CARDI·OH

Ohio Cardiovascular and Diabetes Health Collaborative

SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

In partnership with:

The Ohio State University College of Medicine

University of Toledo College of Medicine and Life Sciences

Ohio University Heritage College of Osteopathic Medicine

Northeast Ohio Medical University

University of Cincinnati College of Medicine

Boonshoft School of Medicine Wright State University

medtapp

Government Resource Center

Ohio Department of Medicaid

Project ECHO®

Cardi-OH ECHO

Innovations in Diabetes and Cardiovascular Health

January 26, 2023

Today's Presenters

FACILITATOR

Goutham Rao, MD
Case Western Reserve University

DIDACTIC PRESENTER

Kathleen Dungan, MD, MPH
The Ohio State University

LEAD DISCUSSANTS

Karen Bailey, MS, RDN, LD, CDCES
Ohio University

Danette Conklin, PhD
Case Western Reserve University

Kathleen Dungan, MD, MPH
The Ohio State University

CASE PRESENTERS

Nathaniel Harris, MD
UC Health West Chester Family Medicine

Kyle Smith, MSN
Equitas Health

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*:
  - Danette Conklin, PhD; Kathleen Dungan, MD, MPH; Ian Neeland, MD; Adam T. Perzynski, PhD; Goutham Rao, MD; Christopher A. Taylor, PhD, RDN, LD, FAND; Yasir Tarabichi, MD; Jackson Wright, MD, PhD

- 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; Carolyn Ievers-Landis, PhD; Kelsey Ufholz, PhD; James Werner, PhD, MSSA
- 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 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.

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

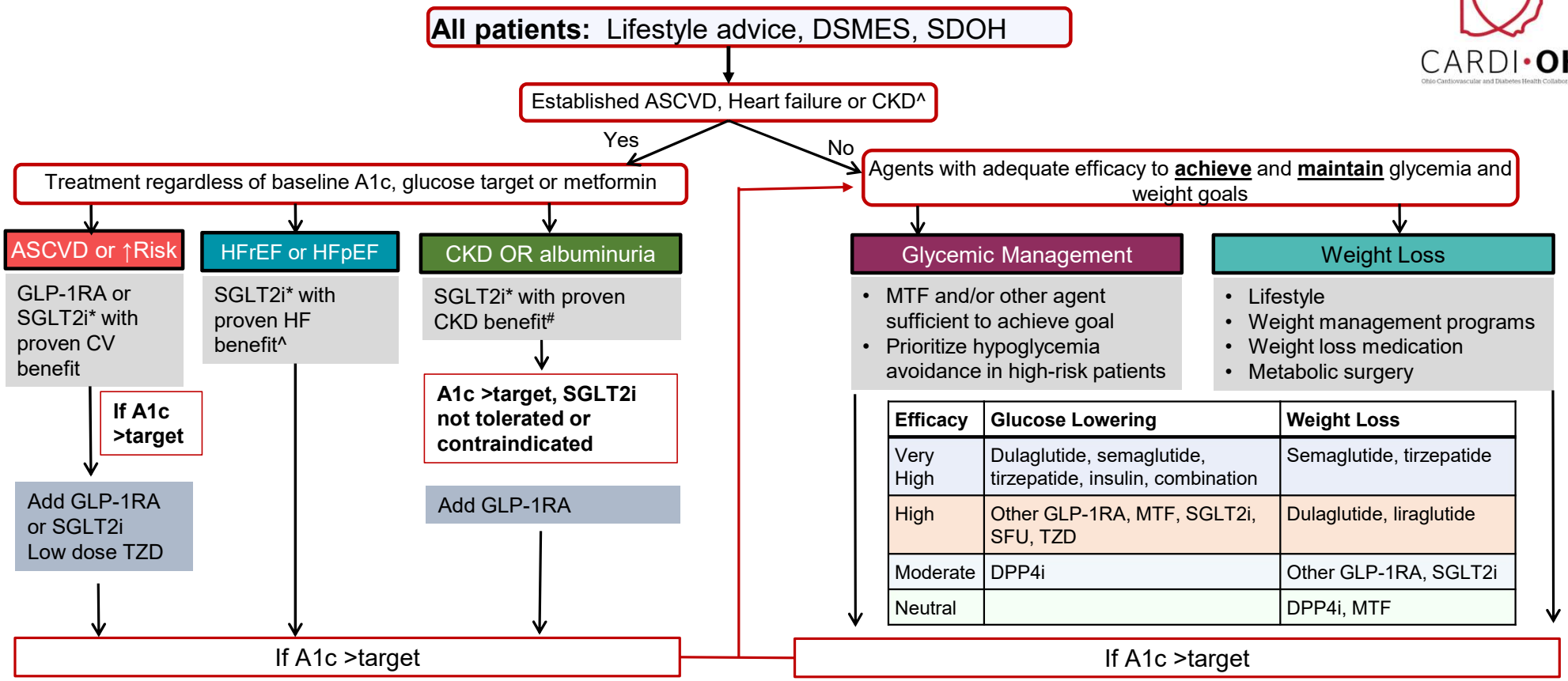
The Ohio State University

Learning Objectives

CARDI·OH
Ohio Cardiovascular and Diabetes Health Collaborative

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/EASD Consensus 2022



^Empagliflozin/dapagliflozin have shown benefit in dedicated HF studies. Canagliflozin/ertugliflozin demonstrated reduction in hospitalization for HF in CV outcomes trials. #Dapagliflozin/canagliflozin demonstrated benefit in dedicated renal studies. Empagliflozin demonstrated reduction in CKD progression in CV outcomes trials. *start if eGFR >20 ml/min/1.73 m2, continue until HD or transplant

DSMES=diabetes self-management education and support, ASCVD=atherosclerotic cardiovascular disease, HFrEF=heart failure with reduced ejection fraction, HFpEF=heart failure with preserved ejection fraction, CKD=chronic kidney disease, GLP-1RA=glucagon-like peptide-1 receptor agonist, SGLT2i=sodium-glucose cotransporter-2 inhibitor, TZD=thiazolidinedione, SFU=sulfonylurea,

Davies et al. Diabetologia. 2022;65(12):1925-1966. doi: 10.1007/s00125-022-05787-2.

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	Daily	
Liraglutide	Victoza	1.6, 1.2, 1.8 mg	Daily	
Exenatide QW	Bydureon	2 mg	Weekly	
Semaglutide	Ozempic	0.5, 1.0 mg	Weekly	
	Rybelsus	3, 7, 14 mg PO	Daily	
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

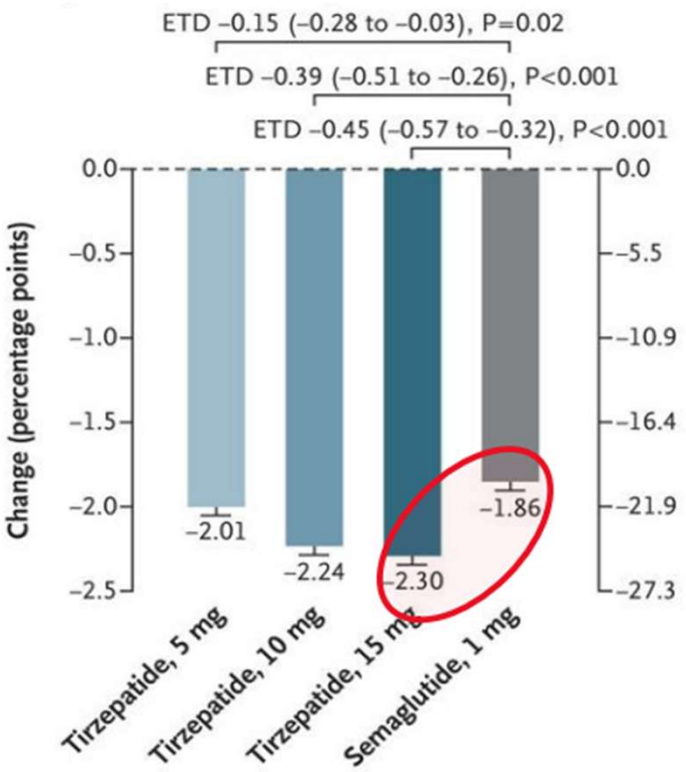
CARDI·OH
Ohio Cardiovascular and Diabetes Health Collaborative

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?

CARDI·OH
Ohio Cardiovascular and Diabetes Health Collaborative

SGLT2i

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

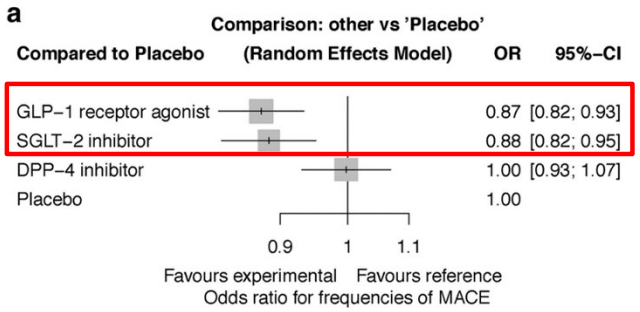
GLP-1 RA

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

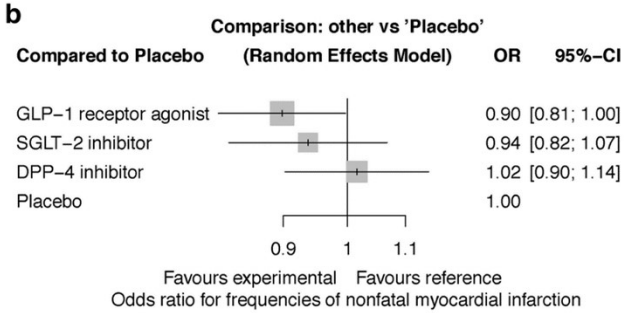
Weight loss in both
No hypoglycemia in either

Meta-Analyses of CVOTs

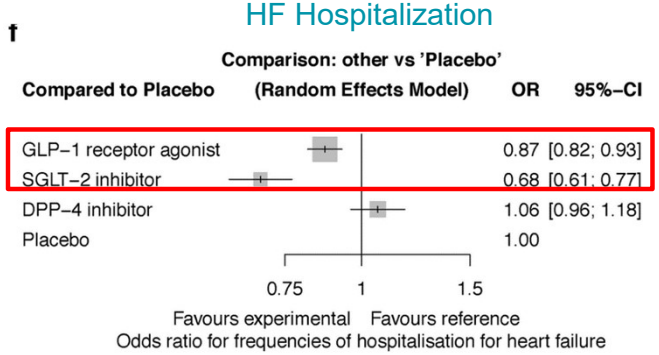
3-point MACE



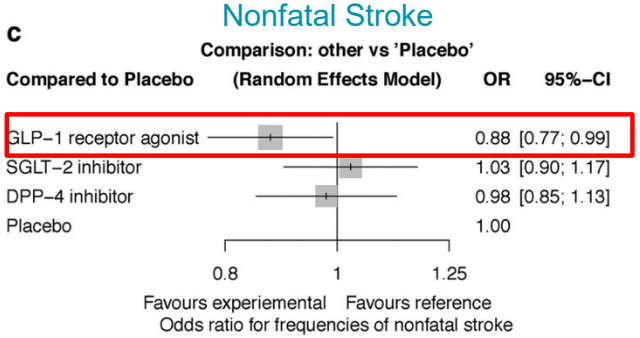
Nonfatal MI



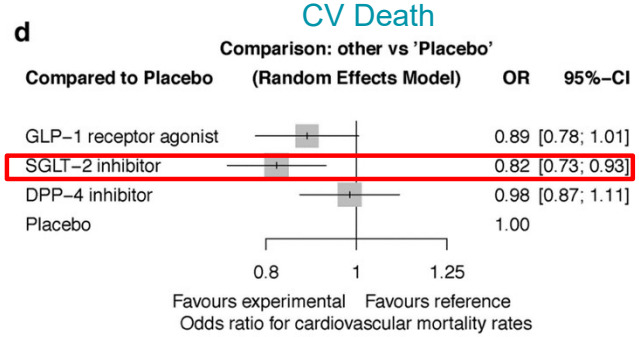
HF Hospitalization



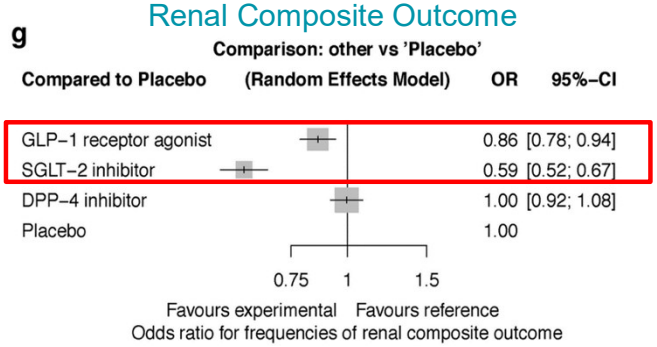
Nonfatal Stroke



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

CARDI·OH
Ohio Cardiovascular and Diabetes Health Collaborative

- 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

CARDI·OH
Ohio Cardiovascular and Diabetes Health Collaborative

- 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