



CARDI•OH

Ohio Cardiovascular and Diabetes Health Collaborative



In partnership with:



Cardi-OH ECHO

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

September 29, 2022

Assistance & Contact Information



- Please enter your name and practice name into the Chat to record attendance
- Use the Chat feature to ask questions or contribute to the discussion at any time
- Feel free to unmute during Q&A or discussion
- If you need to get in touch with us,
 - **Technology concerns or troubleshooting**
 - Rick Cornachione, IT Support: rx553@case.edu; 440-796-2221
 - **General comments or questions**
 - Claire Rollins, Clinic Coordinator: ceh68@case.edu; 216-926-1676
 - Goutham Rao, MD, Facilitator: Goutham.Rao@UHhospitals.org

Please do not hesitate to contact us with any questions or comments!



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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:
 - Marilee Clemons, PharmD; Danette Conklin, PhD; Kathleen Dungan, MD, MPH; Adam T. Perzynski, PhD; Goutham Rao, MD; Christopher A. Taylor, PhD, RDN, LD, FAND*
- 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.

** For more information about exemptions or details, see www.acme.org/standards



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.



Type 2 Diabetes: Emerging and Future Pharmacotherapies

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Division of Endocrinology, Diabetes & Metabolism

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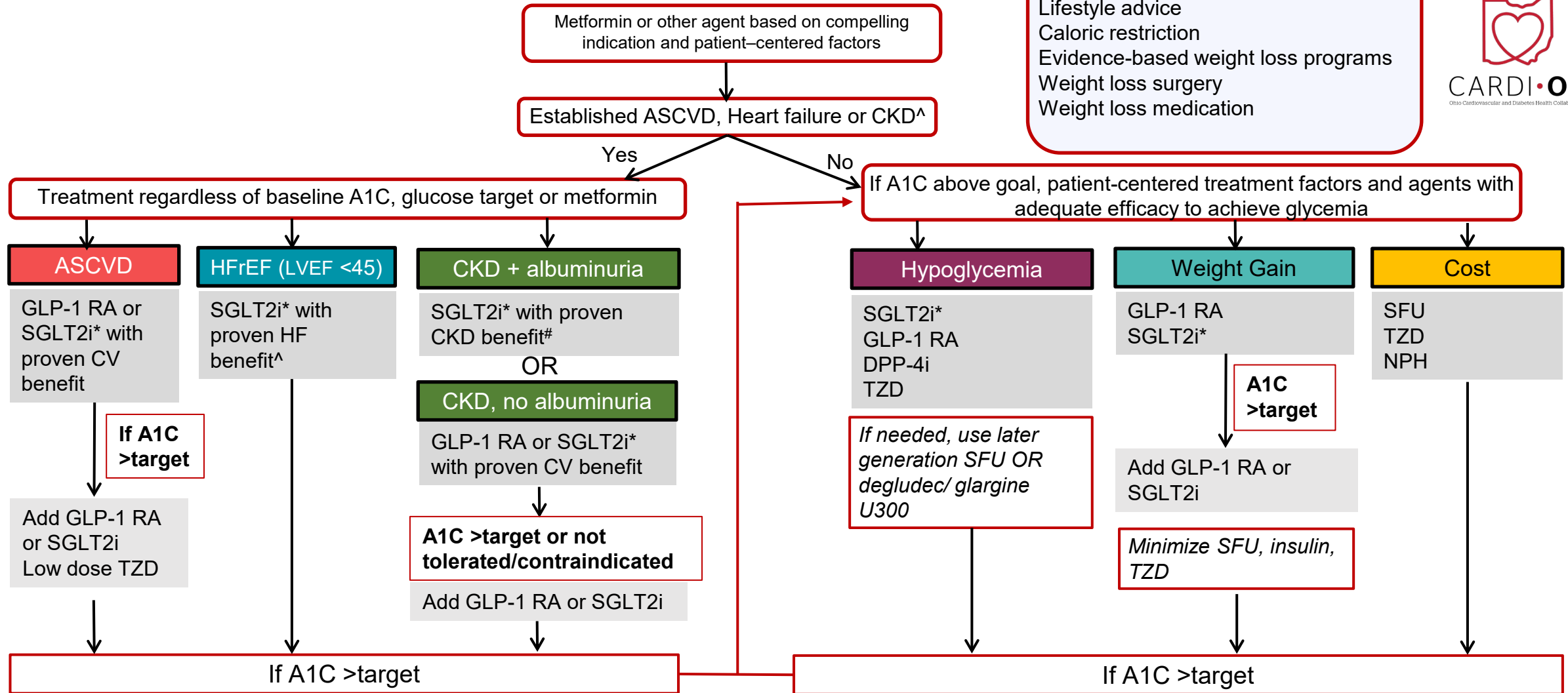
Learning Objectives

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

All Patients

Lifestyle advice
Caloric restriction
Evidence-based weight loss programs
Weight loss surgery
Weight loss medication



*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

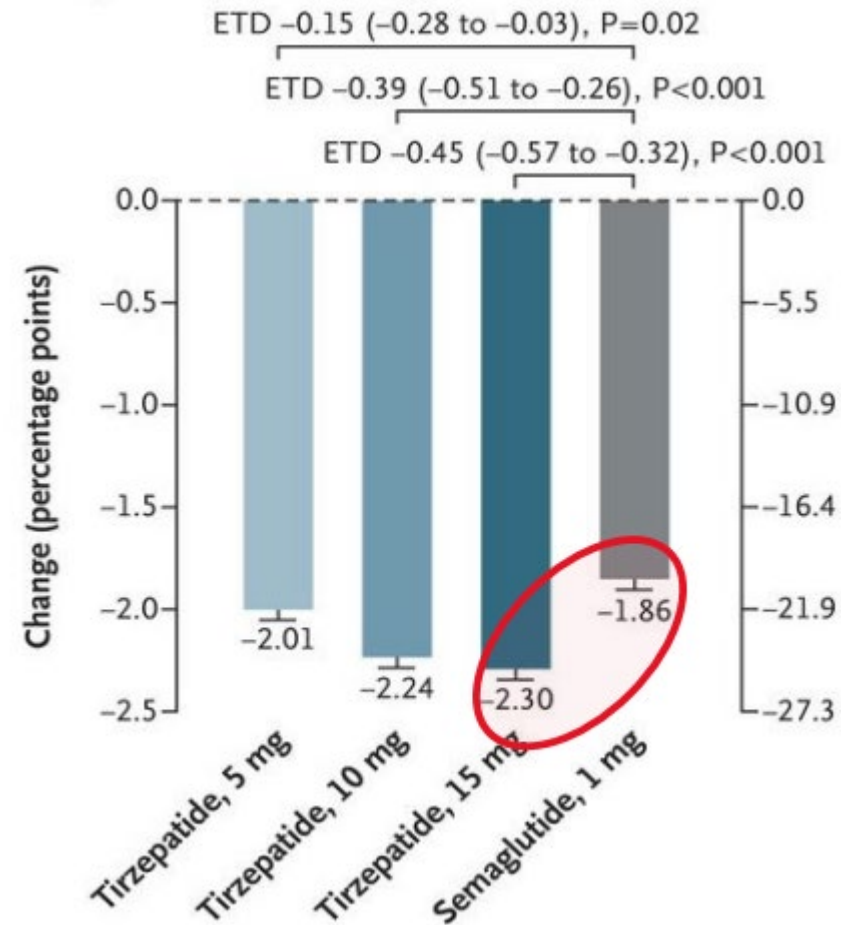
SGLT2 Inhibitors

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

SGLT2i or GLP-1 RA?

SGLT2i

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

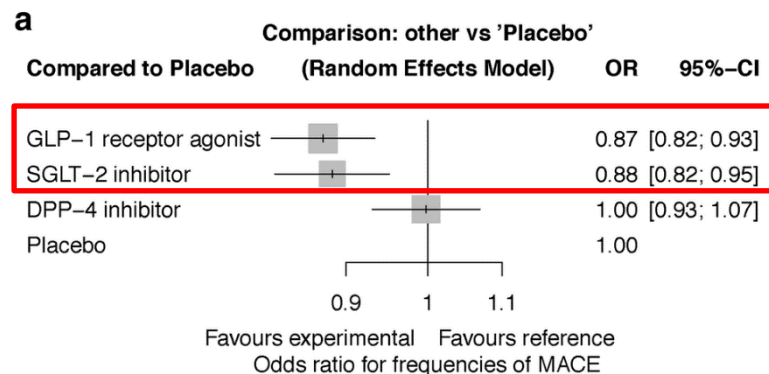
GLP-1 RA

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

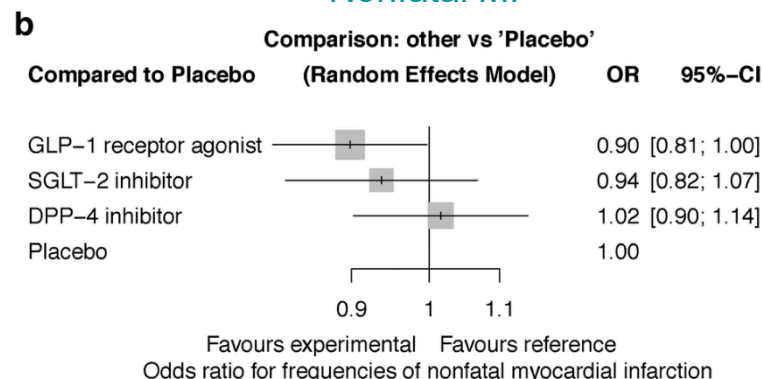
Weight loss in both
No hypoglycemia in either

Meta-Analyses of CVOTs

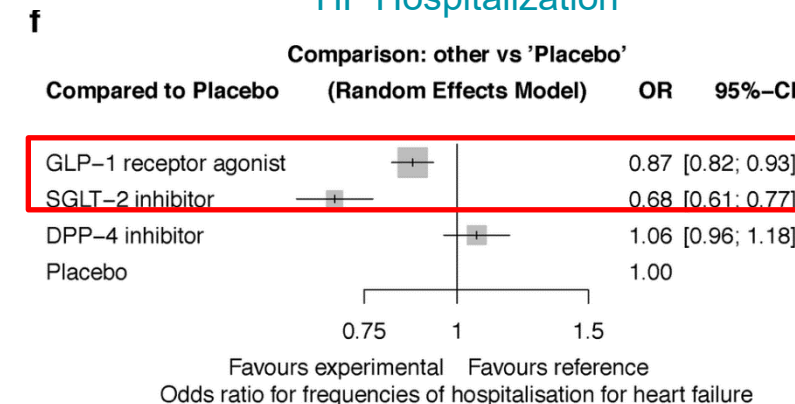
3-point MACE



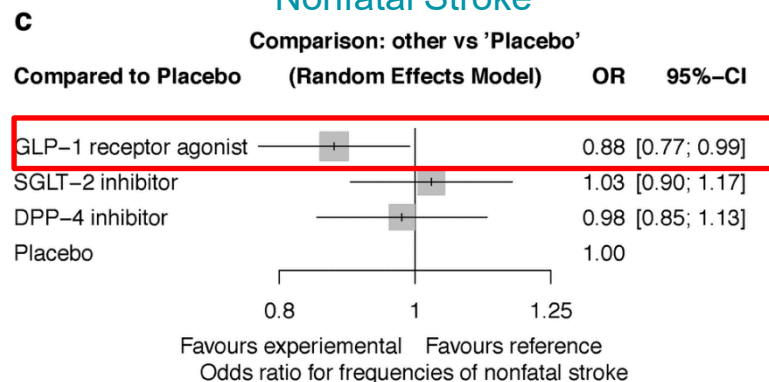
Nonfatal MI



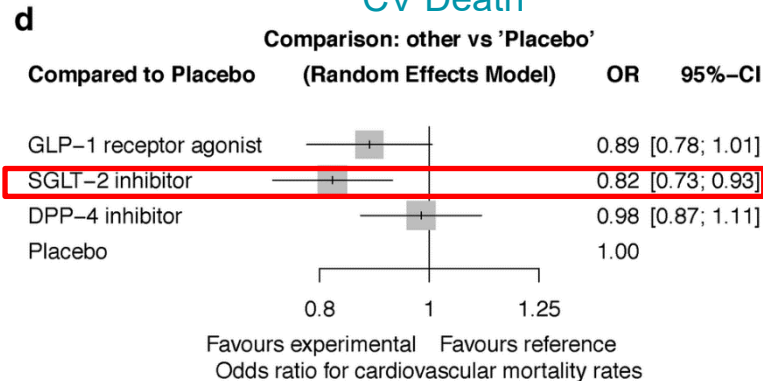
HF Hospitalization



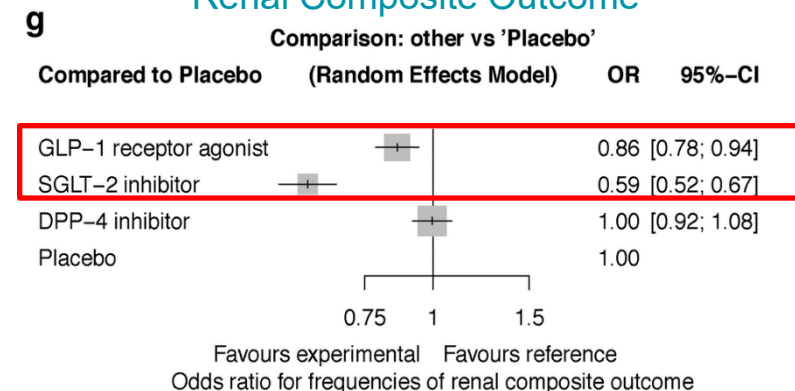
Nonfatal Stroke



CV Death



Renal Composite Outcome



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



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



Future Approaches

- Adult-onset DM sub-types¹
- 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	<ul style="list-style-type: none"> Metformin in combination with <ul style="list-style-type: none"> 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

- 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



Thank you!

Questions/Discussion



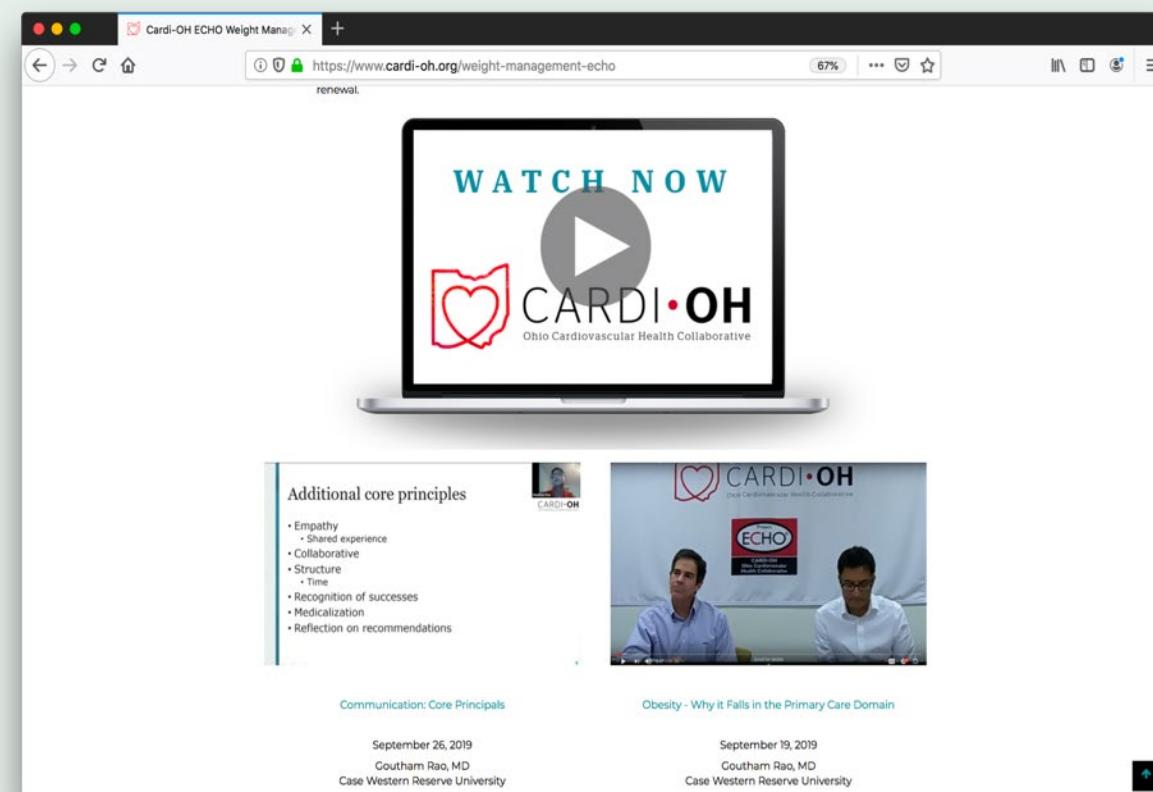
Watch Cardi-OH TeleECHO Clinic Recordings



Register on Cardi-OH.org to watch the current clinic:
cardi-oh.org/user/register

Current Clinic page (access recordings):
cardi-oh.org/echo/cardiovascular-prevention-fall-2022

Access previous Cardi-OH TeleECHO Clinics:
cardi-oh.org/echo/archived-clinics





Reminders



- A Post-Clinic Survey has been emailed to you.
Please complete this survey **by Friday at 5:00 PM.**
- Need to contact us? Email ECHO@Cardi-OH.org

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- *The MetroHealth System designates this educational activity for a maximum of 1 AMA PRA Category 1 Credit(s)TM. Physicians should only claim credit commensurate with the extent of their participation in the activity.*