



# The Scientific Times

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## ADA Guidelines 2021 Standards of Medical Care in Diabetes

### ADA announces new evidence-based guidelines and recommendations

**ADA**



The American Diabetes Association (ADA) is one of the leading voluntary health organizations fighting to bend the curve on the diabetes epidemic and help people living with diabetes thrive. For nearly 80 years the ADA has been driving discovery and research to treat, manage and prevent diabetes, while working relentlessly for a cure.

The ADA has developed and provided diabetes care standards, guidelines and related documents since 1989, and its clinical practice recommendations are integral resources for health care professionals.

A multidisciplinary expert committee including members of ADA updates the Standards of Care annually. The Standards of Medical Care in Diabetes 2021 – provides the latest in comprehensive, evidence based recommendations for the diagnosis and treatment of children & adults with type 1, type 2, or gestational diabetes; strategies for prevention or delay of type 2 diabetes; and therapeutic approaches that can reduce

complications, mitigate cardiovascular (CV) and renal risk and improve health outcomes.

**The current ADA guidelines included some of the key updates:**

1. Evidence for diabetes treatment for people also managing chronic kidney disease (CKD) and heart failure.
2. The use of technology for diabetes management and individualized care as

well as recommendations for continuous glucose monitoring (CGM) for people with diabetes.

3. Important information on addressing social determinants of health in diabetes.
4. Barriers to and critical times for diabetes self-management education and support (DSMES).
5. Vaccine-specific updates, including those related to COVID-19.

### COVID-19 Corner : Care is better than Cure!



- The “Immunizations” subsection has been significantly revised. More information has been added to the discussion of each vaccine, including
- During the coming year it is expected that vaccines for COVID-19 will become available and people with

important considerations related to coronavirus disease 2019 (COVID-19).

diabetes would be a priority population. The COVID-19 vaccine will likely become a routine part of the annual preventive schedule for people with diabetes.

### Diabetes Technology : The importance of CGM during pandemic and beyond

- New information added to diabetes technology section to consider CGM as useful tool for people with diabetes on multiple daily injections, continuous subcutaneous insulin infusions and other forms of insulin therapy regardless of age or diabetes type.

- The section provides advice on use of time in range data for glycemic monitoring, particularly during the COVID-19 pandemic when remote monitoring is preferable.

#### Inside this issue:

ADA Overview	1
COVID-19 Corner	1
Diabetes Technology	1
Diabetes Prevention	2
Pharmacological Therapy for Diabetes	2
Glucose-lowering Medication in T2DM	3
CVD Risk Management	4
Renal Risk Management	5

# DIABETES can be prevented or delayed :

## What Steps need to be Taken?

- Patients must be advised to achieve and maintain 7% loss of initial body weight and increase moderate intensity physical activity (such as brisk walking) to at least 150 mins/week.
- A variety of eating patterns like low-carbohydrate, Dietary Ap-

proaches to Stop Hypertension (DASH) are associated with lower risk of developing Type 2 Diabetes (T2DM).

- Certified technology-assisted diabetes prevention programs may be effective in preventing T2DM and should be considered.

- Metformin therapy for prevention of T2DM should be considered in those with prediabetes, especially for those with BMI  $\geq 35$  kg/m<sup>2</sup>, those aged <60 years, and women with prior gestational diabetes mellitus.



To know your risk of prediabetes click below-

[CLICK HERE](#)



## Pharmacological Therapy for Diabetes: Are There any Updates?

### Pharmacological Therapy for Type 1 Diabetes

- Most people with type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or continuous insulin infusion.
- Most people with type 1 diabetes should use rapid-acting insulin analogs to reduce hypoglycemia risk.
- Patients with type 1 diabetes should receive education on how to match



prandial insulin doses to carbohydrate intake, pre-meal blood glucose and anticipated physical activity.

### Pharmacological Therapy for Type 2 Diabetes (T2DM)

- **Metformin** is the preferred initial pharmacological agent for the treatment of T2DM unless contraindicated.
- **Early combination therapy** can be considered in some patients at treatment initiation to extend the time to treatment failure.
- **Combination Therapy:** Initial combination therapy should be considered in patients presenting with A1C levels **1.5 - 2.0 %** above target.
- The **VERIFY** trial demonstrated that initial combination therapy (Metformin + Vildagliptin) is superior to sequential addition of medications for extending primary and secondary failure.
- These results have not been generalized to DPP-4i other than Vildagliptin.
- Other options for first line therapy: Sulfonylureas, Dipeptidyl peptidase 4 inhibitor (DPP-4i), Sodium-Glucose linked transporter 2 inhibitor (SGLT2i) or Alpha-glucosidase inhibitors, if Metfor-

min not tolerated.

- In patients with T2DM, a glucagon-like peptide 1 receptor agonist is preferred to Insulin when possible.
- Algorithm for pharmacological management of T2DM was revised to include a dedicated decision pathway for CKD and a dedicated decision pathway for heart failure, with updates to reflect consensus interpretation of clinical trial data.



To know your ASCVD score, click below-

[CLICK HERE](#)

# Glucose Lowering Medication in T2DM: A Patient-Centric Approach



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

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

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

**+ASCVD/Indicators of High Risk**

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

ETHER/ OR  
GLP-1 RA with proven CVD benefit<sup>1</sup> OR SGLT2i with proven CVD benefit<sup>1</sup>

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<sup>1</sup>

- TZD<sup>2</sup>
- DPP-4i if not on GLP-1 RA
- Basal insulin<sup>3</sup>
- SU<sup>4</sup>

**+HF**

Particularly HFREF (LVEF  $<45\%$ )

SGLT2i with proven benefit in this population<sup>5,7</sup>

**+CKD**

DKD and Albuminuria<sup>8</sup>

NO

PREFERABLY

SGLT2i with primary evidence of reducing CKD progression

OR  
SGLT2i with evidence of reducing CKD progression in CVOTs<sup>5,8,9</sup>

OR  
GLP-1 RA with proven CVD benefit<sup>1</sup> if SGLT2i not tolerated or contraindicated

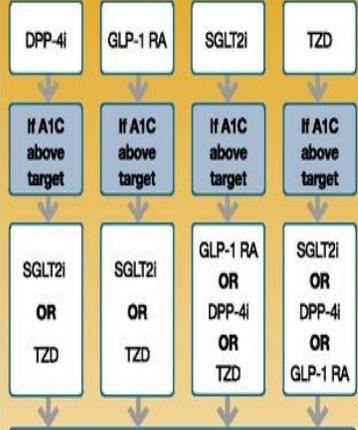
For patients with TZD and CKD<sup>9</sup> (e.g., eGFR  $<60$  mL/min/1.73 m<sup>2</sup>) and thus at increased risk of cardiovascular events

ETHER/ OR  
GLP-1 RA with proven CVD benefit<sup>1</sup> OR SGLT2i with proven CVD benefit<sup>1,7</sup>

NO

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA



If A1C above target

Continue with addition of other agents as outlined above

If A1C above target

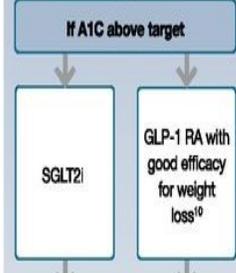
Consider the addition of SU<sup>4</sup> OR basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia<sup>3</sup>

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS



If A1C above target



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<sup>4</sup> • TZD<sup>2</sup> • Basal insulin

COST IS A MAJOR ISSUE<sup>11,12</sup>



If A1C above target



If A1C above target

Insulin therapy basal insulin with lowest acquisition cost

OR  
Consider other therapies based on cost

- Proven CVD benefit means it has label indication of reducing CVD events
- Low dose may be better tolerated though less well studied for CVD effects
- Degludec or U-100 glargine have demonstrated CVD safety
- Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i
- Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
- 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.

- Proven benefit means it has label indication of reducing heart failure in this population
- Refer to Section 11: Microvascular Complications and Foot Care
- Degludec / glargine U-300 < glargine U-100 / detemir < NPH Insulin
- Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
- 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)
- 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.

# CVD Risk Management: Right steps to Reduce the Risk!



- For patients with blood pressure >120/80 mmHg, lifestyle intervention consists of weight loss when indicated, a DASH-style eating pattern including reducing sodium and increasing potassium intake, moderation of alcohol intake, and increased physical activity.

- For individuals with diabetes and hypertension at higher CV



risk (existing ASCVD or 10-year ASCVD risk  $\geq 15\%$ ), a blood pressure target of <130/80 mmHg may be appropriate, if it can be safely attained.

- For patients treated with an Angiotensin Converting Enzyme (ACE) inhibitor, Angiotensin Receptor Blocker (ARB), or diuretic, serum creatinine, estimated glomerular filtration rate (eGFR) and serum potassium levels should be monitored at least annually.
- SGLT2i and GLPI RA are well approved by various regulatory authorities for CV risk reductions apart from their glucose lowering ability.



- In DAPA-HF trial SGLT2i, Dapagliflozin has demonstrated significant risk reduction in worsening of heart failure and CV death in patients with Heart Failure with reduced ejection fraction (HFrEF). The effect of Dapagliflozin was consistent regardless of the presence or absence of T2DM.
- EMPA-REG and CANVAS trials have demonstrated that Empagliflozin and Canagliflozin respectively showed significant risk reduction in composite outcome of MI, Stroke, and CV death.

## Hypertension

- ACE inhibitors or ARBs as first-line therapy for hypertension in people with diabetes and coronary artery disease (CAD) has been added as recommendation.



- ACE inhibitors or ARBs are recommended first-line therapy for hypertension in people with diabetes and CAD.

## Lipid management



### Recommendation:

- Treatment for hypertension should include drug classes demonstrated to reduce CV events in patients with diabetes.

The ODYSSEY OUTCOMES trial has been added to the “Combination Therapy for LDL Cholesterol Lowering” subsection.

- In **ODYSSEY OUTCOMES** trial, 18924 patients (~28% of whom had diabetes) with recent

acute coronary syndrome (ACS) were randomized to receive PCSK9 inhibitor **Alirocumab** or placebo every 2 weeks. Over a median follow up of 2.8 years, there was a significant 15% ( $p < 0.001$ ) reduction in the rate of composite end point (death from coronary heart disease, nonfatal MI, fatal or nonfatal ischemic stroke or unstable angina requiring hospitalization) with Alirocumab versus placebo.



- Similar results were observed for **Evolocumab** in **FOURIER** Trial.

## Anti-platelet agents

- Recommendations were added to the “Antiplatelet Agents” subsection regarding long-term dual antiplatelet therapy and combination therapy with Aspirin plus low dose Rivaroxaban, respectively.

### Recommendation:

- Dual antiplatelet therapy

(DAPT) with low-dose Aspirin and a P2Y12 inhibitor is reasonable for a year after an ACS and may have benefits beyond this period.

- Long term treatment with DAPT should be considered for patients with prior coronary intervention, high ischemic risk, and low bleeding risk to prevent major adverse CV events.

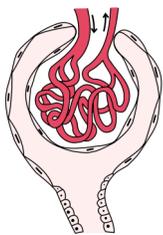
- Combination therapy with Aspirin plus low dose Rivaroxaban should be considered for patient with stable coronary and/or peripheral artery disease and low bleeding risk to prevent major adverse limb and CV events.



## Renal Risk Management: Healthy Kidney is Risk Free Kidney

- At least annually, urinary albumin (e.g., spot urinary albumin-to-creatinine ratio) and estimated glomerular filtration (eGFR) rate should be assessed in patients with type 1 diabetes with duration of  $\geq 5$  years and in all patients with T2DM regardless of treatment.

- In patients with T2DM and diabetic kidney disease, consider use of



**SGLT2 inhibitors** additionally for CV risk reduction when eGFR and urinary albumin creatinine

(UACR) are  $\geq 30$  mL/min/1.73 m<sup>2</sup> or  $>300$  mg/g, respectively.

- In **CREDESCENCE trial, Canagliflozin** was shown to significantly reduce the development of End Stage Renal Disease (ESRD). Additionally, it also showed significant risk reduction in renal and CV death. This benefit was on background of ACE inhibitor or ARB therapy.
- In patients with CKD who are at increased risk for CV events, use of a glucagon-like peptide 1 receptor agonist reduces renal end point, primarily albuminuria, progression of albuminuria, and CV events.

- ACE inhibitors or ARBs are the preferred first-line agent for blood pressure treatment among patients with diabetes, hypertension, eGFR  $< 60$  mL/min/1.73 m<sup>2</sup>, and UACR  $\geq 300$  mg/g Creatinine because of their proven benefits for prevention of CKD progression.
- SGLT2 inhibitors and GLP-1 RAs should be considered for patients with T2DM and CKD who require another drug added to Metformin to attain target A1C or cannot use or tolerate Metformin.

**For any scientific queries on the above topic**

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