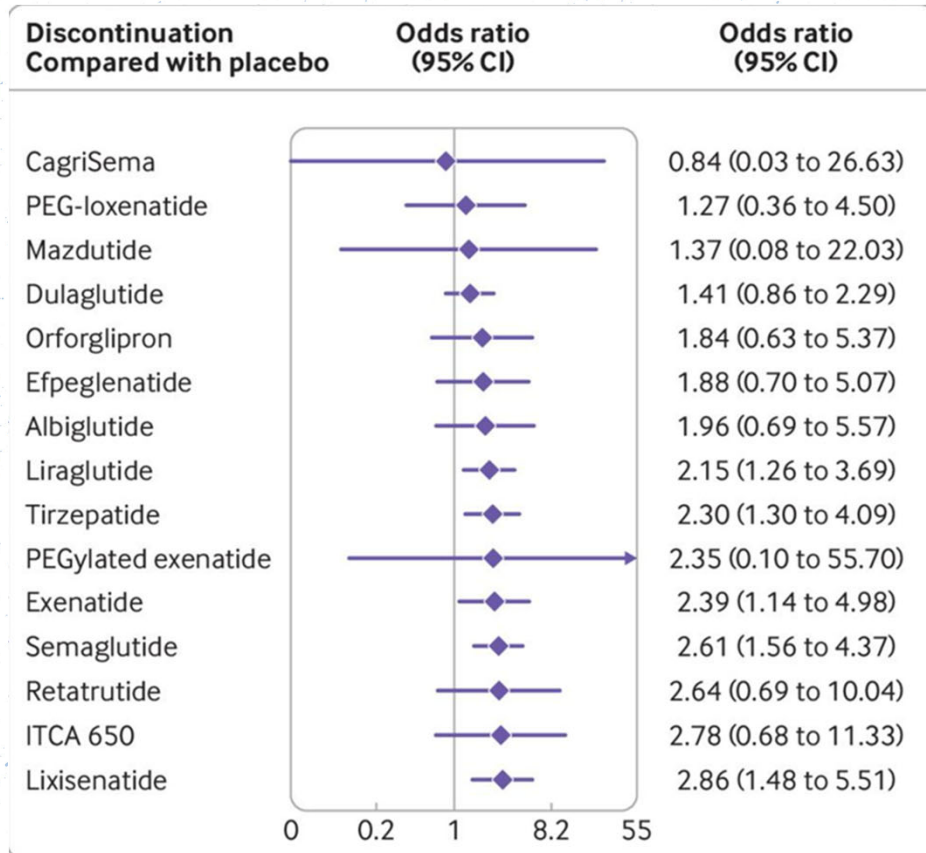
- Thyroid c-cell tumors
- MEN-2
- Active pancreatitis or chronic pancreatitis (<1% pancreatitis in meta-analysis)
- Severe Gastroparesis



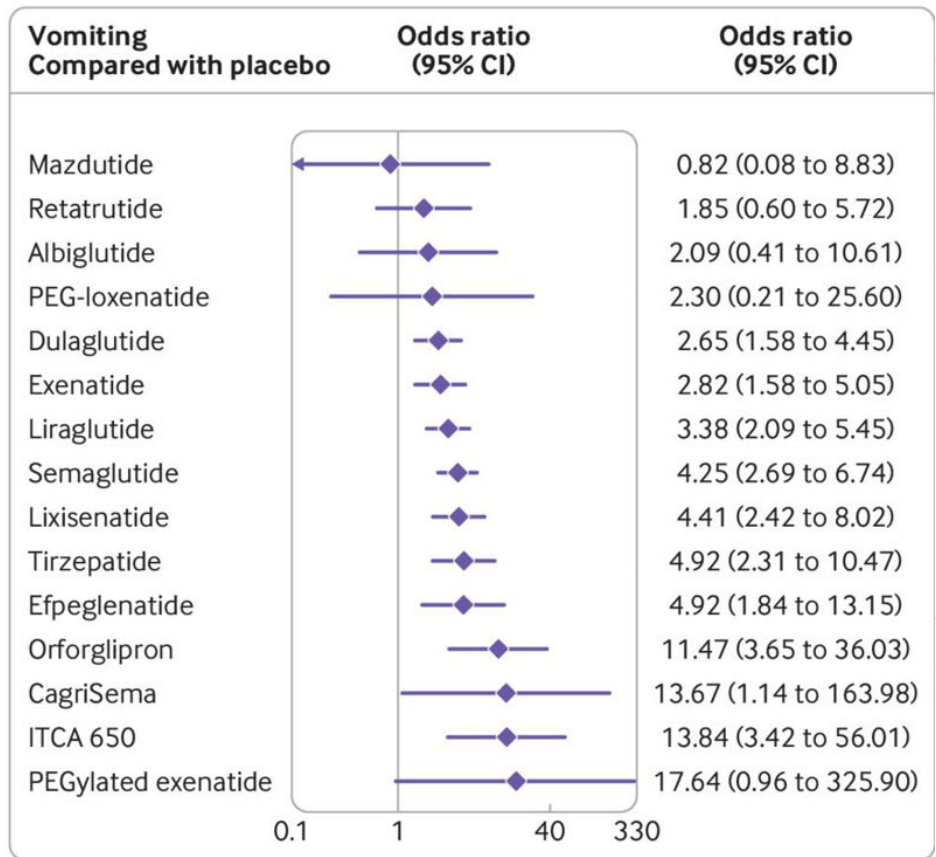
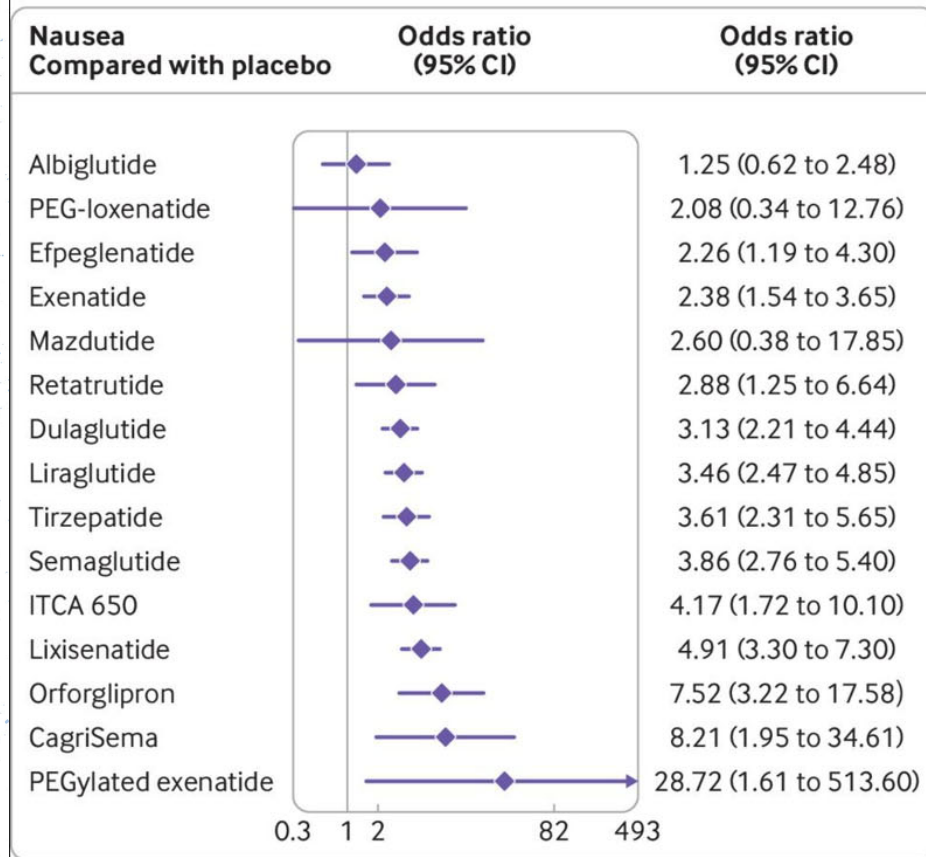


# **YAO H, ZHANG A, LI D, WU Y, WANG C, WAN J ET AL. COMPARATIVE EFFECTIVENESS OF GLP-1 RECEPTOR AGONISTS ON GLYCAEMIC CONTROL, BODY WEIGHT, AND LIPID PROFILE FOR TYPE 2 DIABETES: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS *BMJ* 2024; 384:E076410**

- Metanalysis of 76 trials involving 15 GLP-1s and 39, 246 patients across 56 countries with type 2 diabetes.
- Had to include a placebo arm and be at least 12 weeks in duration.
- Study duration length varied from 12 to 78 weeks with mean age of 56.79 years (18-65yo), mean HbA1C of 8.13% and mean BMI of 31.73.
- Study compared A1C lowering, weight loss and other metabolic indicators among GLP-1s as well as adverse effects.



Yao H, Zhang A, Li D, Wu Y, Wang C, Wan J et al. Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis *BMJ* 2024; 384:e076410



Yao H, Zhang A, Li D, Wu Y, Wang C, Wan J et al. Comparative effectiveness of GLP-1 receptor agonists on glycaemic control, body weight, and lipid profile for type 2 diabetes: systematic review and network meta-analysis *BMJ* 2024; 384:e076410

## MITIGATING SIDE EFFECTS

- Patient Selection – make sure you are prescribing for an appropriate indication and ask patients about symptoms of gastroparesis.
- Set expectations – inform patients that GI side effects including nausea are very common but that side effects are usually not bad enough that patients stop taking the medication and symptoms improve with time.
- Give guidance on how to treat symptoms if they arise
  - Water and fiber supplements for constipation.
  - Loperamide for diarrhea.
  - Pepcid or omeprazole for heartburn.



# MITIGATING SIDE EFFECTS



- Steps that can reduce nausea
  - Eat slowly.
  - Stop eating when you feel full.
  - Avoid Greasy high fat foods, pineapples, apples, broccoli and brussel sprouts.
  - Consider dietician referral for diet analysis.
- Pause dose escalation
- Return to previously tolerated dose
- Switch to an alternative GLP-1

# OTHER THINGS TO KNOW



## **KAHOOT.IT QUESTION 12**

- Go to Kahoot.it
- Enter the game code shown
- Put in a nickname
- Points are given for correct answers.
- The faster the correct answer is given, the more points that are awarded
- No points taken away for incorrect answers
- Be first. Be right.



## OTHER THINGS TO KNOW



- Women respond better to GLP-1s for weight loss than men.
- Older adults are not well represented in clinical trials and data regarding body composition is limited (concerns regarding muscle mass loss).
- Lots of developing evidence for GLP-1 use in NAFLD and MASH.
- Animal studies suggesting reduction in alcohol intake.
- Due to delayed gastric emptying, American Society of Anesthesiologists recommends holding one dose of medication prior to surgery (consensus rather than actual evidence).
- Effective with insulin therapy (usually decrease insulin dosage by 10% when adding).
- No need to prescribe a DPP-4 with a GLP-1.





## OTHER THINGS TO KNOW

- Be on the look out for:
  - SURPASS-CVOT – Tirzepatide clinical trial assessing for cardiovascular benefit (comparison to dulaglutide).
  - High dose oral semaglutide (can it keep up the efficacy?).
  - CagriSema Phase 3 clinical trials (can it keep up the efficacy?).
  - Retatrutide and Mazdutide N/V rate in Phase 3 clinical trials.
  - NAFLD and MASH FDA approval.
  - Human trials for Alcohol Use Disorder

# CONCLUSION

## CONCLUSION AND DISCUSSION

- GLP-1s are very effective for glycemic control with Tirzepatide the most effective currently approved agent.
- GLP-1s are very effective for weight loss in patient with and without diabetes with Tirzepatide the most effective currently approved agent.
- SQ Semaglutide has been shown in clinical trials to reduce the risk of cardiovascular events in patients with known cardiovascular disease and diabetes or obesity.
- SQ Semaglutide has been shown to reduce the risk of renal events in patient with Type 2 diabetes, microalbuminuria and reduced eGFR.
- N/V/D and constipation remain the most common adverse effects of GLP-1 treatment and clinicians should educate patients and use strategies to reduce the risk.



## CONCLUSION AND DISCUSSION

- Questions?

# THANK YOU

