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

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OHIO UNIVERSITY Heritage College of Osteopathic Medicine

Northeast Ohio MEDICAL UNIVERSITY

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Ohio Department of Medicaid

Project ECHO®

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Cardi-OH ECHO Tackling Type 2 Diabetes

Thursday, October 8, 2020

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.
  - Siran M. Koroukian, PhD receives grant funds for her role as a co-investigator on a study funded by Celgene.
  - 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.
  - Martha Sajatovic, MD receives grant support as PI of studies with Nuromate and Otsuka, study design consulting fees from Alkermes, Otsuka, Neurocrine, and Health, and publication development royalties from Springer Press and Johns Hopkins University.
  - 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

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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

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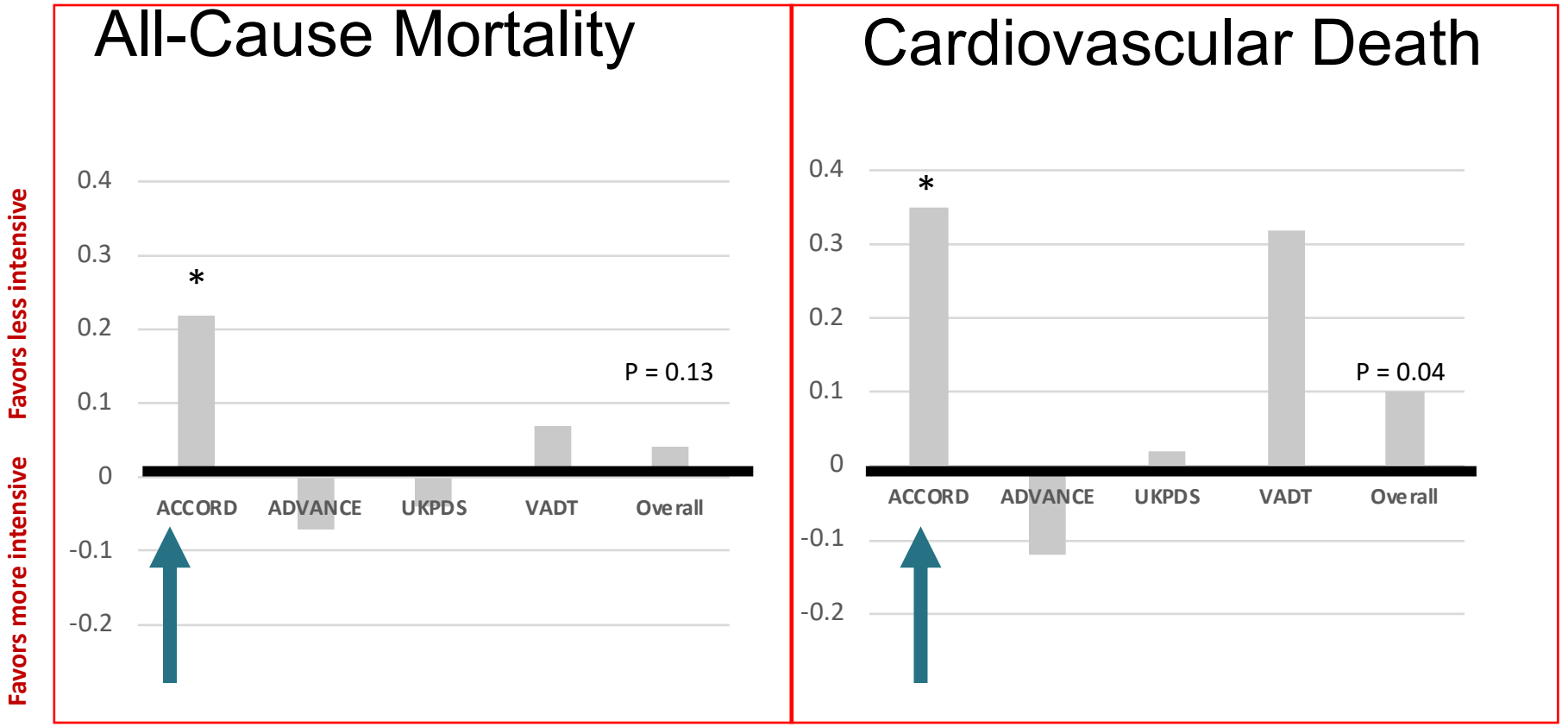

*p<0.05

Diabetologia 2009;52:2288-98

UKPDS: Legacy Effect of Earlier Glucose Control

After median 8.5 years post-trial follow-up

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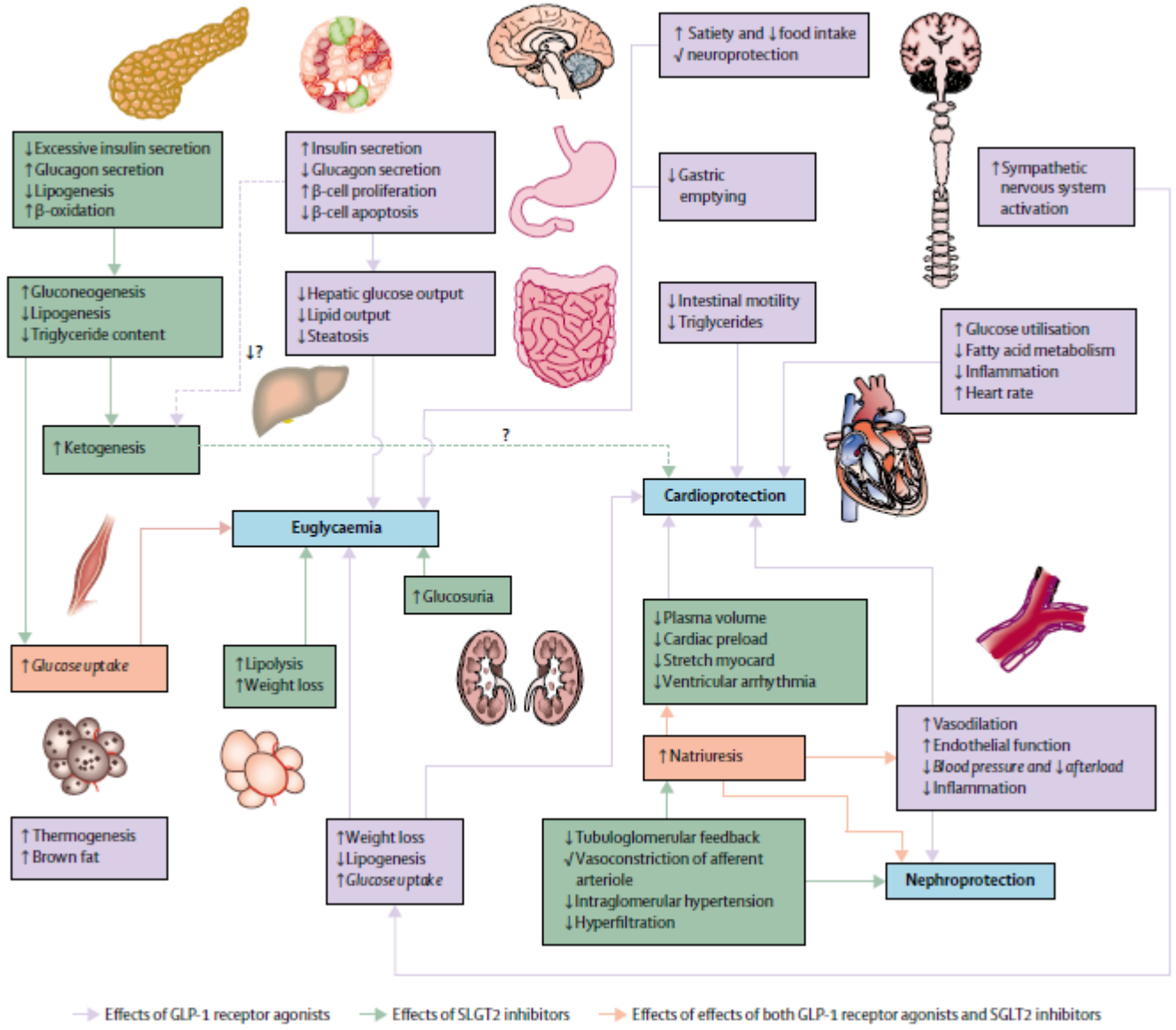
Aggregate Endpoint		**1997**	**2007**
Any diabetes related endpoint	*RRR:*	12%	**9%**
	P:	0.029	**0.040**
Microvascular disease	*RRR:*	25%	**24%**
	P:	0.0099	**0.001**
Myocardial infarction	*RRR:*	16%	**15%**
	P:	0.052	**0.014**
All-cause mortality	*RRR:*	6%	**13%**
	P:	0.44	**0.007**

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

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).

* non-insulin

Meta-analysis of CVOT

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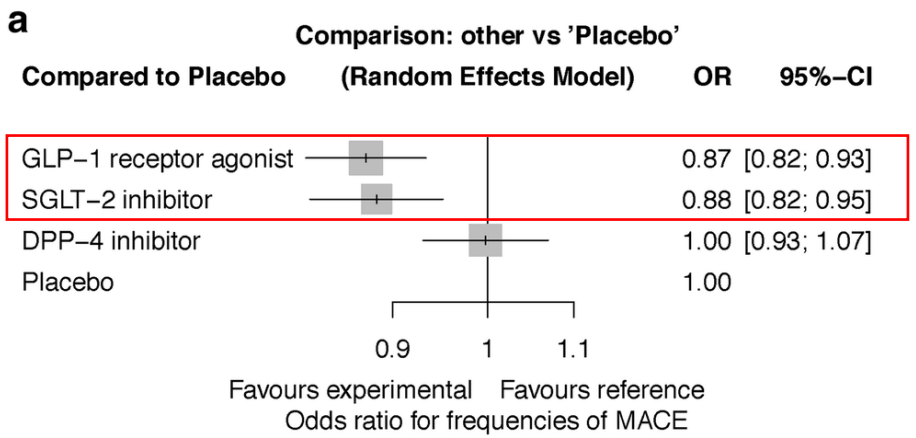
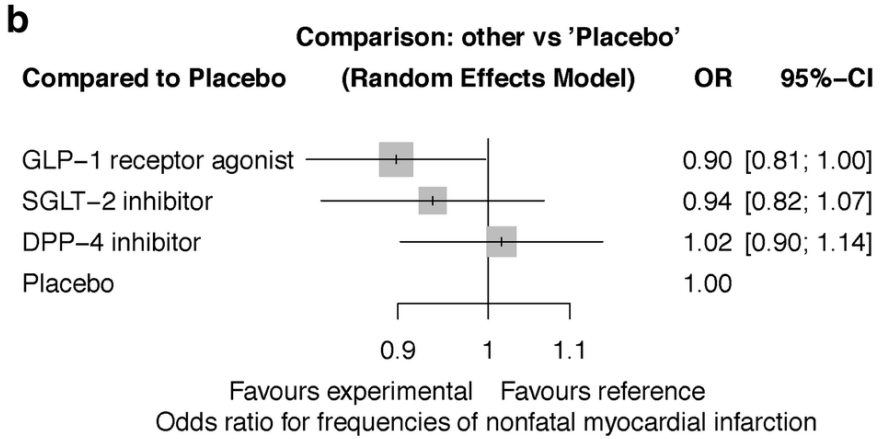
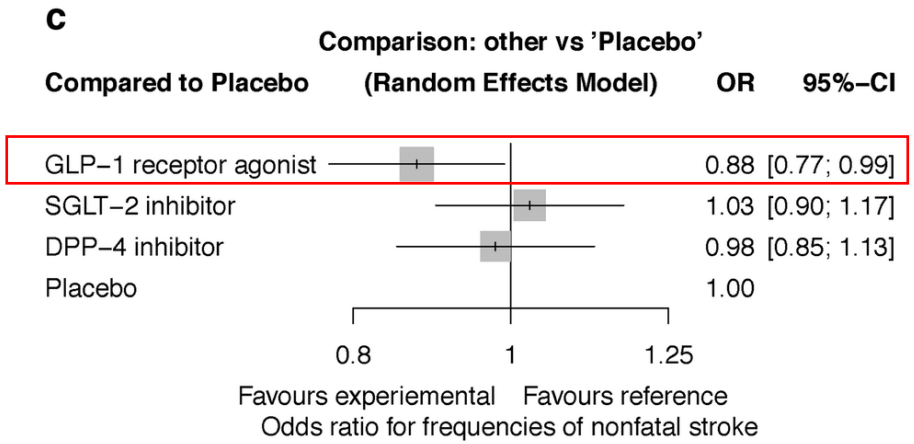
3-point MACE



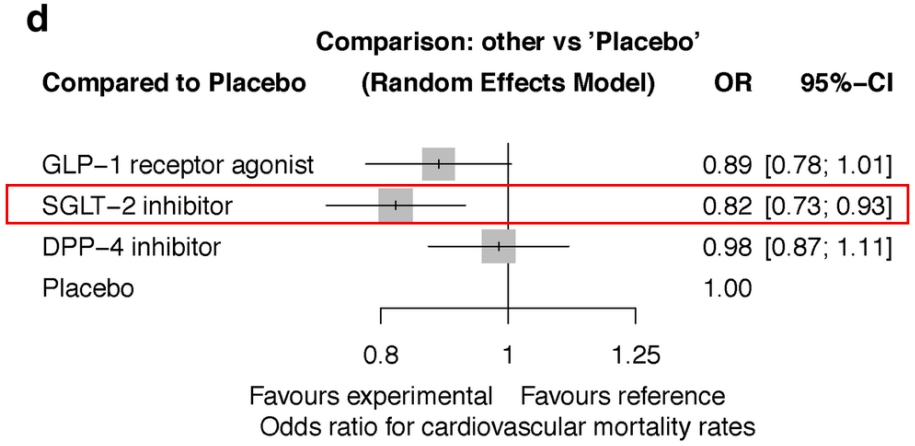
Nonfatal MI



Nonfatal Stroke



CV Death

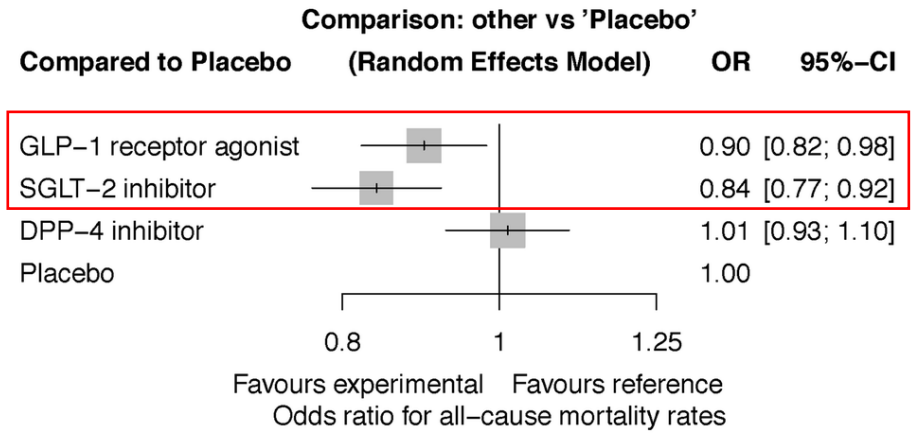


- Meta-analysis of CV outcomes trials
- Did not include CAROLINA, REWIND, PIONEER 6 or VERTIS

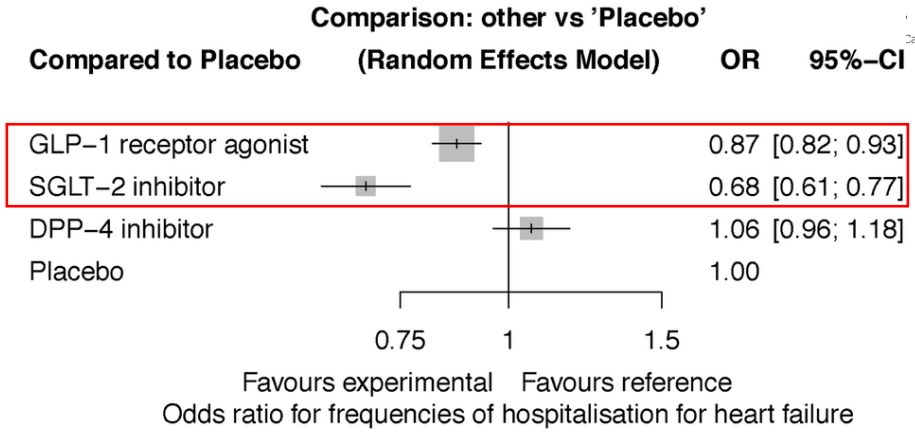
Fei et al. Cardiovasc Diabetol. 2019;18(1):112.

Meta-analysis of CVOT

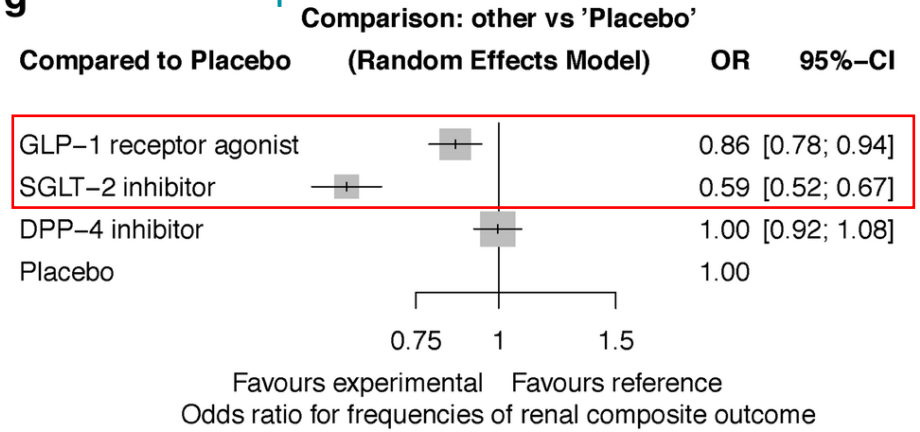
e All-cause Death



f HF hospitalization

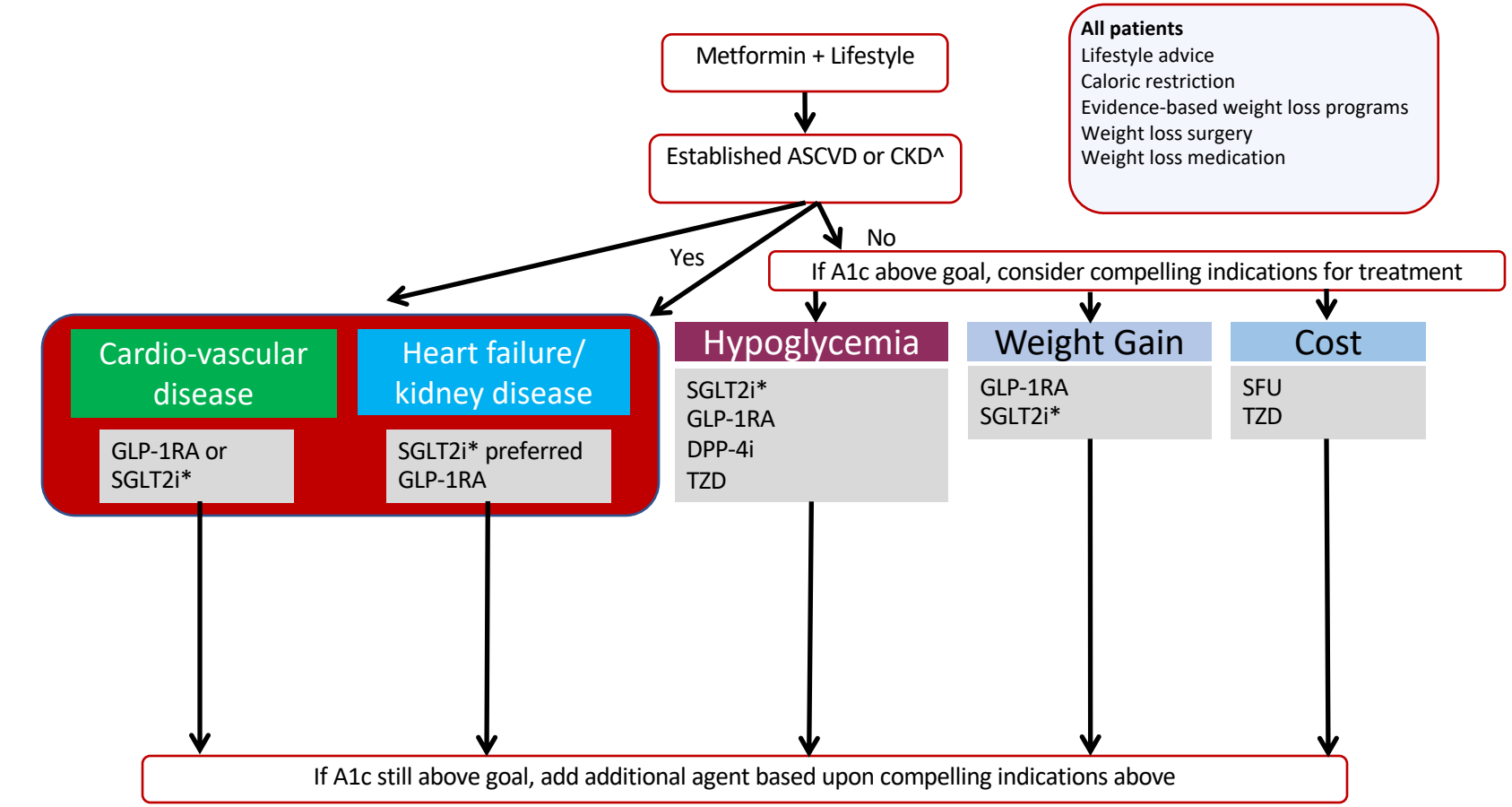


g Renal Composite Outcome



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

ADA Standards of Care 2020



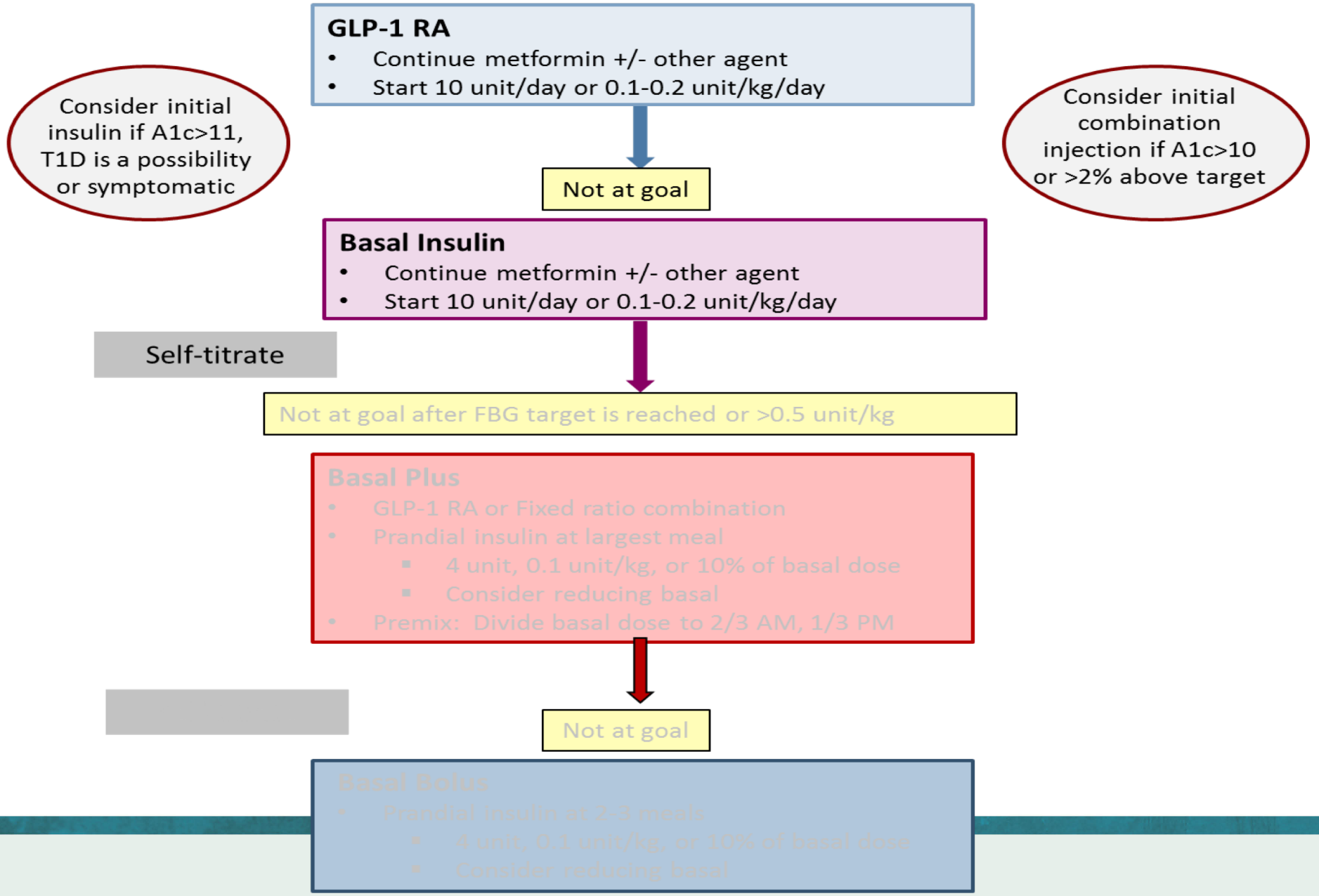
ASCVD=atherosclerotic cardiovascular disease, CKD=chronic kidney disease, GLP-1RA=glucagon-like peptide-1 receptor agonist, SGLT28i=sodium-glucose cotransporter-2 inhibitor, AGI=alpha-glucosidase inhibitor, SFU=sulfonylurea, TZD=thiazolidinedione

*if adequate eGFR

^Medication added regardless of baseline HbA1c

Diabetes Care 2020;43(S1):S1-S212

Intensifying to Injectable Therapies



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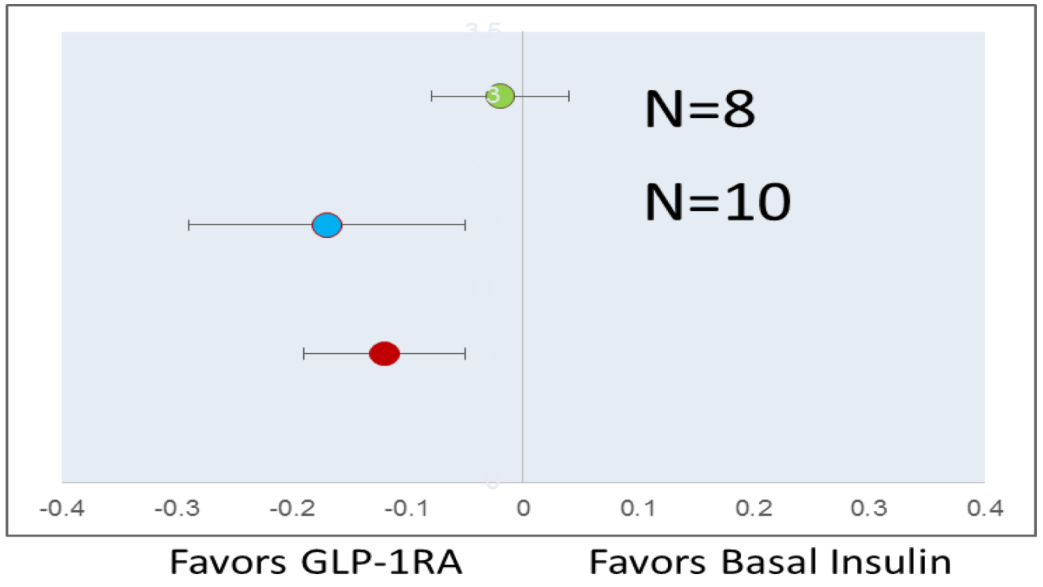
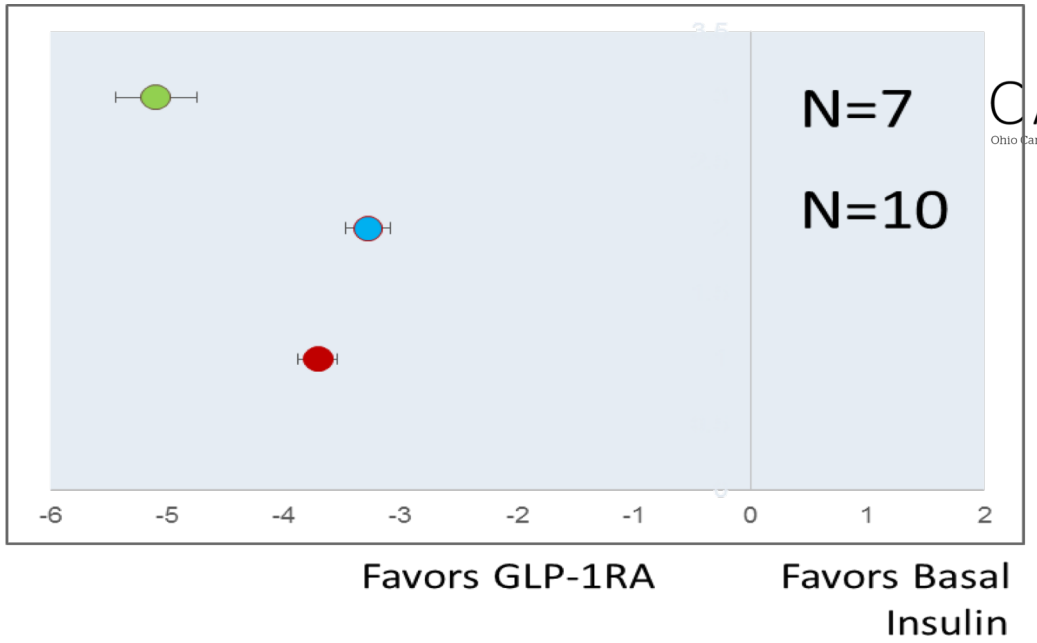
Davies et al. Dia Care 2018;41:2669-2701

GLP-1RA or Basal Insulin?





HbA1c:
Treatment difference 0.12% (p<0.0001)
Driven by long-acting GLP-1RA

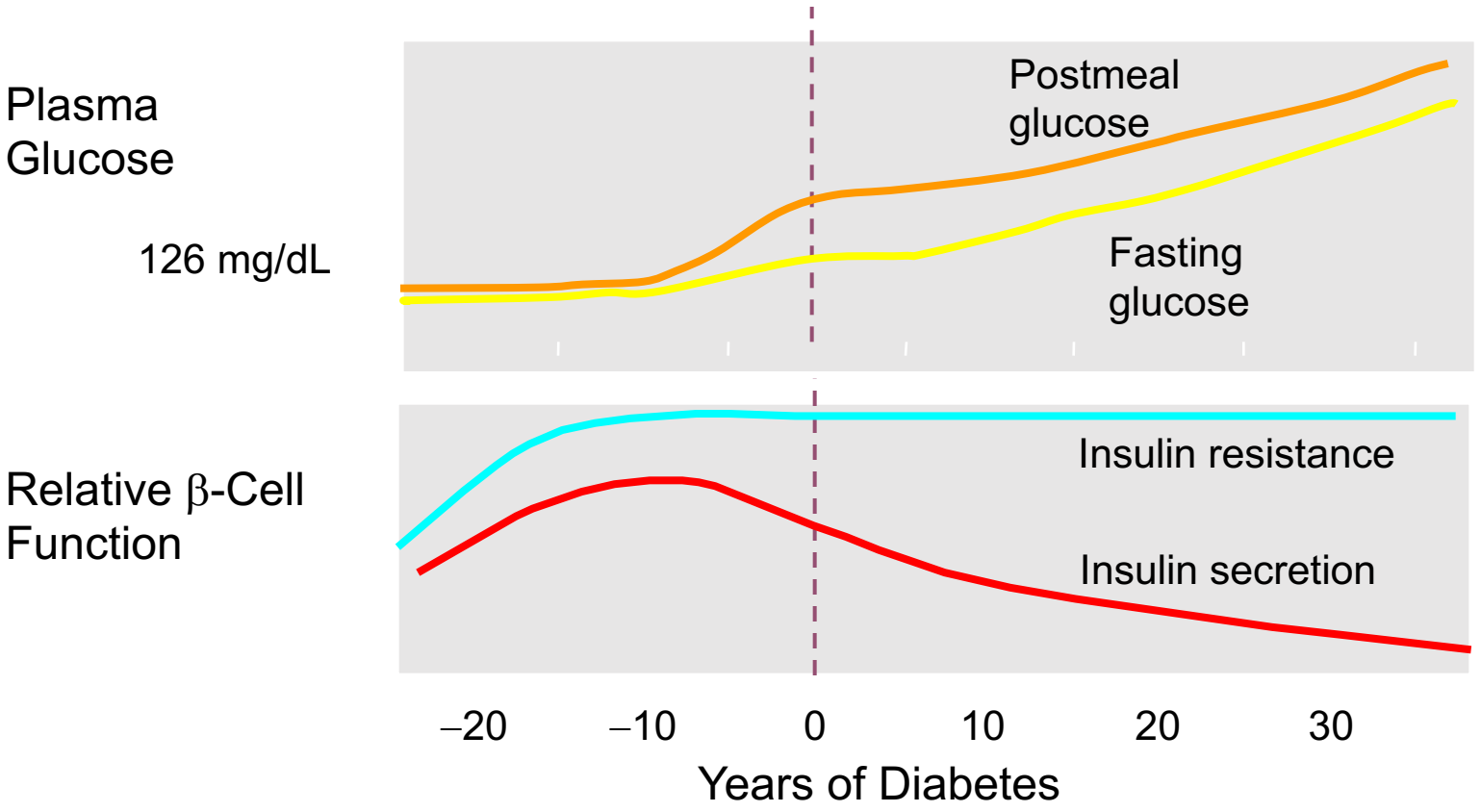
Exenatide BID
Long-acting GLP-1 (Exenatide QW, Dulaglutide, Albiglutide, Liraglutide)
Overall

Weight:
Treatment difference 3.7 kg (p<0.0001)

Hypoglycemia: 15% less (p<0.0001)

Abd El Aziz, Diabetes Obes Metabl 2017;19(2):216-227

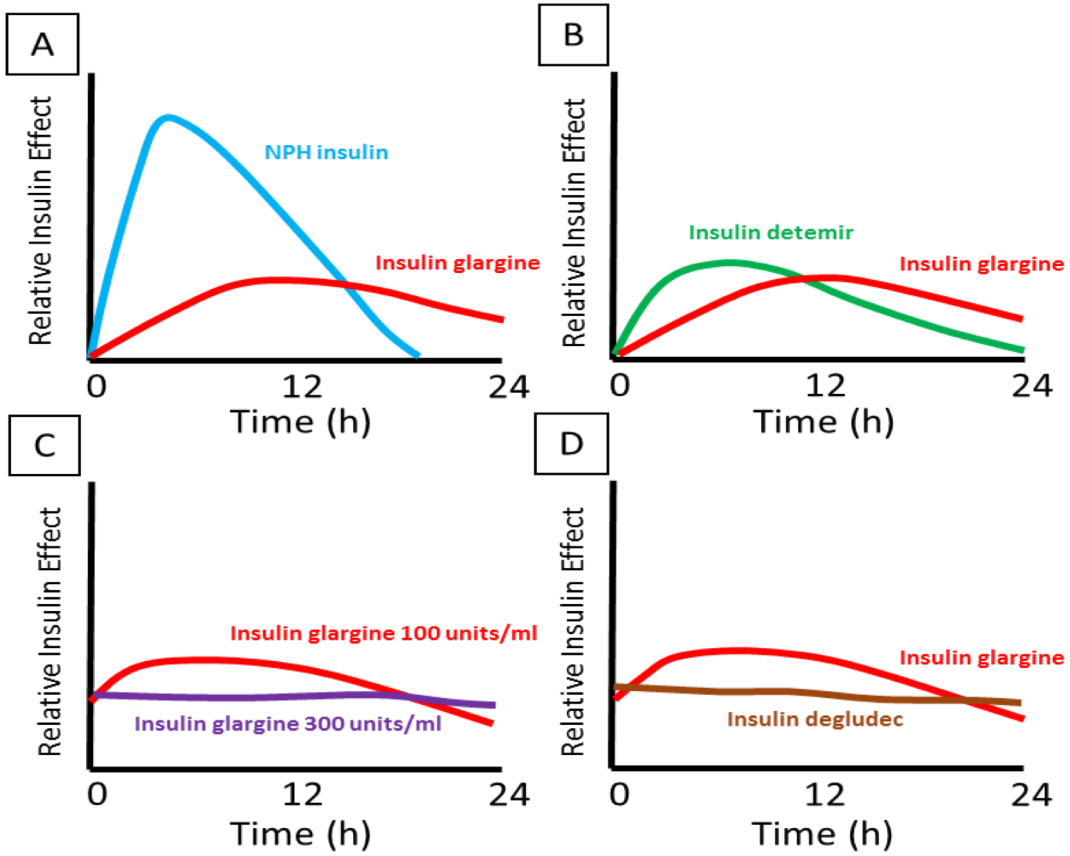
Natural History of T2DM



- 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.

Basal Insulins

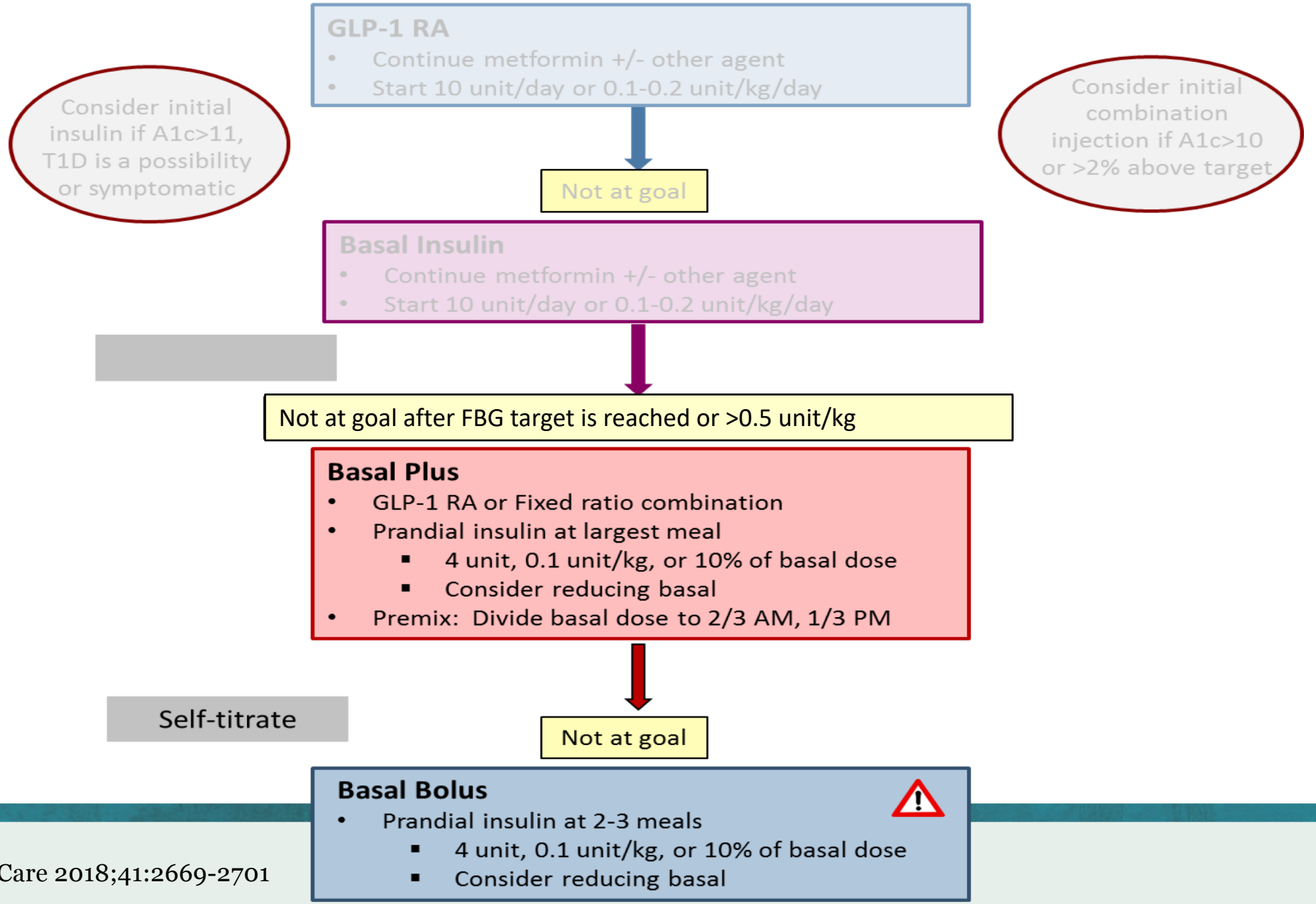


<u>Ultra-long acting:</u>

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

Pettus et al. Diabetes Metab Res Rev 2015;

Intensifying to Basal Plus



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Davies et al. Dia Care 2018;41:2669-2701

Optimizing Basal Bolus insulin

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- Review adherence, simplify
- Refer to DSME
- Use insulin sparing Rx
- Manage carbohydrates, activity
- Insulin analogues, especially if hypoglycemia
- Ultra-long acting insulins (if needed)
- Concentrated insulins (>250 unit/day)
- Delivery: pump, smart pens, inhaled insulin

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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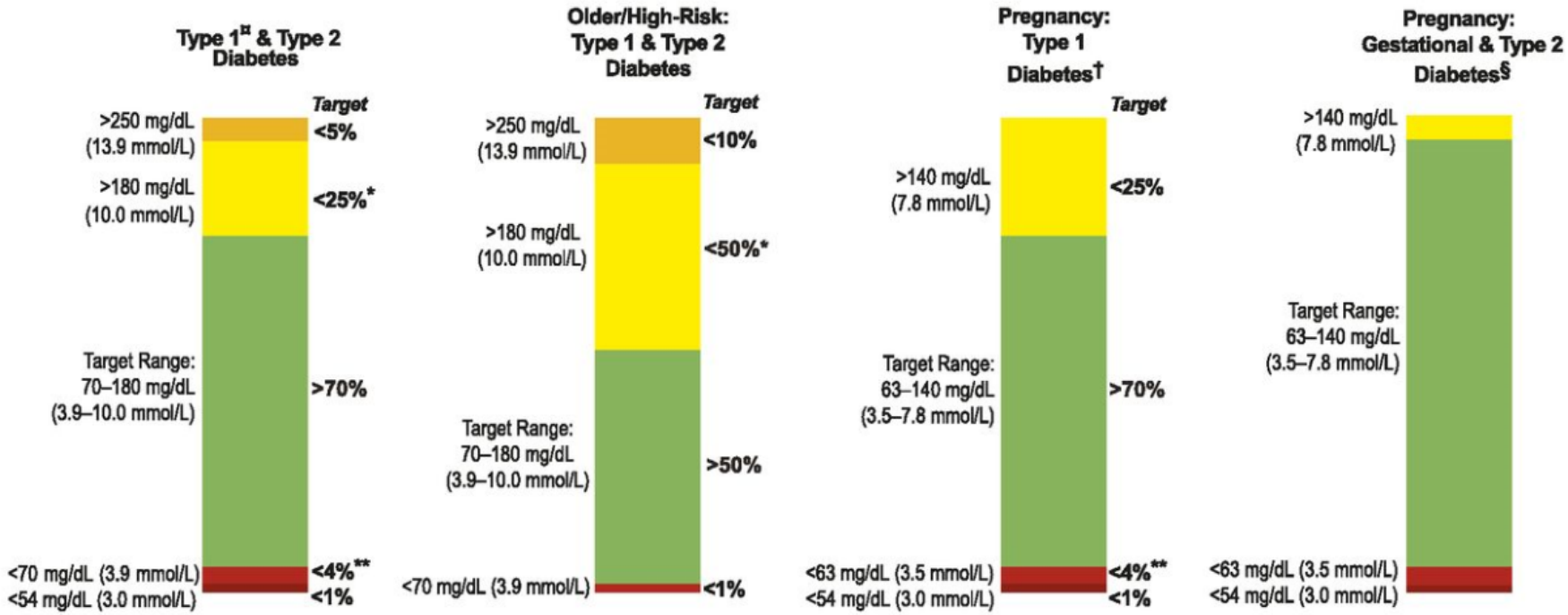

¤ For age <25 yr., if the A1C goal is 7.5%, then set TIR target to approximately 60%. (See *Clinical Applications of Time in Ranges* section in the text for additional information regarding target goal setting in pediatric management.)

† 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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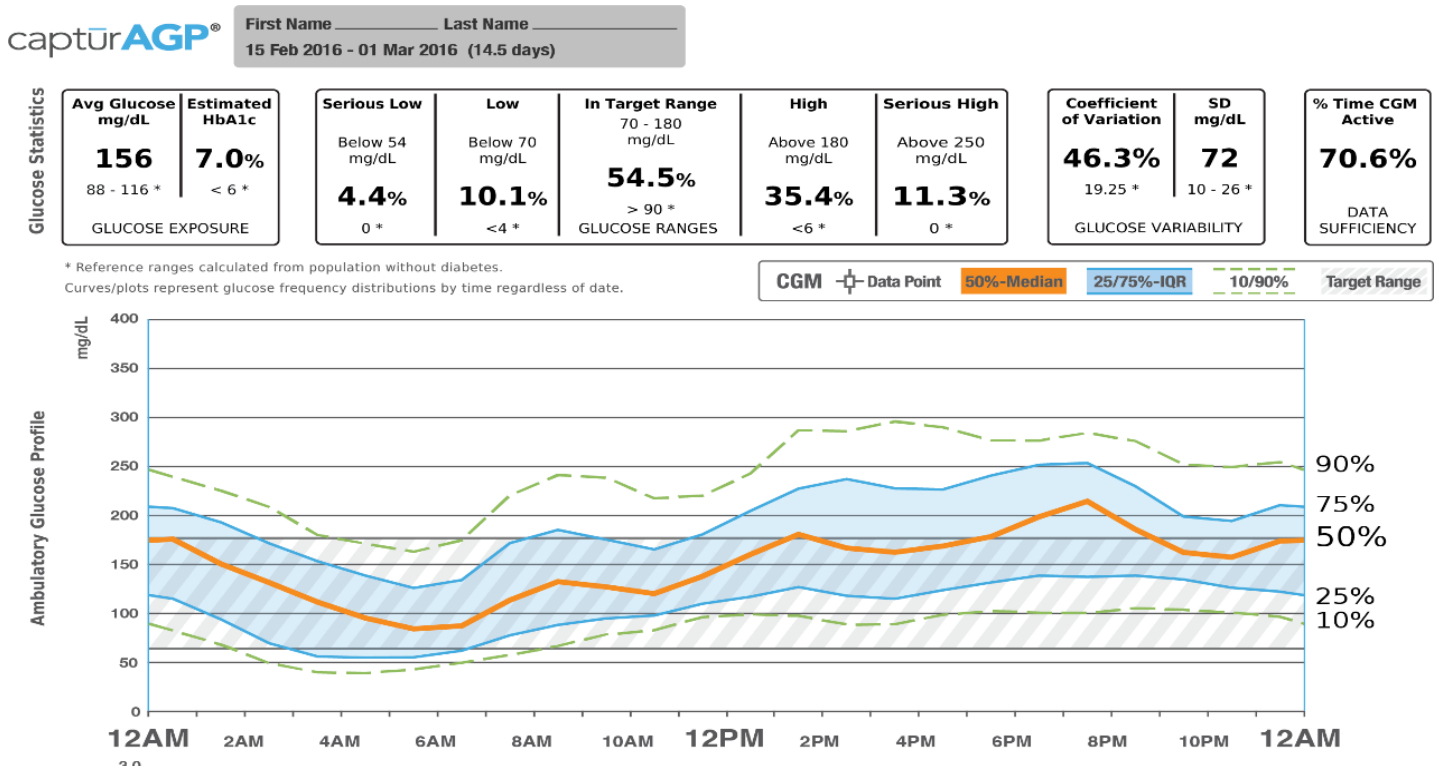

Standardized Reporting Format
14 days
Daily glucose profiles are combined to make a one day (24-hour) picture.
Gray: target range
Orange: median glucose
Blue: area between blue lines shows 50% of the glucose values
Green: 10% of values are above (90% top line) and 10% are below (10% bottom line)

Connected Devices

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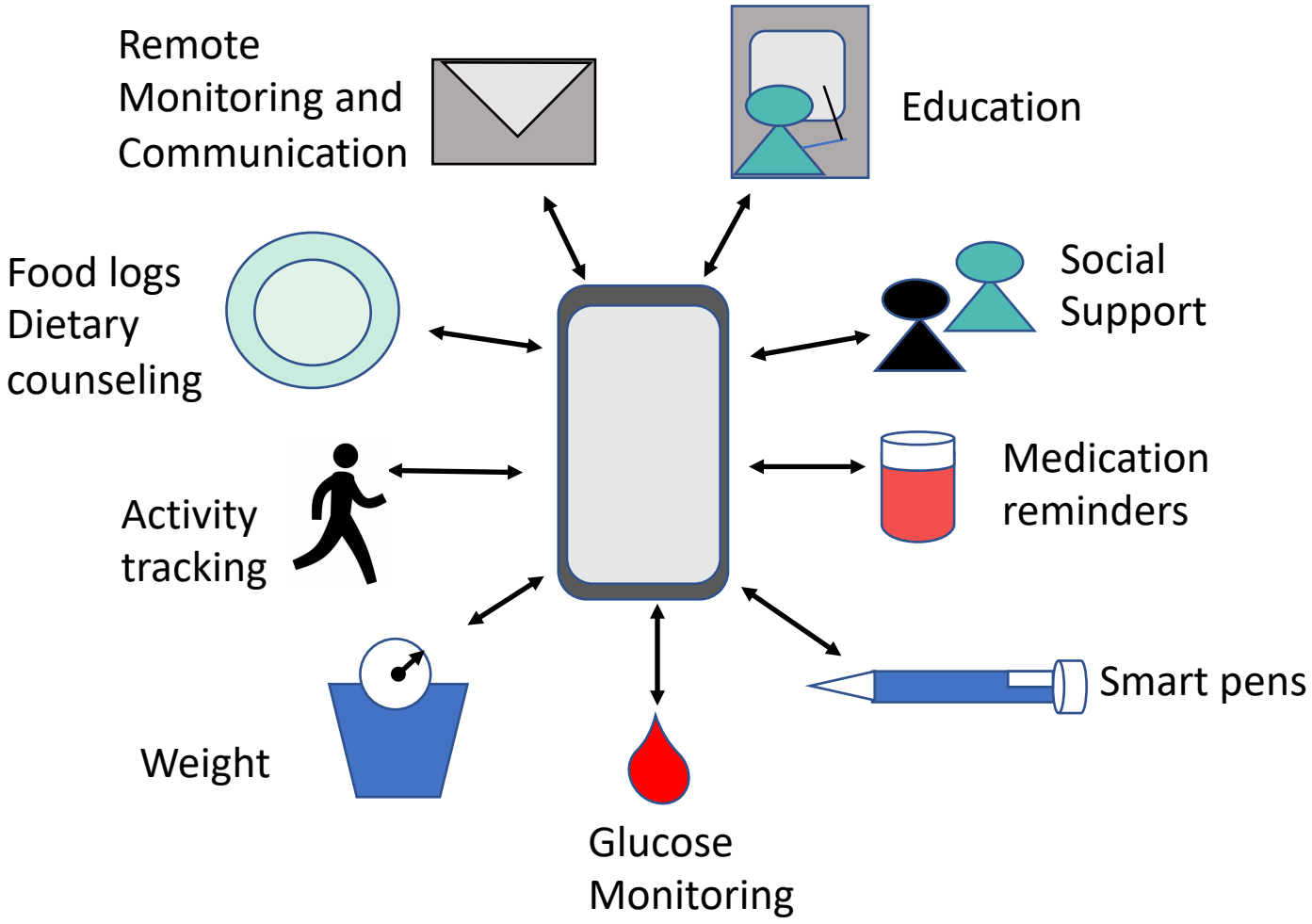
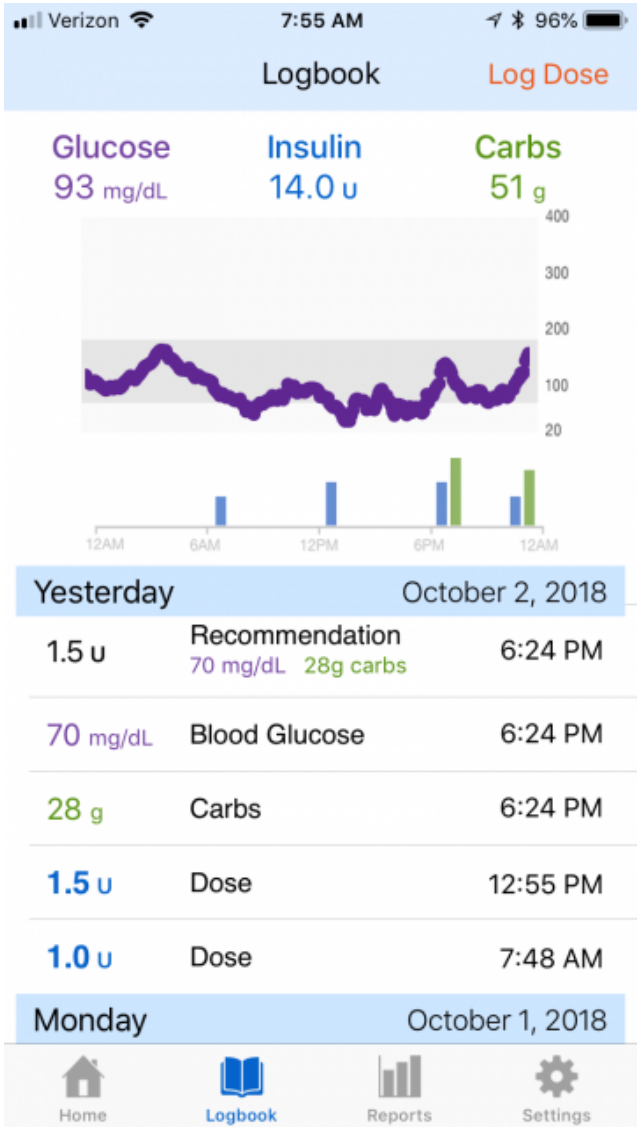
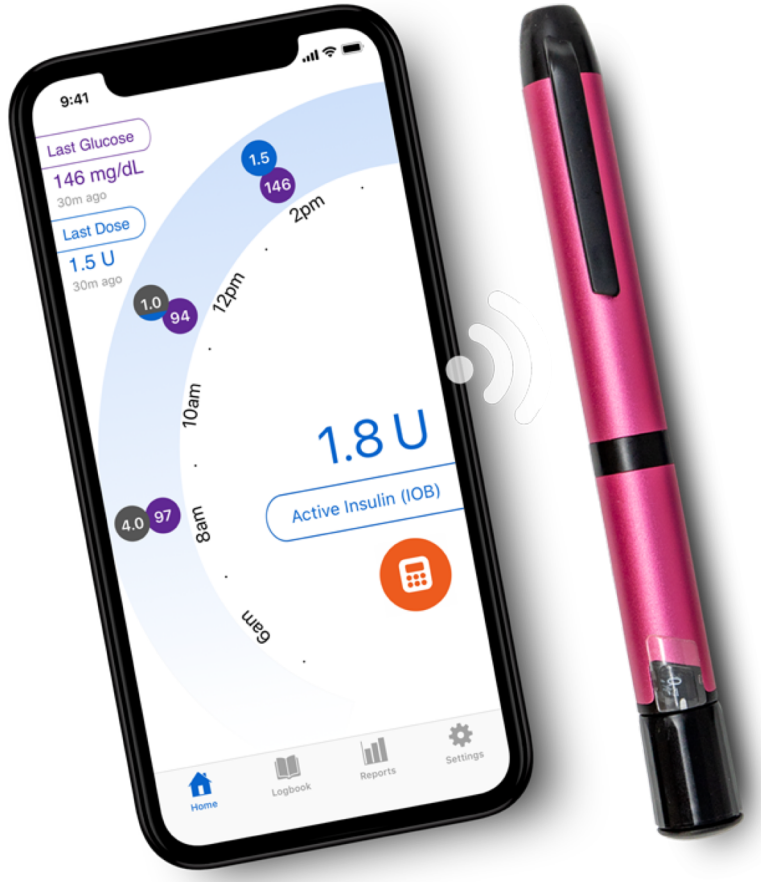


Ashrafzadeh S et al. *Cell Metab*. 2019;29(3):564-575.

Smartpens

- $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