

Management of Hyperglycemia in Type 2 Diabetes

Celeste C. Thomas MD, MS

Disclosures

In compliance with the accrediting board policies, the American Diabetes Association requires the following disclosure to the participants:

Celeste C. Thomas MD, MS

Disclosed no conflict of interest

ADA-EASD Position Statement Update: Management of Hyperglycemia in T2DM, 2015

- PATIENT-CENTERED CARE
- BACKGROUND
 - Epidemiology and health care impact
 - Relationship of glycemic control to outcomes
 - Overview of the pathogenesis of type 2 diabetes
- ANTI-HYPERGLYCEMIC THERAPY
- Glycemic targets
- Therapeutic options
 - Lifestyle
 - Oral agents & non-insulin injectables
 - Insulin

ADA-EASD Position Statement Update: Management of Hyperglycemia in T2DM, 2015

- 3. ANTIHYPERGLYCEMIC THERAPY
 - Implementation Strategies
 - Initial drug therapy
 - Advancing to dual combination therapy
 - Advancing to triple combination therapy
 - Transitions to and titrations of insulin
- 4. OTHER CONSIDERATIONS
 - Age
 - Weight
 - Sex/racial/ethnic/genetic differences
 - Comorbidities (*CAD, HF, CKD, Liver disease, Hypoglycemia-prone*)
- 5. FUTURE DIRECTIONS / RESEARCH NEEDS

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. Consider using decision aids.
- Shared Decision Making – a collaborative process between patient and clinician, using best available evidence and taking into account the patient's preferences and values
- Final decisions regarding lifestyle choices ultimately lie with the patient.

ADA-EASD Position Statement Update: Management of Hyperglycemia in T2DM, 2015

2. BACKGROUND

- Relationship of glycemic control to microvascular and macrovascular outcomes.

Impact of Intensive Therapy for Diabetes: Summary of Major Clinical Trials

Study	Microvasc		CVD		Mortality	
	Initial Trial	Long Term Follow-up	Initial Trial	Long Term Follow-up	Initial Trial	Long Term Follow-up
UKPDS	↓	↓	↔	↓	↔	↓
DCCT / EDIC*	↓	↓	↔	↓	↔	↓
ACCORD	↓		↔		↑	
ADVANCE	↓		↔		↔	
VADT	↓		↔		↔	

Kendall DM, Bergenstal RM. © International Diabetes Center 2009

UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998;352:854.

Holman RR et al. *N Engl J Med*. 2008;359:1577. DCCT Research Group. *N Engl J Med* 1993;329:977.

Nathan DM et al. *N Engl J Med*. 2005;353:2643. Gerstein HC et al. *N Engl J Med*. 2008;358:2545.

Patel A et al. *N Engl J Med* 2008;358:2560. Duckworth W et al. *N Engl J Med* 2009;360:129. (erratum:

Moritz T. *N Engl J Med* 2009;361:1024) . Writing Group for the DCCT/EDIC Research Group. *JAMA*. 2015;313(1):45-53.

* in T1DM



Initial Trial



Long Term Follow-up



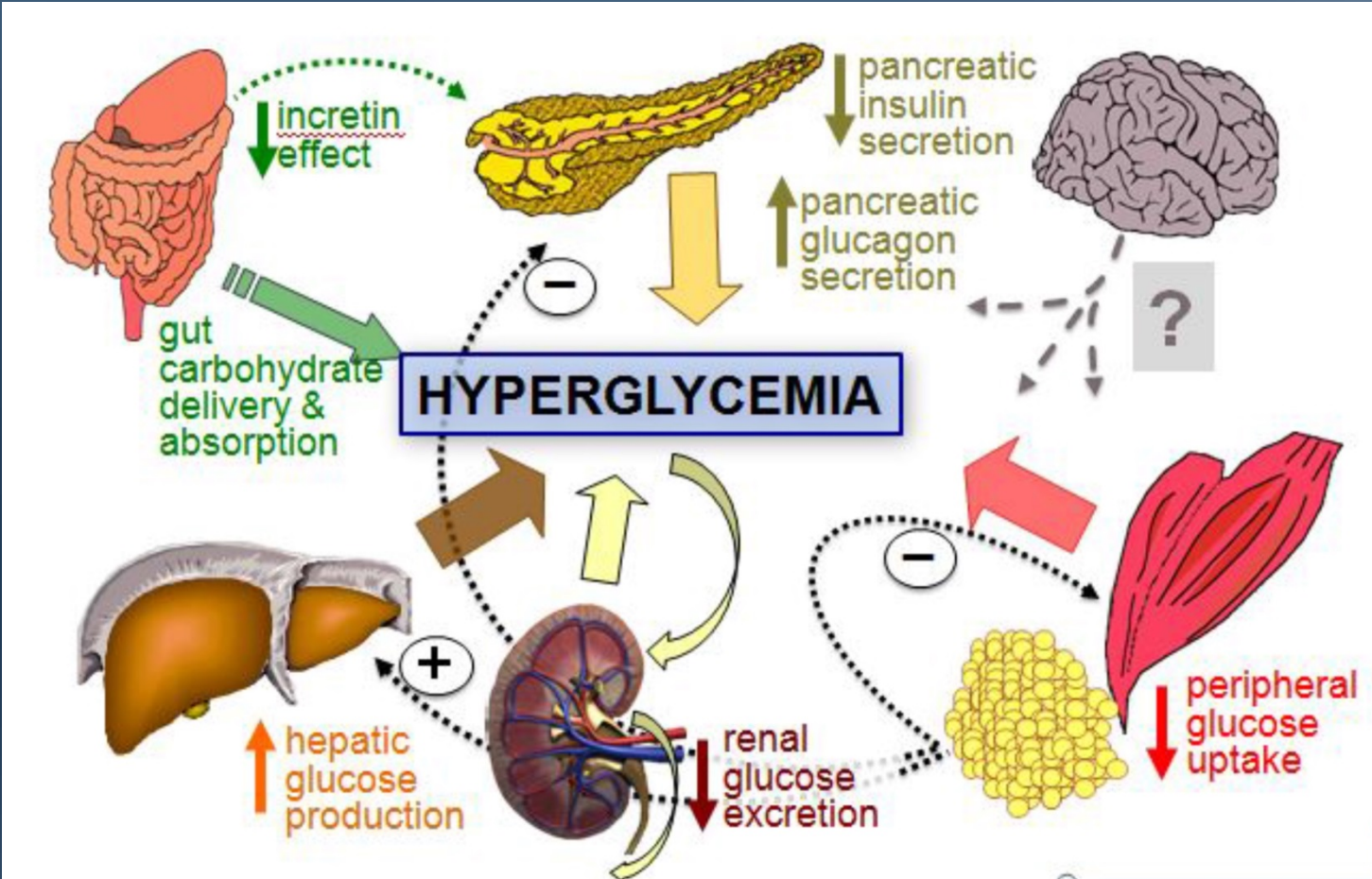
American Diabetes Association.

ADA-EASD Position Statement Update: Management of Hyperglycemia in T2DM, 2015

2. BACKGROUND

- Overview of the pathogenesis of T2DM
 - Insulin secretory dysfunction
 - Insulin resistance (muscle, fat, liver)
 - Increased endogenous glucose production
 - Decreased incretin effect
 - Deranged adipocyte biology

Multiple, Complex Pathophysiological Abnormalities in T2DM



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

Glycemic Recommendations for Non-Pregnant Adults with Diabetes: Treatment Should be Individualized

A1C

- **<7.0%***

Preprandial capillary plasma glucose

- **80–130 mg/dL***
(4.4–7.2 mmol/L)

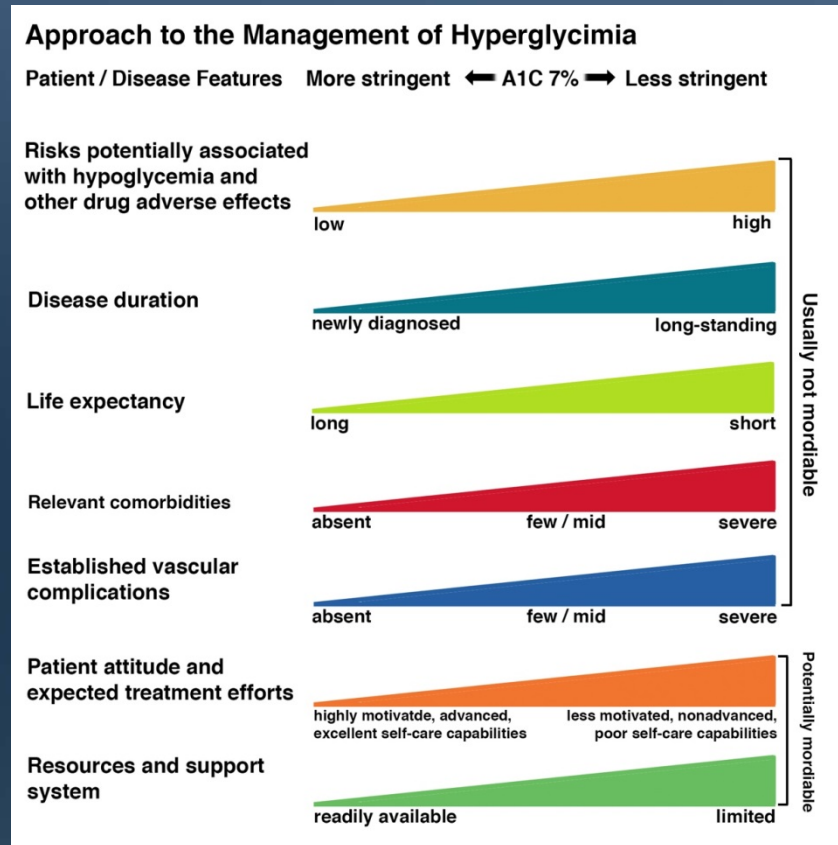
Peak postprandial capillary plasma glucose†

- **<180 mg/dL***
(<10.0 mmol/L)

* More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.

† Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes

Approach to the Management of Hyperglycemia



Adapted from:

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic Targets. *Diabetes Care* 2017;40(Suppl. 1):S48–S56.

Inzucchi SE, et al. *Diabetes Care*. 2015;38:140–149.

Approach to the Management of Hyperglycemia by Patient/Disease Feature – Drug Adverse Effects

Patient / Disease Features **More stringent** ← **A1C 7%** → **Less stringent**

**Risks potentially associated
with hypoglycemia and
other drug adverse effects**

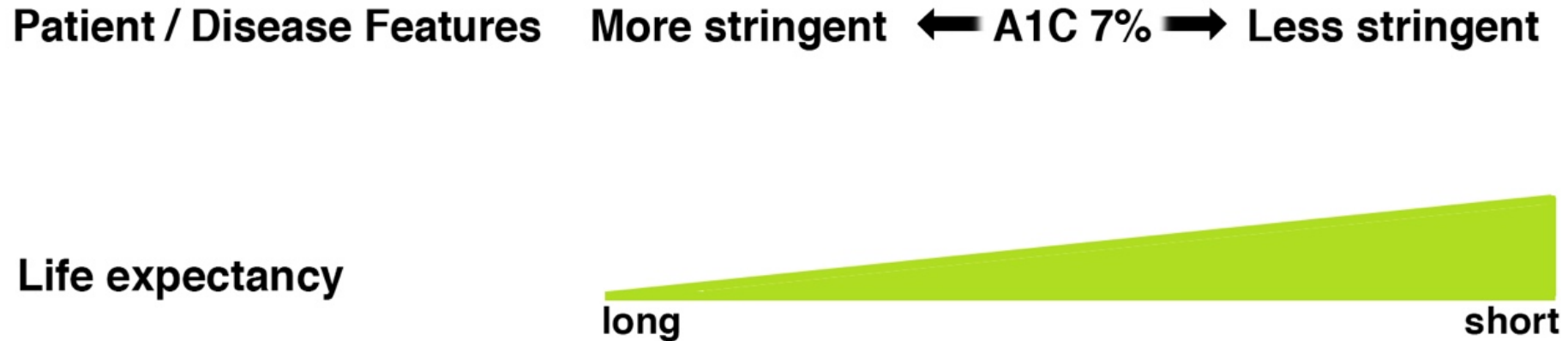


Adapted from:

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic Targets. *Diabetes Care* 2017;40(Suppl. 1):S48–S56.

Inzucchi SE, et al. *Diabetes Care*. 2015;38:140–149.

Approach to the Management of Hyperglycemia by Patient/Disease Feature – Life Expectancy



Adapted from:

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic Targets. *Diabetes Care* 2017;40(Suppl. 1):S48–S56.

Inzucchi SE, et al. *Diabetes Care*. 2015;38:140–149.

Approach to the Management of Hyperglycemia by Patient/Disease Feature – Established Vascular Complications

Patient / Disease Features **More stringent** ← **A1C 7%** → **Less stringent**

Established vascular complications



Adapted from:

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic Targets. *Diabetes Care* 2017;40(Suppl. 1):S48–S56.

Inzucchi SE, et al. *Diabetes Care*. 2015;38:140–149.

Approach to the Management of Hyperglycemia By Patient/Disease Feature – Patient Attitude and Expected Treatment Efforts

Patient / Disease Features **More stringent** ← **A1C 7%** → **Less stringent**

**Patient attitude and
expected treatment efforts**

highly motivated, advanced,
excellent self-care capabilities

less motivated, nonadvanced,
poor self-care capabilities



Adapted from:

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic Targets. *Diabetes Care* 2017;40(Suppl. 1):S48–S56.

Inzucchi SE, et al. *Diabetes Care*. 2015;38:140–149.

Approach to the Management of Hyperglycemia by Patient/Disease Feature – Resources and Support System

Patient / Disease Features **More stringent** ← **A1C 7%** → **Less stringent**

Resources and support system

readily available

limited



Adapted from:

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic Targets. *Diabetes Care* 2017;40(Suppl. 1):S48–S56.
Inzucchi SE, et al. *Diabetes Care*. 2015;38:140–149.

Lifestyle Management

Lifestyle management is a fundamental aspect of diabetes care and includes

- **Diabetes self-management education (DSME)**
- **Diabetes self-management support (DSMS)**
- **Nutrition therapy**
- **Physical activity**
- **Smoking cessation counseling**
- **Psychosocial care**

ADA-EASD Position Statement Update: Anti-Hyperglycemic Therapy in T2DM

Therapeutic options: Oral Agents & Non-Insulin Injectables

Most Popular in the U.S. And Europe

Metformin
Sulfonylureas
Thiazolidinediones
DPP-4 Inhibitors
SGLT-2 Inhibitors
GLP-1 Receptor Agonists

Less Commonly Used

Meglitinides
A-Glucosidase Inhibitors
Colesevelam
Dopamine-2 Agonists
Amylin Mimetics

American Diabetes Association Standards of Medical Care in Diabetes. Pharmacologic Approaches to Glycemic Treatment. *Diabetes Care* 2017;40(Suppl. 1):S64-S74.

Inzucchi SE, et al. *Diabetes Care*. 2015;38:140-149.

Inzucchi SE et al. *Diabetologia* 2015;58(3):429-442.

Diabetes Care 2012;35:1364-1379. *Diabetologia* 2012;55:1577-1596.

Properties of Anti-Hyperglycemic Agents

Oral Class	Mechanism	Advantages	Disadvantages	Cost
Biguanides	<ul style="list-style-type: none"> • Activates AMP-kinase (?other) • ↓ Hepatic glucose production 	<ul style="list-style-type: none"> • Extensive experience • Rare hypoglycemia • ↓ CVD (UKPDS) • Relatively higher A1C efficacy 	<ul style="list-style-type: none"> • Gastrointestinal • Vitamin B12 deficiency Lactic acidosis (rare) • B-12 deficiency • Contraindications eGFR <30 mL/min/1.73m²/acidosis, hypoxia, dehydration, etc. 	Low
Sulfonylureas	<ul style="list-style-type: none"> • Closes K_{ATP} channels on β-cell; plasma membranes • ↑ Insulin secretion 	<ul style="list-style-type: none"> • Extensive experience • ↓ Microvascular risk • Relatively higher A1C efficacy 	<ul style="list-style-type: none"> • Hypoglycemia • ↑ Weight 	Low
Meglitinides (glinides)	<ul style="list-style-type: none"> • Closes K_{ATP} channels on β-cell; plasma membranes • ↑ Insulin secretion 	<ul style="list-style-type: none"> • ↓ Postprandial glucose excursions • Dosing flexibility 	<ul style="list-style-type: none"> • Hypoglycemia • ↑ Weight • Frequent dosing schedule 	Mod.
TZDs	<ul style="list-style-type: none"> • PPAR-g activator • ↑ Insulin sensitivity 	<ul style="list-style-type: none"> • Rare hypoglycemia • Relatively higher A1C efficacy • Durability • ↓ TGs (pio) • ? ↓ CVD events (pio, PROactive) • ↓risk of stroke and I in pts. Without diabetes and with insulin resistance and a history of recent stroke or TIA (IRIS, pio) 	<ul style="list-style-type: none"> • ↑ Weight • Edema/heart failure • Bone fractures • ↑ LDL-C (rosi) 	Low

Properties of Anti-Hyperglycemic Agents

Oral Class	Mechanism	Advantages	Disadvantages	Cost
A-Glucosidase inhibitors	<ul style="list-style-type: none"> • Inhibits a-glucosidase • Slows intestinal carbohydrate digestion / absorption 	<ul style="list-style-type: none"> • Rare hypoglycemia • ↓ post-prandial glucose excursions • ↓ CVD events in prediabetes (STOP-NIDDM) • Nonsystemic 	<ul style="list-style-type: none"> • Generally modest A1C efficacy • Gastrointestinal side effects • Frequent dosing schedule 	Low to Mod.
DPP-4 inhibitors	<ul style="list-style-type: none"> • Inhibits DPP-4 activity • Increases incretin (GLP-1, GIP) concentrations • ↑ insulin secretion, ↓ glucagon secretion (glucose dependent) 	<ul style="list-style-type: none"> • Rare hypoglycemia • Well tolerated 	<ul style="list-style-type: none"> • Angioedema / urticaria and other immune-mediated dermatological effects • ? Acute pancreatitis • ? ↑ Heart failure hospitalizations 	High
Bile acid sequestrants	<ul style="list-style-type: none"> • Bind bile acids in intestinal tract, increasing hepatic bile acid production • ? ↓ Hepatic glucose production and ? ↑ incretin levels 	<ul style="list-style-type: none"> • Rare hypoglycemia • ↓ LDL-C 	<ul style="list-style-type: none"> • Modest ↓ A1C • Constipation • ↑ TGs • May ↓ absorption of other medications 	High
Dopamine-2 Agonists	<ul style="list-style-type: none"> • Activates DA receptor • Modulates hypothalamic regulation of metabolism • ↑ insulin sensitivity 	<ul style="list-style-type: none"> • Rare hypoglycemia • ? ↓ CVD events 	<ul style="list-style-type: none"> • Modest ↓ A1C efficacy • Dizziness/syncope • Nausea • Fatigue • Rhinitis 	High
SGLT2 inhibitors	<ul style="list-style-type: none"> • Inhibits SGLT2 in proximal nephron • Blocks glucose reabsorption by the kidney, increasing glucosuria 	<ul style="list-style-type: none"> • Rare hypoglycemia • ↓ Weight • ↓ BP • Associated with lower CVD event rate and mortality in patients with CVD 	<ul style="list-style-type: none"> • GU infections • Polyuria • Volume depletion/hypotension/dizziness • ↑ LDL-C • ↑ Cr (transient) • DKA, urinary tract infections leading to urosepsis, pyelonephritis 	High

American Diabetes Association Standards of Medical Care in Diabetes. Pharmacologic Approaches to Glycemic Treatment. *Diabetes Care* 2017;40(Suppl. 1):S64-S74. *Diabetes Care* 2015;38:140-149; *Diabetologia* 2015;10.1077/s00125-014-3460-0

Properties of Anti-Hyperglycemic Agents

Injectable Class	Mechanism	Advantages	Disadvantages	Cost
GLP-1 receptor agonists	<ul style="list-style-type: none"> • Activates GLP-1 R • ↑ Insulin ,↓ glucagon (glucose dependent), • ↓ gastric emptying • ↑ satiety 	<ul style="list-style-type: none"> • Rare hypoglycemia • ↓ Weight • ↓ Postprandial glucose excursions • ↓ Some CV risk factors • Associated with lower CV event rate and mortality in patients with CVD 	<ul style="list-style-type: none"> • Gastrointestinal side effects • ↑ Heart rate • ? Acute pancreatitis • C-cell hyperplasia/medullary thyroid tumors in animals • Injectable • Training requirements 	High
Amylin mimetics	<ul style="list-style-type: none"> • Activates amylin receptors • ↓ glucagon secretion • ↓ gastric emptying • ↑ satiety 	<ul style="list-style-type: none"> • ↓ Postprandial glucose • ↓ Weight 	<ul style="list-style-type: none"> • Modest ↓ A1C • Gastrointestinal side effects • Injectable • Hypo if insulin dose not reduced • Frequent dosing schedule • Training requirements 	High
Insulin	<ul style="list-style-type: none"> • Activates insulin receptor • ↑ glucose disposal • ↓ hepatic glucose production • Suppresses ketogenesis 	<ul style="list-style-type: none"> • Nearly universal response • Theoretically unlimited efficacy • ↓ Microvascular risk (UKPDS) 	<ul style="list-style-type: none"> • Hypoglycemia • Weight gain • Training requirements • Patient and Provider reluctance • Injectable (except inhalable) • Pulmonary toxicity (inhaled insulin) 	High (cost is based on lowest-priced member of the class)

American Diabetes Association Standards of Medical Care in Diabetes. Pharmacologic Approaches to Glycemic Treatment. *Diabetes Care* 2017;40(Suppl. 1):S64-S74. *Diabetes Care* 2015;38:140-149; *Diabetologia* 2015;10.1077/s00125-014-3460-0

Anti-Hyperglycemic Therapy in T2DM: General Recommendations

Start with Monotherapy unless:

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300mg/dl,
or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

Monotherapy

Metformin

Lifestyle Management

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS*	low

Anti-Hyperglycemic Therapy in T2DM: Dual Therapy

Dual Therapy

Metformin +

Lifestyle Management

	Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 3-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient - & disease-specific factors):

Anti-Hyperglycemic Therapy in T2DM: Triple Therapy

Triple Therapy

Metformin +

Lifestyle Management

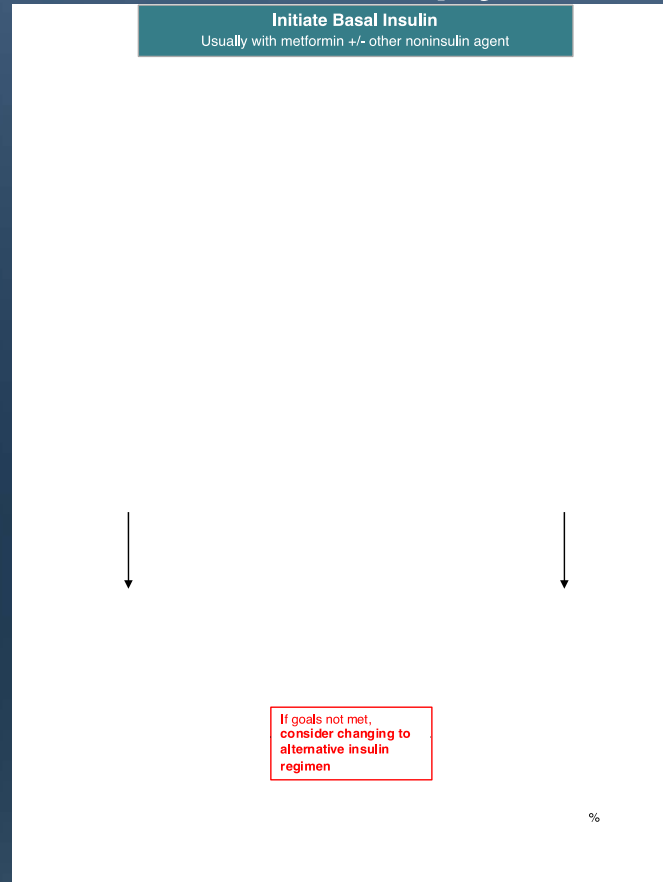
Sulfonylurea +		Thiazolidinedione +		DPP-4 inhibitor +		SGLT2 inhibitor +		GLP-1 receptor agonist +		Insulin (basal) +	
	TZD		SU		SU		SU		SU		TZD
or	DPP-4-i	or	DPP-4-i	or	TZD	or	TZD	or	TZD	or	DPP-4-i
or	SGLT2-i	or	SGLT2-i	or	SGLT2-i	or	DPP-4-i	or	SGLT2-i	or	SGLT2-i
or	GLP-1-RA	or	GLP-1-RA	or	Insulin	or	GLP-1-RA	or	Insulin	or	GLP-1-RA
or	Insulin	or	Insulin			or	Insulin				

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

Combination Injectable Therapy

(See Figure 8.2)

Combination Injectable Therapy For Type 2 Diabetes



Inzucchi SE, et al. *Diabetes Care*. 2015;38:140–149.

American Diabetes Association Standards of Medical Care in Diabetes. Pharmacologic Approaches to Glycemic Treatment. *Diabetes Care* 2017;40(Suppl. 1):S64-S74.

Choosing an Agent to Avoid Hypoglycemia

Monotherapy		Metformin	Lifestyle Management	
EFFICACY*		high		
HYPO RISK		low risk		
WEIGHT		neutral/loss		
SIDE EFFECTS		GI/lactic acidosis		
COSTS*		low		

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy		Metformin +					Lifestyle Management	
	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)		
EFFICACY*	high	high	intermediate	intermediate	high	highest		
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk		
WEIGHT	gain	gain	neutral	loss	loss	gain		
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia		
COSTS*	low	low	high	high	high	high		

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy		Metformin +					Lifestyle Management	
	Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +		
	TZD	SU	SU	SU	SU	TZD		
or	DPP-4-i	DPP-4-i	TZD	TZD	TZD	DPP-4-i		
or	SGLT2-i	SGLT2-i	SGLT2-i	DPP-4-i	SGLT2-i	SGLT2-i		
or	GLP-1-RA	GLP-1-RA	Insulin [§]	GLP-1-RA	Insulin [§]	GLP-1-RA		
or	Insulin [§]	Insulin [§]	Insulin [§]	Insulin [§]	Insulin [§]			

Inzucchi SE, et al. Diabetes Care. 2015;38:140–149.
 American Diabetes Association Standards of Medical Care in Diabetes. Pharmacologic Approaches to Glycemic Treatment. Diabetes Care 2017;40(Suppl. 1):S64-S74.

Choosing an Agent to Avoid Weight Gain

Monotherapy		Metformin		Lifestyle Management		
EFFICACY*	high					
HYPO RISK	low risk					
WEIGHT	neutral/loss					
SIDE EFFECTS	G/Lactic acidosis					
COSTS*	low					
If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):						
Dual Therapy		Metformin +		Lifestyle Management		
	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high
If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):						
Triple Therapy		Metformin +		Lifestyle Management		
	Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
	TZD	SU	SU	SU	SU	TZD
or	DPP-4-i	DPP-4-i	TZD	TZD	TZD	DPP-4-i
or	SGLT2-i	SGLT2-i	SGLT2-i	DPP-4-i	SGLT2-i	SGLT2-i
or	GLP-1-RA	GLP-1-RA	Insulin ⁶	GLP-1-RA	Insulin ⁶	GLP-1-RA
or	Insulin ⁶	Insulin ⁶	Insulin ⁶	Insulin ⁶		

Inzucchi SE, et al. Diabetes Care. 2015;38:140–149.

American Diabetes Association Standards of Medical Care in Diabetes. Pharmacologic Approaches to Glycemic Treatment. Diabetes Care 2017;40(Suppl. 1):S64-S74.

Choosing an Agent to Avoid to Minimize Cost

Monotherapy Metformin Lifestyle Management

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	lactic acidosis
COSTS*	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy Metformin + Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy Metformin + Lifestyle Management

Sulfonylurea +		Thiazolidinedione +		DPP-4 inhibitor +		SGLT2 inhibitor +		GLP-1 receptor agonist +		Insulin (basal) +	
	TZD		SU		SU		SU		SU		TZD
or	DPP-4-i	or	DPP-4-i	or	TZD	or	TZD	or	TZD	or	DPP-4-i
or	SGLT2-i	or	SGLT2-i	or	SGLT2-i	or	DPP-4-i	or	SGLT2-i	or	SGLT2-i
or	GLP-1-RA	or	GLP-1-RA	or	Insulin ⁹	or	GLP-1-RA	or	Insulin ⁹	or	GLP-1-RA
or	Insulin ⁹	or	Insulin ⁹			or	Insulin ⁹				

Inzucchi SE, et al. Diabetes Care. 2015;38:140–149.

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Therapeutic Options: Insulins

Human Insulins

Neutral protamine Hagedorn (NPH)

Regular human insulin

Pre-mixed formulations

Insulin Analogues

Basal analogues (glargine, detemir, degludec)

Rapid analogues (lispro, aspart, glulisine)

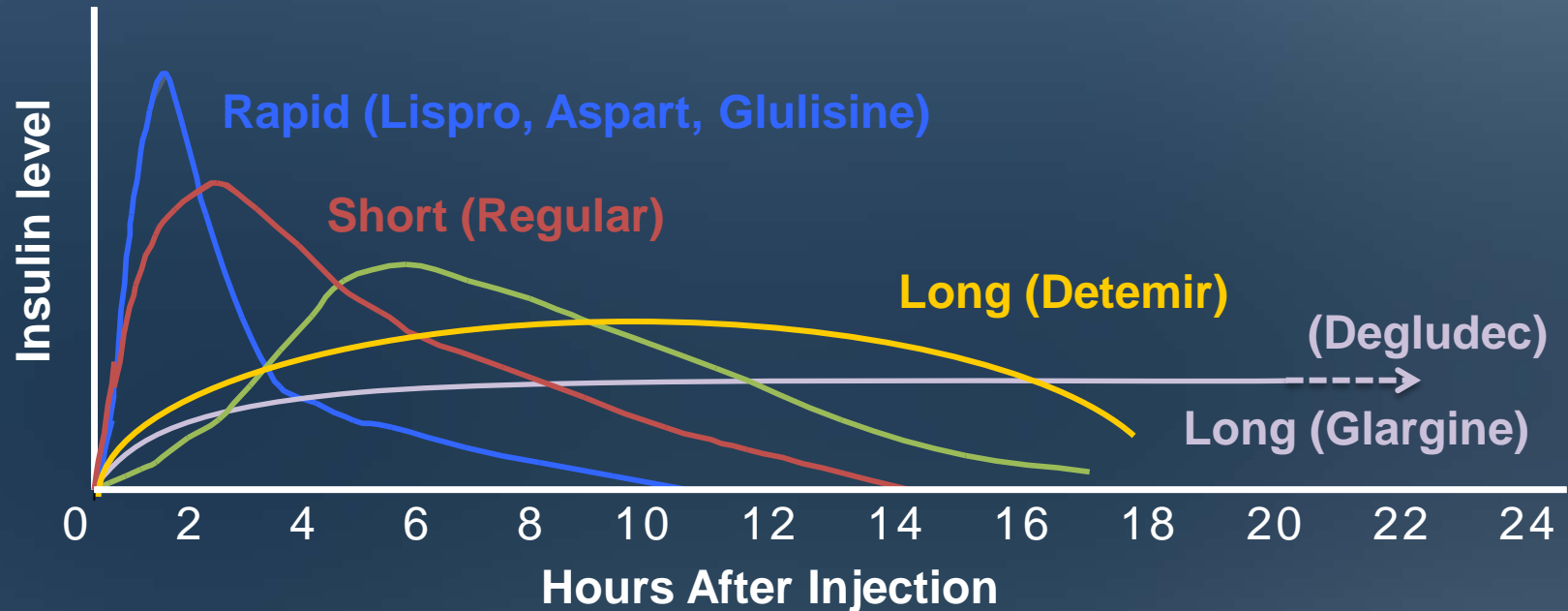
Pre-mixed formulations

Biosimilar Insulin

Basaglar (a biosimilar version of insulin glargine); long-acting



Anti-Hyperglycemic Therapy: Insulins



Approach to Starting and Adjusting Insulin in T2DM

Initiate Basal Insulin

Usually with metformin +/- other noninsulin agent

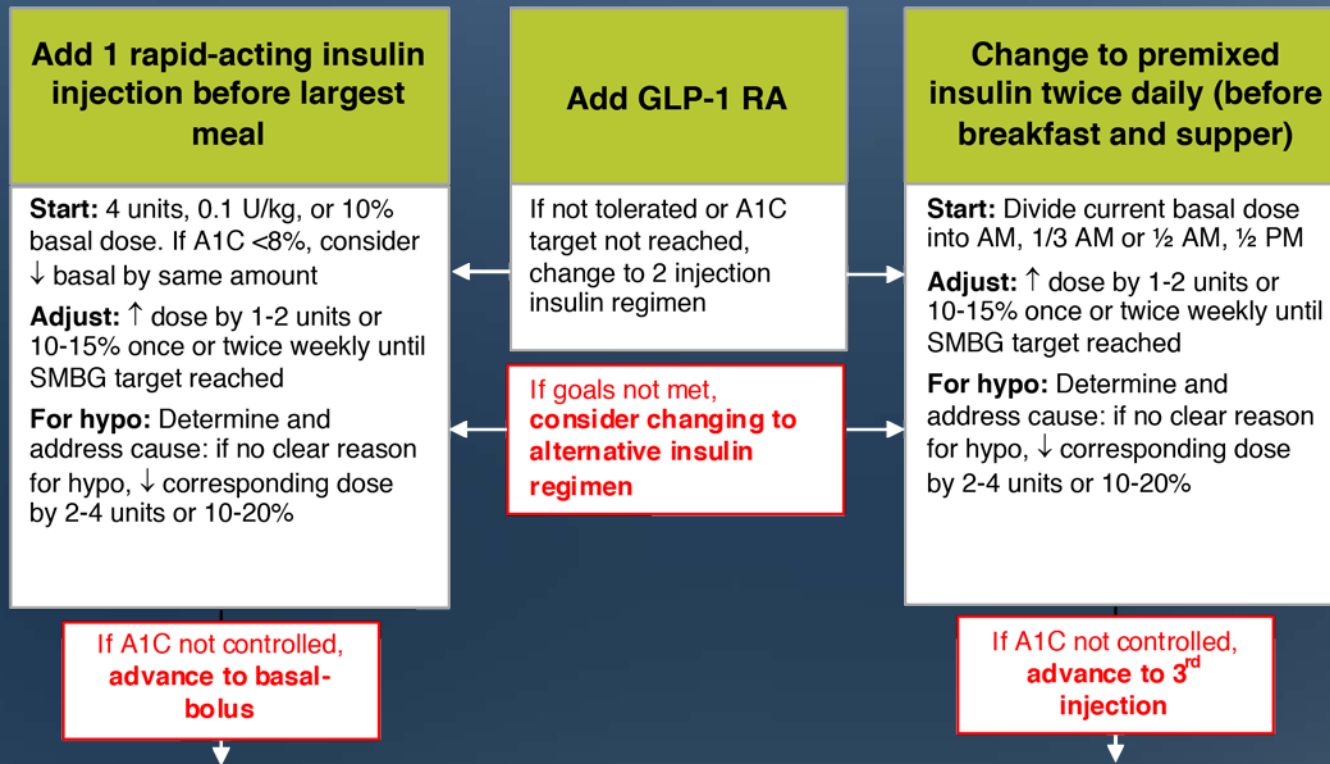
Start: 10 U/day or 0.1-0.2 U/kg/day

Adjust: 10-15% or 2-4 units once or twice weekly to reach FBG target

For hypo: Determine & address cause; if no clear reason for hypo,
↓ dose by 4 units or 10-20%

If A1C not controlled, **consider combination injectable therapy**

Approach to Starting and Adjusting Insulin in T2DM



Adapted from:
American Diabetes Association Standards of Medical Care in Diabetes. Pharmacologic Approaches to Glycemic Treatment. *Diabetes Care* 2017;40(Suppl. 1):S64-S74.
Inzucchi SE, et al. *Diabetes Care*. 2015;38:140-149.

Approach to Starting and Adjusting Insulin in T2DM

Add ≥ 2 rapid-acting insulin injections before meals ('basal-bolus')

Start: 4 units, 0.1 U/kg, or 10% basal dose/meal. If A1C <8%, consider \downarrow basal by same amount

Adjust: \uparrow dose(s) by 1-2 units or 10-15% once or twice weekly to achieve SMBG target

For hypo: Determine and address cause: if no clear reason for hypo, \downarrow corresponding dose by 2-4 units or 10-20%

If goals not met,
**consider changing to
alternative insulin
regimen**

Change to premixed analog insulin 3 times daily (breakfast, lunch and dinner)

Start: Add additional injection before lunch

Adjust: \uparrow dose by 1-2 units or 10-15% once or twice weekly until SMBG target reached

For hypo: Determine and address cause: if no clear reason for hypo, \downarrow corresponding dose by 2-4 units or 10-20%

Other Considerations in Designing an Optimal Glucose Lowering Drug Regimen for Patients

Age

Weight

Sex / racial / ethnic / genetic differences

Comorbidities

- Coronary artery disease
- Heart Failure
- Chronic kidney disease
- Liver dysfunction
- Hypoglycemia-prone

Identifying and addressing barriers to medication adherence

- Cost
- Side effects

Adapted from:

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Inzucchi SE, et al. *Diabetes Care*. 2015;38:140–149.

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

Future Directions/Research Needs

Comparative effectiveness research

- Focus on important clinical outcomes

Contributions of genomic research

Perpetual need for clinical judgment!

Key Points

Glycemic targets & BG-lowering therapies must be individualized, based on a variety of patient and disease characteristics.

Diet, exercise, & education: foundation of any T2DM therapy program

Unless contraindicated, metformin remains the optimal first-line drug.

- After metformin, data are limited. Combination therapy with 1-2 other oral / injectable agents is reasonable. Try to minimize side effects.
- Ultimately, many patients will require insulin therapy alone or in combination with other agents to maintain BG control.
- All treatment decisions should be made in conjunction with the patient (focusing on his or her preferences, needs & values.)

Comprehensive CV risk reduction - a major focus of therapy

Case Study: Introduction

- Mrs. G, a 58-year-old African American female, has had type 2 diabetes for 8 years
- She is currently being treated for hypertension (12 years) and dyslipidemia (10 years)
- She is concerned about her uncontrolled blood glucose level, a recent increase in weight (5 lbs)
- She is a non-smoker and only occasionally consumes alcohol
- Walks 15-20 minutes, three times a week
- Her diet has improved over the last 5 years after consultation with a registered dietitian, but she admits to having a “sweet tooth”



(Continued...)

Case Study (cont'd)

- **Physical exam:**
 - General examination normal, No pallor, cyanosis, clubbing or lymphadenopathy
 - Height, 5'2" (157 cm); weight, 152 lbs (69 kg)
 - BMI, 27.8 kg/m²
 - BP, 132/86 mmHg
 - Pulse 80/min, regular, peripheral pulses well felt
 - Systemic examination- normal
 - Foot examination is normal
 - Fundus examination :Grade I non proliferative diabetic retinopathy
- **Medication history:** Glimepiride 2 mg daily BID • Metformin sustained release preparations 1000 mg daily • Telmisartan 40 mg daily • Atorvastatin 10 mg at night • Aspirin 75 mg at night

(Continued...)

Case Study (cont'd)

- Lab results (recent):

A1C	8%
FPG	130 mg/dL
2-hour postprandial (dinner)	252 mg/dL
Total cholesterol	197 mg/dL
HDL-C	35 mg/dL
LDL-C	101 mg/dL
TG	147 mg/dL
Blood Urea Nitrogen	19 mg/dL
Creatinine	1.3 mg/dL
Urine routine	Sugar, ketones, negative

Case Study: Discussion Question

From the lab results, which plasma glucose patterns of hyperglycemia are present?

- A. Fasting
- B. Preprandial
- C. Postprandial
- D. Nocturnal
- E. B and C above

Case Study: Discussion Question

A drug from which of the following drug classes could you consider to intensify Mrs. G's treatment to manage her postprandial hyperglycemia?

- A. GLP-1 receptor agonist
- B. DPP-4 inhibitor
- C. SGLT2 inhibitor
- D. Basal insulin
- E. A, B, C, or D above

Case Study: Think-Pair-Share

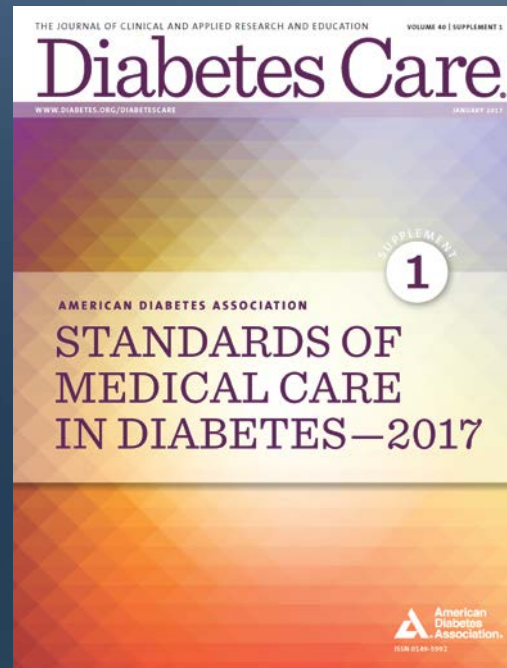
- Do you agree with introducing a GLP-1 receptor agonist to Mrs. G's treatment plan?
- Is there another option you would have tried first?
- Would you discontinue the sulfonylurea or add the GLP-1 receptor agonist to the metformin/sulfonylurea?

Helpful Resources

Guidelines

- Full version
- Abridged version for PCPs
- Free app
- Pocket cards with key figures
- Free webcast for continuing education credit

Professional.Diabetes.org/SOC



Professional Education

- Live programs
- Online self-assessment programs
- Online webcasts



[Professional.Diabetes.org/CE](https://www.professional.diabetes.org/CE)

Diabetes Self-Management Education

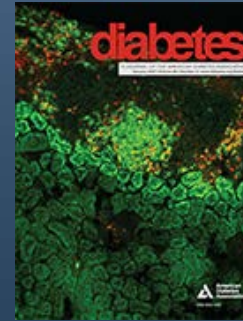
- Find a recognized Diabetes Self-Management program
- Become a recognized DSME program
- Tools and resources for DSME programs
- Online education documentation tools



[Professional.Diabetes.org/ERP](https://www.professionaldiabetes.org/ERP)

Professional Membership

- Journals
- Meeting, book and journal discounts
- Career center
- Quarterly member newsletter



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Thank You!