

### The Diabetes Guidelines Trek: The Next Generation

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### Inpatient Diabetes Guidelines

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The speaker has no conflict to disclose.

### Learning Objectives

1. Review AACE/ADA Guidelines for the management of acute and chronic hyperglycemia.
2. Discuss current clinical practice trends in hyperglycemic management.
3. Summarize these guidelines through the review of common patient scenarios.

### Current Inpatient Guidelines

- American Diabetes Association (ADA)
  - Standards of Medical Care in Diabetes.
  - Diabetes Care, 35, Suppl 1, January 2012
- Endocrine Society (ES)
  - Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Settings: An Endocrine Society Clinical Practice Guideline.
  - J Clin Endocrinol Metab, January 2012, 97(1):16-38.

Which of the following is the best method to assess diabetes at admission?

1. A1c
2. Plasma glucose
3. A1c + plasma glucose

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### General Inpatient Recommendations

- All patients with DM have that identified in their medical record.
- All patients with DM should have an order for glucose monitoring with results available to all members of the healthcare team.
- An A1c should be obtained at admission if no results for previous 2-3 months are available.

### Transition from Home to Hospital

- ES Guidelines:
  - Insulin therapy is preferred method of achieving glycemic control in hospitalized patients with hyperglycemia.

### Transition from Home to Hospital

- ES Guidelines:
  - Suggest the discontinuation of oral hypoglycemic agents and initiation of insulin therapy for the majority of patients with type 2 diabetes at the time of admission for acute illness.

ES Guidelines

### Critically Ill Patients

- Initiate insulin at a threshold no higher than 180mg/dl
- Goal range of 140-180mg/dl
- More stringent goals MAY be appropriate if can be achieved without significant hypoglycemia
- IV insulin protocol should be employed to keep patient in desired range without severe hypoglycemia.

ADA & ES Guidelines

### Non-critically Ill Patients

- No clear evidence for specific glucose goals.
- Generally: fasting glucose <140mg/dl and random glucose <180mg/dl are reasonable.
- Tighter control is acceptable in stable patients with previous tight control.
- Less stringent goals acceptable in those with severe co-morbidities.

ADA & ES Guidelines

Which of the following is the biggest weakness of A1c for diagnosis in inpatients?

1. Low specificity
2. Low sensitivity
3. Low specificity & sensitivity

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### A1c for Inpatients

- Useful in differentiating between chronic diabetes and stress-induced or diabetes associated with hospitalization
- Almost 100% specificity
  - Diabetes will be present if A1c above 6.5%
- Only 55-60% sensitivity
  - May miss 40-45% of cases of true diabetes

ES Guidelines

### Transition from IV Continuous Insulin Infusion (CII) to sc Insulin Therapy

- Scheduled sc insulin should begin 1-2 hrs prior to discontinuation of CII in patients with previous history of diabetes.
- In those without history of diabetes, begin sc insulin 1-2 hrs prior to dc of CII if patient required more than 2u/hr of insulin

ES Guidelines

### Patients receiving Enteral Nutrition (EN) or Parenteral Nutrition (PN)

- POC can be discontinued in patients without history of diabetes if glucose <140mg/dl 24-48 hrs after achieving caloric goals.
- PRN insulin orders should be provided for all patients with EN & PN
- Scheduled insulin therapy should be started if persistent requirement (>12hrs) for prn insulin is demonstrated.

### Self Management in the Hospital

- Appropriate if:
  - Patient is a competent adult
  - Stable consciousness
  - Reasonably stable insulin requirements
  - Tolerating standard, stable oral diet
- Insulin pumps may be appropriate if:
  - Patient was on a pump at home
  - Policies detailing pump use inpatient are advisable

ADA Guidelines

### Discharge Planning

- Medication reconciliation
- Fill prescriptions & counsel prior to discharge
- Transmit discharge summary to primary physician as soon as possible
- Schedule outpatient follow-up prior to discharge
- Structured discharge communication

### Inpatient Diabetes Self Management Education

- Identify provider for outpatient follow-up,
- Assess level of understanding of:
  - Diagnosis of diabetes
  - SMBG
  - Glucose goals
- Recognition & treatment of hyper- & hypoglycemia,
- Sick day management,
- Proper use and disposal of needles & syringes.

### Inpatient Summary

- Insulin is preferred the treatment in most acutely ill patients
- A1c testing should be performed at admission (unless recently done), but results interpreted cautiously
- Diabetes education is an essential component of the inpatient management of diabetes

Which of the following is **NOT** recommended as an essential component of Diabetes Self-Management Education (DSME) to be covered with patients before hospital discharge?

- Assess level of understanding of SMBG goals
- Appropriate levels of exercise
- Proper sick day management
- Recognition and treatment of hypoglycemia

Which of the following statements regarding the sensitivity and specificity of A1c for diagnosis of diabetes in the inpatient setting is **TRUE**?

- A1c testing has a low specificity but high sensitivity among inpatients
- A1c testing has low specificity and sensitivity among inpatients
- A1c testing has a low sensitivity but high specificity among inpatients
- A1c testing has high specificity and sensitivity among inpatients

Critically ill patients in intensive care units should have uncontrolled hyperglycemia treated with which of the following methods?

- Subcutaneous sliding scale regular insulin
- Insulin detemir or glargine subcutaneously every 12 hours  $\pm$  regular insulin every 3 hours.
- The patient's home meds as tolerated  $\pm$  regular insulin sliding scale
- IV insulin infusion using protocol with demonstrated efficacy

Point-of-care testing may be discontinued in patients receiving parenteral nutrition if their glucose is under what level for  $\geq 48$  hours after achieving caloric goals?

- 110 mg/dl
- 140mg/dl
- 180mg/dl
- 200mg/dl

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## Disclosure

- Consultant / Clinical Investigator: Takeda, BMS-AZ Advanced Practitioner Advisory
- Speaker's Bureau / governing board: Takeda, BMS-AZ, Novo-Nordisk, Abbott Diabetes Care, Amylin, Merck, Johnson & Johnson Diabetes Institute
- Any potential conflicts were resolved through peer review.

## Guideline Comparison

The ADA and AACE Guidelines for risk factors for T2DM screening are the same.

1. True
2. False
3. Not Sure

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### Comparison for Risk Factors for Screening

<p><b>ADA</b></p> <ul style="list-style-type: none"> <li>• Screen for diabetes at <b>age 45</b> and <b>every 3 yrs</b> after, or adults of any age with BMI <math>\geq 25</math> kg.M<sup>2</sup> and one or more additional risk factors</li> </ul>	<p><b>AACE</b></p> <ul style="list-style-type: none"> <li>• <b>Annually</b> screen all at risk individuals starting at <b>age 30</b> (FPG or OGTT)</li> </ul>
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2012 Clinical Practice Recommendations Diabetes Care; 2012;35(suppl 1). American Association of Clinical Endocrinologists. Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus. Endocr Pract. 2009; 15(suppl 1).

### ADA & AACE Guidelines: Additional Risk Factors for Screening

- Physically inactive
- First-degree relative with diabetes
- Members of a high risk race/ethnicity
- Delivered baby > 9 lbs or GDM
- Hypertensive (BP  $\geq 140/90$  mmHg)
- HDL cholesterol <35 mg/dL and/or TG levels >250 mg/dL
- Women with polycystic ovary syndrome (PCOS)
- A1c > 5.7%, IGT or IFG on previous testing
- Other conditions associated with insulin resistance (obesity, acanthosis nigricans)
- History of CVD

2012 Clinical Practice Recommendations Diabetes Care; 2012;35(suppl 1). American Association of Clinical Endocrinologists. Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus. Endocr Pract. 2009; 15(suppl 1).

SL labs results show an A1c of 6.5 on 2 separate occasions. SL diagnosis would be:

1. No diabetes
2. Pre-diabetes
3. Diabetes
4. An A1c cannot be used to diagnosis diabetes

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### A1c to Diagnosis Diabetes

- A1c levels  $\geq 6.5\%$  are associated with an increased risk of blood vessel damage
- A1c can now be used to diagnosis diabetes:
  - Normal: < 5.7%
  - People “at risk” (formerly known as pre-diabetes): 5.7% to 6.4%
  - Diabetes:  $\geq 6.5\%$
- For diagnostic purposes, A1c tests should be performed in clinical lab (not POC testing)

2012 Clinical Practice Recommendations Diabetes Care; 2012;35(suppl 1).

WUZZLE #1



Glycemic Control Recommendations

Target Treatment Goals	AAACE/ACE <sup>1</sup> 2011	ADA <sup>2</sup> 2011
A1c	≤ 6.5%	< 7.0%
Fasting glucose	Fasting plasma glucose: < 110 mg/dL	Preprandial capillary plasma glucose: 70 – 130 mg/dL
Postprandial glucose	2-hr postprandial glucose: < 140 mg/dL	Peak postprandial capillary plasma glucose: < 180 mg/dL

1. AAACE Diabetes Mellitus Clinical Practice Guidelines Task Force. *Endocr Pract.* 2007;13 (Suppl 1)  
 2. Standards of Medical Care in Diabetes—2012. *Diabetes Care.* 2012; 35 (Suppl 1)

Case SL:

SL is newly diagnosed with T2DM x 2 months  
 A1c is 8.6%. BMI 32  
 Occupation: interstate truck driver.  
 What should SL's (target) A1c goal be?

1. < 6.5%
2. < 7.0 %
3. < 7.5%
4. < 8.0%
5. unsure

Case: JC

JC (79 y.o.) T2DM x 22 years.  
 A1c is 8.1% (x 4 years); BMI-25; S.Cr – 1.1  
 Metformin 1000mg BID  
 Glimpiride 4mg daily.  
 JC resides in an assisted living apartment & has limited mobility  
 What should JC's (target) A1c goal be?

1. < 6.5%
2. < 7.0 %
3. < 7.5%
4. < 8.0%
5. unsure

Glycemic Goals in Adults

A1c Controversy

- Is "tight" (intensive) control appropriate for every person with T2DM? (e.g., A1c < 7%)
  - Lowering A1c to below 7% has shown reduction in microvascular complications.
  - Controversy over A1c < 7% and benefit in macrovascular complications.

*Diabetes Care.* 2012; 35(Suppl 1)

2012 ADA Glycemic Goals in Adults

- A1c < 7% is appropriate and effective when implemented "soon" after diagnosis
- More stringent A1c < 6.5% for selected individuals: (if attainable without hypo or other ADR's.)
  - Short duration of diabetes
  - Long life expectancy
  - No significant CVD
- Less stringent A1c < 8% appropriate for:
  - Long duration of uncontrolled diabetes
  - History of severe hypo episodes
  - Limited life expectancy
  - Advanced micro & macro complications / co-morbid conditions

*Diabetes Care.* 2012; 35(Suppl 1)

### 2011 AACE: Glycemic Goals in Adults

Less Stringent  
( $< 8\%$ )

(ADA  $< 7\%$ ;  
AACE  $\leq 6.5\%$ )

More Stringent  
(as close to normal  
[6%] as possible)

- Longer duration of diabetes
- Limited life expectancy
- Presence of complications
- Greater concern about hypoglycemia

- Shorter duration of diabetes
- Longer life expectancy
- No significant CVD

Handelsman Y et al. *Endocr Pract.* 2011;17:287-302.

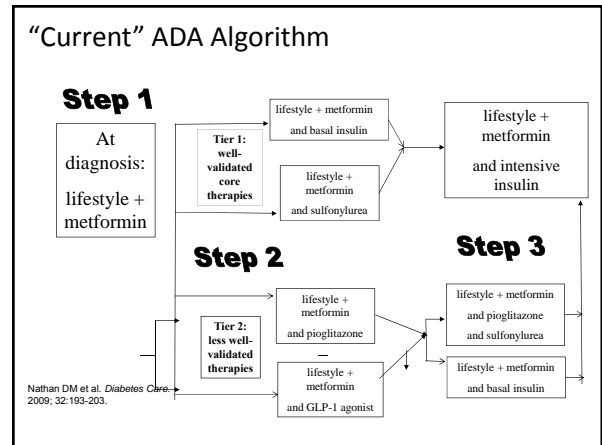
SR has had T2DM for 6 years.  
Admission A1c = 8.5%. Meds prior to admission:

- metformin 1000mg BID
- saxagliptin 5mg daily
- lisinopril 20mg daily
- atorvastatin 20mg daily

What do you recommend for discharge planning

1. Continue preadmission medications
2. Increase dose of preadmission diabetes medications
3. Add a third oral agent
4. Discontinue saxagliptin and add GLP-1 agonist
5. Add basal insulin
6. Add basal-bolus insulin

## Algorithm Comparison



### Clinical Practice Recommendations 2012 Revisions

**New ADA/EASD guidelines expected in early 2012**

- Therapy for T2DM
  - At time of diagnosis:
    - Metformin (unless contraindicated) + Lifestyle
  - Newly diagnosed T2DM with markedly symptomatic and/ or elevated BG or A1c
    - Insulin therapy +/- additional agents
  - If non-insulin monotherapy at max dose does not achieve or maintain A1c target over 3-6 months, add:
    - Second oral agent
    - GLP-1 agonist
    - Insulin

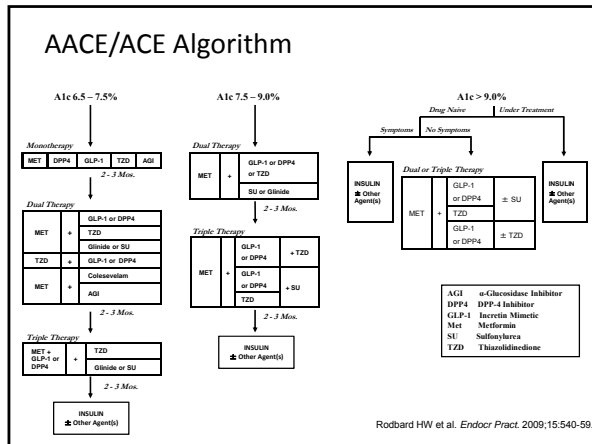
Standards of Medical Care in Diabetes—2012. *Diabetes Care.* 2012; 35 (Suppl 1)

### AACE/ACE Algorithm

Algorithm is stratified by A1c level

- **A1c  $\leq 7.5\%$** 
  - Start with monotherapy. If monotherapy fails, progress to dual and then to triple therapy. Finally, insulin therapy should be initiated, with or without additional agents.
- **A1c 7.6%–9.0%**
  - Begin dual therapy because no single agent is likely to achieve the A1c goal. If dual therapy fails, progress to triple therapy and then to insulin therapy, with or without additional orally administered agents.
- **A1c  $> 9.0\%$** 
  - If the patient is asymptomatic, begin with triple therapy. If the patient is symptomatic, or therapy with similar medications has failed, initiate insulin therapy, either with or without additional orally administered agents.

Rodbard HW et al. *Endocr Pract.* 2009;15:540-59.



### 2012 ACP Guidelines

- American College of Physicians:
  - Recommendation #1:
    - When lifestyle modifications do not achieve glycemic goals – add oral pharmacotherapy
  - Recommendation #2:
    - For most T2DM, initial monotherapy – metformin
  - Recommendation #3:
    - When lifestyle and metformin monotherapy fail, add second drug.

Ann Intern Med. 2012; 156:218-231

### WUZZLE # 2

### Key Points to Consider when Selecting Pharmacotherapy for T2DM

- How long the patient has had diabetes (duration of disease)
- Which blood glucose level is not at target (e.g., fasting, postprandial, or both)
- Patient preference for route of administration (e.g., oral, inhaled, injectable)
- The degree of HbA1c-lowering effect required to achieve goal
- The side effect profile and the patient's tolerability
- Co-existing conditions (eg, CVD, depression, osteoporosis, etc)

Burke S., Cornell S. *Clinician Reviews.* 2008;18:28-34.

### Additional Considerations when Selecting Pharmacotherapy for T2DM

- Undesired Drug Effects:
  - Protect remaining B-cell function
  - Minimize hypoglycemic risks
  - Minimize weight gain

### Pharmacotherapy Options

- Insulin**
  - Bolus insulin**
    - Insulin lispro (Humalog)
    - Insulin aspart (NovoLog)
    - Insulin glulisine (Apidra)
    - Regular human insulin
      - (Humulin R)
      - (Novolin R)
  - Basal insulin**
    - Insulin NPH
      - (Humulin N)
      - (Novolin N)
    - Insulin detemir (Levemir)
    - Insulin glargine (Lantus)
    - Insulin degludec \*\***
- Oral Medications**
  - α-glucosidase inhibitors (AGI)
  - Dipeptidyl peptidase-4 (DPP-4) inhibitors (gliptins)
  - Dopamine agonists
  - Glinides
  - Biguanides
  - Sulfonylureas
  - Sodium Glucose Co-Transporter-2 inhibitors \*\***
  - Thiazolidinediones (TZDs or glitazones)
- Non-insulin injectable agents**
  - Glucagon-like peptide-1 (GLP-1) agonists
  - Amylinomimetic

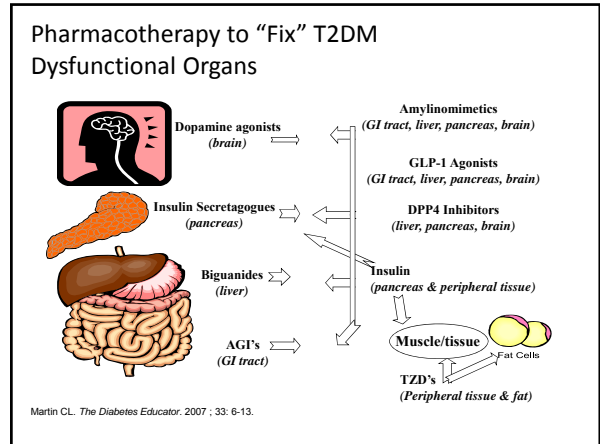
**\*\*Not FDA approved at this time**



How many dysfunctional (broken) organs are currently identified in T2DM?

1. 1-2
2. 3-5
3. 6-7

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Diabetes Medications and their effect on blood glucose	
Medication	Effect on blood glucose
Alpha-glucosidase inhibitors	Post-prandial
Biguanides (metformin)	Fasting
DPP-4 inhibitors (gliptins)	Post-prandial
Dopamine agonists	Post-prandial
Glinides	Post-prandial
GLP-1 agonists	Short acting – Post-prandial Long acting – Fasting & Postprandial
Pramlintide (amylinomimetic)	Post-prandial
Sulfonylureas	Fasting & Post-prandial
Thiazolidinediones	Fasting & Post-prandial
Insulin (Basal)	Fasting
Insulin (Bolus)	Post-prandial

Pharmacotherapy Comparison					
	Weight Effect	Hypoglycemia	b-cell protection	CVD benefits	Other considerations
α-glucosidase inhibitors (AGI)	neutral	Low risk	Possible	possible	GI adverse effects
Amylinomimetics	loss	low risk	possible	yes	GI adverse effects (nausea), cost, injectable
Biguanides	loss	low risk	possible	yes	Inexpensive, GI adverse effects
DPP-4 Inhibitors (gliptins)	neutral	low risk	possible	yes	minimal adverse effects, cost
Dopamine agonist	neutral or loss	Low risk	unknown	yes/no	GI adverse effects , hypotension
GLP-1 agonists	loss	low risk	possible	yes	GI adverse effects (nausea), cost, injectable
Insulin	gain	+ risk – bolus low risk - basal	possible	possible	best A1c lowering, injectable
Secretagogues (Sulfonylureas & Glinides)	gain	+ risk	no	no	immediate short-term response, inexpensive
TZD's (glitazones)	gain	low risk	possible	yes/no	4-8 weeks for response, redistribution of subcutaneous/visceral fat, edema, bone loss- adverse effects

Typical A1c Reductions		
Monotherapy	Route of Administration	A1c (%) Reduction
Sulfonylurea	Oral	1.5–2.0
Metformin	Oral	1.5
Glitazones	Oral	1.0–1.5
Meglitinides	Oral	0.5–2.0
α-Glucosidase Inhibitors	Oral	0.5–1.0
Dopamine agonists	Oral	0.4
DDP-4 Inhibitors	Oral	0.5-0.7
GLP-1 agonists	Injectable	0.8-1.5
Amylin analogs	Injectable	0.6
Insulin	Injectable	Open to target

Unger J et al. *Postgrad Med*. 2010;122:145-57.

## WUZZLE #3

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### Take Home Message

- **The longer we wait – the more damage is done!**
  - T2DM is a multiple broken organ disease
  - Monotherapy rarely works and only for short term.
- **Earlier diagnosis and treatment needed**
  - AACE guidelines start with drug therapy + lifestyle modification
    - Drug therapy is determined on the patient's A1c level (and A1c goal)
- **Individualize glycemic goals and therapy**
  - One size does NOT fit all
- **Key consideration in therapy**
  - Save the  $\beta$ -cell
  - Minimize hypoglycemia
  - Minimize weight gain