# Latest Treatment Strategies for Type 2 Diabetes and Cardiovascular Disease

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# Cardiovascular Risk and Diabetes

Type 2 Diabetes (T2D) is a significant risk factor for cardiovascular disease (CVD)

- Cardiovascular complications are *main cause of mortality* in T2D patients
- The Emerging Risk Factors Collaboration: Diabetes and CVD

  N=698,782; 102 prospective studies; 52,765 events

  - Cardiovascular heart disease death HR = 2.31
  - Non-fatal myocardial infarction HR = 1.82
  - Ischemic cerebral vascular accident HR = 2.27
  - Hemorrhagic cerebral vascular accident HR = 1.84
- Duration of diabetes is associated with higher risk of cardiovascular disease
- Diabetes + CV disease (MI or CVA) reduces life expectancy

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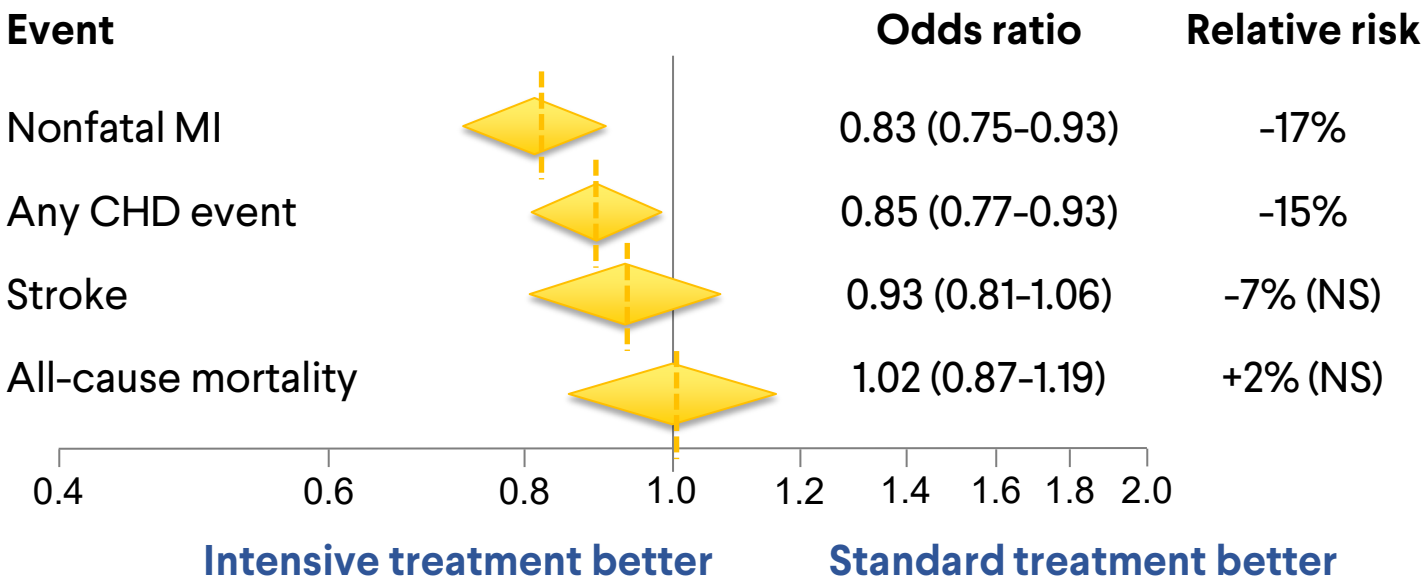
# Prior Landmark Clinical Trials: Intensive Glucose Control and Macrovascular Risk in T2D

**Meta-analysis of Five Prospective RCTs Assessing Effect of Intensive Glucose Lowering on CV Outcomes (ACCORD, ADVANCE, PROactive, UKPDS, VADT)**




Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials. Lancet. 2009 May 23;373(9677):1765-7.

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# Macrovascular Risk Reduction in Type 2 Diabetes

- Hypertension control
- Dyslipidemia control
- Smoking cessation
- Glycemic control
- Aspirin therapy
- Lifestyle modification
- Weight loss

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# Cardiovascular Risk and Diabetes

- Intensive vs. conventional glucose control in older studies did not reduce short term all-cause, CV or non-CV mortality
  - Lowering HbA1c below conventional targets did not confer CV benefit
  - Intensive control confirmed reduction in microvascular disease
- Newer diabetes drugs (SGLT-2 inhibitor and GLP-1 receptor analogs) have consistently shown cardiovascular and renal protection in large cardiovascular outcome trials
- Individualized diabetes management approach is important for:
  - HbA1c lowering
  - Microvascular risk reduction (nephropathy, retinopathy, neuropathy)
  - Macrovascular risk reduction (ASCVD, Heart failure, diabetic kidney disease)

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# Pharmacologic Treatment for T2D

Two classes of newer DM2 therapy with added cardiovascular benefits.

- **Sodium-Glucose CoTransporter 2 (SGLT2) Inhibitors**
- **Glucagon-Like Peptide 1 (GLP-1) Receptor Agonists**

- Each will be reviewed for:
  - Mechanism
  - Summary of CV outcome trials (CVOT)
  - Benefits
  - Adverse effects
  - Dosing

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# Pharmacologic Treatment for T2D With Existent Cardiovascular Disease

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## SGL T2 inhibitors:

- Canagliflozin
- Empagliflozin
- Dapagliflozin
- Ertugliflozin

## Human analog GLP-1 RA:

- Liraglutide
- Dulaglutide*
- Semaglutide
- Albiglutide (off the market)

*Only drug with primary prevention indication

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# Medications for T2D with CV Benefit

| SGLT2 Inhibitors | GLP-1 RAs |
|---|---|
| Oxidative stress-induced endothelial cell dysfunction | Oxidative stress-induced endothelial cell dysfunction |
| Inflammation and atherogenesis | Inflammation and atherogenesis |
| Glucose lowering effect | Glucose lowering effect |
| Natriuretic / diuretic effect | Natriuretic / diuretic effect |
| RAAS effect | RAAS effect |
| Uriscosuric effect | |
| Beta hydroxybutyrate increase | |

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# SGLT2 Inhibitors Benefits

- Improved Glycemia
  - Rare hypoglycemia
- Weight loss
  - Average weight loss of 1-3 kg
- ↓ Blood pressure
- ↓ Triglycerides
- Oral route
- Cardiac and renal protection

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# Cardiovascular Safety Studies

| | | Previous CVD% |
|---|---|---|
| SGLT2 Inhibitors | | |
| EMPA-REG OUTCOME | Empagliflozin | 99 |
| CANVAS | Canagliflozin | 65 |
| DECLARE TIMI 58 | Dapagliflozin | 40 |
| CREDENCE (renal study) | Canagliflozin | 50 |
| VERTIS | Ertugliflozin | 73 |
| GLP-1RAs | | |
| ELIXA | Lixisenatide | 100 |
| LEADER | Liraglutide | ~81 |
| SUSTAIN-6 | Semaglutide | ~83 |
| EXSCEL | Exenatide | 73 |
| Harmony Outcomes | Albiglutide | 100 |
| REWIND | Dulaglutide | 31 |
| PIONEER 6 | Oral semaglutide | 35 |

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# SGLT2 Inhibitors

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## Mechanisms for Cardioprotection

- Reduce preload and afterload segment
- Improved profile of anti-inflammatory vs. pro-inflammatory cytokine
- Reduced cardiac fibrosis
- Increased hematocrit and erythropoietin production
- Increased cardiac metabolic efficiency

## Mechanisms for Renoprotection

- Glycosuria
- Natriuresis
- Decreased glomerular pressure
- Reduced albuminuria

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# Physiological Effects of SGLT2 Inhibitors

Selectively blocks the transporter responsible for > 90% of glucose reabsorption in the nephron (SGLT2).

- This results in reduced absorption of glucose and sodium, leading to glycosuria and natriuresis.
- Greatest rate of glycosuria occurs during periods of hyperglycemia.
- Risk for hypoglycemia is not significant

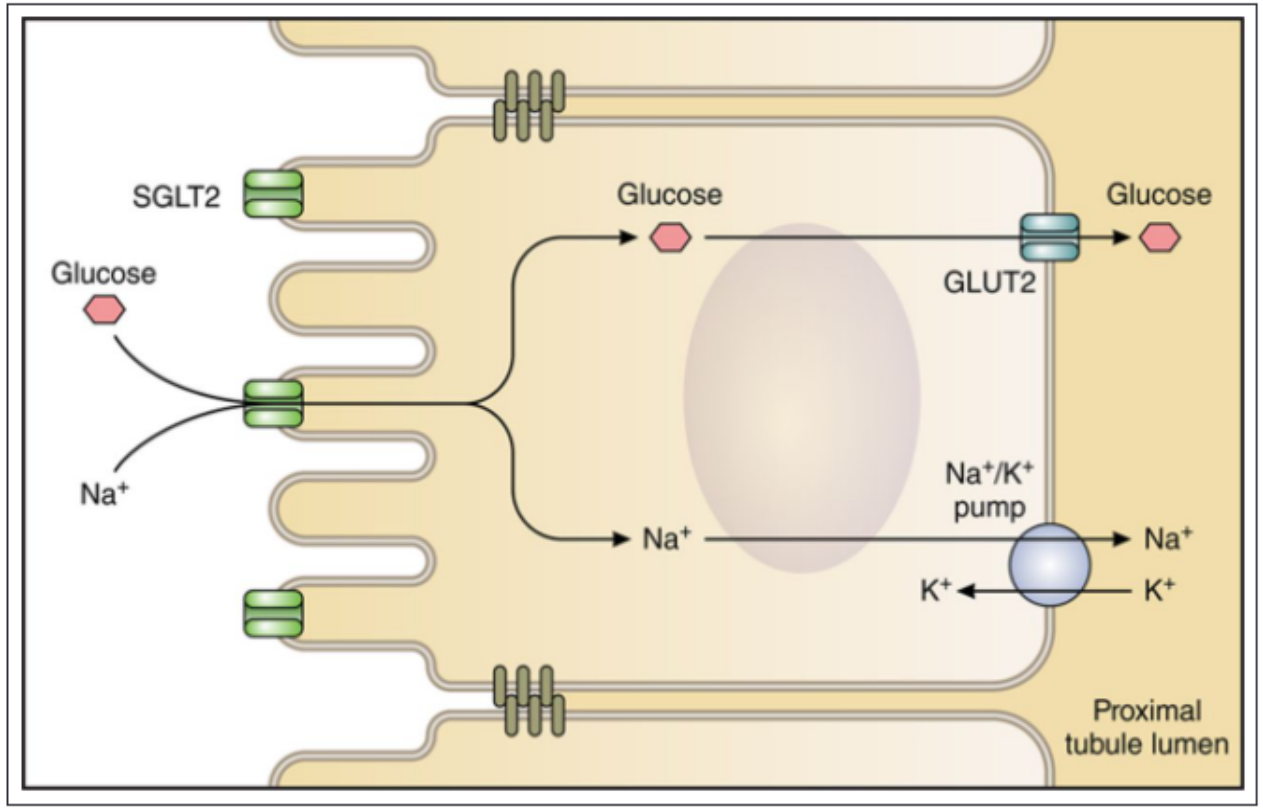


**Figure 1. The sodium-glucose cotransporter-2 (SGLT2) mechanism in the proximal tubule.** Modified from Bakris et al[4] with permission of the publisher. Copyright © 2009, Elsevier.

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# SGLT2 inhibitors: Summary of CV Outcome Trials

| | MACE HR (95%CI) | CV Death HR (95%CI) | HHF HR (95%CI) |
|---|---|---|---|
| **EMPA-REG (empagliflozin)** | 0.86 (0.74-0.99) | 0.62 (0.49-0.77) | 0.65 (0.50-0.85) |
| **CANVAS (canagliflozin)** | 0.86 (0.75-0.97) | 0.87 (0.72-1.06) | 0.67 (0.52-0.87) |
| **DECLARE-TIMI (dapagliflozin)** | 0.93 (0.84-1.03) | 0.98 (0.82-1.17) | 0.73 (0.61-0.88) |
| **VERTIS-CV (ertugliflozin)** | 0.97 (0.85-1.11) | 0.92 (0.77-1.11) | 0.70 (0.54-0.90) |

MACE = composite of death from CV cause, nonfatal MI and nonfatal stroke; CV death = cardiovascular death; HHF = hospitalization for heart failure

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# SGLT-2 inhibitors in Patients with Proteinuria

| | Canagliflozin (CREDENCE) | Dapagliflozin (DAPA-CKD) |
|---|---|---|
| Proportion without diabetes | 0% | 32% |
| Duration | 2.6 years | 2.4 years |
| Primary Outcome Composite Components | Hemodialysis, GFR‹15, Doubling in Creatinine, Renal or CV death | 50% GFR reduction ESKD, Renal or CV death |
| Primary Outcome [HR (95% CI)] | 0.80 (0.67-0.95) | 0.61 (0.51-0.72) |
| Renal Composite outcome (worsening GFR, ESKD, renal death) | 0.66 (0.53–0.81) | 0.56 (0.45–0.68) |
| ESKD (HD or GFR ‹15) | 0.68 (0.54–0.86) | 0.64 (0.50–0.82) |
| CV Death or Hospitalization HF | 0.69 (0.57–0.83) | 0.71 (0.55–0.92) |
| CV death | 0.78 (0.61-1.00) | 0.81 (0.58–1.12) |
| Hospitalizations HF | 0.61 (0.47–0.80) | |
| All-cause mortality | 0.83 (0.68–1.02) | 0.69 (0.53–0.88) |

Guerron AD, Davis GM, Pasquel FJ. Advances in Pharmaco-Therapeutics, Metabolic Surgery, and Technology for Diabetes. Endocrinol Metab Clin North Am. In press.

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# SGLT-2 inhibitors in patients with heart failure and reduced ejection fraction (with and without diabetes)

| | **Dapagliflozin (DAPA-HF)** | **Empagliflozin (EMPEROR HF)** |
|---|---|---|
| Proportion without diabetes | 58% | 50% |
| Duration | 1.5 years | 1.3 years |
| Primary Outcome Composite Components | CV death, urgent visit or Hospitalization for HF | CV death or Hospitalization for HF |
| Primary Outcome [HR (95% CI)] | **0.74 (0.65 to 0.85)** | **0.75 (0.65 to 0.86)** |
| CV Death or Hospitalization HF | **0.75 (0.65 to 0.85)** | **0.75 (0.65 to 0.86**) |
| CV death | **0.82 (0.69 to 0.98)** | 0.92 (0.75 to 1.12) |
| Hospitalizations HF | **0.70 (0.59 to 0.83)** | **0.69 (0.59 to 0.81)** |
| All-cause mortality | 0.83 (0.71 to 0.97) | 0.92 (0.77 to 1.10) |

Guerron AD, Davis GM, Pasquel FJ. Advances in Pharmaco-Therapeutics, Metabolic Surgery, and Technology for Diabetes. Endocrinol Metab Clin North Am. In press.

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# SGLT2 Inhibitors: Summary of CV Outcome Trials

For T2D patients with or *without established CVD*

- Reduced hospitalization for heart failure
- Renoprotection

For T2D patients *with established CVD*

- Reduced MACE (EMPA-REG, CANVAS, CREDENCE)
- Reduced hospitalization for heart failure
- Renoprotection
- Some cases of reduced mortality (EMPA-REG, CREDENCE)

Cardiorenal benefit also shown in patients without diabetes (DAPA-CKD, DAPA-HF, EMPEROR HF) [1]

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# SGLT2 Inhibitors: Adverse Effects

- Genital mycotic infections (women › men)
- Urinary tract infections
- Polyuria
- Volume depletion/hypotension/dizziness
- ↑ LDL-C
- ↑ Creatinine (transient)
- DKA/ euglycemic DKA
- Increased rate of lower extremity amputations (seen in CANVAS, not CREDENCE)
  - CANVAS: numerically low numbers but statistically significant; 6.3 vs. 3.4%, HR 1.97 (95%CI 1.41-2.75)
- Side effect of Fournier's gangrene
- Increased risk of bone fractures

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# SGLT2 Inhibitors Dosing

- Canagliflozin (Invokana) – 100 or 300mg oral once daily
  - Dose adjust if eGFR‹ 60 mL/min/1.73m2
- Dapagliflozin (Farxiga) – 5 or 10mg oral once daily
  - Dose adjust if eGFR‹ 45 mL/min/1.73m2
- Empagliflozin (Jardiance) – 10 or 25mg oral once daily
  - Dose adjust if eGFR‹ 45 mL/min/1.73m2
- Ertugliflozin (Steglatro) – 5 or 15mg oral once daily
  - Dose adjust if eGFR‹ 60 mL/min/1.73m2

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# Glucagon-Like Peptide 1 Receptor Agonists (GLP-1RA)

Currently available drugs:

- Exenatide (Byetta, Bydureon)
- Liraglutide (Victoza)
- Lixisenatide (Adlyxin, component of Soliqua) (Available in US as a fixed ratio combination drug)
- Semaglutide (Ozempic, Rybelsus)
- Dulaglutide (Trulicity)

Mechanisms for Cardioprotection:

- GLP-1 receptor is expressed in cardiomyocytes and coronary endothelial cells
- Improved left ventricular and endothelial function

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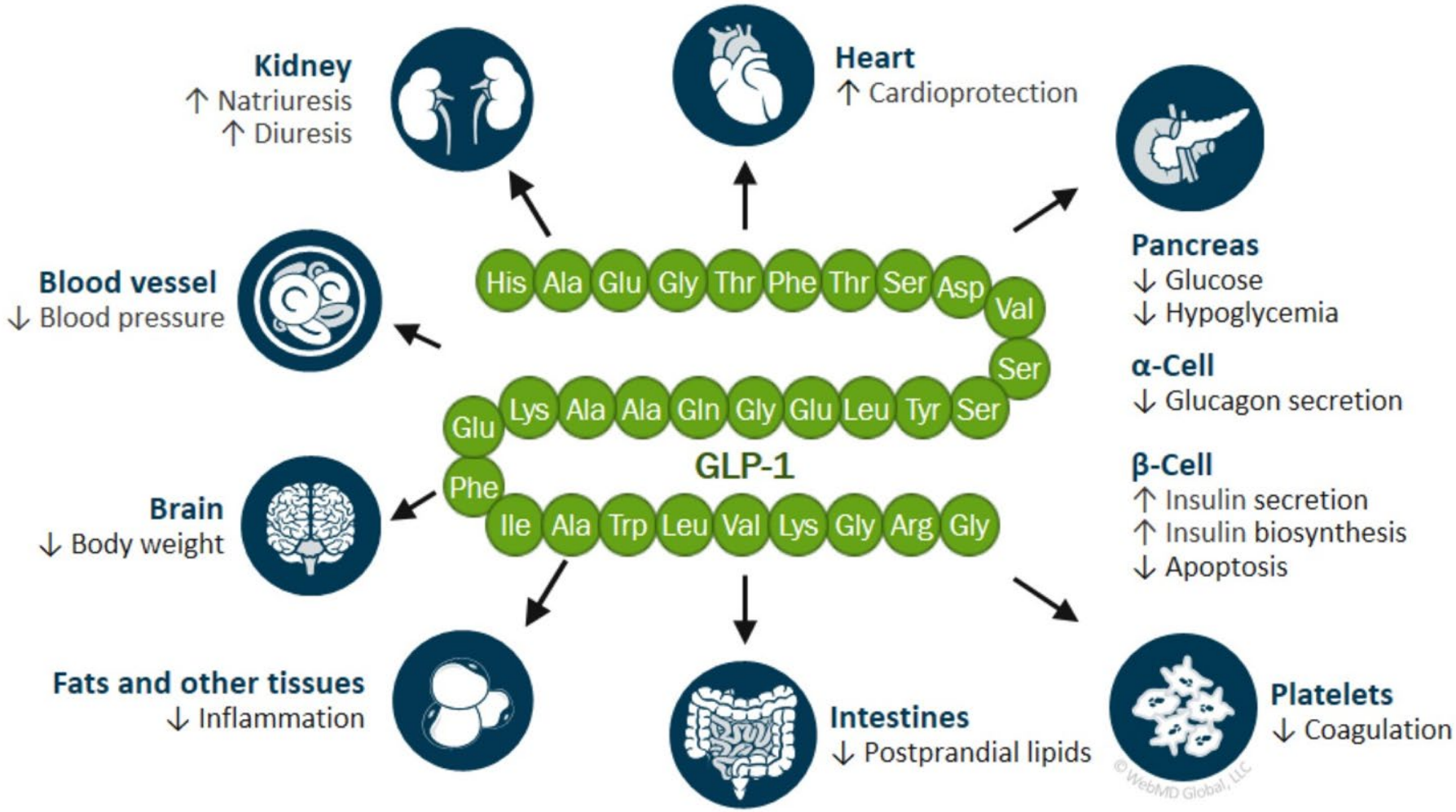
# GLP-1 RAs: Mechanism of Action




Drucker DJ. *Cell Metab.* 2016;24:15-30.

# GLP-1 RA: Summary of CV Outcome Trials

| | Lixisenatide | Liraglutide | Semaglutide | Exenatide | Albiglutide | Dulaglutide |
|---|---|---|---|---|---|---|
| MACE, HR (95% CI) | 1.02 (0.89-1.17) | **0.87 (0.78-0.97)** | **0.74 (0.58-0.95)** | 0.91 (0.83-1.00) | **0.78 (0.68-0.90)** | **0·88 (0.79-0.99)** |
| CV death, HR (95% CI) | 0.98 (0.78-1.22) | **0.78 (0.66-0.93)** | 0.98 (0.65-1.48) | 0.88 (0.76-1.02) | 0.93 (0.73-1.19) | 0·91 (0.78-1.06) |
| Fatal or nonfatal MI, HR (95% CI) | 1.03 (0.87-1.22) | 0.86 (0.73-1.00) | 0.74 (0.51-1.08) | 0.97 (0.85-1.10) | **0.75 (0.61-0.90)** | 0·96 (0.79-1.15) |
| Fatal or nonfatal stroke, HR (95% CI) | 1.12 (0.79-1.58) | 0.86 (0.71-1.06) | **0.61 (0.38-0.99)** | 0.85 (0.70-1.03) | 0.86 (0.66-1.14) | **0·76 (0.62-0.94)** |
| All-cause mortality, HR (95% CI) | 0.94 (0.78-1.13) | **0.85 (0.74-0.97)** | 1.05 (0.74-1.50) | **0.86 (0.77-0.97)** | 0.95 (0.79-1.16) | 0.90 (0.80-1.01) |
| HF hospitalization, HR (95% CI) | 0.96 (0.75-1.23) | 0.87 (0.73-1.05) | 1.11 (0.77-1.61) | 0.94 (0.78-1.13) | | 0·93 (0.77-1.12) |

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# GLP1 Receptor Agonists Summary of CV Outcome Trials

- All trials met non-inferiority
- Superiority for MACE
  - Semaglutide, liraglutide, albiglutide, dulaglutide
- Reduced ischemic events (stroke or MI)
- Renoprotection in meta-analysis (mediated by reduction in albuminuria)
- Potential benefit for heart failure hospitalization (small effect in meta-analysis)
- Mortality benefit seen only in LEADER

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# GLP1 Receptor Agonists Benefits

- ↓ Postprandial glucose excursions
- Weight loss
  - Average weight loss of 2-4 kg
- Increased satiety
- ↓ LDL-C and ↓triglycerides
- Low rate of hypoglycemia
- Cardiac and renal protection

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# GLP-1 RA: Adverse Effects

- Gastrointestinal side effects
  - Nausea, vomiting most common
  - Diarrhea
  - Association with acute gallstone disease
- ↑ Heart rate
- Acute pancreatitis
  - Risk not confirmed in CVOT

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# GLP1 Receptor Agonists: Adverse Effects

- C-cell hyperplasia/medullary thyroid tumors in animals . Do not prescribe if personal or family history of multiple endocrine neoplasia syndrome type 2.
- Increased risk of worsening retinopathy with semaglutide
  - SUSTAIN-6 trial: semaglutide vs. placebo, 3.0 vs. 1.8%, HR 1.76, 95% CI 1.11-2.78.

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# GLP1 Receptor Agonists Dosing

- Exenatide
  - Byetta - 5 or 10 mcg SC twice daily. (Not recommended for CrCl ‹30 ml/min)
  - ER formulation (Bydureon) - 2mg SC once weekly. (Not recommended with eGFR‹45 mL/min/1.73m2)
- Liraglutide
  - Victoza – 0.6, 1.2 or 1.8mg SC once daily. (Use with caution with severe renal impairment).

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# GLP1 Receptor Agonists Dosing

- Lixisenatide
  - 10-20mg SC once daily. Not recommended with eGFR‹15 mL/min/1.73m2
- Semaglutide
  - Ozempic – 0.25, 0.5, or 1.0 mg SC once weekly
  - Rybelsus – 3, 7 or 14 mg oral once daily
- Dulaglutide
  - Trulicity - 0.75, 1.5, 3.0, or 4.5 mg SC once weekly

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# Drug selection: SGLT2-i vs. GLP1-RA

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- Can begin with metformin monotherapy for T2D but consider adding GLP-1 RA or SGLT2-i independent of HbA1c target.
- Can consider beginning therapy with GLP-1 RA or SGLT2-i prior to metformin in patients with higher risk.

- **If atherosclerotic CVD or stroke predominates: Choose GLP-1 RA with proven benefit**
- **If heart failure or CKD predominates: Choose SGLT2-I with proven benefit**

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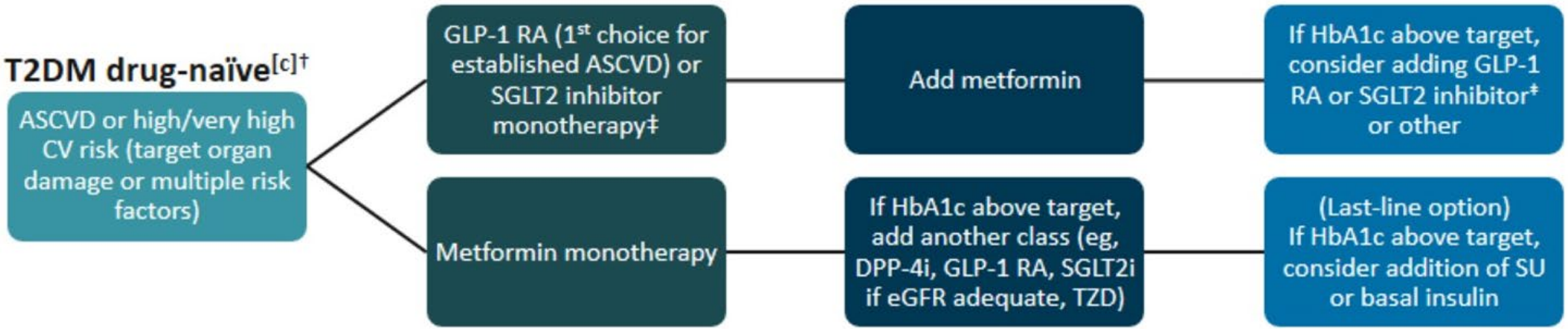
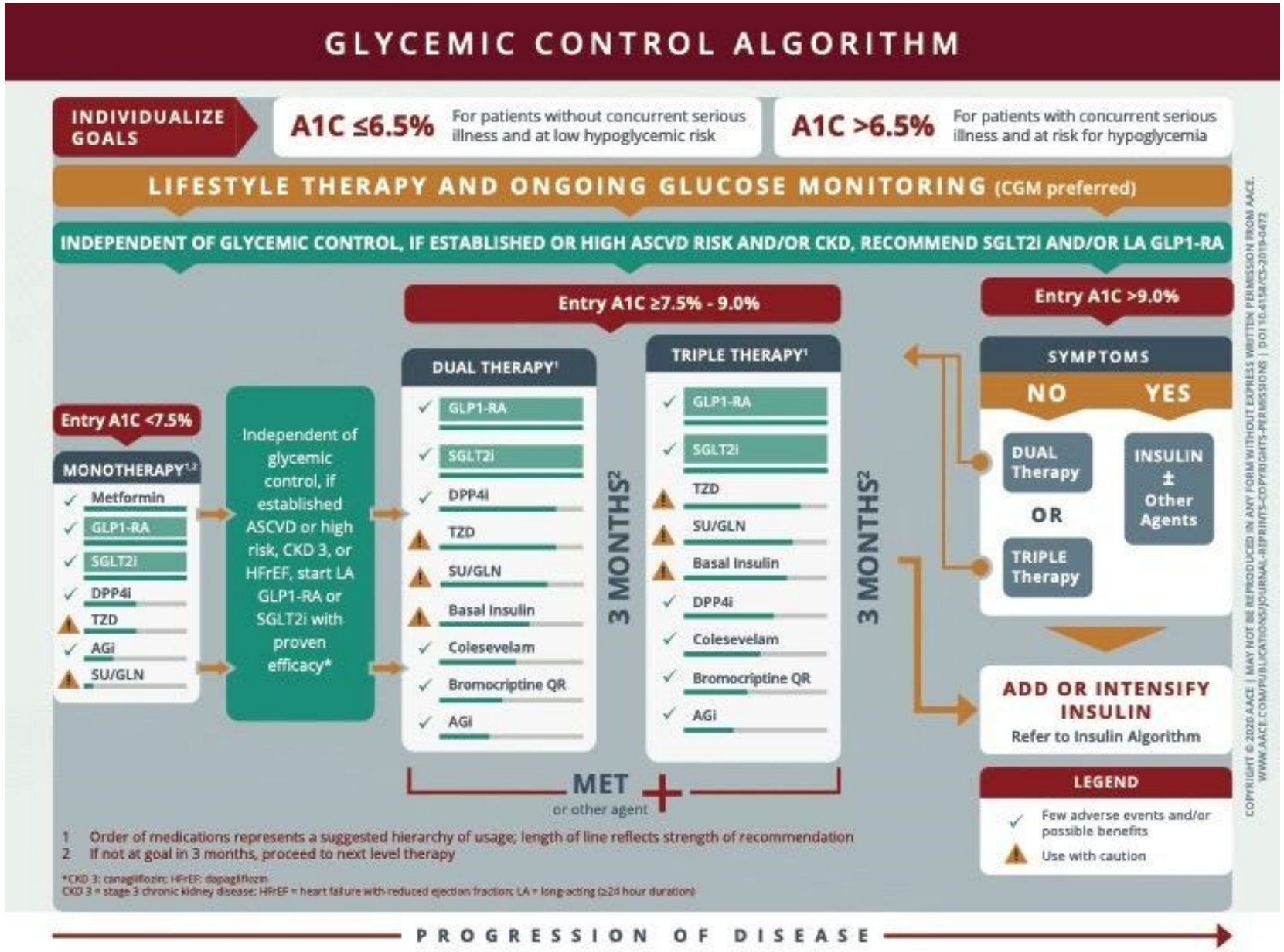
# Guideline Updates 2019-2020

## ACC/AHA*, AACE/ACE, and ESC/EASD recommend GLP-1 RA monotherapy as first-line option for patients with T2DM and established or at high risk for ASCVD[a-c]




*For adults with T2DM and additional ASCVD risk factors (IIb, B-R).
†Please refer to original figure for more detail. ‡Use drugs with proven CVD benefit.
a. Arnett DK, et al. *Circulation*. 2019;140:e596-e646; b. Garber AJ, et al. *Endocr Pract*. 2020;26:107-139;
c. Consentino F, et al. *Eur Heart J*. 2020;41:255-323.




AACE/ACE Comprehensive Type 2 Diabetes Algorithm App. American Association of Clinical Endocrinologists (AACE) 25th Annual Scientific & Clinical Congress, May 25-29, 2016. Orlando, FL.

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# AACE/ACE Comprehensive Type 2 Diabetes Management Algorithm

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## PROFILES OF ANTIHYPERGLYCEMIC MEDICATIONS

| | MET | GLP1-RA | SGLT2i | DPP4i | AGI | TZD (moderate dose) | SU / GLN | COLSVL | BCR-QR | INSULIN | PRAML |
|---|---|---|---|---|---|---|---|---|---|---|---|
| HYPO | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral | Moderate/ Severe / Mild | Neutral | Neutral | Moderate to Severe | Neutral |
| WEIGHT | Slight Loss | Loss | Loss | Neutral | Neutral | Gain | Gain | Neutral | Neutral | Gain | Loss |
| RENAL / GU | Contra-indicated if eGFR [illegible] mL/min/ 1.73 m² | Contra-indicated; Potential Benefit of LA GLP1-RA | Not Indicated for eGFR <45 mL/ [illegible] See #1; Genital Mycotic Infections; Potential CKD Benefit; See #1 | Dose Adjustment Necessary [illegible]; Effective in Reducing Albuminuria | Neutral | Neutral | More Hypo Risk | Neutral | Neutral | More Hypo Risk | Neutral |
| GI Sx | Moderate | Moderate | Neutral | Neutral | Moderate | Neutral | Neutral | Mild | Moderate | Neutral | Moderate |
| CHF | Neutral | Neutral | Prevent HF Hospitalization Manage HfrEF; See #2 | See #4 | Neutral | Moderate | Neutral | Neutral | Neutral | CHF Risk | Neutral |
| CARDIAC ASCVD | | Potential Benefit of LA GLP1-RA | See #3 | | | May Reduce Stroke Risk | Possible ASCVD Risk | Lowers LDL-C | Safe | Neutral | |
| BONE | Neutral | Neutral | Neutral | Neutral | Neutral | Moderate Fracture Risk | Neutral | Neutral | Neutral | Neutral | Neutral |
| KETOACIDOSIS | Neutral | Neutral | DKA Can Occur in Various Stress Settings | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral |

https://pro.aace.com/disease-state-resources/diabetes/clinical-practice-guidelines-treatment-algorithms/comprehensive

- Few adverse events or possible benefits
- Use with caution
- Likelihood of adverse effects

1. Canagliflozin indicated for eGFR ≥30 mL/min/1.73 m² in patients with CKD 3 + albuminuria.
2. Dapagliflozin—potential primary prevention of HF hospitalization & demonstrated efficacy in HFrEF.
3. Empagliflozin—FDA approved to reduce CV mortality. Canagliflozin—FDA approved to reduce MACE events.
4. Possible increased hospitalizations for heart failure with alogliptin and saxagliptin.

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DOI 10.4158/CS-2019-0472

https://pro.aace.com/disease-state-resources/diabetes/clinical-practice-guidelines-treatment-algorithms/comprehensive

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**FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)**

**INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†**

NO

**CONSIDER INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE***

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

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## +ASCVD/Indicators of High Risk

- Established ASCVD
- Indicators of high ASCVD risk (age ≥55 years with coronary, carotid, or lower-extremity artery stenosis >50%, or LVH)

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

**If A1C above target**

If further intensification is required or patient is unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV benefit and/or safety:

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]
- DPP-4i if not on GLP-1 RA
- Basal insulin[3]
- SU[4]

## +HF

Particularly HFrEF (LVEF <45%)

SGLT2i with proven benefit in this population[5,6,7]

## +CKD

DKD and Albuminuria[8]

NO

**PREFERABLY**

SGLT2i with primary evidence of reducing CKD progression

**OR**

SGLT2i with evidence of reducing CKD progression in CVOTs[5,6,8]

**OR**

GLP-1 RA with proven CVD benefit[1] if SGLT2i not tolerated or contraindicated

**For patients with T2D and CKD[8] (e.g., eGFR <60 mL/min/1.73 m²) and thus at increased risk of cardiovascular events**

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1,7]

## IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

### COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

| DPP-4i | GLP-1 RA | SGLT2i | TZD |
|---|---|---|---|
| If A1C above target | If A1C above target | If A1C above target | If A1C above target |
| SGLT2i **OR** TZD | SGLT2i **OR** TZD | GLP-1 RA **OR** DPP-4i **OR** TZD | SGLT2i **OR** DPP-4i **OR** GLP-1 RA |

**If A1C above target**

Continue with addition of other agents as outlined above

**If A1C above target**

Consider the addition of SU[4] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[9]

### COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/OR

- GLP-1 RA with good efficacy for weight loss[10]
- SGLT2i

**If A1C above target**

- SGLT2i
- GLP-1 RA with good efficacy for weight loss[10]

**If A1C above target**

If quadruple therapy required, or SGLT2i and/or GLP-1 RA not tolerated or contraindicated, use regimen with lowest risk of weight gain

**PREFERABLY**

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

- SU[4] • TZD[2] • Basal insulin

### COST IS A MAJOR ISSUE[11,12]

- SU[4]
- TZD[12]

**If A1C above target**

- TZD[12]
- SU[4]

**If A1C above target**

**Insulin therapy** basal insulin with lowest acquisition cost

**OR**

Consider other therapies based on cost

1. Proven CVD benefit means it has label indication of reducing CVD events
2. Low dose may be better tolerated though less well studied for CVD effects
3. Degludec or U-100 glargine have demonstrated CVD safety
4. Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i
5. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
6. Empagliflozin, canagliflozin, and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin and dapagliflozin have primary renal outcome data. Dapagliflozin and empagliflozin have primary heart failure outcome data.
7. Proven benefit means it has label indication of reducing heart failure in this population
8. Refer to Section 11: Microvascular Complications and Foot Care
9. Degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
10. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
11. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
12. Consider country- and region-specific cost of drugs. In some countries TZDs are relatively more expensive and DPP-4i are relatively cheaper.

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

* Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

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# Medication Access/Medication Cost

- Despite promising data described above, many patients are unable to utilize these classes of medications due to high cost involved and economic hardship.
- Uninsured patients, and even some insured patients, with high copays or deductibles may be limited in their ability to obtain diabetes medications with the best profiles for organ protection.
- Often a particular insurance company will only cover one agent within a particular class so ability to select a specific drug may be limited.
- Be aware of limitations when prescribing and consider options for cost-reduction or alternative medications if cost remains prohibitive.

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# Conclusions

Diabetes is a multifactorial disease

Many people with T2DM have ASCVD, kidney disease, and/or HF

Role for PCPs, cardiologists, nephrologists, and diabetologists in risk management for T2DM and CVD, or CKD, or risk factors

We can prevent progression of diabetes complications

Latest guidelines recommend SGLT2 inhibitors and GLP-1 RAs for organ protection in individualized diabetes care

Novel glucose-lowering drugs have a role beyond T2DM: in HF, ASCVD, and kidney disease

# Practice Patient Scenario 1

A 52-year-old male presents for follow up of his diabetes shortly after a recent hospitalization with a STEMI, and status post 2 cardiac stents placed. He is currently feeling well. He has been taking metformin 1000mg twice daily and glipizide 5mg once daily for diabetes therapy. HbA1c is currently 6.7%. He denies hypoglycemia events at home and reports home glucose monitoring values are 78-120 mg/dl. BMI is 32.

**Question**: What would you recommend to patient regarding his diabetes therapy at this time?

**Answer Choices:**

A. No change to therapy as diabetes is well controlled
B. Increase glipizide to 5mg twice daily to reduce HbA1c ‹ 6.5%
C. Add basal insulin for tighter glycemic control
D. Add GLP1-RA and discontinue glipizide

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# Practice Patient Scenario 1

**Correct Answer:** Add GLP1-RA and discontinue glipizide

**Rationale**: Although HbA1c is in the target range, given the presence of active ASCVD the patient would benefit from cardioprotection via addition of a GLP1-RA, along with weight loss benefit. Since some glucose values are borderline low it would be prudent to discontinue the sulfonylurea when adding his GLP1-RA to prevent hypoglycemia. Higher sulfonylurea and adding basal insulin would not confer cardioprotection and could raise the risk of hypoglycemia.

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# Practice Patient Scenario 2

49-year-old male is seen in the emergency department for a skin infection. His lab work is notable for HbA1c 7.5%. He has not seen a doctor for several years but reports having a history of an MI in his early 40s. He was never told of diabetes or prediabetes in the past. He has no medical insurance and mentions having trouble paying his rent. He usually eats fast food and notes that it is the most affordable option for him.

**Question**: What would you recommend for diabetes therapy?

**Answer Choices:**

A. Lifestyle modification and metformin
B. Lifestyle modification and SGLT2-I
C. Lifestyle modification and GLP1-RA
D. Lifestyle modification, SGLT2-i and GLP1-RA

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# Practice Patient Scenario 2

**Correct Answer**: Lifestyle modification and metformin

**Rationale**: Although this patient's history of CAD would indicate a benefit for adding GLP1-RA, given his lack of insurance and trouble affording basic expenses it would be unlikely that this patient could afford this therapy (or SGLT2-i). Metformin is available as a generic and relatively inexpensive medication option for patients without insurance. Cost factors should be considered for patients when prescribing medications.

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