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

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Ohio Department of Medicaid

Project ECHO®

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Cardi-OH ECHO

Your Patient with Diabetes at Risk for Heart Disease: A Series of Case Discussions

October 21, 2021

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Disclosure Statements

- The following planners, speakers, and/or content experts of the CME activity have financial relationships with commercial interests to disclose:
  - Marilee Clemons reports receiving consulting fees from Novo Nordisk.
  - Kathleen Dungan, MD, MPH reports receiving consulting fees from Eli Lilly, Novo Nordisk and Boehringer, research support from Sanofi, , Viacyte, and Abbott and presentation honoraria from UpToDate, Elsevier, ACHL, and CMHC.
  - 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 Mideast.
  - Jackson T. Wright, Jr., MD, PhD reports receiving fees for serving as an advisor to Medtronic.
  - These financial relationships are outside the presented work.
- All other planners, speakers, and/or content experts of the CME activity have no financial relationships with commercial interests to disclose.

Person-Centered Language Recommendations

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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 “sex” when referring to the biological distinction.
- **Race**: Race is a social construct that is broadly used to categorize people based on physical characteristics, behavioral patterns, and geographic location. Race is not a proxy for biology or genetics. Examining health access, quality, and outcome data by race and ethnicity allows the healthcare system to assist in addressing the factors contributing to inequity and ensure that the health system serves the needs of all individuals.
- **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 “inner-city.”

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

New and Emerging Treatments 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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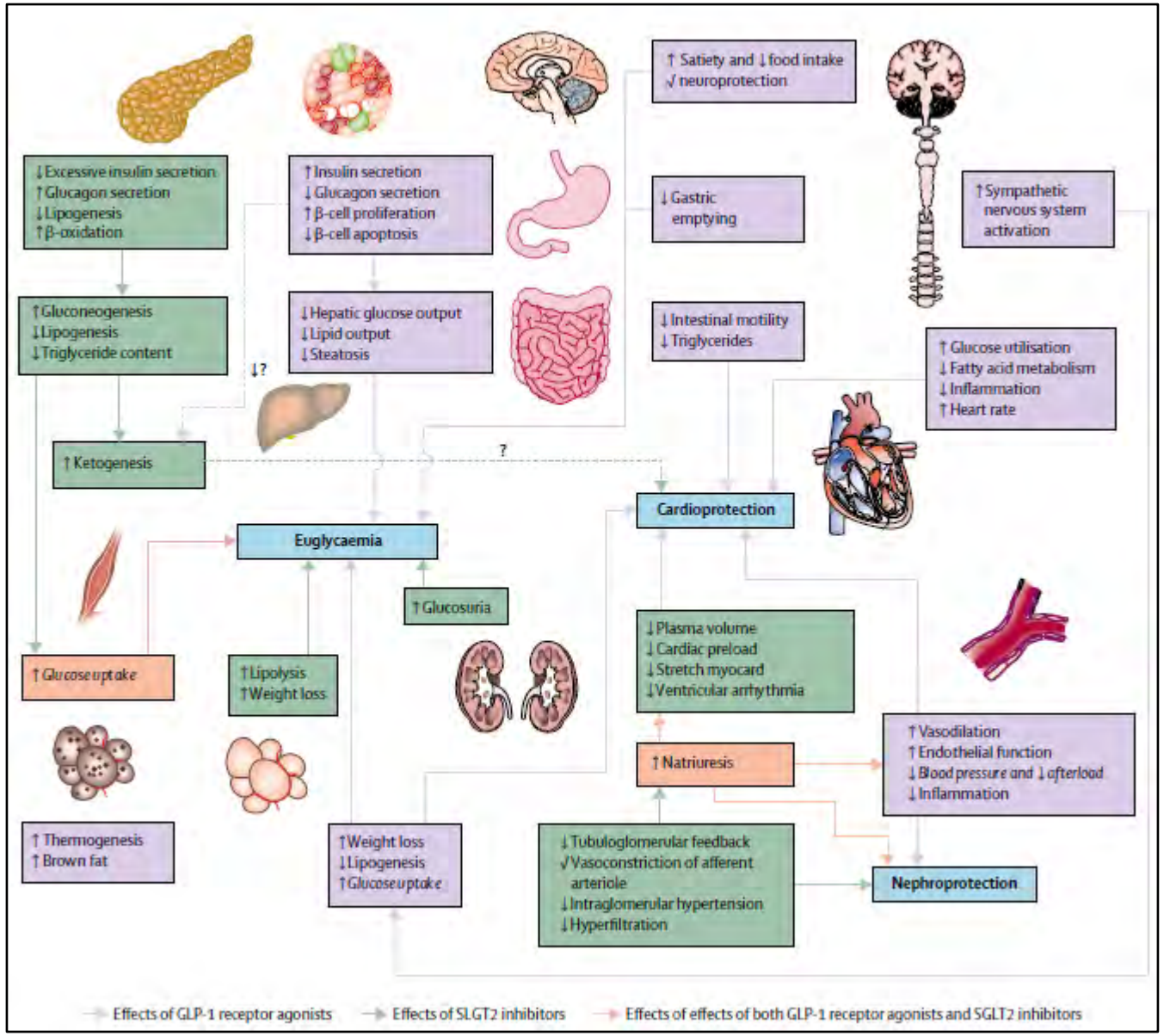
1. Describe the role and benefits (including cardiovascular benefits) of GLP-1 agonists and SGLT-2 inhibitors in the care of patients with type 2 diabetes.
2. Describe current recommendations for selection and titration of insulin therapy.
3. Highlight the role of continuous glucose monitoring in patients with diabetes.

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				

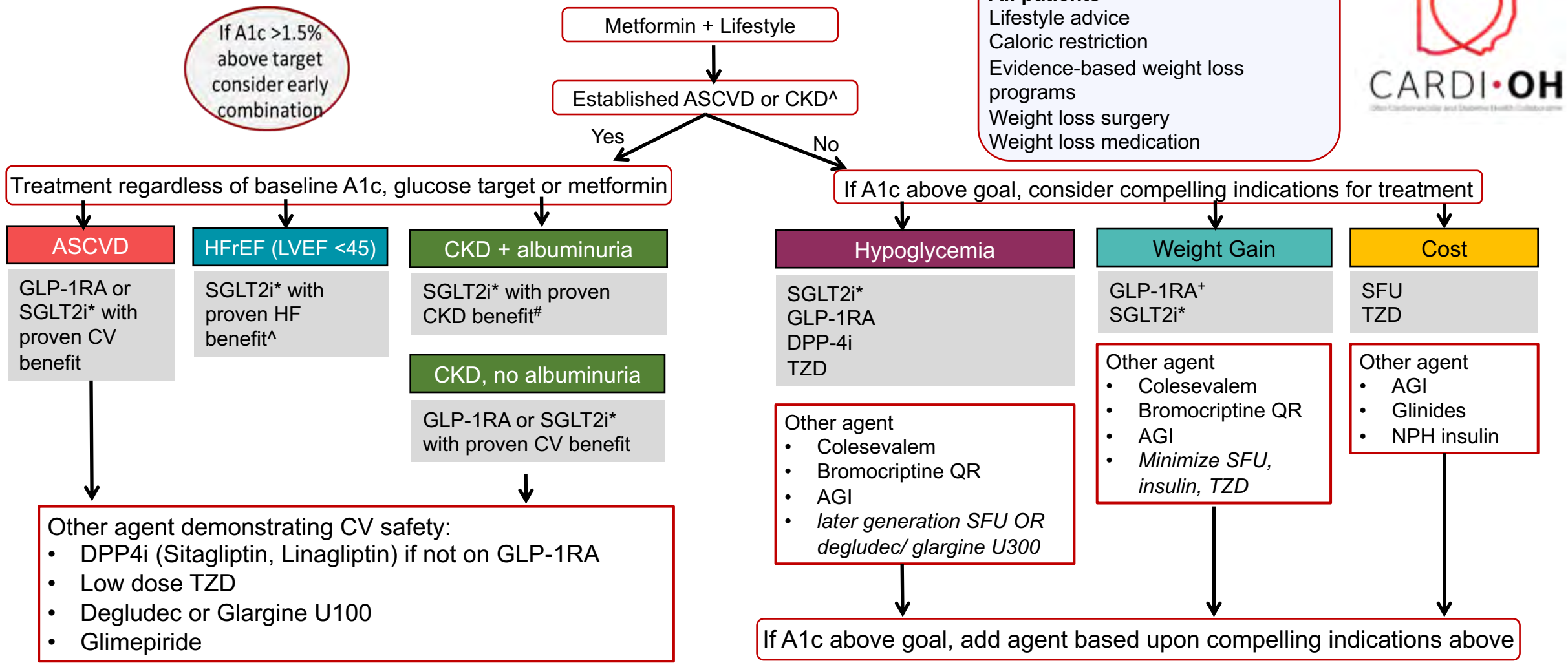
Study	ELIXA[6]	LEADER[7]	SUSTAIN 6[8]	EXSCEL[9]	REWIND[10]	HARMONY[11]	PIONEER 6
GLP1-RA	lixisenatide	liraglutide	semaglutide	exenatide LR	dulaglutide	albiglutide	Oral sema
Comparator	placebo	placebo	placebo	placebo	placebo	placebo	Placebo
N	6068	9340	3297	14,752	9901	9463	3183
Results	2015	2015 ✚	2016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

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

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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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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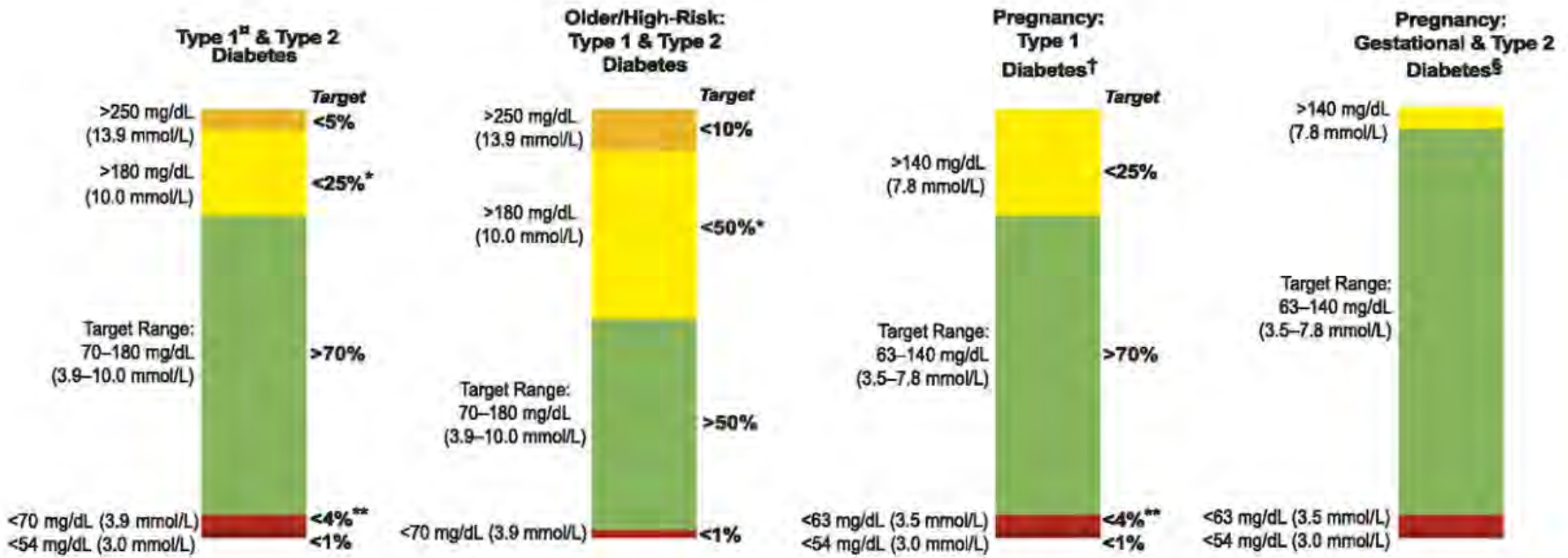

¤ For age <25 yr., if the A1C goal is 7.5%, then set TIR target to approximately 60%. (See *Clinical Applications of Time in Ranges* section in the text for additional information regarding target goal setting in pediatric management.)

† 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)

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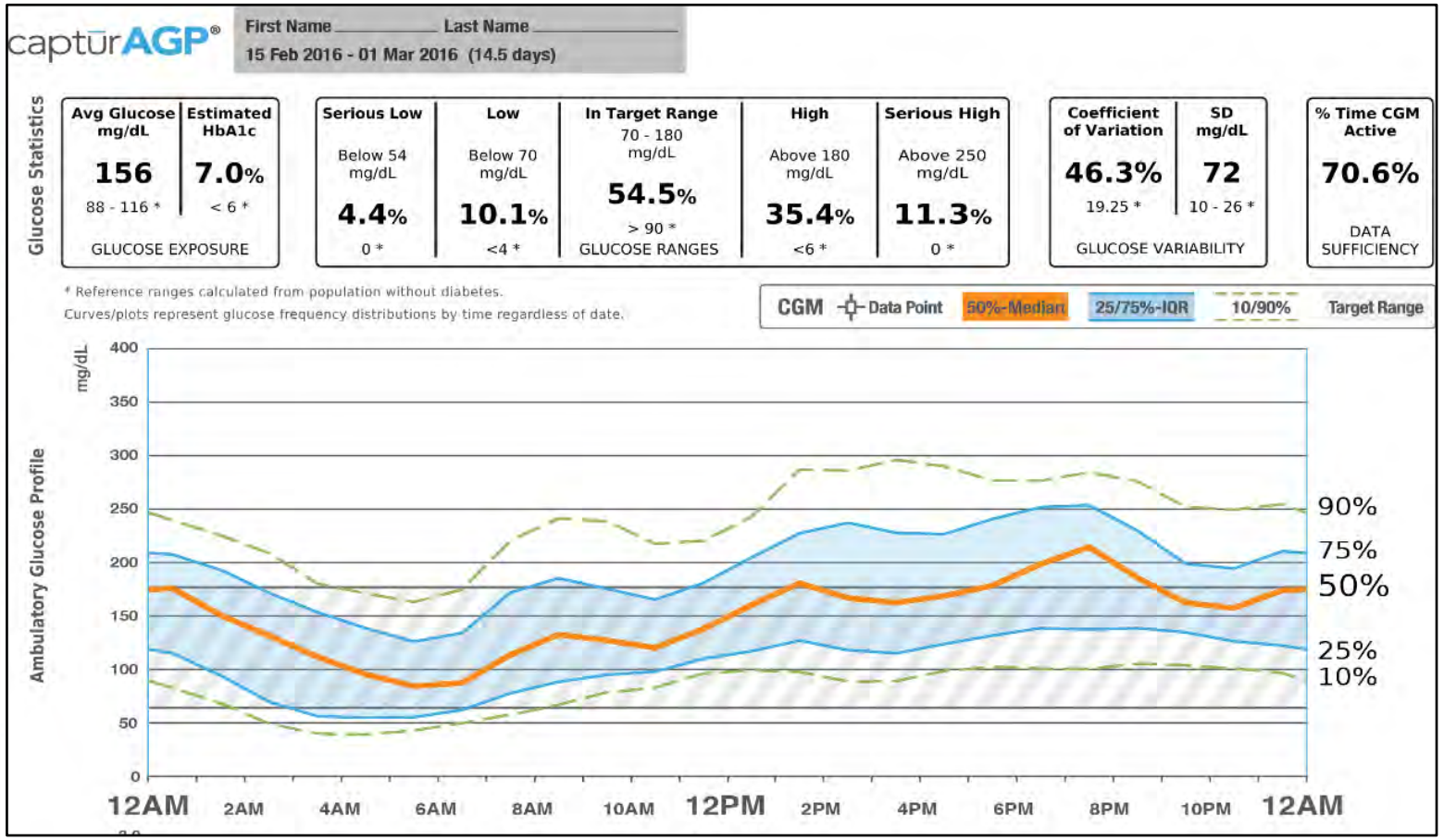

Standardized Reporting Format
14 days
Daily glucose profiles are combined to make a one day (24-hour) picture.
Gray: target range
Orange: median glucose
Blue: area between blue lines shows 50% of the glucose values
Green: 10% of values are above (90% top line) and 10% are below (10% bottom line)

Thank you!

Questions/Discussion