# AACE/ACE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM

# 2017

## TASK FORCE


Alan J. Garber, MD, PhD, FACE, *Chair*

Martin J. Abrahamson, MD
Joshua I. Barzilay, MD, FACE
Lawrence Blonde, MD, FACP, MACE
Zachary T. Bloomgarden, MD, MACE
Michael A. Bush, MD
Samuel Dagogo-Jack, MD, FACE
Ralph A. DeFronzo, MD
Daniel Einhorn, MD, FACP, FACE
Vivian A. Fonseca, MD, FACE
Jeffrey R. Garber, MD, FACP, FACE
W. Timothy Garvey, MD, FACE
George Grunberger, MD, FACP, FACE
Yehuda Handelsman, MD, FACP, FNLA, FACE
Irl B. Hirsch, MD
Paul S. Jellinger, MD, MACE
Janet B. McGill, MD, FACE
Jeffrey I. Mechanick, MD, FACP, FACE, FACN, ECNU
Paul D. Rosenblit, MD, PhD, FNLA, FACE
Guillermo Umpierrez, MD, FACP, FACE


 DOI 10.4158/EP161682.CS

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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 therapy, including medically supervised weight loss, is key to managing type 2 diabetes. |
| 2. | Weight loss should be considered as a lifelong goal in all patients with prediabetes and T2D who also have overweight or obesity, utilizing behavioral interventions and weight loss medications as required to achieve chronic therapeutic goals. |
| 3. | The A1C target must be individualized. |
| 4. | Glycemic control targets include fasting and postprandial glucoses. |
| 5. | The choice of therapies must be individualized on basis of patient characteristics, impact of net cost to patient, formulary restrictions, personal preferences, etc. |
| 6. | Minimizing risk of hypoglycemia is a priority. |
| 7. | Minimizing risk of weight gain is a priority. |
| 8. | 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. |
| 9. | This algorithm stratifies choice of therapies based on initial A1C. |
| 10. | Combination therapy is usually required and should involve agents with complementary actions. |
| 11. | Comprehensive management includes lipid and blood pressure therapies and related comorbidities. |
| 12. | Therapy must be evaluated frequently until stable (e.g., every 3 months) and then less often. |
| 13. | The therapeutic regimen should be as simple as possible to optimize adherence. |
| 14. | This algorithm includes every FDA-approved class of medications for diabetes. |

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# LIFESTYLE THERAPY

## RISK STRATIFICATION FOR DIABETES COMPLICATIONS

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

| | | | |
|---|---|---|---|
| **Nutrition** | • Maintain optimal weight<br>• Calorie restriction (if BMI is increased)<br>• Plant-based diet; high polyunsaturated and monounsaturated fatty acids | • Avoid *trans* fatty acids; limit saturated fatty acids | • Structured counseling<br>• Meal replacement |
| **Physical Activity** | • 150 min/week moderate exertion (eg. walking, stair climbing)<br>• Strength training<br>• Increase as tolerated | • Structured program<br>• Wearable technologies | • Medical evaluation/ clearance<br>• Medical supervision |
| **Sleep** | • About 7 hours per night<br>• Basic sleep hygiene | • Screen OSA<br>• Home sleep study | • Referral to sleep lab |
| **Behavioral Support** | • Community engagement<br>• Alcohol moderation | • Discuss mood with HCP | • Formal behavioral therapy |
| **Smoking Cessation** | • No tobacco products | • Nicotine replace-ment therapy | • Referral to structured program |

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

## STEP 1 — EVALUATION FOR COMPLICATIONS AND STAGING

**CARDIOMETABOLIC DISEASE | BIOMECHANICAL COMPLICATIONS**

| BMI < 25 | NO COMPLICATIONS | COMPLICATIONS | |
|---|---|---|---|
| | BMI ≥ 25 | BMI ≥ 25 | |
| NO OVERWEIGHT OR OBESITY | OVERWEIGHT OR OBESITY | MILD TO MODERATE | SEVERE |
| | STAGE 0 | STAGE 1 | STAGE 2 |

## 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): | 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 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

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

### ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

- DYSLIPIDEMIA ROUTE
- HYPERTENSION ROUTE

### NORMAL GLYCEMIA

Progression

### OVERT DIABETES

PROCEED TO HYPERGLYCEMIA ALGORITHM

### 1 PRE-DM CRITERION

Intensify Weight Loss Therapies

### MULTIPLE PRE-DM CRITERIA

Low-risk Medications
- Metformin
- Acarbose

Consider with Caution
- TZD
- GLP-1 RA

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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# 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 | HIGH | VERY HIGH | EXTREME |
|---|---|---|---|
| | 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 |

**RISK LEVELS:**
- **HIGH:** DM but no other major risk and/or age <40
- **VERY HIGH:** DM + major ASCVD risk(s) (HTN, Fam Hx, low HDL-C, smoking, CKD3,4)*
- **EXTREME:** DM plus established clinical CVD

**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, colesevelam, 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, colesevelam, 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

## HYPERTENSION

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

ACEi or ARB

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

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

If not at goal (2–3 months)

Add calcium channel blocker, ß-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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# 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

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# GLYCEMIC CONTROL ALGORITHM

## LIFESTYLE THERAPY
(Including Medically Assisted Weight Loss)

### Entry A1C < 7.5%

**MONOTHERAPY***

- ✓ 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%

**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 and/or possible benefits
- ! Use with caution

* Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation

## PROGRESSION OF DISEASE

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# 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

**Glycemic Control Not at Goal***

## INTENSIFY (Prandial Control)

**Add GLP-1 RA**

Or SGLT-2i
Or DPP-4i

**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

**Basal Bolus**

- Begin prandial insulin before each meal
- 50% Basal / 50% Prandial TDD 0.3–0.5 U/kg
- 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%

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# PROFILES OF ANTIDIABETIC MEDICATIONS

| | MET | GLP-1 RA | SGLT-2i | DPP-4i | AGi | TZD (moderate dose) | 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 | Contrain-dicated if eGFR < 30 mL/min/1.73 $m^2$ | Exenatide Not Indicated CrCl < 30<br>Possible Benefit of Liraglutide | Not Indicated for eGFR < 45 mL/min/1.73 $m^2$<br>Genital Mycotic Infections<br>Possible Benefit of Empagliflozin | Dose Adjustment Necessary (Except Linagliptin)<br>Effective in Reducing Albuminuria | Neutral | Neutral | More Hypo Risk | Neutral | Neutral | More Hypo Risk | Neutral |
| GI Sx | Moderate | Moderate | Neutral | Neutral | Moderate | Neutral | Neutral | Mild | Moderate | Neutral | Moderate |
| CHF | Neutral | Possible Benefit of Liraglutide | Possible Benefit of Empagliflozin | Possible Risk for Saxagliptin and Alogliptin | Neutral | Moderate | More CHF Risk | Neutral | Neutral | More CHF Risk | Neutral |
| CARDIAC* / ASCVD | | Possible CV Benefit | Possible CV Benefit | Neutral | | May Reduce Stroke Risk | ? | Benefit | Safe | Neutral | |
| BONE | Neutral | Neutral | Canagliflozin Warning | Neutral | Neutral | Moderate Fracture Risk | Neutral | Neutral | Neutral | Neutral | Neutral |
| KETOACIDOSIS | Neutral | Neutral | DKA Occurring in T2D in Various Stress Settings | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral |

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect | * FDA indication to prevent CVD death in diabetes plus prior CVD events

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