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Ohio Cardiovascular and Diabetes Health Collaborative

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Cardi-OH ECHO

What's New in Cardiovascular Prevention? A Series of Case-Based Discussions

September 29, 2022

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Disclosure Statements

- The following speakers have a relevant financial interest or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of their presentation:
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- The remaining speakers have no financial relationships with any commercial interest related to the content of this activity:
  - Karen Bailey, MS, RDN, LD, CDCES; Kristen Berg, PhD; Elizabeth Beverly, PhD; James Werner, PhD, MSSA; Jackson Wright, MD, PhD
- The following members of the planning committee DO NOT have any disclosures/financial relationships from any ineligible companies:
  - Shari Bolen, MD; Richard Cornachione; Carolyn Henceroth; Gillian Irwin; Michael W. Konstan, MD; Elizabeth Littman; Devin O'Neill; Steven Ostrolencki; Ann Nevar; Claire Rollins; Catherine Sullivan

* These financial relationships are outside the presented work.
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Person-Centered Language Recommendations

The ADA and the APA recommend language that emphasizes inclusivity and respect:

- **Gender**: Gender is a social construct and social identity; use term “gender” when referring to people as a social group. Sex refers to biological sex assignment; use term “assigned sex” when referring to the biological distinction.
- **Race**: Race is a social construct that is used broadly to categorize people based on physical characteristics, behaviors, and geographic location. Race is not a proxy for biology or genetics. Examining health access, quality, and outcome data by allows the healthcare system to assist in addressing the factors contributing to inequity.
- **Sexual Orientation**: Use the term “sexual orientation” rather than “sexual preference” or “sexual identity.” People choose partners regardless of their sexual orientation; however, sexual orientation is not a choice.
- **Disability**: The nature of a disability should be indicated when it is relevant. Disability language should maintain the integrity of the individual. Language should convey the expressed preference of the person with the disability.
- **Socioeconomic Status**: When reporting SES, provide detailed information about a person’s income, education, and occupation/employment. Avoid using pejorative and generalizing terms, such as “the homeless” or “poor.”
- **Violent Language**: Avoid sayings like ‘killing it,’ ‘pull the trigger,’ ‘take a stab at it,’ ‘off the reservation,’ etc.

Flanagin A et al., 2021, JAMA; Dickinson JK et al., Diabetes Care, 2017; American Psychological Association, 2021; ODM, 2021.

Type 2 Diabetes: Emerging and Future Pharmacotherapies

Kathleen Dungan, MD, MPH

Professor and Associate Director of Clinical Services

Division of Endocrinology, Diabetes & Metabolism

The Ohio State University

Learning Objectives

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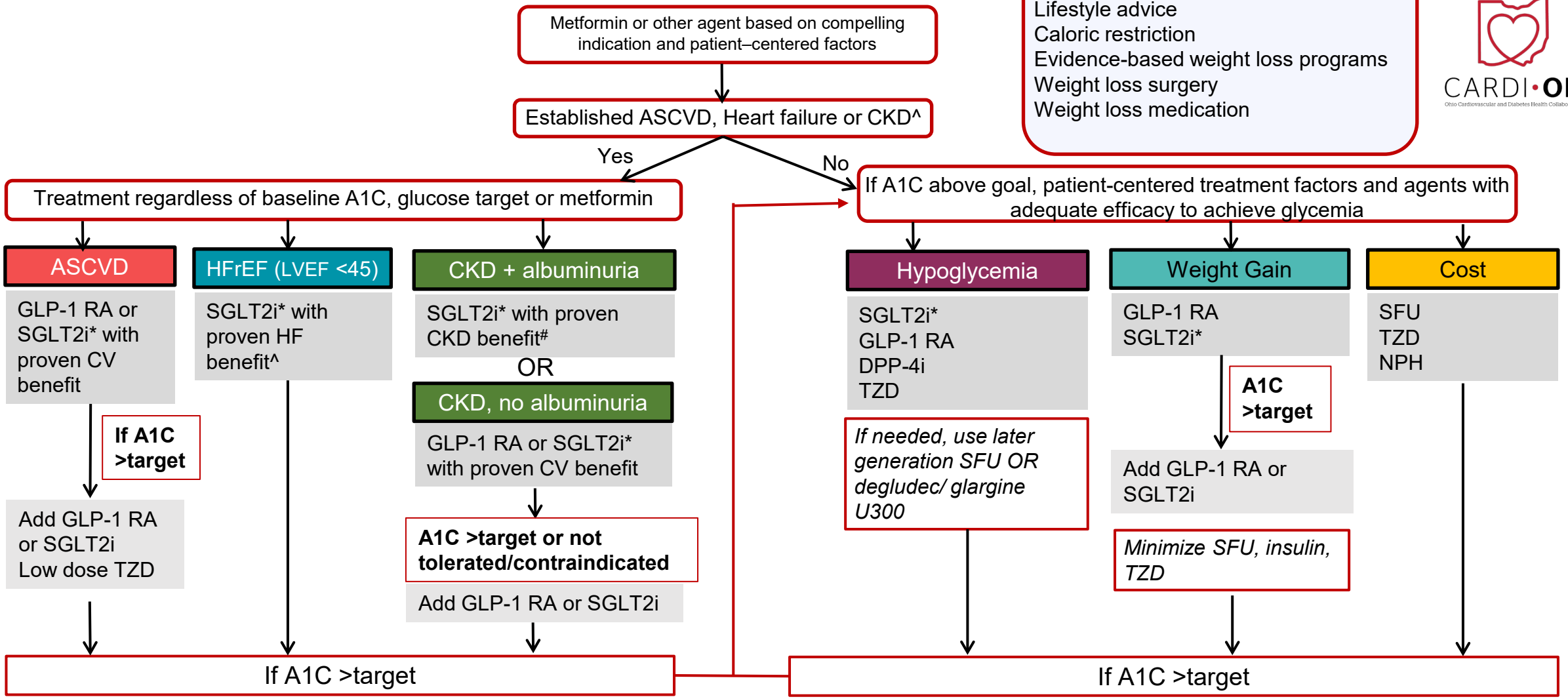
1. List and describe currently available GLP-1 agonists and SGLT-2 inhibitor medications.
2. Describe the future landscape of diabetes pharmacotherapies.
3. Describe Medicaid coverage for newer diabetes pharmacotherapies

Pharmacologic Management, ADA Standards of Care 2022



***if adequate eGFR, ^Empagliflozin and dapagliflozin have shown benefit in dedicated HF studies. Canagliflozin and ertugliflozin have demonstrated reduction in hospitalization for HF in CV outcomes trials. #Dapagliflozin and canagliflozin have demonstrated benefit in dedicated renal outcomes studies. Empagliflozin has demonstrated reduction in CKD progression in CV outcomes trials.**

ASCVD=atherosclerotic cardiovascular disease, CKD=chronic kidney disease, GLP-1 RA=glucagon-like peptide-1 receptor agonist, SGLT2i=sodium-glucose cotransporter-2 inhibitor, AGI=alpha-glucosidase inhibitor, SFU=sulfonylurea, TZD=thiazolidinedione

American Diabetes Association Professional Practice Committee. 9. Pharmacologic approaches to glycemic treatment: *Standards of Medical Care in Diabetes—2022*. Diabetes Care 2022;45(Suppl. 1):S125–S143

GLP-1 Receptor Agonists

Generic Name	Brand Name	Dose Forms	Dosing Interval	Cautions
Exenatide BID	Byetta	5, 10 µg	BID	C-cell tumors/ MEN-2 advanced CKD gastroparesis pancreatitis?
Lixisenatide	Lyxumia	10, 20 µg	QD	
Liraglutide	Victoza	1.6, 1.2, 1.8 µg	Daily	
Exenatide QW	Bydureon	2 mg	Weekly	
Semaglutide	Ozempic	0.5, 1.0 mg	Weekly	
	Rybelsus	3, 7, 14 mg PO		
Dulaglutide	Trulicity	0.75, 1.5 mg	Weekly	

- No inherent hypoglycemia
- Modest weight and BP reduction
- Nausea/vomiting, usually self-limited

GLP-1 R Activation
Intermittent
Continuous: better A1C reduction, better tolerability

SGLT2 Inhibitors

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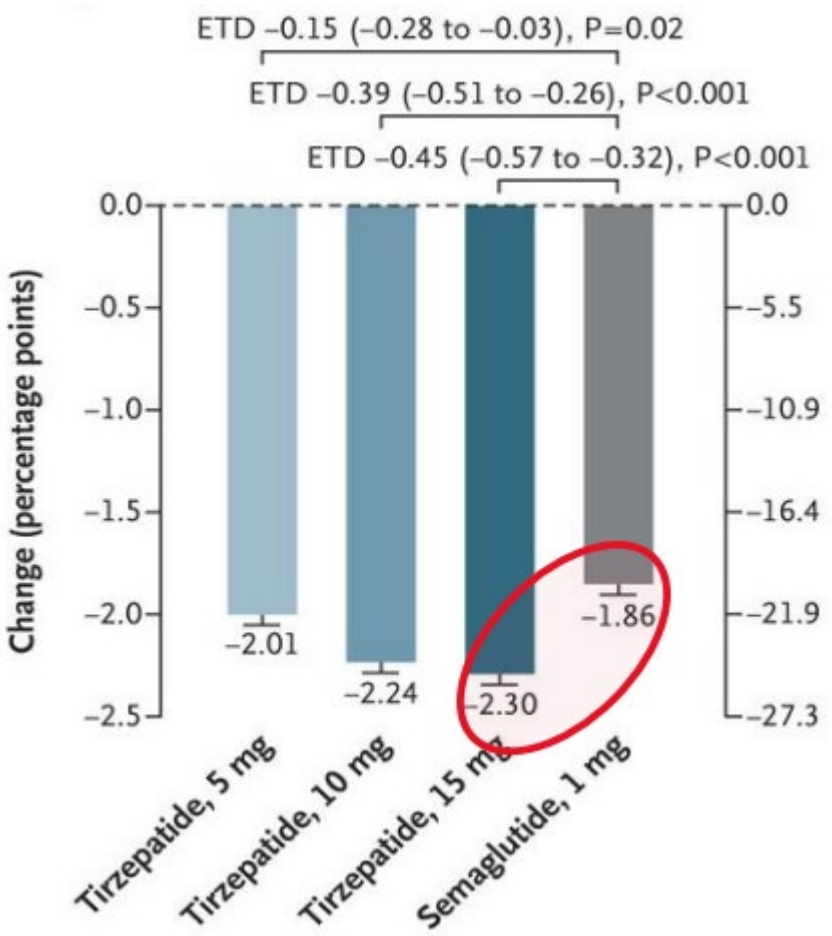
Name	Starting Dose	Max Dose	Primary Effect	Cautions
Canagliflozin (Invokana®)	100 mg daily	300 mg daily	Block renal glucose reabsorption	UG infection fluid/electrolyte euglycemic DKA Amputation? (C)
Empagliflozin (Jardiance®)	10 mg daily	25 mg daily		
Dapagliflozin (Farxiga®)	5 mg daily	10 mg daily		
Ertugliflozin (Steglatro®)	5 mg daily	15 mg daily		

- Modest blood pressure, weight reduction
- No hypoglycemia
- Small rise in Cr early but long-term renoprotection

Tirzepatide

- GLP-1/GIP analogue
- Superior A1C/weight loss/QOL vs. semaglutide 1.0 mg
- Similar tolerability
- No comparisons with semaglutide 2 mg or higher
- No CV outcomes data (yet)



N=1878, 40 week RCT
Additional 5.5 kg weight loss vs. semaglutide

Frias JP et al. N Engl J Med 2021; 385:503-515.

SGLT2i or GLP-1 RA?

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SGLT2i

- ASCVD, HF benefit
- Renal benefit
- Minimal A1C reduction at lower eGFR

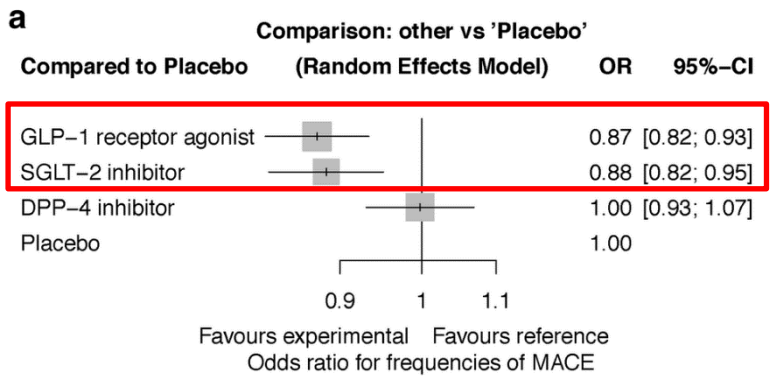
GLP-1 RA

- ASCVD, especially stroke benefit
- Possible renal benefit
- Greater A1C reduction

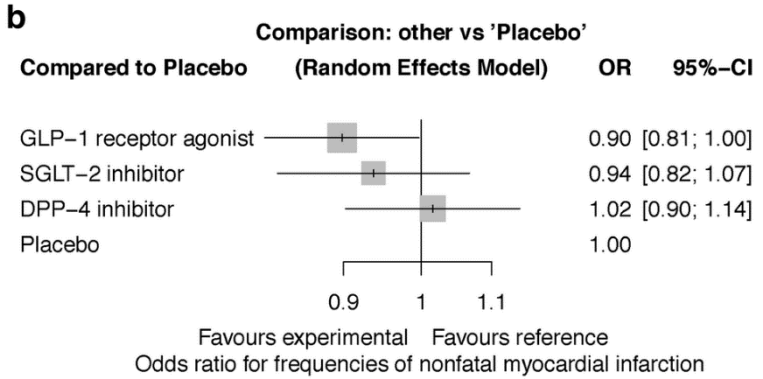
Weight loss in both
No hypoglycemia in either

Meta-Analyses of CVOTs

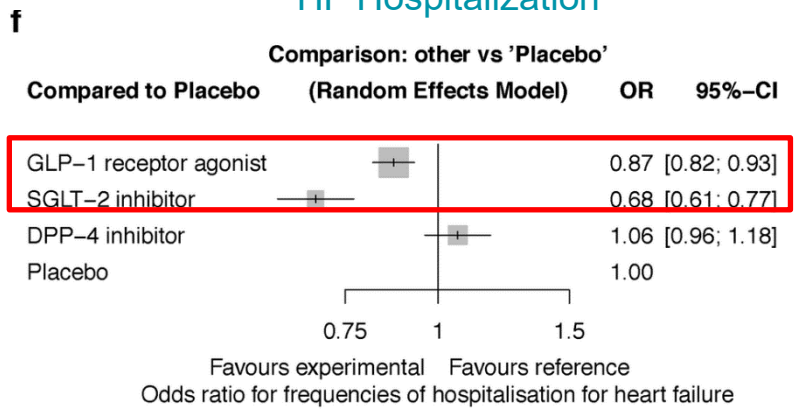
3-point MACE



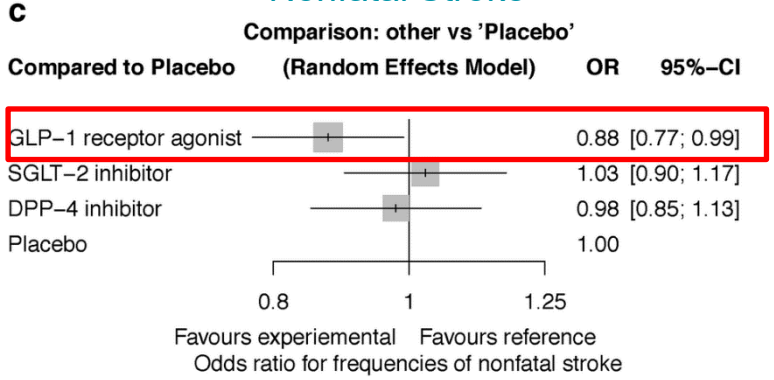
Nonfatal MI



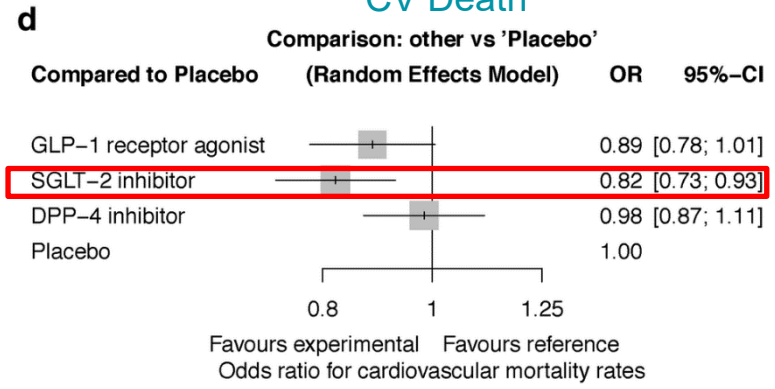
HF Hospitalization



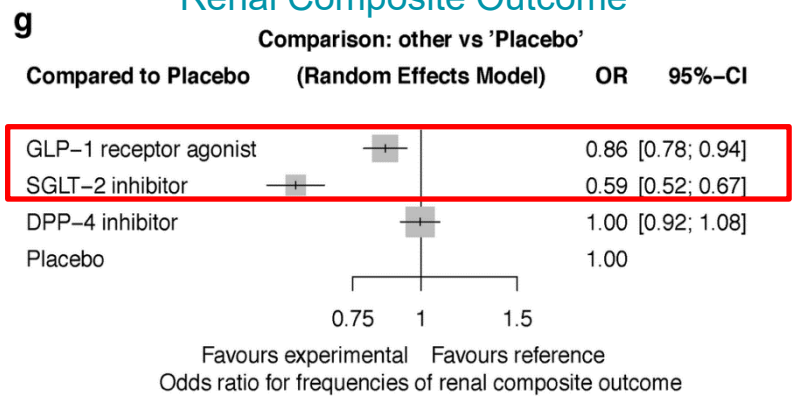
Nonfatal Stroke



CV Death



Renal Composite Outcome



- Meta-analysis of CV outcomes trials
- Did not include CAROLINA, REWIND, PIONEER 6 or VERTIS

Fei et al. Cardiovasc Diabetol. 2019;18(1):112.

Future Therapies

- Once weekly basal insulin (Icodec)
- Glucose responsive insulin
- Combined peptides: GLP-1/GIP, GLP-1/glucagon receptor dual agonist, GLP-1/glucagon/GIP
- Others
  - Glucagon receptor antagonist
  - G-protein-coupled receptor ligands
  - Hormone/enzyme/receptors
  - PPARs: insulin sensitizers
  - Glimins: correction of mitochondrial dysfunction

Perreault l, Skyler JS, Rosenstock J. Rev Endocrinol. 2021 Jun;17(6):364-377. doi: 10.1038/s41574-021-00489-y.
Shah et al. Ther Adv Endocrinol Metab 2021;12:1-30. DOI: 10.1177/ 20420188211042145.

Future Approaches

- Adult-onset DM sub-types[1]
- Precision medicine:[2]
  - Patient-level markers predict response to therapy, complications
  - Emphasis on clinical utility, equity
- Early combination therapy in some patients at treatment initiation to extend the time to treatment failure.[3,4]
- Connected devices for monitoring and treatment

1. Ahlqvist et al. Lancet Diabetes Endocrinol. 2018;6(5):361-369.
2. Nolan et al. ADA/EASD Precision Medicine in Diabetes Initiative. Diabetes Care. 2022;45(2):261-266.
3. Davies et al. ADA Standards of Care. Dia Care 2022;45(Suppl. 1):S125–S143.
4. Garber et al. AACE Consensus Statement. Endocr Pract 2019;25(1):69-100.

Table 1. 2022 Ohio Medicaid Preferred Diabetes Formulary *As of July 2022*

Drug Class	Preferred
Non-Insulin	

Metformin and combination	• Metformin in combination with
	  ○ Pioglitazone
	  ○ Glyburide
	  ○ Canagliflozin, empagliflozin
	  ○ Sitagliptin, linagliptin
	  ○ Repaglinide
	• Metformin ER (Glucophage XR)

Sulphonylurea SFU	glimepiride, glipizide, glyburide
Glucagon-like peptide-1 receptor agonist GLP-1 RA	Byetta (exenatide), Trulicity (dulaglutide), Victoza (liraglutide)
Sodium-glucose cotransporter-2 inhibitor SGLT2i	Farxiga (dapagliflozin), Invokana (canagliflozin), Jardiance (empagliflozin)
Dipeptidyl peptidase-4 inhibitor DPP-4i	Januvia (sitagliptin), Tradjenta (linagliptin)
Thiazolidinedione TZD	pioglitazone
Alpha glucosidase inhibitor AGI	acarbose, miglitol
Glinide	nateglinide, repaglinide

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- No step therapy is required for most medications on formulary
- Continuous glucose monitors are now covered without the need for prior authorization

Insulin	
Basal	Lantus (glargine), Levemir (detemir), Toujeo (glargine U-300), Tresiba (degludec)[5]
Bolus	Apidra (glulisine), aspart, Humalog (lispro) U-100, Humulin R (regular insulin) U-500, lispro, Novolog (aspart) U100
Premix	Humalog 50/50 (lispro protamine/lispro), Humalog 75/25 (lispro protamine/lispro), Humulin 70/30 (insulin isophane/regular insulin), aspart protamine/aspart, Novolog 70/30 (aspart protamine/aspart)

[5] Step therapy

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Thank you!

Questions/Discussion