Highlights Patient Centered Approach to Managing Type 2 DM

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Patient Centered Approach to Managing Type 2 DM

1. Discuss a patient centered approach to manage hyperglycemia.
2. State strategies to treat hyperglycemia from lifestyle to medications.
3. Discuss how the unique characteristics of patients determine the best approach to hyperglycemic management.

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Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach

Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

American Diabetes Association.

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

EASD

American Diabetes Association.

EASD

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ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

EASD

1. 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.**

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ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

EASD

2. BACKGROUND

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

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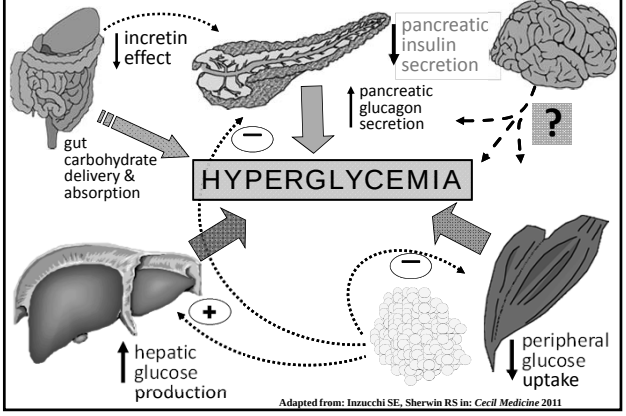
Main Pathophysiological Defects in T2DM



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

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

3. ANTI-HYPERGLYCEMIC THERAPY

- **Glycemic targets**
  - **HbA1c < 7.0%** (mean PG ~150-160 mg/dl [8.3-8.9 mmol/l])
  - Pre-prandial PG <130 mg/dl (7.2 mmol/l)
  - Post-prandial PG <180 mg/dl (10.0 mmol/l)
  - **Individualization** is key:
    - Tighter targets (6.0 - 6.5%) - younger, healthier
    - Looser targets (7.5 - 8.0%+) - older, comorbidities, hypoglycemia prone, etc.
  - Avoidance of hypoglycemia

PG = plasma glucose

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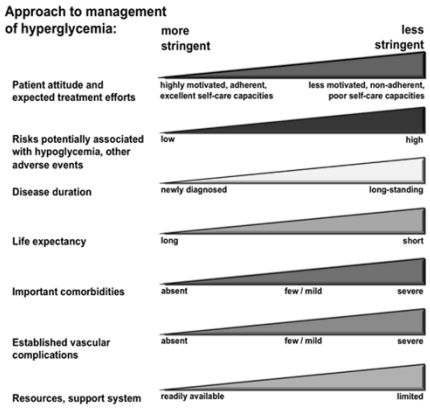

Figure 1

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(Adapted with permission from: Ismail-Beigi et al. *Ann Intern Med* 2011;154:554)

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

3. ANTI-HYPERGLYCEMIC THERAPY

- **Therapeutic options: Lifestyle**
  - **Weight optimization**

  - **Healthy diet**

  - **Increased activity level**

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American Diabetes Association. ADA-EASD Position Statement: Management of Hyperglycemia in T2DM EASD

3. ANTI-HYPERGLYCEMIC THERAPY

- **Therapeutic options:**

Oral agents & non-insulin injectables

- Metformin
- Sulfonylureas
- Thiazolidinediones
- DPP-4 inhibitors
- GLP-1 receptor agonists
- Meglitinides
- α-glucosidase inhibitors
- Bile acid sequestrants
- Dopamine-2 agonists
- Amylin mimetics

Diabetes Care **2012;35:1364–1379**
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Oral Diabetes Medications

Diabetes PocketCard™

Class/Main Action	Name(s)	Daily Dose Range	Considerations
Biguanides *Decrease hepatic glucose output. American Diabetes Association recommends start at diagnosis of type 2.*	metformin (Glucophage)	500–2500 mg *(usually BID w/meal)*	Take caution if creat>1.4 women, >1.5 men, CHF on meds, >80 yrs, binge drinker, liver disease, during IV dye study, illness. Eliminated via kidney. Side effects include nausea, B12 deficiency, bloating, diarrhea. Take w/ meals. Lowers A1c 1.0% – 2.0%.
	Extended Release-XR (Glucophage XR)	*(1x daily w/dinner)* 500–2000 mg
	(Glumetza)	500–2000 mg
	(Fortamet)	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. Side effects include hypoglycemia and weight gain. Eliminated via kidney.
	glipizide: (Glucotrol*) (Glucotrol XL)	2.5–40 mg 2.5–20 mg	*Take Glucotrol on an empty stomach. Take Glucotrol XL with first meal.
	glimepiride (Amaryl)	1.0–8 mg	Lowers A1c 1.0%–2.0%.
Meglitinides *Stimulates rapid insulin "burst."*	repaglinide (Prandin)	0.5–4 mg w/meals (metabolized in liver)	Take before meals. Side effects may include hypoglycemia and weight gain.
	nateglinide (Starlix)	60–120 mg w/meals (eliminated via kidney)	Lowers A1c 1.0%–2.0%.

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
DPP – 4 Inhibitors *"Incretin Enhancers" Prolongs action of gut hormones = increased insulin secretion, delayed 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 headache, flu-like symptoms. Report signs of pancreatitis (abdominal pain, nausea, vomiting).
	saxagliptin (Onglyza)	Up to 5 mg daily (eliminated via kidney*, feces)	
	linagliptin (Tradjenta)	5 mg daily (eliminated via feces)	Lowers A1c 0.6%–0.8%.
Thiazolidinediones "TZDs" *Increase insulin sensitivity.*	pioglitazone (Actos)	15–45 mg daily	**Black Box Warning:** TZDs may cause or worsen CHF. Monitor for edema and weight gain. Increased peripheral fracture risk. * No new pts to be started on Avandia. Actos may increase risk of bladder cancer. Lowers A1c 0.5%–1.0%
	rosiglitazone (Avandia) ***restricted access****	4–8 mg daily	
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. Start at one tab daily, increase 0.8 mg each wk as tolerated. Side effects: nausea, headache, fatigue, hypotension, syncope, somnolence. Lowers A1c 0.6%–0.9%.
Glucosidase Inhibitors *Delay carb absorption.*	acarbose (Precose) miglitol (Glyset)	25–100 mg w/meals; 300 mg max daily dose	Start with low dose, increase at 4-8 wk intervals to decrease GI effects. Caution with liver or kidney problems. Lowers A1c 0.5%–1.0%.
Combination medications *Observe precautions of each component drug.*	Glucovance: Glucophage + Glyburide Metaglip: Metformin + Glipizide * Avandamet: Avandia + Metformin * Avandaryl: Avandia + Amaryl * *Restricted access*		Actoplus Met: Actos + Metformin Duetact: Actos + Amaryl Janumet: Januvia + Metformin Kombiglyze XR: Onglyza + Metformin XR Juvisync: Januvia + Zocor

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ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

3. ANTI-HYPERGLYCEMIC THERAPY

- **Therapeutic options: Insulin**
  - **Human Neutral protamine Hagedorn (NPH)**
  - **Human Regular**
  - **Basal analogues (glargine, detemir)**
  - **Rapid analogues (lispro, aspart, glulisine)**
  - **Pre-mixed varieties**

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Insulin PocketCard™

Diabetes PocketCard™

Action		Insulin Name	Onset	Peak	Effective Duration	Considerations
Bolus	Rapid Acting Analogs	Aspart (Novolog)	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.
		Lispro (Humalog)				
		Glulisine (Apidra)				
	Short Acting	Regular	30 - 60 min	2 - 3 hrs	5 - 8 hrs	
Basal	Intermediate	NPH	2 - 4 hrs	4 - 10 hrs	10 - 16 hrs	
	Long Acting	Detemir (Levemir)	3 - 8 hrs	No peak	6 - 24 hrs	
		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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ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

3. ANTI-HYPERGLYCEMIC THERAPY

- **Implementation strategies:**
  - **Initial therapy**
  - **Advancing to dual combination therapy**
  - **Advancing to triple combination therapy**
  - **Transitions to & titrations of insulin**

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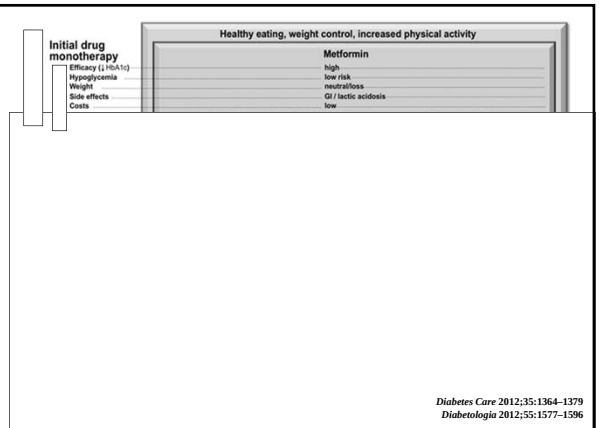

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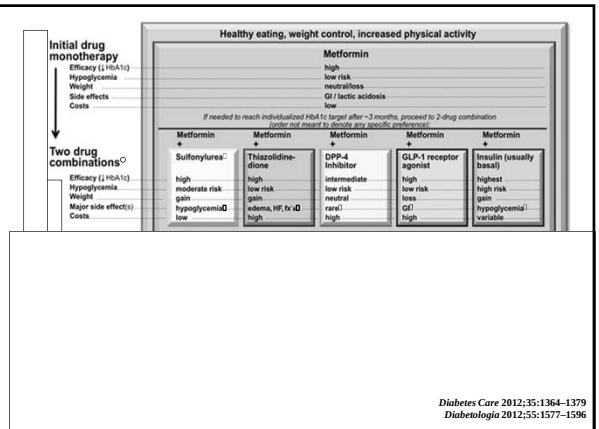
Fig. 2. T2DM Antihyperglycemic Therapy: General Recommendations



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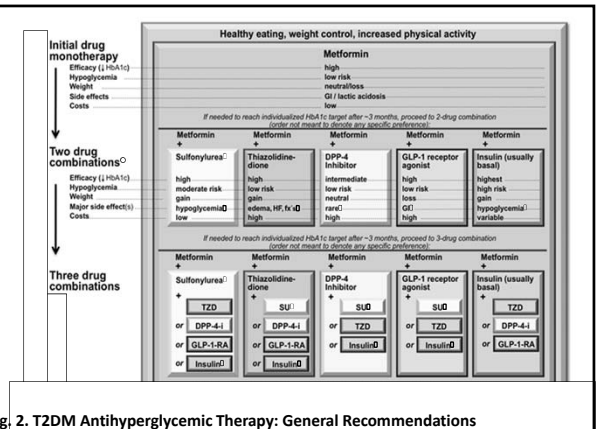

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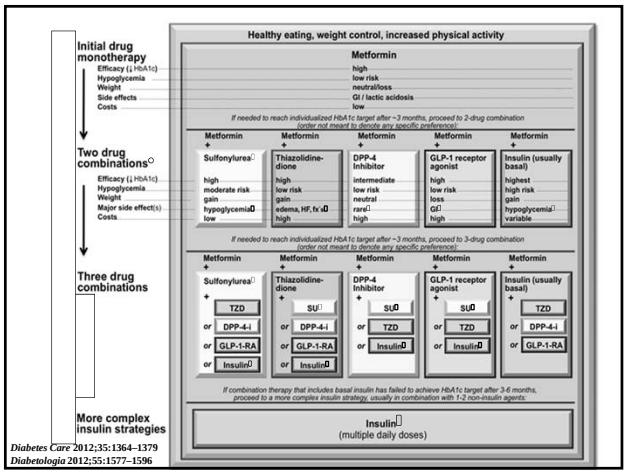

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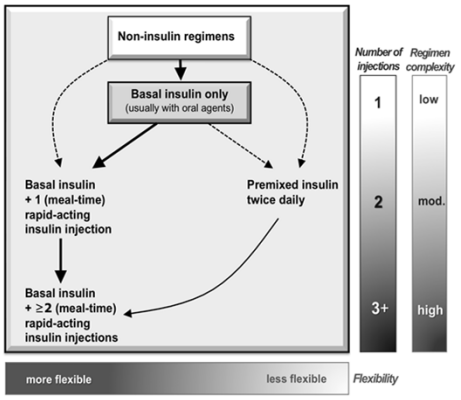

Fig. 3. Sequential Insulin Strategies in T2DM

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4. OTHER CONSIDERATIONS

- **Age**
- **Weight**
- **Sex / racial / ethnic / genetic differences**
- **Comorbidities**
  - **Coronary artery disease**
  - **Heart Failure**
  - **Chronic kidney disease**
  - **Liver dysfunction**
  - **Hypoglycemia**

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4. OTHER CONSIDERATIONS

- **Age: Older adults**
  - 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**
✓HbA1c <7.5–8.0% if tighter targets not easily achieved
✓Focus on drug safety

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4. OTHER CONSIDERATIONS

- **Weight**
  - Majority of T2DM patients overweight / obese
  - Intensive lifestyle program
  - Metformin
  - GLP-1 receptor agonists
  - ? Bariatric surgery
  - Consider LADA in lean patients

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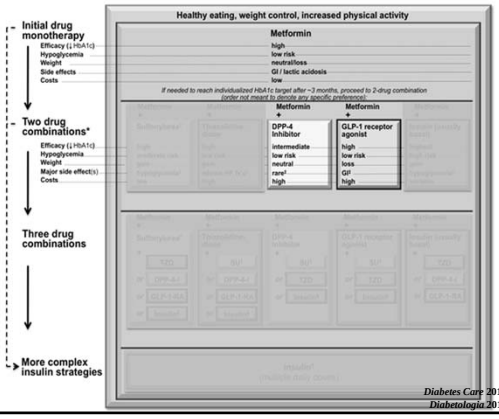
Adapted Recommendations: When Goal is to Avoid Weight Gain



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4. OTHER CONSIDERATIONS

- **Comorbidities**
  - **Coronary Disease** ----->
  - **Heart Failure**
  - **Renal disease**
  - **Liver dysfunction**
  - **Hypoglycemia**

- Metformin: CVD benefit (UKPDS)
- Avoid hypoglycemia
- ? SUs & ischemic preconditioning
- ? Pioglitazone & ↓ CVD events
- ? Effects of incretin-based therapies

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4. OTHER CONSIDERATIONS

- **Comorbidities**
  - **Coronary Disease**
  - **Heart Failure** ------->
  - **Renal disease**
  - **Liver dysfunction**
  - **Hypoglycemia**

- Metformin: May use unless condition is unstable or severe
- Avoid TZDs
- ? Effects of incretin-based therapies

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ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

4. OTHER CONSIDERATIONS

- **Comorbidities**
  - **Coronary Disease**
  - **Heart Failure**
  - **Renal disease** -->
  - **Liver dysfunction**
  - **Hypoglycemia**

- Increased risk of hypoglycemia
- Metformin & lactic acidosis
  - US: stop @SCr ≥ 1.5 (1.4 women)
  - UK: half-dose @GFR < 45 & stop @GFR < 30
- Caution with SUs (esp. glyburide)
- DPP-4-i's – dose adjust for most
- Avoid exenatide if GFR < 30

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4. OTHER CONSIDERATIONS

- **Comorbidities**
  - **Coronary Disease**
  - **Heart Failure**
  - **Renal disease**
  - **Liver dysfunction**
  - **Hypoglycemia** ----→

> ➢ Emerging concerns regarding association with increased morbidity / mortality
> ➢ Proper drug selection is key in the hypoglycemia prone

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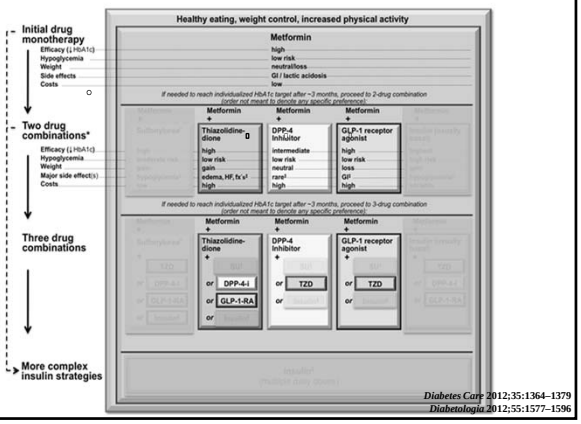
Adapted Recommendations: When Goal is to Avoid Hypoglycemia



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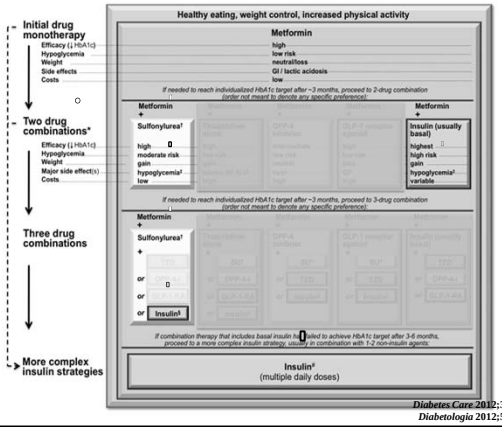
Adapted Recommendations: When Goal is to Minimize Costs



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4. FUTURE DIRECTIONS / RESEARCH NEEDS

- **Comparative effectiveness research**
  - Focus on important clinical outcomes
- **Contributions of genomic research**
- **Perpetual need for clinical judgment!**

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ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

KEY POINTS

- Glycemic targets & BG-lowering therapies must be individualized.
- Diet, exercise, & education: foundation of any T2DM therapy program
- Unless contraindicated, metformin = optimal 1st-line drug.
- After metformin, data are limited. Combination therapy with 1-2 other oral / injectable agents is reasonable; minimize side effects.
- Ultimately, many patients will require insulin therapy alone / in combination with other agents to maintain BG control.
- All treatment decisions should be made in conjunction with the patient (focus on preferences, needs & values.)
- Comprehensive CV risk reduction - a major focus of therapy.

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ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

Invited Reviewers

James Best, *The University of Melbourne, Australia*
Henk Bilo, *Isala Clinics, Zwolle, Netherlands*
John Boltri, *Wayne State University, Detroit, MI*
Thomas Buchanan, *Univ of So California, LA, CA*
Paul Callaway, *University of Kansas,Wichita, KS*
Bernard Charbonnel, *University of Nantes, France*
Stephen Colagiuri, *The University of Sydney, Australia*
Samuel Dagogo-Jack, *Univ of Tenn, Memphis, TN*
Margo Farber, *Detroit Medical Center, Detroit, MI*
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Andrew Wolf, *Univ of Virginia Charlottesville, VA*
Bernard Zinman, *University of Toronto, Ontario, Canad*

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