AACE/ACE COMPREHENSIVE DIABETES MANAGEMENT ALGORITHM

2015

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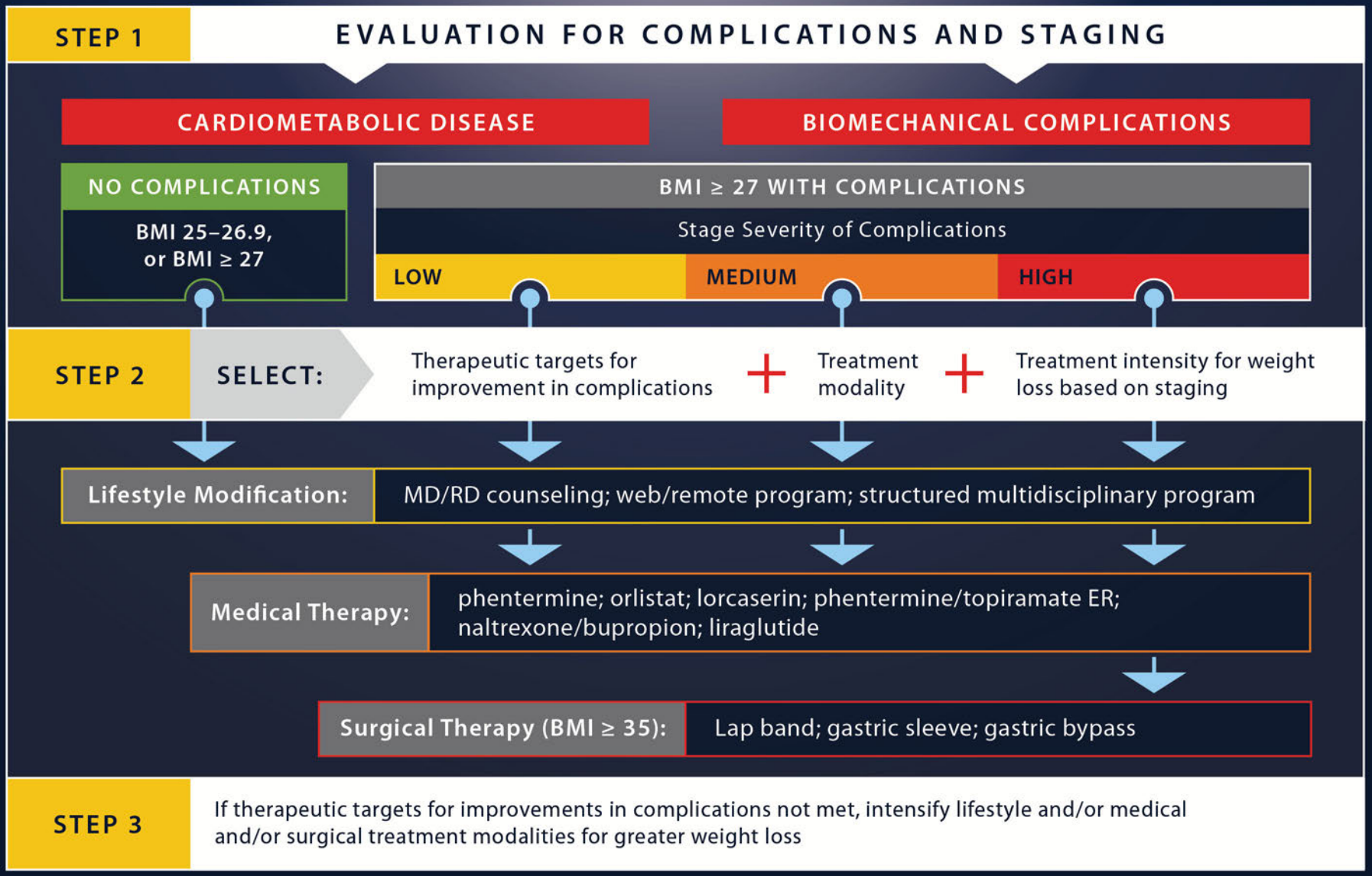
TABLE OF CONTENTS

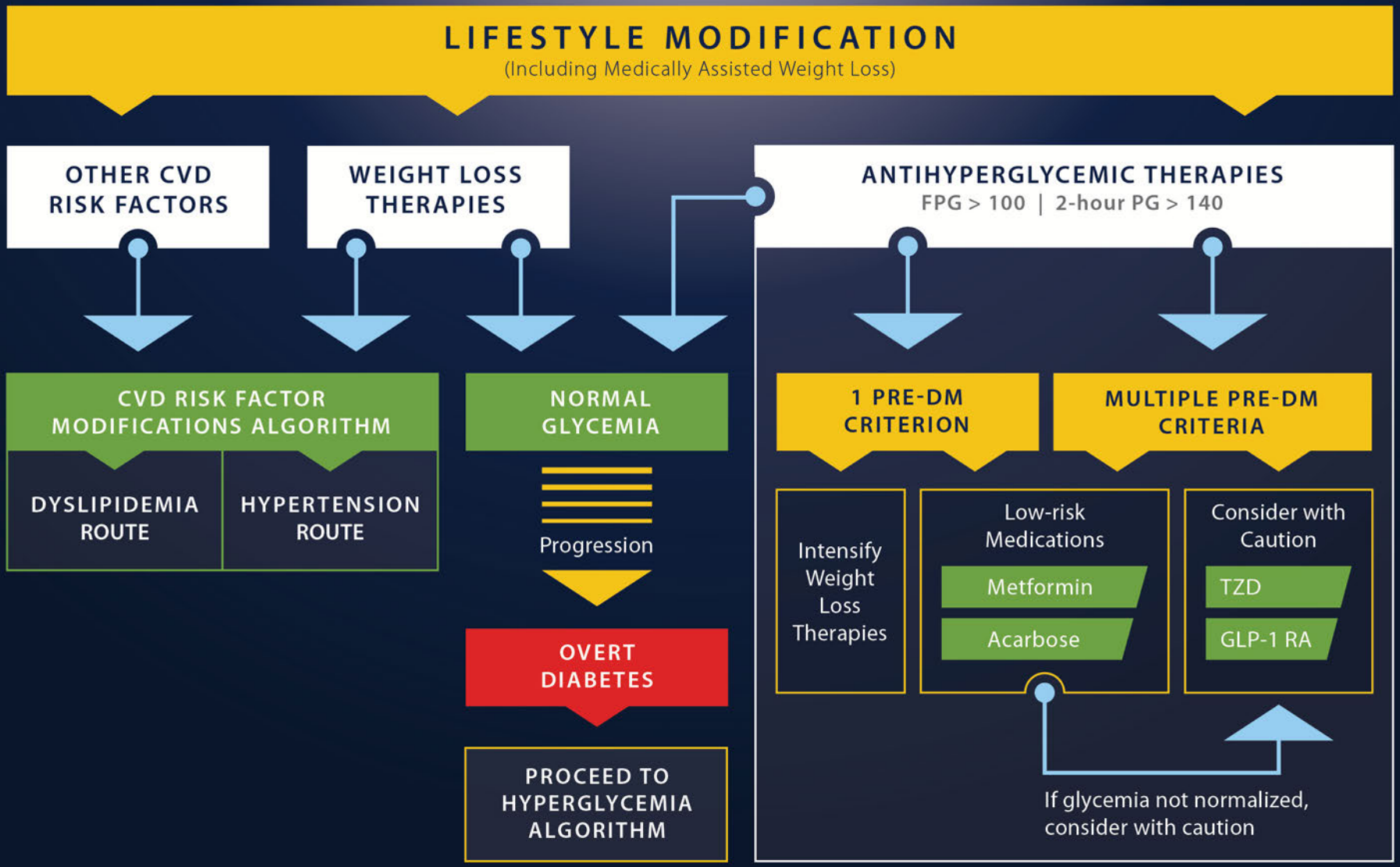
Comprehensive Diabetes Algorithm

Complications-Centric Model for Care of the Overweight/Obese Patient



PREDIABETES ALGORITHM

IFG (100–125) | IGT (140–199) | METABOLIC SYNDROME (NCEP 2005)



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

Glycemic Control Algorithm

LIFESTYLE MODIFICATION
(Including Medically Assisted Weight Loss)

Entry A1c < 7.5%

MONOTHERAPY*

- ✓ Metformin
- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ✓ AGi
- ⚠ TZD
- ⚠ SU/GLN

If not at goal in 3 months proceed to Double Therapy

Entry A1c ≥ 7.5%

DUAL THERAPY*

MET 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

TRIPLE THERAPY*

MET or other 1st-line agent + 2nd-line agent +

- ✓ GLP-1 RA
- ✓ SGLT-2i
- ⚠ TZD
- ⚠ Basal insulin
- ✓ DPP-4i
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ⚠ SU/GLN

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

Entry A1c > 9.0%

SYMPTOMS

NO	YES
DUAL Therapy OR TRIPLE Therapy	INSULIN ± Other Agents

ADD OR INTENSIFY INSULIN
Refer to Insulin Algorithm

LEGEND
- ✓ Few adverse events or possible benefits
- ⚠ Use with caution

* Order of medications listed represents a suggested hierarchy of usage

PROGRESSION OF DISEASE

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 basal insulin started (basal analogs preferred to NPH)

****Glycemic Goal:**

- <7% for most patients with T2DM; 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

Glycemic Control Not at Goal**

INTENSIFY (prandial control)

Add GLP-1 RA

or SGLT-2i
or DPP-4i

Add Prandial Insulin

TDD 0.3–0.5 U/kg

- 50% Basal Analog
- 50% Prandial Analog
- Less desirable: NPH and regular insulin or premixed insulin

Insulin titration every 2–3 days to reach glycemic goal:

- Increase prandial dose by 10% for any meal if the 2-hr postprandial or next premeal glucose is > 180 mg/dL
- Premixed: Increase TDD by 10% if fasting/premeal BG > 180 mg/dL
- If fasting AM hypoglycemia, reduce basal insulin
- If nighttime hypoglycemia, reduce basal and/or pre-supper or pre-evening snack short/rapid-acting insulin
- If between-meal daytime hypoglycemia, reduce previous premeal short/rapid-acting insulin

CVD RISK FACTOR MODIFICATIONS ALGORITHM

DYSLIPIDEMIA

THERAPEUTIC LIFESTYLE CHANGES (See Obesity Algorithm)

LIPID PANEL: Assess CVD Risk

STATIN THERAPY

If TG > 500 mg/dL, fibrates, omega-3 ethyl esters, 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	MODERATE: DM but no other major risk and/or age <40	HIGH: DM + major CVD risk(s) (HTN, Fam Hx, low HDL-C, smoking) or CVD*
	DESIRABLE LEVELS	DESIRABLE LEVELS
LDL-C (mg/dL)	<100	<70
Non-HDL-C (mg/dL)	<130	<100
TG (mg/dL)	<150	<150
TC/HDL-C	<3.5	<3.0
Apo B (mg/dL)	<90	<80
LDL-P (nmol/L)	<1200	<1000

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

TO LOWER LDL-C: Intensify statin, add ezetimibe &/or colesevelam &/or niacin
TO LOWER Non-HDL-C, TG: Intensify statin &/or add OM3EE &/or fibrates &/or niacin
TO LOWER Apo B, LDL-P: Intensify statin &/or ezetimibe &/or colesevelam &/or niacin

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

* EVEN MORE INTENSIVE THERAPY MIGHT BE WARRANTED

HYPERTENSION

GOAL: SYSTOLIC ~130, DIASTOLIC ~80 mm Hg

ACEi or ARB

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

ACEi or ARB + Thiazide ✓ / Calcium Channel Blocker ✓ / ß-blocker ✓

If not at goal (2–3 months)

Add ß-blocker or calcium channel 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, spironolactone)

Achievement of target blood pressure is critical

PROFILES OF ANTIDIABETIC MEDICATIONS

	MET	GLP-1 RA	SGLT-2i	DPP-4i	AGi	TZD	SU / GLN	COLSVL	BCR-QR	INSULIN	PRAML
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/ Severe / Mild	Neutral	Neutral	Moderate to Severe	Neutral
WEIGHT	Slight Loss	Loss	Loss	Neutral	Neutral	Gain	Gain	Neutral	Neutral	Gain	Loss
RENAL/ GU	Contra-indicated CKD Stage 3B,4,5	Exenatide Contra-indicated CrCl < 30	Genital Mycotic Infections	Dose Adjustment May be Necessary (Except Linagliptin)	Neutral	May Worsen Fluid Retention	More Hypo Risk	Neutral	Neutral	More Hypo Risk & Fluid Retention	Neutral
GI Sx	Moderate	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral	Mild	Moderate	Neutral	Moderate
CHF	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate	Neutral	Neutral	Neutral	Neutral	Neutral
CVD	Benefit		Increased LDL			Neutral	?		Safe		
BONE	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate Bone Loss	Neutral	Neutral	Neutral	Neutral	Neutral

Few adverse events or possible benefits — Use with caution — Likelihood of adverse effects

PRINCIPLES OF THE AACE ALGORITHM FOR THE TREATMENT OF TYPE 2 DIABETES

1) Lifestyle optimization and education are essential for all patients with diabetes. Lifestyle modification designed for weight loss, including medical and surgical interventions approved for the treatment of obesity, should be considered as primary approaches for therapeutic benefits in overweight and obese patients with diabetes, and for prevention of diabetes in high risk patients with prediabetes. The treatment of overweight/obesity in patients with type 2 diabetes and prediabetes should proceed according to the Obesity Treatment Algorithm. Effective interventions for weight loss involve a multidisciplinary team. The need for medical therapy for weight loss or glycemic control should not be considered as a failure of lifestyle management, but as an adjunct to it.
2) The A1c target must be individualized, based on numerous factors, such as age, comorbid conditions, duration of diabetes, risk of hypoglycemia, patient motivation, adherence, life expectancy, etc. An A1c of 6.5% or less is still considered optimal if it can be achieved in a safe and affordable manner, but higher targets may be appropriate and may change in a given individual over time.
3) Minimizing risk of hypoglycemia is a priority. It is a matter of safety, adherence, and cost.
4) Minimizing risk of weight gain is a priority. It too is a matter of safety, adherence, and cost.
5) Glycemic control targets include fasting and postprandial glucose as determined by self blood glucose monitoring.
6) The choice of therapies must be individualized based on attributes of the patient (as above) and the medications themselves (see *Profiles of Antidiabetic Medications*). Attributes of medications that affect their choice include: risk of inducing hypoglycemia, risk of weight gain, ease of use, cost, and safety impact of kidney, heart, or liver disease. This algorithm includes every FDA-approved class of medications for diabetes. This algorithm also stratifies choice of therapies based on initial A1c.
7) The algorithm provides guidance to what therapies to initiate and add, but respects individual circumstances that would make different choices.
8) Therapies with complementary mechanisms of action must typically be used in combinations for optimum glycemic control.
9) Effectiveness of therapy must be evaluated frequently until stable (e.g. every 3 months) using multiple criteria including A1c, SMBG records including both fasting and post-prandial data, documented and suspected hypoglycemia, and monitoring for other potential adverse events (weight gain, fluid retention, hepatic, renal, or cardiac disease), and monitoring of comorbidities, relevant laboratory data, concomitant drug administration, diabetic complications, and psycho-social factors affecting patient care.
10) Safety and efficacy should be given higher priorities than initial acquisition cost of medications per se since cost of medications is only a small part of the total cost of care of diabetes. In determining the cost of a medication, consideration should be given to monitoring requirements, risk of hypoglycemia and weight gain, etc.
11) The algorithm should be as simple as possible to gain physician acceptance and improve its utility and usability in clinical practice.
12) The algorithm should serve to help educate the clinician as well as to guide therapy at the point of care.
13) The algorithm should conform, as nearly as possible, to a consensus for current standard of practice of care by expert endocrinologists who specialize in the management of patients with type 2 diabetes and have the broadest experience in outpatient clinical practice.
14) The algorithm should be as specific as possible, and provide guidance to the physician with prioritization and a rationale for selection of any particular regimen.
15) Rapid-acting insulin analogs are superior to Regular because they are more predictable.
16) Long-acting insulin analogs are superior to NPH insulin because they provide a fairly flat response for approximately 24 hours and provide better reproducibility and consistency both between subjects and within subjects, with a corresponding reduction in the risk of hypoglycemia.

This document represents the official position of the American Association of Clinical Endocrinologists and the American College of Endocrinology. Where there were no RCTs or specific FDA labeling for issues in clinical practice, the participating clinical experts utilized their judgment and experience. Every effort was made to achieve consensus among the committee members. Many details that could not be included in the graphic summary (Figure) are described in the text.

All necessary author disclosures are made to AACE and are on file at the main office. Please contact Lori Clawges at AACE for further inquiries.