AACE/ACE COMPREHENSIVE
TYPE 2 DIABETES
MANAGEMENT ALGORITHM

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS
AMERICAN COLLEGE OF ENDOCRINOLOGY

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# Principles of the AACE/ACE Comprehensive Type 2 Diabetes Management Algorithm

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<tr>
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<th>Description</th>
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<tbody>
<tr>
<td>1.</td>
<td>Lifestyle modification underlies all therapy (e.g., weight control, physical activity, sleep, etc.)</td>
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<tr>
<td>2.</td>
<td>Avoid hypoglycemia</td>
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<tr>
<td>3.</td>
<td>Avoid weight gain</td>
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<td>4.</td>
<td>Individualize all glycemic targets (A1C, FPG, PPG)</td>
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<td>5.</td>
<td>Optimal A1C is ≤6.5%, or as close to normal as is safe and achievable</td>
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<td>6.</td>
<td>Therapy choices are affected by initial A1C, duration of diabetes, and obesity status</td>
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<td>7.</td>
<td>Choice of therapy reflects cardiac, cerebrovascular, and renal status</td>
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<td>8.</td>
<td>Comorbidities must be managed for comprehensive care</td>
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<td>9.</td>
<td>Get to goal as soon as possible—adjust at ≤3 months until at goal</td>
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<td>10.</td>
<td>Choice of therapy includes ease of use and affordability</td>
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<tr>
<td>11.</td>
<td>A1C ≤6.5% for those on any insulin regimen as long as CGM is being used</td>
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</table>
# Lifestyle Therapy

## Risk Stratification for Diabetes Complications

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

<table>
<thead>
<tr>
<th>Category</th>
<th>Interventions</th>
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</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 |
**Comprehensive Model for Care of the Patient with Overweight/Obesity**

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

- **BMI <25**
  - No complications
  - No overweight or obesity

- **BMI ≥25**
  - Overweight or obesity
  - Stage 0

- **BMI ≥25**
  - Complications
  - Stage 1
  - Stage 2

**Cardiometabolic Disease | Biomechanical Complications**

**Step 2: Select**

- 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 are 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.

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PREDIABETES ALGORITHM
IFG (100-125) | IGT (140-199) | METABOLIC SYNDROME (NCEP 2001)

LIFESTYLE THERAPY
(Including Medically Assisted Weight Loss)

TREAT ASCVD RISK FACTORS
WEIGHT LOSS THERAPIES

ASCVD RISK FACTOR MODIFICATIONS ALGORITHM
DYSLIPIDEMIA ROUTE
HYPERTENSION ROUTE

NORMAL GLYCEMIA
Progression

OVERT DIABETES

TREAT HYPERGLYCEMIA
FPG >100 | 2-hour PG >140

1 PRE-DM CRITERION
Multiple PRE-DM CRITERIA

Intensify Weight Loss Therapies
Low-risk Medications
Metformin
Acarbose
Consider with Caution
TZD
GLP-1RA

LEGEND
Orlistat, lorcaserin, phentermine/topiramate ER, naltrexone/bupropion, liraglutide 3 mg, or bariatric surgery as indicated for obesity treatment

If glycemia not normalized

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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

<table>
<thead>
<tr>
<th></th>
<th>HIGH</th>
<th>VERY HIGH</th>
<th>EXTREME</th>
</tr>
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<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:**

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

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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**GLYCEMIC CONTROL ALGORITHM**

**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

**LIFESTYLE THERAPY** (Including Medically Assisted Weight Loss)

**Entry A1C < 7.5%**

**MONOTHERAPY**
- Metformin
- GLP1-RA
- SGLT2i
- DPP4i
- TZD
- AGI
- SU/GLN

If not at goal in 3 months proceed to Dual Therapy

**Entry A1C ≥ 7.5%**

**DUAL THERAPY**
- GLP1-RA
- SGLT2i
- DPP4i
- TZD
- Basal Insulin
- Colesevelam
- Bromocriptine QR
- AGI
- SU/GLN

If not at goal in 3 months proceed to Triple Therapy

**Entry A1C > 9.0%**

**TRIPLE THERAPY**
- GLP1-RA
- SGLT2i
- DPP4i
- TZD
- Basal Insulin
- Colesevelam
- Bromocriptine QR
- AGI
- SU/GLN

If not at goal in 3 months proceed to or intensify insulin therapy

**SYMPTOMS**

NO
- DUAL Therapy

OR
- INSULIN ± Other Agents

YES
- TRIPLE Therapy

ADD OR INTENSIFY INSULIN
- Refer to Insulin Algorithm

**LEGEND**

✓ Few adverse events and/or possible benefits

⚠ Use with caution

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1. Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation
2. Certain GLP1-RAs and SGLT2is have shown CVD and CKD benefits—preferred in patients with those complications
3. Include one of these medications if CHD present
**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

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**Intensify (Prandial Control)**

- **Add GLP1-RA**
  - Or SGLT2i
  - Or DPP4i
- **Add Prandial Insulin**
  - Basal Plus 1, Plus 2, Plus 3
  - Start: 10% of basal dose or 5 units
  - Basal Bolus
  - 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>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>
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<tbody>
<tr>
<td>HYPO</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>
<td>Neutral</td>
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<tr>
<td>WEIGHT</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>RENAL / GU</td>
<td>Contra-indicated if eGFR &lt;30 mL/min/1.73 m²</td>
<td>Exenatide Not Indicated</td>
<td>eGFR &lt;45 mL/min</td>
<td>Not Indicated for eGFR &lt;45 mL/min</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
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<tr>
<td>GI Sx</td>
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<td>Mild</td>
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<td>CHF</td>
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<td>See #1</td>
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<td>See #3</td>
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<td>Moderate</td>
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<td>CHF Risk</td>
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<td>Moderate Fracture Risk</td>
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<td>BONE</td>
<td>Neutral</td>
<td>Neutral</td>
<td>DKA Can Occur in Various Stress Settings</td>
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<td>KETOACIDOSIS</td>
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- Few adverse events or possible benefits
- Use with caution
- Likelihood of adverse effects

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.

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