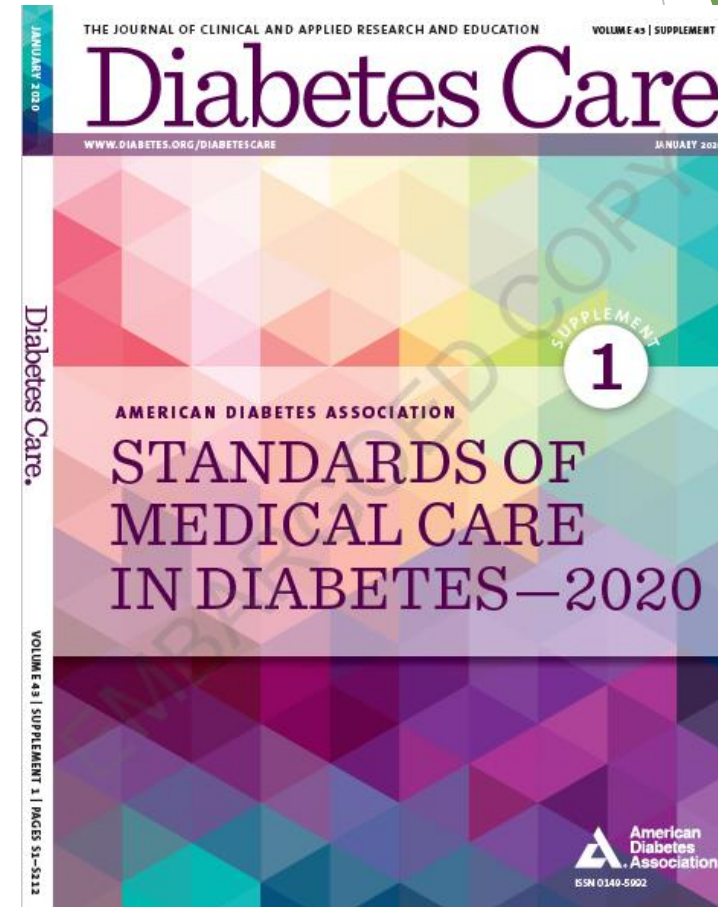# Standards of Medical Care in Diabetes - 2020

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Alaska Native Tribal Health Consortium
Diabetes Program
October 2020

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

Objectives: At the end of this session, participants will be able to

- Outline ADA diagnostic criteria for Diabetes and Pre-Diabetes

- Review Goals of Care from Standards of Medical Care in Diabetes 2020 from the ADA

  - Glucometer vs Continuous Glucose Monitoring (CGM)

- Review pharmacologic recommendations of glycemic treatment for type 2 diabetes

- Review Other Maintenance Care for Diabetes

1. Type of DM
2. CV hx, CV risk? Aspirin?
3. A1C/ fasting glucose? Hypoglycemia events?
4. BP/ACEi?
5. LDL/statin?
6. CKD/ eGFR & microalbumin/cr ratio
7. Eye (retinopathy?)/ Dental
8. Foot (neuropathy?)
9. Tobacco/ Etoh/ other drugs
10. Vaccines: pneumovax/flu/zoster
11. Diet and activities

► I have no conflict of interest to disclose for this presentation.

PRE-diabetes

Table 2.5—Criteria defining prediabetes*

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)
OR
2-h PG during 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)
OR
A1C 5.7–6.4% (39–47 mmol/mol)

Table 2.3—Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in overweight or obese (BMI $\geq$25 kg/m^2 or $\geq$23 kg/m^2 in Asian Americans) adults who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension ($\geq$140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - Women with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. Patients with prediabetes (A1C $\geq$5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

CVD, cardiovascular disease; GDM, gestational diabetes mellitus.

ADA 2020

Diagnosis of Diabetes

Table 2.2—Criteria for the diagnosis of diabetes

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG ≥200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; WHO, World Health Organization; 2-h PG, 2-h plasma glucose. *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

CLASSIFICATION

Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency)
2. Type 2 diabetes (due to a progressive loss of β-cell insulin secretion frequently on the background of insulin resistance)
3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)
4. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)

ADA 2020

DECISION CYCLE FOR PATIENT-CENTERED GLYCEMIC MANAGEMENT IN TYPE 2 DIABETES

Agree to use CGM

REVIEW AND AGREE ON MANAGEMENT PLAN

- Review management plan
- Mutual agreement on changes
- Ensure agreed modification of therapy is implemented in a timely fashion to avoid clinical inertia
- Decision cycle undertaken regularly (at least once/twice a year)

ASSESS KEY PATIENT CHARACTERISTICS

- Current lifestyle
- Comorbidities, i.e., ASCVD, CKD, HF
- Clinical characteristics, i.e., age, HbA_{1c}, weight
- Issues such as motivation and depression
- Cultural and socioeconomic context

ONGOING MONITORING AND SUPPORT INCLUDING:

- Emotional well-being
- Check tolerability of medication
- Monitor glycemic status
- Biofeedback including SMBG, weight, step count, HbA_{1c}, blood pressure, lipids

GOALS OF CARE

- Prevent complications
- Optimize quality of life

CONSIDER SPECIFIC FACTORS THAT IMPACT CHOICE OF TREATMENT

- Individualized HbA_{1c} target
- Impact on weight and hypoglycemia
- Side effect profile of medication
- Complexity of regimen, i.e., frequency, mode of administration
- Choose regimen to optimize adherence and persistence
- Access, cost, and availability of medication

For those with more complex regimen

IMPLEMENT MANAGEMENT PLAN

- Patients not meeting goals generally should be seen at least every 3 months as long as progress is being made; more frequent contact initially is often desirable for DSMES

AGREE ON MANAGEMENT PLAN

- Specify SMART goals:
  - **S**pecific
  - **M**easurable
  - **A**chievable
  - **R**ealistic
  - **T**ime limited

SHARED DECISION MAKING TO CREATE A MANAGEMENT PLAN

- Involves an educated and informed patient (and their family/caregiver)
- Seeks patient preferences
- Effective consultation includes motivational interviewing, goal setting, and shared decision making
- Empowers the patient
- Ensures access to DSMES

Access to self management

ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose

ADA 2020

Glucometer

- Correlation between greater SMBG frequency and lower A1C.

- Patient should be taught how to use SMBG data to adjust food intake, exercise, or pharmacologic therapy

Continuous Glucose Monitoring (CGM) - covered by health insurance

- Real-time CGM (rtCGM)

- Intermittently scanned CGM (iCGM)

- Blinded CGM
  - Professional version
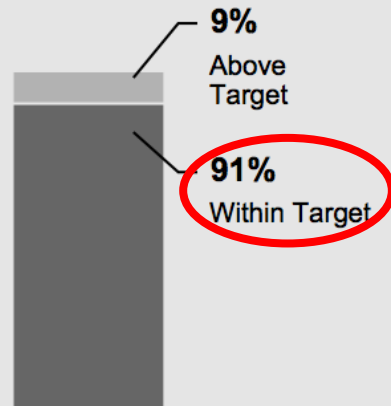 - Like a "cardiac holter monitoring" but for blood glucose
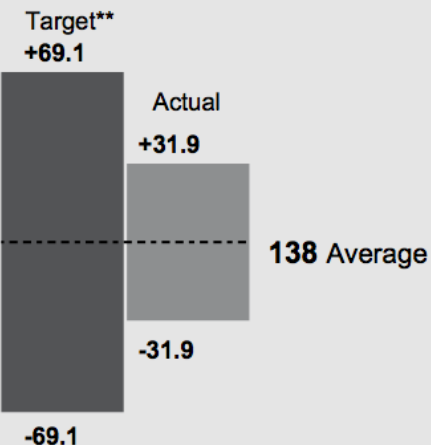
Glucometer

Jan 15, 2020 - Feb 11, 2020 (28 days)

Glucose (mg/dL)
SELECTED REPORTING PERIOD

Tests

9%
Above Target

91%
Within Target

Standard Deviation

Target**
+69.1

Actual
+31.9

138 Average

-31.9

-69.1

Average	138	mg/dL
High	252	mg/dL
Low	100	mg/dL
Standard Deviation	31.9	
Total Tests	33	
Avg. Tests/Day	1.6	
Days without tests	7	
Hypo Events	0	

Target Range:70-180 mg/dL   ** Target Standard Deviation < (Average/2)   Hypo Threshold: 60 mg/dL

TRENDS(Last 90 days)

90 DAYS   60 DAYS   30 DAYS

350

180

70

mg/dL
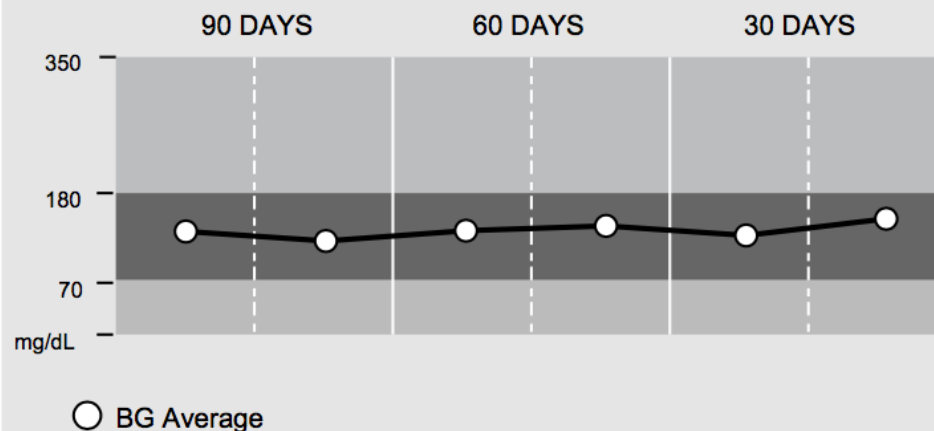
○ BG Average

	30 DAYS	90 DAYS
Average	134	130
High	252	252
Low	96	89
Standard Deviation	32.1	26.4
Total Tests	38	137
Avg. Tests/Day	1.7	2.1
Days without tests	7	25
Hypo Events	0	0

Continuous Glucose Monitoring

- Libre Freestyle personal – Abbot (Pro available)
    - No calibration needed
    - Need to scan to get data
    - 14 day wear sensor
    - Reader vs iphone/android
- Dexcom G6, G5 (Pro available)
    - G5: still require calibration twice a day
    - G6: no calibration required : 10 days
    - Continuous data
    - Hypoglycemia/hyperglycemia alarm
- Guardian Connect – Medtronics : 6 days
    - Requires 2-3x calibration a day
    - Continuous data
    - Hypoglycemia/hyperglycemia alarm
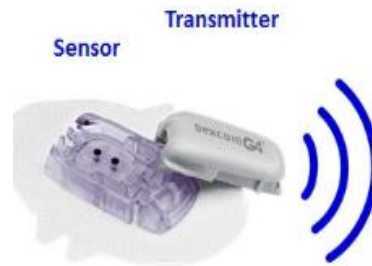
Time in Range vs A1C

Limitation of A1C:

▶ - no daily fluctuations or variability

▶ - avg glucose over previous 3 months

▶ - no time in range

Average Glucose

164 mg/dL

*88-116**

Time In Range

Above 180 mg/dL
(above 250 mg/dL: 7%) — **33**%

In Target Range
70-180 mg/dL — **64**%

Below 70 mg/dL
(below 54 mg/dL: 0%) — **3**%
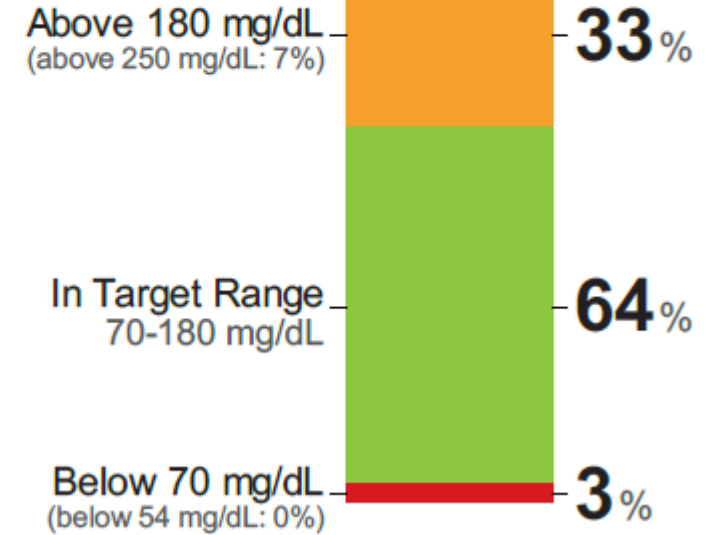
THE MANY FACES OF A 7% A1C
(and an average blood glucose of 154 mg/dl)

180 mg/dl — 70 mg/dl — 12 am — 12 pm — 12 am

40% High — 40% In-Range — 20% Low

25% High — 5% Low — 70% In-Range

100% In-Range

https://diatribe.org/time-range
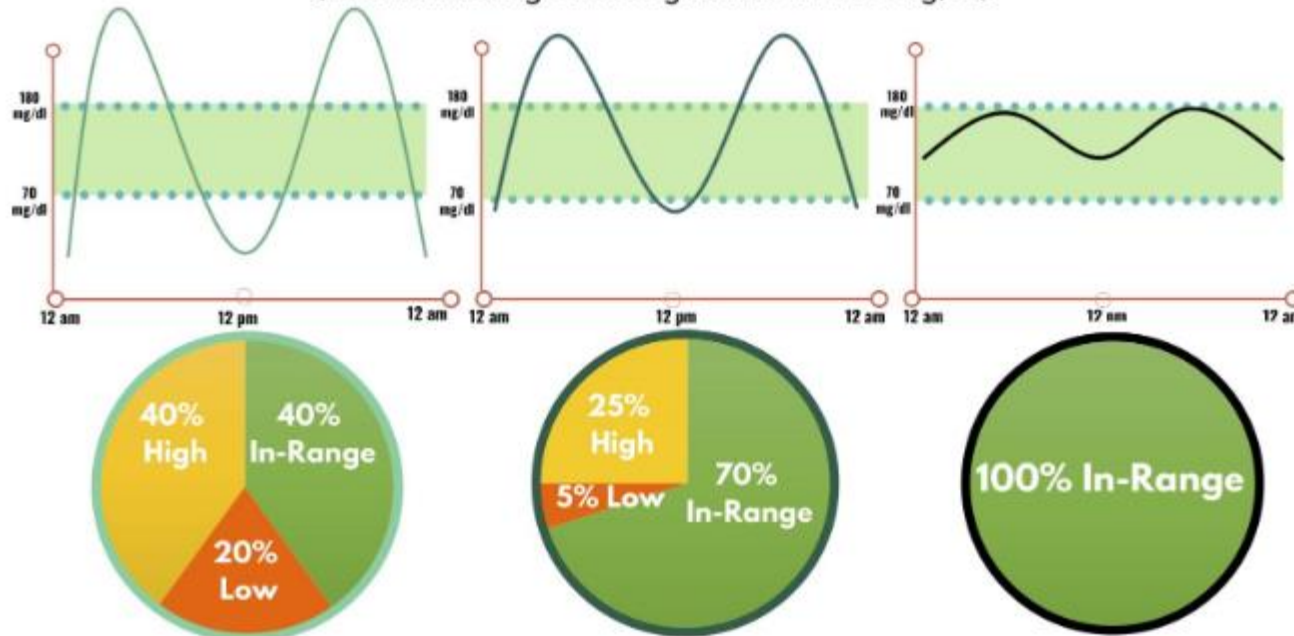
Consider CGM

- Type 1 DM (MDI or pump therapy)
- Type 2 DM on insulin (MDI or pump therapy)
- Patients with high risk of hypoglycemia
- Large variability (i.e. low fasting glucose, still with high A1C)

Individualized based on patient's needs, desires, skill levels, and availability

- To help with glycemic pattern and fluctuation, mean glucose level, time in range, prevent hyper/hypo-glycemia

*insufficient evidence in type2 DM not using insulin or using basal insulin only. However, assessing fasting glucose with self-management blood glucose does result in lower A1C (ADA, 2020)

- CPT code 95251 can be billed for **interpretation** of either personal or professional CGM
- CPT code 95250 is for the **placement** of professional CGM.
- CPT code 95249 is for **placement** of personal CGM

Consider to include

CGM data reviewed for time (i.e. 2 weeks, 4 weeks)

Data Capture or average daily scans

Average glucose :_____

Time in Range (TIR) 70-180mg/dl: _____% time

Pattern noted: postprandial hyperglycemia/ hypoglycemia event at night

Hypoglycemia events/time: _____

- 18F with DM1
- Medtronics insulin pump

GLUCOSE STATISTICS AND TARGETS

February 1, 2020 - February 14, 2020 — 14 Days
% Time CGM is Active — 85%

Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges Target Range 70-180 mg/dL	**Targets** % of Readings (Time/Day) Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)
Each 5% increase in time in range (70-180 mg/dL) is clinically beneficial.	

Average Glucose — 208 mg/dL
Glucose Management Indicator (GMI) — 8.3 %
Glucose Variability — 38.1%
Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES

Very High >250 mg/dL	31%	(7h 26min)
High 181-250 mg/dL	32%	(7h 41min)
Target Range 70-180 mg/dL	34%	(8h 10min)
Low 54-69 mg/dL	3%	(43min)
Very Low <54 mg/dL	0%	(0min)
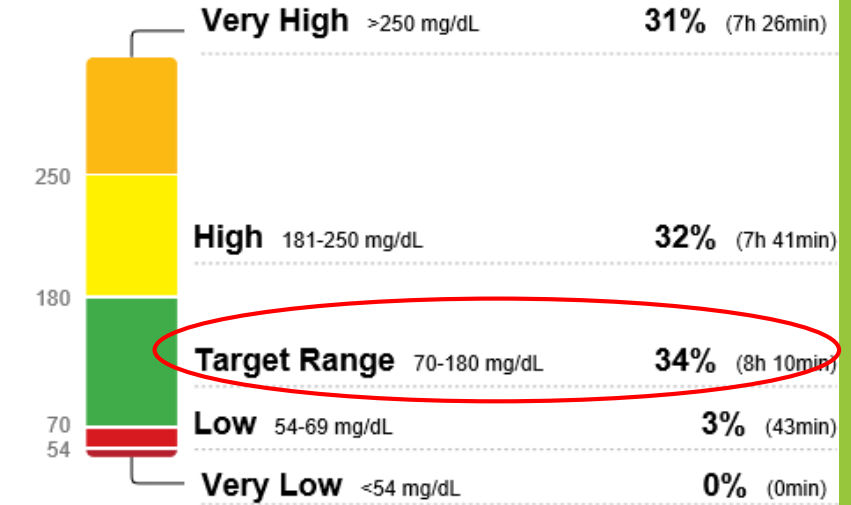
AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.
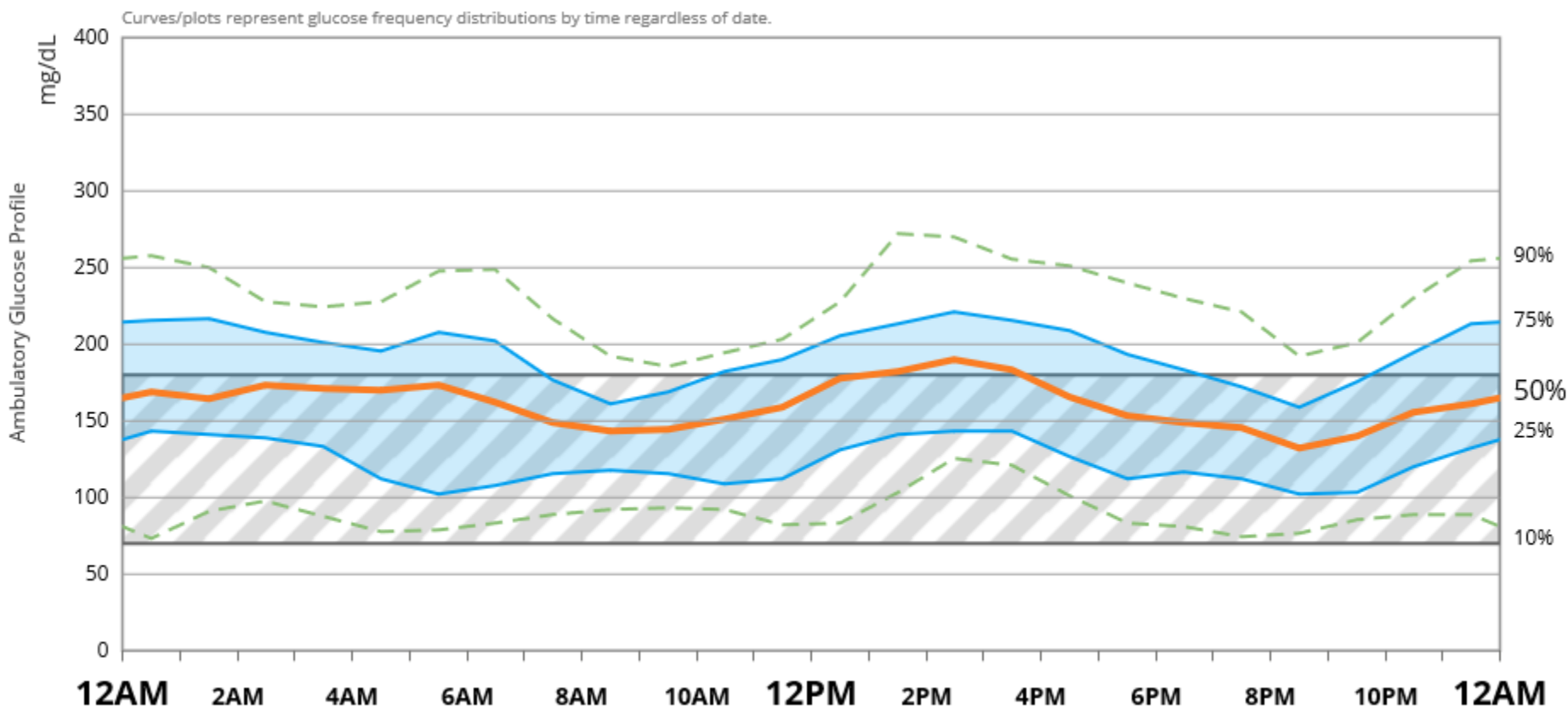
Individualized Care

TABLE 4. Summary of Glycemic Recommendations for Many Nonpregnant Adults With Diabetes

A1C	<7.0% (53 mmol/mol)*
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (10.0 mmol/L)

▸ Patient preference/resources

▸ Established Complications/Comorbidities?

Approach to Individualization of Glycemic Targets

Patient / Disease Features	More stringent ⟵ A1C 7% ⟶ Less stringent
Risks potentially associated with hypoglycemia and other drug adverse effects	low — high
Disease duration	newly diagnosed — long-standing
Life expectancy	long — short
Important comorbidities	absent — few / mild — severe
Established vascular complications	absent — few / mild — severe
Patient preference	highly motivated, excellent self-care capabilities — preference for less burdensome therapy
Resources and support system	readily available — limited

Usually not modifiable

Potentially modifiable

ADA 2020

For older adults: 7.5, 8, 8.5

Table 12.1—Framework for considering treatment goals for glycemia, blood p

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5% (58 mmol/mol)
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%† (69 mmol/mol)

ADA 2020

64F hx of DM2 (over 15years), hypertension/hyperlipidemia, NSTEMI Oct 2019 found to have CAD s/p DES in LAD x2 here for follow-up in January 2020.

▶ Adopted and lives with 3 grandchildren

▶ Cooks dinners at home, works on the village elders committee

▶ Takes all her pills at night before going to bed because she is too busy in the morning

▶ Current meds: aspirin81, clopidegrel 75, metop50, Lisinopril 20, metformin 1000mg daily, empagliflozin 10mg (started in Oct on discharge with cardiology), atorvastatin 80mg

▶ Vitals: HR 84, bp 135/80, SpO2 98% on RA, BMI 33.5 (weight 75kg, height 5')

▶ Labs: Jan 2020 - hgb 14, plt 285, CO_2 23, glucose 201, bun/cr 15/1.0, eGFR >60, microalbumin/cr 45, A1C 8.8, total cholesterol 189, triglyceride 165, HDL 60, LDL 110

▶ What is her goal A1C?

▶ How should we reach her goal A1C?

FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF[†]　　**NO**

CONSIDER INDEPENDENTLY OF BASELINE A1C OR INDIVIDUALIZED A1C TARGET

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

ASCVD PREDOMINATES
- Established ASCVD
- Indicators of high ASCVD risk (age ≥55 years with coronary, carotid or lower extremity artery stenosis >50%, or LVH)

PREFERABLY
GLP-1 RA with proven CVD benefit[1]
------ OR ------
SGLT2i with proven CVD benefit[1] if eGFR adequate[2]

If A1C above target

If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:
- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit[1]
- DPP-4i if not on GLP-1 RA
- Basal insulin[4]
- TZD[5]
- SU[6]

HF OR CKD PREDOMINATES
- Particularly HFrEF (LVEF <45%)
- CKD: Specifically eGFR 30-60 mL/min/1.73 m² or UACR >30 mg/g, particularly UACR >300 mg/g

PREFERABLY
SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate[3]
------ OR ------
If SGLT2i not tolerated or contraindicated or if eGFR less than adequate[2] add GLP-1 RA with proven CVD benefit[1]

If A1C above target

- Avoid TZD in the setting of HF
Choose agents demonstrating CV safety:
- For patients on a SGLT2i, consider adding GLP-1 RA with proven CVD benefit[1]
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin[4]
- SU[6]

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
If A1C above target	If A1C above target	If A1C above target	If A1C above target
SGLT2i[2] OR TZD	SGLT2i[2] OR TZD	GLP-1 RA OR DPP-4i OR TZD	SGLT2i[2] OR DPP-4i OR GLP-1 RA

If A1C above target

Continue with addition of other agents as outlined above

If A1C above target

Consider the addition of SU[6] OR basal insulin:
- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[7]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/OR
GLP-1 RA with good efficacy for weight loss[8]　　SGLT2i[2]

If A1C above target

SGLT2i[2]　　GLP-1 RA with good efficacy for weight loss[8]

If A1C above target

If quadruple therapy required, or SGLT2i and/or GLP-1 RA not tolerated or contraindicated, use regimen with lowest risk of weight gain

PREFERABLY
DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:
- SU[6] · TZD[5] · Basal insulin

COST IS A MAJOR ISSUE[9-10]

SU[6]	TZD[10]

If A1C above target

TZD[10]	SU[6]

If A1C above target

- Insulin therapy basal insulin with lowest acquisition cost
  OR
- Consider DPP-4i OR SGLT2i with lowest acquisition cost[10]

---

1. Proven CVD benefit means it has label indication of reducing CVD events
2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CREDENCE. Dapagliflozin has primary heart failure outcome data from DAPA-HF
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects

6. Choose later generation SU to lower risk of hypoglycemia, Glimepiride has shown similar CV safety to DPP-4i
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

LVH = Left Ventricular Hypertrophy; HFrEF = Heart Failure reduced Ejection Fraction; UACR = Urine Albumin-to-Creatinine Ratio; LVEF = Left Ventricular Ejection Fraction

ADA 2020

CVOT:	EMPA-REG
SGLT2-i	Empagliflozin (0% 1°P)
3-P MACE	14% RRR (HR=0.86; 0.74-0.99)
CV Death	38% RRR (HR=0.62; 0.49-0.77)
CV Death *or* HHF	34% RRR (HR=0.66; 0.55-0.79)
All-cause death	32% RRR HR=0.68 (0.57-0.82)
Non-fatal MI	NS (HR=0.87; 0.70-1.09)
Non-fatal Stroke	NS (HR=1.24; 0.92-1.67)
HHF	35% RRR (HR=0.65; 0.50-0.85)
CKD Progression	39% RRR (HR = 0.61; 0.53-0.70)

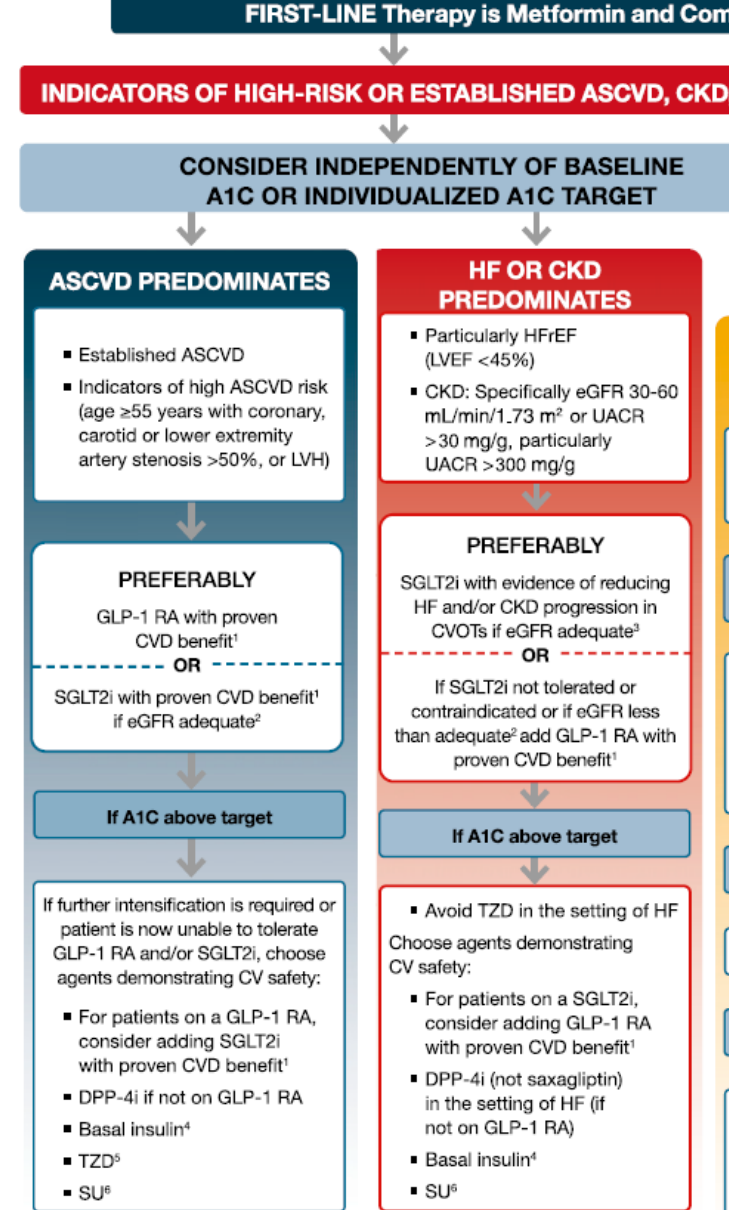| CVOT (non-ACS):	LEADER
GLP-1 RA	Liraglutide (19% 1°P)
3-P MACE	13% RRR (HR=0.87; 0.78-0.97)
CV Death *or* HHF	
CV Death	22% RRR (HR=0.78; 0.66-0.93)
All-cause death	15% RRR HR=0.85 (0.74-0.97)
Non-fatal MI	NS HR=0.88 (0.75-1.03)
Non-fatal Stroke	NS HR=0.89 (0.72-1.11)
HHF	NS HR=0.87 (0.73-1.05)
CKD Progression mainly ↓albuminuria	22% RRR (HR=0.78; 0.67-0.92)

ASCVD+ : GLP1 vs SGLT2i

- **Liraglutide**
- Semaglutide (weekly)
- Dulaglutide (weekly)

1. **Contraindication: <u>HX idiopathic pancreatitis</u>, medullary thyroid cancer or MEN syndrome, caution with gastroparesis, gall bladder disease, GERD**
2. No dosage adjustment in renal or liver disease
3. Side-effects: nausea, diarrhea, constipation

- **Empagliflozin**
  - eGFR <45 mL/min = recommend not to initiate, do not discontinue
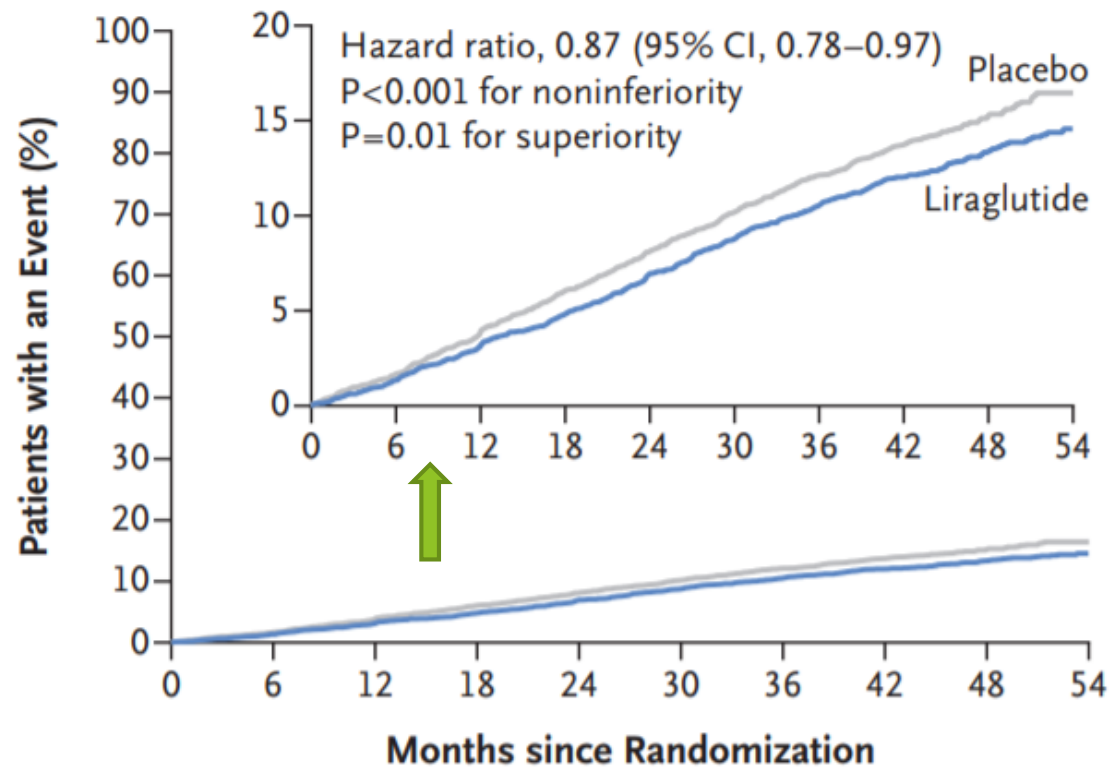 - eGFR <30 = contraindicated
- Canagliflozin
  - eGFR 30 to <60 mL/min = 100 mg
  - eGFR < 45 mL/min = do not initiate
1. **Side-effects: UTI, mycotic infections, vulvovaginitis, dehydration, euglycemic DKA**

FIRST-LINE Therapy is Metformin and Com

INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD,

CONSIDER INDEPENDENTLY OF BASELINE A1C OR INDIVIDUALIZED A1C TARGET

ASCVD PREDOMINATES	HF OR CKD PREDOMINATES
■ Established ASCVD ■ Indicators of high ASCVD risk (age ≥55 years with coronary, carotid or lower extremity artery stenosis >50%, or LVH)	■ Particularly HFrEF (LVEF <45%) ■ CKD: Specifically eGFR 30-60 mL/min/1.73 m² or UACR >30 mg/g, particularly UACR >300 mg/g

PREFERABLY GLP-1 RA with proven CVD benefit[1] ---- OR ---- SGLT2i with proven CVD benefit[1] if eGFR adequate[2]	**PREFERABLY** SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate[3] ---- OR ---- If SGLT2i not tolerated or contraindicated or if eGFR less than adequate[2] add GLP-1 RA with proven CVD benefit[1]
If A1C above target	**If A1C above target**
If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety: ■ For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit[1] ■ DPP-4i if not on GLP-1 RA ■ Basal insulin[4] ■ TZD[5] ■ SU[6]	■ Avoid TZD in the setting of HF Choose agents demonstrating CV safety: ■ For patients on a SGLT2i, consider adding GLP-1 RA with proven CVD benefit[1] ■ DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA) ■ Basal insulin[4] ■ SU[6]

1. Proven CVD benefit means it has label indication of reducing CVD events
2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
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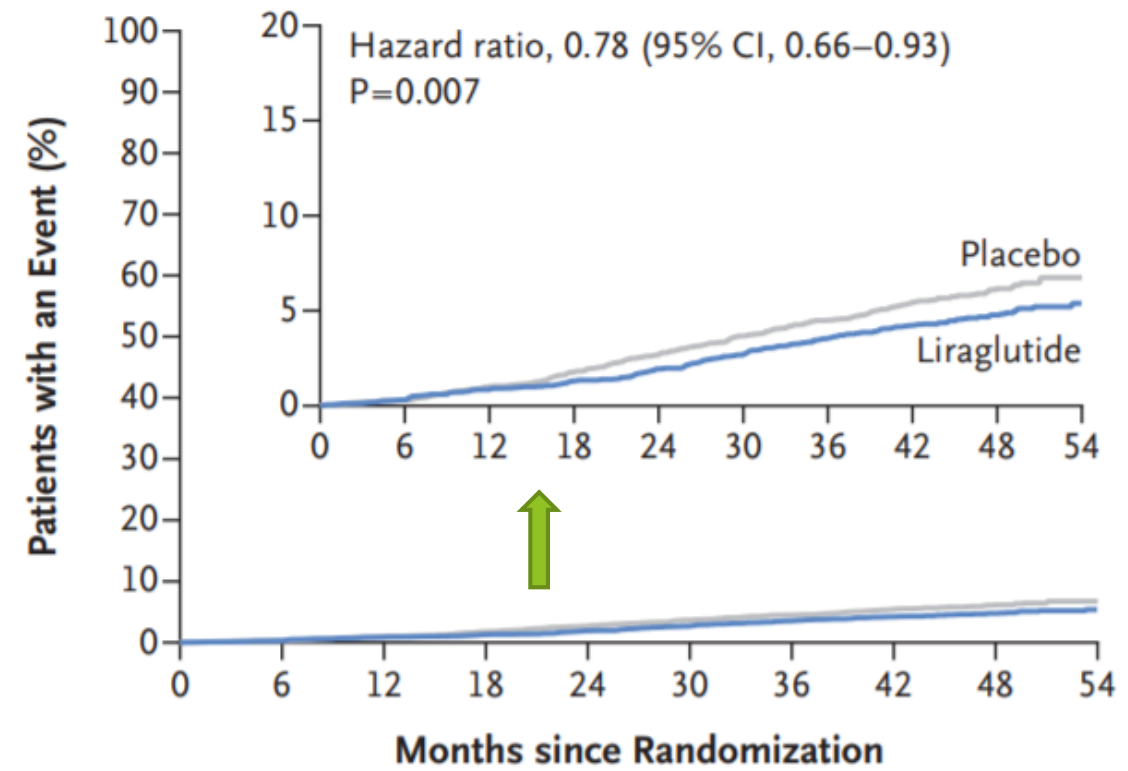5. Low dose may be better tolerated though less well studied for CVD effects

ADA 2020

A Primary Outcome

Hazard ratio, 0.87 (95% CI, 0.78–0.97)
P<0.001 for noninferiority
P=0.01 for superiority

Placebo

Liraglutide

Patients with an Event (%)

Months since Randomization

No. at Risk
Liraglutide 4668 4593 4496 4400 4280 4172 4072 3982 1562 424
Placebo   4672 4588 4473 4352 4237 4123 4010 3914 1543 407
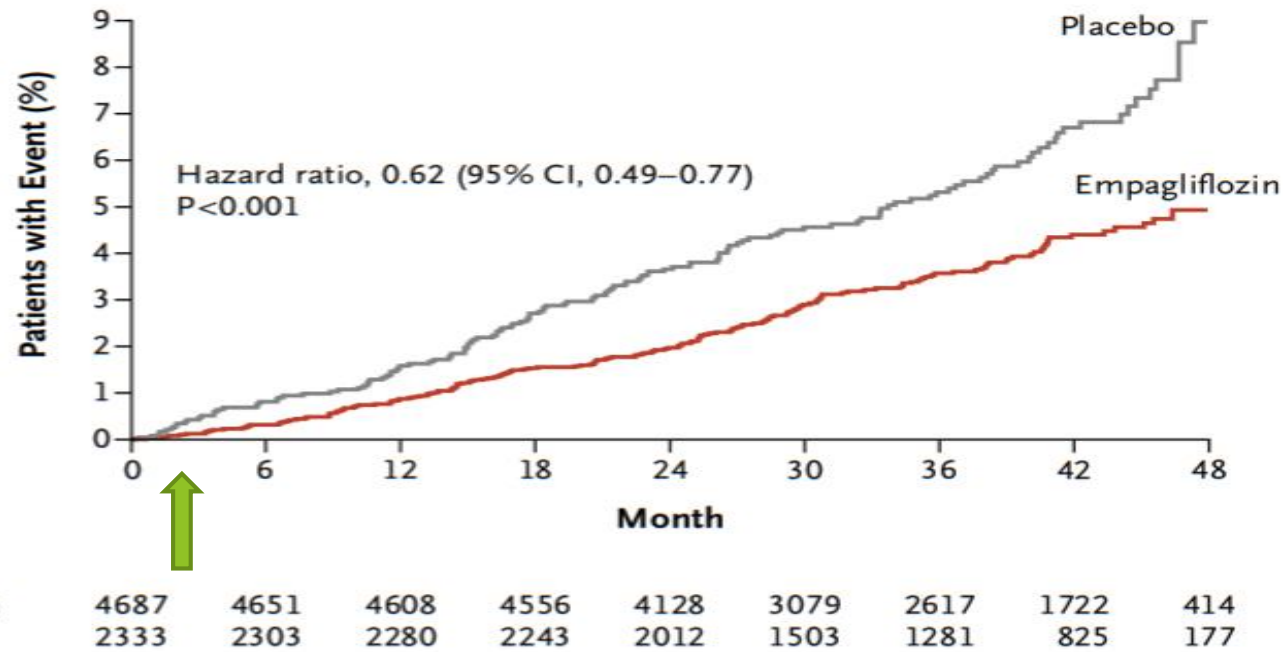
B Death from Cardiovascular Causes

Hazard ratio, 0.78 (95% CI, 0.66–0.93)
P=0.007

Placebo

Liraglutide

Patients with an Event (%)

Months since Randomization

No. at Risk
Liraglutide 4668 4641 4599 4558 4505 4445 4382 4322 1723 484
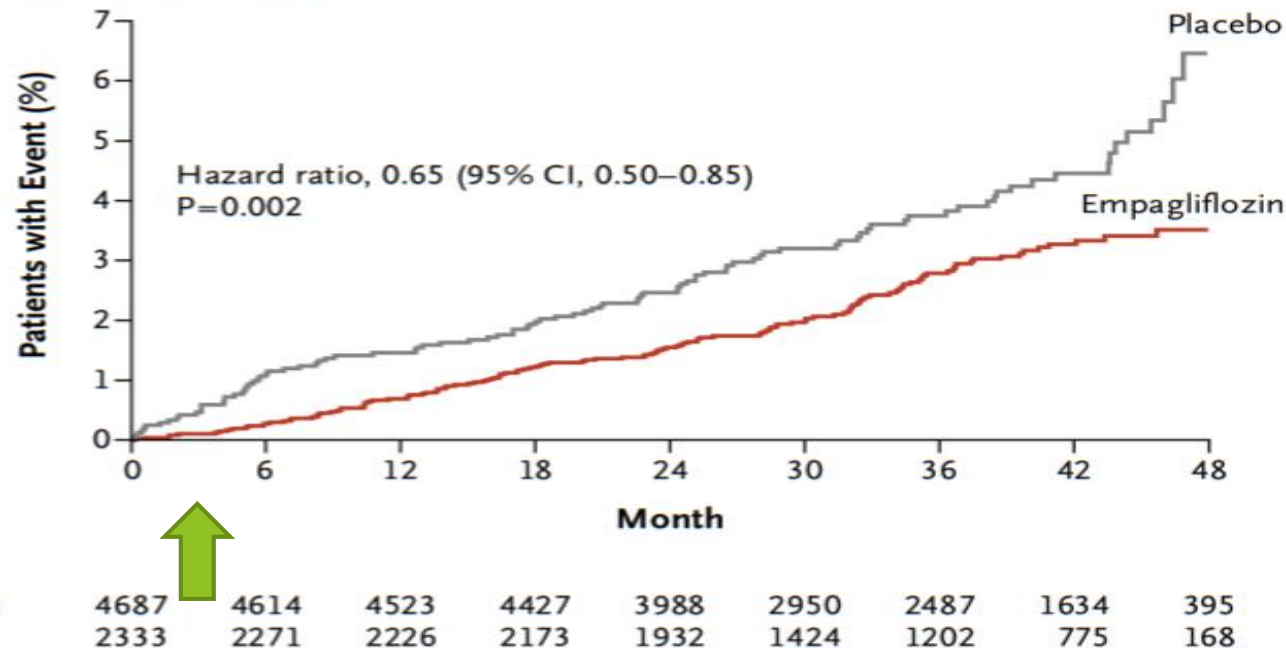Placebo   4672 4648 4601 4546 4479 4407 4338 4267 1709 465

LEADER trial

GLP-1 (Do not use together with DDP4, saxagliptin)

Generic Name	Brand Name	Usual Dosing	Benefits
Liraglutide	Victoza	1.2-1.8mg sc **daily** (start at 0.6mg)	Reduction in CV events Weight loss
Semaglutide	Ozempic	1mg sc **weekly** (start at 0.25mg or 0.5mg)	Reduction in CV events Weight loss
Exanatide (Extended Release)	Bydureon	2mg **weekly**	Weekly dosing
Dulaglutide	Trulicity	0.75mg sc **weekly** 1.5mg sc weekly	Weight loss

B Death from Cardiovascular Causes

Patients with Event (%)

Hazard ratio, 0.62 (95% CI, 0.49–0.77)
P<0.001

Placebo

Empagliflozin

Month

No. at Risk

Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

D Hospitalization for Heart Failure

Patients with Event (%)

Hazard ratio, 0.65 (95% CI, 0.50–0.85)
P=0.002

Placebo

Empagliflozin

Month

No. at Risk

Empagliflozin	4687	4614	4523	4427	3988	2950	2487	1634	395
Placebo	2333	2271	2226	2173	1932	1424	1202	775	168

EMPA-REG trial

SGLT2-I (reduce other diuretics by half, know CrCl)

| Generic Name	Brand Name	Usual Dosing	Cautions	Benefit
Canagliflozin	Invokana®	100-300 mg once daily	CrCl 45 to <60 mL/min => 100 mg CrCl < 30 mL/min contraindicated	Reduce proteinuria
Dapagliflozin	Farxiga®	5-10 mg once daily	CrCl <30 mL/min contraindicated	Reduce proteinuria and HF hospitalization
Empagliflozin	Jardiance®	10-25 mg once daily	CrCl <45 mL/min not recommended to start	Reduce CV death

A Primary Composite Outcome

Hazard ratio, 0.70 (95% CI, 0.59–0.82)
P=0.00001

Placebo

Canagliflozin

Months since Randomization
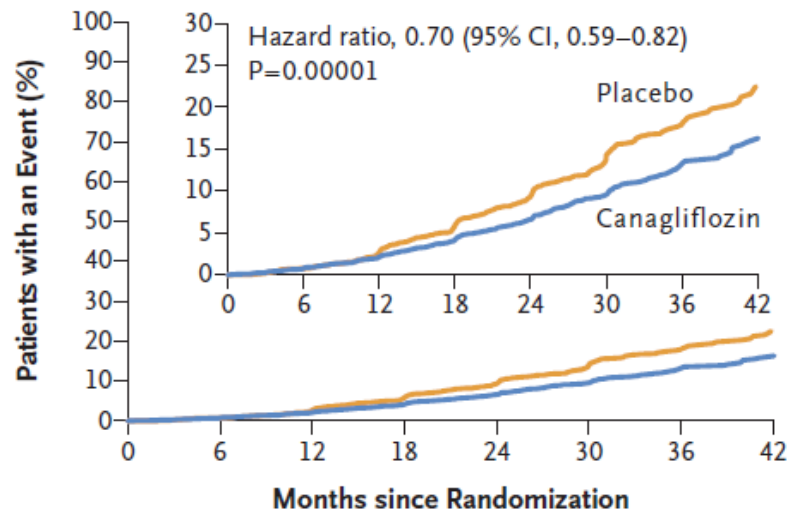
No. at Risk
Placebo   2199 2178 2132 2047 1725 1129 621 170
Canagliflozin 2202 2181 2145 2081 1786 1211 646 196

B Renal-Specific Composite Outcome

Hazard ratio, 0.66 (95% CI, 0.53–0.81)
P<0.001

Placebo

Canagliflozin

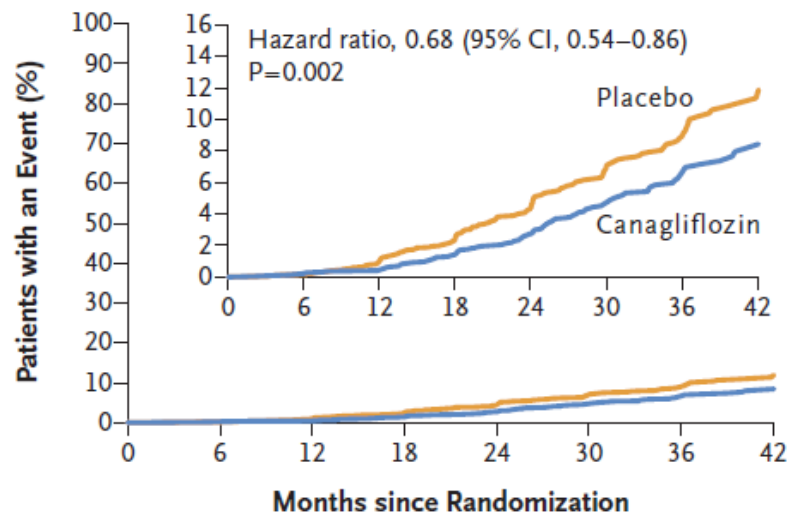Months since Randomization
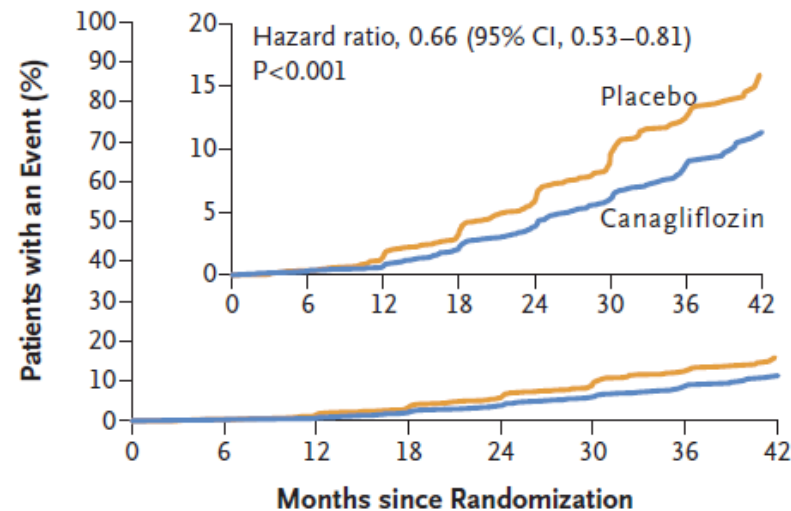
No. at Risk
Placebo   2199 2178 2131 2046 1724 1129 621 170
Canagliflozin 2202 2181 2144 2080 1786 1211 646 196

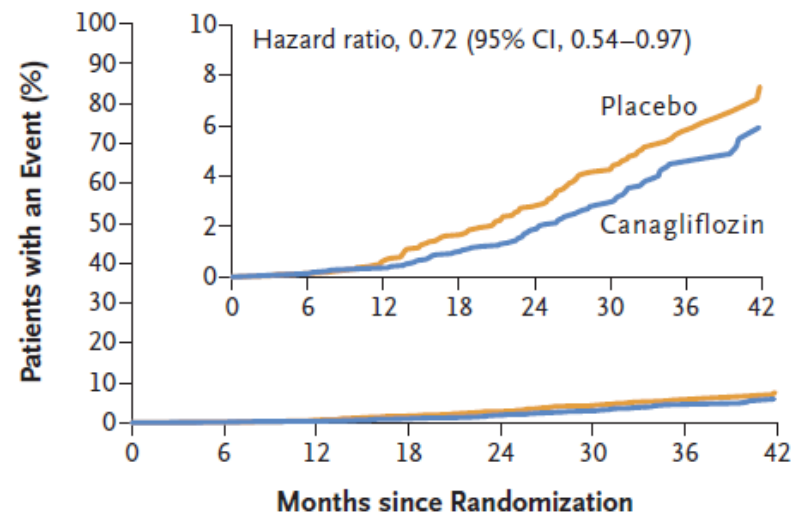**C** End-Stage Kidney Disease

Hazard ratio, 0.68 (95% CI, 0.54–0.86)
P=0.002

Placebo

Canagliflozin

Months since Randomization

No. at Risk
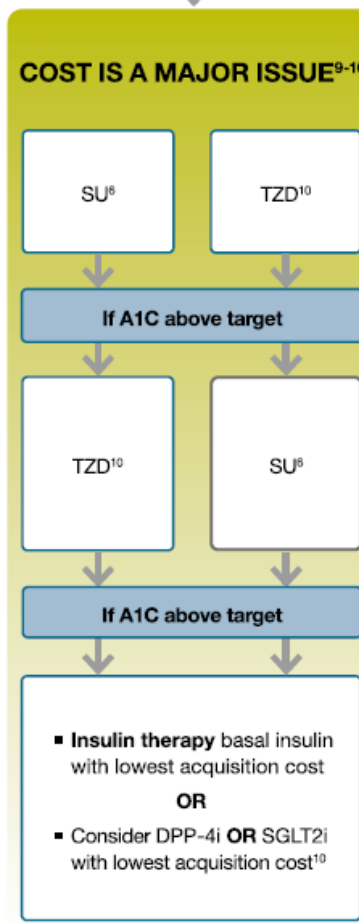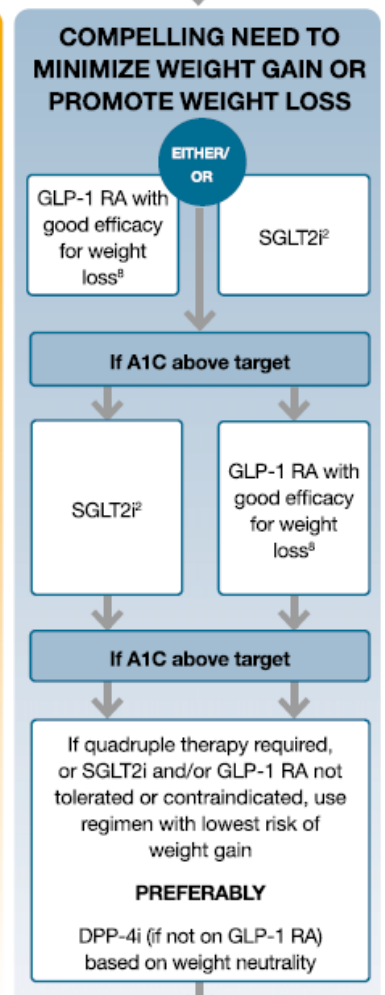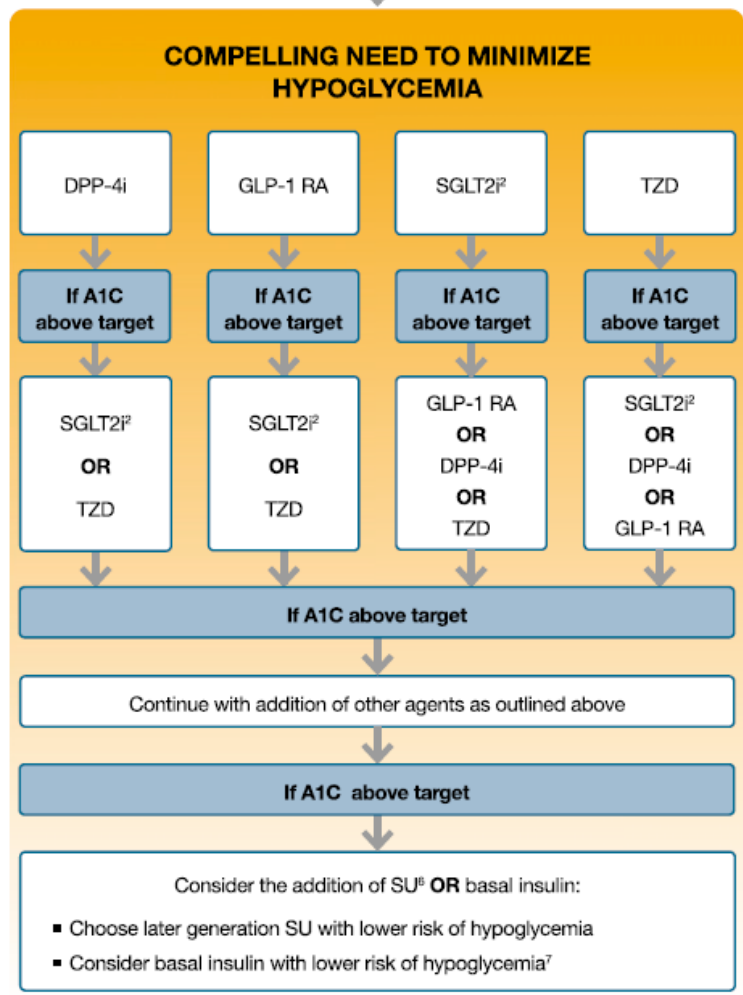Placebo   2199 2182 2141 2063 1752 1152 641 178
Canagliflozin 2202 2182 2146 2091 1798 1217 654 199

D Dialysis, Kidney Transplantation, or Renal Death

Hazard ratio, 0.72 (95% CI, 0.54–0.97)

Placebo

Canagliflozin

Months since Randomization

No. at Risk
Placebo   2199 2183 2147 2077 1776 1178 653 180
Canagliflozin 2202 2184 2148 2100 1811 1236 661 199

Credence trial

NO

THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
If A1C above target	If A1C above target	If A1C above target	If A1C above target
SGLT2i[2] **OR** TZD	SGLT2i[2] **OR** TZD	GLP-1 RA **OR** DPP-4i **OR** TZD	SGLT2i[2] **OR** DPP-4i **OR** GLP-1 RA

If A1C above target

Continue with addition of other agents as outlined above

If A1C above target

Consider the addition of SU[6] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[7]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/ OR

GLP-1 RA with good efficacy for weight loss[8]	SGLT2i[2]

If A1C above target

SGLT2i[2]	GLP-1 RA with good efficacy for weight loss[8]

If A1C above target

If quadruple therapy required, or SGLT2i and/or GLP-1 RA not tolerated or contraindicated, use regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

COST IS A MAJOR ISSUE[9-10]

SU[6]	TZD[10]

If A1C above target

TZD[10]	SU[6]

If A1C above target

- **Insulin therapy** basal insulin with lowest acquisition cost **OR**
- Consider DPP-4i **OR** SGLT2i with lowest acquisition cost[10]

6. Choose later generation SU to lower risk of hypoglycemia, Glimepiride has shown similar CV safety to DPP-4i
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
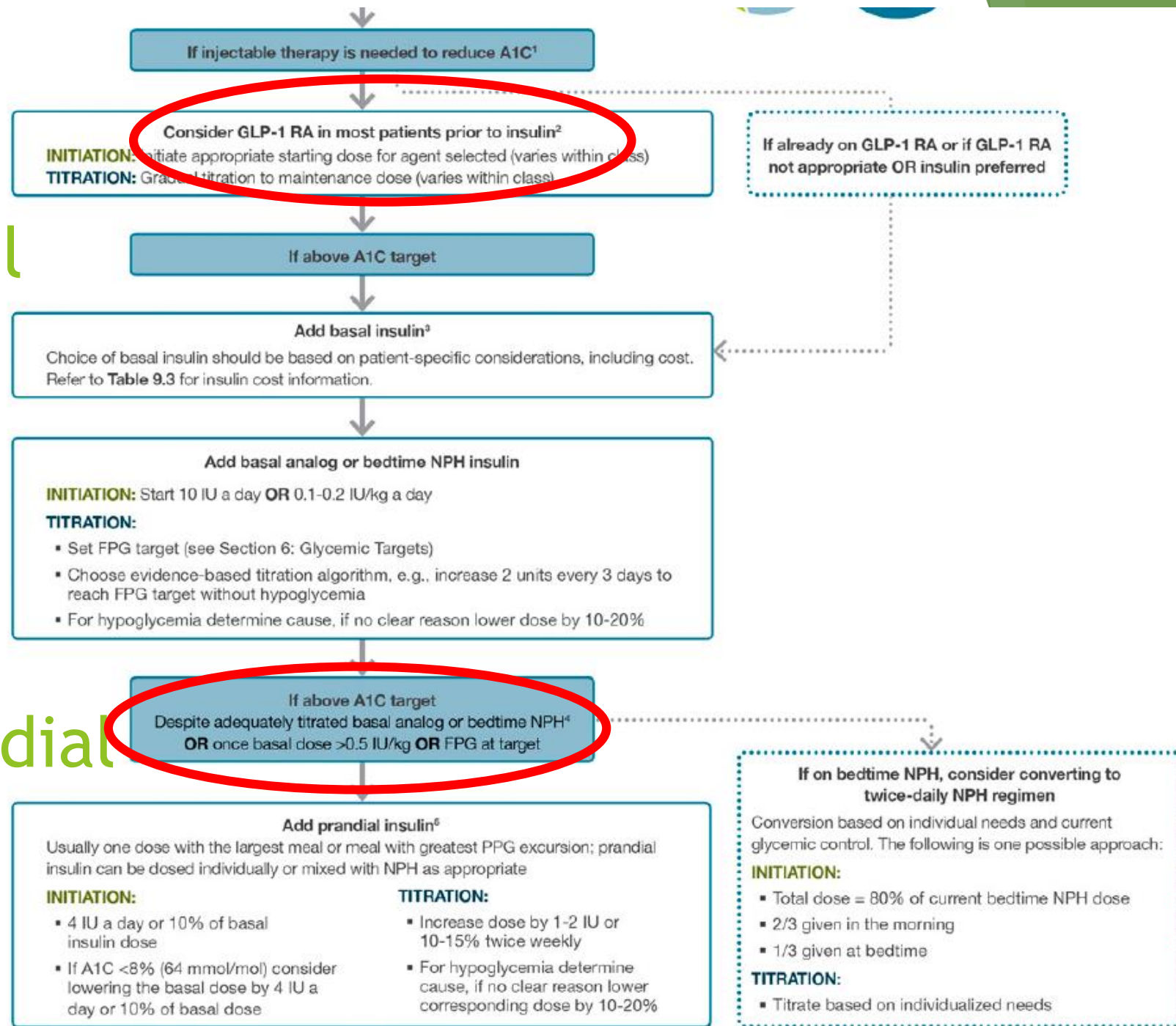8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide

ADA 2020

Insulin – Basal

Insulin – Prandial

If injectable therapy is needed to reduce A1C[1]

Consider GLP-1 RA in most patients prior to insulin[2]
INITIATION: Initiate appropriate starting dose for agent selected (varies within class)
TITRATION: Gradual titration to maintenance dose (varies within class)

If already on GLP-1 RA or if GLP-1 RA not appropriate OR insulin preferred

If above A1C target

Add basal insulin[3]
Choice of basal insulin should be based on patient-specific considerations, including cost. Refer to **Table 9.3** for insulin cost information.

Add basal analog or bedtime NPH insulin
INITIATION: Start 10 IU a day **OR** 0.1–0.2 IU/kg a day
TITRATION:
- Set FPG target (see Section 6: Glycemic Targets)
- Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG target without hypoglycemia
- For hypoglycemia determine cause, if no clear reason lower dose by 10-20%

If above A1C target
Despite adequately titrated basal analog or bedtime NPH[4]
OR once basal dose >0.5 IU/kg **OR** FPG at target

Add prandial insulin[6]
Usually one dose with the largest meal or meal with greatest PPG excursion; prandial insulin can be dosed individually or mixed with NPH as appropriate

INITIATION:
- 4 IU a day or 10% of basal insulin dose
- If A1C <8% (64 mmol/mol) consider lowering the basal dose by 4 IU a day or 10% of basal dose

TITRATION:
- Increase dose by 1-2 IU or 10-15% twice weekly
- For hypoglycemia determine cause, if no clear reason lower corresponding dose by 10-20%

If on bedtime NPH, consider converting to twice-daily NPH regimen
Conversion based on individual needs and current glycemic control. The following is one possible approach:
INITIATION:
- Total dose = 80% of current bedtime NPH dose
- 2/3 given in the morning
- 1/3 given at bedtime
TITRATION:
- Titrate based on individualized needs

ADA 2020

64F hx of DM2 (over 15years), hypertension/hyperlipidemia, NSTEMI Oct 2019 found to have CAD s/p DES in LAD x2 here for follow-up

- Adopted and lives with 3 grandchildren
- Cooks dinners at home, works on the village elders committee
- Takes all her pills at night before going to bed because she is too busy in the morning
- Current meds: aspirin81, clopidegrel 75, metop50, Lisinopril 20, metformin 1000mg daily, empagliflozin 10mg (started in Oct on discharge with cardiology), atorvastatin 80mg
- Vitals: HR 84, bp 135/80, SpO2 98% on RA, BMI 33.5 (weight 75kg, height 5')
- Labs: Jan 2020 - hgb 14, plt 285, CO2 23, glucose 201, bun/cr 15/1.0, eGFR >60, microalbumin/cr 45, A1C 8.8, total cholesterol 189, triglyceride 165, HDL 60, LDL 110

- Is her blood pressure at goal?
- Is her lipid at goal?

Blood Pressure

- Using **ASCVD 10-yr risk**
  - >15%
  - <15%

- Per Dr. Trowbridge (Cardiology)
  - individualized care
  - as close to 'normal' blood pressure as possible

10.4 For individuals with diabetes and hypertension at higher cardiovascular risk (existing atherosclerotic cardiovascular disease or 10-year atherosclerotic cardiovascular disease risk >15%), a blood pressure target of <130/80 mmHg may be appropriate, if it can be safely attained. **C**

10.5 For individuals with diabetes and hypertension at lower risk for cardiovascular disease (10-year atherosclerotic cardiovascular disease risk <15%), treat to a blood pressure target of <140/90 mmHg. **A**

ADA 2020

LDL

- Use ASCVD 10 year Risk APP from ACA/ACC

- low (<5%)

- borderline (5-<7.5%)

- intermediate (7.5%-<20%)

- high risk (≥20%)

Primary Prevention

Recommendations

10.19 For patients with diabetes aged 40–75 years without atherosclerotic cardiovascular disease, use moderate-intensity statin therapy in addition to lifestyle therapy. **A**

10.20 For patients with diabetes aged 20–39 years with additional atherosclerotic cardiovascular disease risk factors, it may be reasonable to initiate statin therapy in addition to lifestyle therapy. **C**

10.21 In patients with diabetes at higher risk, especially those with multiple atherosclerotic cardiovascular disease risk factors or aged 50–70 years, it is reasonable to use high-intensity statin therapy. **B**

10.22 In adults with diabetes and 10-year atherosclerotic cardiovascular disease risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL cholesterol levels by 50% or more. **C**

Secondary Prevention

Recommendations

10.23 For patients of all ages with diabetes and atherosclerotic cardiovascular disease, high-intensity statin therapy should be added to lifestyle therapy. **A**

10.24 For patients with diabetes and atherosclerotic cardiovascular disease considered very high risk using specific criteria, if LDL cholesterol is ≥70 mg/dL on maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor). **A** Ezetimibe may be preferred due to lower cost.

10.25 For patients who do not tolerate the intended intensity, the maximally tolerated statin dose should be used. **E**

ADA 2020

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering	≥50%	30%–49%	<30%
Statins	Atorvastatin (40 mg‡) 80 mg Rosuvastatin 20 mg (40 mg	Atorvastatin 10 mg (20 mg) Rosuvastatin (5 mg) 10 mg Simvastatin 20–40 mg§	Simvastatin 10 mg
	…	Pravastatin 40 mg (80 mg) Lovastatin 40 mg (80 mg) Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 1–4 mg	Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg

Triglyceride

10.29 For patients with fasting triglyceride levels ≥500 mg/dL, evaluate for secondary causes of hypertriglyceridemia and consider medical therapy to reduce the risk of pancreatitis. **C**

10.30 In adults with moderate hypertriglyceridemia (fasting or non-fasting triglycerides 175–499 mg/dL), clinicians should address and treat lifestyle factors (obesity and metabolic syndrome), secondary factors (diabetes, chronic liver or kidney disease and/or nephrotic syndrome, hypothyroidism), and medications that raise triglycerides. **C**

10.31 In patients with atherosclerotic cardiovascular disease or other cardiovascular risk factors on a statin with controlled LDL cholesterol but elevated triglycerides (135–499 mg/dL), the addition of icosapent ethyl can be considered to reduce cardiovascular risk. **A**

Maintenance Care

Table 4.4—Referrals for initial care management
- Eye care professional for annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian nutritionist for medical nutrition therapy
- Diabetes self-management education and support
- Dentist for comprehensive dental and periodontal examination
- Mental health professional, if indicated

▶ Annual:

  ▶ Foot exam – monofilament test

  ▶ DM Eye exam – dilated eye exam

  ▶ Dental exam

  ▶ Microalbumin/cr ratio (if elevated, consider q6month)

  ▶ Meet with a registered RD

q3-6months

  ○ A1C if not at goal, or q6month if at goal

  ○ Lipid panel if not at goal, or annual if at goal

Maintenance Care

▶ Vaccines

  ▶ On dx of DM: PPSV23

  ▶ After 65yo: PCV13 and PPSV23 (again, at least 5yrs after last dose of PPSV23)

Other:

  ○ TB screening

  ○ HCV screening

  ○ Routine vaccines as regular population: annual flu vaccine, tetanus vaccine q10yr, etc

Recommendation tab
- dynamic workbook

Recommendation	Due ∧	Last Action	Rec...	Source	Orders
▼ Adult Abnormal Weight Counseling					
COU - Abnormal Weight Counseling	Overdue (12 months)	Ordered (12 months a...	Every 1 yr	--	
▼ Dental Management					
DEN - Dental Exam	Today	--	Every 1 yr	--	
▼ Depression Screening					
SCR - Depression Screening	Overdue (15 months)	Not at all (2 years a...	Every 1 yr	--	
▼ Diabetes Management					
DM - Eye Exam 🗋	Overdue (22 months)	--	Every 1 yr	--	
DM - Foot Exam 🗋	Overdue (3 years)	1:2016061300000000	Every 1 yr	--	
DM - Statin Therapy if ages 40-75	Overdue (10 months)	Undone (22 months a...	Every 1 yr	--	Orders ∨
▼ Healthy Adult					
IMM - Influenza Vaccine - Age... 🗋	Overdue (3 weeks)	0.500000 mL (10 m...	Seasonal	--	Orders ∨
IMM - Tetanus Vaccine - Age 19+...	Overdue (7 years)	0.000000 unit(s) (...	Every 10 yr	--	ORDER - Td Pres

In Summary

- Diagnosis of Diabetes and Pre-Diabetes:
  - fasting glucose vs A1C
- Review Goals of Care from Standards of Medical Care in Diabetes 2020 from ADA
  - holistic approach, individualized A1C goal, short-term vs long-term goal, and re-assess
- Review of 2020 ADA pharmacologic recommendations of glycemic treatment for type 2 diabetes
  - CV Disease? Titration of medications, DM technology
- Other Maintenance Care for Diabetes
  - A1C, lipid panel, microalbumin urine, GFR
  - Eye, foot, dental, vaccines, screening for TB, HCV, HBV
  - Consider NAFLD work-up in DM2 and obese patients

1. Type of DM
2. CV hx, CV risk? Aspirin?
3. A1C/ fasting glucose? Hypoglycemia events?
4. BP/ACEi?
5. LDL/statin?
6. CKD/ eGFR & microalbumin/cr ratio
7. Eye (retinopathy?)/ Dental
8. Foot
9. Tobacco/ Etoh/ other drugs
10. Vaccines: pneumovax/flu/zoster
11. Diet and activities

Questions?

- alin@anthc.org

- Tigertext ANTHC: Lin, Ai-Ling

- ANTHC Diabetes Program: 907-729-1125, Case Manager: 907-729-3928