

Reviewing Diabetes Guidelines

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Objectives:

At the conclusion of this knowledge-based lesson, successful participants should be able to:

- Describe the treatment algorithms for type 2 diabetes from the American Diabetes Association and from the American Association of Clinical Endocrinologists.
- Identify the goals of therapy for diabetes treatment.
- Discuss the role of new agents to treat diabetes.

There are nearly 24 million Americans with diabetes in the United States, and every year 1.3 million people are diagnosed with type 2 diabetes. That translates to nearly 3,500 persons a day! In order to manage this growing epidemic, we must incorporate several different treatment modalities to best manage care for our patients with diabetes: lifestyle changes, preventative health screenings, nutrition counseling, medications, and support groups. Even among the diabetes medications, there are over twenty different choices on the market today. How do we provide the best care possible when there are so many options available?

The Guidelines

There are several groups that have published their own set of guidelines for the treatment of type 2 diabetes in non-pregnant adult patients.

Both the American Diabetes Association/European Association for the Study of Diabetes (ADA/EASD) and the American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) are leading organizations that have produced guidelines outlining a treatment roadmap for optimal care of patients with diabetes. While these documents advocate many similar practice principles, it is important to consider the differences between the two. The provider must ultimately tailor diabetes treatment to the individual patient in accordance with published guidelines and clinical experience.

Monitoring Diabetes

When monitoring patients with diabetes, both organizations advocate the use of regular hemoglobin A1C testing. Regular

testing, at least two times per year in patients meeting treatment targets and quarterly in patients who are not meeting goals or whose therapy has changed. This blood test provides an approximate 3-month snapshot of an individual's glycemic control. The ADA recommends an A1C goal of $\leq 7\%$ while the AACE/ACE goal is $\leq 6.5\%$. Each publication provides justification for its respective recommendation. For most patients the ADA prefers a less-intensive goal to prevent hypoglycemic events. The ADA advocates for providers to consider lower A1C goals for individual patients, if this can be achieved without significant hypoglycemia. These patients generally have a shorter duration of diabetes, long life expectancy and no significant CVD. In contrast, the AACE/ACE advocates for an A1C goal of $\leq 6.5\%$ for all patients.

Therapeutic Options

Both organizations have published their own algorithms for treating individuals with type 2 diabetes. The AACE/ACE guidelines determine a patient's treatment by stratifying individuals according to their current A1C level. The AACE/ACE algorithm cites six goal priorities for medication selections-

1. minimize risk and severity of hypoglycemia
2. minimize risk of weight gain
3. include major classes of FDA approved medications
4. selection of therapy based on A1C stratification and documented

5. ability of medication to lower A1C
5. consideration of both fasting and post prandial glucose as targets
6. consideration of total cost of therapy including medication, supplies, hypoglycemia, adverse events and diabetes associated complications.

For patients with A1C levels of 7.5% or lower AACE/ACE concludes a goal of 6.5% can be achieved with monotherapy. Metformin is the preferred agent and is usually the most appropriate initial choice unless there is a contraindication, such as renal disease. If A1C goals are not being reached, the guidelines recommend additional oral medications first, then insulin if A1C levels are still high. If insulin is to be started in a patient, there are four general approaches that can be taken:

- basal insulin, using a long-acting insulin (glargine or detemir), generally given once daily;
- premixed insulins, using a rapid-acting analogue and protamine (NovoLog or Humalog Mix), usually given twice daily with breakfast and dinner but occasionally used only with the largest meal;
- basal-bolus insulin or multiple daily injections, using rapid-acting insulin analogues at mealtime—aspart, lispro, or glulisine along with one of the long-acting insulin analogues, glargine or detemir;
- a meal-time insulin regimen, involving use of the rapid-acting

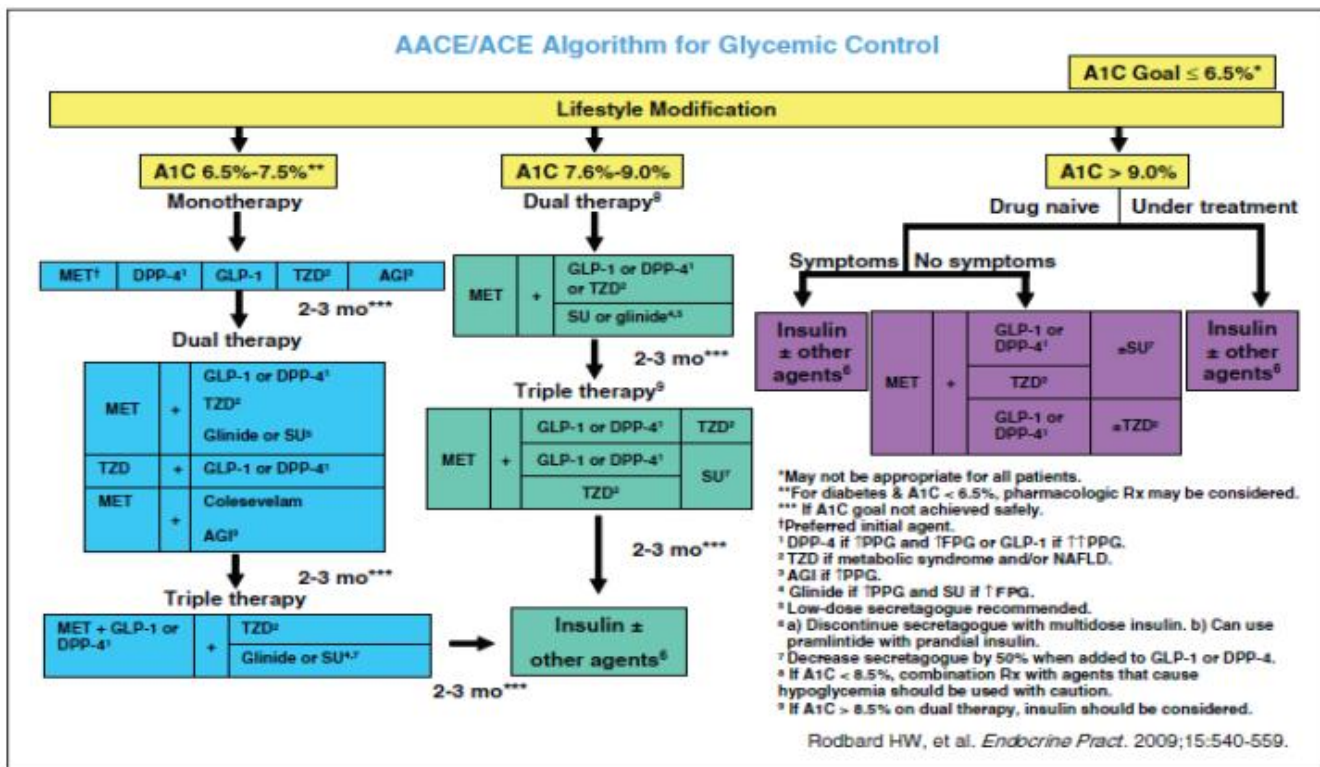


Figure 1

insulin analogues, but without a basal or long-acting insulin component is an additional option. This may be possible if the patient is being treated with an insulin sensitizer (metformin) that provides adequate control of fasting plasma glucose.

The AACE/ACE guidelines recommend against the use of intermediate-acting insulins such as insulin N or insulin R because their duration of action does not adequately mimic the body's normal physiology. As a result, these agents are often associated with an increased risk of hypoglycemia.

Figure 1 details the AACE/ACE stratification by A1C and recommended combinations based on the patients A1C. For example,

according to the AACE/ACE guidelines a patients whose A1C is 8%, would have the provider consider four different medication combinations

1. Metformin plus a GLP-1
2. Metformin plus a DPP-4 inhibitor
3. Metformin plus a TZD
4. Metformin plus a sulfonylurea or glinide

ADA/EASD Guidelines

The ADA guidelines selected specific therapies on their effectiveness in lowering glucose, extraglycemic effects that may reduce long term complications, the medications safety profile, tolerability, ease of use, and cost. The algorithm takes into account the characteristics of the individual interventions and advocates

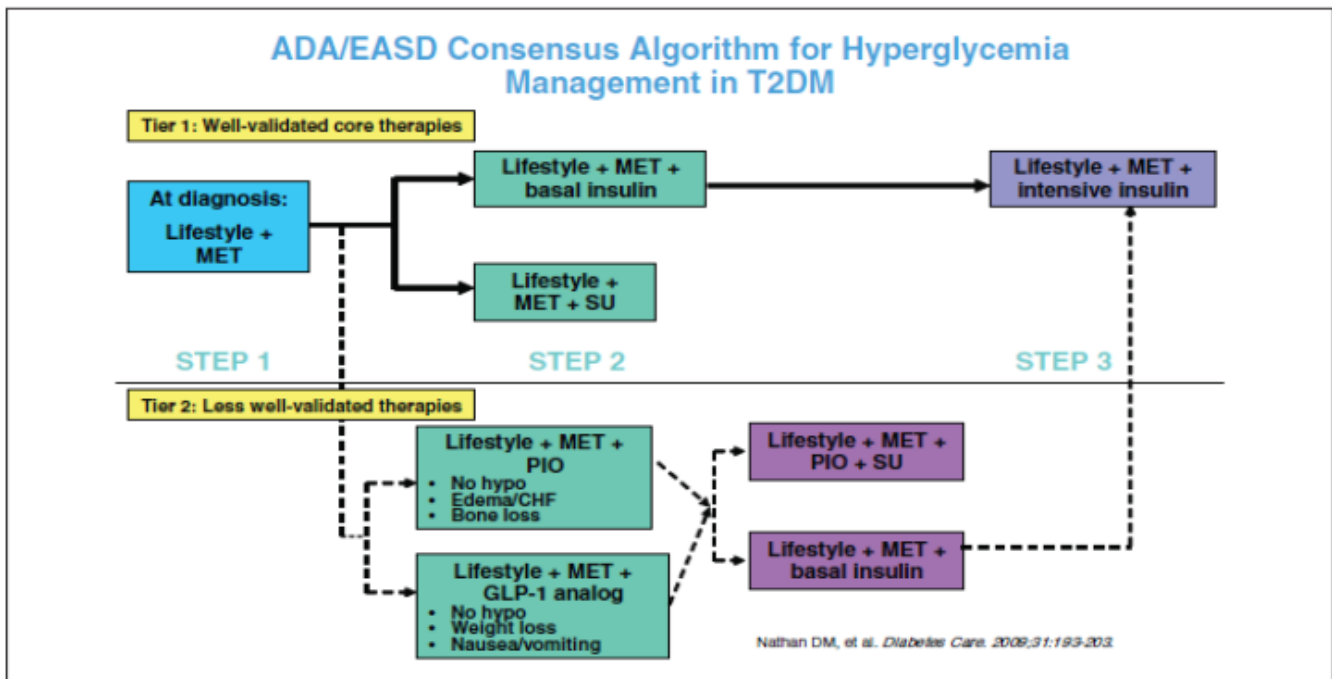


Figure 2

for aggressive lowering of glycemia as close to the time of diagnosis as possible. Similarly to AACE/ACE, metformin is the preferred initial agent along with lifestyle changes (diet, exercise, and weight loss). If lifestyle intervention and the maximal tolerated dose of metformin fail to achieve glycemic targets, another medication should be added within 2-3 months. If A1C is less than 8.5%, a sulfonylurea (other than glyburide or chlorpropamide) or basal insulin should be added. Higher A1C's should be treated with metformin and insulin. The algorithm also includes second-line "less well-validated" therapies (i.e. less clinical trial data, less outcome data, and less clinical experience than other therapies) for use in selected clinical settings such as a reduced risk of hypoglycemia. These options suggest using pioglitazone or a GLP-1 agonist (exenatide or liraglutide) in addition to metformin and lifestyle changes. Although addition of a third agent can be considered, this

- Algorithm Abbreviations**
- MET= metformin
 - SU= sulfonylurea
 - DPP-4= dipeptidyl peptidase 4 inhibitor
 - GLP-1= glucagon-like peptide 1 agonist
 - TZD= thiazolidinediones
 - AGI= alpha glucosidase inhibitor
 - PIO= pioglitazone

approach is usually not preferred since the same level of glycemic control can be achieved with insulin.

The ADA algorithm provides specific instructions for initiating and maintaining a patient on insulin. They recommend starting with bedtime intermediate-acting insulin or bedtime or morning long-acting insulin at a dose of 10 units or 0.2 units per kilogram. Regular monitoring of fasting blood glucose levels in the morning should be performed so

the insulin dose can be titrated, typically by 2 units every few days, to achieve fasting glucose levels of 70-130 mg/dL. If A1C levels are above target after 2-3 months, blood glucose testing should be performed before lunch, dinner, and

bedtime to determine if additional meal-time injections are needed. While on insulin, both sets of guidelines recommend discontinuing diabetes drugs that either increase the risk of hypoglycemia or are not approved for use with

insulin (sulfonylureas and exenatide). Metformin should continue to be administered with insulin unless the patient develops a contraindication.

Newer Agents

Both sets of guidelines address the role of newer classes of diabetes medications that are helping patients manage their disease. Glucagon-like peptide-1 (GLP-1) agonists such as exenatide and liraglutide are two injectable drugs that stimulate the pancreas to release insulin at mealtimes, decrease glucagon release, and increase satiety. Dipeptidyl peptidase 4 (DPP-4) inhibitors such as sitagliptin, saxagliptin, and the recently approved linagliptin are oral agents that enhance the effect of GLP-1 by preventing its breakdown. These agents reduce a patient's A1C by approximately 0.5 to 1% with relatively little risk of hypoglycemia, and are weight neutral or support weight loss. In light of these observations, the AACE/ACE guidelines favor the use of these agents over sulfonylureas or thiazolidinediones when adding on to metformin therapy. On the other hand, the ADA guidelines consider these agents to be "less well-validated" therapies.

Self-Monitored Blood Glucose

Self-monitoring of blood glucose (SMBG) is an important element in adjusting or adding new drug therapies and, in particular, titrating insulin doses. The need for and number of required SMBG measurements are not clear and are dependent on the medications used. Oral agents that are not likely to cause hypoglycemia do not usually require SMBG. The AACE/ACE guidelines recommend daily SMBG checks for patients on bedtime basal insulin or dinnertime premixed insulin. For

each additional injection of insulin per day, SMBG should be increased in frequency to ensure successful titration of each dose. The ADA guidelines suggest targeting daily fasting and preprandial glucose levels when SMBG is employed. ADA guidelines target a fasting plasma glucose of 90-130 mg/dL and a postprandial plasma glucose of <180 mg/dL. AACE/ACE guidelines target a fasting plasma glucose of <110 mg/dL and a postprandial plasma glucose of <140 mg/dL.

The implications of uncontrolled diabetes can lead to long-term consequences that increase human suffering and reduced quality of life. Much of the complications that occur can be substantially reduced by interventions that achieve glucose levels close to the nondiabetic range. When we use guidelines provided by the leading organizations in diabetes, the American Diabetes Association, the European Association for the Study of Diabetes, the American Association of Clinical Endocrinologists/American College of Endocrinology we provide an evidence-based level of diabetes care to our patients.

References:

- ◆ Rodbard, H W, Jellinger, P S, Davidson, J A, et al. (2009). Statement by an American association of clinical endocrinologists/American college of endocrinology consensus panel on type 2 diabetes mellitus: An algorithm for glycemic control. *Endocrine practice*, 15(6), 540-59.
- ◆ Nathan, D M, Buse, J B, Davidson, M B, et al. (2009). Medical management of hyperglycemia in type 2 diabetes: A consensus algorithm for the initiation and adjustment of therapy: A consensus statement of the American diabetes association and the European association for

the study of diabetes. *Diabetes care*, 32(1), 193-203.

◆ Ray, K, Seshasai, S R, Wijesuriya, S, et al. (2009). Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: A meta-analysis of

randomized controlled trials. *Lancet*, 373(9677), 1765-72.

◆ American Diabetes Association. Standards of Medical Care in Diabetes - 2011. *Diabetes Care*. 2011;34 (Suppl 1):S11-S61.

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1) Which of the following organizations have published guidelines for the treatment of Type 2 diabetes?

- A. American Diabetes Association
- B. American Association of Endocrinologists
- C. American Academy of Pediatrics
- D. A and B are correct

2) True or False: a patient with type 2 diabetes with an A1C level of 7.5% is considered at goal according to the ADA guidelines.

- A. True
- B. False

3) LS is a 67-year old male with good renal function who has just been diagnosed with diabetes. His A1C level is 7%. Which of the following medications would be the most appropriate first-line therapy?

- A. Glyburide
- B. Metformin
- C. Rosiglitazone
- D. Pioglitazone

4) All of the following are medications that increase the risk of hypoglycemia except

- A. Glyburide
- B. Glipizide
- C. Exenatide
- D. Insulin aspart

5) Which of the following fasting blood glucose levels would be in target for a patient with type 2 diabetes according to the ADA guidelines?

- A. 65 mg/dL
- B. 109 mg/dL
- C. 133 mg/dL
- D. 140 mg/dL

6) Which of the following medications is not included in the ADA algorithm's two tiers of preferred agents?

- A. Metformin
- B. Pioglitazone
- C. Basal insulin
- D. Sitagliptin

7) JT is a 50 year old male currently being treated for type 2 diabetes with metformin, glipizide, and glargine. His diabetes team has decided to add on bolus insulin to help better control his blood glucose. Which of these medications should be discontinued with the addition of aspart?

- A. Metformin.
- B. Glipizide
- C. Glargine
- D. B and C are correct

8) GLP-1 agonist reduce a patient's A1C by about

- A. 0.2-0.5%
- B. 0.5-1%
- C. 1-2%

9) Which of the following basal-bolus insulin regimens are correctly paired?

- A. Detemir-glargine
- B. Glulisine-aspart
- C. Glargine-lispro
- D. NPH-detemir

10) True or False: When initiating basal insulin, bedtime long-acting insulin is an appropriate choice.

- A. True
- B. False