

# Individualized Glycemic Goals and Choosing Therapy in Type 2 Diabetes

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University of Washington  
Cardiometabolic  
ECHO



# Dualities

- Research: Medtronic Diabetes, Insulet, Beta Bionics
- Consulting: Abbot, Roche, Bigfoot, GWave

# To Understand Glycemic Goals, How Does One Measure Glycemia?

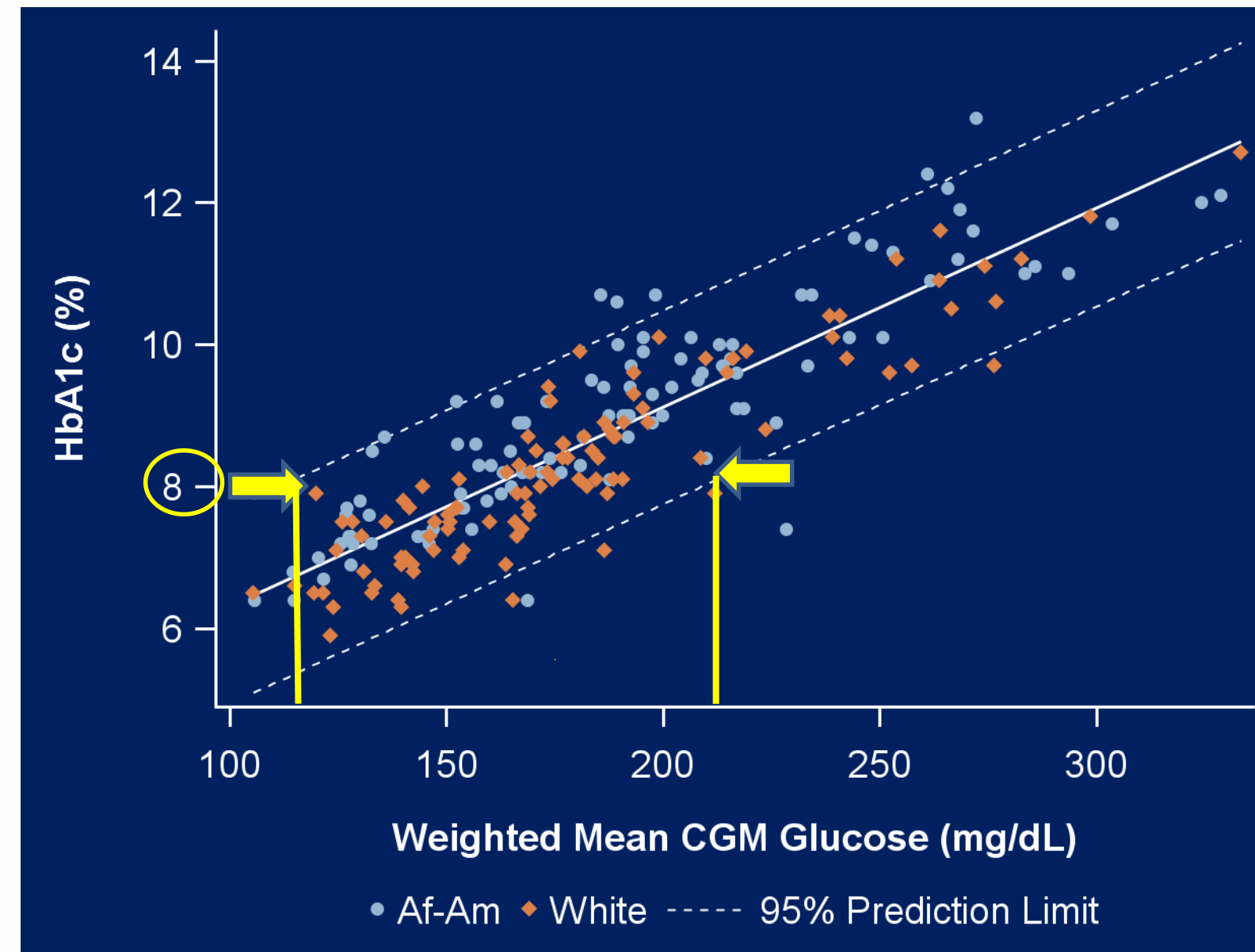
- A. Fasting blood glucose
- B. Frequent home blood glucose  
monitoring
- C. HbA1c
- D. Continuous glucose  
monitoring (CGM)

# Study #1: Average Glucose Versus A1C

A1C (%)	AG (mg/dL [95% CI])
5	97 (76-120)
6	126 (100-152)
7	154 (123-185)
8	183 (147-217)
9	212 (170-249)
10	249 (192-282)
11	269 (217-314)
12	298 (240-347)

- 1. One can't compare the A1C levels between 2 people
- 2. Each A1C comprises a wide mean glucose range
- 3. This does not take away from A1C use in a clinical trial

# Study #2: Mean CGM Glucose by HbA1c – Overall (N=208)





# Glucose Management Indicator (GMI): A New Term for Estimating A1C From Continuous Glucose Monitoring

*Diabetes Care* 2018;41:2275–2280 | <https://doi.org/10.2337/dc18-1581>



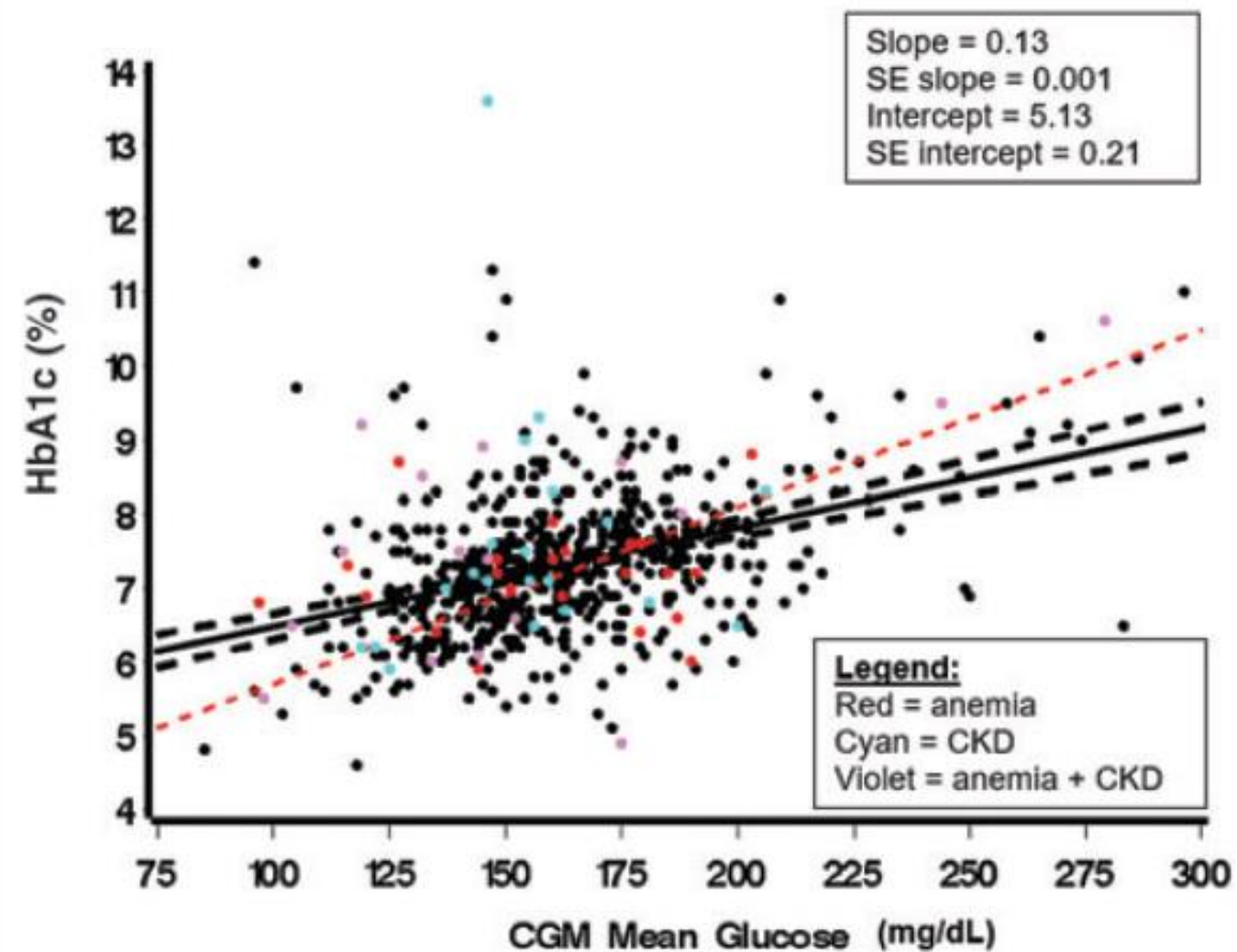
*Richard M. Bergenstal,<sup>1</sup> Roy W. Beck,<sup>2</sup>  
Kelly L. Close,<sup>3</sup> George Grunberger,<sup>4</sup>  
David B. Sacks,<sup>5</sup> Aaron Kowalski,<sup>6</sup>  
Adam S. Brown,<sup>7</sup> Lutz Heinemann,<sup>8</sup>  
Grazia Aleppo,<sup>9</sup> Donna B. Ryan,<sup>10</sup>  
Tonya D. Riddlesworth,<sup>2</sup> and  
William T. Cefalu<sup>11</sup>*

## What Every Provider and Patient needs to Understand in 2022

- Glycemic Management Indicator (GMI): a metric calculated by CGM-based formula from a population of mean glucose data (previously called “estimated A1C”)
- Is now on most but now all downloads. Can also find on CGM apps

# Why GMI is so important

N=641 using CGM with mean duration of data = 25 days, A1C measured within 30 days of CGM download



CGM Discordance:

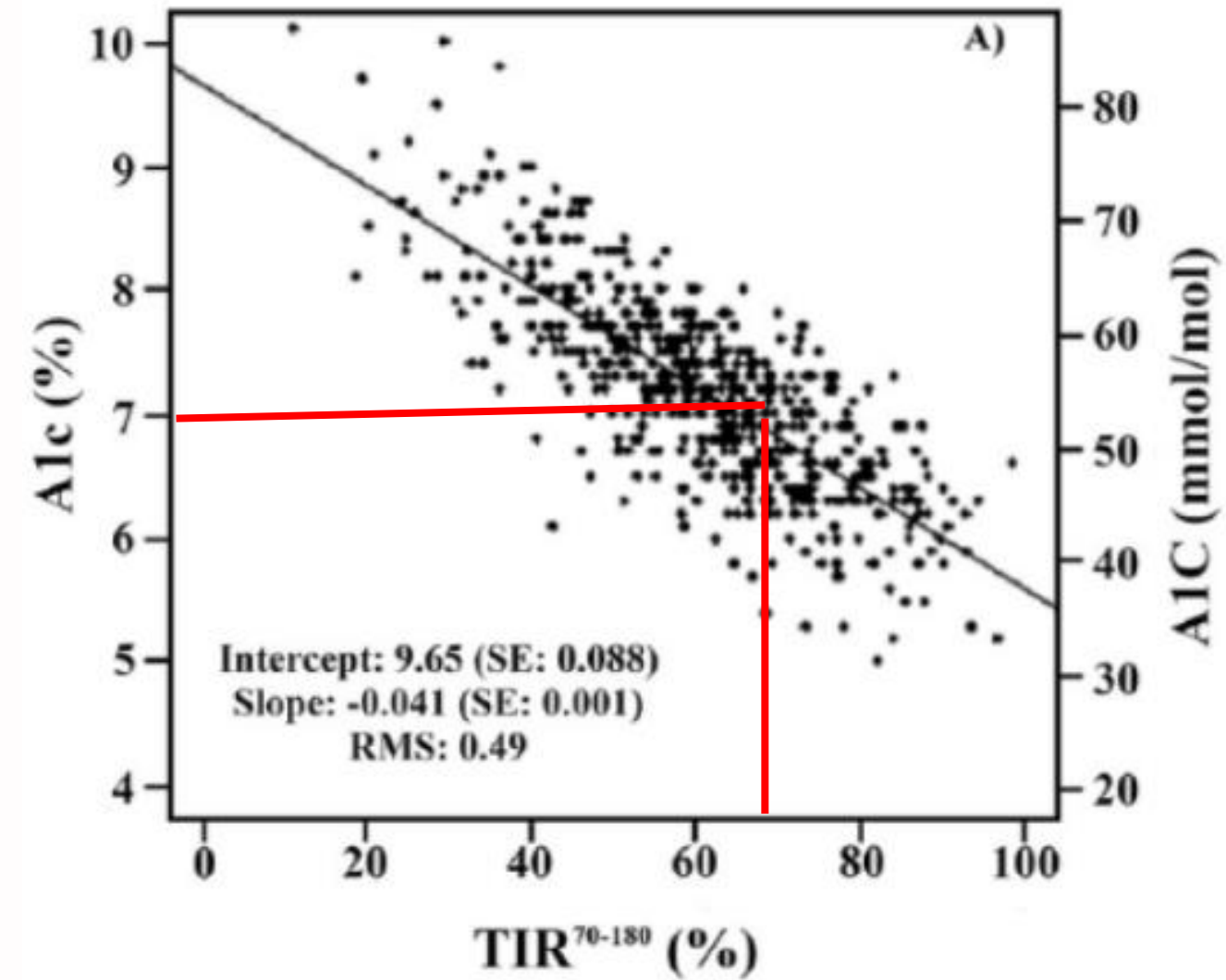
11% < 0.1%

50%  $\geq$  0.5%

22%  $\geq$  1.0%

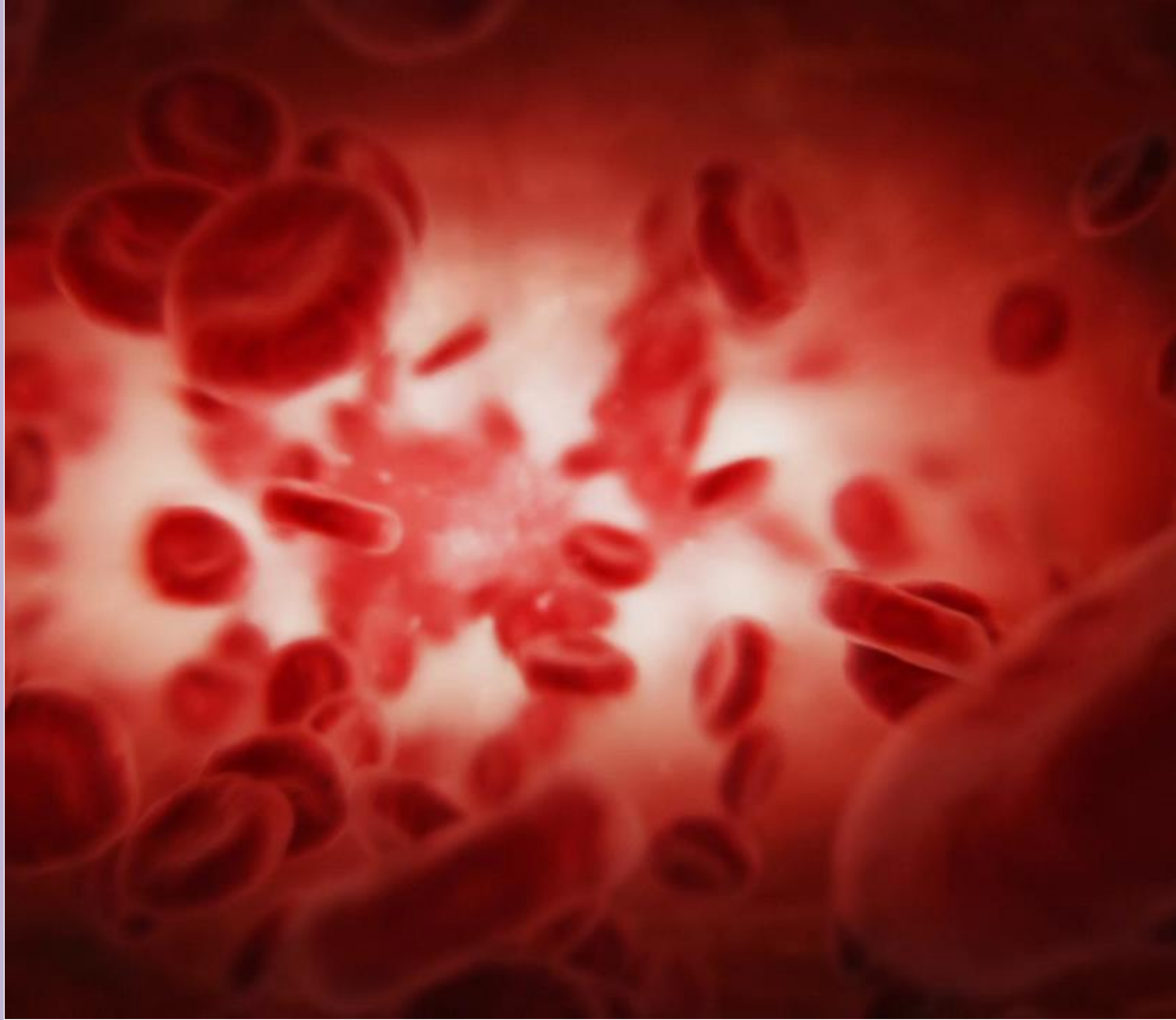
Increased discordance with eGFR < 60

A time-in-range of 70% is close to a HbA1c of 7% (but there is a lot of variability!)



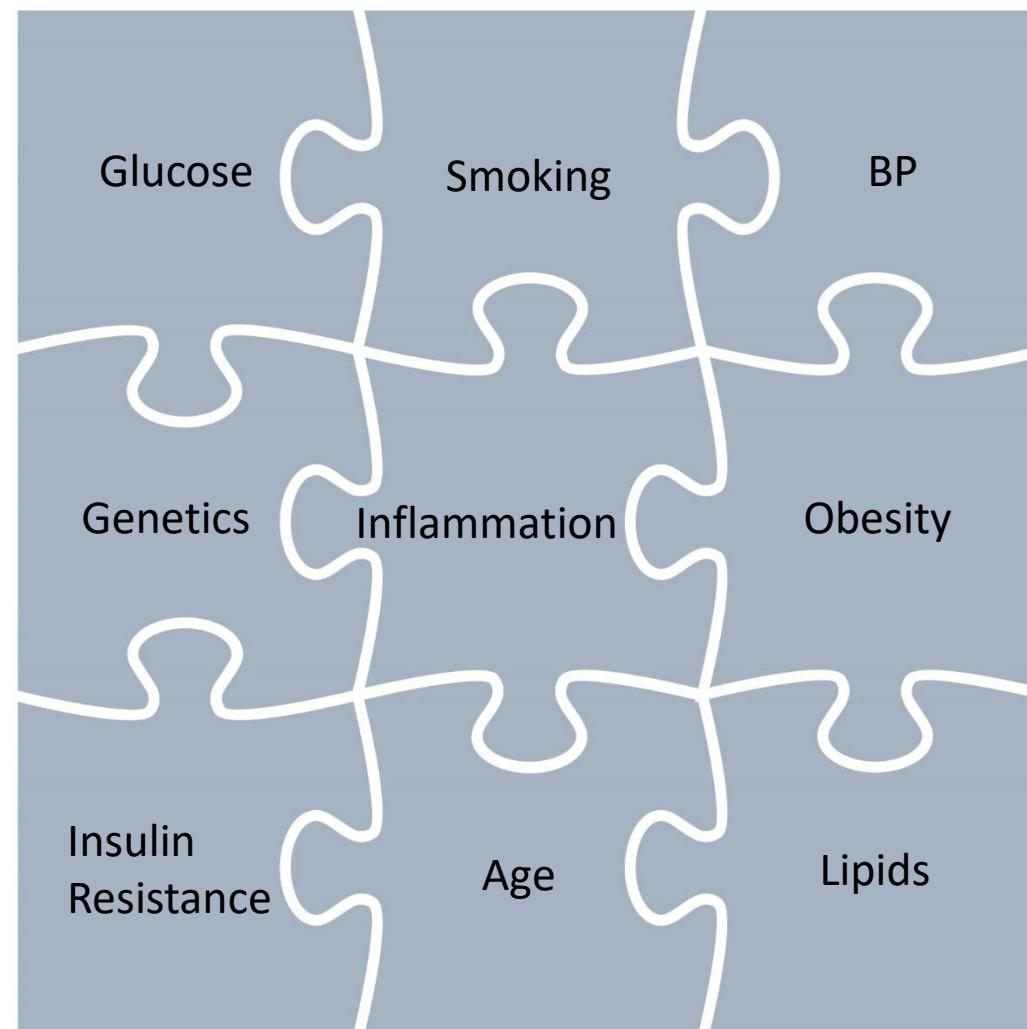


**HbA1c Works Great  
for a Population, But  
Not For Individual  
Patients in Assessing  
Glycemic Control**

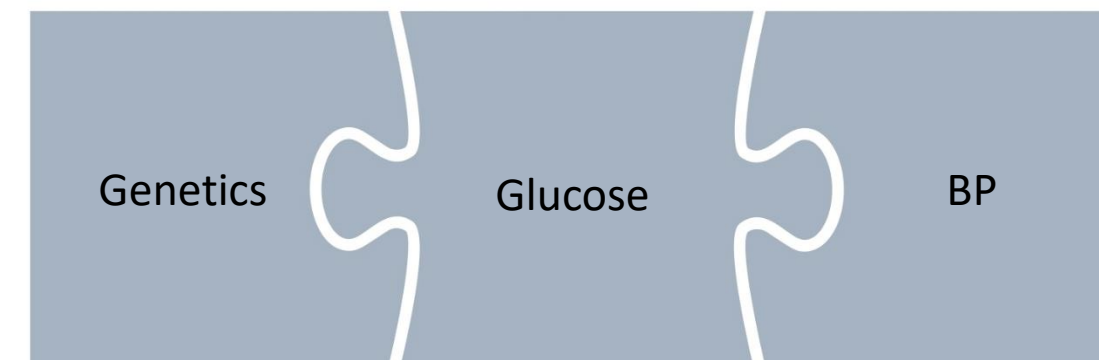


# The Puzzles of Diabetes & Its Complications

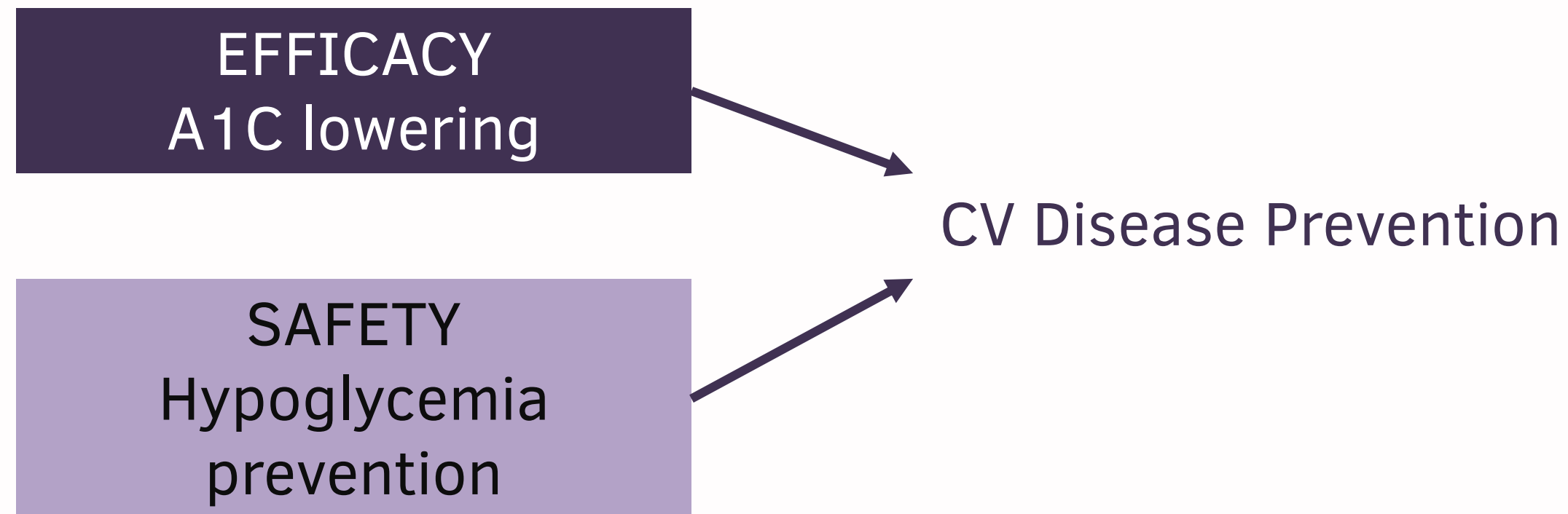
## Macrovascular Complications



## Microvascular Complications



# Management of T2D in 2022





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# **Guidance for Industry**

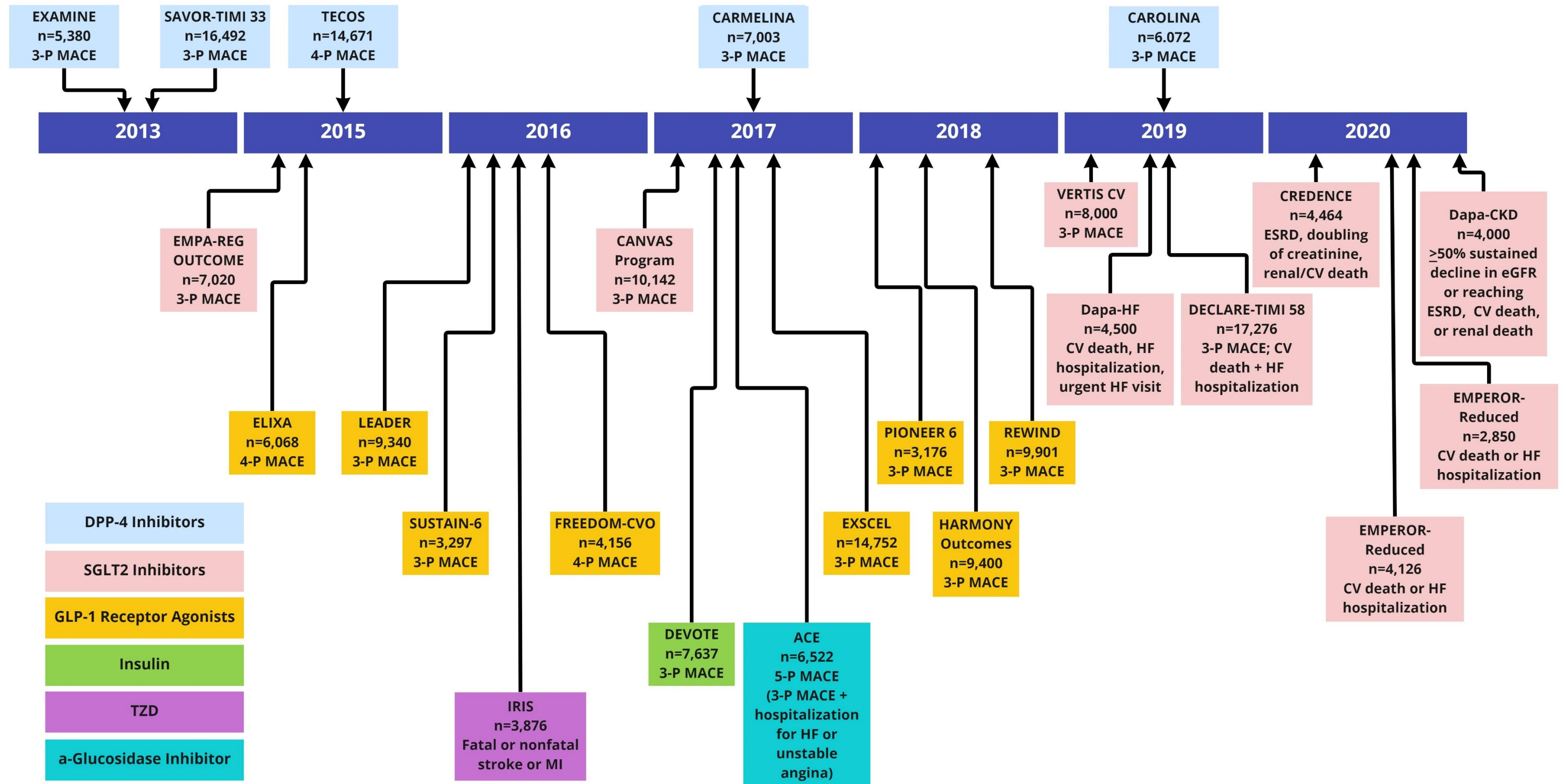
## **Diabetes Mellitus — Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes**

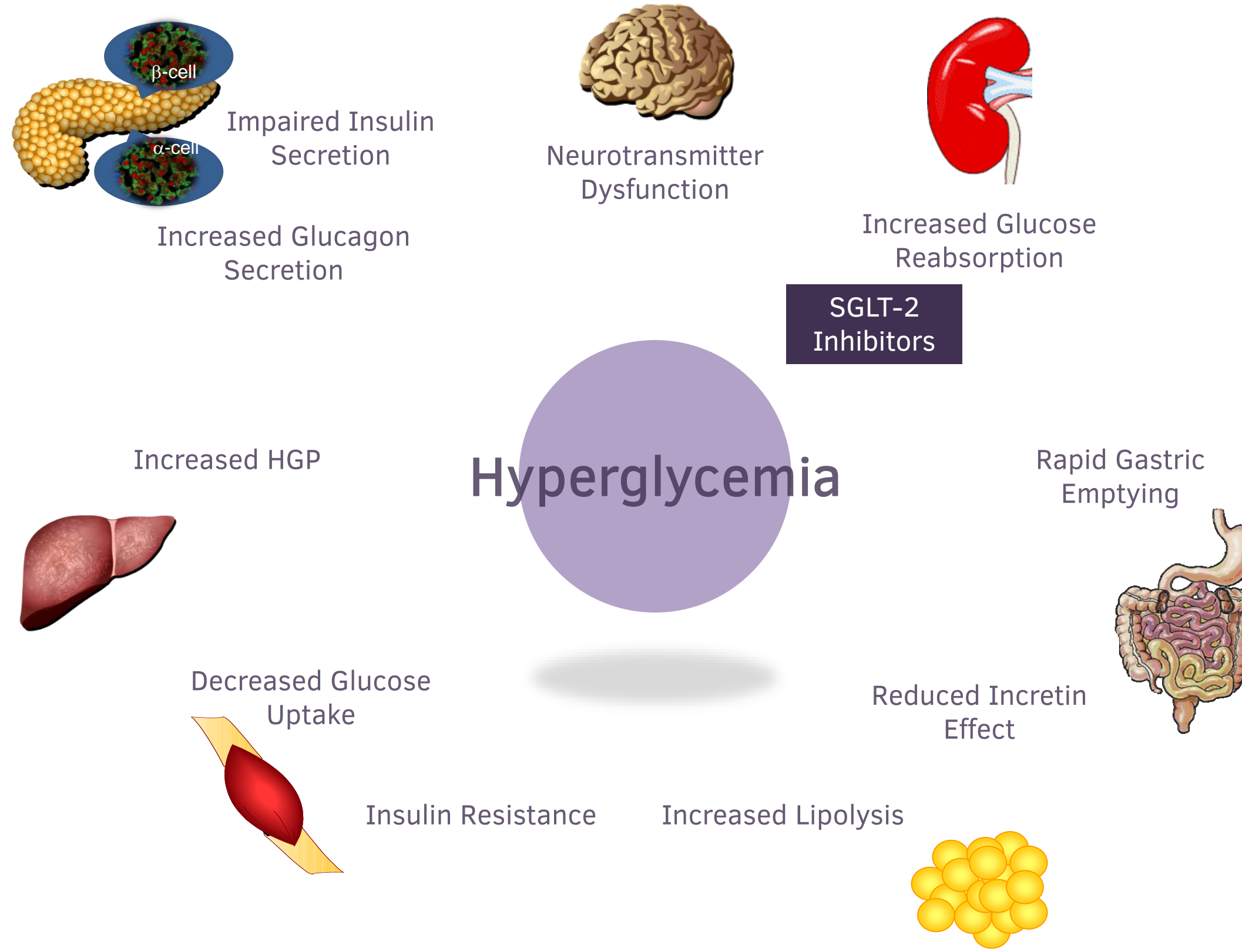
**U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER)**

**December 2008  
Clinical/Medical**

## **FDA Guidance for Industry, Dec 2008**

“To establish the safety of a new antidiabetic therapy to treat type 2 diabetes, sponsors should demonstrate that the therapy will not result in an unacceptable increase in cardiovascular risk.”



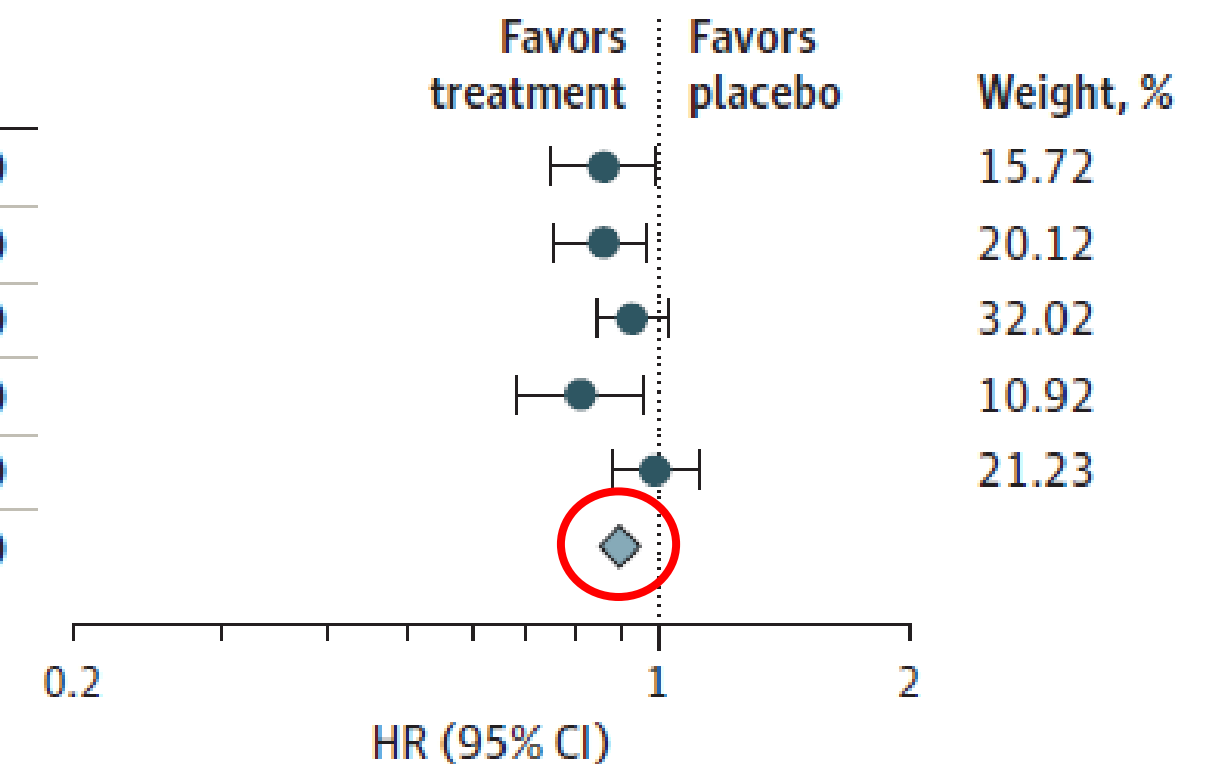




# Effect of SGLT-2s on MACE

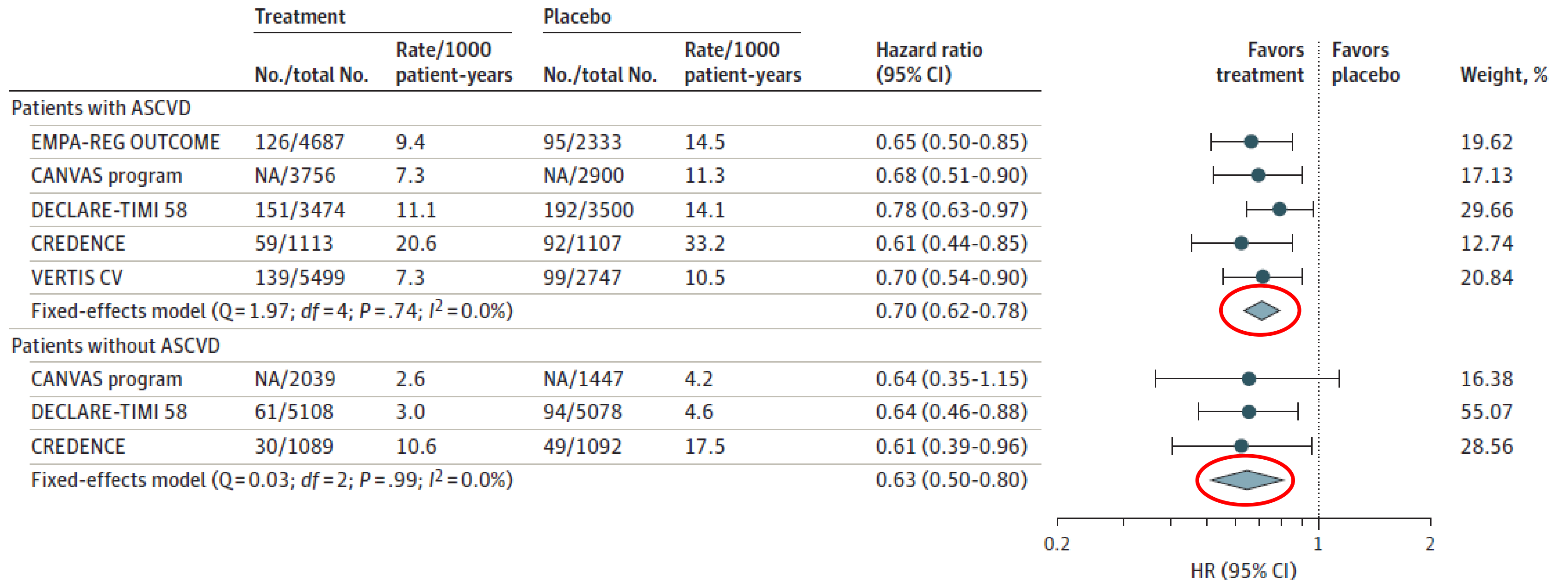
## A Overall MACEs

	Treatment		Placebo		Hazard ratio (95% CI)
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	
EMPA-REG OUTCOME	490/4687	37.4	282/2333	43.9	0.86 (0.74-0.99)
CANVAS program	NA/5795	26.9	NA/4347	31.5	0.86 (0.75-0.97)
DECLARE-TIMI 58	756/8582	22.6	803/8578	24.2	0.93 (0.84-1.03)
CREDENCE	217/2202	38.7	269/2199	48.7	0.80 (0.67-0.95)
VERTIS CV	735/5499	40.0	368/2747	40.3	0.99 (0.88-1.12)
Fixed-effects model (Q= 5.22; df= 4; P= .27; I <sup>2</sup> = 23.4%)					0.90 (0.85-0.95)



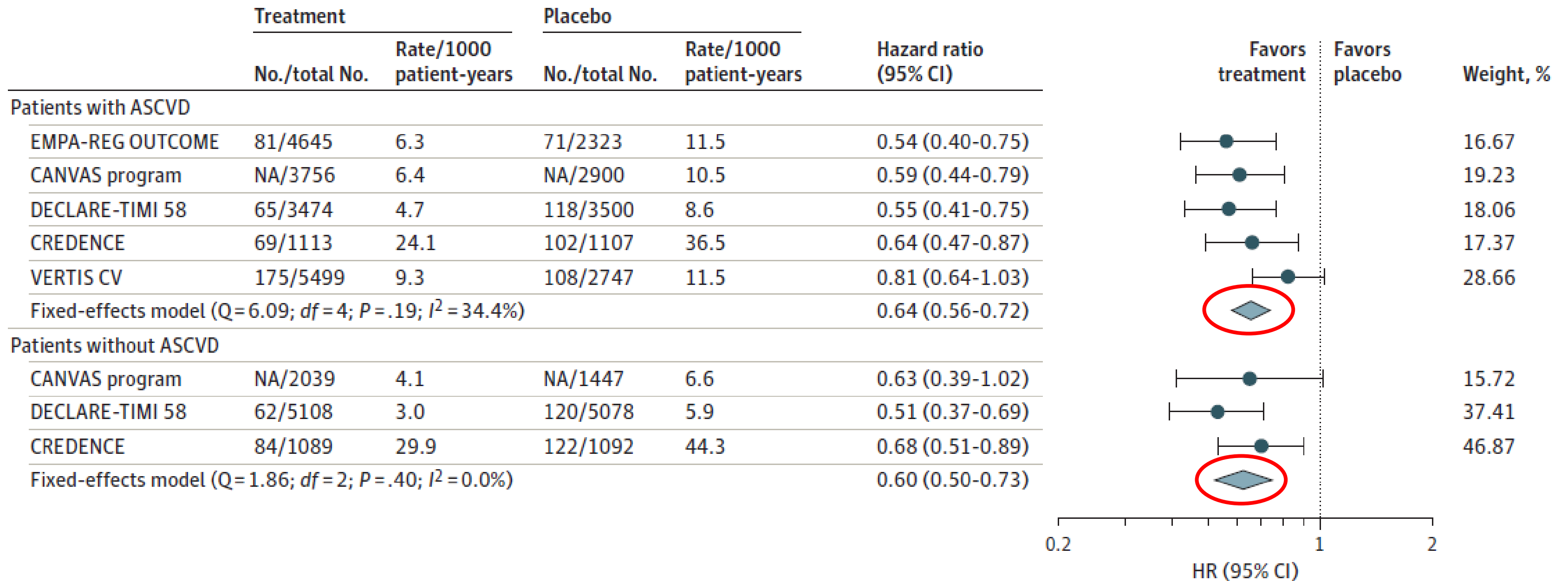
# Effect of SGLT-2s on Hospitalization for HF

## B HHF by ASCVD status

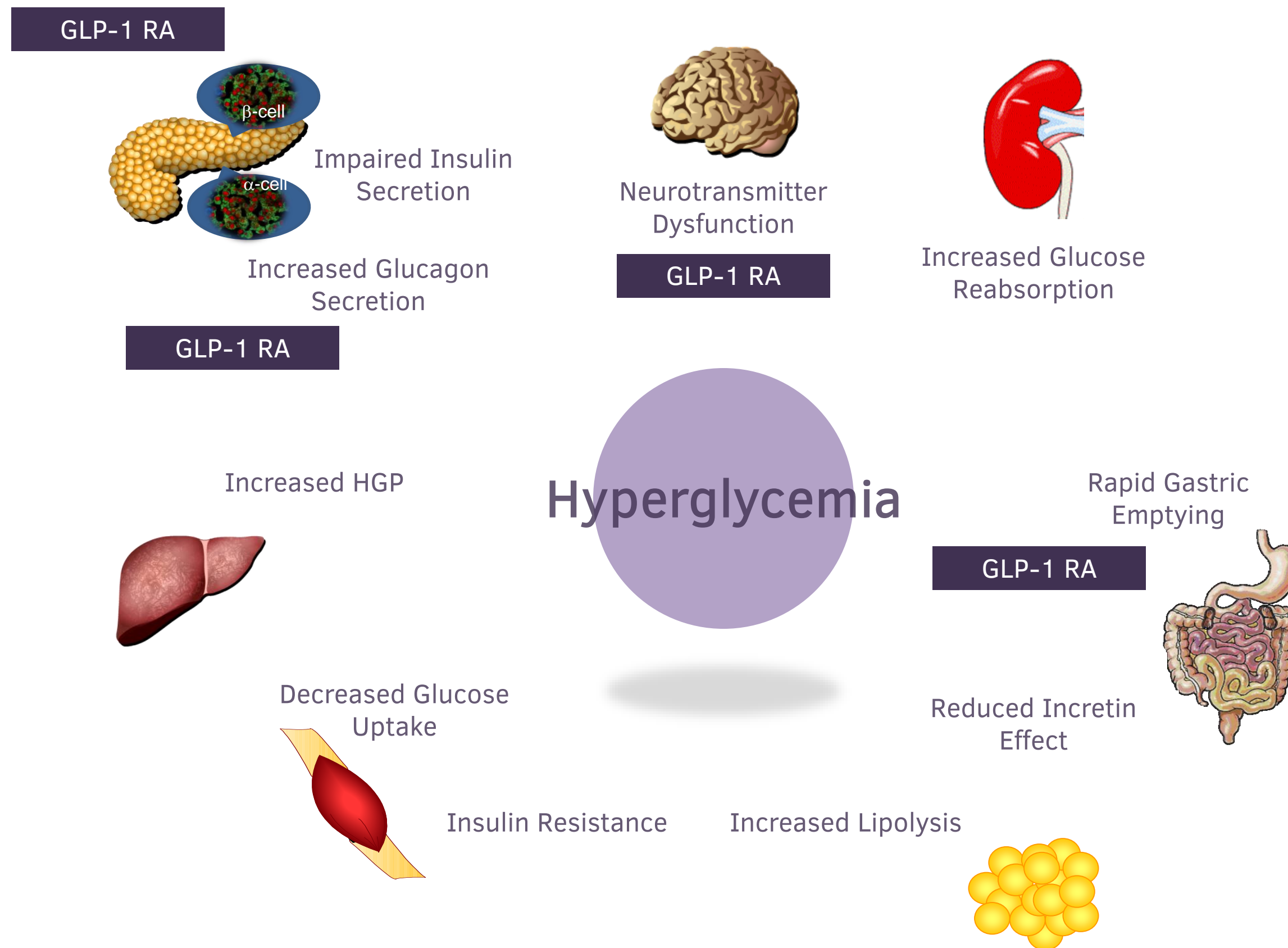


# Effect of Effect of SGLT-2s on *Renal Outcomes*

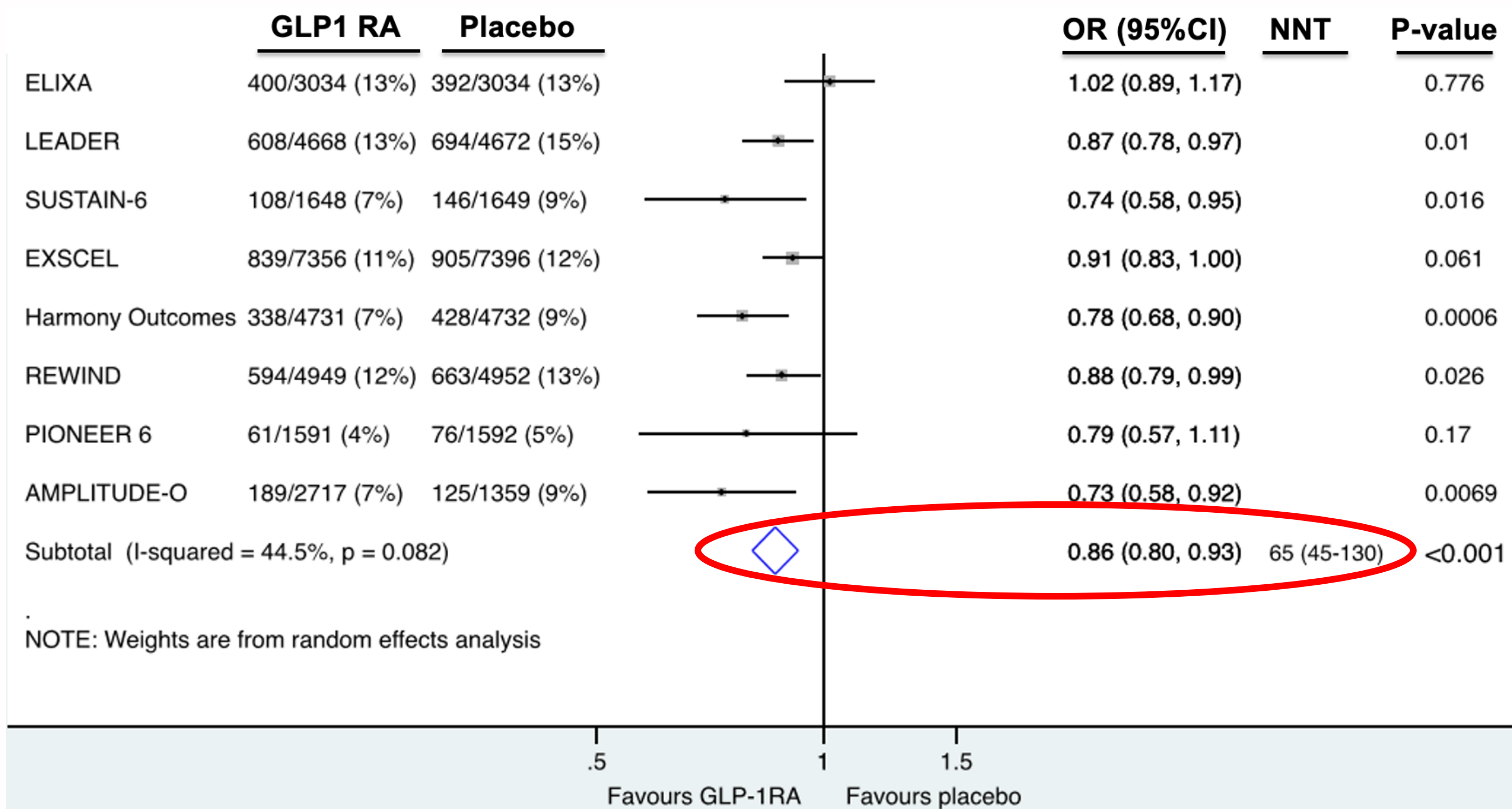
## B Kidney outcomes by ASCVD status





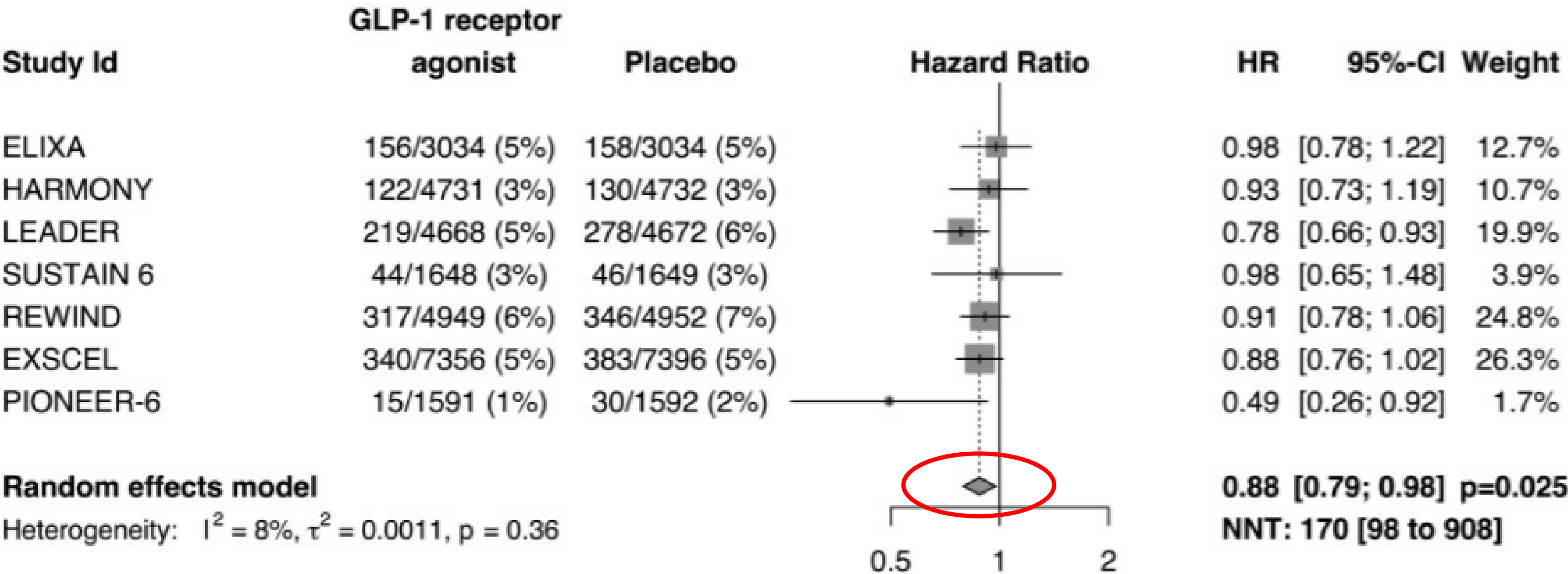


# Effect on GLP RAs on MACE



# The Effect of GLP1-Ras on CV Death

## Cardiovascular death





# Key Components of 2022 ADA/EASD Rx of Hyperglycemia Guidelines

- All people with T2D should be offered access to on-going Diabetes Self-Management Education Support (DSMES) programs
- Facilitating medication adherence should be specifically considered when selecting glucose-lowering medications
- GLP-1 RAs and SGLT-2i's for CV or renal benefit for people with type 2 diabetes should now be *considered independently* of baseline or target A1c.
- GLP-1 RAs are now the first-line injectable therapy for type 2 diabetes

FIRST-LINE THERAPY depends on comorbidities, patient-centered treatment factors, including cost and access considerations, and management needs and generally includes metformin and comprehensive lifestyle modification^

ASCVD/INDICATORS OF HIGH RISK, HF, CKD†

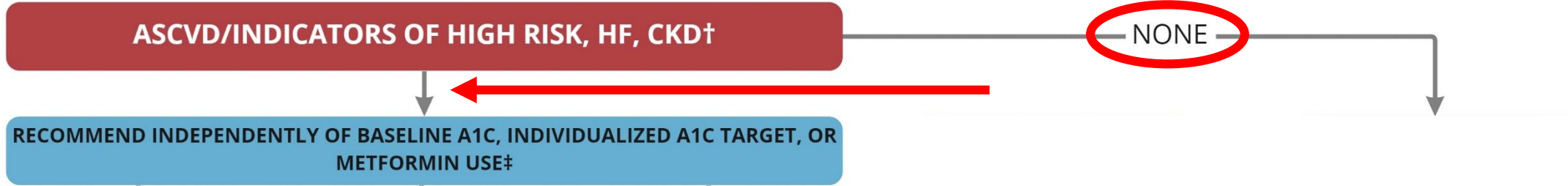
NONE

RECOMMEND INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE‡

TO AVOID  
THERAPEUTIC  
INERTIA REASSESS  
AND MODIFY  
TREATMENT  
REGULARLY (3-6  
MONTHS)

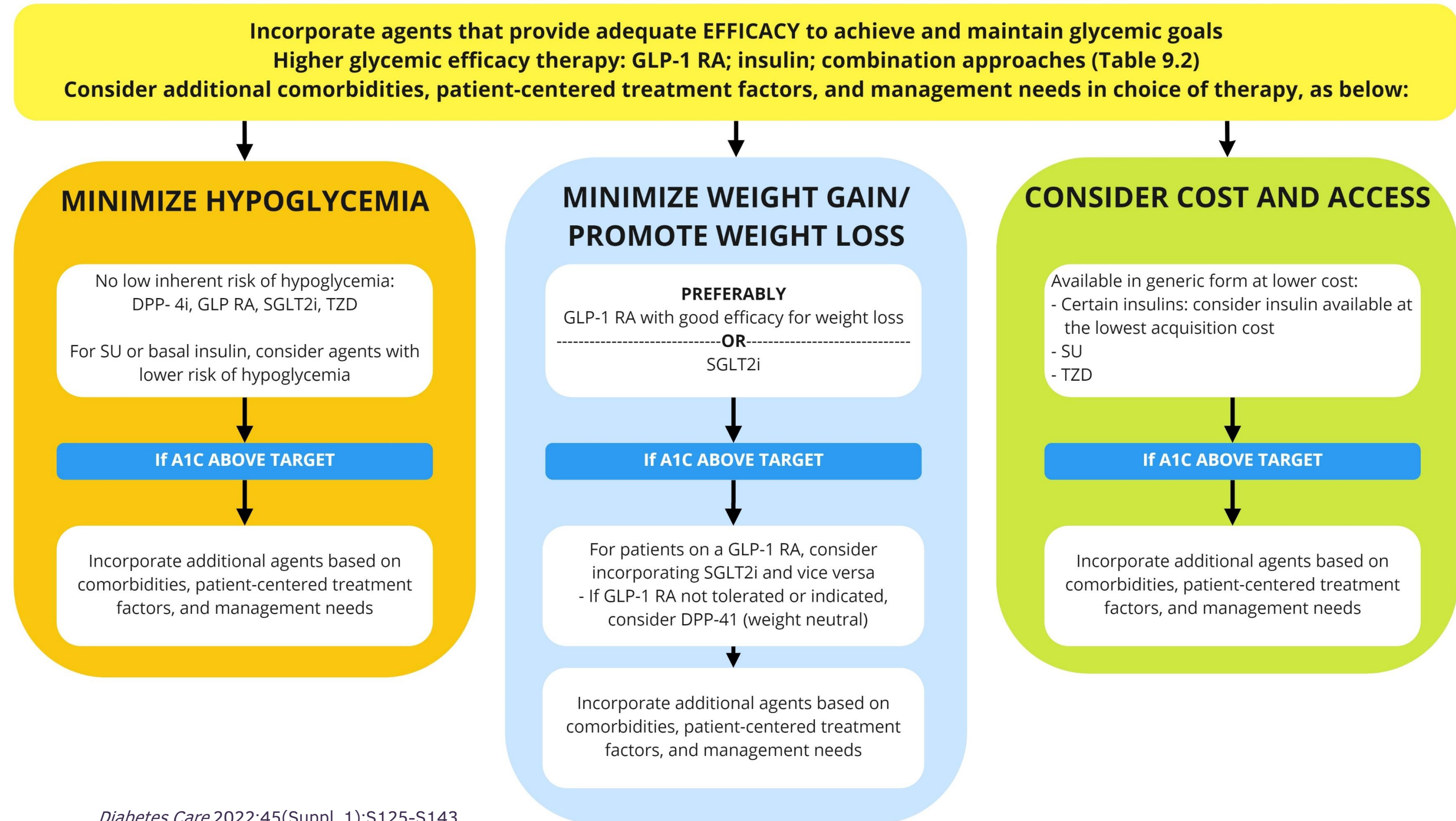
1. First-line therapy depends on comorbidities, patient centered treatment factors, including cost and access considerations, and management needs and generally includes metformin and comprehensive lifestyle modification

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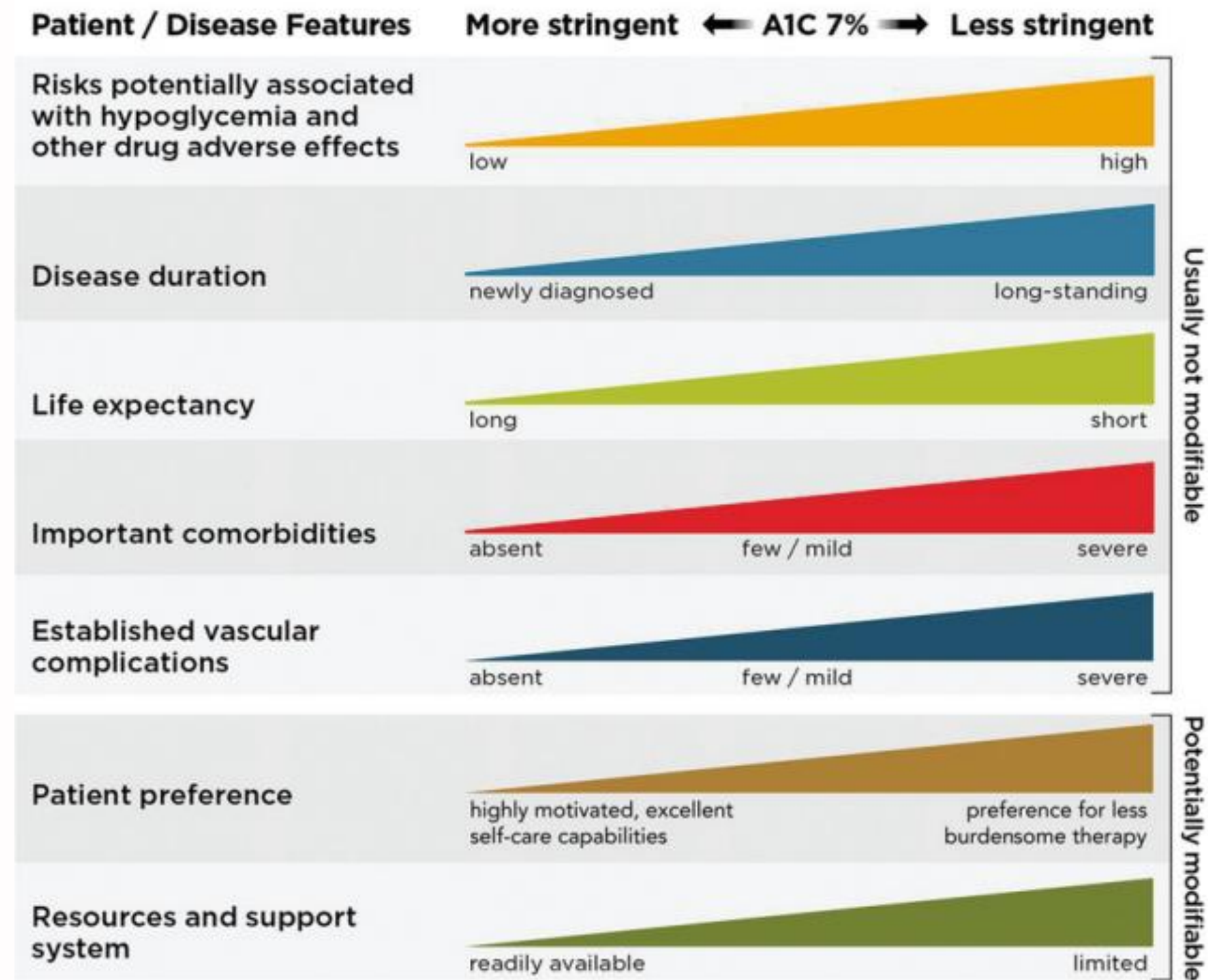
TO AVOID  
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# If No Risk of ASCVD, HF, or CKD and HbA1C is Above Target

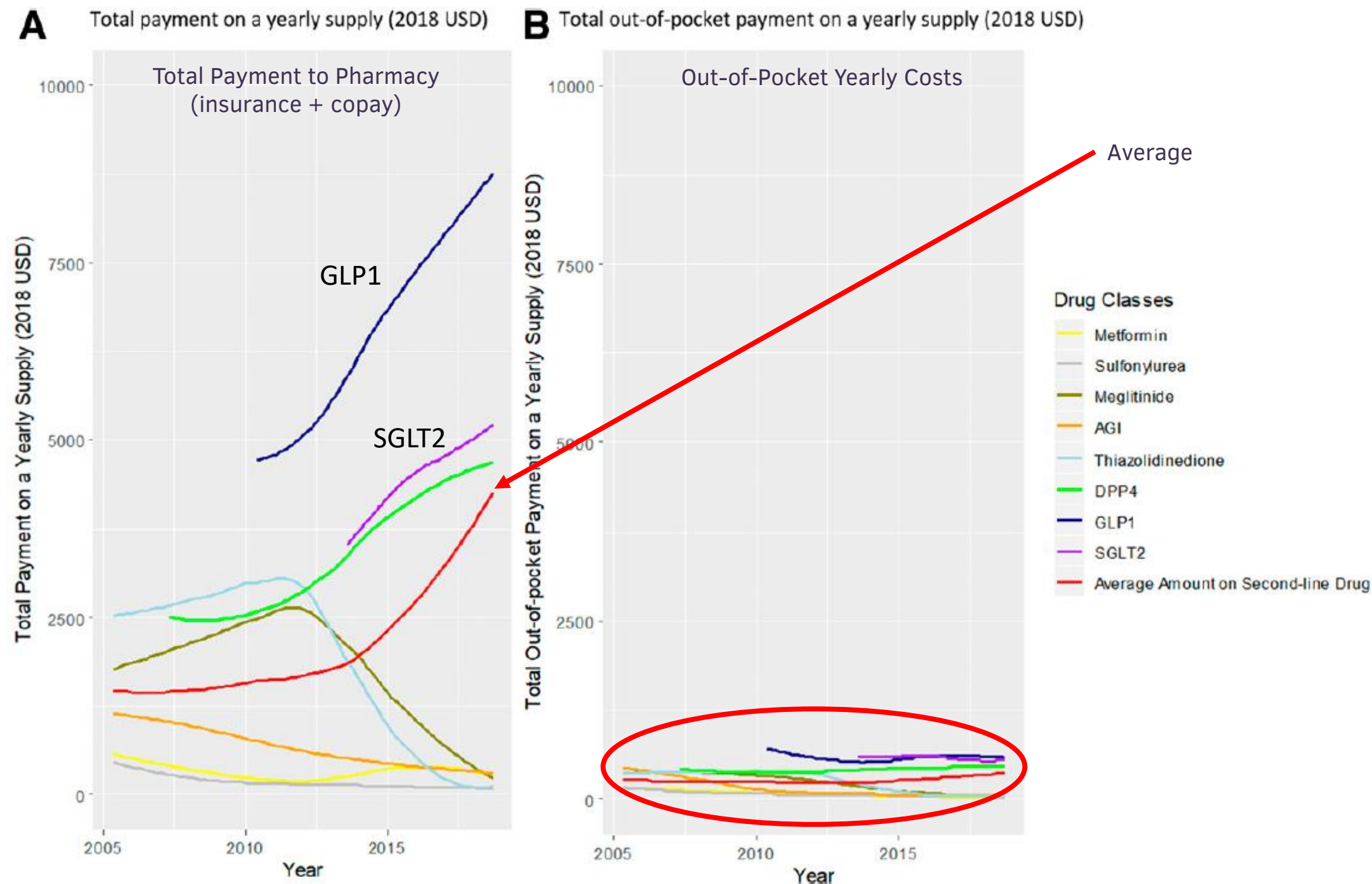




# Approach to Individualization of Glycemic Targets



# Fact to Consider: The Cost of Non-Insulin Agents



Increase in costs from the launch of DPP4i's, GLP1RAs, and SGLT2i's were 88%, 78%, and 37%, respectively, while the OOP costs were relatively stable.

Figure 3. Rates of Treatment With Sodium-Glucose Cotransporter 2 Inhibitor by Race/Ethnicity in the Cohort Over Time

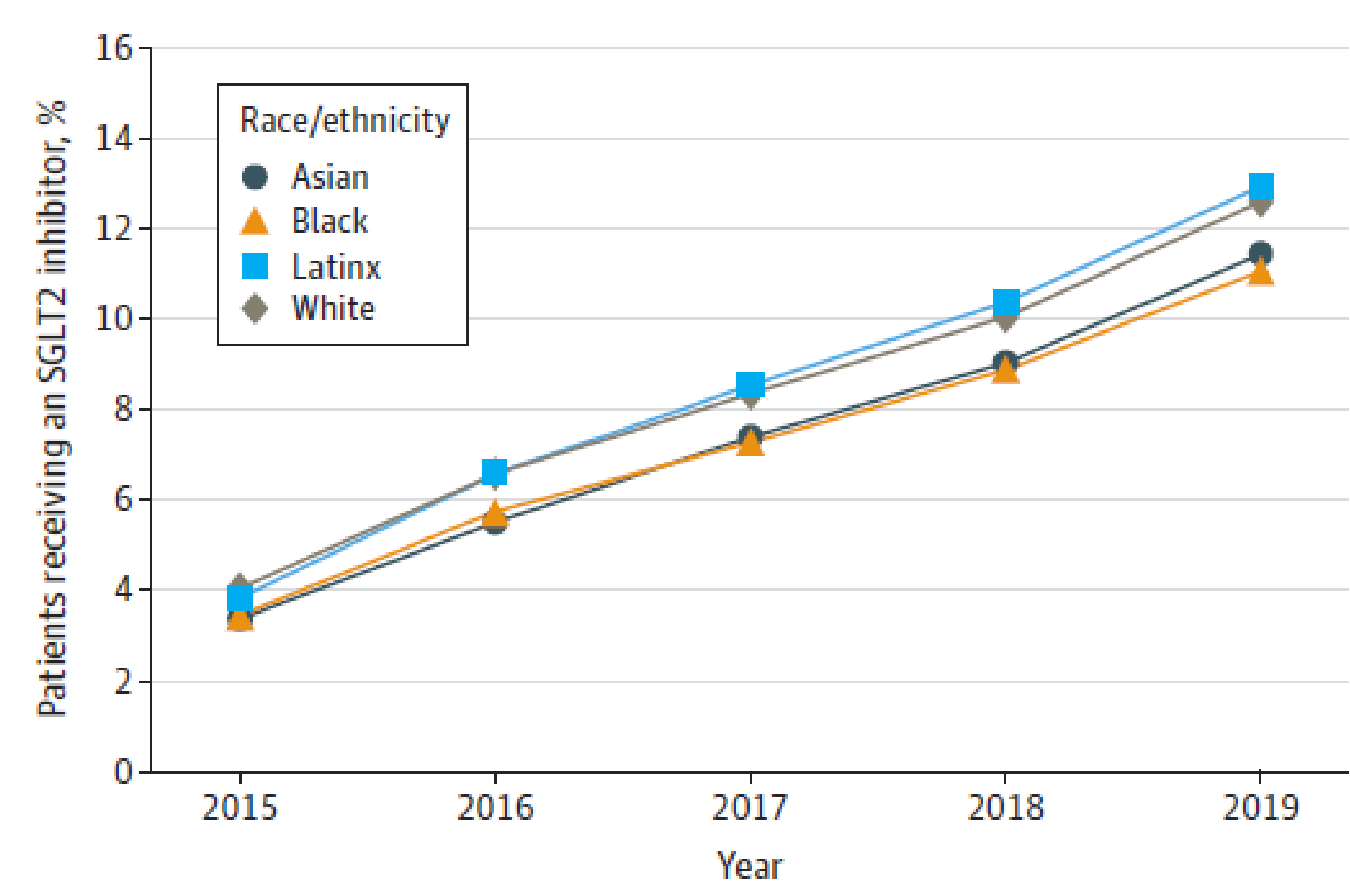
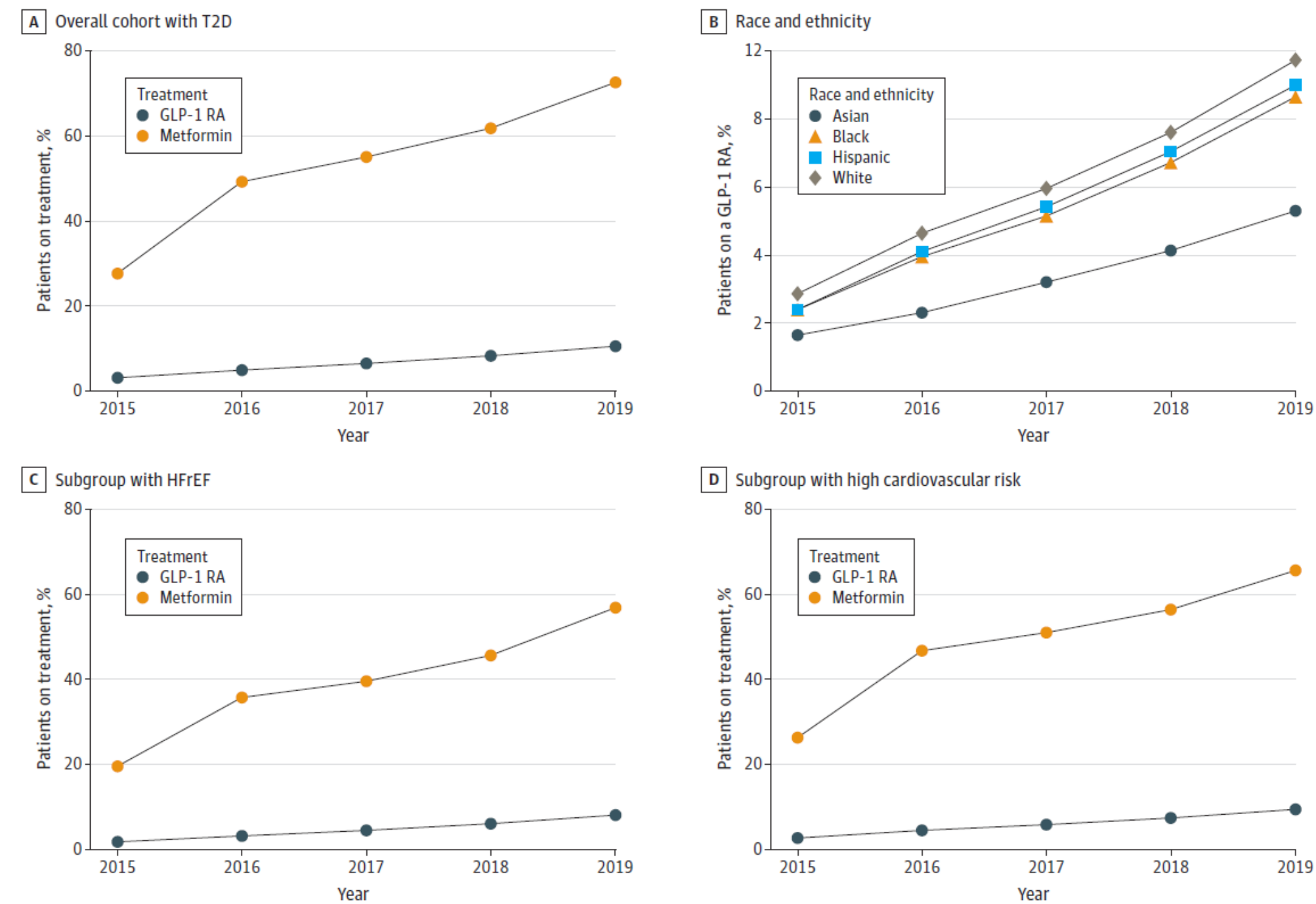


Figure 2. Accumulated Rates of GLP-1 RA Use Among a Cohort of Patients with T2D, By Race & Ethnicity and by Subgroup, 2015 to 2019





# Conclusions

- For individuals (but not populations), using HbA1c as your glycemic metric can result in problems.
  - Ideally, one should perform at least one CGM to see if there is a discordance
- The etiology of macrovascular complications is more complex than microvascular disease
- Lifestyle is still the cornerstone of T2D therapy
- Data has emerged that for HF, CKD, and ASCVD, SGLT2i's and GLP1i's should be used early in therapy.
- Glycemic goals (TIR or HbA1c) need to be individualized.
  - When hypoglycemic agents are required, the fundamental goal is as low as possible without disabling hypoglycemia.

# Cardiometabolic teleECHO™ Clinic

## Patient Recommendation Form



**Presentation Date:** April 6 20022      **Presenter name:** Peter Berberian, MD

**Presenter Facility:** Sea Mar Community Health Clinic

- **Recap:** 55 y/o Latino male with type 2 DM, obesity (BMI 43), h/o severe covid and pulmonary fibrosis on home oxygen, hypertensive heart disease wo CHF, hypertriglyceridemia, microalbuminuria with normal creatinine and a h/o PE. On 8-12 units of prandial insulin and 40 units of basal insulin. Dulaglutide was attempted to prescribe but not received
1. In a non-judgement way, assess the total insulin dose and review nutritional intake and any barriers such as cost or schedule to insulin dosing
  2. Request personal CGM for this patient as they meet the criteria
  3. Ensure patient is rotating sites and is attempting to use insulin “naïve” site to ensure good absorption
  4. Stop sitagliptin and convert metformin to 750mg XR 2 in the morning
  5. Add liraglutide 0.6mg daily per his formulary and increase every 7-10 days to goal of 1.8mg
  6. Two choices for insulin:
    - Increase to 14 units with meals and continue 40 units basal insulin. Continue to titrate prandial insulin by 2-3 units once on max dose of liraglutide
    - Consider Novolog 70/30 mixed insulin prior to breakfast and dinner 45 -50 units(34-37 basal/ 13-15 units prandial) in order to min number of injection a day. Once on max dose of liraglutide, if needed titrate by 4 units and 5 units Novolog with lunch for sugars >150. (This helps him meet the 3 or more injections of daytime insulin criteria)
  7. Consider SGLT-2I in future given microalbuminuria and CV disease

Nicole Ehrhardt, MD

Nicole Ehrhardt

Physician Signature Nicole ehrhardt

PLEASE NOTE that Project ECHO® case consultations do not create or otherwise establish a provider-patient relationship between any UW or ECHO clinician and any patient whose case is being presented in a Project ECHO® setting