The 13th Diabetes in Practice

Updates on Patient-Centered Management of Diabetes

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Metabolic Management in Diabetes Care

Panel:

Farhad Hossein Panah; M.D.
Endocrinologist

Hamidreza Aghaei Meybodi; M.D.
Endocrinologist

Hengameh Abdi; M.D.
Endocrinologist

Syed Adel Jahed; M.D.
Endocrinologist

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When Diabetes Meets MASLD: A Metabolic Duo

Navigating MASLD in Type 2 Diabetes

Hengameh Abdi; M.D.
Endocrinologist

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Clinical Case Scenario

55 y/o female, T2DM 10 years ago, First time visit in your clinic for her diabetes control.

PMHx:

- Dyslipidemia for 10 years, HTN for 5 years

FHx:

- T2DM in first-degree relatives
- No family history of premature CAD

SHx:

- Sedentary lifestyle
- Non-Smoker
- Non-drinker

Daily medications:

- **Metformin/Linagliptin** 500/2.5 mg BD
- **Gliclazide MR** 30 mg QD
- **Atorvastatin** 20 mg QD
- **Losartan** 50 mg QD

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Clinical Case Scenario

55 y/o female, T2DM 10 years ago, First time visit in your clinic for her diabetes control.

Physical examination:
Unremarkable
Office BP: 140/90 mm/Hg
BMI: 27 kg/m^2

Paraclinical Data:
ECG: Normal Sinus Rythm
Echocardiography report:
EF:55%, Mild LVH
Sonography:
Grade 2 fatty liver

Lab Data:
HbA1c: 8.3%
Cr: 1.1 mg/dL, **eGFR:** 56 mL/min/1.73 m^2
Total Chol: 205 mg/dL
LDL: 115 mg/dL
HDL: 40 mg/dL
TG: 250 mg/dL
UACR: 20 mg/g
AST: 32 IU/L
ALT: 20 IU/L
Platelet Count: 200 10^3/uL
K:5.2 mEq/L

FIB-4 score: 1.97

10-year ASCVD risk: 8.4%

Daily Medications:

Met+Lina 500/2.5 mg BD, **Gliclazide 30** mg daily, **Ator 20** mg QD, **Losar 50** mg daily

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Clinical Scenario

- F/55 y/o (postmenopause)
- T2D for 10 yr
- HTN for 5 yr
- No clinical ASCVD
- Never-smoker
- No Alcohol consumption
- Overweight (BMI: 27 kg/m²)
- Not meeting goal BP (140/90 mmHg)
- HbA1c: 8.3%
- Not meeting goal LDL-C (115 mg/dL); TG: 250 mg/dL, HDL-C: 40 mg/dL
- CKD: G3a-A1/Moderately increased risk
- FIB-4 index score: 1.97
- Medications:
  - Metformin, Linagliptin, Gliclazide
  - Atorvastatin 20 mg daily
  - Losartan 50 mg daily

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Metabolic dysfunction associated steatotic liver disease (MASLD)

- Hepatic steatosis in conjunction with at least one cardiometabolic risk factor (traits of metabolic syndrome) in the absence of secondary causes of steatosis

At least 1 out of 5:

- ☐ BMI ≥ 25 kg/m² [23 Asia] **OR** WC > 94 cm (M) 80 cm (F) **OR** ethnicity adjusted equivalent
- ☐ Fasting serum glucose ≥ 5.6 mmol/L [100 mg/dL] **OR** 2-hour post-load glucose levels ≥ 7.8 mmol/L [≥140 mg/dL] **OR** HbA1c ≥ 5.7% [39 mmol/L] **OR** type 2 diabetes **OR** treatment for type 2 diabetes
- ☐ Blood pressure ≥ 130/85 mmHg **OR** specific antihypertensive drug treatment
- ☐ Plasma triglycerides ≥ 1.70 mmol/L [150 mg/dL] **OR** lipid lowering treatment
- ☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [40 mg/dL] (M) and ≤ 1.3 mmol/L [50 mg/dL] (F) **OR** lipid lowering treatment

WC Iran:
M & F: 90 cm

Rinella ME, et al. Hepatology. 2023;78:1966-1986.

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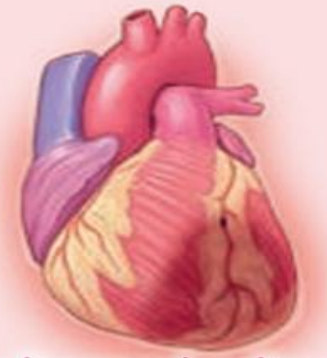
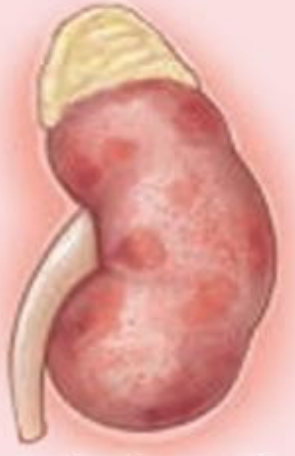
Clinical implications of MASLD in people with prediabetes and diabetes



Cardiovascular disease, heart failure, and certain arrhythmias (atrial fibrillation)

Cirrhosis or HCC



Chronic kidney disease (stage ≥3)

Certain extrahepatic cancers (e.g., colorectal cancer)

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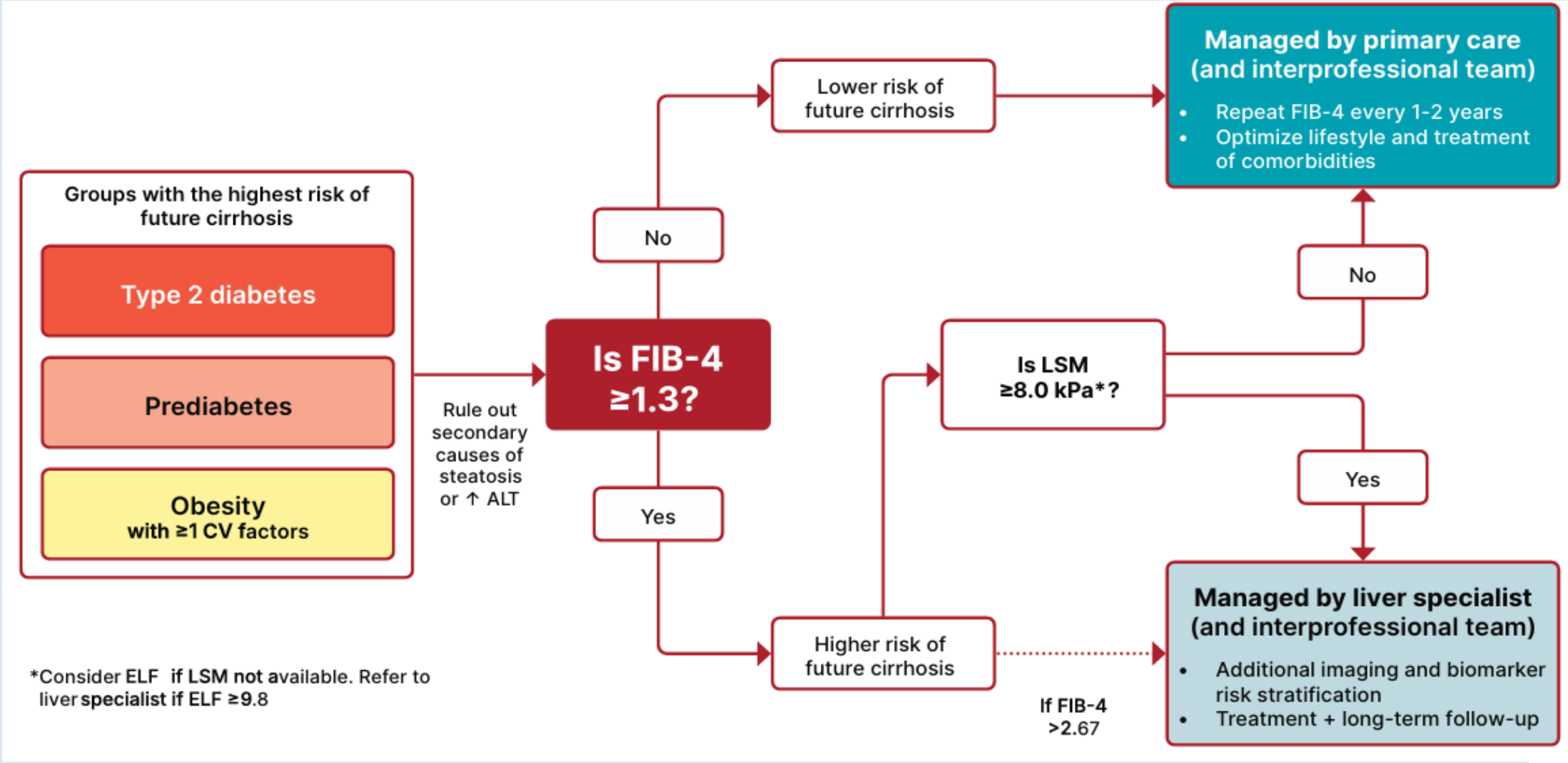
Targher G, et al. N Engl J Med 2025;393:683-98.

Diagnostic algorithm for risk stratification and prevention of cirrhosis in individuals with MASLD



American Diabetes Association. Diabetes Care 2025;48(Suppl. 1):S59-S85.

Weight loss

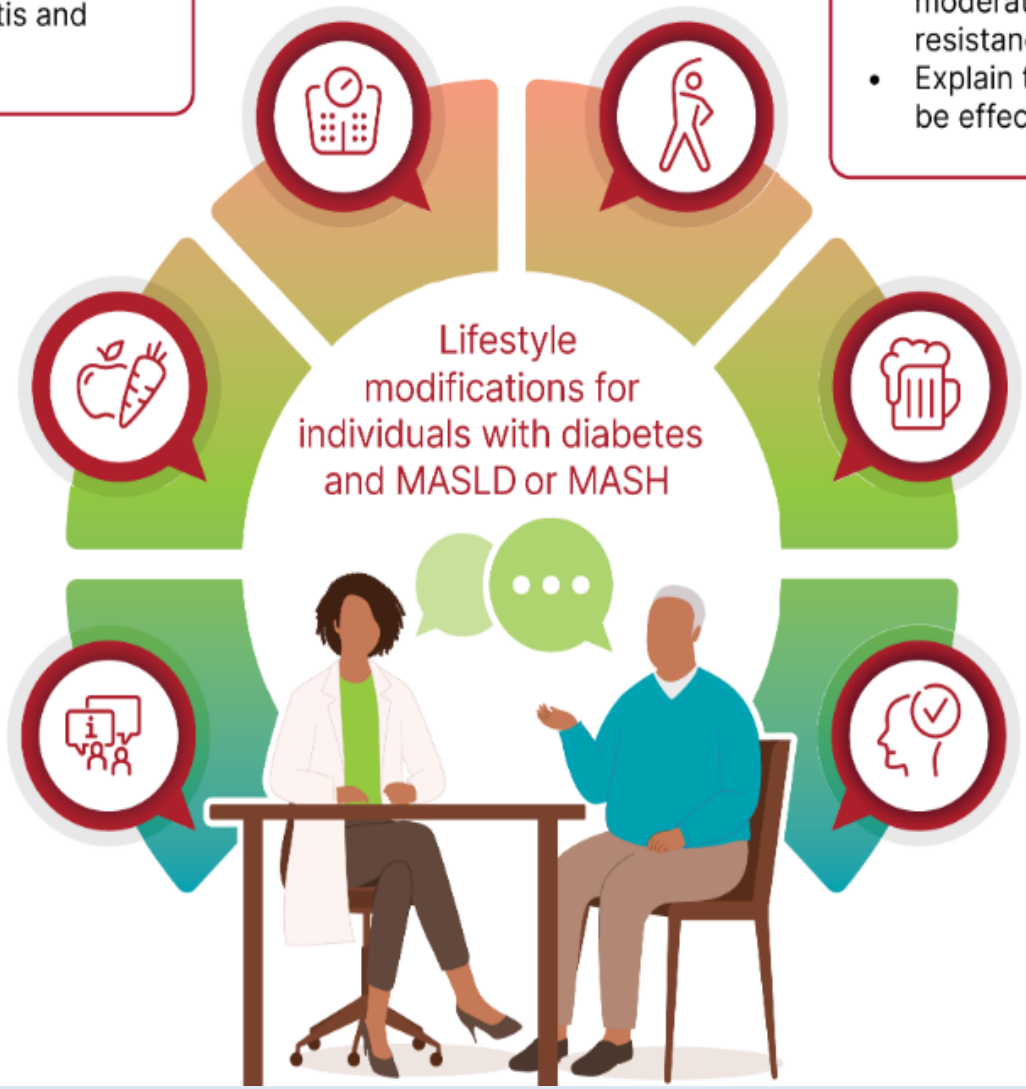
- Encourage calorie deficit that promotes weight loss
- ~5% weight reduction to reduce steatosis
- ~7-10% to reverse steatohepatitis and liver fibrosis

Physical activity

- Discuss goal of performing ≥150 min/week moderate-intensity aerobic activity and resistance activities 2-3 times/week
- Explain that brief sessions (~10 min) can be effective ways to reach goal

Nutrition (healthy eating)

- Emphasize a high-fiber, whole foods eating pattern with personalized goals, that is low in saturated fat and added sugar
- Individuals should abstain from sugar-containing beverages and minimize consumption of ultraprocessed foods



Alcohol

- Assess intake at every visit
- Recommend minimizing alcohol intake in MASLD
- Individuals should abstain if moderate fibrosis is present (≥F2)

DSMES

- Support behavior change to address factors complicating diabetes management
- Address lifestyle modification with medical nutrition therapy

Behavioral health

- Promote stress reduction via positive health behaviors
- Screen for depression and anxiety at least annually and refer to behavioral health professionals when indicated
- Advise adequate sleep and quitting smoking

Cusi K, et al. Diabetes Care 2025;48:1057-1082.

Liver effects of glucose-lowering medications

	Medication	Effect in MASLD and MASH*			
		Hepatic steatosis	Steatohepatitis	Fibrosis regression	Reduction of fibrosis progression
Phase 3 trial	Semaglutide**	Beneficial	Beneficial	Beneficial	Potential benefit
Phase 2 trial	Tirzepatide***†	Potential benefit	Potential benefit	Potential benefit	Potential benefit
	Pioglitazone†	Potential benefit	Potential benefit	Potential benefit	Potential benefit
	SGLT2 inhibitors	Potential benefit	?	?	?
	Metformin¶	Neutral	Neutral	Neutral	Neutral
	DPP-4 inhibitors¶	Neutral	?	?	?
	Insulin¶	Potential benefit	?	?	?
	Sulfonylureas¶	Neutral	?	?	?

Cusi K, et al. Diabetes Care 2025;48:1057-1082.

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Semaglutide in Metabolic-Related Steatohepatitis

A Research Summary based on Sanyal AJ et al. | 10.1056/NEJMoa2413258 | Published on April 30, 2025

ESSENCE study

BMI:
34.3±7.2 kg/m²
T2D:
55.4%

WHY WAS THE TRIAL DONE?

Metabolic dysfunction–associated steatohepatitis (MASH) is a severe form of metabolic dysfunction–associated steatotic liver disease characterized by steatosis, hepatocyte damage, and inflammation. In a previous phase 2 trial involving patients with MASH, treatment with semaglutide, a glucagon-like peptide-1 receptor agonist, resulted in better outcomes than placebo.

HOW WAS THE TRIAL CONDUCTED?

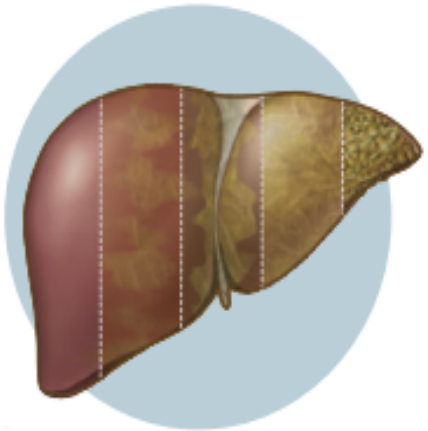
1197 adults with biopsy-defined MASH and fibrosis stage 2 or 3 were randomly assigned to receive once-weekly subcutaneous semaglutide at a dose of 2.4 mg or placebo for 240 weeks. The primary end points were the resolution of steatohepatitis with no worsening of liver fibrosis and a reduction in liver fibrosis with no worsening of steatohepatitis.

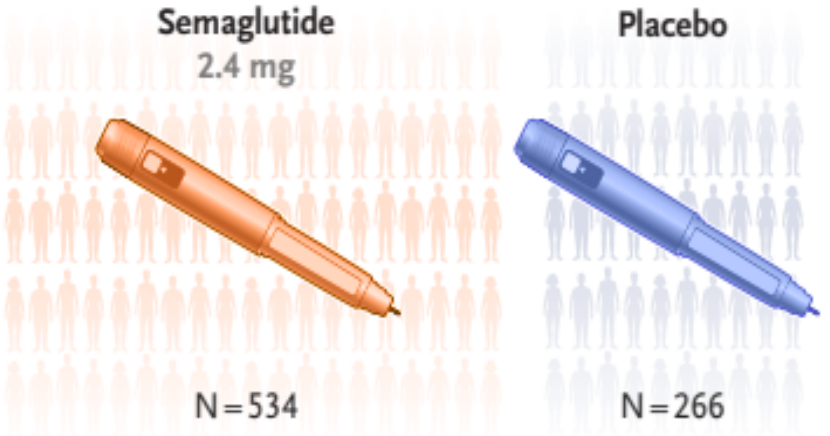
TRIAL DESIGN

- Phase 3
- Randomized
- Double-blind
- Placebo-controlled
- Location: 253 clinical sites in 37 countries

Patients

- 800 adults
- Mean age, 56 years
- Women 57%; Men: 43%





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RESULTS

At a planned interim analysis at week 72 involving the first 800 patients, resolution of steatohepatitis with no worsening of liver fibrosis occurred in a higher percentage of patients treated with semaglutide than with placebo. Reduction in liver fibrosis with no worsening of steatohepatitis was also reported in a higher percentage of patients treated with semaglutide than with placebo. The most common adverse events in both groups were gastrointestinal disorders, including nausea, diarrhea, and constipation.

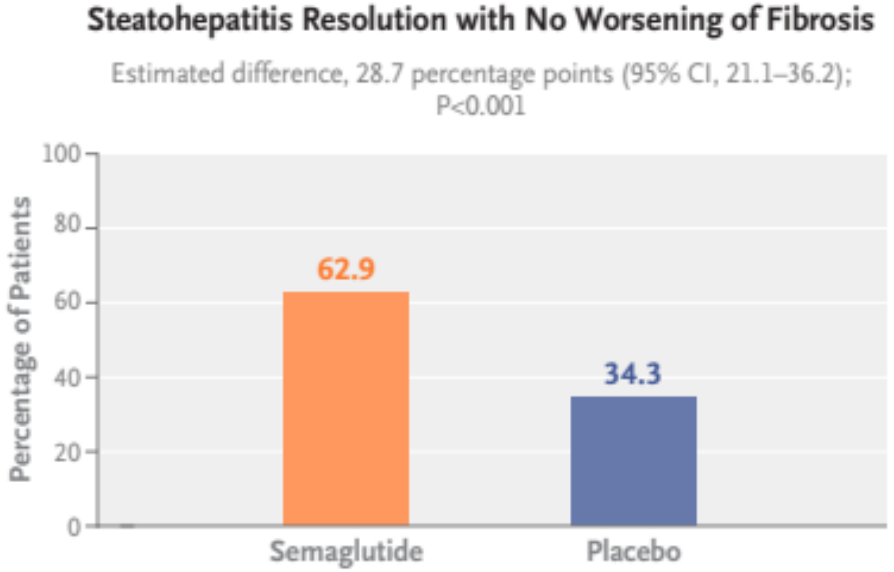
LIMITATIONS AND REMAINING QUESTIONS

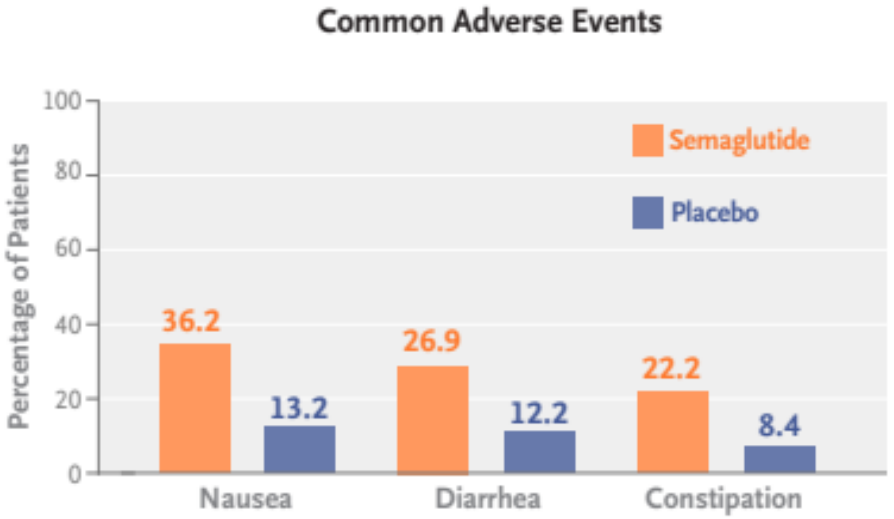
- More than two thirds of the patients were White, which may limit the generalizability of the results.
- Data regarding biomarkers of alcohol consumption were lacking.
- Given the small number of lean patients, definitive conclusions about benefit in this population cannot be drawn.

CONCLUSIONS

In an interim analysis of a phase 3 trial involving patients with MASH and moderate or advanced liver fibrosis, once-weekly semaglutide improved liver histologic results over 72 weeks.

NEJM QUICK TAKE | EDITORIAL





NNT: ~3.5

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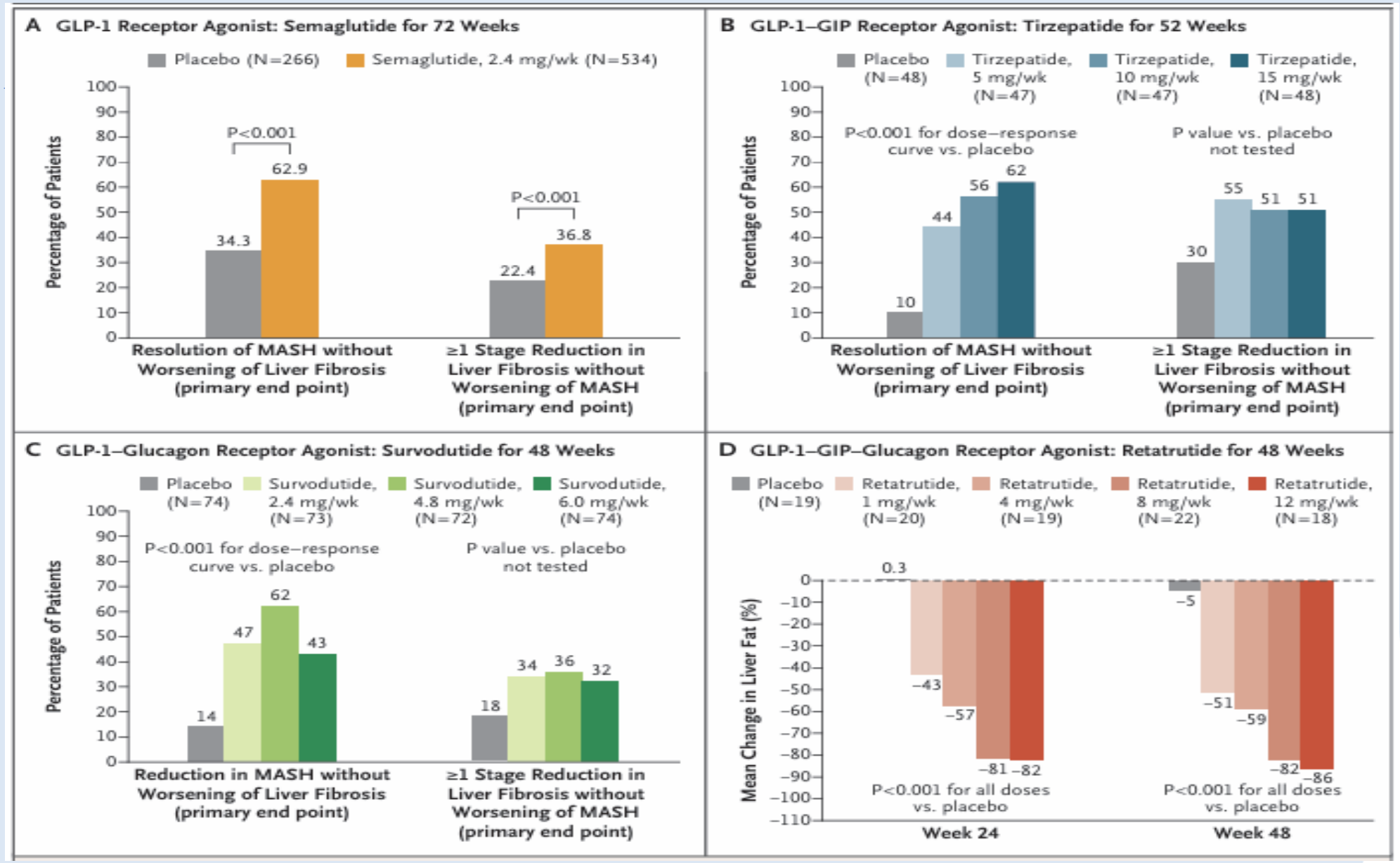
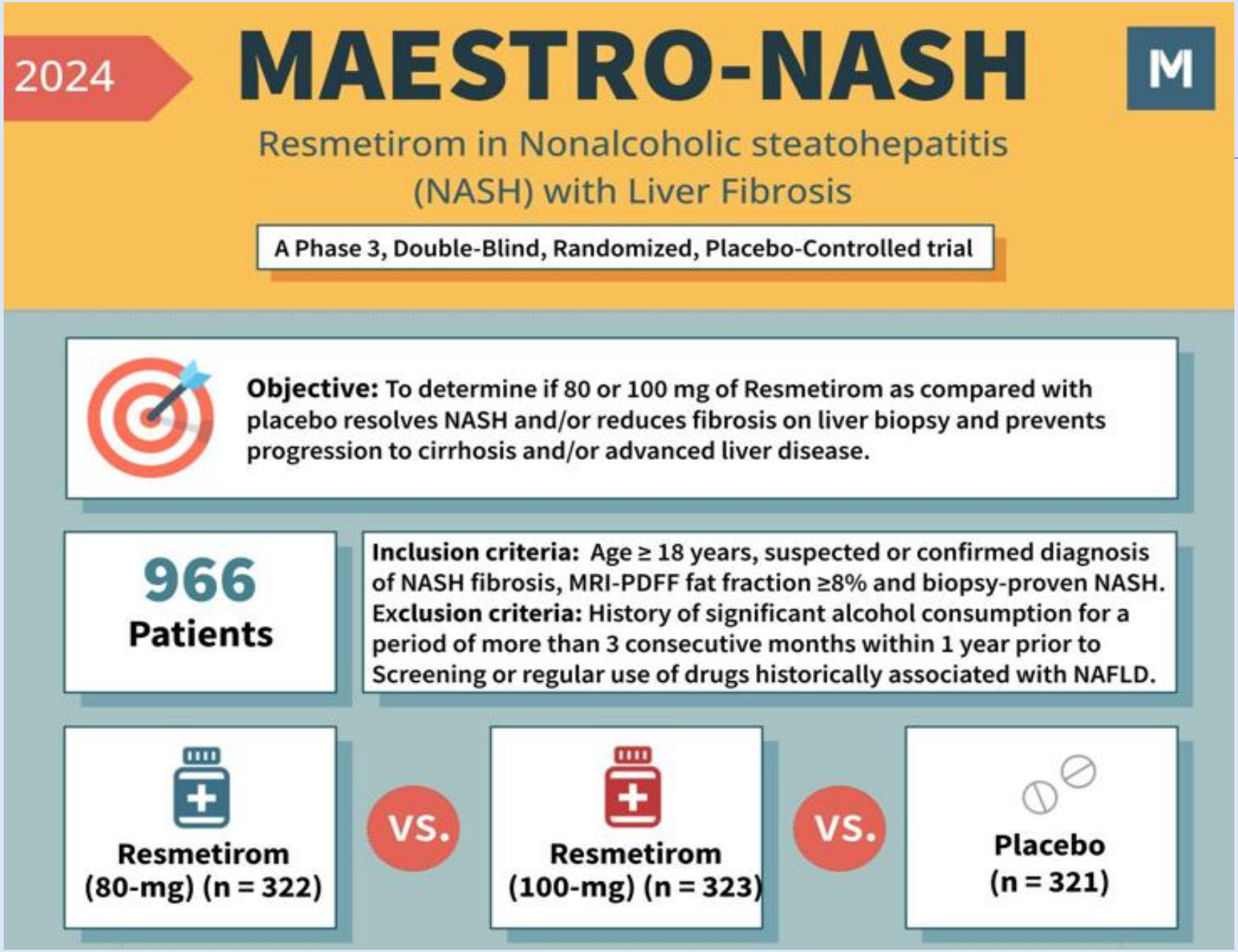
Sanyal, AJ, et al. N Engl J Med 2025;392:2089-99.

Incretins in MASLD and MASH



Targher G, et al. N Engl J Med 2025;393:683-98.



an oral, liver-directed, thyroid hormone receptor beta selective agonist

- **Resmetirom 100 mg:**

BMI: 36.2±7.4 kg/m²
T2D: 66%
GLP-1RA use: ~13%

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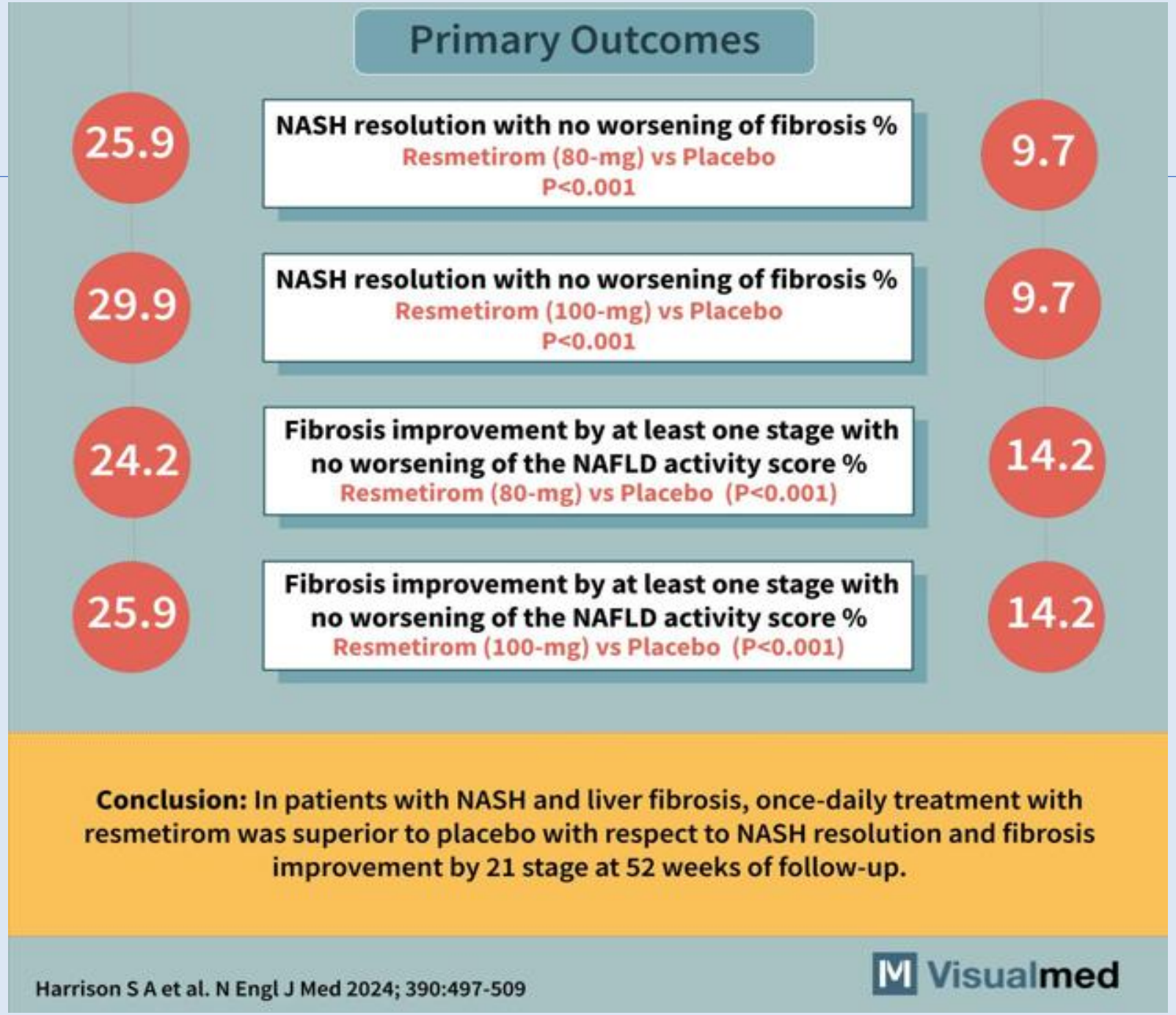

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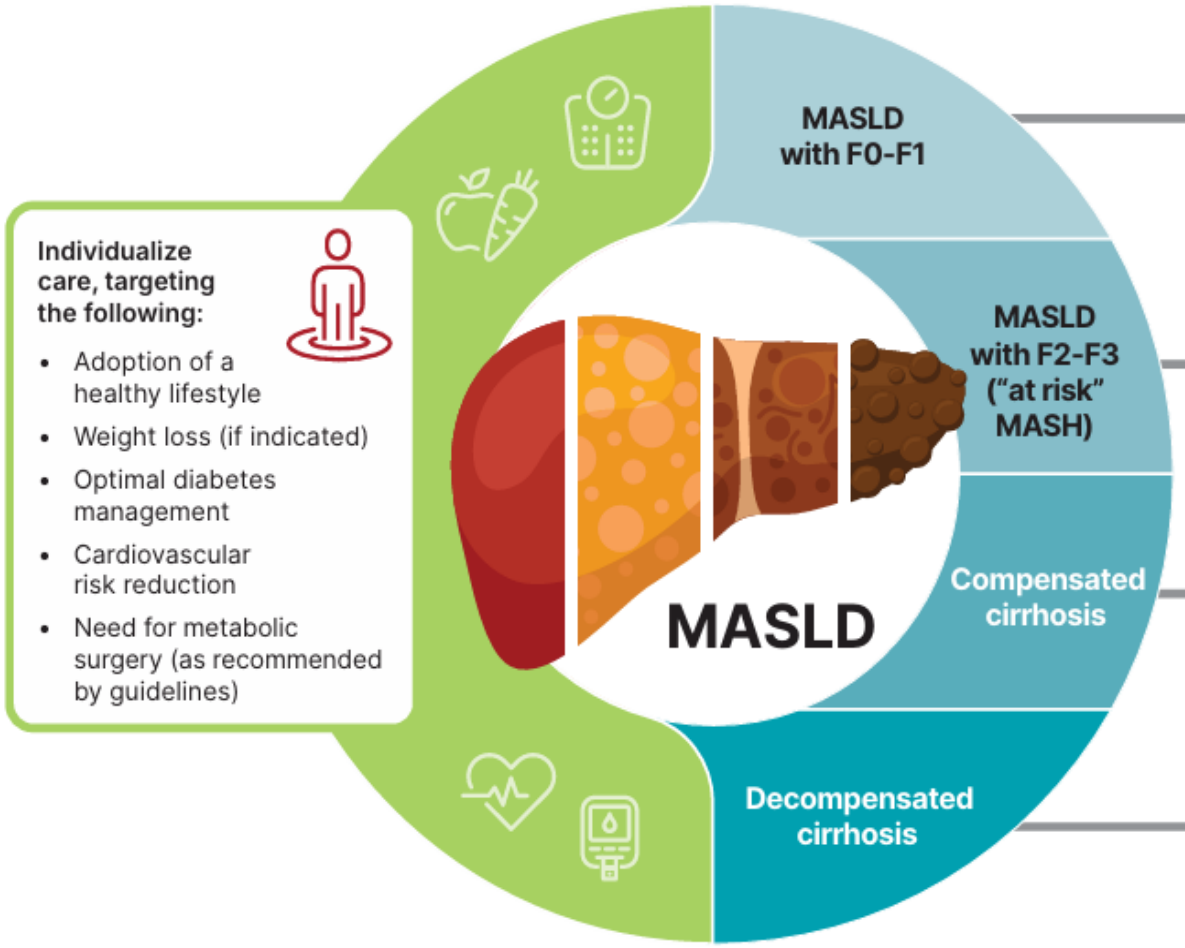
Wrap UP

Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) Treatment Algorithm



Obesity pharmacotherapy	Diabetes pharmacotherapy	MASH pharmacotherapy
Prefer GLP-1 RA, dual GIP and GLP-1 RA	Prefer GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone, SGLT2i	Not indicated

Obesity pharmacotherapy	Diabetes pharmacotherapy	MASH pharmacotherapy
Prefer GLP-1 RA, dual GIP and GLP-1 RA	Prefer GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone	Resmetirom

Obesity pharmacotherapy	Diabetes pharmacotherapy	MASH pharmacotherapy
As with F2-F3 with caution*	As with F2-F3 with caution*	ⓘ AVOID

Obesity pharmacotherapy	Diabetes pharmacotherapy	MASH pharmacotherapy
ⓘ AVOID	Only use insulin	ⓘ AVOID

American Diabetes Association. Diabetes Care 2025;48(Suppl. 1):S59-S85.

Fine-tuning patient care: Tackling Residual Risk in Diabetic Kidney Disease

Syed Adel Jahed; M.D.
Endocrinologist

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Clinical Case Scenario

A 60-year-old man with a 12-year history of T2DM and HTN is seen for follow-up.

He reports mild ankle edema but no dyspnea or orthopnea.

PMHx:

- Dyslipidemia for 12 years, HTN for 5 years

FHx:

- No family history of premature CAD

SHx:

- Sedentary lifestyle
- Non-Smoker
- Non-drinker

Daily medications:

- **Metformin/Empagliflozin** 1000/12.5 mg Daily
- **Glargine** 20 units QHS
- **Atorvastatin** 20 mg QD
- **Telmisartan/Amlodipine** 80/5 mg Daily

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Clinical Case Scenario

Physical examination:

Lower Limbs:

- Peripheral pulses: 2+
- Symmetric mild non pitting ankle edema

Office BP: 120/75 mm/Hg

HR: 76 bpm and regular

BMI: 29 kg/m^2

Paraclinical Data:

ECG: Normal Sinus Rythm

Echocardiography report:

EF:55%, Mild LVH

Lab Data:

HbA1c: 7.1%

Cr: 1.8 mg/dL, **eGFR:** 43 mL/min/1.73 m^2

Total Chol: 130 mg/dL

LDL: 70 mg/dL

HDL: 30 mg/dL

TG: 150 mg/dL

UACR: 180 mg/g

AST: 30 IU/L

ALT: 34 IU/L

Platelet: 280 10^3/uL

K: 4.6 mEq/L

Na: 140 mEq/L

FIB-4 score: 1.1

10-year ASCVD risk: 16.3%

Daily Medications:

Met+Empa 1000/12.5 mg daily, **Glargine 20 U** QHS, **Ator 20** mg QD, **Telmi/Amlo 80/5** mg daily

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Goals of Care

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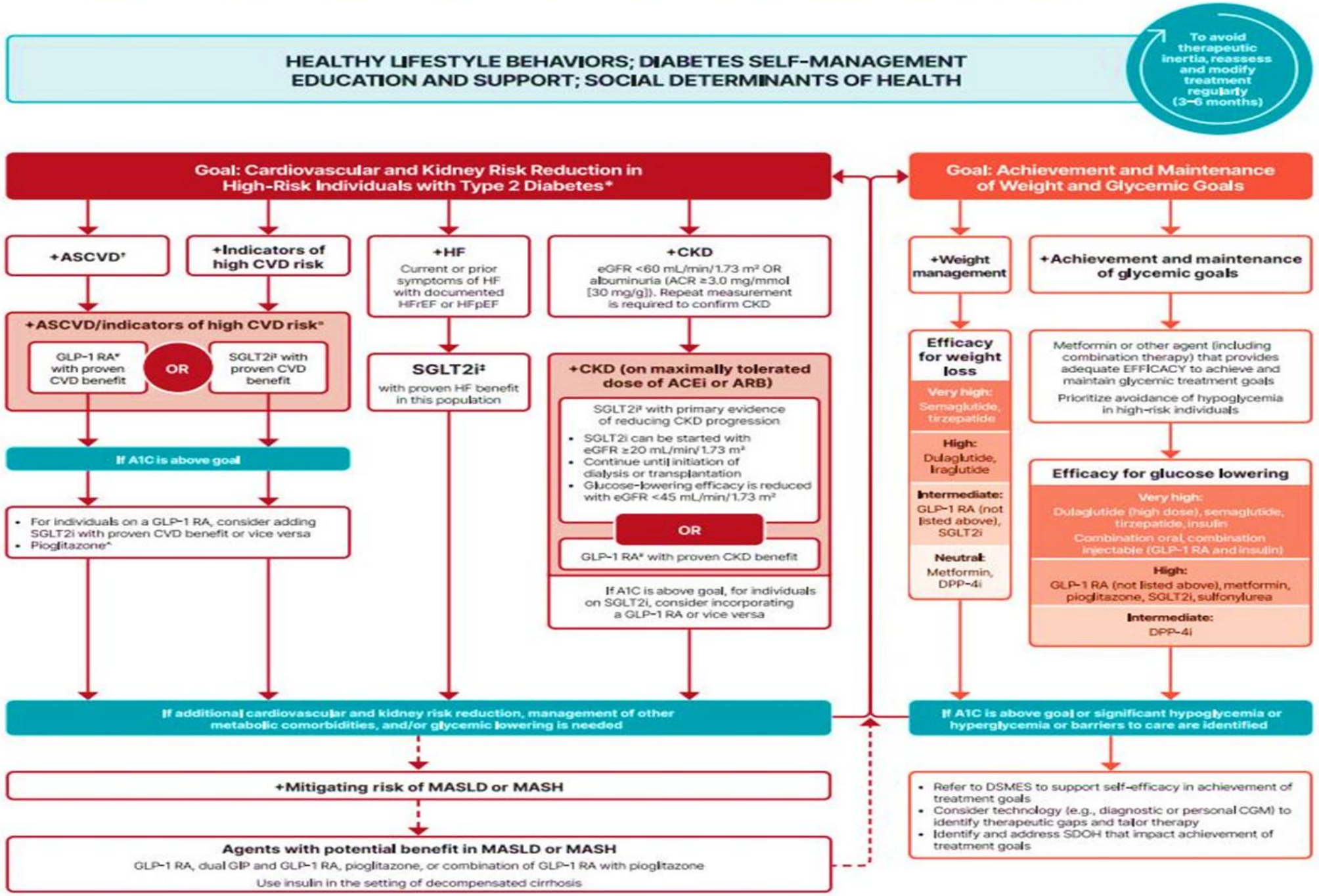
Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes - 2025*. *Diabetes Care* 2025;48(Suppl. 1):S59-S85

Use of Glucose-Lowering Medications in the Management of Type 2 Diabetes



Pharmacologic Approaches to Glycemic Treatment:
Standards of Care in Diabetes - 2025 Diabetes Care 2025;48(Suppl. 1):S181-S206

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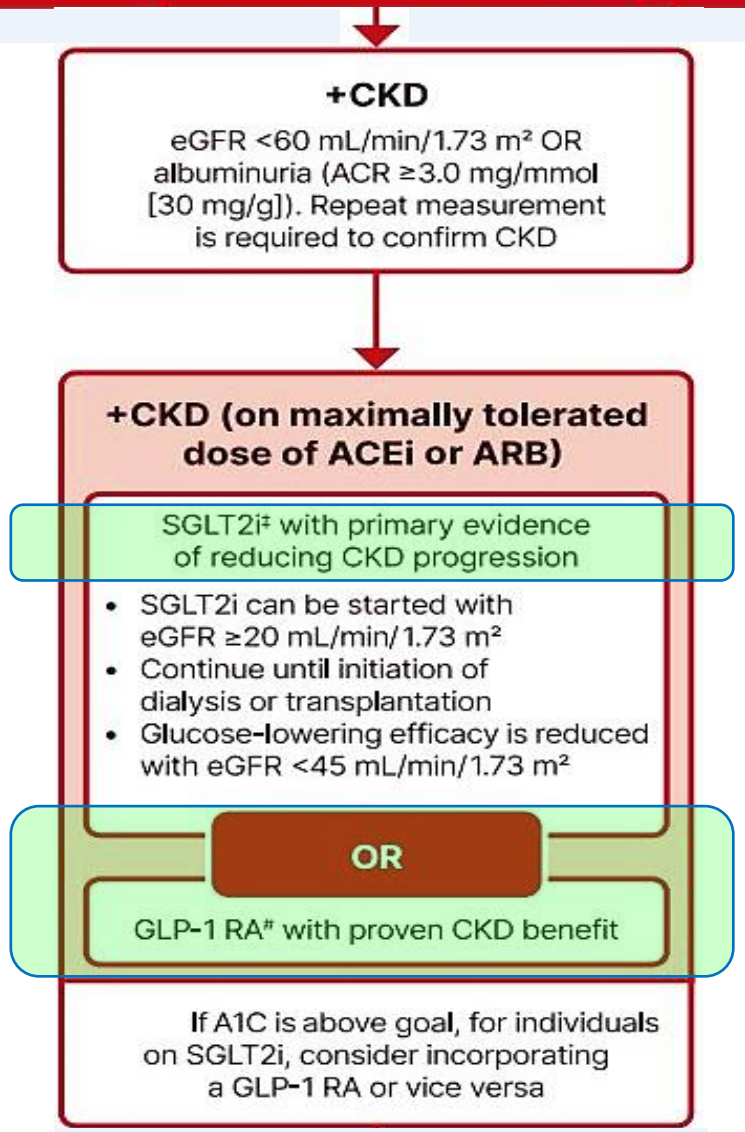
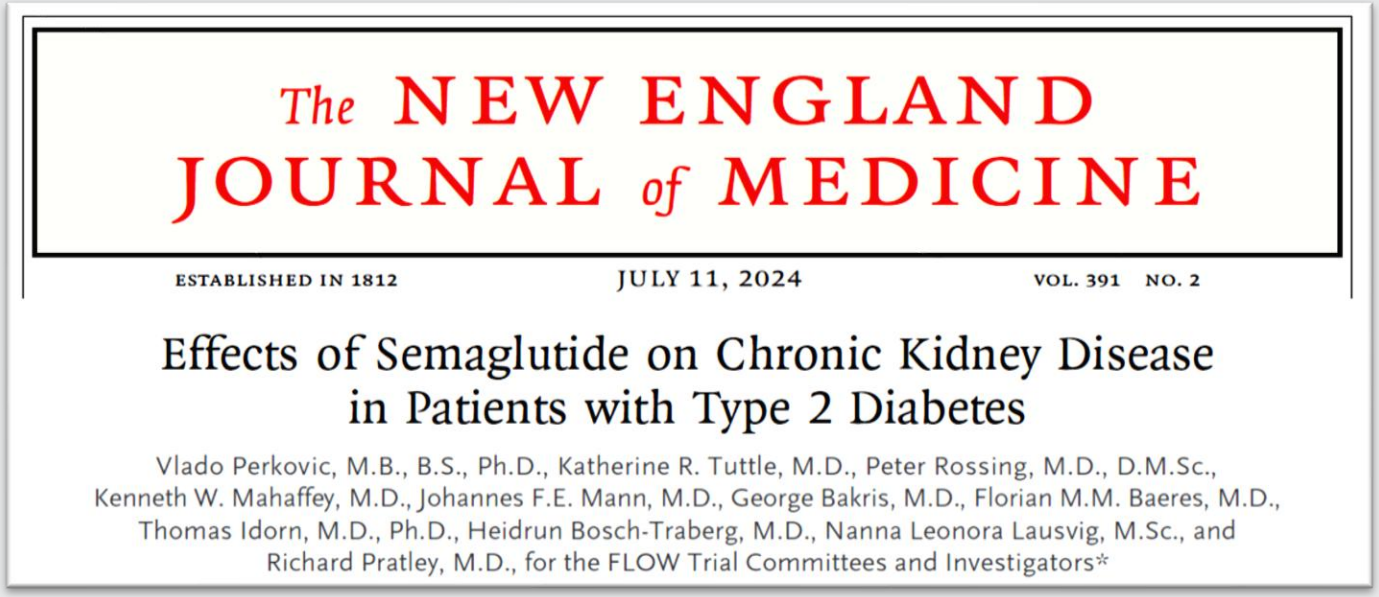
Goal: Cardiovascular and Kidney Risk Reduction in High-Risk Individuals with Type 2 Diabetes*



9.13 In adults with T_2D who have CKD (with confirmed eGFR 20–60 mL/min/1.73 m^2 and/or albuminuria), an $SGLT_2i$ or GLP-1 RA with demonstrated benefit in this population should be used for both glycemic management **(irrespective of A_{1C})** and for slowing progression of CKD and reduction in cardiovascular events. The glycemic benefits of $SGLT_2i$ are reduced at eGFR <45 mL/min/1.73 m^2. **A**

9.14 In adults with T_2D and eGFR <30 mL/min/1.73 m^2, a GLP-1 RA is preferred for glycemic management due to lower risk of hypoglycemia and for cardiovascular event reduction. **B**

Pharmacologic Approaches to Glycemic Treatment:
Standards of Care in Diabetes - 2025 Diabetes Care 2025;48(Suppl. 1):S181-S206



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 11, 2024 VOL. 391 NO. 2

Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes

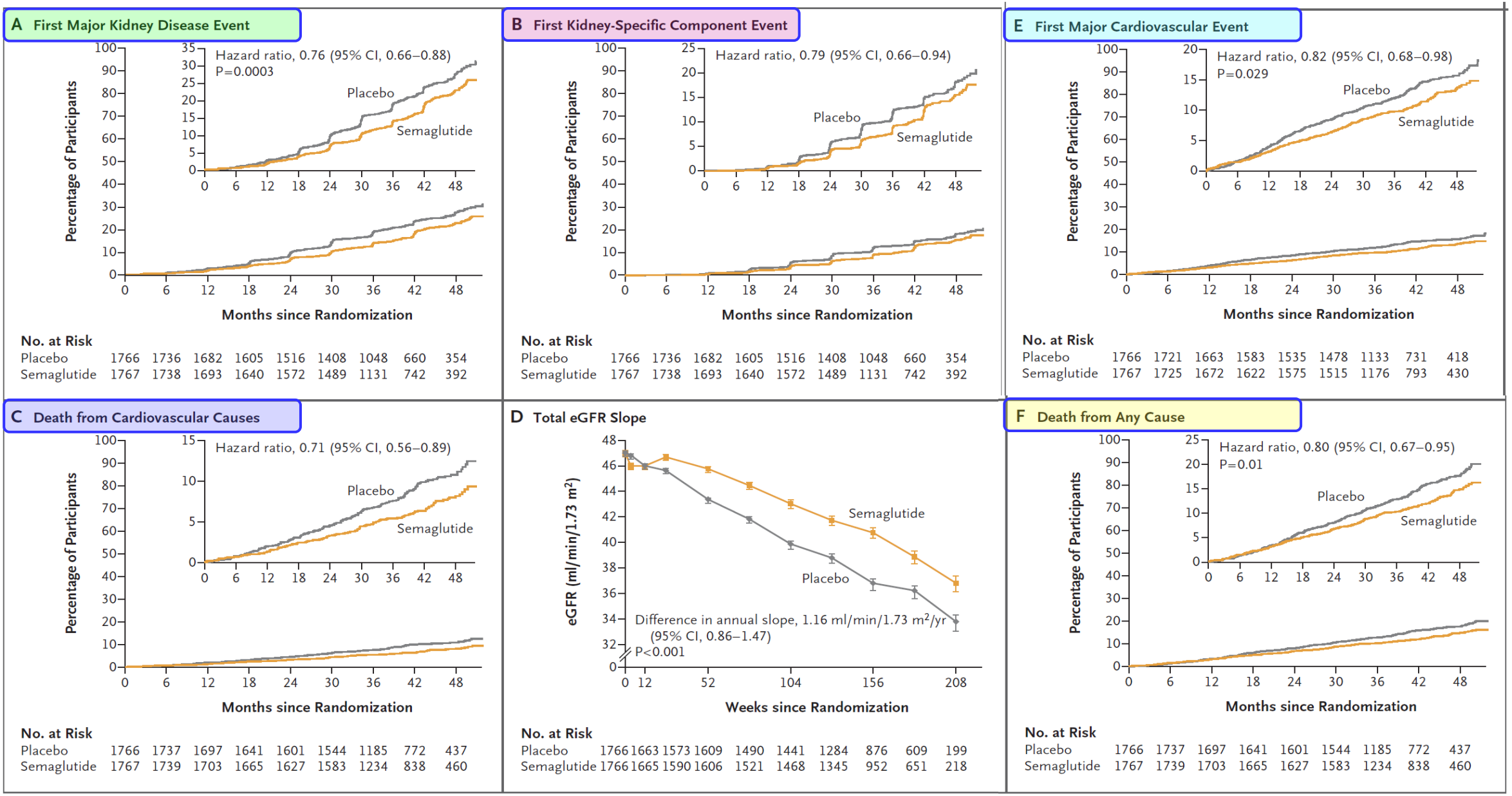
Vlado Perkovic, M.B., B.S., Ph.D., Katherine R. Tuttle, M.D., Peter Rossing, M.D., D.M.Sc., Kenneth W. Mahaffey, M.D., Johannes F.E. Mann, M.D., George Bakris, M.D., Florian M.M. Baeres, M.D., Thomas Idorn, M.D., Ph.D., Heidrun Bosch-Traberg, M.D., Nanna Leonora Lausvig, M.Sc., and Richard Pratley, M.D., for the FLOW Trial Committees and Investigators*

FLOW Trial

- **T_2D and CKD**
  - eGFR of 50 to 75 ml/min/1.73 m2 and a UACR of >300 and <5000 mg/gr
  - eGFR of 25 to <50 ml/min/1.73 m2 and a UACR of >100 and <5000 mg/gr
- Semaglutide, SC, at a dose of 1.0 mg weekly or placebo
  - 1767 semaglutide group; 1766 placebo group
  - median follow-up: 3.4 years
- The **primary outcome** was major kidney disease events, a composite of
  - the onset of kidney failure (dialysis, transplantation, or an eGFR of <15 ml/min/1.73 m2)
  - at least a 50% reduction in the eGFR from baseline
  - death from kidney-related or cardiovascular causes.
- Prespecified confirmatory secondary outcomes were tested hierarchically.

Diabetes Academy GABRIC

Perkovic, V. Et al. *N Engl J Med* 2024;391:109-21.. DOI: 10.1056/NEJMoa2403347



FLOW Trial

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Perkovic, V. Et al. *N Engl J Med* 2024;391:109-21.. DOI: 10.1056/NEJMoa2403347

American Diabetes Association® 2025

Section 11.

Chronic Kidney Disease and Risk Management

(https://doi.org/10.2337/dc25-S011)

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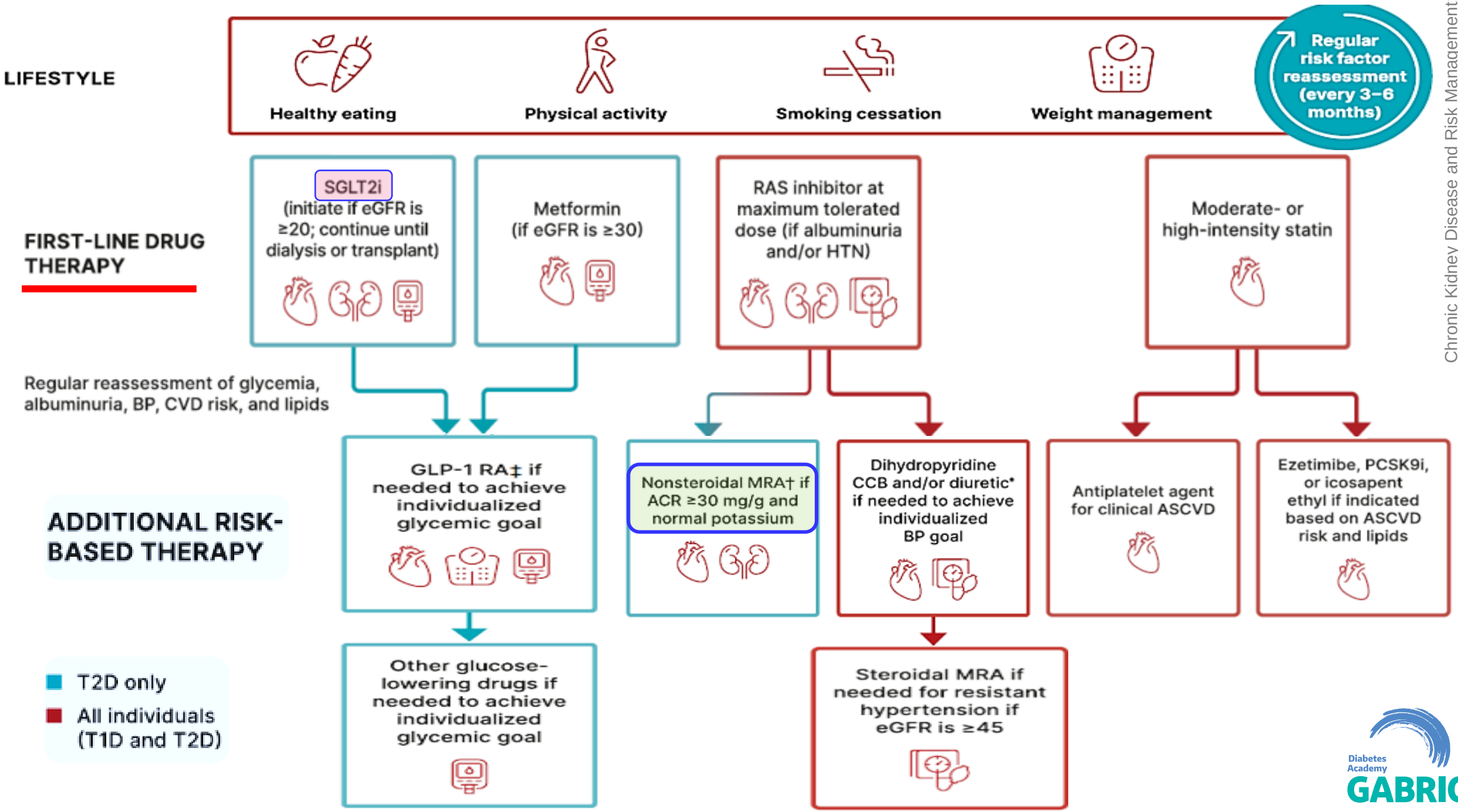
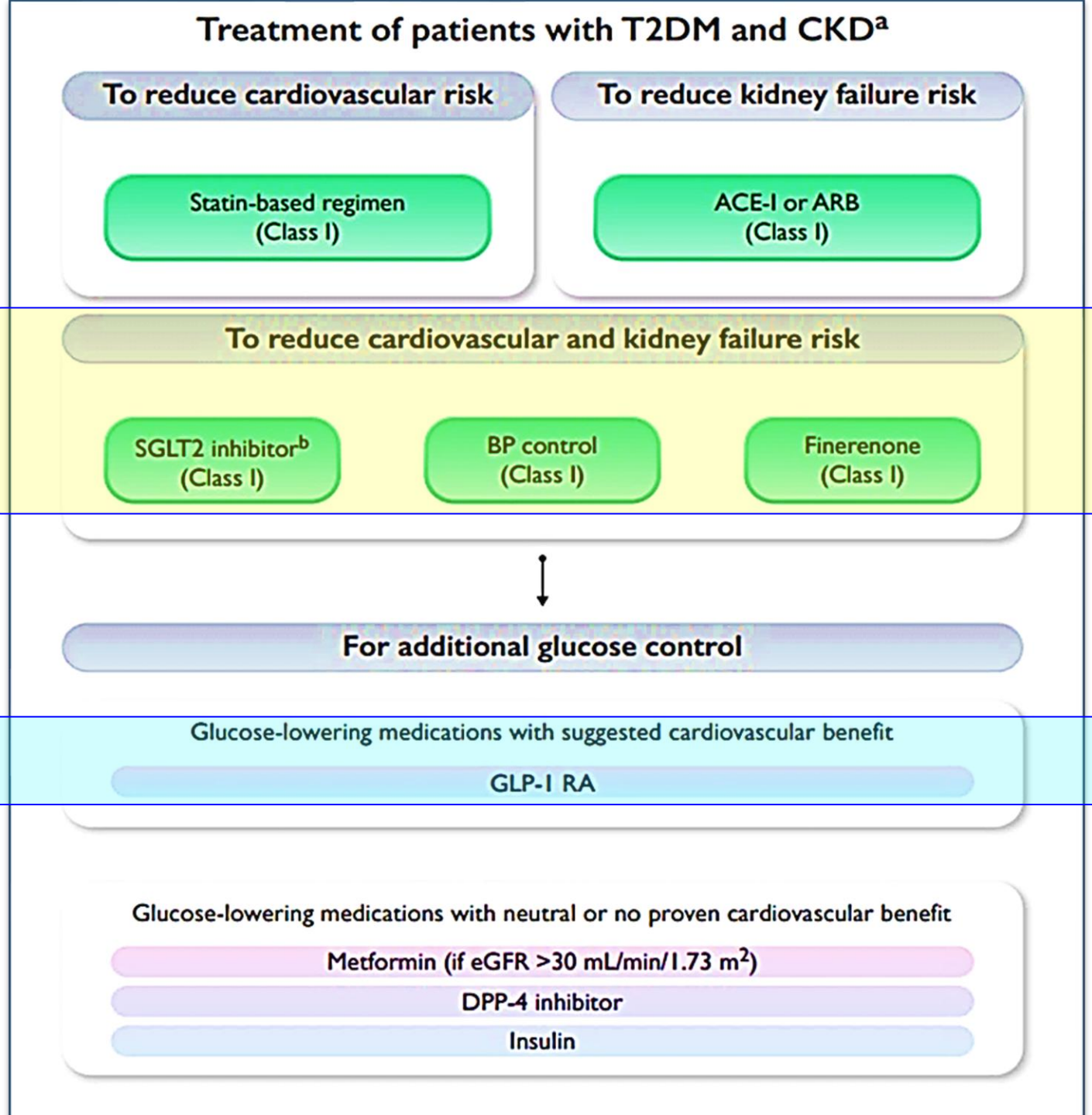


Chronic Kidney Disease and Risk Management: *Standards of Care in Diabetes .2025 Diabetes Care* 2025;48(Suppl. 1):S238-S251



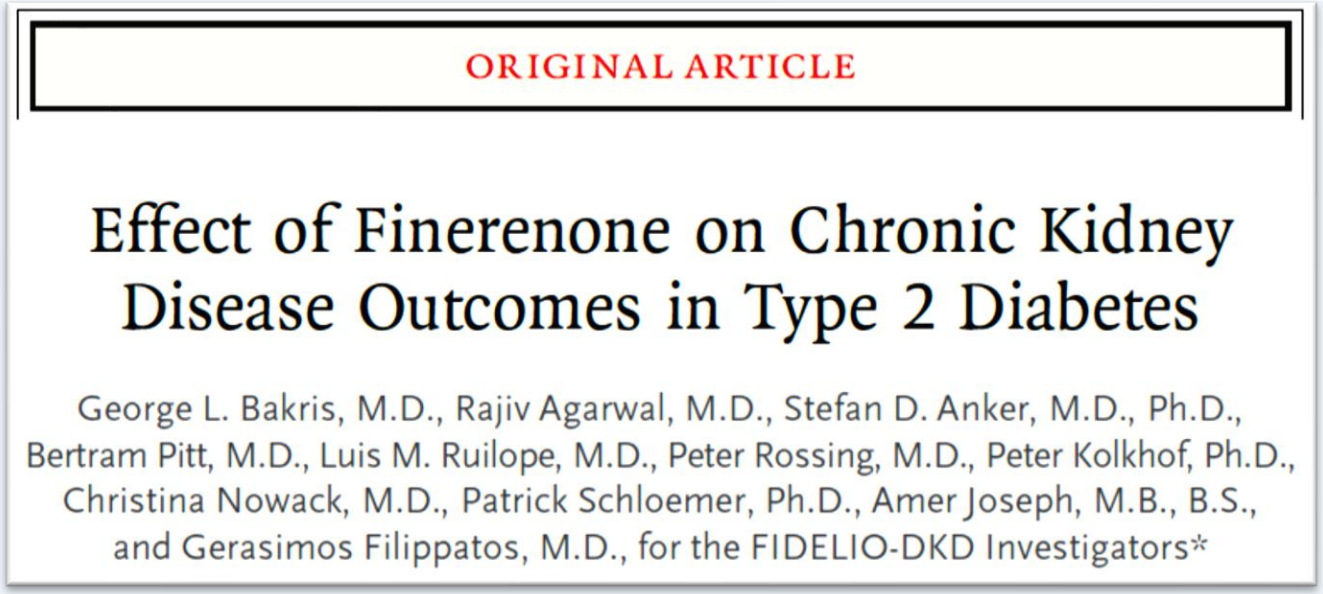
ESC European Society of Cardiology

Recommendations for the Treatment of Patients with T_2DM

to Reduce CKD Risk[1]

European Heart Journal (2023) 00, 1–98

Diabetes Academy GABRIC



ORIGINAL ARTICLE

Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes

George L. Bakris, M.D., Rajiv Agarwal, M.D., Stefan D. Anker, M.D., Ph.D., Bertram Pitt, M.D., Luis M. Ruilope, M.D., Peter Rossing, M.D., Peter Kolkhof, Ph.D., Christina Nowack, M.D., Patrick Schloemer, Ph.D., Amer Joseph, M.B., B.S., and Gerasimos Filippatos, M.D., for the FIDELIO-DKD Investigators*

FIDELIO-DKD Trial

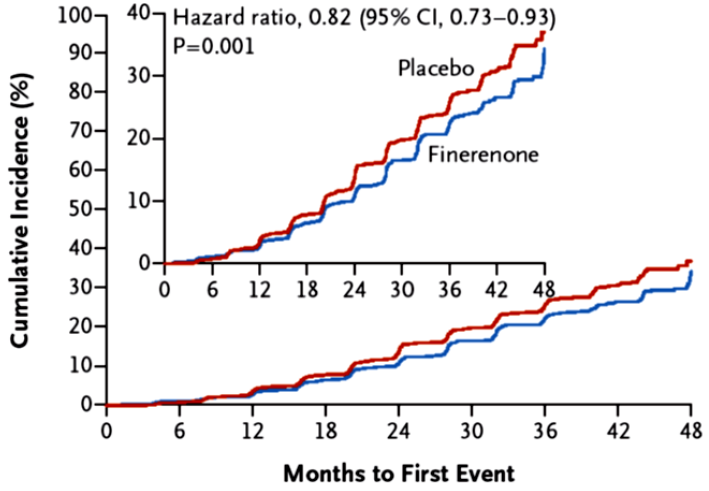
- 5734 patients with CKD and T_2D, in a 1:1 ratio, received finerenone or placeboe.
  - UACR of >30 and <300 mg/gr & eGFR of 25 to <60 ml/min/1.73 m2 & diabetic retinopathy
  - UACR of >300 and <5000 mg/gr & eGFR of 25 to 75 ml/min/1.73 m2 and
- A median follow-up of 2.6 years
- The **primary composite outcome** was:
  - kidney failure
  - a sustained decrease of at least 40% in the eGFR from baseline,
  - death from renal causes
- The key secondary composite outcome, was death from cardiovascular causes, nonfatal MI, nonfatal stroke, or hospitalization for heart failure.

Diabetes Academy GABRIC

Bakris G, et al. *N Engl J Med* 2020;383:2219-29. DOI: 10.1056/NEJMoa2025845

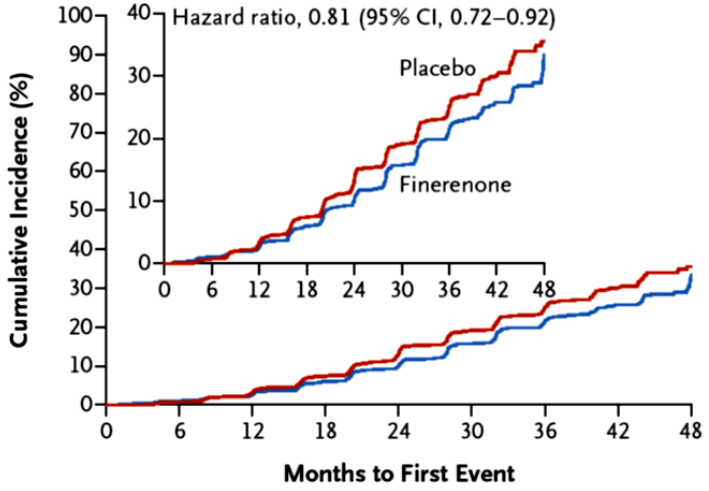
FIDELIO-DKD Trial

A Primary Composite Outcome



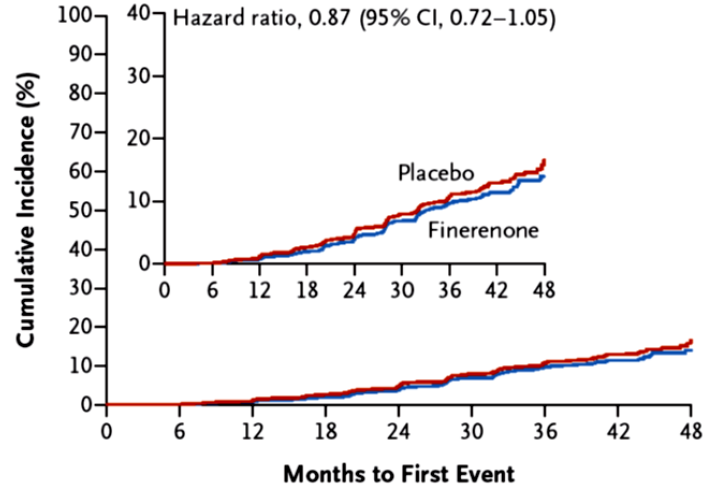
No. at Risk									
Placebo	2841	2724	2586	2379	1758	1248	792	453	82
Finerenone	2833	2705	2607	2397	1808	1274	787	441	83

B Sustained Decrease of ≥40% in the eGFR from Baseline



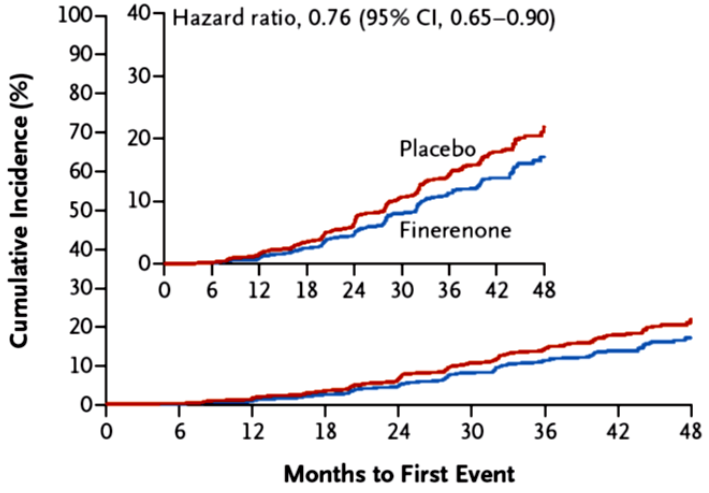
No. at Risk									
Placebo	2841	2722	2588	2379	1758	1249	793	453	82
Finerenone	2833	2703	2606	2396	1808	1275	788	442	83

C Kidney Failure



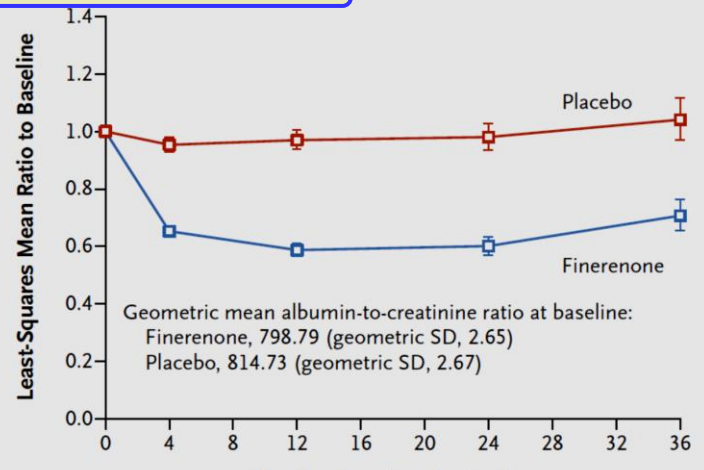
No. at Risk									
Placebo	2841	2741	2645	2508	1911	1390	892	513	103
Finerenone	2833	2733	2658	2506	1932	1393	897	510	104

D Secondary Composite Outcome



No. at Risk									
Placebo	2841	2740	2636	2490	1887	1364	873	499	98
Finerenone	2833	2732	2655	2492	1915	1377	883	501	101

A Urinary Albumin-to-Creatinine Ratio



No. of Patients					
Finerenone	2831	2725	2582	1841	856
Placebo	2840	2726	2598	1825	834
Mean Change from Baseline (percent)					
Finerenone	Ref.	−34.7	−41.3	−39.9	−29.3
Placebo	Ref.	−4.7	−3.0	−2.0	4.1

Diabetes Academy GABRIC

Bakris G, et al. *N Engl J Med* 2020;383:2219-29. DOI: 10.1056/NEJMoa2025845

ORIGINAL ARTICLE

Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes

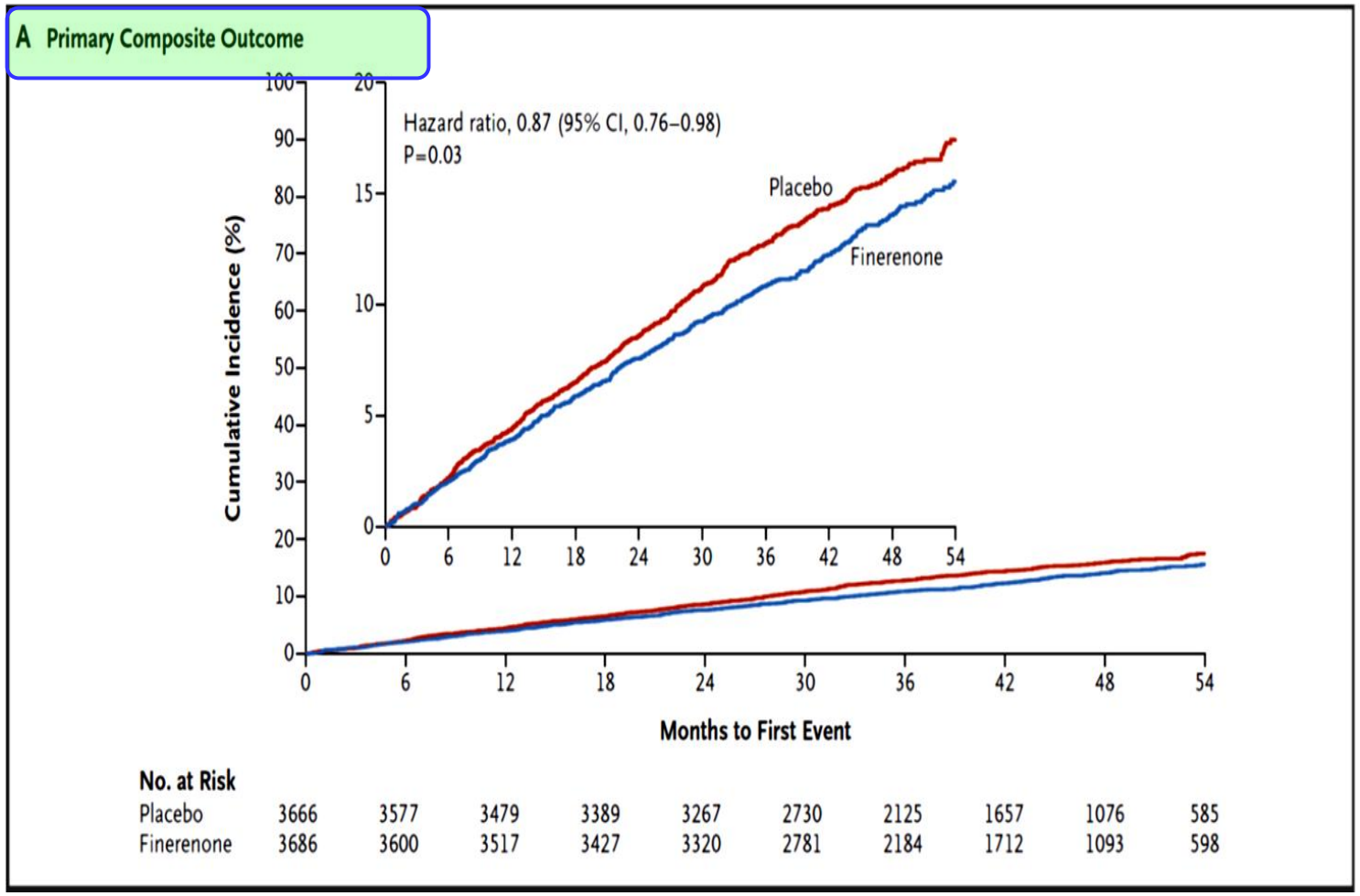
B. Pitt, G. Filippatos, R. Agarwal, S.D. Anker, G.L. Bakris, P. Rossing, A. Joseph, P. Kolkhof, C. Nowack, P. Schloemer, and L.M. Ruilope, for the FIGARO-DKD Investigators*

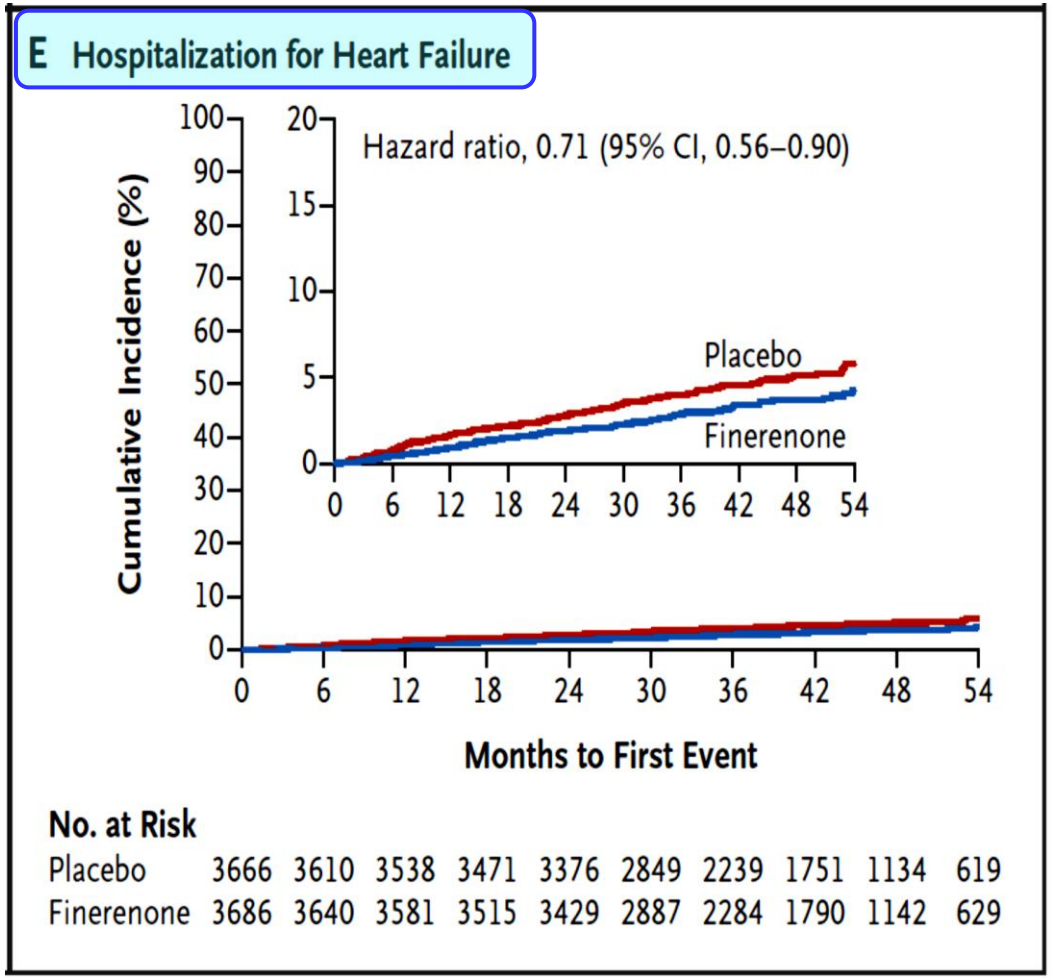
FIGARO-DKD Trial

- 7437 patients with CKD and T_2D, in a 1:1 ratio, received finerenone or placebo.
  - UACR of >30 and <300 mg/gr & eGFR of 25 to <90 ml/min/1.73 m2
  - UACR of >300 and <5000 mg/gr & eGFR of >60 ml/min/1.73 m2
- A median follow-up of 3.4 years
- The **primary composite outcome** was:
  - death from cardiovascular causes
  - nonfatal MI
  - nonfatal stroke
  - hospitalization for heart failure
- The first secondary outcome was a composite of kidney failure, a sustained decrease from baseline of at least 40% in the eGFR, or death from renal causes.

Diabetes Academy GABRIC

Pitt B, et al. *N Engl J Med* 2021;385:2252-63. DOI: 10.1056/NEJMoa2110956





FIGARO-DKD Trial

Pitt B, et al. *N Engl J Med* 2021;385:2252-63. DOI: 10.1056/NEJMoa2110956

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Clinical Case Scenario

My advise:

- Start Semaglutide, 0.25 mg, weekly/SC
  - Gradual decrease in Glargine dose

&

- Start Finerenone, 10 mg, OD

Daily Medications:

Met+Empa 1000/12.5 mg daily, **Glargine 20 U** QHS, **Ator 20** mg QD, **Telmi/Amlo 80/5** mg daily