

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS  
AMERICAN COLLEGE OF ENDOCRINOLOGY

AACE/ACE COMPREHENSIVE  
**TYPE 2 DIABETES**  
MANAGEMENT ALGORITHM



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## COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM

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# 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  $\leq 6.5\%$ , or as close to normal as is safe and achievable
6. Therapy choices are affected by initial A1C, duration of diabetes, and obesity status
7. Choice of therapy reflects cardiac, cerebrovascular, and renal status
8. Comorbidities must be managed for comprehensive care
9. Get to goal as soon as possible—adjust at  $\leq 3$  months until at goal
10. Choice of therapy includes ease of use and affordability
11. A1C  $\leq 6.5\%$  for those on any insulin regimen as long as CGM is being used

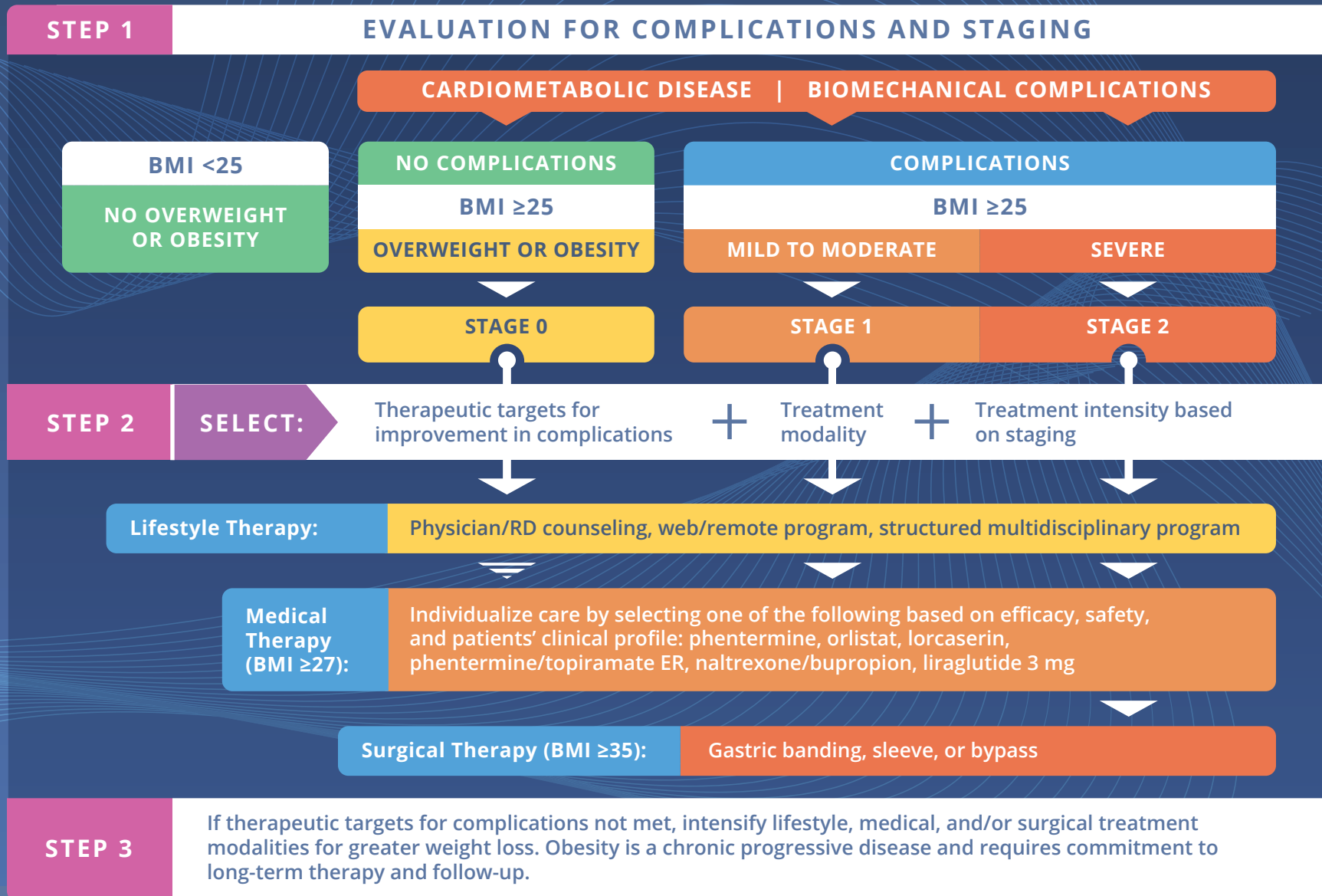
# LIFESTYLE THERAPY

## RISK STRATIFICATION FOR DIABETES COMPLICATIONS

### INTENSITY STRATIFIED BY BURDEN OF OBESITY AND RELATED COMPLICATIONS

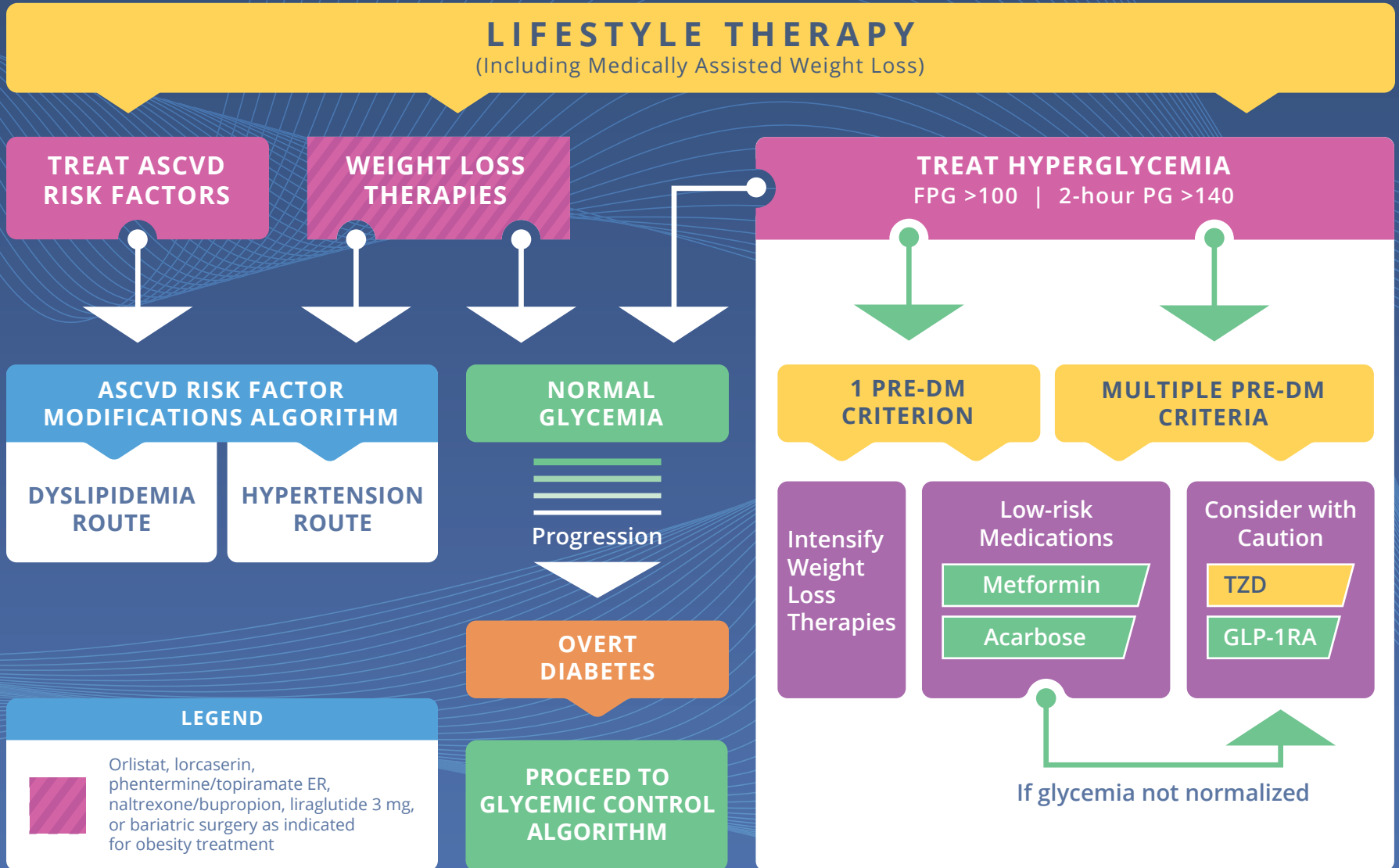
|                           |  |   |   |   |
|---------------------------|--|---|---|---|
| <b>Nutrition</b>          | <ul style="list-style-type: none"> <li>Maintain optimal weight</li> <li>Calorie restriction (if BMI is increased)</li> <li>Plant-based diet; high polyunsaturated and monounsaturated fatty acids</li> </ul> | + | <ul style="list-style-type: none"> <li>Avoid <i>trans</i> fatty acids; limit saturated fatty acids</li> </ul> | <ul style="list-style-type: none"> <li>Structured counseling</li> <li>Meal replacement</li> </ul>           |
| <b>Physical Activity</b>  | <ul style="list-style-type: none"> <li>150 min/week moderate exertion (e.g., walking, stair climbing)</li> <li>Strength training</li> <li>Increase as tolerated</li> </ul>                                   | + | <ul style="list-style-type: none"> <li>Structured program</li> <li>Wearable technologies</li> </ul>           | <ul style="list-style-type: none"> <li>Medical evaluation/clearance</li> <li>Medical supervision</li> </ul> |
| <b>Sleep</b>              | <ul style="list-style-type: none"> <li>About 7 hours per night</li> <li>Basic sleep hygiene</li> </ul>   | + | <ul style="list-style-type: none"> <li>Screen OSA</li> <li>Home sleep study</li> </ul>                        | <ul style="list-style-type: none"> <li>Referral to sleep lab</li> </ul>                                     |
| <b>Behavioral Support</b> | <ul style="list-style-type: none"> <li>Community engagement</li> <li>Alcohol moderation</li> </ul>   | + | <ul style="list-style-type: none"> <li>Discuss mood with HCP</li> </ul>                                       | <ul style="list-style-type: none"> <li>Formal behavioral therapy</li> </ul>                                 |
| <b>Smoking Cessation</b>  | <ul style="list-style-type: none"> <li>No tobacco products</li> </ul>  | + | <ul style="list-style-type: none"> <li>Nicotine replacement therapy</li> </ul>                                | <ul style="list-style-type: none"> <li>Referral to structured program</li> </ul>                            |

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



# PREDIABETES ALGORITHM

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



# ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

## DYSLIPIDEMIA

## HYPERTENSION

**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          | RISK LEVELS:<br><span style="color: yellow;">■</span> <b>HIGH:</b><br>DM but no other major risk and/or age <40<br><span style="color: orange;">■</span> <b>VERY HIGH:</b><br>DM + major ASCVD risk(s) (HTN, Fam Hx, low HDL-C, smoking, CKD3,4)*<br><span style="color: red;">■</span> <b>EXTREME:</b><br>DM plus established clinical CVD |
|-------------------|------------------|------------------|------------------|---|
|                   | DESIRABLE LEVELS | DESIRABLE LEVELS | DESIRABLE LEVELS |   |
| 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              |   |

**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, colesovelam, or niacin  
**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 and/or add ezetimibe, PCSK9i, colesovelam, and/or niacin  
**To lower LDL-C in FH:\*\*** Statin + PCSK9i

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

\* EVEN MORE INTENSIVE THERAPY MIGHT BE WARRANTED \*\* FAMILIAL HYPERCHOLESTEROLEMIA

**GOAL: SYSTOLIC <130, DIASTOLIC <80 mm Hg**

**ACEi or ARB**

For initial blood pressure >150/100 mm Hg:  
**DUAL THERAPY**

|                    |   |                           |
|--------------------|---|---------------------------|
| <b>ACEi or ARB</b> | + | 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

**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%

Entry A1C ≥7.5%

Entry A1C >9.0%

### MONOTHERAPY<sup>1</sup>

- ✓ Metformin
- ✓ GLP1-RA<sup>2,3</sup>
- ✓ SGLT2i<sup>2,3</sup>
- ✓ DPP4i
- ! TZD
- ✓ AGi
- ! SU/GLN

If not at goal in 3 months proceed to Dual Therapy

### DUAL THERAPY<sup>1</sup>

- ✓ GLP1-RA<sup>2,3</sup>
  - ✓ SGLT2i<sup>2,3</sup>
  - ✓ DPP4i
  - ! TZD
  - ! Basal Insulin
  - ✓ Colesevelam
  - ✓ Bromocriptine QR
  - ✓ AGi
  - ! SU/GLN
- MET** or other 1st-line agent

If not at goal in 3 months proceed to Triple Therapy

### TRIPLE THERAPY<sup>1</sup>

- ✓ GLP1-RA<sup>2,3</sup>
  - ✓ SGLT2i<sup>2,3</sup>
  - ! TZD
  - ! Basal Insulin
  - ✓ DPP4i
  - ✓ Colesevelam
  - ✓ Bromocriptine QR
  - ✓ AGi
  - ! SU/GLN
- MET** or other 1st-line agent + 2nd-line agent

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

### SYMPTOMS

NO YES

DUAL Therapy

OR

TRIPLE Therapy

INSULIN ± Other Agents

**ADD OR INTENSIFY INSULIN**

Refer to Insulin Algorithm

### LEGEND

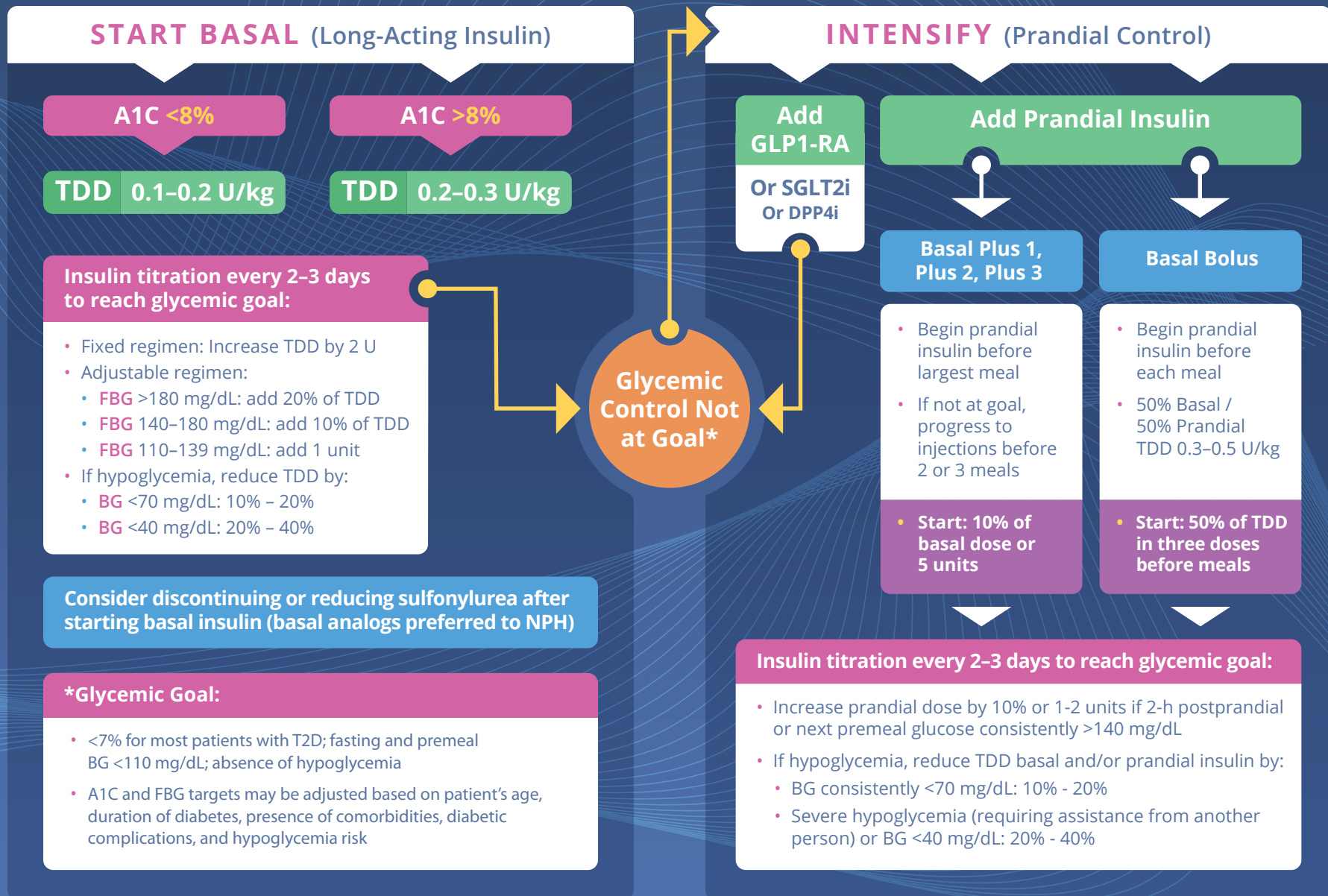
- ✓ Few adverse events and/or possible benefits
- ! Use with caution

- 1 Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation
- 2 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

PROGRESSION OF DISEASE



# ALGORITHM FOR ADDING/INTENSIFYING INSULIN



# PROFILES OF ANTIDIABETIC MEDICATIONS

|                     | MET   | GLP1-RA                                   | SGLT2i   | DPP4i   | AGi      | TZD<br>(moderate dose)       | SU<br>GLN                    | COLSVL                    | BCR-QR   | INSULIN               | PRAML    |
|---------------------|---|---|--|---|----------|------------------------------|------------------------------|---------------------------|----------|-----------------------|----------|
| <b>HYPO</b>         | Neutral   | Neutral                                   | Neutral  | Neutral   | Neutral  | Neutral                      | Moderate/<br>Severe<br>Mild  | Neutral                   | Neutral  | Moderate<br>to Severe | Neutral  |
| <b>WEIGHT</b>       | Slight Loss   | Loss                                      | Loss   | Neutral   | Neutral  | Gain                         | Gain                         | Neutral                   | Neutral  | Gain                  | Loss     |
| <b>RENAL / GU</b>   | Contra-<br>indicated<br>if eGFR <30<br>mL/min/<br>1.73 m <sup>2</sup> | Exenatide<br>Not<br>Indicated<br>CrCl <30 | Not Indicated for<br>eGFR <45 mL/<br>min/1.73 m <sup>2</sup> | Dose<br>Adjustment<br>Necessary<br>(Except<br>Linagliptin)<br><br>Effective in<br>Reducing<br>Albuminuria | Neutral  | Neutral                      | More<br>Hypo Risk            | Neutral                   | Neutral  | More<br>Hypo Risk     | Neutral  |
|                     |   | Possible<br>Benefit of<br>Liraglutide     | Genital Mycotic<br>Infections                                |   |          |                              |                              |                           |          |                       |          |
| <b>GI Sx</b>        | Moderate  | Moderate                                  | Neutral  | Neutral   | Moderate | Neutral                      | Neutral                      | Mild                      | Moderate | Neutral               | Moderate |
| <b>CHF</b>          | Neutral   | See #1                                    | See #2   | See #3  | Neutral  | Moderate                     | Neutral                      | Neutral                   | Neutral  | CHF Risk              | Neutral  |
| <b>CARDIAC</b>      |   |   |  |   |          | ASCVD                        | May<br>Reduce<br>Stroke Risk | Possible<br>ASCVD<br>Risk | Benefit  | Safe                  |          |
| <b>BONE</b>         | Neutral   | Neutral                                   | Neutral  | Neutral   | Neutral  | Moderate<br>Fracture<br>Risk | Neutral                      | Neutral                   | Neutral  | Neutral               | Neutral  |
| <b>KETOACIDOSIS</b> | Neutral   | Neutral                                   | DKA Can Occur<br>in Various<br>Stress Settings               | Neutral   | Neutral  | Neutral                      | Neutral                      | Neutral                   | Neutral  | Neutral               | Neutral  |

- 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.