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Comprehensive Type 2 Diabetes Algorithm

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## 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>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nutrition</strong></td>
<td>- Maintain optimal weight&lt;br&gt;- Calorie restriction&lt;br&gt;- Plant-based diet; high polyunsaturated and monounsaturated fatty acids&lt;br&gt;- Avoid trans fatty acids; limit saturated fatty acids&lt;br&gt;- Structured counseling&lt;br&gt;- Meal replacement</td>
</tr>
<tr>
<td><strong>Physical Activity</strong></td>
<td>- 150 min/week moderate exertion (eg. walking, stair climbing)&lt;br&gt;- Strength training&lt;br&gt;- Increase as tolerated&lt;br&gt;- Structured program&lt;br&gt;- Medical evaluation/clearance&lt;br&gt;- Medical supervision</td>
</tr>
<tr>
<td><strong>Sleep</strong></td>
<td>- About 7 hours per night&lt;br&gt;- Screen for obstructive sleep apnea</td>
</tr>
<tr>
<td><strong>Behavioral Support</strong></td>
<td>- Community engagement&lt;br&gt;- Screen for mood disorders&lt;br&gt;- Refer to mental healthcare professional&lt;br&gt;- Behavioral therapy</td>
</tr>
<tr>
<td><strong>Smoking Cessation</strong></td>
<td>- No tobacco products&lt;br&gt;- Structured programs</td>
</tr>
</tbody>
</table>

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STEP 1
EVALUATION FOR COMPLICATIONS AND STAGING

CARDIOMETABOLIC DISEASE | BIOMECHANICAL COMPLICATIONS

NO COMPLICATIONS
BMI ≥ 25

COMPLICATIONS
BMI 25–26.9
BMI ≥ 27: Stage Severity of Complications

MILD TO MODERATE

SEVERE

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):
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.

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PRE-DIABETES 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

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

TREAT HYPERGLYCEMIA MODIFICATIONS ALGORITHM

LEGEND

MULTIPLE PRE-DM CRITERIA

1 PRE-DM CRITERION

Low-risk Medications
Metformin
Acarbose

Consider with Caution
TZD
GLP-1 RA

PROCEED TO HYPERGLYCEMIA ALGORITHM

OVERT DIABETES

If glycemia not normalized

LEGEND

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

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**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
GLYCEMIC CONTROL ALGORITHM

LIFESTYLE THERAPY
(Including Medically Assisted Weight Loss)

Entry A1C < 7.5%
- Metformin
- GLP-1 RA
- SGLT-2i
- DPP-4i
- TZD
- AGi
- SU/GLN

If not at goal in 3 months proceed to Dual Therapy

Entry A1C ≥ 7.5%
- Metformin or other 1st-line agent
- GLP-1 RA
- SGLT-2i
- DPP-4i
- TZD
- Basal Insulin
- Colesevelam
- Bromocriptine QR
- AGi
- SU/GLN

If not at goal in 3 months proceed to Triple Therapy

Entry A1C > 9.0%
- Basal insulin
- DPP-4i
- Colesevelam
- Bromocriptine QR
- AGi
- SU/GLN

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

MONOTHERAPY*

DUAL THERAPY*

TRIPLE THERAPY*

ADD OR INTENSIFY INSULIN
Refer to Insulin Algorithm

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

PROGRESSION OF DISEASE

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r 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

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% decrease
  - BG < 40 mg/dL: 20%–40% decrease

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%

ALGORITHM FOR ADDING/INTENSIFYING INSULIN

Glycemic Goal:
- A1C < 8%
- A1C > 8%

START BASAL (Long-Acting Insulin)

A1C < 8%
- TDD 0.1–0.2 U/kg

A1C > 8%
- TDD 0.2–0.3 U/kg

Infusion pump is the preferred method for basal insulin delivery

Glycemic Control Not at Goal*:

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

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%

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

Oral hypoglycemic agents may be added or intensified after starting basal insulin

Oral hypoglycemic agent selection may be based on patient’s age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk

Add Pranidal Insulin

- Insulin titration every 2–3 days to reach glycemic goal:
  - Start: 50% of TDD in three doses before meals
  - 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% decrease
      - BG < 40 mg/dL: 20%–40% decrease

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

Add Prandial Insulin
- 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

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%

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DYSLIPIDEMIA

LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

LIPID PANEL: Assess ASCVD Risk

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>HIGH</th>
<th>VERY HIGH</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C (mg/dL)</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Non-HDL-C (mg/dL)</td>
<td>&lt;130</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>&lt;150</td>
</tr>
<tr>
<td>TC/HDL-C</td>
<td>&lt;3.5</td>
</tr>
<tr>
<td>Apo B (mg/dL)</td>
<td>&lt;90</td>
</tr>
<tr>
<td>LDL-P (nmol/L)</td>
<td>&lt;1200</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

Intensify lifestyle therapy (weight loss, physical activity, dietary changes) and glycemic control; consider additional therapy IF NOT AT DESIRABLE LEVELS:

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

ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

ACHE or ARB

ACEi or ARB

Calcium Channel Blocker

ACEi or ARB

ACEi or ARB

ACEi or ARB + Calcium Channel Blocker

ACEi or ARB + Calcium Channel Blocker + β-blocker

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide + Diuretic

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide + Diuretic + Other

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide + Diuretic + Other + Additional Choices

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide + Diuretic + Other + Additional Choices + Achievement of target blood pressure is critical

GOAL: SYSTOLIC <130, DIASTOLIC <80 mm Hg

For initial blood pressure >150/100 mm Hg:

DUAL THERAPY

ACEi or ARB

ACEi or ARB

ACEi or ARB

ACEi or ARB + Calcium Channel Blocker

ACEi or ARB + Calcium Channel Blocker + β-blocker

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide + Diuretic

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide + Diuretic + Other

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide + Diuretic + Other + Additional Choices

ACEi or ARB + Calcium Channel Blocker + β-blocker + Thiazide + Diuretic + Other + Additional Choices + Achievement of target blood pressure is critical
### Profiles of Antidiabetic Medications

<table>
<thead>
<tr>
<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>HYPO</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>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>Gain</td>
</tr>
<tr>
<td>RENAL/GU</td>
<td>Contraindicated CKD Stage 3B,4,5</td>
<td>Exenatide Not Indicated CrCl &lt; 30</td>
<td>Not Effective with eGFR &lt; 45, Genital Mycotic Infections</td>
<td>Dose Adjustment Necessary (Except Linagliptin)</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
</tr>
<tr>
<td>GI Sx</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>
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<tr>
<td>CHF</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td>ASCVD</td>
<td>Benefit</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Safe</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td>BONE</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>
</tr>
</tbody>
</table>

**Legend:**
- **Green** Few adverse events or possible benefits
- **Yellow** Use with caution
- **Red** Likelihood of adverse effects
- **Question Mark** Uncertain effect
1. Lifestyle therapy, including medically supervised weight loss, is key to managing type 2 diabetes.

2. The A1C target must be individualized.

3. Glycemic control targets include fasting and postprandial glucoses.

4. The choice of therapies must be individualized on basis of patient characteristics, impact of net cost to patient, formulary restrictions, personal preferences, etc.

5. Minimizing risk of hypoglycemia is a priority.

6. Minimizing risk of weight gain is a priority.

7. 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.

8. This algorithm stratifies choice of therapies based on initial A1C.

9. Combination therapy is usually required and should involve agents with complementary actions.

10. Comprehensive management includes lipid and blood pressure therapies and related comorbidities.

11. Therapy must be evaluated frequently until stable (e.g., every 3 months) and then less often.

12. The therapeutic regimen should be as simple as possible to optimize adherence.

13. This algorithm includes every FDA-approved class of medications for diabetes.