AACE/ACE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM

2017

TASK FORCE

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# 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 Overweight/Obese Patient</td>
</tr>
<tr>
<td>IV.</td>
<td>Prediabetes Algorithm</td>
</tr>
<tr>
<td>V.</td>
<td>ASCVD Risk Factor Modifications Algorithm</td>
</tr>
<tr>
<td>VI.</td>
<td>Goals for Glycemic Control</td>
</tr>
<tr>
<td>VII.</td>
<td>Glycemic Control Algorithm</td>
</tr>
<tr>
<td>VIII.</td>
<td>Algorithm for Adding/Intensifying Insulin</td>
</tr>
<tr>
<td>IX.</td>
<td>Profiles of Antidiabetic Medications</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>1.</td>
<td>Lifestyle therapy, including medically supervised weight loss, is key to managing type 2 diabetes.</td>
</tr>
<tr>
<td>2.</td>
<td>Weight loss should be considered as a lifelong goal in all patients with prediabetes and T2D who also have overweight or obesity, utilizing behavioral interventions and weight loss medications as required to achieve chronic therapeutic goals.</td>
</tr>
<tr>
<td>3.</td>
<td>The A1C target must be individualized.</td>
</tr>
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<td>4.</td>
<td>Glycemic control targets include fasting and postprandial glucose levels.</td>
</tr>
<tr>
<td>5.</td>
<td>The choice of therapies must be individualized on the basis of patient characteristics, impact of net cost to patient, formulary restrictions, personal preferences, etc.</td>
</tr>
<tr>
<td>6.</td>
<td>Minimizing risk of hypoglycemia is a priority.</td>
</tr>
<tr>
<td>7.</td>
<td>Minimizing risk of weight gain is a priority.</td>
</tr>
<tr>
<td>8.</td>
<td>Initial acquisition cost of medications is only a part of the total cost of care which includes monitoring requirements, risk of hypoglycemia, weight gain, safety, etc.</td>
</tr>
<tr>
<td>9.</td>
<td>This algorithm stratifies choice of therapies based on initial A1C.</td>
</tr>
<tr>
<td>10.</td>
<td>Combination therapy is usually required and should involve agents with complementary actions.</td>
</tr>
<tr>
<td>11.</td>
<td>Comprehensive management includes lipid and blood pressure therapies and related comorbidities.</td>
</tr>
<tr>
<td>12.</td>
<td>Therapy must be evaluated frequently until stable (e.g., every 3 months) and then less often.</td>
</tr>
<tr>
<td>13.</td>
<td>The therapeutic regimen should be as simple as possible to optimize adherence.</td>
</tr>
<tr>
<td>14.</td>
<td>This algorithm includes every FDA-approved class of medications for diabetes.</td>
</tr>
</tbody>
</table>
## LIFESTYLE THERAPY
### RISK STRATIFICATION FOR DIABETES COMPLICATIONS

<table>
<thead>
<tr>
<th>Intensity Stratified by Burden of Obesity and Related Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nutrition</strong></td>
</tr>
<tr>
<td>- Maintain optimal weight</td>
</tr>
<tr>
<td>- Calorie restriction (if BMI is increased)</td>
</tr>
<tr>
<td>- Plant-based diet; high polyunsaturated and monounsaturated fatty acids</td>
</tr>
<tr>
<td>- Avoid trans fatty acids; limit saturated fatty acids</td>
</tr>
<tr>
<td>- Structured counseling</td>
</tr>
<tr>
<td>- Meal replacement</td>
</tr>
<tr>
<td>- Medical supervision</td>
</tr>
</tbody>
</table>

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COMPICATIONS-CENTRIC MODEL FOR CARE OF THE PATIENT WITH OVERWEIGHT/OBESITY

**STEP 1**

**EVALUATION FOR COMPLICATIONS AND STAGING**

**CARDIOMETABOLIC DISEASE | BIOMECHANICAL COMPLICATIONS**

<table>
<thead>
<tr>
<th>BMI &lt; 25</th>
<th>BMI ≥ 25</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO OVERWEIGHT OR OBESITY</td>
<td>OVERWEIGHT OR OBESITY</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):**  
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

STATIN THERAPY
If TG > 500 mg/dL, fibrates, Rx-grade omega-3 fatty acids, niacin

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>HIGH</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:
- Intensify statin, add ezetimibe, PCSK9i, colesvealam, or niacin
- Intensify statin and/or add Rx-grade OM3 fatty acid, fibrate, and/or niacin
- Intensify statin and/or add ezetimibe, PCSK9i, colesvealam, and/or niacin Statin + PCSK9i

TO LOWER Non-HDL-C, TG:
- Intensify statin and/or add Rx-grade OM3 fatty acid, fibrate, and/or niacin

TO LOWER Apo B, LDL-P:
- Intensify statin, add ezetimibe, PCSK9i, colesvealam, or niacin

TO LOWER LDL-C in FH: **
- Intensify statin, add ezetimibe, PCSK9i, colesvealam, or niacin

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

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

HYPERTENSION

GOAL: SYSTOLIC <130, DIASTOLIC <80 mm Hg

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
**GOALS FOR GLYCEMIC CONTROL**

**INDIVIDUALIZE GOALS**

**A1C ≤ 6.5%**
For patients without concurrent serious illness and at low hypoglycemic risk

**A1C > 6.5%**
For patients with concurrent serious illness and at risk for hypoglycemia
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

**Intensify** (Prandial Control)

- Add GLP-1 RA
- Or SGLT-2i
- Or DPP-4i

**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%

**Glycemic Control Not at Goal***

**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

Consider discontinuing or reducing sulfonylurea after starting basal insulin (basal analogs preferred to NPH)

**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

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## Profiles of Antidiabetic Medications

<table>
<thead>
<tr>
<th></th>
<th>MET</th>
<th>GLP-1 RA</th>
<th>SGLT-2i</th>
<th>DPP-4i</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>Moderate/Severe</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</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>Gain</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>Not Indicated for eGFR &lt; 45 mL/min/1.73 m²</td>
<td>Genital Mycotic Infections</td>
<td>Dose Adjustment Necessary (Except Linagliptin)</td>
<td>Effective in Reducing Albuminuria</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
<td>Neutral</td>
<td>More Hypo Risk</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>Neutral</td>
<td>Mild</td>
<td>Moderate</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>CHF</strong></td>
<td>Neutral</td>
<td>Possible Benefit of Liraglutide</td>
<td>Possible Benefit of Empagliflozin</td>
<td>Possible Risk for Saxagliptin and Alogliptin</td>
<td>Neutral</td>
<td>Moderate</td>
<td>More CHF Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More CHF Risk</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>CARDIAC</strong>*</td>
<td>Neutral</td>
<td>Possible Benefit of Liraglutide</td>
<td>Possible Benefit of Empagliflozin</td>
<td>Possible CV Benefit</td>
<td>Neutral</td>
<td>Moderate</td>
<td>More CHF Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More CHF Risk</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>ASCVD</strong></td>
<td>Neutral</td>
<td>Possible CV Benefit</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></td>
</tr>
<tr>
<td><strong>BONE</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Canagliflozin Warning</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>KETOACIDOSIS</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>DKA Occurring in T2D 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>
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**Legend:**
- Few adverse events or possible benefits
- Use with caution
- Likelihood of adverse effects
- ? Uncertain effect
- * FDA indication to prevent CVD death in diabetes plus prior CVD events

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