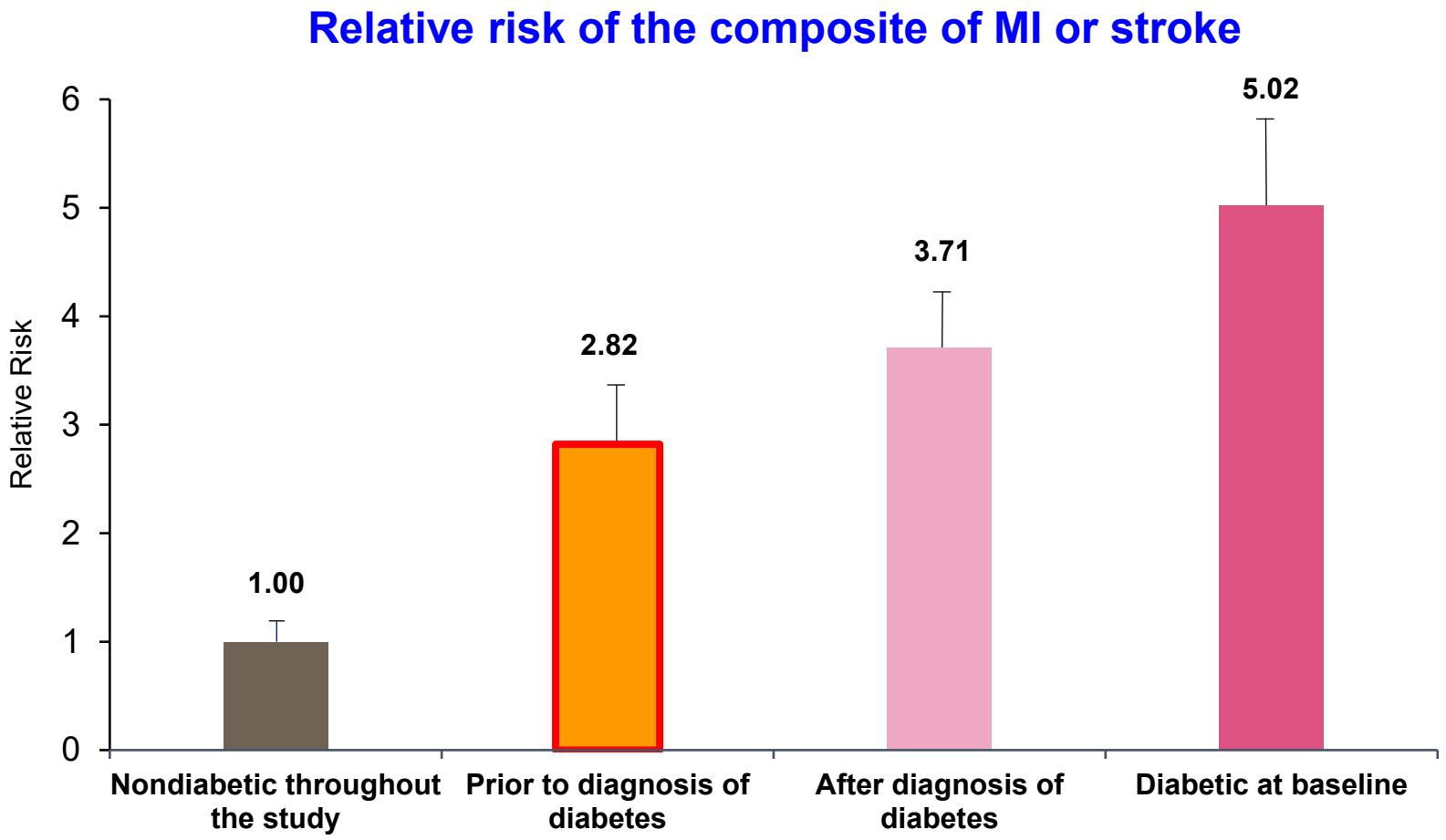
# Cardiometabolic diseases: Tackling the unmet need in CV risk reduction

**FRANCESCO GIORGINO, M.D., PH.D.**

PROFESSOR OF ENDOCRINOLOGY, UNIVERSITY OF BARI ALDO MORO
SENIOR VICE PRESIDENT, EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES (EASD)


# There is a Substantially Elevated Risk of CVD Even Prior to Clinical Diagnosis of Type 2 Diabetes

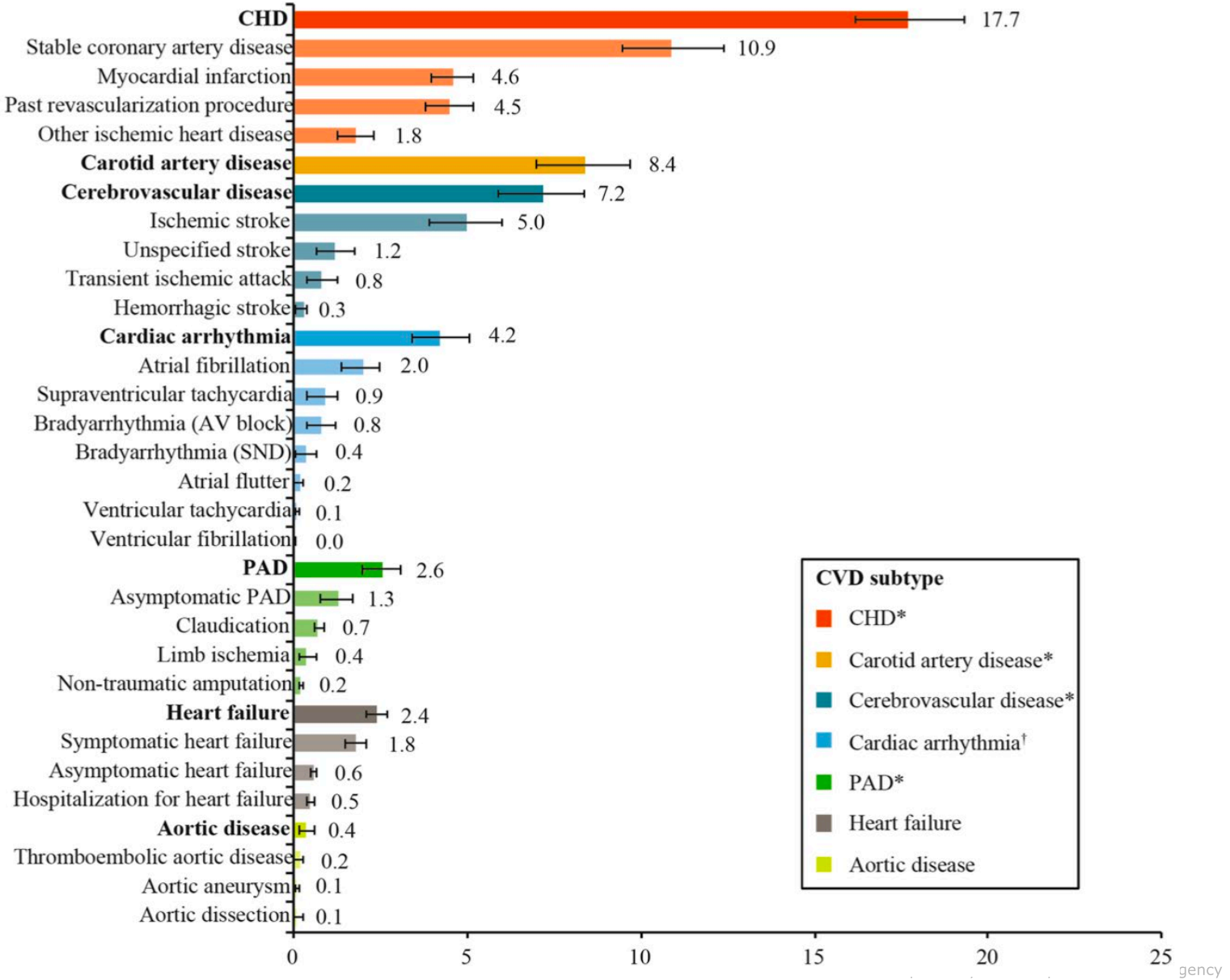
117,629 female nurses without diagnosed CVD at baseline were followed for 20 years; of these, 1508 had Type 2 diabetes at baseline.




CVD, cardiovascular disease; MI, myocardial infarction

Hu F, et al. *Diabetes Care* 2002; 25:1129–1134

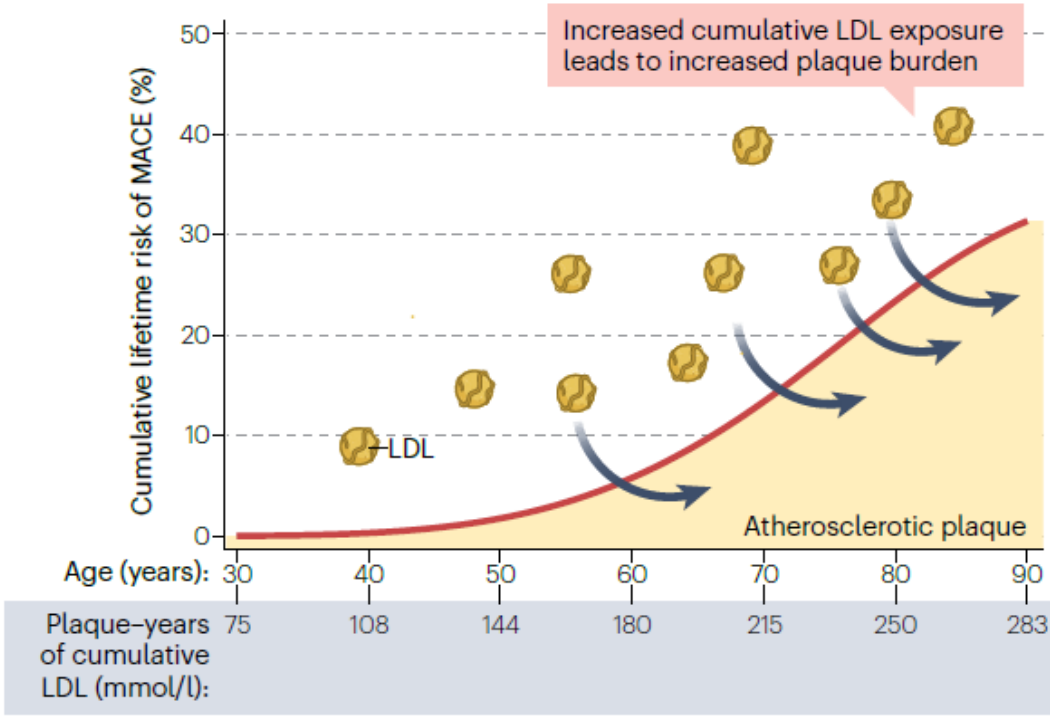
# Worldwide Prevalence and Subtypes of CV Complications in T2D CAPTURE study - 2019

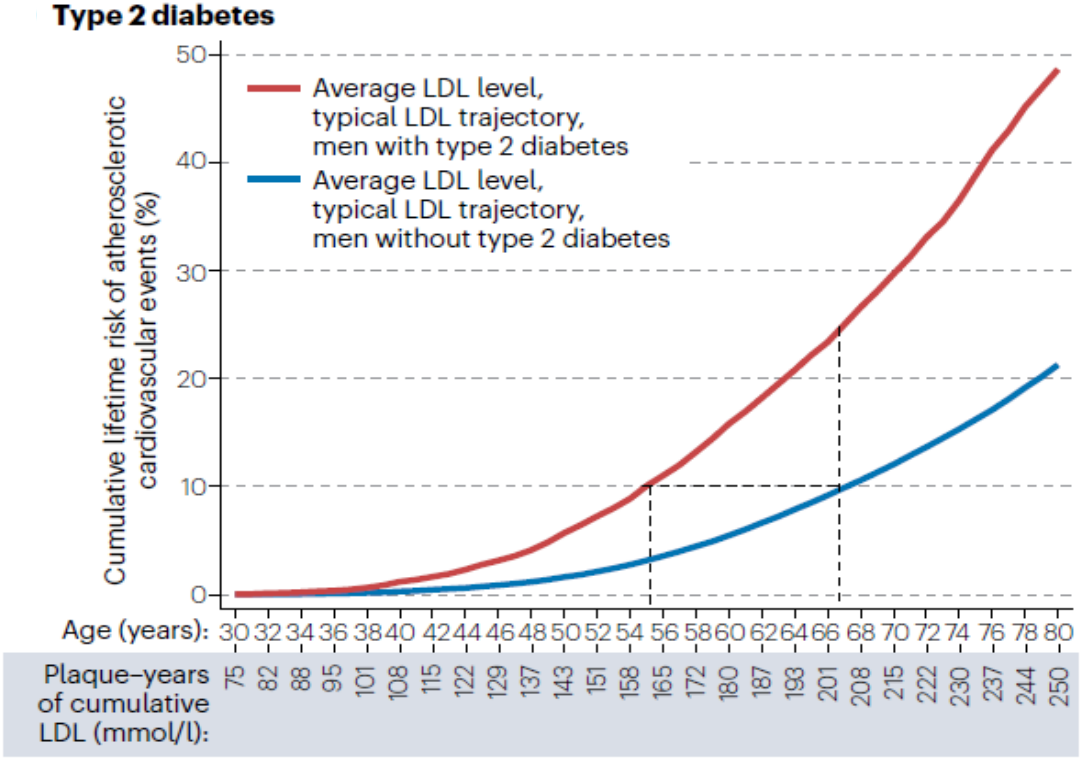



- Non-interventional, cross-sectional study
- 13 countries (Australia, China, Japan, Czech Republic, France, Hungary, Italy, Argentina, Brazil, Mexico, Israel, Kingdom of Saudi Arabia, Turkey)
- N=9832 T2D adults
- Median diabetes duration 10.7 years
- Median HbA1c 7.3%
- Overall CVD 34.8%

Mosenzon O et al. *Cardiovasc Diabetol* 2021

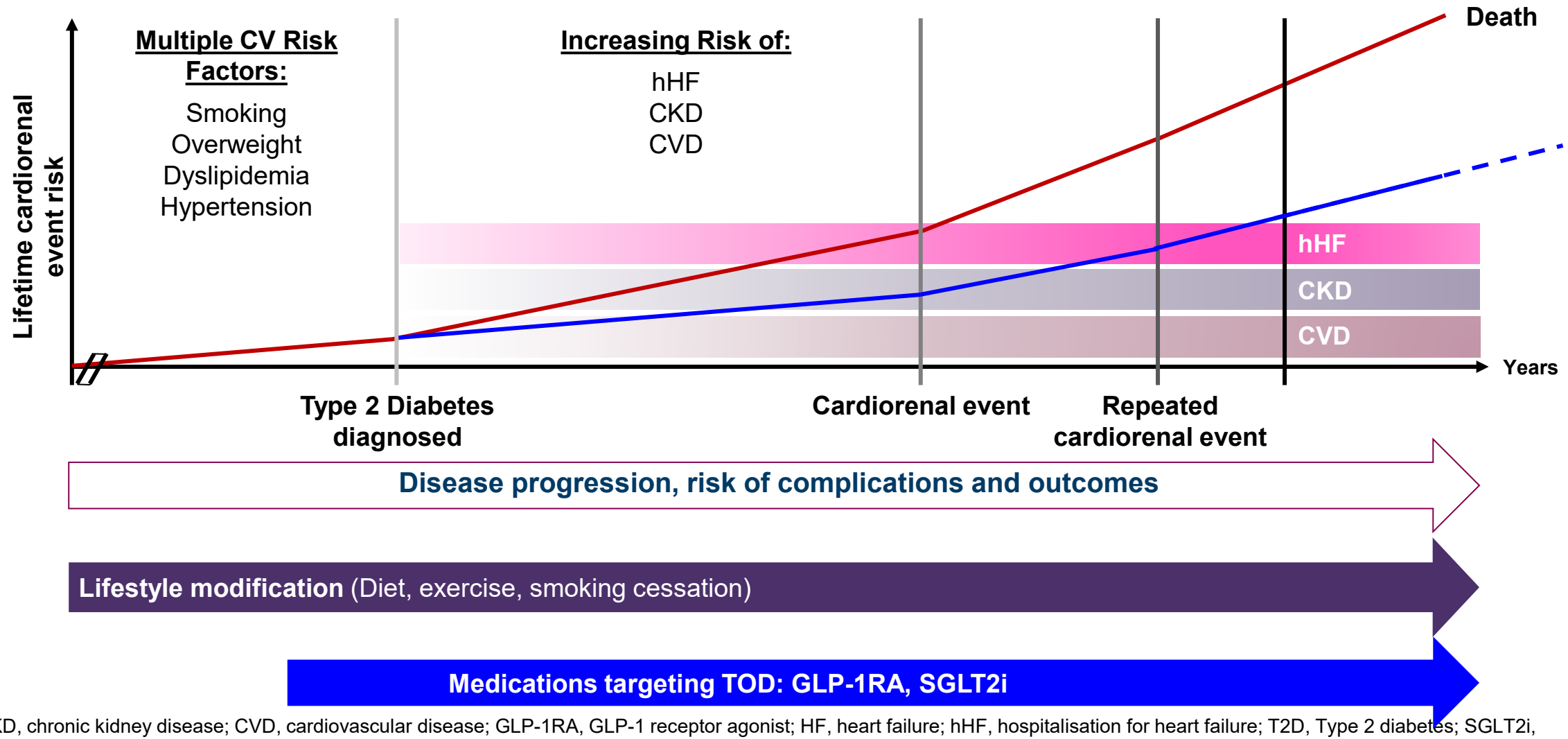
# In People with Type 2 Diabetes, the Cumulative Lifetime Risk of ASCVD Events Is Higher than in People without Diabetes




Ference BA, Braunwald E, Catapano AL. *Nat Rev Cardiol.* 2024 Oct;21(10):701-716

# Prevention and Treatment of Cardiorenal Events in T2D




CKD, chronic kidney disease; CVD, cardiovascular disease; GLP-1RA, GLP-1 receptor agonist; HF, heart failure; hHF, hospitalisation for heart failure; T2D, Type 2 diabetes; SGLT2i, sodium-glucose transporter inhibitor; TOD; target organ damage.

adapted from **Giorgino F, et al., Diabetes Obes Metab 2020**

# Cardiovascular and Kidney Outcomes and Mortality With Long-Acting Injectable and Oral GLP-1 RA in Type 2 Diabetes: A Systematic Review and Meta-analysis of Randomized Trials

**Do long-acting glucagon-like peptide 1 receptor agonists, including subcutaneous and oral formulations, improve cardiovascular and kidney outcomes and mortality in type 2 diabetes?**

Systematic review & meta-analysis of randomized placebo-controlled trials including new data from SOUL & FLOW

**Major adverse cardiovascular events***

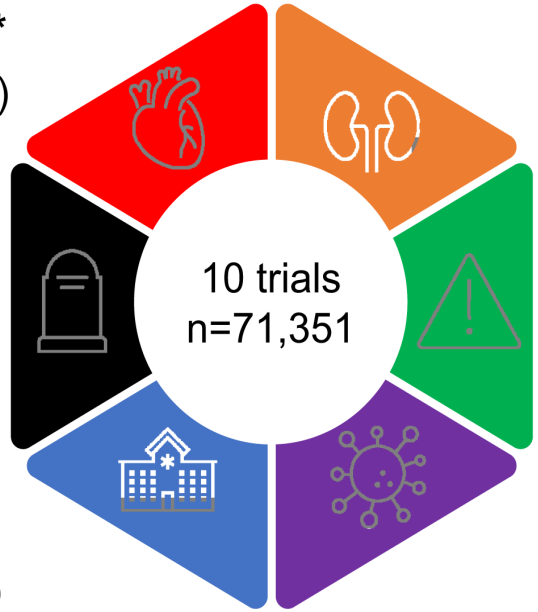
↓ 14% (HR 0.86; 95% CI 0.81, 0.90)

**All-cause mortality***

↓ 12% (HR 0.88; 95% CI 0.82, 0.93)

**Hospitalization for heart failure***

↓ 14% (HR 0.86; 95% CI 0.79, 0.93)




**Composite kidney outcome***

↓ 17% (HR 0.83; 95% CI 0.75, 0.92)

**Safety outcomes**

↔ severe hypoglycemia, retinopathy, pancreatitis

**Safety outcomes (cancers)**

↔ total cancer, pancreatic cancer, any thyroid cancer

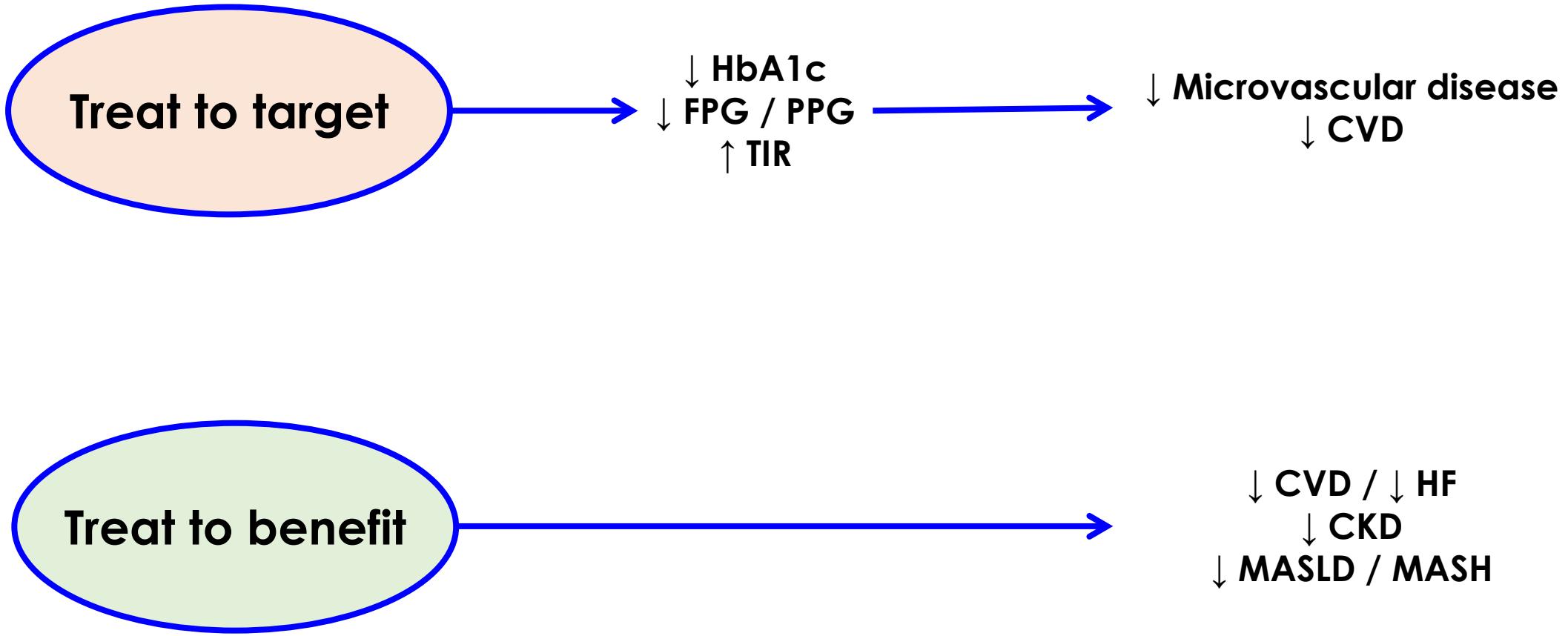
*No significant heterogeneity by drug route (subcutaneous vs. oral)

*PROSPERO registration number: CRD42024607253*



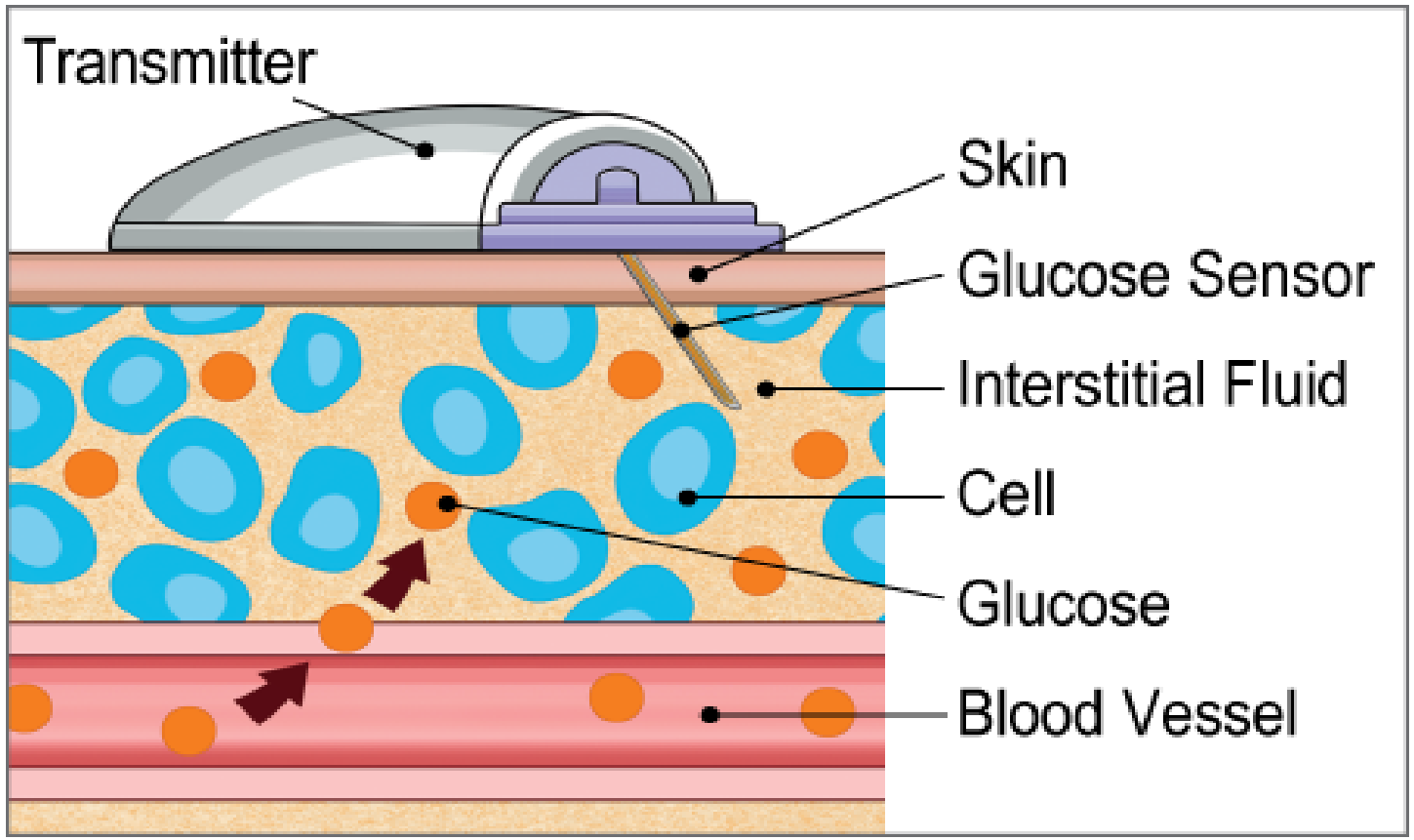
Lee MMY, et al., *Diabetes Care*. 2025

# Evolution in Type 2 Diabetes Therapy




CKD, chronic kidney disease; CVD, cardiovascular disease; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HF, heart failure; PPG, postprandial glucose; TIR, time in range

# CGM and FGM Read Interstitial Glucose

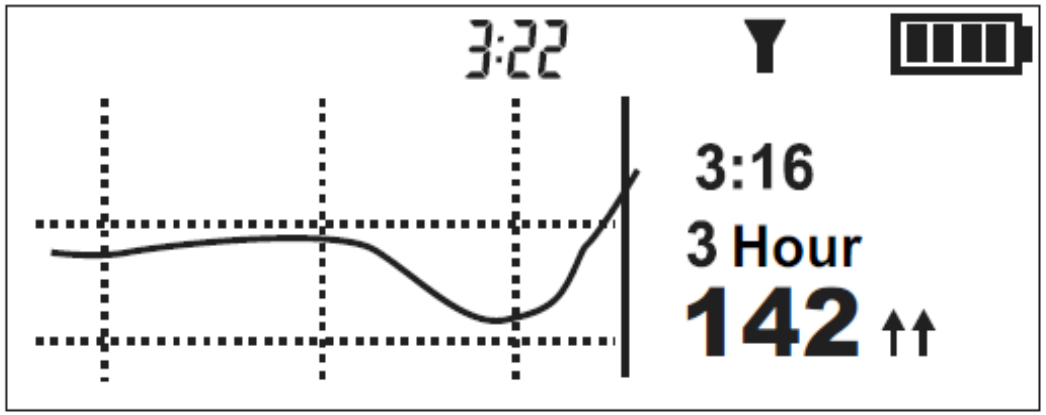


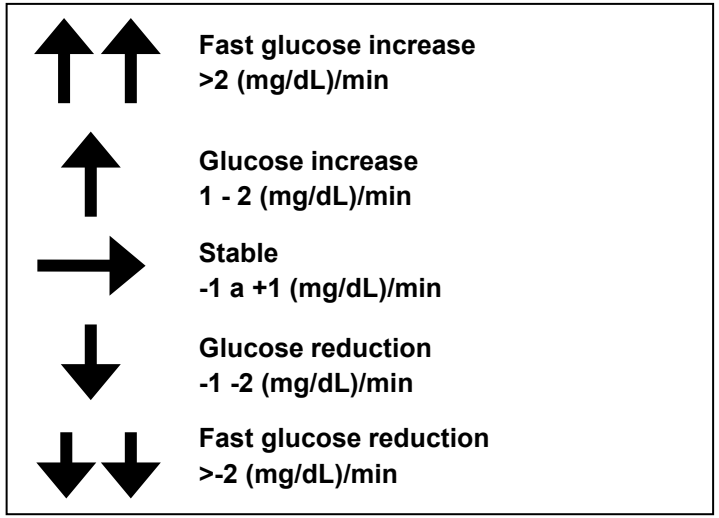

Calibration is needed to convert bioelectric signals in glucose concentration values

A variable lag time (10+ min) is required for blood glucose to reach interstitial fluid

# Interstitial Glucose Sensors

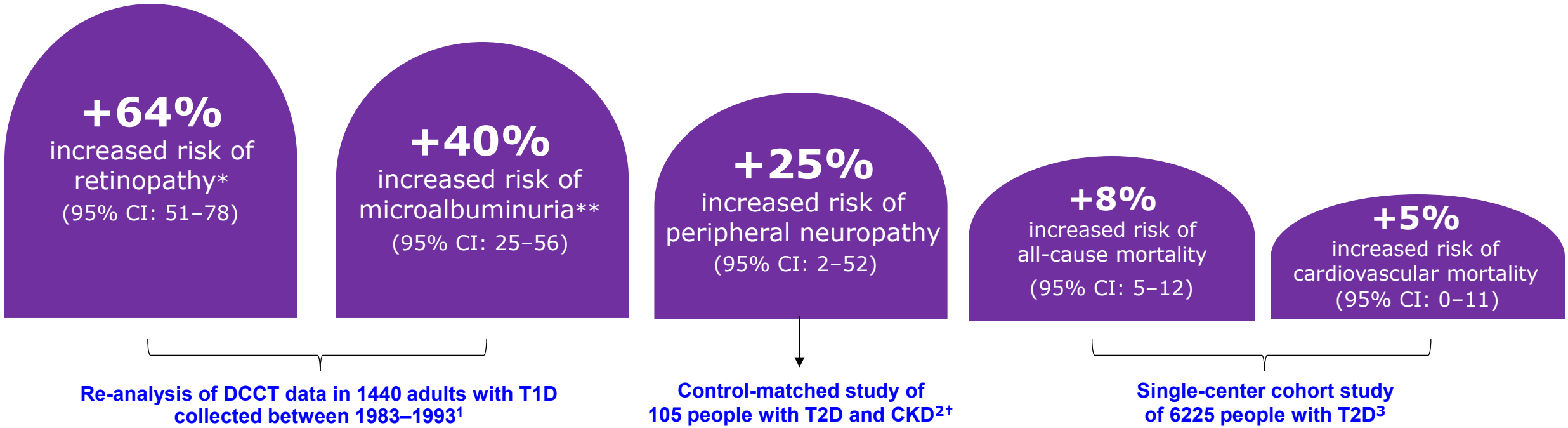
- Actual glucose values *(every 1-5 min)*
- Glucose trends *(graphs)*
- Glucose variation *(arrows)*



# Time-in-Range as a Predictor of Long-Term Complications of Diabetes

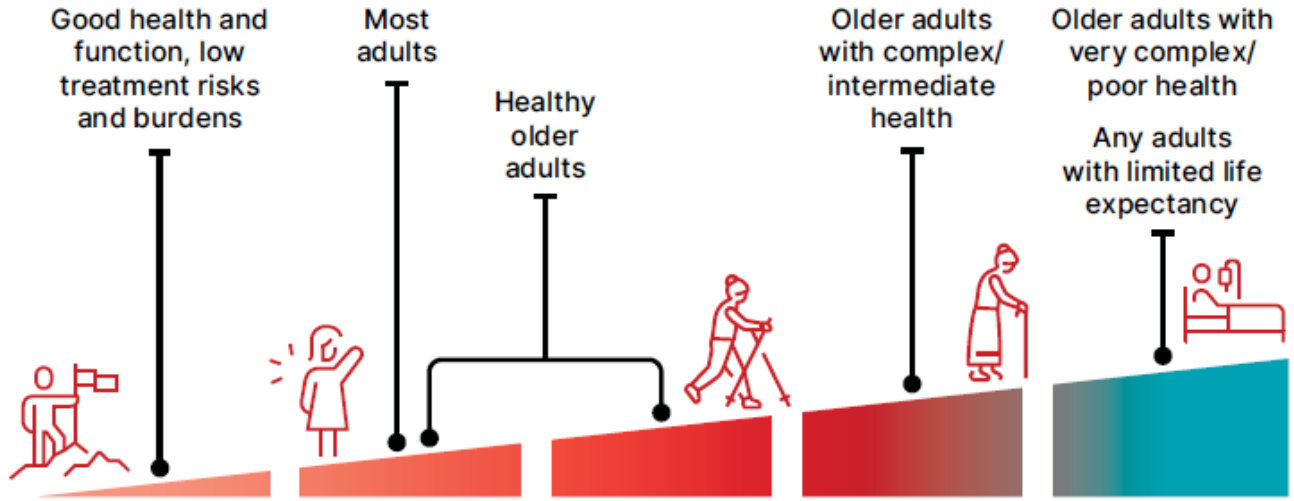
**Each 10% drop-in time-in-range (TIR) was associated with increased frequency of:**




*For assessment of retinopathy, DCCT definitions of primary prevention were used: no retinopathy at baseline (n=726) and retinopathy at baseline (n=714). **For assessment of microalbuminuria, 1283 participants with an AER <30 mg/24 h were included in the analysis. †Out of 105 participants, 81 were participations with moderate-to-severe CKD (eGFR <60 ml/min/1.73m$^2$) and 23 were matched control participants with eGFR ≥ 60 ml/min/1.73m$^2$. ‡HR: 0.54 (CI: 0.40–0.73), for time to first severe hypoglycemia when TIR is >70% (vs TIR ≤50%); HR: 0.60 (CI: 0.43–0.85), for time to first microvascular complication when TIR is >70% (vs TIR ≤50%); HR: 0.69 (CI: 0.52–0.91), for time to first MACE when TIR is >70% (vs TIR ≤50%). CI, confidence interval; CKD, chronic kidney disease; DCCT, Diabetes Control and Complications Trial; MACE, major adverse cardiac events.

1. Beck RW, et al. *Diabetes Care* 2019;42:400–5; 2. Mayeda L, et al. *BMJ Open Diab Res Care* 2020;8:e000991; 3. Lu J, et al. *Diabetes Care* 2021;44:549–55; 4. Bergenstal R, et al. Presented at ADA 2020 (21-LB).

# Individualized Glycemic Goals for Nonpregnant Adults




| A1C goals | <6.5% | <7.0% | <7.5% | <8.0% | No A1C goal |
|---|---|---|---|---|---|
| **CGM goals TIR:** | — | >70% | — | >50% | — |
| • TBR <70 | — | <4% | — | <1% | <1% |
| • TBR <54 | — | <1% | — | <1% | <1% |
| • TAR >180 | — | <25% | — | <50% | Avoid symptomatic hyperglycemia |
| • TAR >250 | — | <5% | — | <10% | |

**Modifying Factors**

| Favor more stringent goal | Favor less stringent goal |
|---|---|
| Short diabetes duration | Long diabetes duration |
| Low hypoglycemia risk | High hypoglycemia risk |
| Low treatment risks and burdens | High treatment risks and burdens |
| Pharmacotherapy with cardiovascular, kidney, weight, or other benefits | Pharmacotherapy without nonglycemic benefits |
| No cardiovascular complications | Established cardiovascular complications |
| Few or minor comorbidities | Severe, life-limiting comorbidities |

**ADA 2026**

*Diabetes Care 2026*

# Use of Glucose-lowering Medications in the Management of Type 2 Diabetes


**ADA-EASD 2026 Consensus**

## GOAL: PREVENT LONGITUDINAL COMPLICATIONS ASSOCIATED WITH T2D

**Incorporate SGLT2i or/and GLP-1-based therapy§ early to modify disease and complication risk***

***PERSONALISE APPROACH***

### Achieve and maintain glycaemic goals

Treatment plan that provides adequate EFFICACY to achieve and maintain glycaemic treatment goals, including combination therapy

**Efficacy for glucose lowering**

- **Very high:** tirzepatide, semaglutide (sq), dulaglutide (high dose), insulin, combination therapy
- **High:** GLP-1RA (not listed above), metformin, pioglitazone, SGLT2i, sulfonylurea
- **Intermediate:** DPP-4i, alpha glucosidase inhibitors

If glycaemia is above goal or significant hypoglycaemia, consider technology (e.g., CGM) to identify therapeutic gaps and tailor therapy

### Weight management

**Achieve and maintain weight management goals:**

Set individualised weight management goals

General lifestyle

Intensive evidence-

### +ASCVD

**+ASCVD/indicators of high CVD risk**

GLP-1-based therapies§ with proven CVD benefit and/or SGLT2i with proven CVD benefit‡

- For individuals on GLP-1-based therapy§, consider adding SGLT2i with proven CVD benefit or vice versa based on indication
- Pioglitazone

### +CKD†

**+CKD**

SGLT2i with primary evidence of reducing CKD progression and/or GLP-1-based therapy§ with proven CKD benefit‡

For individuals on SGLT2i, consider incorporating an GLP-1-based therapy§ or vice versa based on indication

### +HF

**+HFrEF or HFpEF**

SGLT2i with proven HF benefit

**+HFpEF and obesity**

SGLT2i and/or GLP-1-based therapy§‡

### +MASLD or MASH

**Agents with proven or potential benefit in MASLD or MASH**

- GLP-1-based therapy§ and/or pioglitazone
- SGLT2i

Use insulin in the setting of decompensated cirrhosis

### +CKD†

**+CKD**

SGLT2i with primary evidence of reducing CKD progression and/or GLP-1-based

### +HF

**+HFrEF or HFpEF**

SGLT2i with proven HF benefit

**+HFpEF and obesity**

SGLT2i and/or GLP-1-based therapy§‡

### +MASLD or MASH

**Agents with proven or potential benefit in MASLD or MASH**

- GLP-1-based therapy§ and/or pioglitazone
- SGLT2i

Use insulin in the setting of decompensated cirrhosis

* Use combination therapy based on target achievement and individual CVD and CKD

† eGFR <60 mL/min/1.73 m² and/or albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). Repe

‡ While evidence does not suggest simultaneous introduction of a GLP-1-based therapy with SGLT2i, evidence indicates that each will have benefit toward outcome risk reduction.

§ Includes GLP-1 RA and Dual GLP-1/GIP agonist, tirzepatide.

- Continuous glucose monitor; DMES - Diabetes self-management education and

served ejection fraction; HFrEF - Heart failure with reduced ejection fraction;

MASH - Metabolic dysfunction-associated steatohepatitis; MASLD - Metabolic dysfunction-associated steatotic liver disease; OSA - Obstructive sleep apnoea; SGLT2i - SGLT2 inhibitor; T2D - Type 2 diabetes.