

Pharmacotherapy updates: Managing type 2 diabetes mellitus

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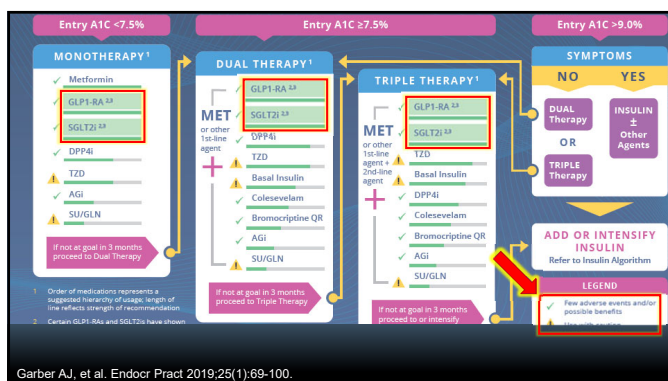
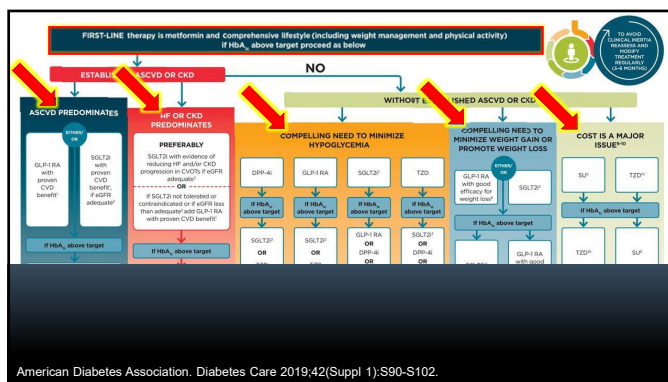
Objectives

- Describe the current clinical practice guidelines for treatment of type 2 diabetes mellitus (DM2)
- Discuss therapy options for DM2 with regard to risks, benefits, cost, and practicality
- Identify therapies for DM2 that are currently in development
- Evaluate the use of technology designed to assist with therapy decisions in people with DM2

Abbreviations

- CGM = continuous glucose monitor
- DKA = diabetic ketoacidosis
- DM1/2 = type 1/2 diabetes mellitus
- DPP-4i = dipeptidyl peptidase-4 inhibitor
- GLP-1 RA = glucagon-like peptide-1 receptor agonist
- SAS = short-acting secretagogue
- SGLT2i = sodium-glucose co-transporter-2 inhibitor
- SMBG = self-monitored blood glucose
- SU = sulfonylurea
- TZD = thiazolidinedione

Clinical practice guidelines



Selecting medications for DM2



What should not be used?



What is the person willing/able to do?



What other benefits will the medication provide?



Which blood sugars am I targeting?

Developing a therapy plan for persons with DM2

Therapy options for DM2

Biguanides

Metformin

DPP-4is

Sitagliptin, saxagliptin, linagliptin, alogliptin

SUs

Glyburide, glimepiride, glipizide

GLP-1 RAs

Exenatide, liraglutide, lixisenatide, dulaglutide, semaglutide

SASs

Repaglinide, nateglinide

SGLT2is

Canagliflozin, dapagliflozin, empagliflozin, ertugliflozin

TZDs

Rosiglitazone, pioglitazone

Insulin

Various products

What are some goals of therapy for DM2?

No numbers allowed!

-  Achieve euglycemia
-  Prevent hypoglycemia
-  Prevent complications
-  Weight loss
-  Improve quality of life

A1C reduction potency of DM meds

*High: >1%
Mod: 0.5-1%*

-  Achieve euglycemia
- HIGH**
 - Insulin (highest)
 - Metformin
 - SUs
 - TZDs
 - GLP-1 RAs
- MOD**
 - SASs
 - DPP-4is
 - SGLT2is

 **Blood glucose targets of DM meds**

-  Achieve euglycemia
- FAST**
 - Metformin
 - TZDs
- MEAL**
 - DPP-4is
 - SASs
- BOTH**
 - SUs
 - GLP-1 RAs
 - SGLT2is
 - Insulin

Meds with increased hypoglycemia risk

 Prevent hypoglycemia

RISK

- SUs
- SASs
- Insulin

RISK FACTORS

- Advanced age
- Renal dysfunction
- Skipping meals
- Poor timing with meals
- Cognitive deficits

 Prevent hypoglycemia

Levels of hypoglycemia

- 1 Glucose 54-69 mg/dL
- 2 Glucose <54 mg/dL
- 3 Altered mental status and/or assistance required

American Diabetes Association. Diabetes Care 2019;42(Suppl 1):S61-S70.

 Prevent hypoglycemia

What are some consequences associated with hypoglycemia?

 Fear

 Seizure

 Falls

 Accidents

 Dementia
Whitler 2009

 Death
Zoungas 2010, McCoey 2012

American Diabetes Association. Diabetes Care 2019;42(Suppl 1):S61-S70.

 Atherosclerotic cardiovascular disease (ASCVD)

 Prevent complications

BENEFIT

- Canagliflozin
- Empagliflozin
- Liraglutide
- Dulaglutide

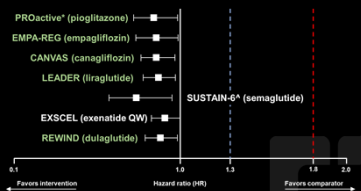
BENEFIT?

- Semaglutide
- Exenatide-QW
- Metformin
- Pioglitazone

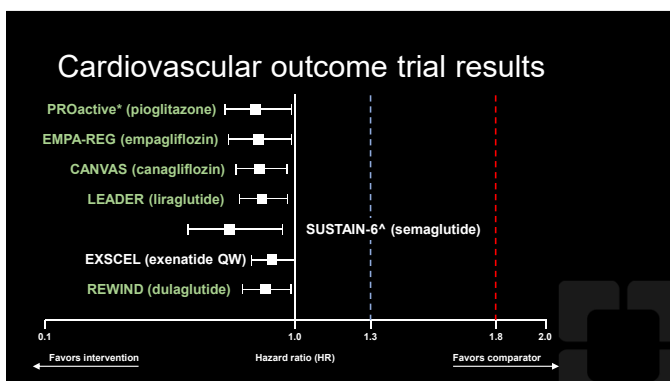
 Atherosclerotic cardiovascular disease (ASCVD)

 Prevent complications

Cardiovascular outcome trial results



* Secondary outcome
^ Superiority not tested






Congestive heart failure (CHF)

 Prevent complications

BENEFIT

- Canagliflozin
- Dapagliflozin
- Empagliflozin

RISK?

- Saxagliptin
- Alogliptin

RISK!

- Rosiglitazone
- Pioglitazone




Chronic kidney disease (CKD)

 Prevent complications

BENEFIT

- Canagliflozin
- Dapagliflozin
- Empagliflozin
- Liraglutide
- Dulaglutide

CAUTION

Most non-insulin DM medications are renally eliminated!




Weight changes with DM meds

 Weight loss

LOSS

- GLP-1 RAs
- SGLT2is
- Metformin (slight)

GAIN

- SUs
- SASs
- TZDs
- Insulin

 Monthly cost of DM meds

High: >\$300/mo
Mod: \$50-300/mo
Low: <\$50/mo

* Except those listed under moderate cost category

Source: goodrx.com

 Improve quality of life

Category	Medications
LOW	- Metformin - SUs - Pioglitazone - SASs
MOD	- Alogliptin - Rosiglitazone - Ertugliflozin
HIGH	- DPP-4is* - SGLT2is* - GLP-1 RAs - Insulin (<u>maybe</u> moderate)

The following is prescribed:

1. Metformin 1,000 mg twice daily
2. Dulaglutide 1.5 mg once weekly
3. Insulin detemir 30 units at bedtime

What will be the monthly cost?

 Improve quality of life

\$250	\$500
\$750	\$1,000

Combination therapy

Combining medications for DM2



Selection depends on
comorbidities



Consider cost when adding
medications



Should add insulin if
symptomatic!

58-year-old woman with
DM2, currently on
metformin 500 mg BID
and glimepiride 1 mg
qAM.

NHY, stage III HF, history
of MI 10 years ago, normal
renal function.

Fasting sugars 140-
post-prandial sugars
elevated, A1C = 8.2%,
no hypoglycemia

Biguanides

DPP-4is

SUs

Liraglutide
Dulaglutide

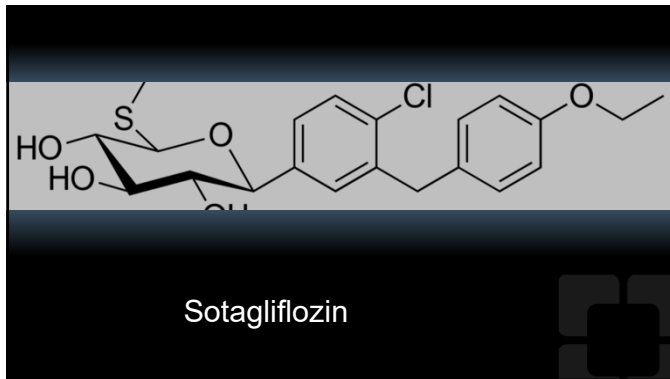
SAs

SGLT2is

TZDs

Insulin

Up and comers...

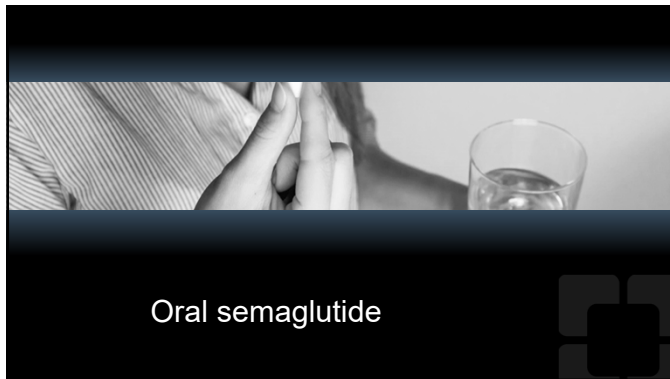


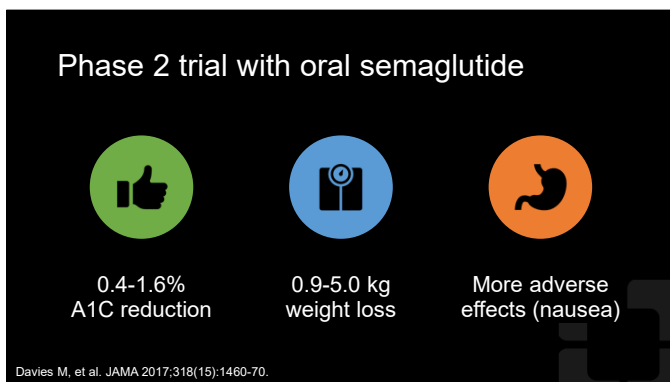
Sotagliflozin

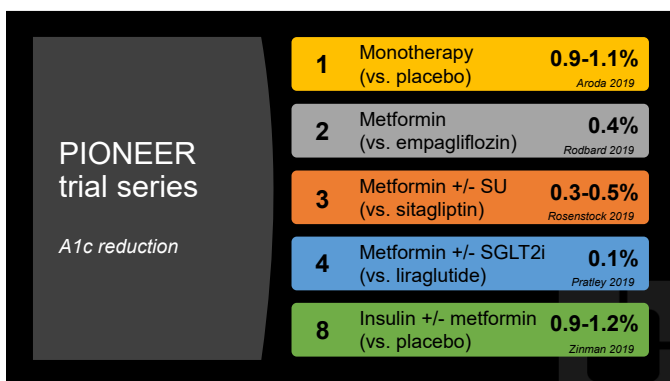
	Dual inhibitor of SGLT1 and SGLT2
	~0.4% A1C reduction ~4x greater risk of DKA Garg 2017, Musso 2019
	Up to a 0.9% A1C reduction ~2 kg weight loss No hypoglycemia or DKA Rosenstock 2015

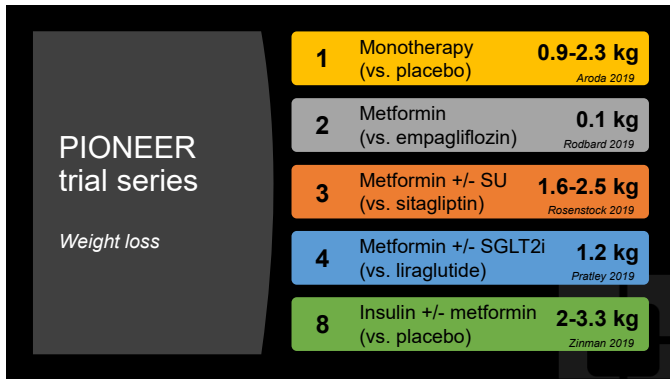
Where do we stand?

	
FDA rejected application for DM1 use in March 2019	Phase 3 trials ongoing for use in DM2









Where do we stand?



Approved by the FDA on
September 20, 2019 (Rybelsus®)



New glucagon dosage forms





Intranasal vs. intramuscular glucagon	
	Nasal: 93-94% IM: 20-50% Yale 2017
	Nasal: 16-26 sec IM: 1.9-2.4 min Yale 2017
	81% preferred nasal over IM Easy to use Less intimidating than injections Yale 2017, Deeb 2018, Seaquist 2018



Emergency kit vs. ready-to-use auto-injector

	Adults: 97.4 vs. 100% Children: 100% Buckingham 2018, Christiansen 2018
	Adults: 15-16 min vs. 13-14 min Christiansen 2018
	Most common = nausea Similar with each device Buckingham 2018, Christiansen 2018

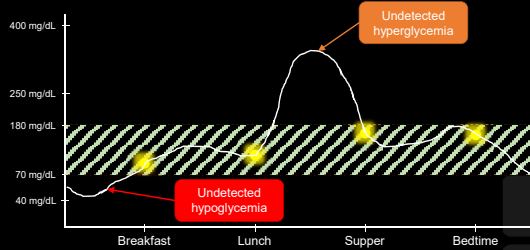
Where do we stand?



Approved by the FDA on September 10, 2019

Using technology with DM2

Continuous glucose monitors (CGMs)



FreeStyle
Libre



Dexcom
G6



Medtronic
Guardian
Sensor 3



Senseonics
Eversense

Age requirement (years)	 FreeStyle Libre	18+
	 Medtronic Guardian Sensor 3	14-75
	 Dexcom G6	2+
	 Senseonics Eversense	18+

Sensor wear time (days)	 FreeStyle Libre	14
	 Medtronic Guardian Sensor 3	7
	 Dexcom G6	10
	 Senseonics Eversense	90

Calibration requirement <i>Check SMBG if:</i> - Low glucose - No trend arrow - No signal - Symptomatic <i>*Better accuracy with 3-4x/day</i>	 FreeStyle Libre	None
	 Medtronic Guardian Sensor 3	Q12H*
	 Dexcom G6	None
	 Senseonics Eversense	Q12H

Non-adjunctive use indication

*Non-adjunctive:
Can replace
glucose meter
checks to make
therapy decisions*

	FreeStyle Libre	✓
	Medtronic Guardian Sensor 3	✗
	Dexcom G6	✓
	Senseonics Eversense	✓

Benefits of using CGM

	A1C reduction (~0.5%)		Improved time in glucose target range
	Reduction in hypoglycemia		Improved aspects of quality of life

What are some factors that might result in insurance companies covering CGM?

Frequent hypoglycemia	Hypoglycemia unawareness
Elevated A1C	Erratic glucose levels
Receiving prandial insulin	Performing frequent SMBG

Insulin pumps



Medtronic
Revel



Tandem
t:slim X2

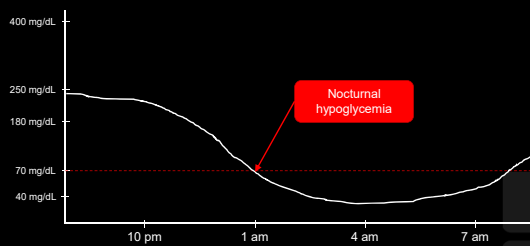


Medtronic
630G/670G

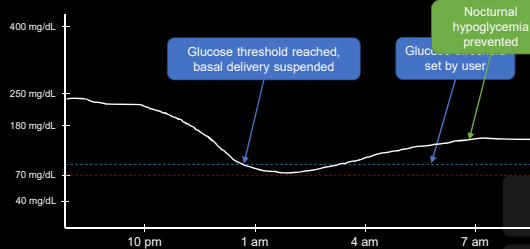


Insulet
Omnipod

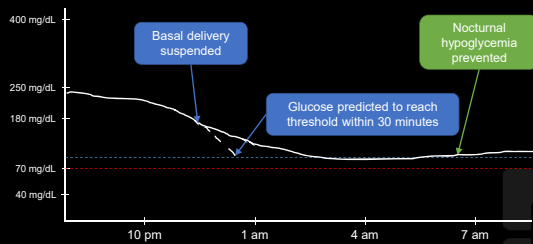
Evolution of insulin pump technology



Threshold suspend



Predictive low glucose suspend



Sensor augmentation availability

	Medtronic Revel	✓
	Medtronic 630G/670G	✓
	Tandem t:slim X2	✓
	Insulet Omnipod	✗

Threshold suspend ability

	Medtronic Revel	✗
	Medtronic 630G/670G	✓
	Tandem t:slim X2	✓
	Insulet Omnipod	✗

Predictive low glucose suspend ability

**Medtronic 670G only*

	Medtronic Revel	✗
	Medtronic 630G/670G	✓*
	Tandem t:slim X2	✓
	Insulet Omnipod	✗

Summary

-  Consider patient-specific factors
-  Remember goals of therapy
-  Incorporate technology when possible
-  Keep an eye out for new therapy options



Questions?

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