



2015 Type 2 Meds Management

Beverly Dyck Thomassian, RN, MPH, BC-ADM, CDE
President, Diabetes Education Services

www.DiabetesEd.net



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Diabetes Meds for Type 2: Objectives



1. Describe the main action of the different categories of type 2 diabetes medications.
2. Discuss using the AACE and ADA 2015 Guidelines to determine best therapeutic approach.
3. Using the ADA Guidelines, describe strategies to initiate and adjust insulin therapy.



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Path to Type 2 Diabetes



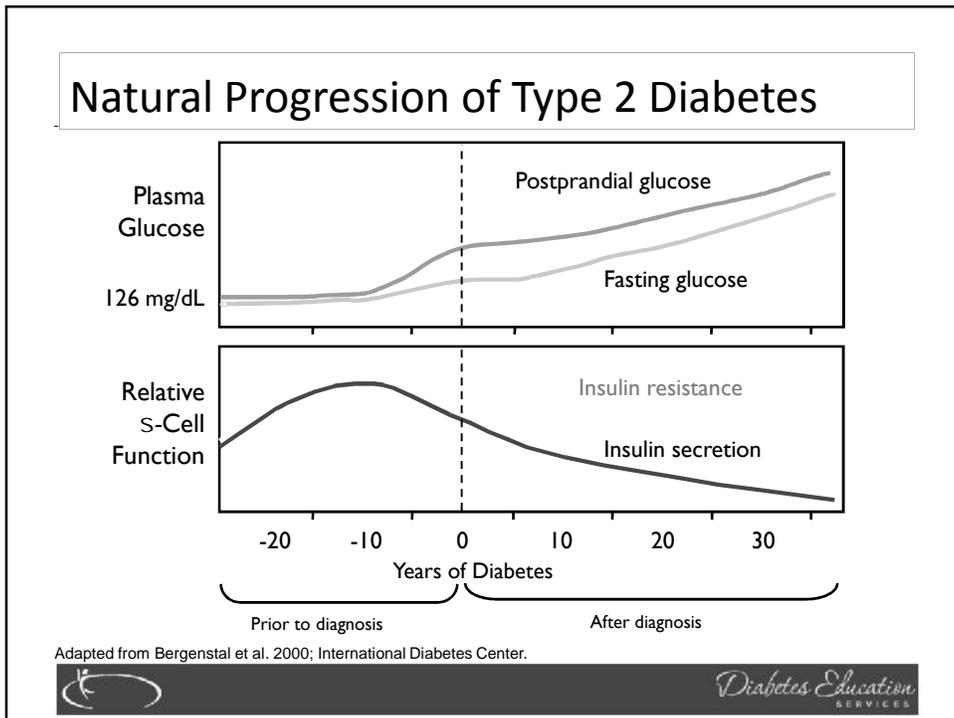
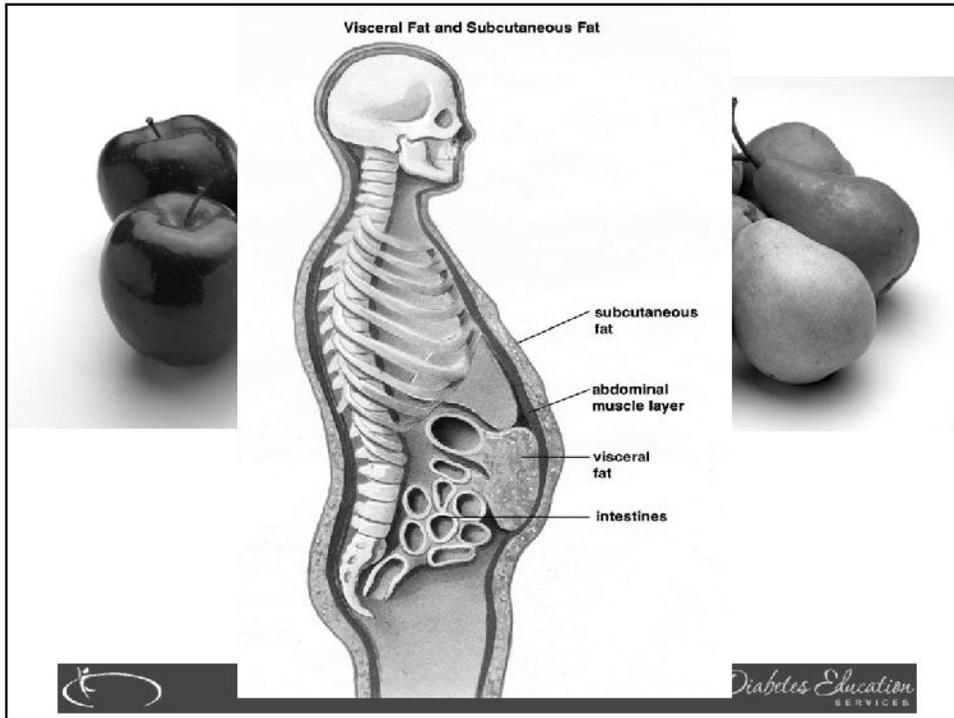
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Patti LaBelle
"divabetic" --
that's a mix of
diabetic and
diva



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Patient Centered Approach

"...providing care that is respectful of and responsive to individual patient preferences, needs, and values - ensuring that patient values guide all clinical decisions."

- Gauge patient's preferred level of involvement.
- Explore, where possible, therapeutic choices.
- Utilize decision aids.
- **Shared** decision making – final decisions re: lifestyle choices ultimately lie with the patient.



ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

Diabetes Care 2012;35:1364–1379
Diabetologia 2012;55:1577–1596



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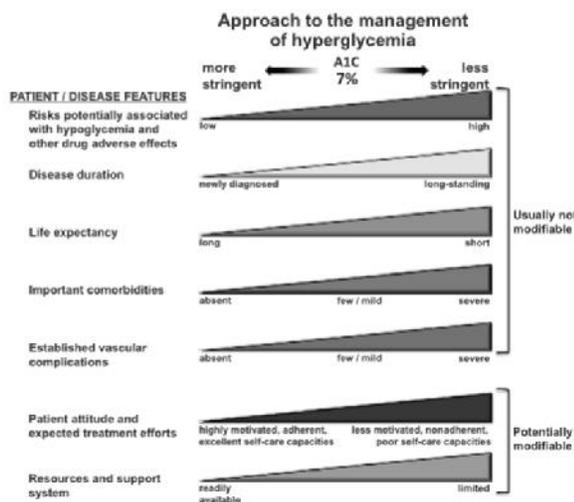


Figure 6.1—Depicted are patient and disease factors used to determine optimal A1C targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. Adapted with permission from Inzucchi et al. (45).

ADA Standards of Care 2015



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Other Considerations

- ▶ Cost
- ▶ Hypoglycemia
- ▶ Age
- ▶ Weight
- ▶ Comorbidities
 - ▶ Kidney disease
 - ▶ Heart disease – CHF, CAD
 - ▶ Liver dysfunction



ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

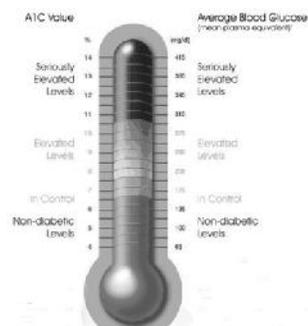
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Glycemic Targets - ADA

- ▶ **Adult non pregnant A1c goals**
 - ▶ **A1c < 7%** - a reasonable goal for adults.
 - ▶ **A1c < 6.5%** - may be appropriate for those without significant risk of hypoglycemia or other adverse effects of treatment.
 - ▶ **A1c < 8%** - may be appropriate for patients with history of hypoglycemia, limited life expectancy, or those with longstanding diabetes and vascular complications.



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GOALS FOR GLYCEMIC CONTROL

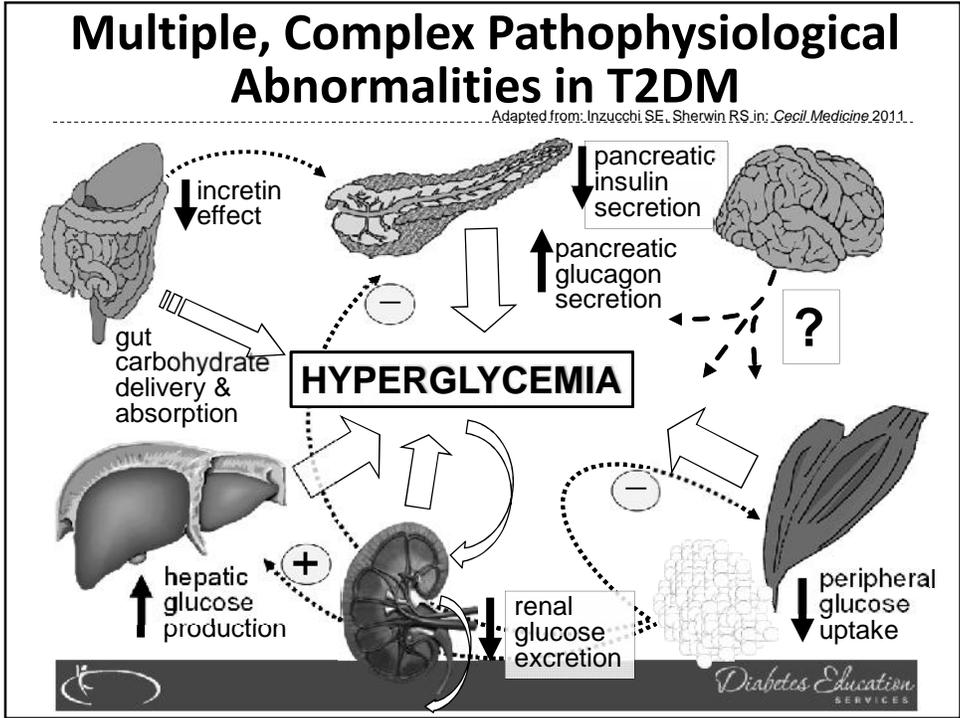
A1c ≤ 6.5%

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

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Antihyperglycemic Therapy – 1st Step

► Lifestyle Changes

- Weight control
- Healthy eating
- Activity



ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

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Oral Diabetes Medications



Class/Main Action	Name(s)	Daily Dose Range	Considerations
Biguanides • Decrease hepatic glucose output • First line med at diagnosis of type 2	metformin (Glucophage)	500 – 2500 mg (usually BID w/meal)	Side effects: nausea, bloating, diarrhea. Use XR to minimize. Lactic acidosis precaution: avoid in pts with creat >1.4 women, 1.5 men, during illness or surgery. Benefits: decreased cholesterol, no wt gain or hypoglycemia. Lowers A1c 1.0% – 2.0%.
	Extended Release-XR (Glucophage XR)	(1x daily w/dinner)	
	glimepiride (Glimetza) (Fortamet)	500 – 2000 mg 500 – 2000 mg 500 – 2500 mg	
Sulfonylureas • Stimulates sustained insulin release	glyburide (Micronase, Diabeta) (Glynase)	1.25 – 20 mg 0.75 – 12 mg	Can take once or twice daily before meals. Side effects include hypoglycemia and weight gain. Eliminated via kidney. Caution: Glyburide most likely to cause hypoglycemia. Lowers A1c 1.0% – 2.0%.
	glipizide (Glucotrol) (Glucotrol XL)	2.5 – 40 mg 2.5 – 20 mg	
	glimapiride (Amaryl)	1.0 – 8 mg	
DPP – 4 Inhibitors • "Incretin Enhancers" • Prolongs action of gut hormones • Increases insulin secretion • Delays gastric emptying	sitagliptin (Januvia)	100 mg daily (eliminated via kidney*)	*If creatinine elevated, see pkg insert for dosing info. No wt gain or hypoglycemia. Side effects include nasopharyngitis, headache and upper-respiratory tract infection. Report signs of pancreatitis (abdominal pain, nausea, vomiting). Lowers A1c 0.6% – 0.8%.
	saxagliptin (Onglyza)	Up to 5 mg daily (eliminated via kidney*, feces)	
	linagliptin (Tradjenta)	5 mg daily (eliminated via feces)	
	alogliptin (Nesina)	25 mg once daily (eliminated via kidney)	

More medications on back. Note: These meds are for people with Type 2 diabetes and should not be used during pregnancy. Content is for educational purposes only; please consult prescribing information for details.

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Class/Main Action	Name(s)	Daily Dose Range	Considerations
SGLT2 Inhibitors • Decrease glucose reabsorption in kidneys • "Glucoretic"	Canagliflozin (Invokana) Dapagliflozin (Farxiga) Empagliflozin (Jardiance)	100 – 300 mg 1x daily 5 – 10 mg 1x daily 10 – 25 mg 1x daily	For all, monitor B/P, K+ and renal function. If GFR<45, stop Invokana. If GFR<60, stop Farxiga. Do not start pts w/ GFR<45 on Jardiance. Side effects: hypotension, UTIs, increased urination, genital infections. Avoid Farxiga in pts w/ bladder cancer. Lowers A1c 0.7% – 1.5%, lowers wt 1 – 3 lbs.
Thiazolidinediones "TZDs" • Increase insulin sensitivity	pioglitazone (Actos) rosiglitazone (Avandia)	15 – 45 mg daily 4 – 8 mg daily	Black Box Warning: TZDs may cause or worsen CHF. Monitor for edema and weight gain. Increased peripheral fracture risk. Actos may increase risk of bladder cancer. Lowers A1c 0.5% – 1.0%
Glucosidase Inhibitors • Delay carb absorption	acarbose (Precose) miglitol (Glyset)	25 – 100 mg w/meals 300 mg max daily dose	Start low dose, increase at 4-8 wk intervals to decrease GI effects. Caution with liver or kidney problems. In case of hypo, treat w/ glucose tabs. Lowers A1c 0.5– 1.0%.
Dopamine Receptor Agonists • Resets circadian rhythm	bromocriptine mesylate—Quick Release "QR" (Cycloset)	1.6 to 4.8 mg a day (each tab 0.8 mg)	Take within 2 hrs of waking. Side effects: nausea, headache, fatigue, hypotension, syncope, somnolence. Lowers A1c 0.6% – 0.9%.
Meglitinides • Stimulates rapid insulin burst	repaglinide (Prandin) nateglinide (Starlix)	0.5 – 4 mg w/meals (metabolized in liver) 60 – 120 mg w/meals (eliminated via kidney)	Take before meals. Side effects may include hypoglycemia and weight gain. Lowers A1c 1.0% – 2.0%.



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Injectables That Lower Glucose

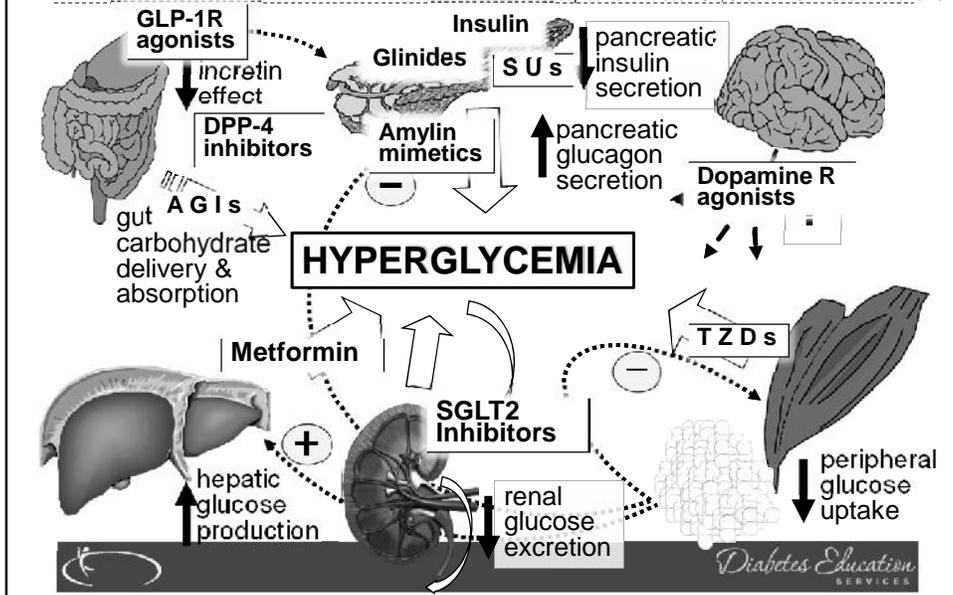
Class/Main Action	Name	Dose Range	Considerations
GLP-1 Agonist "Incretin Mimetic" • Increases insulin release with food • Slows gastric emptying • Promotes satiety • Suppresses glucagon Lowers A1c 0.5 – 1.6% Wt loss of ~ 3lbs	exenatide (Byetta) exenatide XR (Bydureon)	5 or 10 mcg BID (renally excreted) 2mg 1x a week (renally excreted)	Side effects for all: Nausea, vomiting, weight loss, injection site reaction. Report signs of acute pancreatitis (severe abdominal pain, vomiting), stop med. Black box: Thyroid C-cell tumor warning for liraglutide, exenatide XR, albiglutide, and dulaglutide (avoid if family history of medullary thyroid cancer, notify MD of hoarseness, throat lump)
	liraglutide (Victoza)	0.6 - 1.8 mg daily	
	albiglutide (Tanzeum)	30 and 50 mg 1x a week pen injector	
	dulaglutide (Trulicity)	0.75 and 1.5 mg 1x a week pen injector	
Amylin Mimetic • Slows gastric emptying • Suppresses glucagon • Promotes satiety Lowers A1c 0.5 – 1%	pramlintide (Symlin)	Type 1: 15 - 60 mcg; Type 2: 60 - 120 mcg Immediately before major meals	For Type 1 or 2 on insulin. Black box warning: severe hypoglycemic risk 3 hrs post injection. Prevent hypoglycemia, decrease insulin dose when starting pramlintide. Side effects: nausea, weight loss.

The information listed here are general guidelines only; please consult prescribing information for details.



Multiple, Complex Pathophysiological Abnormalities in T2DM

Adapted from: Inzucchi SE, Sherwin RS in: *Cecil Medicine* 2011



Life Study

- ▶ 61 year old overweight woman with type 2 diabetes 3 months. Has been trying to control diabetes with diet and exercise. GFR in 90s. Worried about weight gain.
- ▶ Most recent A1c 6.4%
 - ▶ ADA
 - ▶ AACE
 - ▶ Cash pay



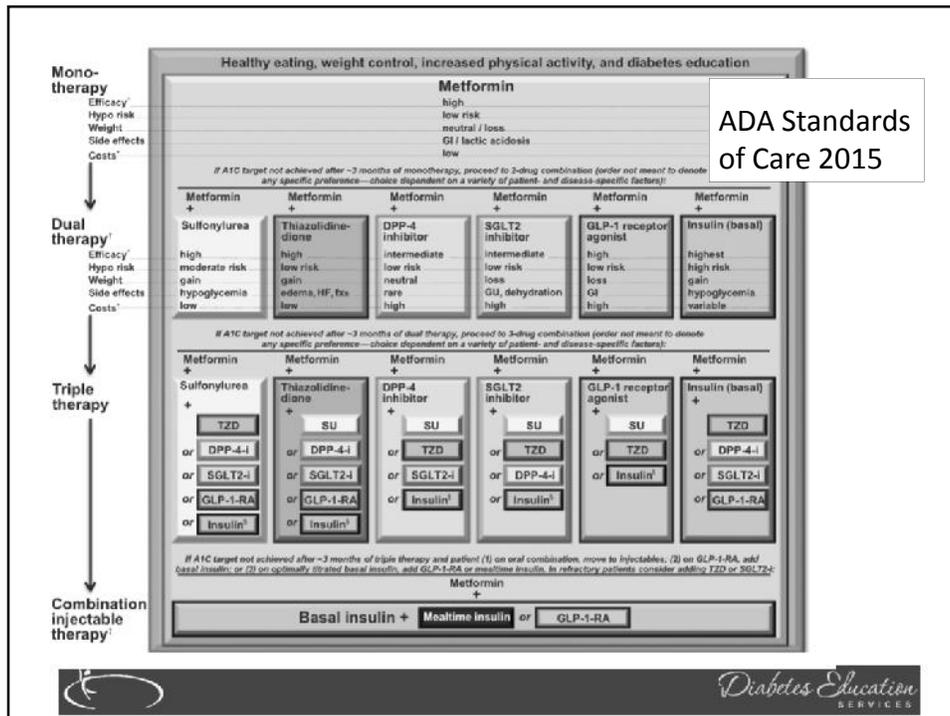
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ADA Step Wise Approach to Hyperglycemia 2015

- ▶ Start with lifestyle coaching
- ▶ When lifestyle alone is not achieving A1c goal – Metformin should be added at, or soon after diagnosis (unless contraindicated).
- ▶ Metformin has a long standing evidence base for efficacy and safety, is cheap and may reduce CV risk.



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When goal is to avoid weight gain

- ▶ These meds are weight neutral
 - ▶ Metformin
 - ▶ DPP-IV Inhibitors: Januvia, Onglyza, Tradjenta, Nesina
 - ▶ Acarbose
- ▶ These meds associated with wt loss
 - ▶ GLP-1 agonists (Byetta, Bydureon, Victoza, Tanzeum, Trulicity)
 - ▶ SGLT-2 Inhibitors (Canagliflozin, Dapagliflozin, Empagliflozin)
 - ▶ Symlin (Pramlintide)



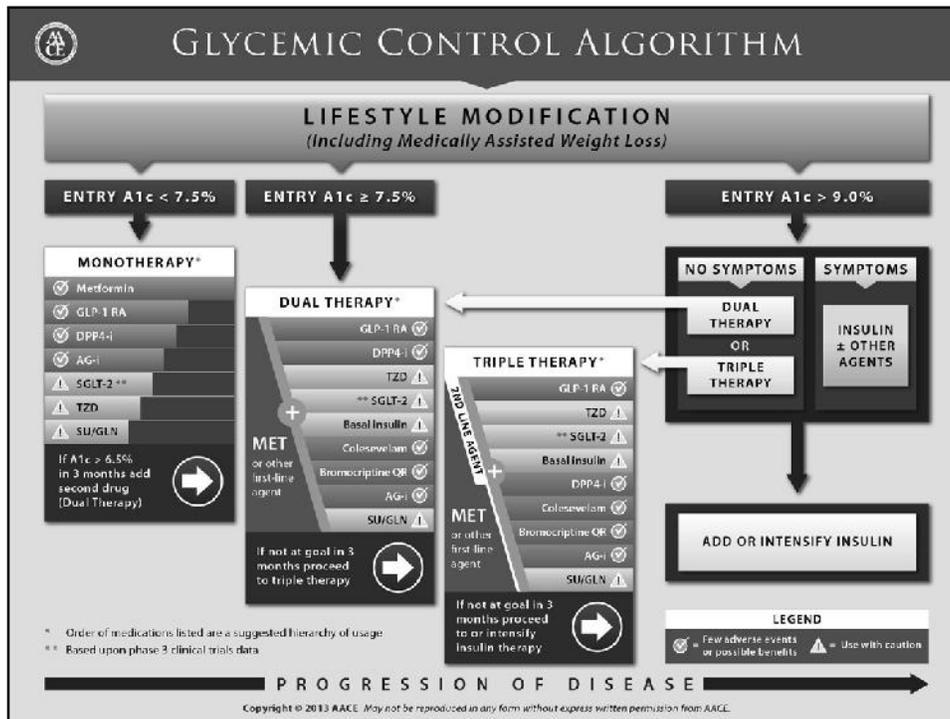
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When goal is to minimize cost

- ▶ Go generic.
- ▶ Oral Meds -Metformin and Sulfonylureas
 - ▶ Walmart offers 3 mo supply of following meds for ~ \$10
 - ▶ Metformin and Metformin XR
 - ▶ Glipizide, Glyburide, Glimepiride
- ▶ Insulins – Oldies but Goodies
 - ▶ NPH, Regular, 70/30 mix
 - ▶ \$25 a vial at Walmart – ReliOn
 - ▶ Vials and needles cheaper



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Life Study

- ▶ 54 year old smoker, creatinine 1.2, BMI 27. Not checking BG, even though he has glucose meter. On Metformin 500mg BID for past 4 months. Had bad experience with hypoglycemia on glyburide.
- ▶ Most recent A1c 7.9%
 - ▶ ADA
 - ▶ AACE



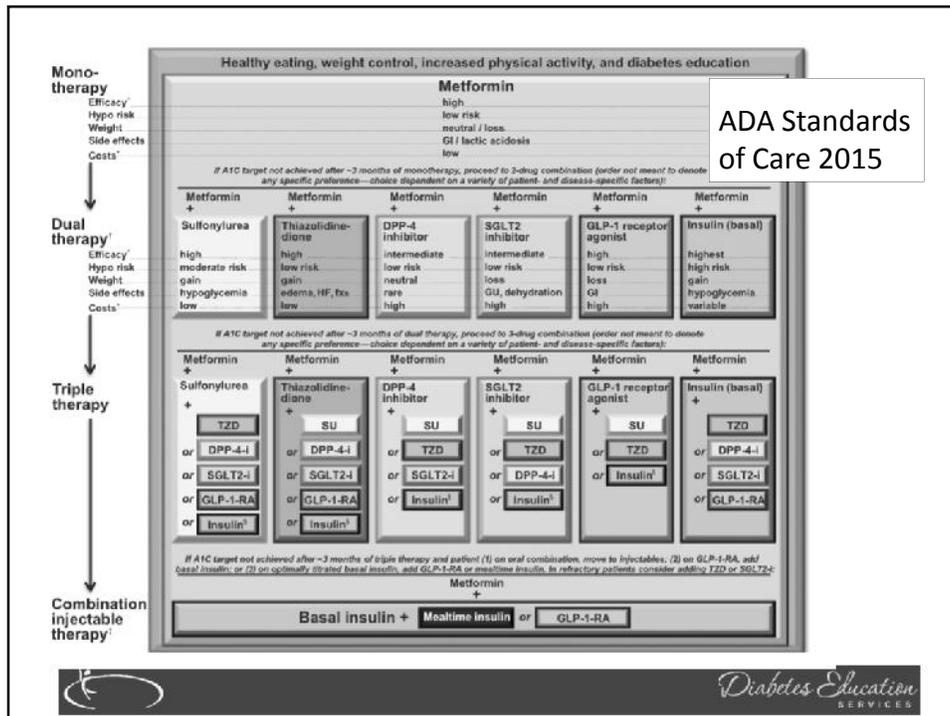
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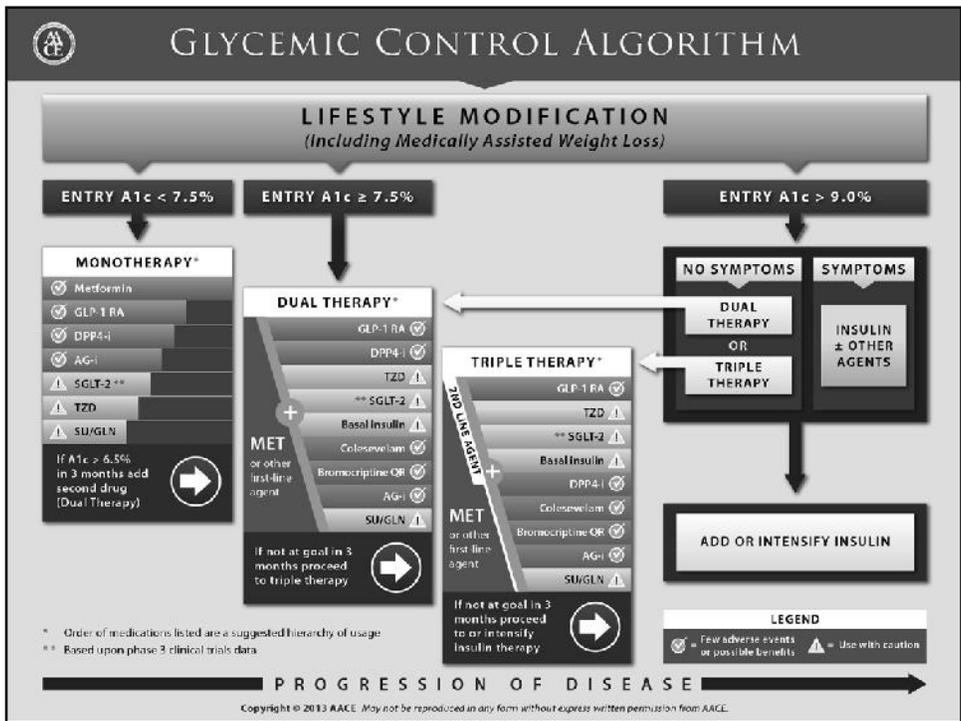
When goal is to avoid Hypoglycemia

- ▶ Avoid sulfonylureas
- ▶ Careful insulin dosing
- ▶ May need to up adjust glucose goals
- ▶ Monitor kidney function
- ▶ Reinforce for patients on insulin to “TIE”
 - ▶ Test
 - ▶ Inject
 - ▶ Eat



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Life Study

- ▶ 71 year old woman with type 2 diabetes for past year. BMI 24. Has been trying to control diabetes by limiting carbs and exercise. Creat 1.6. Good social support.
- ▶ Most recent A1c 8.6%
 - ▶ She has great insurance or
 - ▶ She is cash pay, hates needles



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Older Adults - Considerations



- Reduced life expectancy
- Higher CVD burden
- Reduced GFR
- At risk for adverse events from polypharmacy
- More likely to be compromised from hypoglycemia

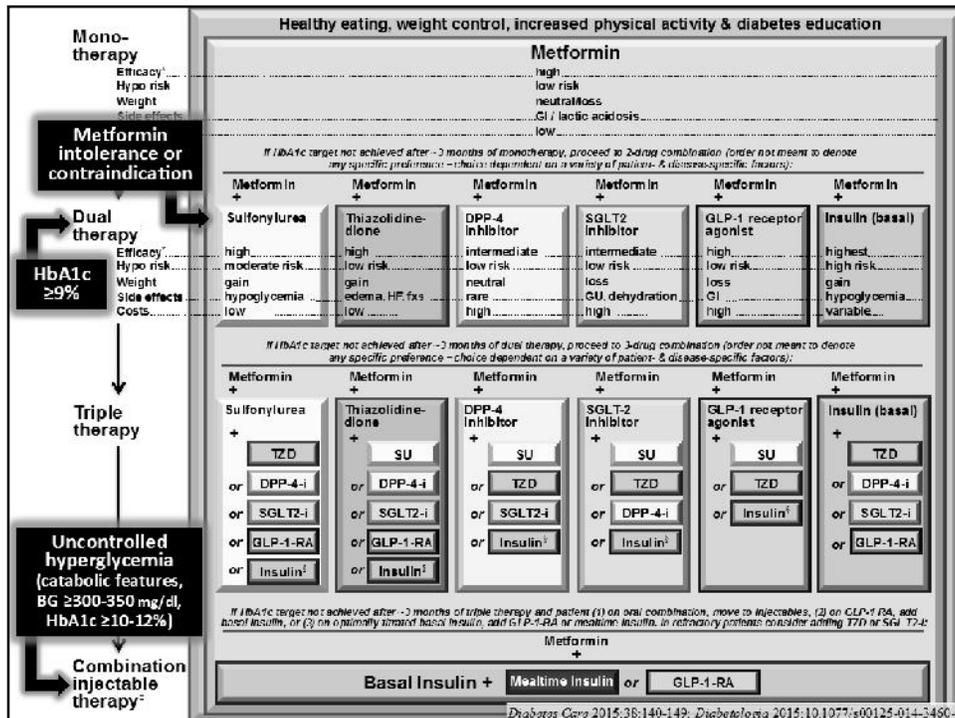
- ✓ Less ambitious targets
- ✓ A1c <7.5–8.0%
- ✓ Focus on drug safety

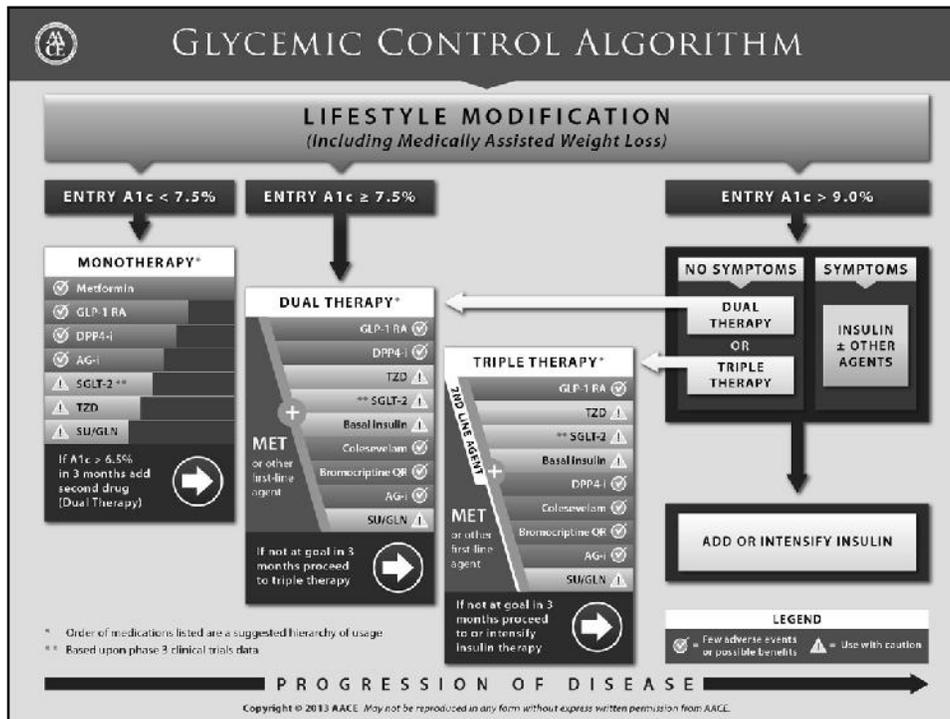
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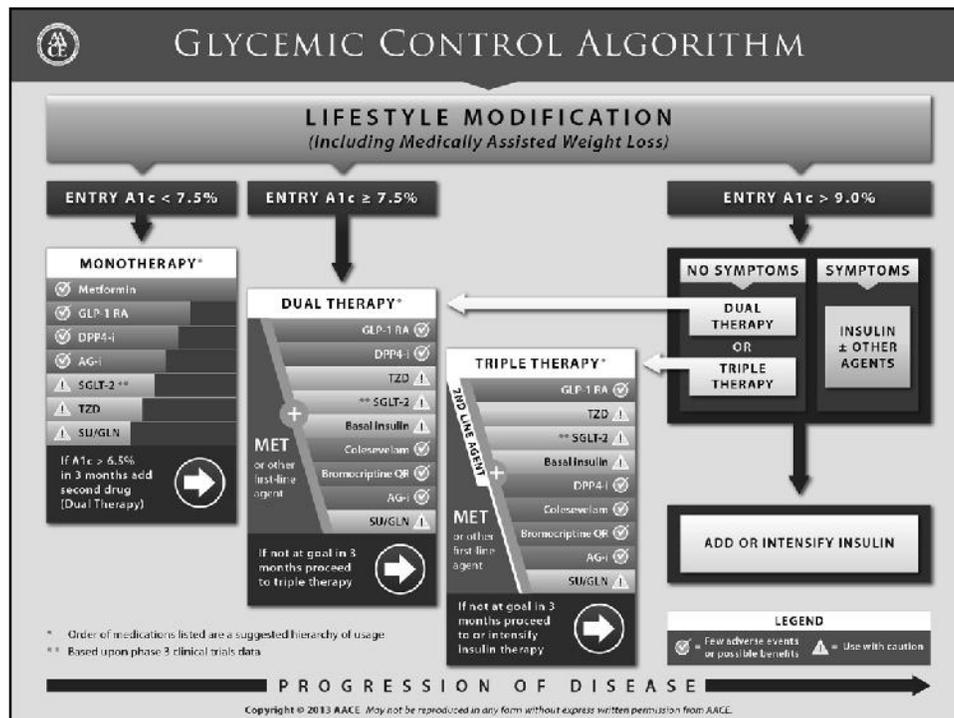
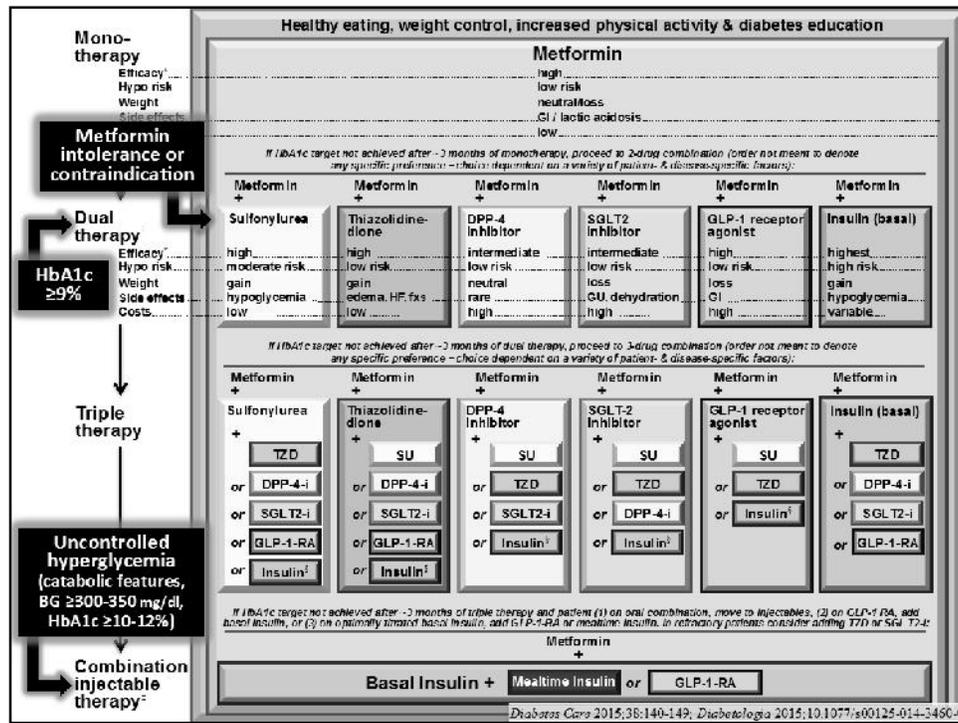


What next?

- ▶ 69 year old male, BMI 31, on Metformin 2000mg a day and Glipizide 40mg a day.
- ▶ A1c 9.1%. Creat 1.2
- ▶ Pt is obese, 11 yr history of diabetes
 - ▶ What next?
 - ▶ Insurance
 - ▶ No insurance



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Case Study



- ▶ 70 yr old, weighs 100kg
- ▶ History of CABG, tobacco
- ▶ A1c – 11.3%, BG 400-500 for past weeks
- ▶ Insulin – 100+ units Lantus at hs (solostar)
- ▶ Oral Meds: Metformin, Invokana
- ▶ Pt can't afford Lantus insulin pen – what other option?



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Insulin PocketCard™

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15
years

Action	Insulin Name	Onset	Peak	Effective Duration	Considerations
Bolus	Rapid Acting Analogs	5 - 15 min	30 - 90 min	< 5 hrs	Bolus insulin lowers after-meal glucose. Efficacy reflected in post-meal BG. Basal insulin controls BG between meals and HS. Efficacy reflected in fasting BG. Side effects: hypoglycemia, weight gain. Typical dosing range: 0.5-1.0 units/kg body wt/day. Discard opened insulin vials after 28 days.
	Aspart (Novolog)				
	Lispro (Humalog)				
Short Acting	Regular	30 - 60 min	2 - 3 hrs	5 - 8 hrs	
	Intermediate	NPH	2 - 4 hrs	4 - 10 hrs	
Basal	Long Acting	Detemir (Levemir)	3 - 8 hrs	No peak	
	Glargine (Lantus)	2 - 4 hrs	No peak	20 - 24 hrs	
Bolus + Basal	Intermediate + rapid	Novolog® Mix 70/30 70/30 = 70% NPA + 30% aspart	5 - 15 min	Dual peaks	10 - 16 hrs
	Humalog® Mix 75/25 = 75% NPL + 25% lispro 50/50 = 50% NPL + 50% lispro				
Intermediate + short	Combo of NPH + Reg 70/30 = 70% NPH + 30% Reg 50/50 = 50% NPH + 50% Reg	30 - 60 min	Dual peaks	10 - 16 hrs	

Adapted from American Association of Clinical Endocrinologists Guidelines 2007. Because insulin action times can vary with each injection, time periods listed here are general guidelines only; please consult prescribing information for details.

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Cost Per Vial in Northern CA

Per vial cost	Walmart	Walgreens	Costco
Regular Insulin	\$25*	\$92	\$99
NPH	\$25*	\$92	\$99
70/30	\$25*	\$92	\$101
Humalog	\$200	\$220	\$178
Novolog	\$197	\$217	\$178
Apidra	\$180	\$246	\$178
Levemir	\$300	\$300	\$300
Lantus	\$226	\$221	\$206



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Case Study

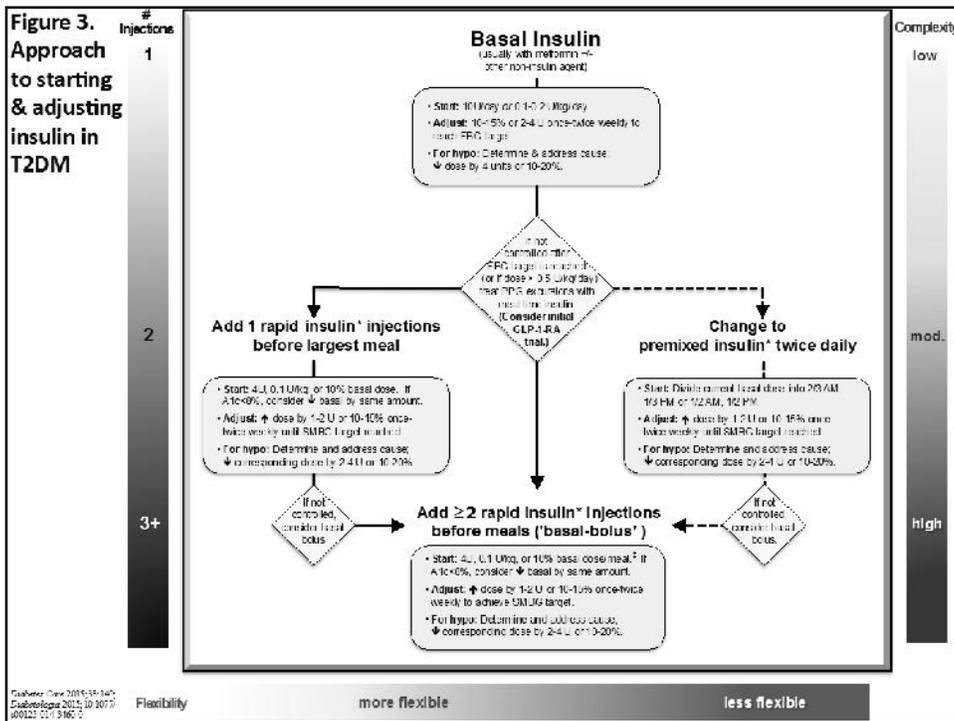


- ▶ 70 yr old, weighs 100kg
- ▶ History of CABG
- ▶ A1c – 11.3%, BG 400-500 for past weeks
- ▶ Insulin – 100+ units Lantus at hs (solostar).
- ▶ Metformin 1000mg BID
- ▶ What is max basal insulin should he be on?



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Case Study



- ▶ 70 yr old, weighs 100kg
- ▶ History of CABG
- ▶ A1c – 11.3%, BG 400-500 for past weeks
- ▶ Insulin – 100+ units Lantus at hs (solostar)
- ▶ Metformin 1000mg BID
- ▶ What is max basal insulin should he be on?
 - ▶ $100\text{kg} \times 0.5 = 50$ units a day
- ▶ What can we do next to improve BG?



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Case Study



What is max basal insulin should he be on?

- ▶ $100\text{kg} \times 0.5 = 50$ units a day
- ▶ What can we do next to improve BG?
 - ▶ Add GLP-1 (Exenatide, Victoza, Trulicity, Tanzeum)
 - ▶ Add bolus insulin to largest meal
 - ▶ Switch him to 70/30 insulin ac breakfast and dinner
 - ▶ Total previous basal dose – 100 units
 - ▶ 2/3 in am – 65 units am (43 NPH and 22 regular)
 - ▶ 1/3 pre dinner – 35 units pm (23 NPH and 12 regular)



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Case Study



- ▶ 70 yr old, weighs 100kg
- ▶ History of CABG, tobacco
- ▶ A1c – 11.3%, BG 400-500 for past weeks
- ▶ What will inform you of how to proceed?



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Critical Points

- ▶ Individualize Glycemic targets & BG-lowering
- ▶ Diet, exercise, & education: foundation T2DM therapy
- ▶ Metformin = optimal 1st-line drug.
- ▶ After metformin, data limited. Combo therapy reasonable
- ▶ Ultimately, many T2 patients will require insulin therapy
- ▶ All treatment decisions should be made in conjunction with the patient (focus on preferences, needs & values.)
- ▶ CV risk reduction - a major focus of therapy.

ADA-EASD Position Statement: Management of
Hyperglycemia in T2DM

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Thank You



- ▶ Have fun tonight
- ▶ Reps here tomorrow
- ▶ Not too late to sign up for Adv Assessment

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