AACE/ACE Comprehensive Type 2 Diabetes Management Algorithm

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Task Force
Alan J. Garber, MD, PhD, FACE, Chair

Martin J. Abrahamson, MD
Joshua I. Barzilay, MD, FACE
Lawrence Blonde, MD, FACP, MACE
Zachary T. Bloomgarden, MD, MACE
Michael A. Bush, MD
Samuel Dagogo-Jack, MD, FACE
Ralph A. DeFronzo, MD

Daniel Einhorn, MD, FACP, FACE
Vivian A. Fonseca, MD, FACE
Jeffrey R. Garber, MD, FACP, FACE
W. Timothy Garvey, MD, FACE
George Grunberger, MD, FACP, FACE
Yehuda Handelsman, MD, FACP, FNLA, FACE
Irl B. Hirsch, MD

Paul S. Jellinger, MD, MACE
Janet B. McGill, MD, FACE
Jeffrey I. Mechanick, MD, FACP, FACE, FACN, ECNU
Paul D. Rosenblit, MD, PhD, FNLA, FACE
Guillermo Umpierrez, MD, FACP, FACE
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<td></td>
<td><strong>PRINCIPLES OF THE AACE/ACE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM</strong></td>
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<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>
<tr>
<td>4.</td>
<td>Glycemic control targets include fasting and postprandial glucose.</td>
</tr>
<tr>
<td>5.</td>
<td>The choice of therapies must be individualized on 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

### Intensity Stratified by Burden of Obesity and Related Complications

<table>
<thead>
<tr>
<th>Component</th>
<th>Intervention Details</th>
<th>Additional Interventions</th>
</tr>
</thead>
</table>
| Nutrition       | • Maintain optimal weight  
• Calorie restriction (if BMI is increased)  
• Plant-based diet; high polyunsaturated and monounsaturated fatty acids | • Avoid trans fatty acids  
• Limit saturated fatty acids  
• Structured counseling  
• Meal replacement |
| Physical Activity| • 150 min/week moderate exertion (e.g., walking, stair climbing)  
• Strength training  
• Increase as tolerated | • Structured program  
• Wearable technologies  
• Medical evaluation/clearance  
• Medical supervision |
| Sleep           | • About 7 hours per night  
• Basic sleep hygiene | • Screen OSA  
• Home sleep study  
• Referral to sleep lab |
| Behavioral Support| • Community engagement  
• Alcohol moderation | • Discuss mood with HCP  
• Formal behavioral therapy |
| Smoking Cessation| • No tobacco products | • Nicotine replacement therapy  
• Referral to structured program |
**Complications-Centric Model for Care of the Patient with Overweight/Obesity**

**Step 1: Evaluation for Complications and Staging**

<table>
<thead>
<tr>
<th>Cardiometabolic Disease</th>
<th>Biomechanical Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI &lt; 25</strong></td>
<td></td>
</tr>
<tr>
<td><strong>BMI ≥ 25</strong></td>
<td></td>
</tr>
<tr>
<td><strong>NO Complications</strong></td>
<td></td>
</tr>
<tr>
<td><strong>BMI ≥ 25</strong></td>
<td><strong>COMPLICATIONS</strong></td>
</tr>
<tr>
<td><strong>Overweight or Obesity</strong></td>
<td><strong>Mild to Moderate</strong></td>
</tr>
<tr>
<td><strong>Stage 0</strong></td>
<td><strong>Stage 1</strong></td>
</tr>
<tr>
<td><strong>Stage 2</strong></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):**
- 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.
ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

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

HIGH

VERY HIGH

EXTREME

LDL-C (mg/dL)
<100
<70
<55

Non-HDL-C (mg/dL)
<130
<100
<80

TG (mg/dL)
<150
<150
<150

Apo B (mg/dL)
<90
<80
<70

RISK LEVELS:

HIGH: DM but no other major risk and/or age <60
VERY HIGH: DM + major ASCVD risk (s HTN, Fam Hx, low HDL-C, smoking, CKD3.4+)
EXTREME: DM plus established clinical CVD

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, colesuvelam, or niacin
Intensify statin and/or add Rx-grade OM3 fatty acid, fibrate, and/or niacin
Intensify statin and/or add ezetimibe, PCSK9i, colesuvelam, 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

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## 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>
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)

*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

INTENSIFY (Prandial Control)

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

- 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%
# 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>Mild</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>Gain</td>
<td>Loss</td>
</tr>
<tr>
<td><strong>RENAI / GU</strong></td>
<td>Contraindicated if eGFR &lt; 30 mL/min/1.73 m²</td>
<td>Exenatide Not Indicated if 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>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>Neutral</td>
</tr>
<tr>
<td><strong>CHF</strong></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>
<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>Neutral</td>
<td>Moderate</td>
<td>More CHF Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More CHF Risk</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>ASCVD</strong></td>
<td>Neutral</td>
<td>Possible CV Benefit</td>
<td>Possible CV Benefit</td>
<td>Neutral</td>
<td>May Reduce Stroke Risk</td>
<td>Moderate</td>
<td>Safe</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>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>
<td>Neutral</td>
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</table>

- 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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