American Diabetes Association® (ADA) 2019

The American Association of Clinical Endocrinologists (AACE)
<p>| 1. | Principles of Treatment of Type 2 Diabetes |
| 2. | Criteria for Testing and Diagnosis for Diabetes or Prediabetes in Asymptomatic Patients |
| 3. | Glycemic Recommendations in Adults |
| 4. | Classification of Hypoglycemia |
| 5. | Goals of Care and Approach to Individualization of Glycemic Targets |
| 6. | Main Oral Drug Classes |
| 7. | Insulin |
| 8. | Glycemic Control Algorithm |
| 9. | Alliance Formulary |
| 10. | Link to Alliance Formulary Document and Prior Authorization Criteria |</p>
<table>
<thead>
<tr>
<th>Principles</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Lifestyle modification underlies all therapy (e.g., weight control, physical activity, sleep etc.)</td>
</tr>
<tr>
<td>2. Avoid hypoglycemia</td>
</tr>
<tr>
<td>3. Avoid weight gain</td>
</tr>
<tr>
<td>4. Individualize all glycemic targets (A1C, FPG, PPG)</td>
</tr>
<tr>
<td>5. Optimal A1C is ≤6.5%, or as close to normal as safe and achievable</td>
</tr>
<tr>
<td>6. Therapy choices are affected by initial A1C, duration of diabetes and obesity</td>
</tr>
<tr>
<td>7. Choice of therapy reflects cardiac, cerebrovascular and renal status</td>
</tr>
<tr>
<td>8. Comorbidities must be managed for comprehensive care</td>
</tr>
<tr>
<td>9. Get to goal as soon as possible</td>
</tr>
<tr>
<td>10. Choice of therapy includes ease of use and cost</td>
</tr>
<tr>
<td>11. A1C ≤6.5% for those on any insulin regimen as long as CGM is being used</td>
</tr>
</tbody>
</table>
Alliance Care Management (CM) works with individuals to improve their health and quality of life.

These services are voluntary and available to all eligible members. Alliance Services include:

- Healthy Weight for Life
- Wellness that Works Support Program (formerly known as Weight Watchers)
- Live Better with Diabetes
- Tobacco Cessation Program
- Complex Case Management

Alliance Care Management Services Referrals and Contact: (800) 700-3874 ext. 5512 or [www.ccah-alliance.org/case_management.html](http://www.ccah-alliance.org/case_management.html).
1. Testing should be considered in overweight or obese (BMI ≥25 kg/m² or ≥23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:

- First-degree relative with diabetes
- High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
- History of CVD
- Hypertension (≥140/90 mmHg or on therapy for hypertension)
- HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
- Women with polycystic ovary syndrome
- Physical inactivity
- Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)

IFG, impaired fasting glucose; IGT, impaired glucose tolerance.
2. Patients with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.

3. Women who were diagnosed with Gestational Diabetes Mellitus (GDM) should have lifelong testing at least every 3 years.

4. For all other patients, testing should begin at age 45 years.

5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

IFG, impaired fasting glucose; IGT, impaired glucose tolerance.
Risk-Based Screening for Type 2 Diabetes or Prediabetes in Asymptomatic Children and Adolescents in a Clinical Setting

Testing should be considered in youth\(^*\) who are overweight (≥85% percentile) or obese (≥95 percentile) [A] and who have one or more additional risk factors based on the strength of their association with diabetes:

- Maternal history of diabetes or GDM during the child’s gestation [A]
- Family history of type 2 diabetes in first- or second-degree relative [A]
- Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander) [A]
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight) [B]

\(^*\) After the onset of puberty or after 10 years of age, whichever occurs earlier. If tests are normal, repeat testing at a minimum of 3-year intervals, or more frequently if BMI is increasing, is recommended.

ADA’s grading system uses A, B, C, or E to show the evidence level that supports each recommendation.

- A—Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered
- B—Supportive evidence from well-conducted cohort studies
- C—Supportive evidence from poorly controlled or uncontrolled studies
- E—Expert consensus or clinical experience
### CRITERIA FOR THE SCREENING AND DIAGNOSIS OF DIABETES

**Tests** | **Prediabetes** | **Diabetes**
--- | --- | ---
A1C | 5.7–6.4%* | ≥6.5%†
FPG | 100–125 mg/dL (5.6–6.9 mmol/L)* | ≥126 mg/dL (7.0 mmol/L)†
OGTT | 140–199 mg/dL (7.8–11.0 mmol/L)* | ≥200 mg/dL (11.1 mmol/L)‡
RPG | | ≥200 mg/dL (11.1 mmol/L)‡

* For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range.
† In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate samples.
‡ Only diagnostic in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis.

RPG, random plasma glucose.
Summary of Glycemic Recommendations for Many Non-Pregnant Adults With Diabetes

<table>
<thead>
<tr>
<th>Tests</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>&lt;7.0% (53 mmol/mol)*</td>
</tr>
<tr>
<td>Pre-prandial capillary plasma glucose</td>
<td>80–130 mg/dL* (4.4–7.2 mmol/L)</td>
</tr>
<tr>
<td>Peak postprandial capillary plasma glucose</td>
<td>&lt;180 mg/dL* (10.0 mmol/L)</td>
</tr>
</tbody>
</table>

*More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.
† Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.
A reasonable A1C goal for many non-pregnant adult patients with diabetes is:

A. Lower than 7%
B. Lower than 5.7%
C. Neither A or B
<table>
<thead>
<tr>
<th>Level</th>
<th>Glycemic criteria/description</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>Glucose &lt;70 mg/dL (3.9 mmol/L) and glucose ≥54 mg/dL (3.0 mmol/L)</td>
<td>Glucose (15–20 g)</td>
</tr>
<tr>
<td>Level 2</td>
<td>Glucose &lt;54 mg/dL (3.0 mmol/L)</td>
<td>Glucagon should be prescribed</td>
</tr>
<tr>
<td>Level 3</td>
<td>A severe event characterized by altered mental and/or physical status requiring assistance</td>
<td>Reevaluation of the treatment regimen</td>
</tr>
</tbody>
</table>

**Treating Low Blood Sugar**

- **Check your blood sugar**
  - Is it in your target range?
  - If you can’t check your blood sugar, treat it anyway
  - If you’re low, follow the Rule of 15

- **The Rule of 15**
  - Eat or drink 15g carbs
  - Wait 15 minutes and check blood sugar
  - If still low, eat another 15g carbs
  - Check again after 15 minutes

- **Fast-acting sugars**
  - ½ cup fruit juice or regular soda
  - 4 or 5 hard candies
  - 3 glucose tablets
GOALS OF CARE
- Prevent complications
- Optimize quality of life

ASSESS KEY PATIENT CHARACTERISTICS
- Current lifestyle
- Comorbidities, i.e., ASCVD, CKD, HF
- Clinical characteristics, i.e., age, HbA1c, weight
- Issues such as motivation and depression
- Cultural and socioeconomic context

CONSIDER SPECIFIC FACTORS THAT IMPACT CHOICE OF TREATMENT
- Individualized HbA1c target
- Impact on weight and hypoglycemia
- Side effect profile of medication
- Complexity of regimen, i.e., frequency, mode of administration
- Choose regimen to optimize adherence and persistence
- Access, cost, and availability of medication

SHARED DECISION MAKING TO CREATE A MANAGEMENT PLAN
- Involves an educated and informed patient (and their family/caregiver)
- Seeks patient preferences
- Effective consultation includes motivational interviewing, goal setting, and shared decision making
- Empowers the patient
- Ensures access to DSMES

AGREE ON MANAGEMENT PLAN
- Specify SMART goals:
  - Specific
  - Measurable
  - Achievable
  - Realistic
  - Time limited

IMPLEMENT MANAGEMENT PLAN
- Patients not meeting goals generally should be seen at least every 3 months as long as progress is being made, more frequent contact initially is often desirable for DSMES

ONGOING MONITORING AND SUPPORT INCLUDING:
- Emotional well-being
- Check tolerability of medication
- Monitor glycemic status
- Biofeedback including SMBG, weight, step count, HbA1c, blood pressure, lipids

REVIEW AND AGREE ON MANAGEMENT PLAN
- Review management plan
- Mutual agreement on changes
- Ensure agreed modification of therapy is implemented in a timely fashion to avoid clinical inertia
- Decision cycle undertaken regularly (at least once/twice a year)

ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose
ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

DYSLIPIDEMIA

LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

LIPID PANEL: Assess ASCVD Risk

STATIN THERAPY
If statin-intolerant:
Try alternate statin, lower statin dose or frequency, or add nonstatin LDL-C-lowering therapies.
Repeat lipid panel; assess adequacy, tolerance of therapy.
Intensify therapies to attain goals according to risk levels.

RISK LEVELS

<table>
<thead>
<tr>
<th>RISK LEVELS</th>
<th>DESIRABLE LEVELS</th>
<th>VERY HIGH</th>
<th>EXTREME</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C (mg/dL)</td>
<td>&lt;100</td>
<td>&lt;70</td>
<td>&lt;55</td>
</tr>
<tr>
<td>Non-HDL-C (mg/dL)</td>
<td>&lt;130</td>
<td>&lt;100</td>
<td>&lt;80</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>&lt;150</td>
<td>&lt;150</td>
<td>&lt;150</td>
</tr>
<tr>
<td>Apo B (mg/dL)</td>
<td>&lt;90</td>
<td>&lt;80</td>
<td>&lt;70</td>
</tr>
</tbody>
</table>

If not at desirable levels:
Intensify lifestyle therapy (weight loss, physical activity, dietary changes) and glycemic control; consider additional therapy.

To lower LDL-C:
To lower Non-HDL-C, TG:
To lower Apo B, LDL-P:
To lower LDL-C in FH:**
Intensify statin, add ezetimibe, PCSK9i, coleselvam, or niacin.
Intensify statin and/or add Rx-grade OM3 fatty acid, fibrate, and/or niacin.
Intensify statin and/or add ezetimibe, PCSK9i, coleselvam, and/or niacin.
Statin + PCSK9i

Assess adequacy & tolerance of therapy with focused laboratory evaluations and patient follow-up.

* EVEN MORE INTENSIVE THERAPY MIGHT BE WARRANTED ** FAMILIAL HYPERCHOLESTEROLEMIA

HYPERTENSION

GOAL: SYSTOLIC <130, DIASTOLIC <80 mm Hg

ACEI or ARB
For initial blood pressure >150/100 mm Hg:
DUAL THERAPY

ACEI or ARB +
Calcium Channel Blocker
β-blocker
Thiazide

If not at goal (2-3 months)
Add calcium channel blocker, β-blocker or thiazide diuretic

If not at goal (2-3 months)
Add next agent from the above group, repeat

If not at goal (2-3 months)
Additional choices (α-blockers, central agents, vasodilators, aldosterone antagonist)

Achievement of target blood pressure is critical
### Approach to Individualization of Glycemic Targets

<table>
<thead>
<tr>
<th>Patient / Disease Features</th>
<th>More stringent</th>
<th>( \text{A1C} 7% )</th>
<th>Less stringent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks potentially associated with hypoglycemia and other drug adverse effects</td>
<td>low</td>
<td>( \text{A1C} 7% )</td>
<td>high</td>
</tr>
<tr>
<td>Disease duration</td>
<td>newly diagnosed</td>
<td>( \text{A1C} 7% )</td>
<td>long-standing</td>
</tr>
<tr>
<td>Life expectancy</td>
<td>long</td>
<td>( \text{A1C} 7% )</td>
<td>short</td>
</tr>
<tr>
<td>Important comorbidities</td>
<td>absent</td>
<td>( \text{A1C} 7% )</td>
<td>few / mild</td>
</tr>
<tr>
<td>Established vascular complications</td>
<td>absent</td>
<td>( \text{A1C} 7% )</td>
<td>few / mild</td>
</tr>
<tr>
<td>Patient preference</td>
<td>highly motivated, excellent self-care capabilities</td>
<td>( \text{A1C} 7% )</td>
<td>preference for less burdensome therapy</td>
</tr>
<tr>
<td>Resources and support system</td>
<td>readily available</td>
<td>( \text{A1C} 7% )</td>
<td>limited</td>
</tr>
<tr>
<td>Drug Class</td>
<td>Examples</td>
<td>Mechanism of Action</td>
<td>Common ADRs</td>
</tr>
<tr>
<td>------------</td>
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<td>---------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Biguanide</td>
<td>Metformin (Glucophage)</td>
<td>Decreases hepatic glucose production and intestinal glucose absorption; Increases insulin sensitivity</td>
<td>N/V/D, Indigestion</td>
</tr>
<tr>
<td>Sulfonylurea</td>
<td>Glimepiride Glipizide Glyburide</td>
<td>Stimulates pancreatic islet beta cell insulin release; Increases insulin sensitivity at peripheral target sites</td>
<td>N/V/D, Hypoglycemia</td>
</tr>
<tr>
<td>Glucagon-like Peptide 1 Receptor Agonists (GLP-1 Agonists)</td>
<td>Trulicity Byetta/Bydureon Victoza Ozempic</td>
<td>Activates glucagon-like-peptide-1 (GLP-1) receptor, increasing insulin secretion, decreasing glucagon secretion, and delaying gastric emptying (incretin mimetic)</td>
<td>N/V/D, Abdominal pain, Dyspepsia, Decreased appetite, MTC</td>
</tr>
<tr>
<td>Dipeptidyl Peptidase-4 Inhibitor (DPP-4 Inhibitors)</td>
<td>Alogliptin Tradjenta Januvia Onglyza</td>
<td>Inhibits dipeptidyl peptidase-4, slowing incretin metabolism, increasing insulin synthesis/release, decreasing glucagon levels</td>
<td>URIs</td>
</tr>
<tr>
<td>Sodium Glucose Co-transporter 2 Inhibitors (SGLT2 Inhibitors)</td>
<td>Steglatro Invokana Farxiga Jardiance</td>
<td>Inhibits sodium-glucose cotransporter 2 (SGLT2), reducing glucose reabsorption and increasing urinary glucose excretion</td>
<td>Genital Mycotic Infections, UTIs, DKA</td>
</tr>
<tr>
<td>Alpha-Glucosidase Inhibitors (AGi)</td>
<td>Acarbose Miglitol</td>
<td>Inhibits pancreatic alpha-amylase and intestinal alpha-glucoside hydrolase, delaying glucose absorption</td>
<td>N/V/D, Abdominal Pain</td>
</tr>
<tr>
<td>Thiazolidinediones (TZDs)</td>
<td>Pioglitazone</td>
<td>Increases insulin sensitivity</td>
<td>URI, Edema, Weight Gain, CHF</td>
</tr>
</tbody>
</table>
# Profiles of Antidiabetic Medications

<table>
<thead>
<tr>
<th></th>
<th>MET</th>
<th>GLP1-RA</th>
<th>SGLT2i</th>
<th>DPP4i</th>
<th>AGi</th>
<th>TZD (moderate dose)</th>
<th>SU</th>
<th>COLSVL</th>
<th>BCR-QR</th>
<th>INSULIN</th>
<th>PRAML</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HYPO</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate to Severe</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>WEIGHT</strong></td>
<td>Slight Loss</td>
<td>Loss</td>
<td>Loss</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Loss</td>
</tr>
<tr>
<td><strong>RENAI / GU</strong></td>
<td>Contra-indicated if eGFR &lt;30 ml/min/1.73 m²</td>
<td>Exenatide Not Indicated CrCl &lt;30</td>
<td>Genital Mycotic Infections</td>
<td>Not Indicated for eGFR &lt;45 ml/min/1.73 m²</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>GI Sx</strong></td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Mild</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>CHF</strong></td>
<td>Neutral</td>
<td>See #1</td>
<td>See #2</td>
<td>See #3</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>CHF Risk</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>ASCVD</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate Fracture Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>BONE</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>KETOACIDOSIS</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>DKA Can Occur in Various Stress Settings</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
</tbody>
</table>

1. Liraglutide—FDA approved for prevention of MACE events.
2. Empagliflozin—FDA approved to reduce CV mortality. Canagliflozin—FDA approved to reduce MACE events.
3. Possible increased hospitalizations for heart failure with alogliptin and saxagliptin.
Due to overlapping mechanism of action, guidelines recommend against the use of which two classes in combination:

A. GLP-1 Agonists + SGLT 2 Inhibitors
B. SGLT 2 Inhibitors + DPP-4 Inhibitors
C. DPP-4 Inhibitors + GLP-1 Agonists
**Algorithm for Adding/Intensifying Insulin**

**Start Basal** (Long-Acting Insulin)

- **A1C <8%**
  - TDD 0.1-0.2 U/kg
  - Insulin titration every 2-3 days to reach glycemic goal:
    - Fixed regimen: Increase TDD by 2 U
    - Adjustable regimen:
      - FBG >180 mg/dL: add 20% of TDD
      - FBG 140-180 mg/dL: add 10% of TDD
      - FBG 110-139 mg/dL: add 1 unit
      - If hypoglycemia, reduce TDD by:
        - BG <70 mg/dL: 10% - 20%
        - BG <40 mg/dL: 20% - 40%
  - Consider discontinuing or reducing sulfonylurea after starting basal insulin (basal analogs preferred to NPH)

- **A1C >8%**
  - TDD 0.2-0.3 U/kg

**Intensify** (Prandial Control)

- **Add GLP1-RA**
  - Or SGLT2i
  - Or DPP4i
  - Basal Plus 1, Plus 2, Plus 3
  - Basal Bolus
    - Start: 10% of basal dose or 5 units

- **Add Prandial Insulin**
  - Basal Bolus
    - Start: 50% of TDD in three doses before meals
  - Basal Plus 1, Plus 2, Plus 3
    - Begin prandial insulin before largest meal
    - If not at goal, progress to injections before 2 or 3 meals
    - Begin prandial insulin before each meal
    - 50% Basal / 50% Prandial TDD 0.3-0.5 U/kg

**Glycemic Control Not at Goal**

- Increase prandial dose by 10% or 1-2 units if 2-h postprandial or next premeal glucose consistently >140 mg/dL
- If hypoglycemia, reduce TDD basal and/or prandial insulin by:
  - BG consistently <70 mg/dL: 10% - 20%
  - Severe hypoglycemia (requiring assistance from another person) or BG <40 mg/dL: 20% - 40%

*Glycemic Goal:

- <7% for most patients with T2D: fasting and premeal BG <110 mg/dL; absence of hypoglycemia
- A1C and FBG targets may be adjusted based on patient’s age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk
Alliance Preferred Antidiabetic Medications Summary

- **Biguanide**
  - Metformin (Glucophage)
  - Metformin ER (Glucophage XR)

- **SU**
  - Glipizide
  - Glimepiride
  - Glyburide

- **AGi**
  - Acarbose

- **TZD**
  - Pioglitazone

- **GLP-1 Agonist**
  - Trulicity*

- **SGLT-2 Inhibitor**
  - Steglatro

- **DPP-4 Inhibitor**
  - Alogliptin

- **Prandial Insulin**
  - Admelog Pen and Vial

- **Basal Insulin**
  - Basaglar Pen

* Requires Prior Authorization
The Alliance provider webpage has valuable resources:

- Pharmacy **Formulary**
- Quick Reference Guides: **Diabetes**
- Prior Authorization **Form**
- Prior Authorization **Criteria**

http://www.ccah-alliance.org/pharmacy.html
• Introduction: Standards of Medical Care in Diabetes 2019. Diabetes Care 2019 Jan; 42(Supplement 1): S1-S2
QUESTIONS?

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