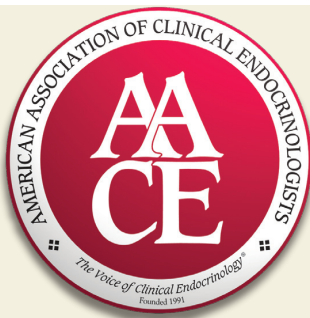




AACE COMPREHENSIVE DIABETES MANAGEMENT ALGORITHM — 2013 —

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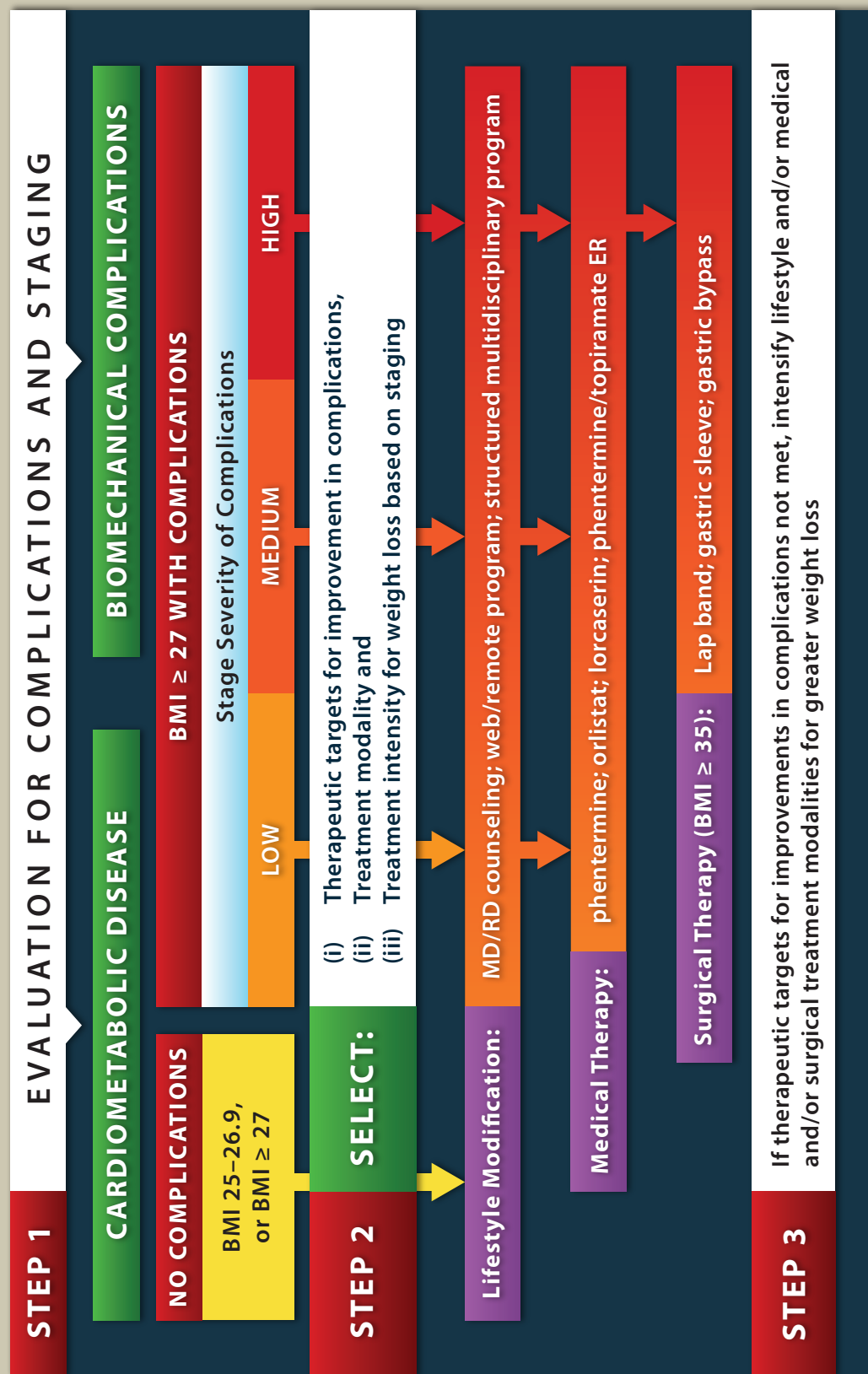
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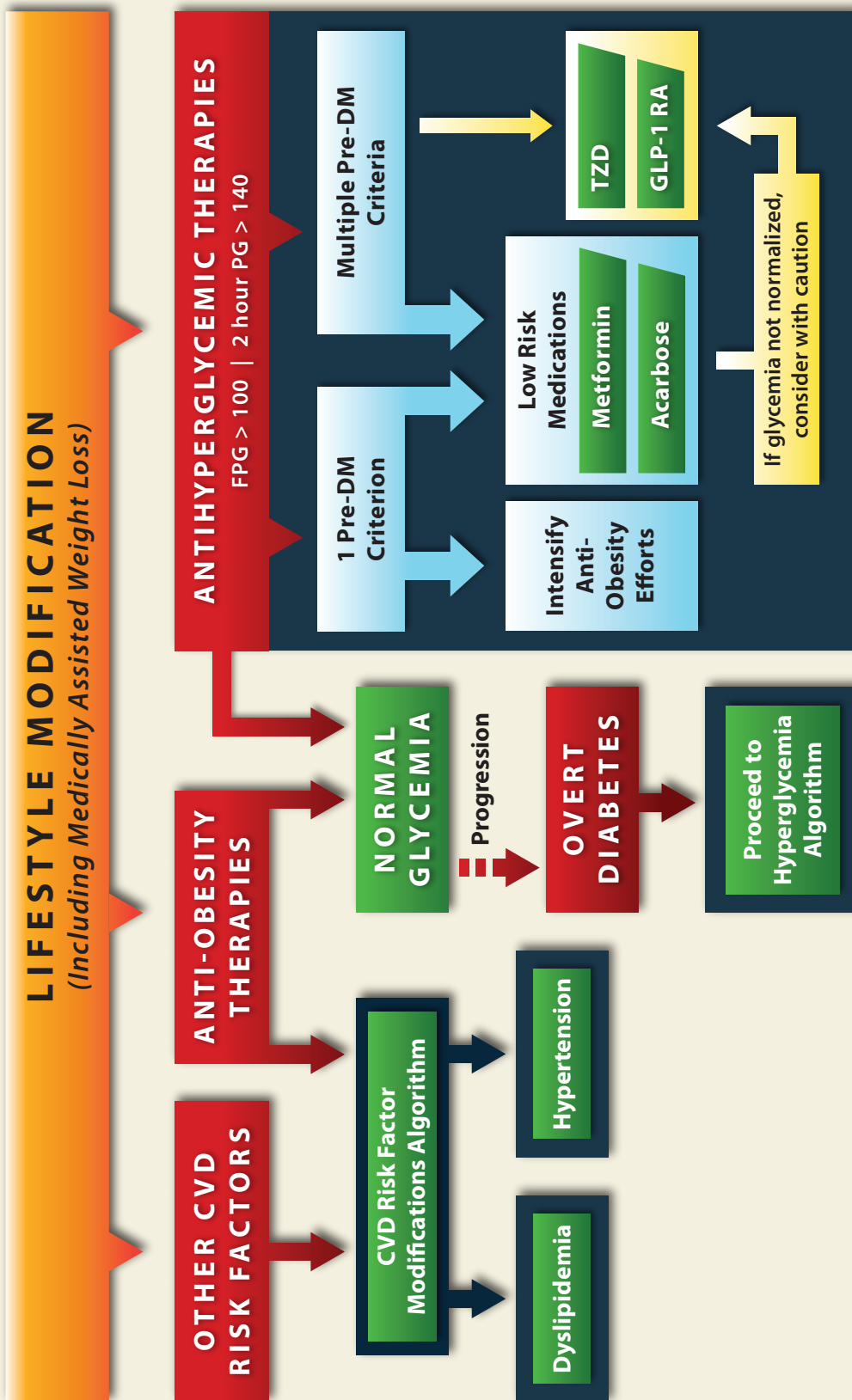


COMPLICATIONS-CENTRIC MODEL FOR CARE OF THE OVERWEIGHT/OBESE PATIENT



PREDIABETES ALGORITHM

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





GOALS FOR GLYCEMIC CONTROL

$A1c \leq 6.5\%$

For healthy patients
without concurrent
illness and at low
hypoglycemic risk

$A1c > 6.5\%$

Individualize goals
for patients with
concurrent 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	DPP4-i	AG-i	SGLT-2**	TZD	SU/GLN
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If A1c > 6.5% in 3 months add second drug (Dual Therapy)

ENTRY A1c ≥ 7.5%

DUAL THERAPY*

GLP-1 RA	DPP4-i	TZD	** SGLT-2	Basal insulin	Colesevelam	Bromocriptine QR	AG-i	SU/GLN
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MET or other first-line agent

If not at goal in 3 months proceed to triple therapy

ENTRY A1c > 9.0%

NO SYMPTOMS	SYMPTOMS
DUAL THERAPY OR TRIPLE THERAPY	INSULIN ± OTHER AGENTS

ADD OR INTENSIFY INSULIN

TRIPLE THERAPY*

GLP-1 RA	TZD	** SGLT-2	Basal insulin	DPP4-i	Colesevelam	Bromocriptine QR	AG-i	SU/GLN
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2ND LINE AGENT + **MET** or other first-line agent

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

* Order of medications listed are a suggested hierarchy of usage
 ** Based upon phase 3 clinical trials data

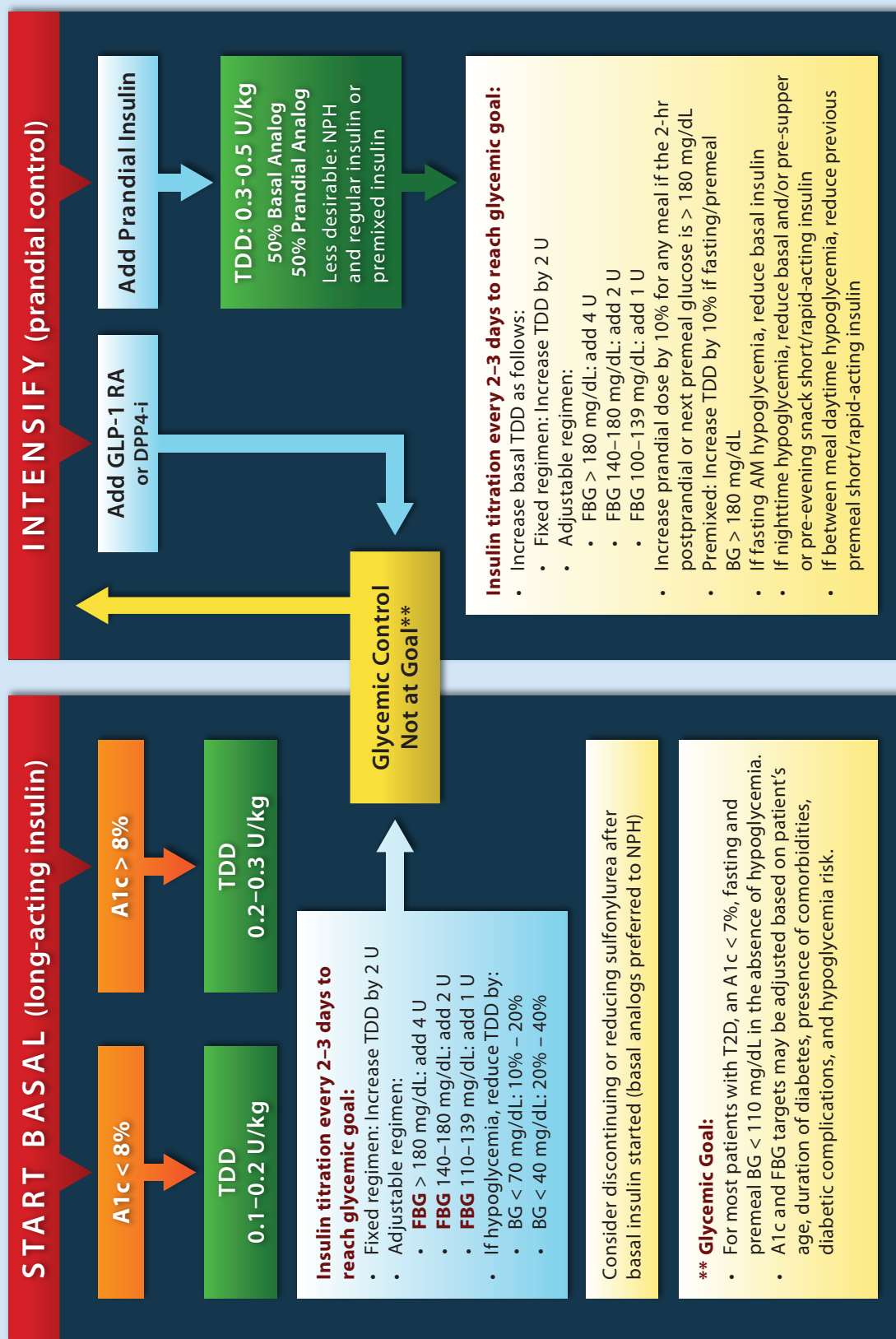
LEGEND
 ✓ = Few adverse events or possible benefits
 ⚠ = Use with caution

PROGRESSION OF DISEASE

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ALGORITHM FOR ADDING/INTENSIFYING INSULIN



CVD RISK FACTOR MODIFICATIONS ALGORITHM



DYSLIPIDEMIA

THERAPEUTIC LIFESTYLE CHANGES (See Obesity Algorithm)

LIPID PANEL: Assess CVD Risk

Statin Therapy

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

If TG > 500 mg/dL, fibrates, omega-3 ethyl esters, niacin

Intensify therapies to attain goals according to risk levels

RISK LEVELS	MODERATE	HIGH
	DM but no other major risk and/or age <40	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 glyemic control; Consider additional therapy

To lower LDL-C:

Intensify statin, add ezetimibe &/or colesvelam &/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 colesvelam &/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

For initial blood pressure >150/100 mm Hg: Dual therapy

ACEi or ARB

ACEi or ARB	+	Thiazide Calcium Channel Blocker β-blocker
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If not at goal (2–3 months)

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



Few adverse events or possible benefits



Use with caution



Likelihood of adverse effects

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



- 1) Lifestyle optimization is essential for all patients with diabetes. This is multifaceted, ongoing, and engages the entire diabetes team. However, such efforts should not delay needed pharmacotherapy, which can be initiated simultaneously and adjusted based on the response to lifestyle efforts. The need for medical therapy should not be interpreted 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, co-morbid 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) Glycemic control targets include fasting and postprandial glucose as determined by self blood glucose monitoring.
- 4) The choice of therapies must be individualized based on attributes of the patient (as above) and the medications themselves (see *Profiles of Anti-Diabetic 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.
- 5) Minimizing risk of hypoglycemia is a priority. It is a matter of safety, adherence, and cost.
- 6) Minimizing risk of weight gain is a priority. It too is a matter of safety, adherence, and cost.
- 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 co-morbidities, 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.