# TABLE OF CONTENTS

**COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM**

<table>
<thead>
<tr>
<th>I.</th>
<th>Principles for Treatment of Type 2 Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>II.</td>
<td>Lifestyle Therapy</td>
</tr>
<tr>
<td>III.</td>
<td>Complications-Centric Model for Care of the Patient with Overweight/Obesity</td>
</tr>
<tr>
<td>IV.</td>
<td>Prediabetes</td>
</tr>
<tr>
<td>V.</td>
<td>ASCVD Risk Factor Modifications</td>
</tr>
<tr>
<td>VI.</td>
<td>Glycemic Control</td>
</tr>
<tr>
<td>VII.</td>
<td>Adding/Intensifying Insulin</td>
</tr>
<tr>
<td>VIII.</td>
<td>Profiles of Antihyperglycemic Medications</td>
</tr>
</tbody>
</table>
# Principles of the AACE/ACE Comprehensive Type 2 Diabetes Management Algorithm

| 1. | Lifestyle modification underlies all therapy (e.g., weight control, physical activity, sleep, etc.) |
| 2. | Avoid hypoglycemia |
| 3. | Avoid weight gain |
| 4. | Individualize all glycemic targets (A1C, FPG, PPG) |
| 5. | Optimal A1C is ≤6.5%, or as close to normal as is safe and achievable |
| 6. | Therapy choices are patient centric based on A1C at presentation and shared decision-making |
| 7. | Choice of therapy reflects ASCVD, CHF, and renal status |
| 8. | Comorbidities must be managed for comprehensive care |
| 9. | Get to goal as soon as possible—adjust at ≤3 months until at goal |
| 10. | Choice of therapy includes ease of use and affordability |
| 11. | CGM is highly recommended, as available, to assist patients in reaching goals safely |
## LIFESTYLE THERAPY

### RISK STRATIFICATION FOR DIABETES COMPLICATIONS

<table>
<thead>
<tr>
<th><strong>Nutrition</strong></th>
<th><strong>Physical Activity</strong></th>
<th><strong>Sleep</strong></th>
<th><strong>Behavioral Support</strong></th>
<th><strong>Smoking Cessation</strong></th>
</tr>
</thead>
</table>
| • Maintain optimal weight  
• Calorie restriction (manage increased weight)  
• Plant-based diet; high polyunsaturated and monounsaturated fatty acids  
+ • Avoid *trans* fatty acids; limit saturated fatty acids  
+ • Technological aids  
+ • Structured counseling  
+ • Meal replacement | • 150 min/week moderate exertion (e.g., walking, stair climbing)  
• Strength training  
• Increase as tolerated  
+ • Structured program  
+ • Wearable technologies  
+ • Medical evaluation/clearance  
+ • Medical supervision | • About 6-8 hours per night  
• Basic sleep hygiene  
+ • Screen sleep disturbances  
+ • Home sleep study  
+ • Referral to sleep study | • Community engagement  
• Alcohol moderation  
+ • Discuss mood with HCP  
+ • Formal behavioral therapy | • No tobacco products  
+ • Nicotine replacement therapy and medications as tolerated  
+ • Referral to structured program |
COMPLICATIONS-CENTRIC MODEL FOR CARE OF THE PATIENT WITH OVERWEIGHT/OBESITY (ADIPOSITY-BASED CHRONIC DISEASE)

**STEP 1 EVALUATION FOR COMPLICATIONS AND STAGING**

**CARDIOMETABOLIC DISEASE | BIOMECHANICAL COMPLICATIONS**

<table>
<thead>
<tr>
<th>BMI &lt;25</th>
<th>NO COMPLICATIONS</th>
<th>BMI ≥25</th>
<th>COMPLICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO OVERWEIGHT OR OBESITY</td>
<td>BMI ≥25</td>
<td>OVERWEIGHT OR OBESITY</td>
<td>BMI ≥25</td>
</tr>
<tr>
<td>STAGE 0</td>
<td>STAGE 1</td>
<td>STAGE 2</td>
<td></td>
</tr>
</tbody>
</table>

**STEP 2 SELECT:**

- Therapeutic targets for improvement in complications
- Treatment modality
- Treatment intensity based on staging

**Lifestyle Therapy:**

- Physician/RD counseling, web/remote program, structured multidisciplinary program

**Medical Therapy (BMI ≥27):**

- Individualize care by selecting one of the following based on efficacy, safety, and patients’ clinical profile: phentermine, orlistat, lorcaserin, phentermine/topiramate ER, naltrexone/bupropion, liraglutide 3 mg

**Surgical Therapy (BMI ≥35):**

- Endoscopic procedures, gastric banding, sleeve, or bypass

**STEP 3**

If therapeutic targets for complications not met, intensify lifestyle, medical, and/or surgical treatment modalities for greater weight loss. Obesity is a chronic progressive disease and requires commitment to long-term therapy and follow-up.
### Dyslipidemia

#### Lifestyle Therapy (Including Medically Assisted Weight Loss)

**Lipid Panel: Assess ASCVD Risk**

<table>
<thead>
<tr>
<th>Risk Levels</th>
<th>High</th>
<th>Very High</th>
<th>Extreme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desirable Levels</td>
<td>&lt;100</td>
<td>&lt;70</td>
<td>&lt;55</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-HDL-C (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>&lt;150</td>
<td></td>
<td>&lt;150</td>
</tr>
<tr>
<td>Apo B (mg/dL)</td>
<td>&lt;90</td>
<td></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:
- If TG >500 mg/dL, fibrates, Rx-grade OM-3 fatty acids, niacin

To lower Non-HDL-C, TG:
- Intensify statin, add ezetimibe, PCSK9i, colesvelam, or niacin

To lower Apo B, LDL-P:
- Intensify statin and/or add ezetimibe, PCSK9i, colesvelam, and/or niacin

To lower LDL-C in FH:**
- Intensify statin + PCSK9i

If TG 135-499:
- Add icosapent ethyl 4 g/day if high ASCVD risk on maximally tolerated statins

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

- 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.
**GLYCEMIC CONTROL ALGORITHM**

**INDIVIDUALIZE GOALS**

<table>
<thead>
<tr>
<th>A1C ≤6.5%</th>
<th>A1C &gt;6.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>For patients without concurrent serious illness and at low hypoglycemic risk</td>
<td>For patients with concurrent serious illness and at risk for hypoglycemia</td>
</tr>
</tbody>
</table>

**LIFESTYLE THERAPY AND ONGOING GLUCOSE MONITORING** (CGM preferred)

**INDEPENDENT OF GLYCEMIC CONTROL, IF ESTABLISHED OR HIGH ASCVD RISK AND/OR CKD, RECOMMEND SGLT2I AND/OR LA GLP1-RA**

**Entry A1C ≥7.5% - 9.0%**

**DUAL THERAPY**

- GLP1-RA
- SGLT2i
- DPP4i
- TZD
- SU/GLN
- Basal Insulin
- Colesevelam
- Bromocriptine QR
- AGi

**TRIPLE THERAPY**

- GLP1-RA
- SGLT2i
- TZD
- SU/GLN or Basal Insulin
- Colesevelam
- Bromocriptine QR
- AGi

**ADD OR INTENSIFY INSULIN**

Refer to Insulin Algorithm

**SYMPTOMS**

- **NO**
  - Dual Therapy
  - OR
  - Other Agents

- **YES**
  - Triple Therapy

**LEGEND**

- Few adverse events and/or possible benefits
- Use with caution

---

1 Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation

2 If not at goal in 3 months, proceed to next level therapy

*CKD 3: canagliflozin; HFrEF: dapagliflozin

CKD 3 = stage 3 chronic kidney disease; HFrEF = heart failure with reduced ejection fraction; LA = long-acting (≥24 hour duration)
**Algorithm for Adding/Intensifying Insulin**

### START BASAL (Long-Acting Insulin)

- **A1C <8%**
  - TDD: 0.1–0.2 U/kg
- **A1C >8%**
  - TDD: 0.2–0.3 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)**

### INTENSIFY (Prandial Control)

- **Add GLP1-RA**
- **Add Prandial Insulin**
  - **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
    - Start: 10% of basal dose or 5 units
  - **Basal Bolus**
    - Begin prandial insulin before each meal
    - 50% Basal / 50% Prandial TDD 0.3–0.5 U/kg
    - Start: 50% of TDD in three doses before meals

**Insulin titration every 2-3 days to reach glycemic 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
### Profiles of Antihyperglycemic Medications

<table>
<thead>
<tr>
<th>Condition</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>GLN</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>Moderate/Severe</td>
<td>Mild</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate to Severe</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>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Loss</td>
</tr>
<tr>
<td><strong>RENAL / GU</strong></td>
<td>Contraindicated if eGFR &lt;30 mL/min/1.73 m²</td>
<td>Exenatide Not Indicated CrCl &lt;30</td>
<td>Dose Adjustment Necessary (Except Linagliptin)</td>
<td>Genital Mycotic Infections</td>
<td>Effective in Reducing Albuminuria</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>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Mild</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>CHF</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Prevent HF Hospitalization</td>
<td>Manage HFpEF; See #2</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>CHF Risk</td>
</tr>
<tr>
<td><strong>CARDIAC</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Potential Benefit of LA GLP1-RA</td>
<td>See #4</td>
<td>Neutral</td>
<td>May Reduce Stroke Risk</td>
<td>Possible ASCVD</td>
<td>Lowers LDL-C</td>
<td>Safe</td>
<td>Neutral</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ASCVD</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Potential Benefit of LA GLP1-RA</td>
<td>See #3</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td></td>
</tr>
<tr>
<td><strong>BONE</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>
<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>
<td>Neutral</td>
</tr>
</tbody>
</table>

- **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.