# 2026 Pharmacologic Therapy for Type 2 Diabetes

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LOUISIANA DEPARTMENT OF HEALTH

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# Speaker


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# Disclosure(s)

In the past 24 months, I have NOT had any financial relationships with any ineligible companies.

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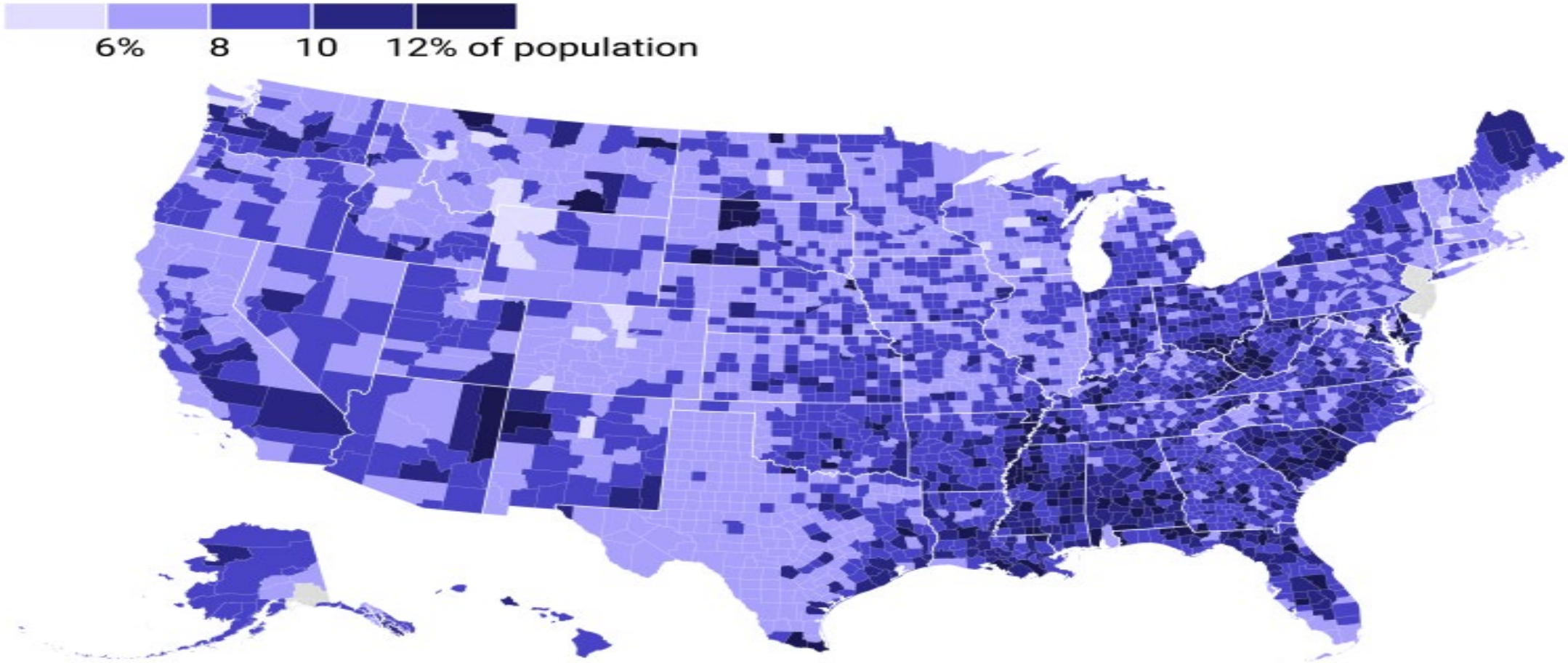
# Objectives

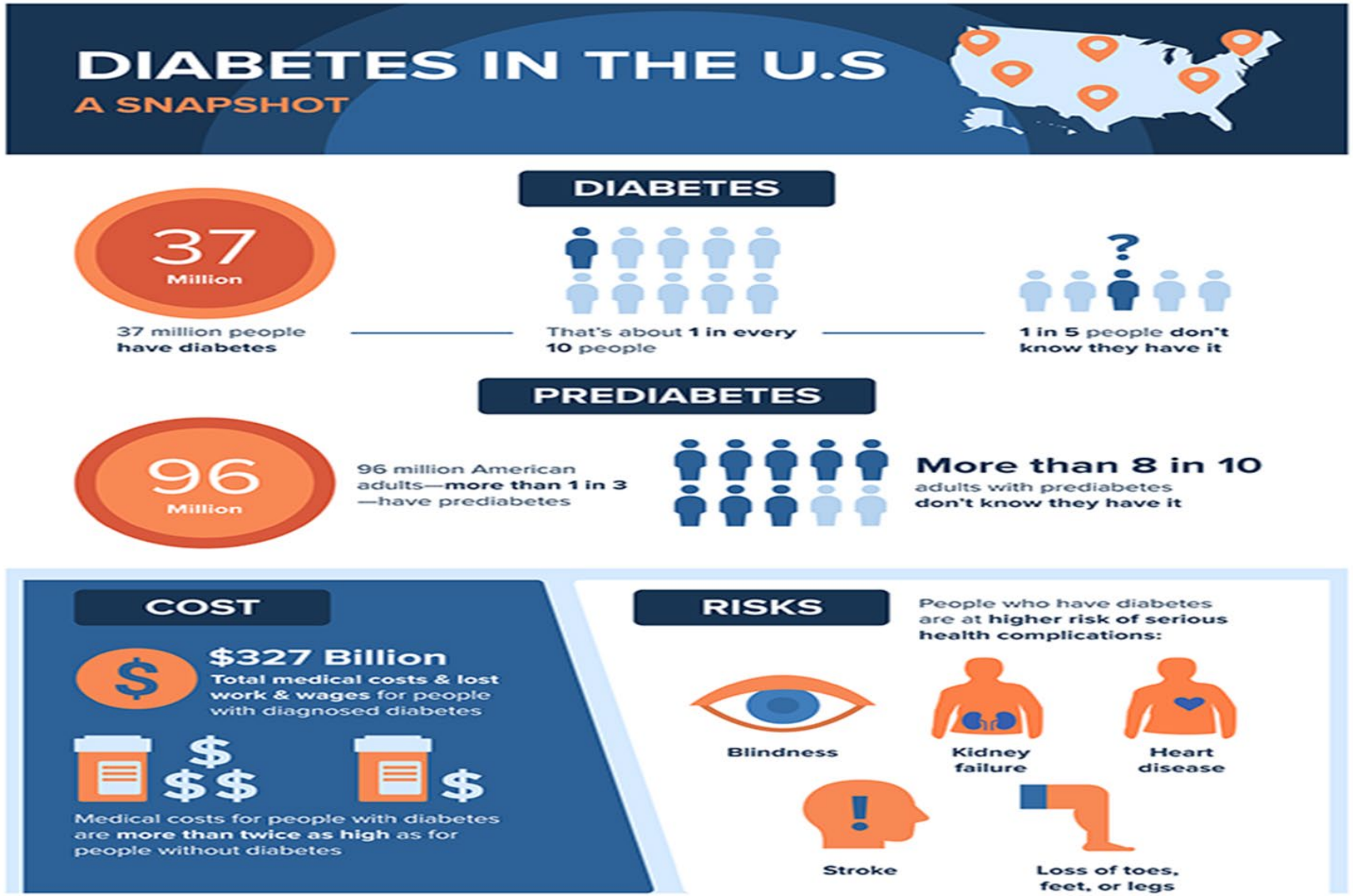
- Review the background, prevalence, and pathophysiology of Type 2 Diabetes
- Evaluate treatment options per the 2026 ADA Diabetes Standards of Care
- Discuss the advantages and disadvantages of different treatment options for type 2 Diabetes.

# The South has highest rates of diabetes

Based on data for adults 20 and over

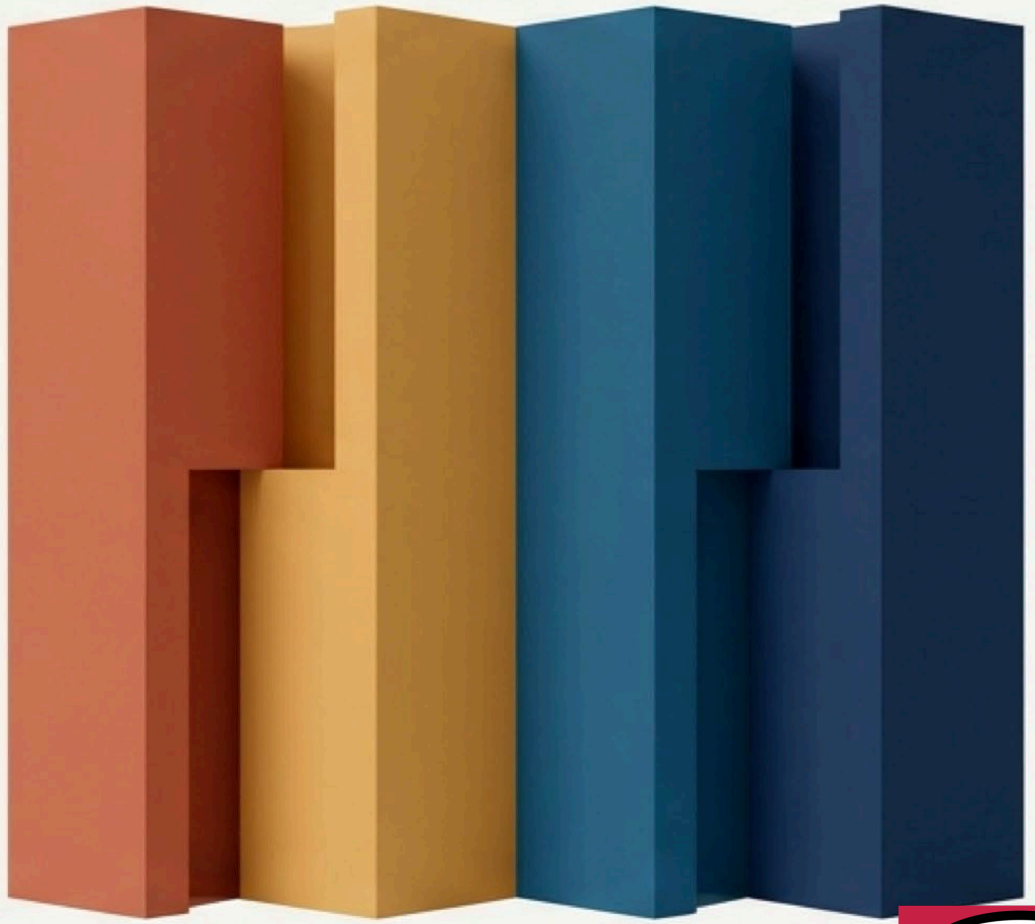



Note: Data not available for New Jersey.
Data source: CDC, age-adjusted prevalence 2019

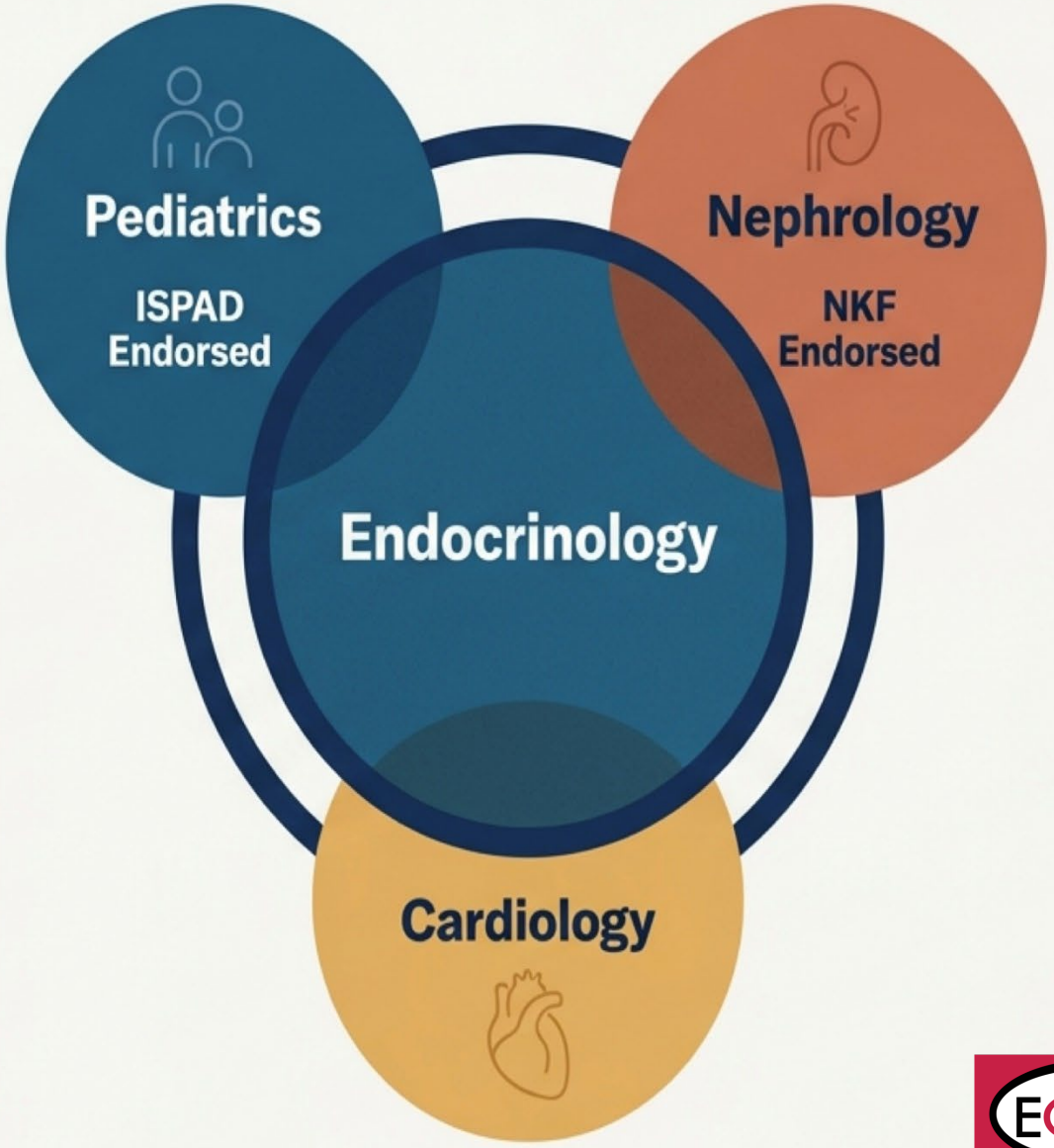

DIABETES IN THE U.S
A SNAPSHOT
DIABETES
37
Million
37 million people have diabetes
That's about 1 in every 10 people
1 in 5 people don't know they have it
PREDIABETES
96
Million
96 million American adults—more than 1 in 3—have prediabetes
More than 8 in 10
adults with prediabetes don't know they have it
COST
$327 Billion
Total medical costs & lost work & wages for people with diagnosed diabetes
Medical costs for people with diabetes are more than twice as high as for people without diabetes
RISKS
People who have diabetes are at higher risk of serious health complications:
Blindness
Kidney failure
Heart disease
Stroke
Loss of toes, feet, or legs

# 2026 ADA Standards of Care: The Clinical Blueprint

Actionable, practice-changing updates for tomorrow's clinic.



# **Diabetes Care** is No Longer a Solo Sport



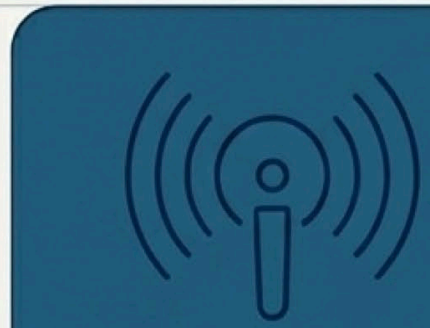

## The Paradigm Shift

The 2026 guidelines mark a definitive move toward multi-disciplinary, collaborative care.

## The Proof

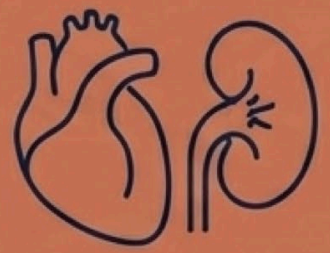
For the first time, major guidelines carry official endorsements endorsements from the NKF and ISPAD. The standard of care now mandates treating the patient across specialties.

# The 4 Pillars of the 2026 Guidelines



## Tech as Foundation

Moving from reactive additions to proactive baselines.

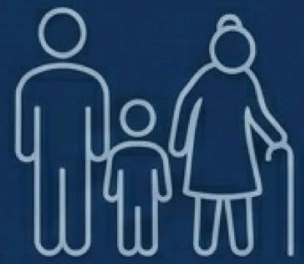


## Organ-First Pharmacology

Prioritizing vital organ protection over mere A1C reduction.

## Proactive Early Detection

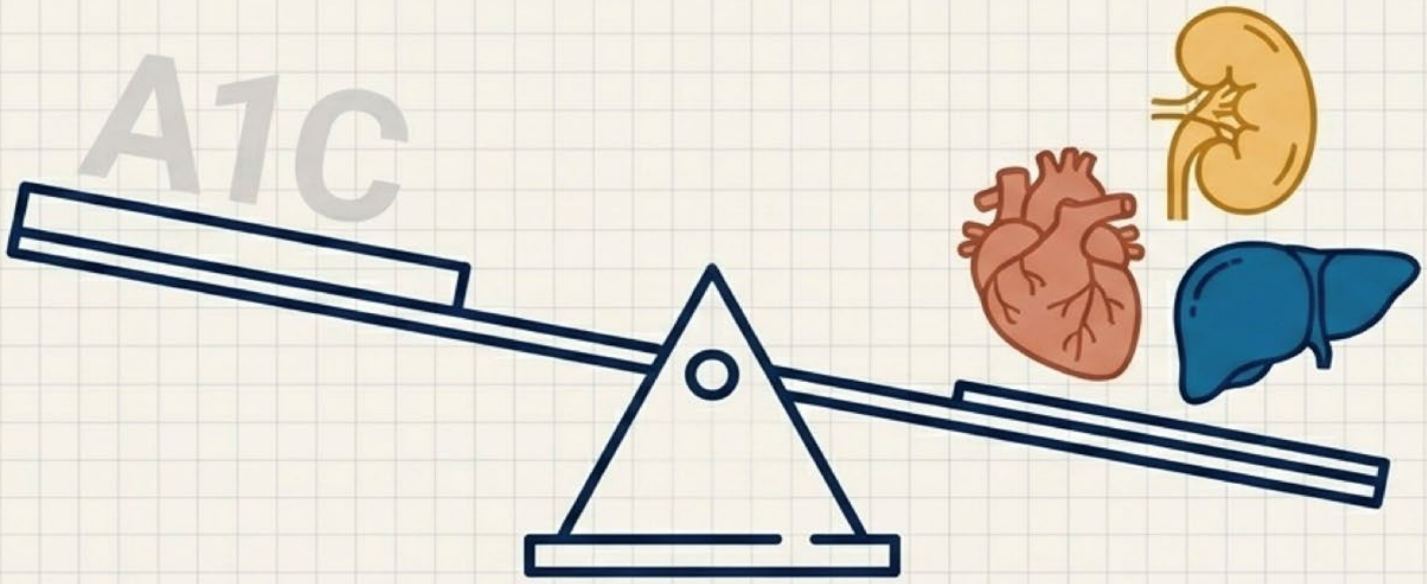
Intervening before symptomatic progression.



## Nuanced Population Care

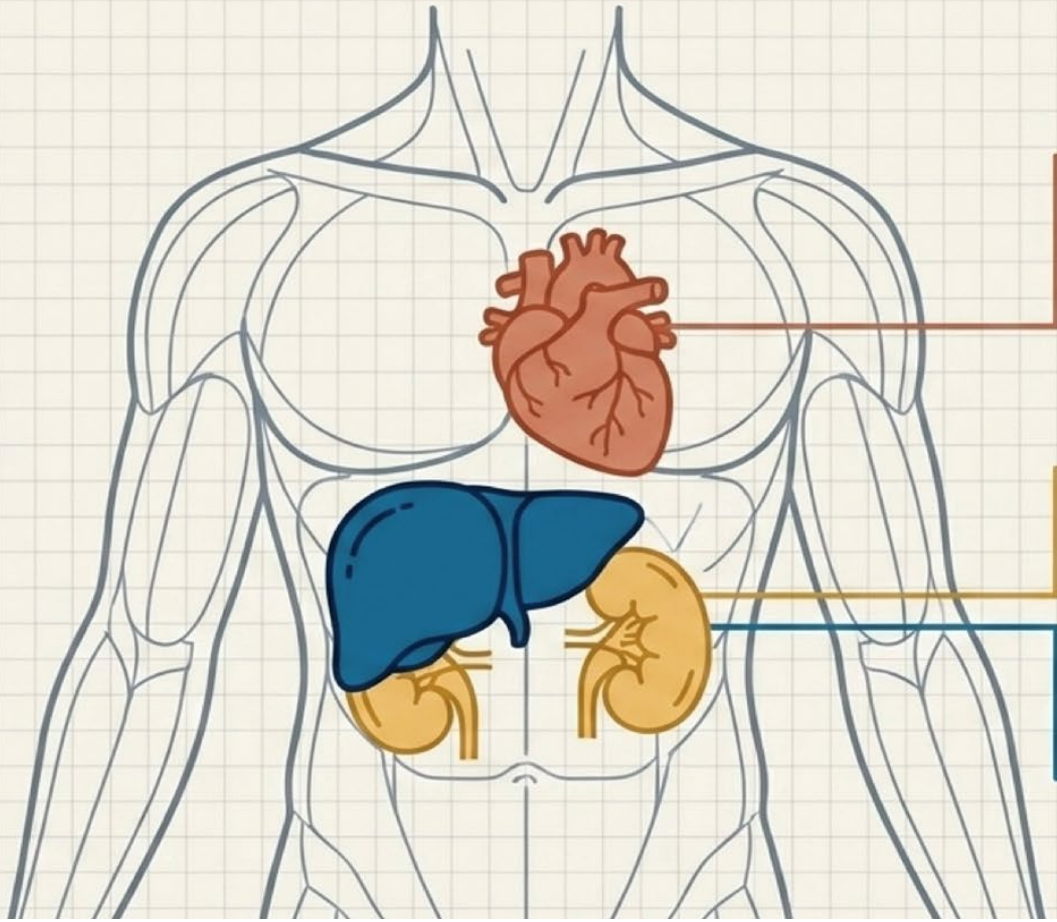
Tailoring intensity for older adults, pediatrics, and pregnancy.

# Beyond the A1C: The Pharmacology Shift




**Lowering glucose is now secondary.** Actively protecting vital organs is the primary driver for therapeutic selection. We now select specific agents specifically for their proven, powerful benefits in preventing and managing major comorbidities.

# The Organ-First Strategy Playbook



**Heart Failure (HFrEF)**
Initiate **GIP/GLP1s** or **GLP1s** to reduce cardiac events.

**CKD**
Simultaneous start protocol:
SGLT2i + nsMRA + RAS inhibitor.

**MASH**
GLP1s are the preferred therapy for glycemic management.

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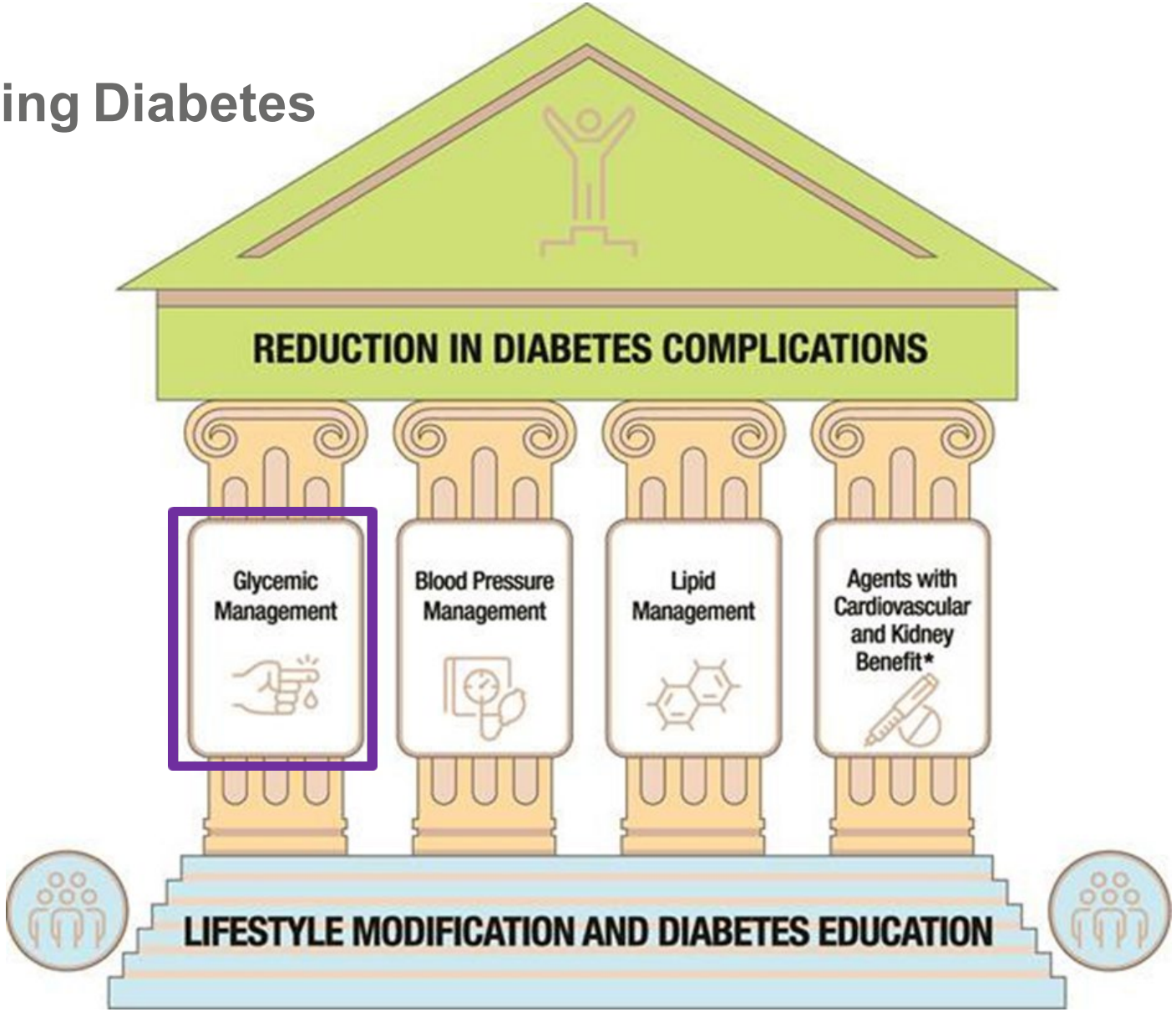
# Pillar Approach to Managing Diabetes Related Complications




American Diabetes Association Professional Practice Committee; Standards of Medical Care in Diabetes—2024. Diabetes Care 1 January 2024; 47.

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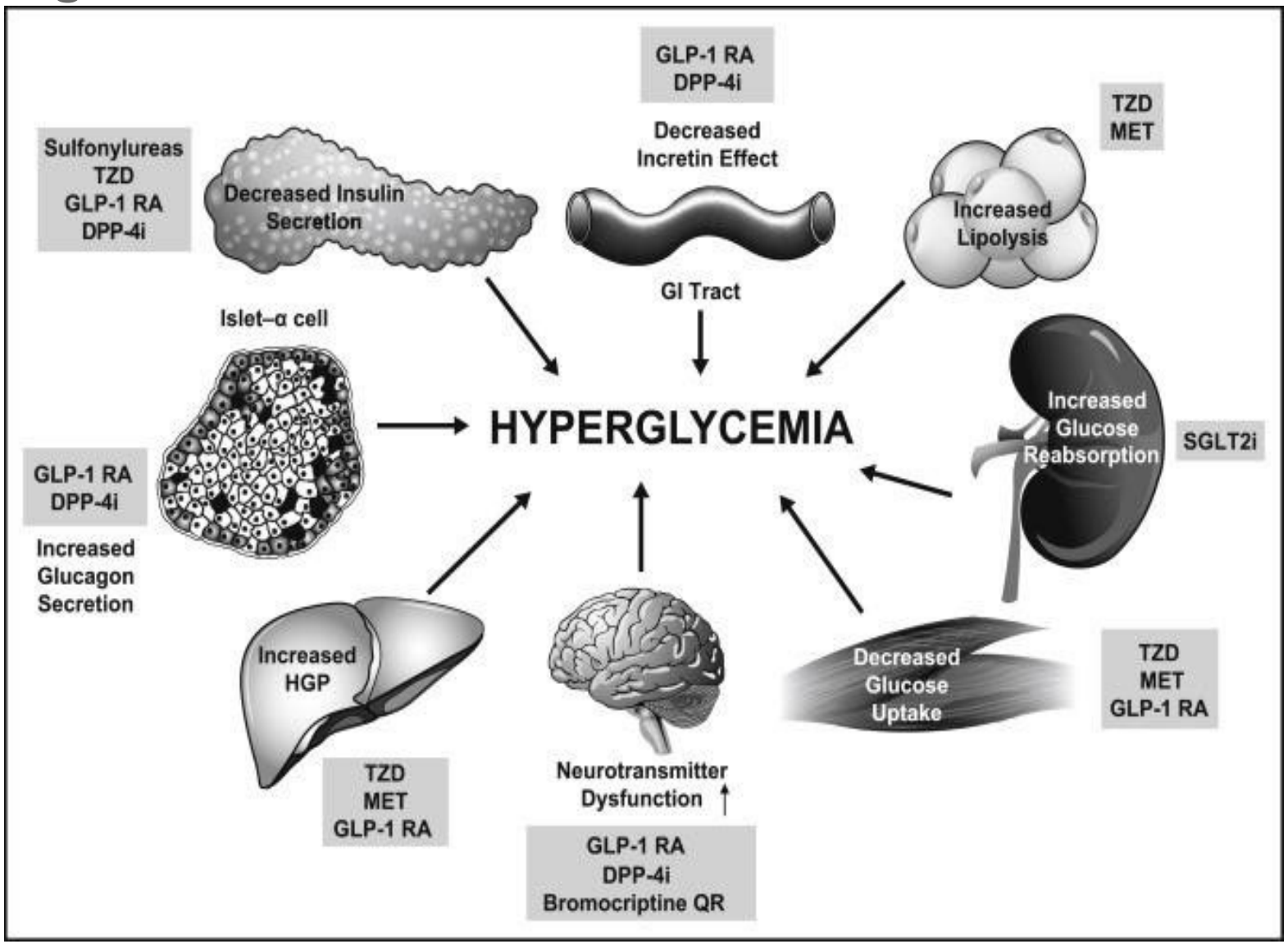
# Glycemic Management




# Therapeutic Considerations


- Metformin
- SGLT2 inhibitors
- GLP1 agonists
- Dual GIP and GLP1 agonists
- Sulfonylureas
- DPP IV inhibitors
- Pioglitazone
- Sulfonylurea (second generation)
- Insulin (human and analog)

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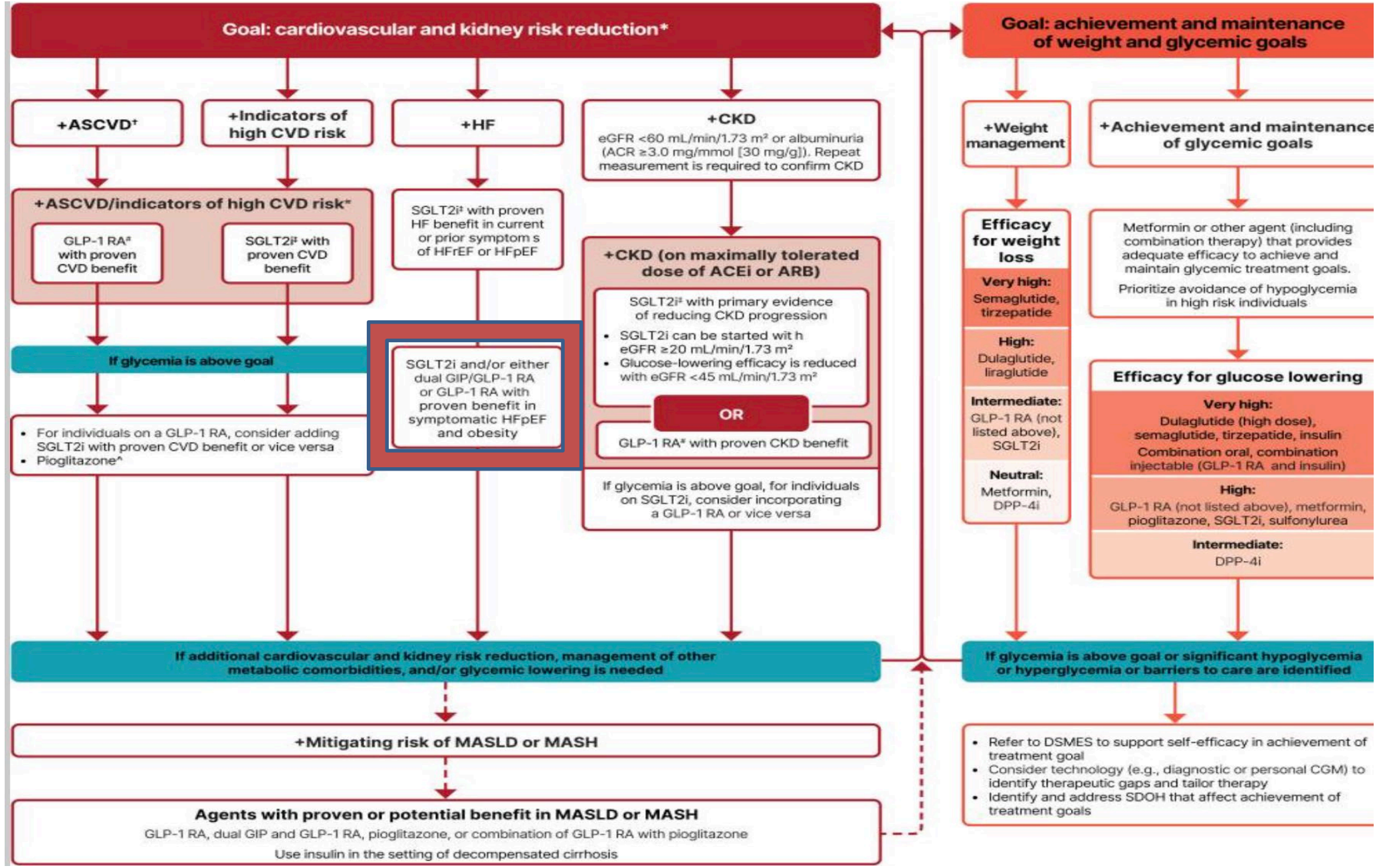
# 2026 Pharmacologic Therapy for Type 2 Diabetes

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# Pharmacological Treatment of Diabetes Mellitus Type II

# Metformin

| | Efficacy[1] | Hypoglycaemia | Weight change[2] | CV effects | | Renal effects | | Oral/SQ | Cost |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Effect on MACE | HF | Progression of DKD | Dosing/use considerations* | | |
| **Metformin** | High | No | Neutral (potential for modest loss) | Potential benefit | Neutral | Neutral | • Contraindicated with eGFR <30 ml/min per 1.73 $m^2$ | Oral | Low |

Traditionally recommended as first-line glucose-lowering therapy for type 2 diabetes, because of its high efficacy in lowering $HbA_{1c}$, minimal hypoglycaemia risk when used as monotherapy, potential for some modest weight loss, good safety profile, low cost

American Diabetes Association.

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

*Diabetes Care* 2022; https://doi.org/10.2337/dci22-0034. *Diabetologia* 2022; https://doi.org/10.1007/s00125-022-05787-2.



EASD European Association for the Study of Diabetes

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# Sulfonylureas

| | Efficacy[1] | Hypoglycaemia | Weight change[2] | CV effects | | Renal effects | | Oral/SQ | Cost |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Effect on MACE | HF | Progression of DKD | Dosing/use considerations* | | |
| **Sulfonylureas (2nd Generation)** | High | Yes | Gain | Neutral | Neutral | Neutral | • Glyburide: generally not recommended in chronic kidney disease<br>• Glipizide and glimepiride: initiate conservatively to avoid hypoglycaemia | Oral | Low |

- High glucose-lowering efficacy, inexpensive and accessible
- A heterogenous group - sulfonylureas with lower risk of hypoglycaemia to be selected when considered for therapy
- No difference in the incidence of MACE in patients at high CV risk treated with glimepiride or linagliptin

American Diabetes Association.

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

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# Thiazolidinediones

| | Efficacy[1] | Hypoglycaemia | Weight change[2] | CV effects | | Renal effects | | Oral/SQ | Cost |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Effect on MACE | HF | Progression of DKD | Dosing/use considerations* | | |
| **Thiazolidinediones** | High | No | Gain | Potential benefit: pioglitazone | Increased risk | Neutral | • No dose adjustment required<br>• Generally not recommended in renal impairment due to potential for fluid retention | Oral | Low |

- High glucose-lowering efficacy, durability of glycaemic effect
- Beneficial effects in NASH seen with pioglitazone
- Side effects (e.g. weight gain, fluid retention) can be mitigated by optimising dosing strategies (e.g. using lower doses) and combining therapy with other medications (SGLT2 inhibitors, GLP-1 RA) that promote weight loss and sodium excretion

American Diabetes Association.

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

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# DPP-4 Inhibitors

| | Efficacy[1] | Hypoglycaemia | Weight change[2] | CV effects | | Renal effects | | Oral/SQ | Cost |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Effect on MACE | HF | Progression of DKD | Dosing/use considerations* | | |
| **DPP-4 Inhibitors** | Intermediate | No | Neutral | Neutral | Neutral (potential risk, saxagliptin) | Neutral | • Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment<br>• No dose adjustment required for linagliptin | Oral | High |

- Intermediate glucose-lowering efficacy, neutral effect on weight, generally well tolerated, minimal risk of hypoglycaemia
- Early combination treatment with metformin and a DPP-4i (vildagliptin) increased glycaemic durability compared to stepwise approach to therapy
- Cardiovascular safety demonstrated

American Diabetes Association.

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

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# SGLT2 Inhibitors

| | Efficacy[1] | Hypoglycaemia | Weight change[2] | CV effects | | Renal effects | | Oral/SQ | Cost |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Effect on MACE | HF | Progression of DKD | Dosing/use considerations* | | |
| **SGLT2 Inhibitors** | Intermediate to high | No | Loss (intermediate) | Benefit: canagliflozin, empagliflozin | Benefit: canagliflozin, dapagliflozin, empagliflozin, ertugliflozin | Benefit: canagliflozin, dapagliflozin, empagliflozin | • See labels for renal dose considerations of individual agents<br>• Glucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR | Oral | High |

- *Glucose-lowering mechanism of action:* Reduce renal tubular glucose reabsorption
- *Clinical Efficacy Profile:* Intermediate to high glucose-lowering efficacy, lower at lower eGFR; low inherent risk of hypoglycaemia; intermediate weight loss
- *Cardiorenal Effects:* Demonstrated protective effects in studied trial populations:
  - Reduction in major adverse cardiovascular events
  - Reduction in overall CV death (with heterogeneity across the class)
  - Reduction in risk of hospitalisation for heart failure
  - Reduction in risk of kidney outcomes
- Increased confidence surrounding safety issues of interest

American Diabetes Association.

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

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# GLP-1 Receptor Agonists

| | Efficacy[1] | Hypogly-caemia | Weight change[2] | CV effects | | Renal effects | | Oral/SQ | Cost |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Effect on MACE | HF | Progression of DKD | Dosing/use considerations* | | |
| **GLP-1 RAs** | High to very high | No | Loss (intermediate to very high) | Benefit: dulaglutide, liraglutide, semaglutide (SQ)<br>Neutral: exenatide once weekly, lixisenatide | Neutral | Benefit for renal endpoints in CVOTs, driven by albuminuria outcomes: dulaglutide, liraglutide, semaglutide (SQ) | • See labels for renal dose considerations of individual agents<br>• No dose adjustment for dulaglutide, liraglutide, semaglutide<br>• Monitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse GI reactions | SQ; oral (semaglutide) | High |

- *Glucose-lowering mechanism of action:* Augment glucose-dependent insulin secretion & glucagon suppression, decelerate gastric emptying, curb post-meal glycaemic increments, reduce appetite, calorie intake and body weight
- *Clinical Efficacy Profile:* High to Very High glucose-lowering efficacy, low inherent risk of hypoglycaemia; intermediate to high weight loss
- *Cardiorenal Effects:* cardioprotective, with evidence of reduction in major adverse cardiovascular events, CV death, fatal or non-fatal MI, fatal or non-fatal stroke, all-cause mortality, composite kidney outcome driven by macroalbuminuria
- Increased confidence surrounding safety areas of interest

American Diabetes Association.

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

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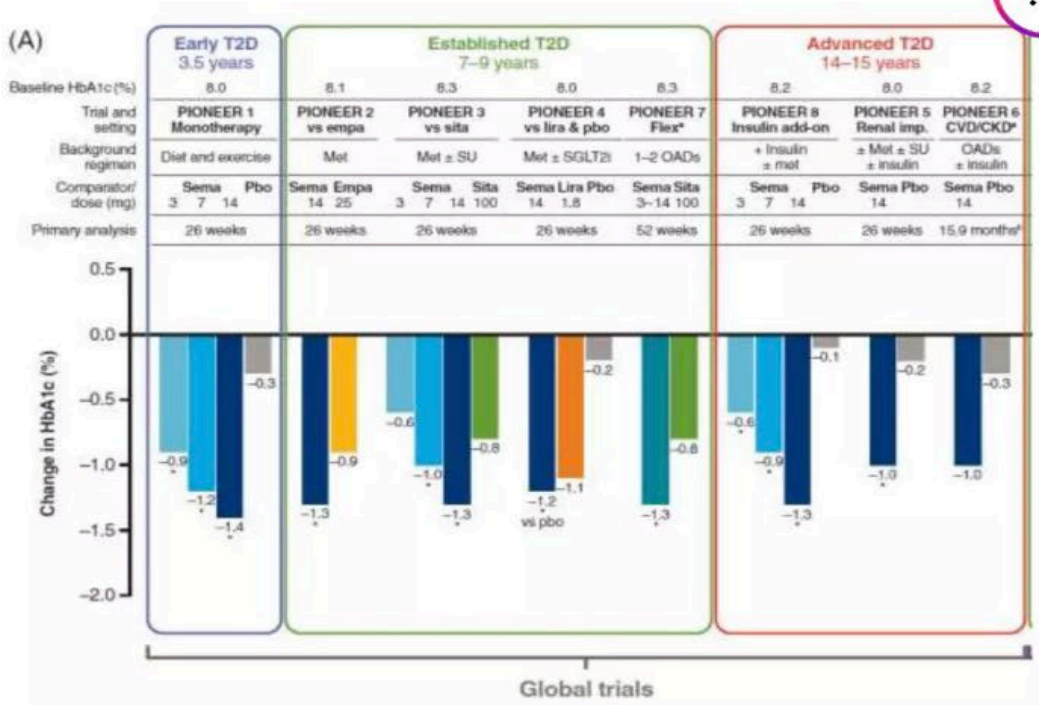
# GLP-1 RA Therapeutic Updates

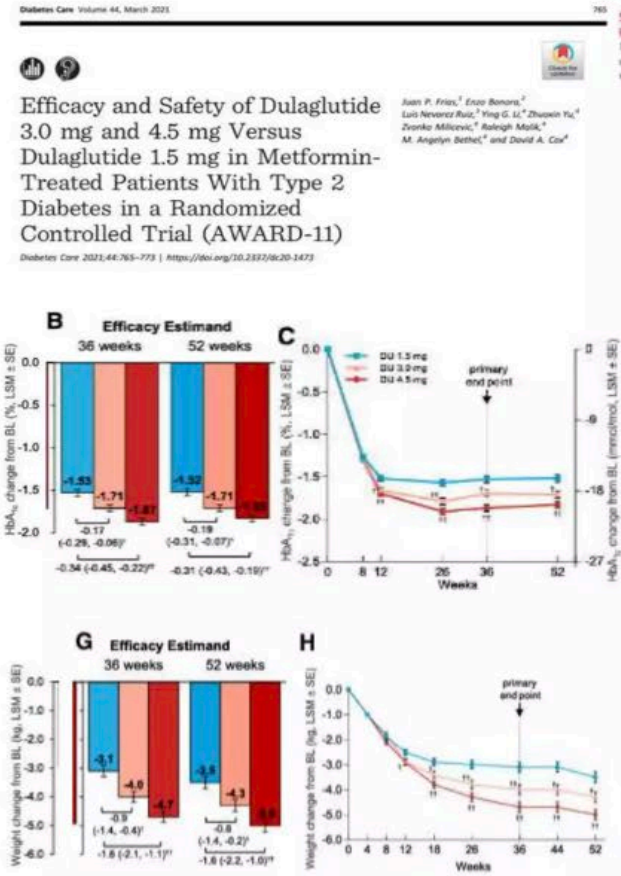
- First oral GLP-1 RA (oral semaglutide) developed and available



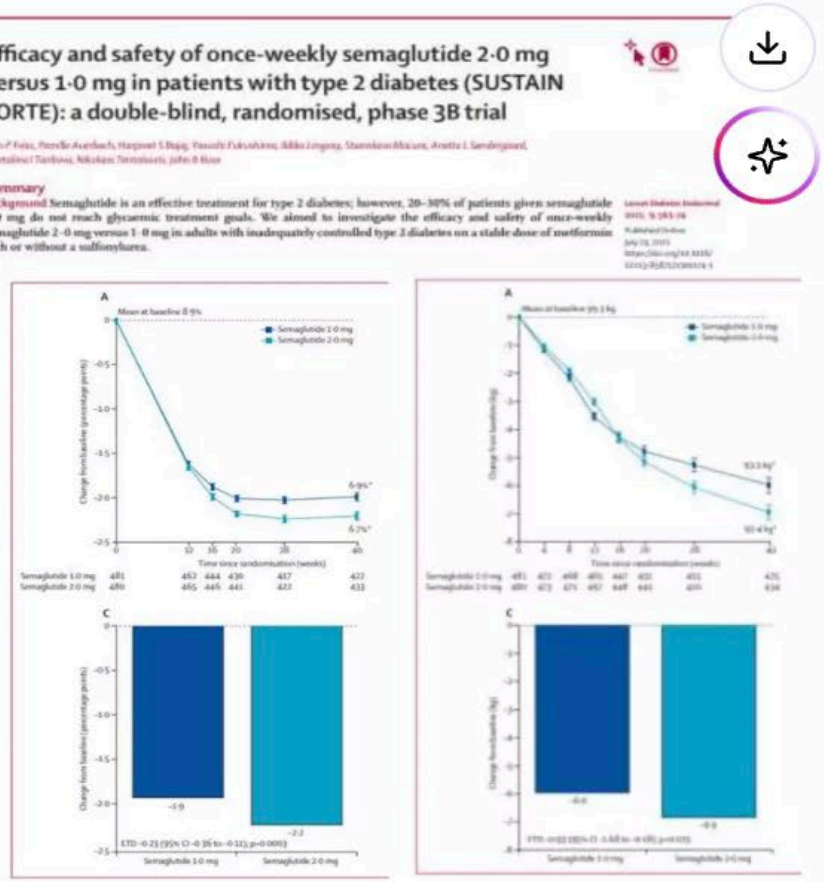

Thethi TK *et al; Diabetes Obes Metab;* 2020; 22:1263-1277

# GLP-1 RA Therapeutic Updates

- First oral GLP-1 RA (oral semaglutide) developed and available
- Higher dose GLP-1 RAs (dulaglutide, semaglutide) with incremental benefits in glucose weight efficacy
- Greater clinical expertise in anticipating and addressing GI effects



Efficacy and Safety of Dulaglutide 3.0 mg and 4.5 mg Versus Dulaglutide 1.5 mg in Metformin-Treated Patients With Type 2 Diabetes in a Randomized Controlled Trial (AWARD-11)



Efficacy and safety of once-weekly semaglutide 2·0 mg versus 1·0 mg in patients with type 2 diabetes (SUSTAIN FORTE): a double-blind, randomised, phase 3B trial

# Glucose-dependent insulinotropic polypeptide (GIP) receptor and GLP-1 receptor agonist (tirzepatide)

| | Efficacy[1] | Hypoglycaemia | Weight change[2] | CV effects | | Renal effects | | Oral/SQ | Cost |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Effect on MACE | HF | Progression of DKD | Dosing/use considerations* | | |
| GIP and GLP-1 RA | Very high | No | Loss (very high) | Under investigation | Under investigation | Under investigation | • See label for renal dose considerations<br>• No dose adjustment<br>• Monitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse GI reactions | SQ | High |

- *Glucose-lowering mechanism of action:* GIP receptor and GLP-1 receptor agonist; enhances first and second-phase insulin secretion, and reduces glucagon levels, both in a glucose-dependent manner
- *Clinical Efficacy profile:* Very high glycaemic efficacy; low inherent risk of hypoglycaemia; weight loss (high); cardiorenal effects unknown (trials in progress)

American Diabetes Association.

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

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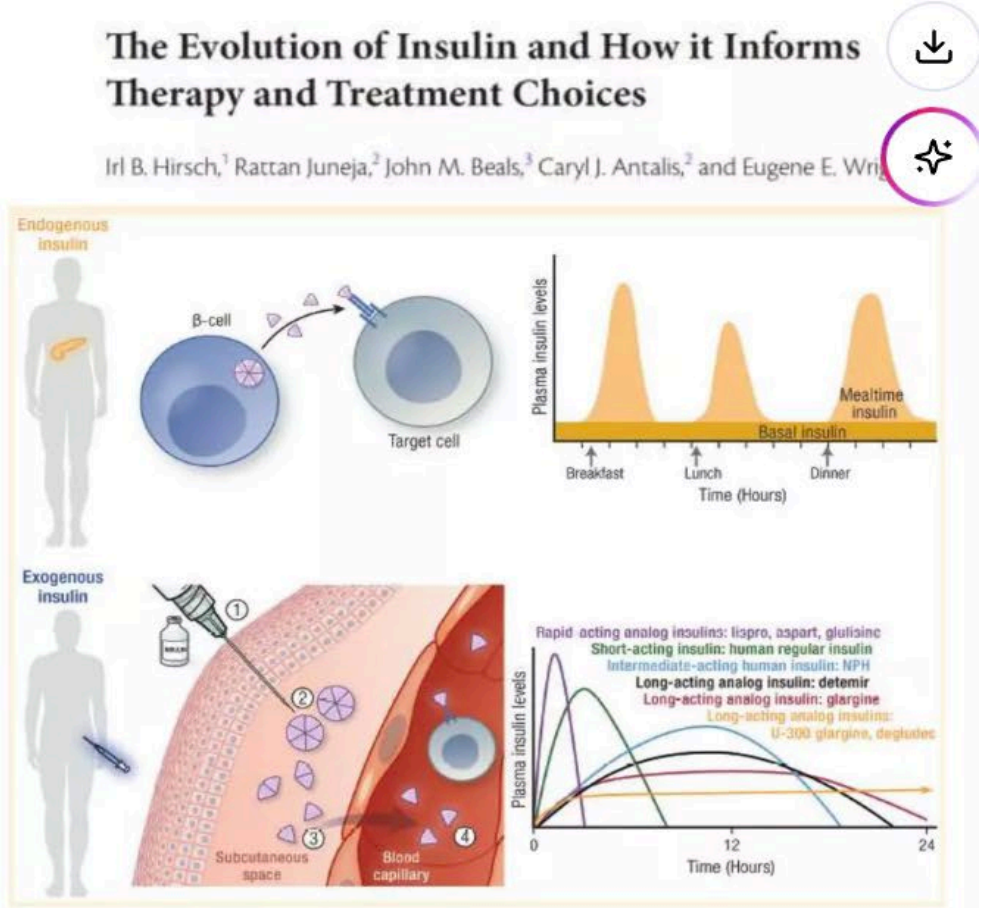
# Insulin

- Advantage of lowering glucose in dose-dependent manner, able to address any level of glycaemia
- *Clinical Profile:* High to very high glycaemic efficacy, increased risk of hypoglycaemia and weight gain; neutral cardiorenal profile
- Efficacy and safety are largely dependent on education and support to facilitate self-management
- Importance of matching insulin to physiologic need




Adapted from Hirsch I *et al*; *Endocr Rev* 2020; 41: 733-755

American Diabetes Association.

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