CARDI·OH

Ohio Cardiovascular and Diabetes Health Collaborative

SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

In partnership with:

THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER

COLLEGE OF MEDICINE AND LIFE SCIENCES THE UNIVERSITY OF TOLEDO

OHIO UNIVERSITY Heritage College of Osteopathic Medicine

Northeast Ohio MEDICAL UNIVERSITY

University of CINCINNATI FAMILY AND COMMUNITY MEDICINE

Boonshoft School of Medicine WRIGHT STATE UNIVERSITY

MedTAPP

OHIO COLLEGES OF MEDICINE GOVERNMENT RESOURCE CENTER

Ohio Department of Medicaid

Project ECHO®

CARDI-OH
Ohio Cardiovascular & Diabetes Health Collaborative

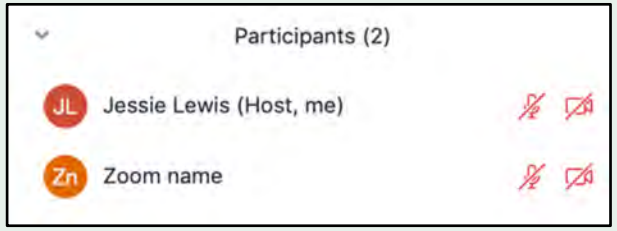
Cardi-OH ECHO Tackling Type 2 Diabetes

Thursday, February 4, 2021

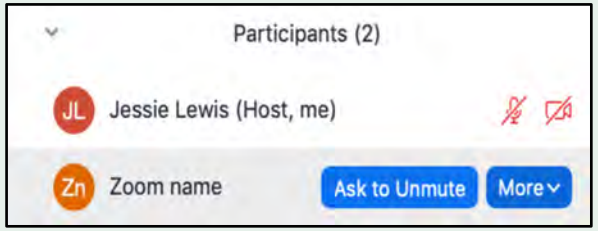
Reminders

- Enter your name and practice name into the Chat to record your attendance
- Rename yourself in the Participant List with your full name and practice name

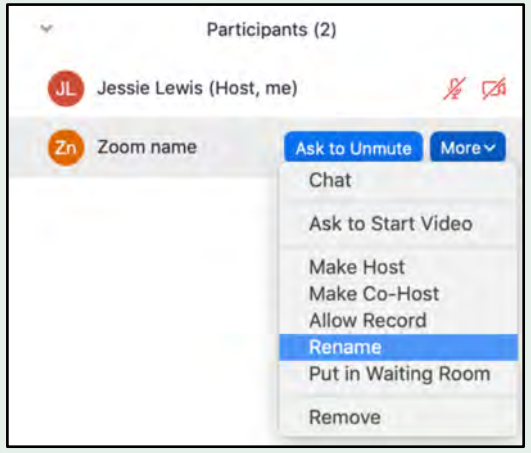
1. Hover over your name



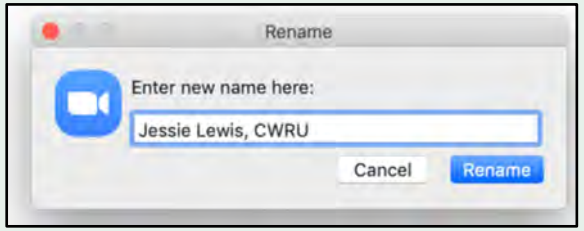
2. Select More



3. Select Rename



4. Type name and practice



- Mute your microphone unless speaking
- Comment or ask questions in the Chat at any time

Cardi-OH ECHO Hub Team

LEAD

Goutham Rao, MD
Case Western Reserve University

FACILITATOR

Kathleen Dungan, MD, MPH
The Ohio State University

DIDACTIC PRESENTER

Kathleen Dungan, MD, MPH
The Ohio State University

CASE PRESENTER

Carrie Cales, NP
Signature Health - Painesville

Structure of ECHO Clinics

Duration	Item
5 minutes	Announcements and introductions
25 minutes	Didactic presentation, followed by Q&A
25 minutes	Case study presentation and discussion
5 minutes	Wrap-up/Post-Clinic Survey completion

Disclosure Statements

- The following planners, speakers, moderators, and/or panelists of the CME activity have financial relationships with commercial interests to disclose:
  - Kathleen Dungan, MD, MPH receives consulting fees from Eli Lilly and Tolerion, institutional research fees from Eli Lilly, Novo Nordisk, and Sanofi Aventis, and presentation honoraria from Nova Biomedical, Integritas, and Uptodate.
  - Adam T. Perzynski, PhD reports being co-owner of Global Health Metrics LLC, a Cleveland-based software company and royalty agreements for book authorship with Springer Nature publishing and Taylor Francis publishing.
  - Christopher A. Taylor, PhD, RDN, LD, FAND reports grant funding for his role as a researcher and presenter for Abbott Nutrition and grant funding for research studies with both the National Cattleman's Beef Association and the American Dairy Association.
  - Jackson T. Wright, Jr., MD, PhD reports research support from the NIH and Ohio Department of Medicaid and consulting with NIH, AHA, and ACC.
  - These financial relationships are outside the presented work.
- All other planners, speakers, moderators, and/or panelists of the CME activity have no financial relationships with commercial interests to disclose.

New and Emerging Therapies for Type 2 Diabetes

Kathleen Dungan, MD, MPH

Professor, Associate Director Clinical Services, Division of Endocrinology, Diabetes & Metabolism

The Ohio State University

Objectives

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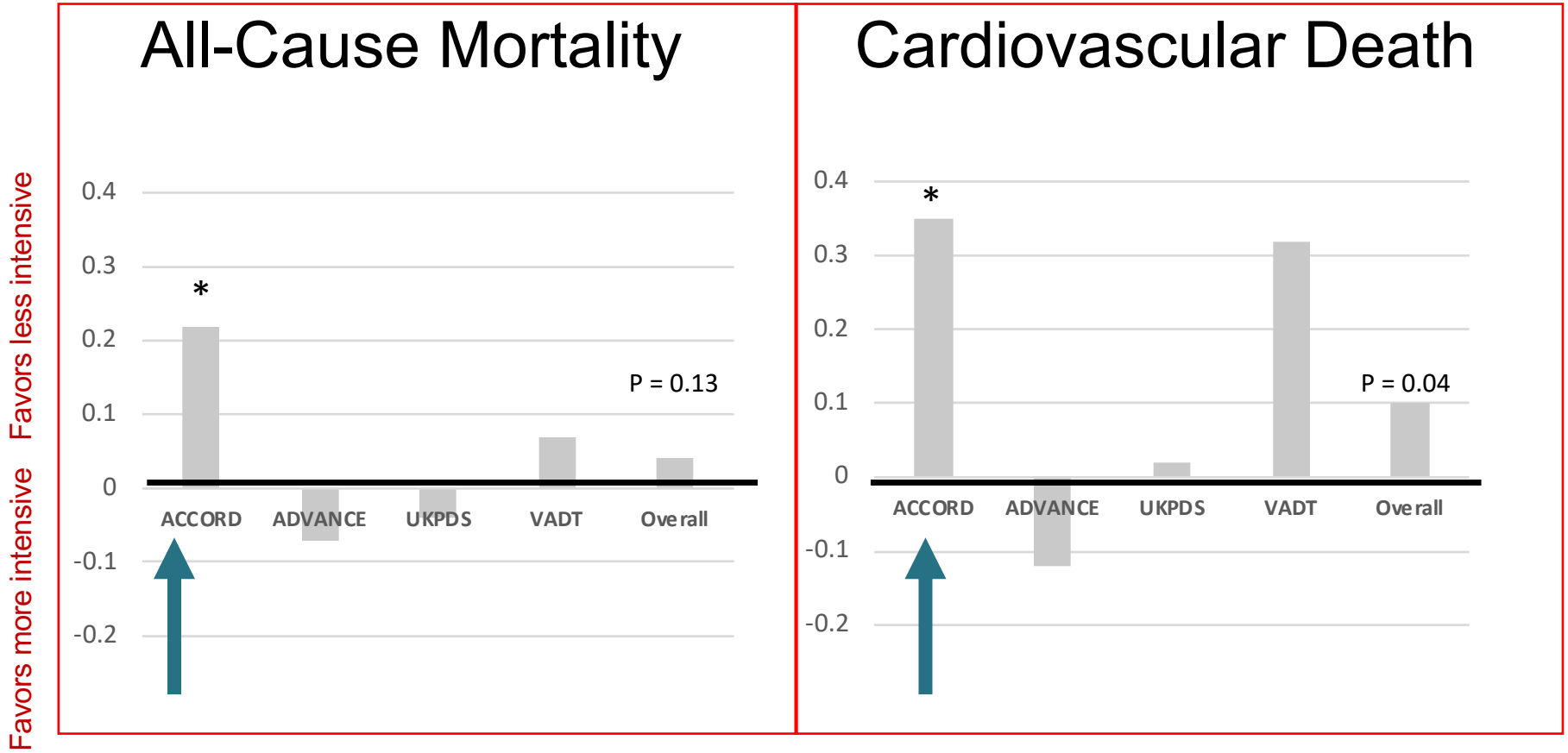
1. Describe the role and benefits (including cardiovascular benefits) of GLP-1 agonists and SGLT-2 inhibitors in the care of patients with type 2 diabetes.
2. Describe current recommendations for selection and titration of insulin therapy.
3. Describe a minimum of 2 developments in the use of technology for improved management of type 2 diabetes.

Meta-analysis: Intensive Glucose Control & Mortality



*p<0.05

Diabetologia 2009;52:2288-98

UKPDS: Legacy Effect of Earlier Glucose Control

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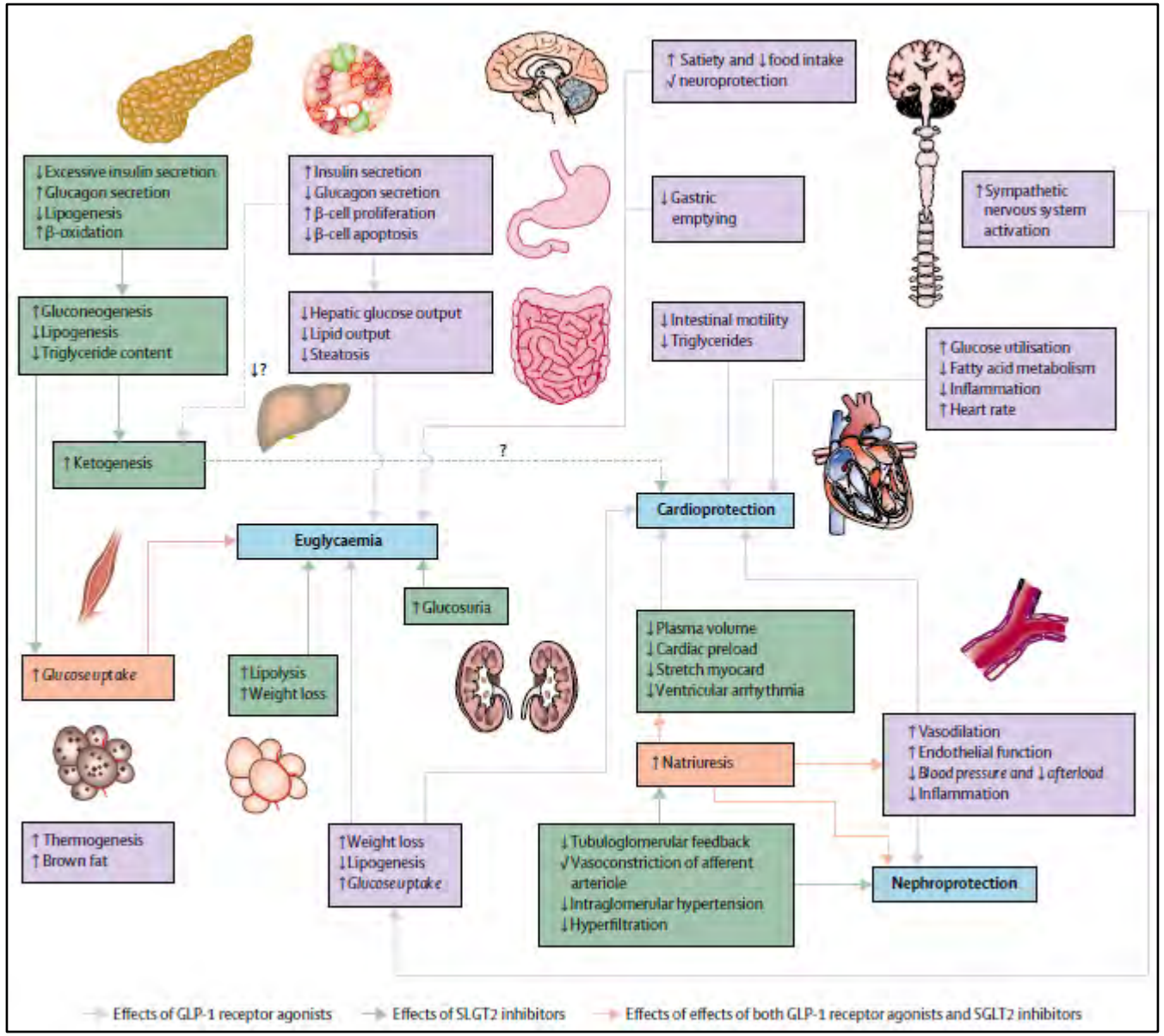
After median 8.5 years post-trial follow-up

Aggregate Endpoint		**1997**	**2007**
Any diabetes related endpoint	*RRR:*	12%	**9%**
	P:	0.029	**0.040**
Microvascular disease	*RRR:*	25%	**24%**
	P:	0.0099	**0.001**
Myocardial infarction	*RRR:*	16%	**15%**
	P:	0.052	**0.014**
All-cause mortality	*RRR:*	6%	**13%**
	P:	0.44	**0.007**

RRR = Relative Risk Reduction, P = Log Rank

GLP-1RA + SGLT2i



- Synergistic effects
  - A1c
  - Weight
  - BP
  - Lipid
- No Hypoglycemia
- Beneficial CV and renal outcomes
  - GLP1RA: atherosclerotic mechanism
  - SGLT2i: plasma volume, fuel metabolism

De Block; Lancet Diabetes Endocrinol 2018;6:349-352

CV Outcomes Trials in T2DM

Study	SAVOR[1]	EXAMINE[2]	TECOS[3]	CARMELINA[4]	CAROLINA[5]
DPP4-i	saxagliptin	alogliptin	sitagliptin	linagliptin	linagliptin
Comparator	placebo	placebo	placebo	placebo	glimepiride (SU)
N	16,492	5380	14,671	6979	6103
Results	NEUTRAL— increase in hospitalization for HF with saxagliptin, possibly alogliptin				

Study	ELIXA[6]	LEADER[7]	SUSTAIN 6[8]	EXSCEL[9]	REWIND[10]	HARMONY[11]	PIONEER 6
GLP1-RA	lixisenatide	liraglutide	semaglutide	exenatide LR	dulaglutide	albiglutide	Oral sema
Comparator	placebo	placebo	placebo	placebo	placebo	placebo	Placebo
N	6068	9340	3297	14,752	9901	9463	3183
Results	2015	2015 ✚	2016 ✚	2017	2019 ✚	2018 ✚	2019

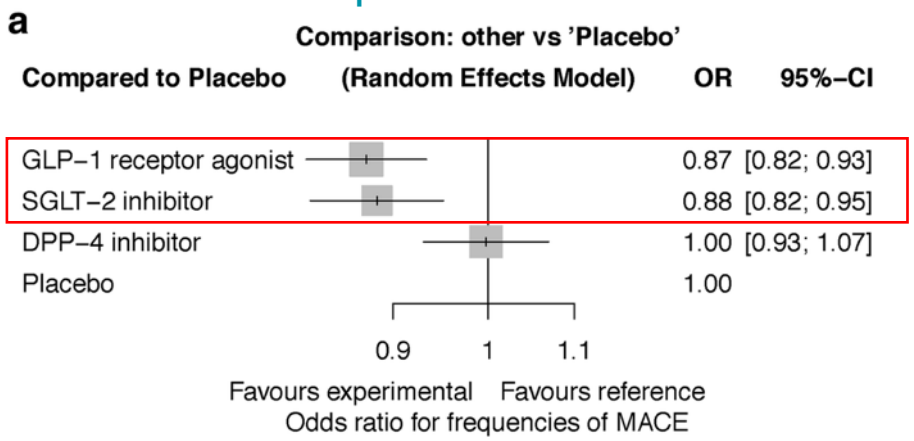
Study	EMPA-REG[12]	CANVAS[13]	(CREDENCE[14])	DECLARE[15]	VERTIS CV[16]
SGLT2-i	empagliflozin	canagliflozin	canagliflozin	dapagliflozin	ertugliflozin
Comparator	placebo	placebo	placebo	placebo	placebo
N	7020	4330	4401	17,160	8246
Results	2015 ✚	2017 ✚	2018 ✚	2018 ✚	2020

✚ Superior for primary outcome vs. placebo *** non-insulin**

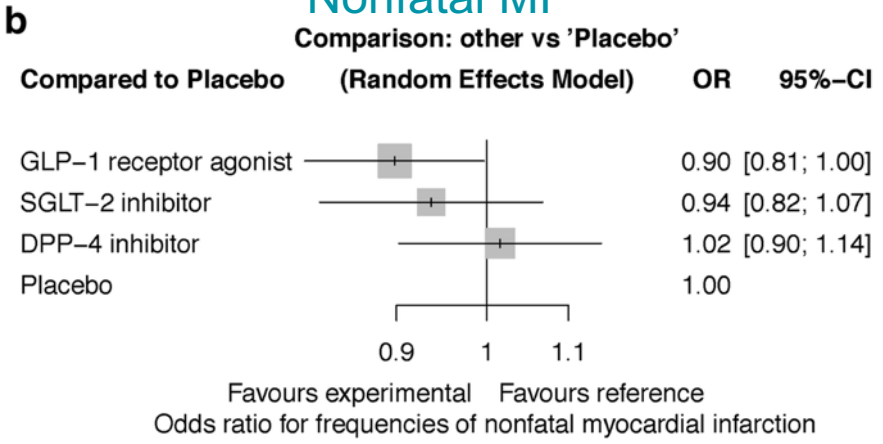
1. NCT01107886 (SAVOR). 2. NCT00968708 (EXAMINE). 3. NCT00790205 (TECOS). 4. NCT01897532 (CARMELINA). 5. NCT01243424 (CAROLINA). 6. NCT01147250 (ELIXA). 7. NCT01179048 (LEADER). 8. NCT01720446 (SUSTAIN 6). 9. NCT01144338 (EXSCEL). 10. NCT01394952 (REWIND). 11. NCT02465515 (HARMONY). 12. NCT01131676 (EMPA-REG). 13. NCT01032629 (CANVAS). 14. NCT02065791 (CREDENCE). 15. NCT01730534 (DECLARE). 16. NCT01986881 (VERTIS CV).

Meta-analysis of CVOT

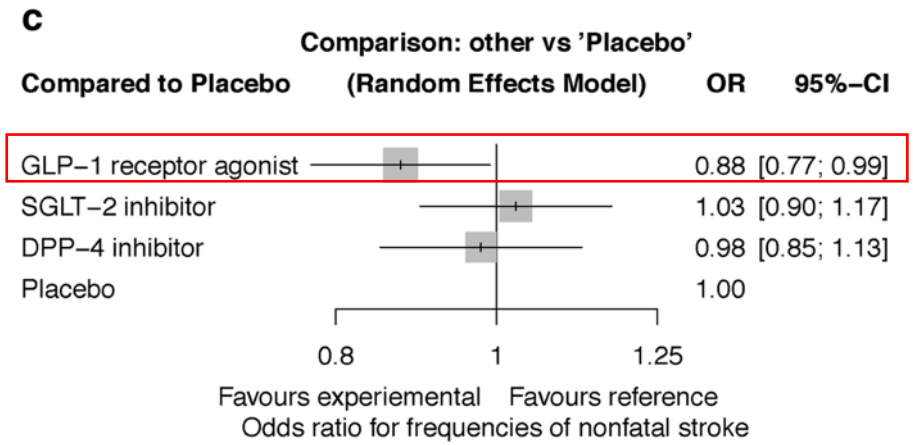
3-point MACE



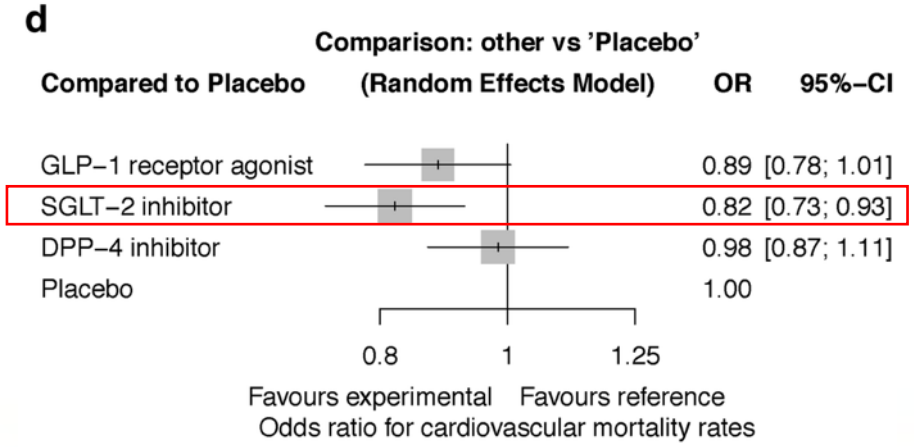
Nonfatal MI



Nonfatal Stroke



CV Death

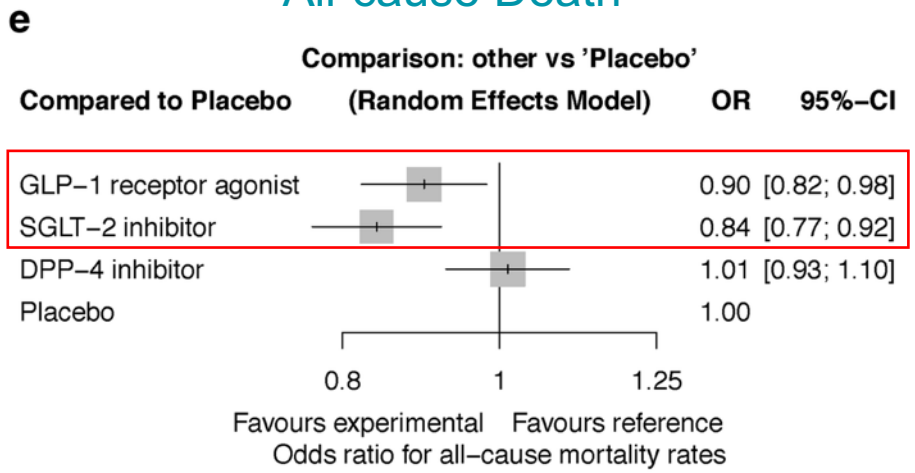


- Meta-analysis of CV outcomes trials
- Did not include CAROLINA, REWIND, PIONEER 6 or VERTIS

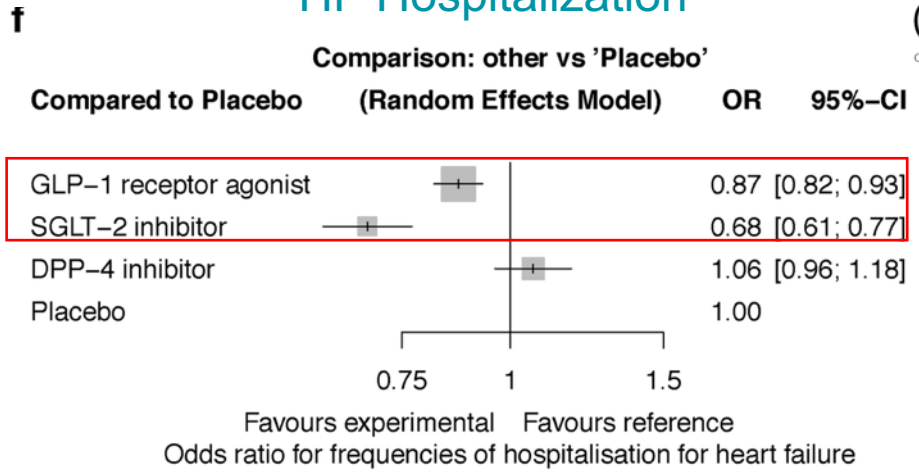
Fei et al. Cardiovasc Diabetol. 2019;18(1):112.

Meta-analysis of CVOT

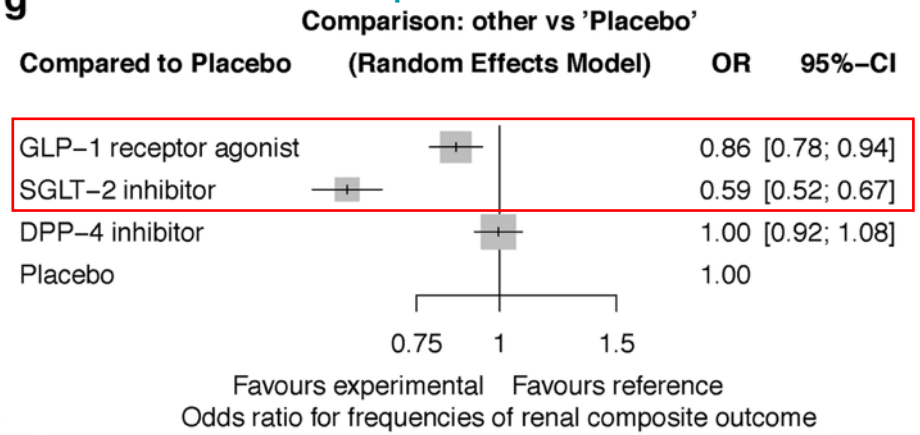
All-cause Death



HF Hospitalization

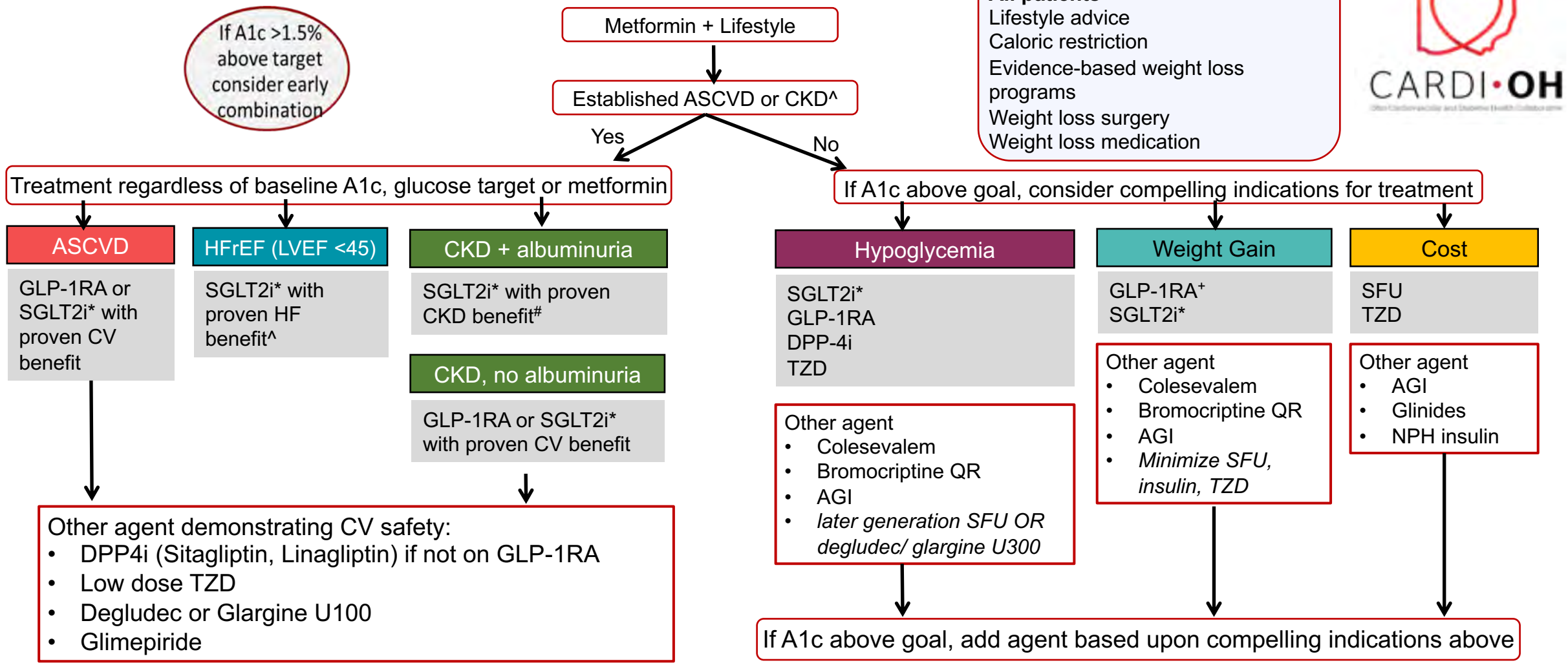


Renal Composite Outcome



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

ADA Standards of Care 2021



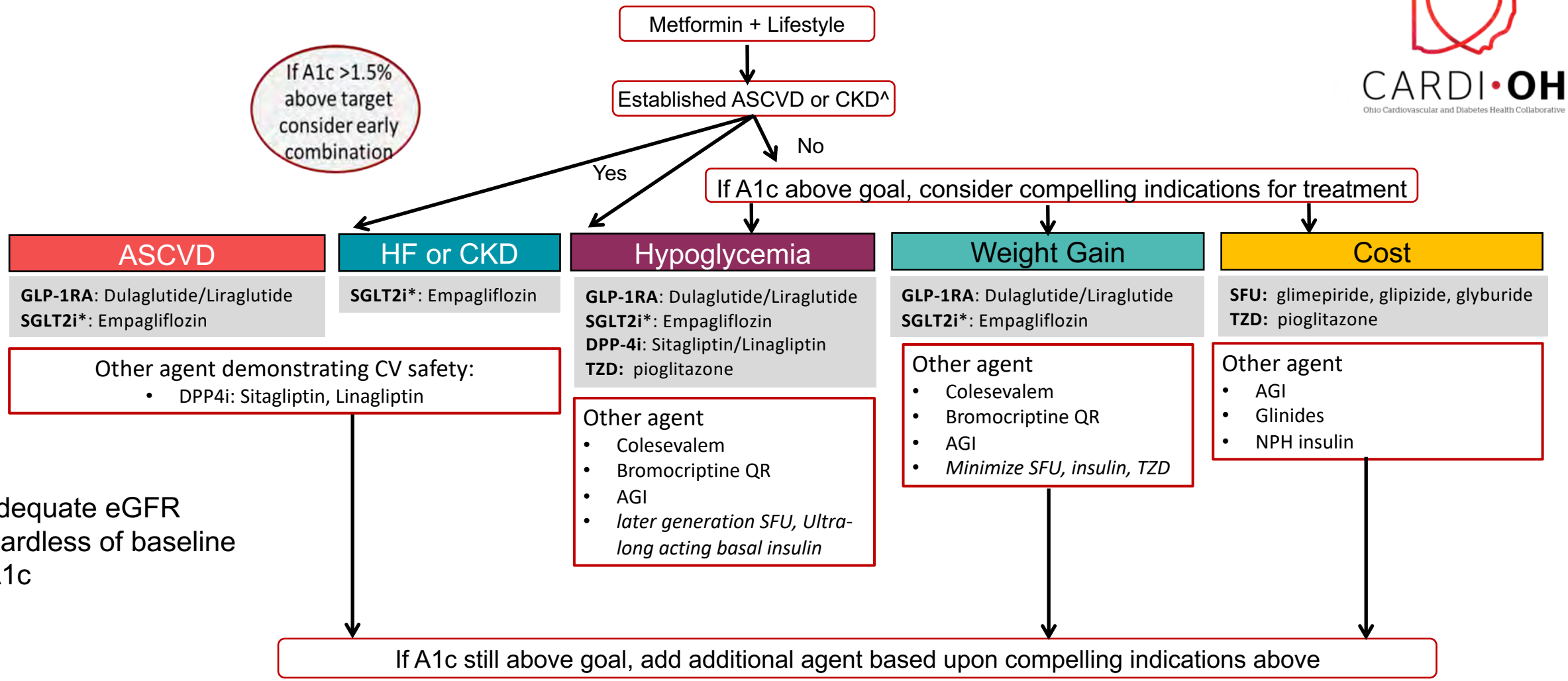
***if adequate eGFR, ^Empagliflozin and dapagliflozin have shown benefit in dedicated HF studies. Canagliflozin has demonstrated reduction in hospitalization for HF in CV outcomes trials. #Dapagliflozin and canagliflozin have demonstrated benefit in dedicated renal outcomes studies. Empagliflozin has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

+Weight loss is greatest with semaglutide > liraglutide >dulaglutide >exenatide >lixisenatide

ASCVD=atherosclerotic cardiovascular disease, CKD=chronic kidney disease, GLP-1RA=glucagon-like peptide-1 receptor agonist, SGLT28i=sodium-glucose cotransporter-2 inhibitor, AGI=alpha-glucosidase inhibitor, SFU=sulfonylurea, TZD=thiazolidinedione

American Diabetes Association Dia Care 2021;44:S111-S124

Pharmacologic management--Medicaid Formulary



*if adequate eGFR
^regardless of baseline HbA1c

ASCVD=atherosclerotic cardiovascular disease, CKD=chronic kidney disease, GLP-1RA=glucagon-like peptide-1 receptor agonist, SGLT28i=sodium-glucose cotransporter-2 inhibitor, AGI=alpha-glucosidase inhibitor, SFU=sulfonylurea, TZD=thiazolidinedione

Intensifying to Injectable Therapies

Consider initial insulin if A1c>11, T1D is a possibility or symptomatic

Basal Insulin Titration
Self-titration more effective
Increase 2 unit every 3 day until tasting glucose at target without hypoglycemia.
If hypoglycemia, if no other cause, reduce dose by 10-20%

Prandial Insulin Titration
Increase 1-2 unit or 10-15% 2x/week to reach post-meal target
If hypoglycemia, if no other cause, reduce corresponding basal or prandial dose by 10-20%

GLP-1 RA
- Continue metformin +/- other agent

Not at goal

Basal Insulin
- Continue metformin +/- other agent
- Start 10 unit/day or 0.1-0.2 unit/kg/day

Not at goal after FBG target is reached or signs of excess basal (>0.5 unit/kg, elevated bedtime-morning and/or post-prandial differential, hypoglycemia, high variability)

Basal Plus
- GLP-1 RA or Fixed ratio combination
- Prandial insulin at largest meal
  - 4 unit, 0.1 unit/kg, or 10% of basal dose
  - Consider reducing basal 10%
- Premix: Divide basal dose to 2/3 AM, 1/3 PM

Not at goal

Basal Bolus
- Prandial insulin at 2-3 meals
  - 4 unit, 0.1 unit/kg, or 10% of basal dose
  - Consider reducing basal

Consider initial combination injection if A1c>10 or >2% above target

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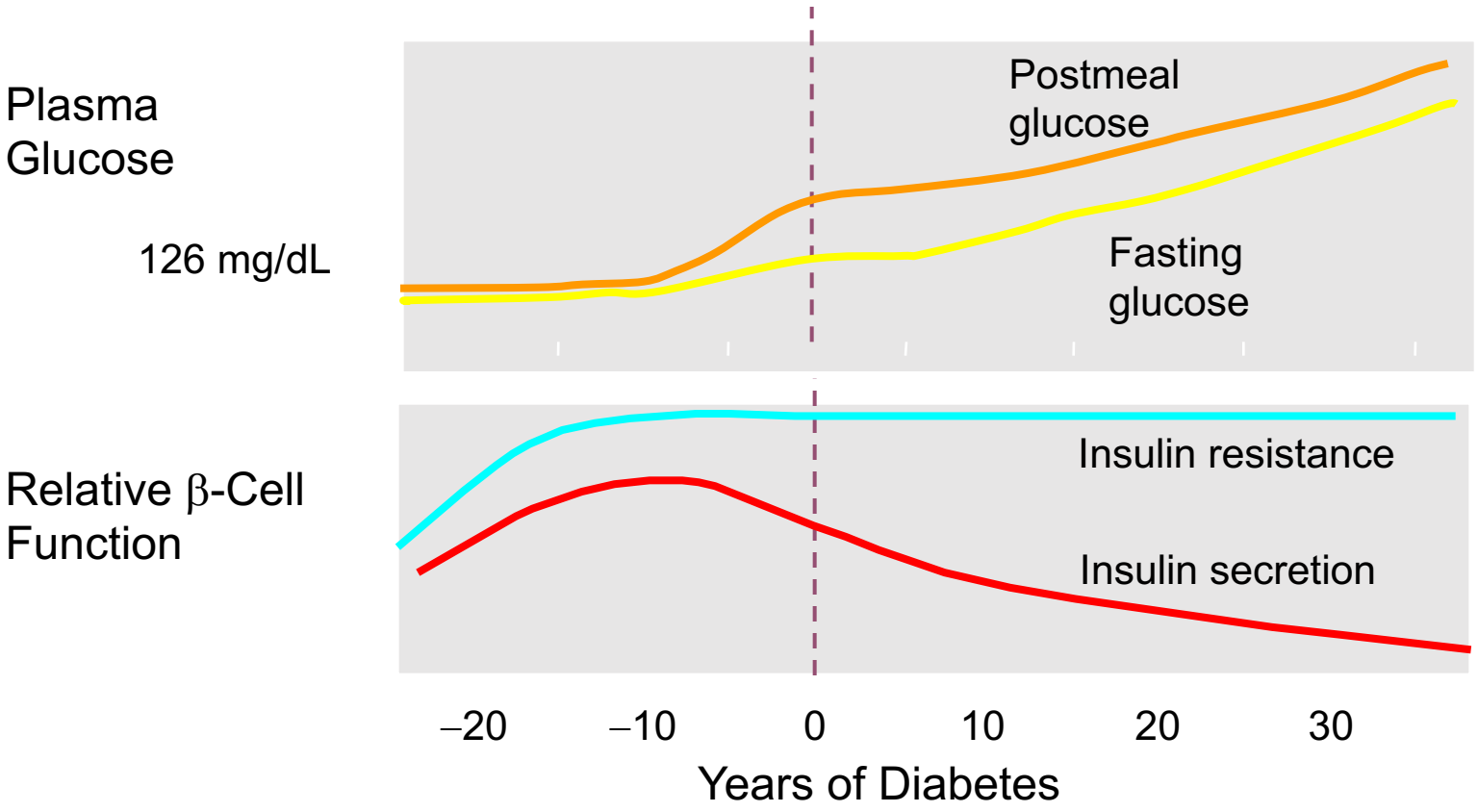
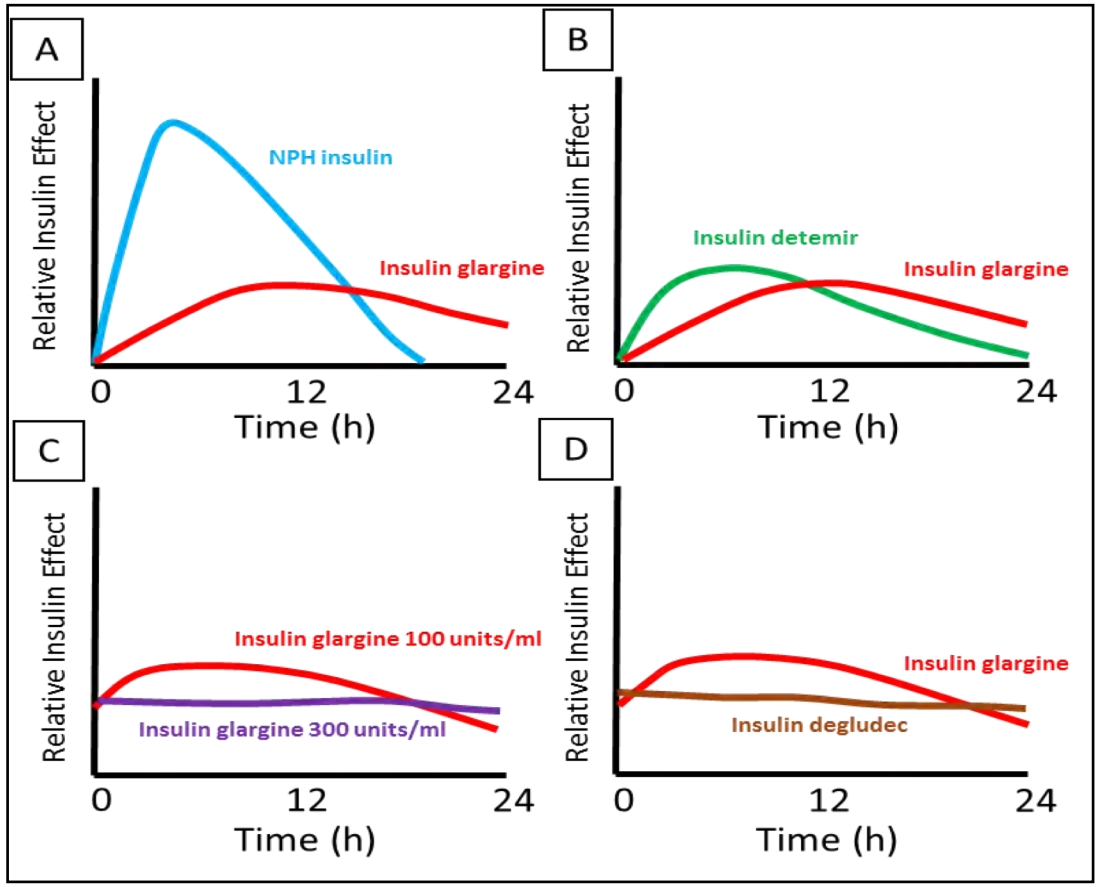
Natural History of T2DM



- Loss of beta cell function begins before diagnosis and progresses
- Insulin resistance does not change over time

Adapted from International Diabetes Center (IDC). Minneapolis, Minnesota. 6-6

Basal Insulins



Ultra-long acting:

- Flatter profile
- Longer duration
- Less hypoglycemia
- Once daily, flexible

Pettus et al. Diabetes Metab Res Rev 2015

Optimizing Basal Bolus Insulin

- Review medication taking, simplify
- Refer to DSMES
- Use insulin sparing Rx
- Manage carbohydrates, activity
- Insulin analogues, especially if hypoglycemia
- Ultra-long acting insulins (if hypoglycemia, need for >50-60 unit/day or to reduce basal injection count)
- Concentrated insulins (U500 if >250 unit/day, otherwise U200 lispro, U300 glargine, U200 Degludec)
- Delivery: smart pens, inhaled insulin
- Use CGM

CGM

- Recommended for all T1D, insulin requiring T2D not meeting targets/hypoglycemia
- Real-time vs. flash
- Some devices do not require calibration, minimal fingersticks
- Education is critical: Greater inaccuracy on day 1 of sensor wear, low BG, rapid glucose swings

Freestyle Libre

Eversense

Dexcom

Medtronic

AACE/ACE GM Consensus Statement, *Endocr Pract.* 2016;22(No. 2) 239,254
Standards of Medical Care in *Diabetes Care* January 2020..
Diabetes Technology-Continuous Subcutaneous Insulin Infusion Therapy and Continuous Glucose Monitoring in Adults: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016;101(11):3922-3937.

Advanced Technologies & Treatments for Diabetes Consensus Congress

Recommendations for CGM Targets

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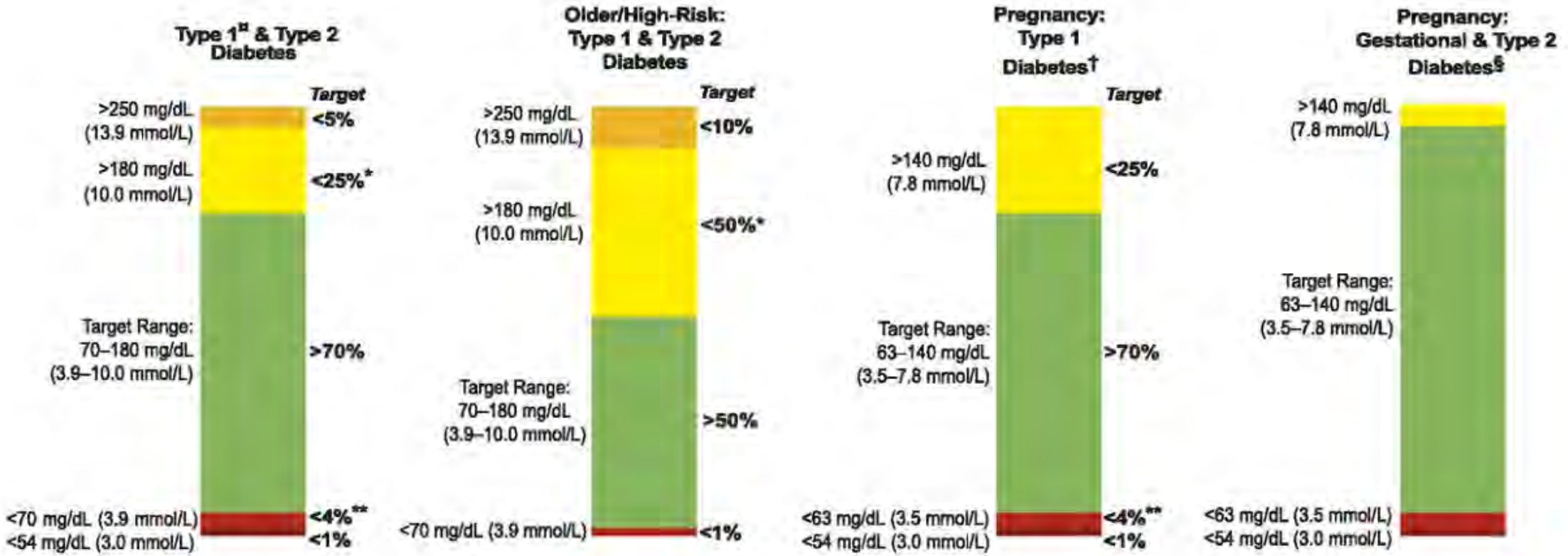


¤ For age <25 yr., if the A1C goal is 7.5%, then set TIR target to approximately 60%. (See *Clinical Applications of Time in Ranges* section in the text for additional information regarding target goal setting in pediatric management.)

† Percentages of time in ranges are based on limited evidence. More research is needed.

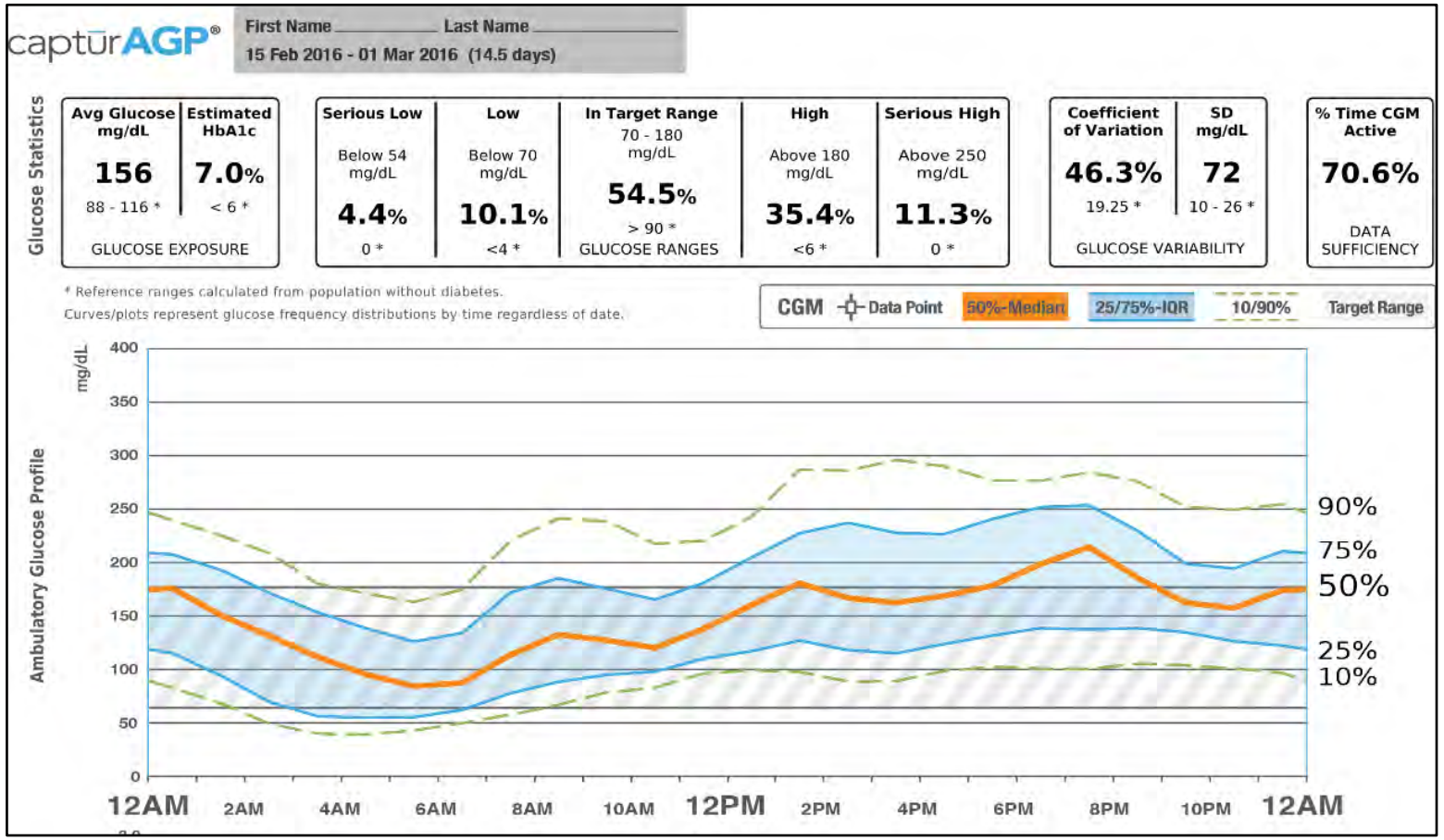
§ Percentages of time in ranges have not been included because there is very limited evidence in this area. More research is needed. Please see *Pregnancy* section in text for more considerations on targets for these groups.

* Includes percentage of values >250 mg/dL (13.9 mmol/L).

** Includes percentage of values <54 mg/dL (3.0 mmol/L).

Battelino et al. Diabetes Care 2019;42:1593–1603

Ambulatory Glucose Profile (AGP)



Standardized Reporting Format
14 days
Daily glucose profiles are combined to make a one day (24-hour) picture.
Gray: target range
Orange: median glucose
Blue: area between blue lines shows 50% of the glucose values
Green: 10% of values are above (90% top line) and 10% are below (10% bottom line)

Connected Devices

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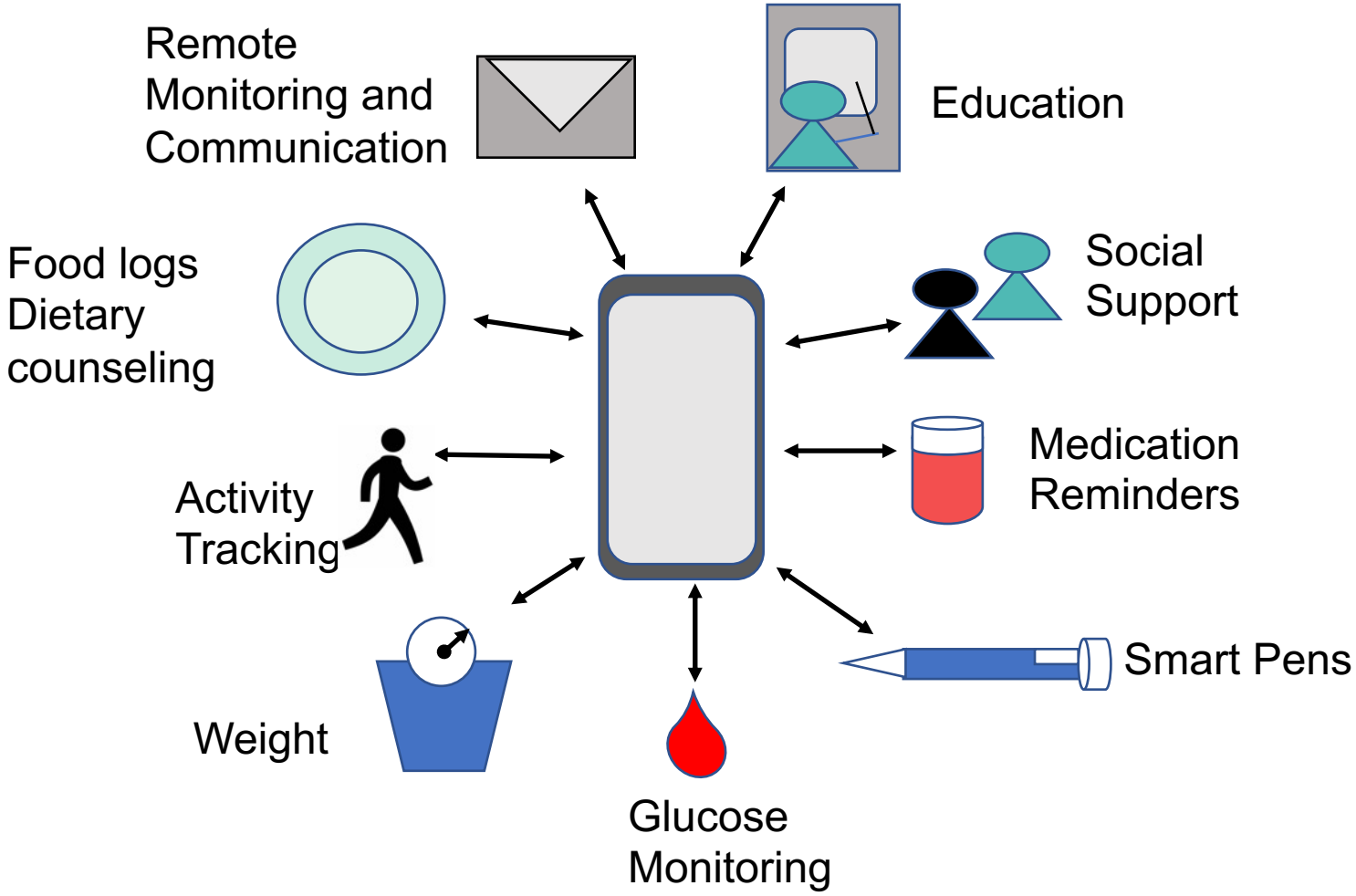
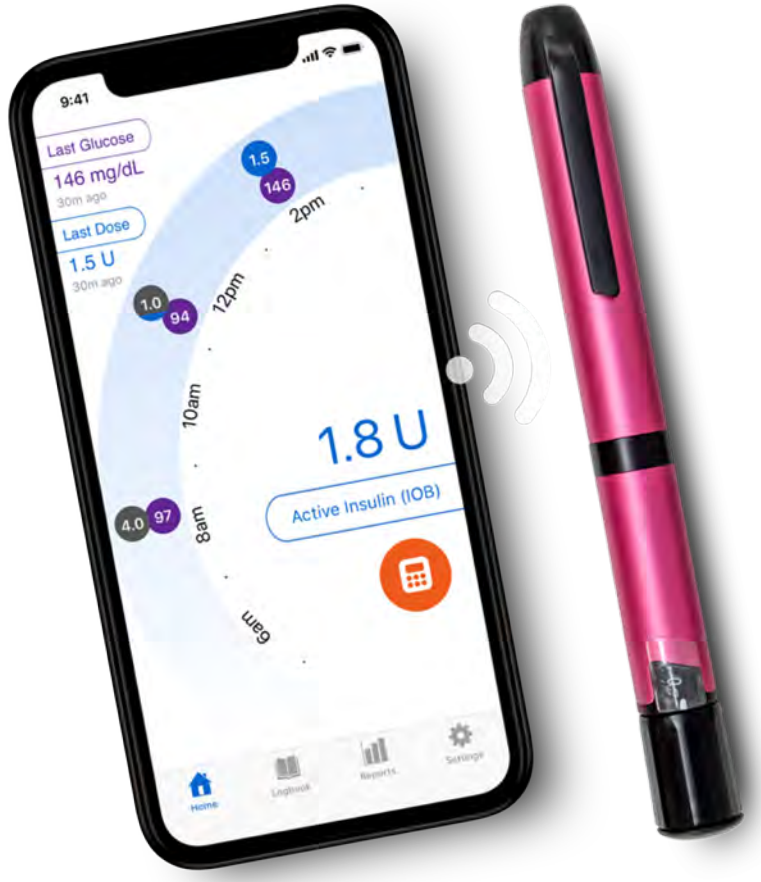


Ashrafzadeh S et al. *Cell Metab*. 2019;29(3):564-575.

Smart Pens

- $35 from Manufacturer
- Lispro/aspart cartridges
- ½ unit increments
- Smartphone App
  - Bolus calculator: carb counting, meal size, fixed
  - Customize by time of day
  - Exercise feature
  - Records actual dose
  - Reminders
- Does not link to meter
- Healthkit



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Bailey et al. Expert Opin Drug Deliv. 2017;14(5):697-703.

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Thank you!

Questions/Discussion

Update Contact Information

A REDCap form will be emailed early next week to update your contact/demographic information.

Your contact information will be shared with:

- Cardi-OH leadership team as a part of internal program evaluation
  - Data will be presented to external audiences in aggregate only (i.e., geographical spread of participants, clinical roles of participants, etc.)
- This Cardi-OH ECHO Tackling Type 2 Diabetes cohort* (name, email address, and practice name and location only)

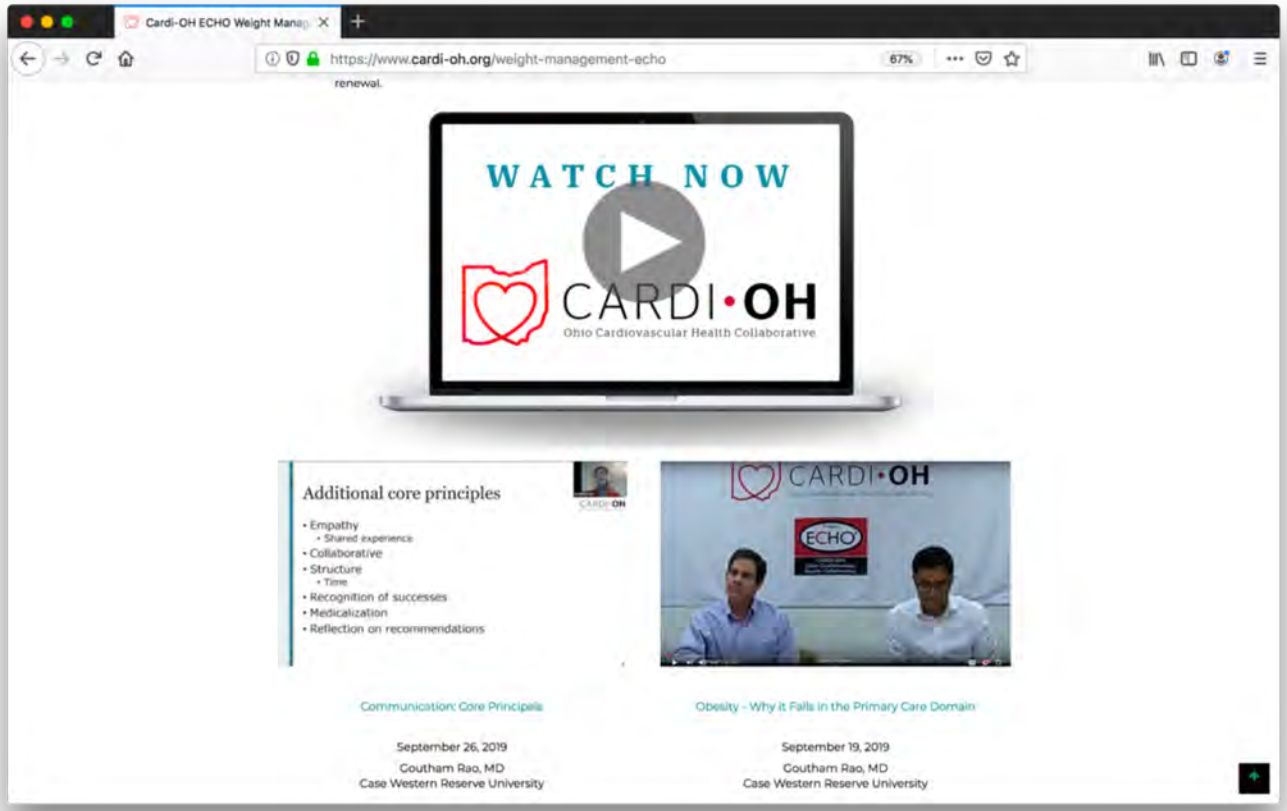
**Email the Clinic Coordinator (jessie.lewis@case.edu) if you wish to OPT OUT of sharing your contact information with this ECHO cohort.*

Please update your contact information by February 18, 2021

Watch Previous Cardi-OH TeleECHO Clinics

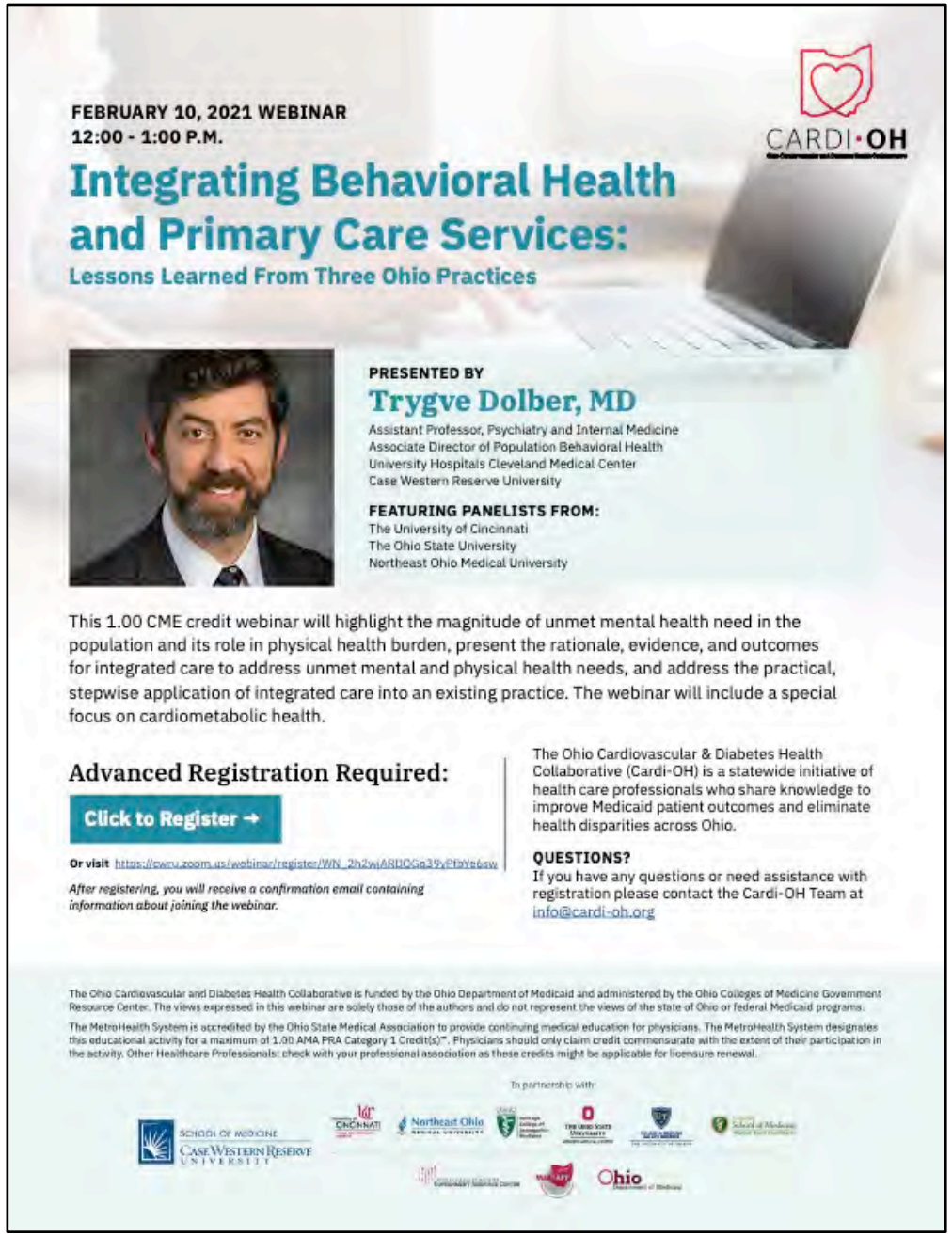
Register on Cardi-OH.org to watch all Tackling Type 2 Diabetes TeleECHO Clinics:

https://www.cardi-oh.org/user/register
https://www.cardi-oh.org/echo/diabetes-spring-2021



Reminders

- A Post-Clinic Survey has been emailed to you.
  Please complete this survey **by Friday at 5:00 PM**.
- *The MetroHealth System is accredited by the Ohio State Medical Association to provide continuing medical education for physicians.*
- *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.*



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Registration Now Open!

February 2021 Webinar

Integrating Behavioral Health and Primary Care Services: Lessons Learned From Three Ohio Practices

Wednesday, February 10, 2021
12:00 – 1:00 PM EST

Register online:
https://www.cardi-oh.org/