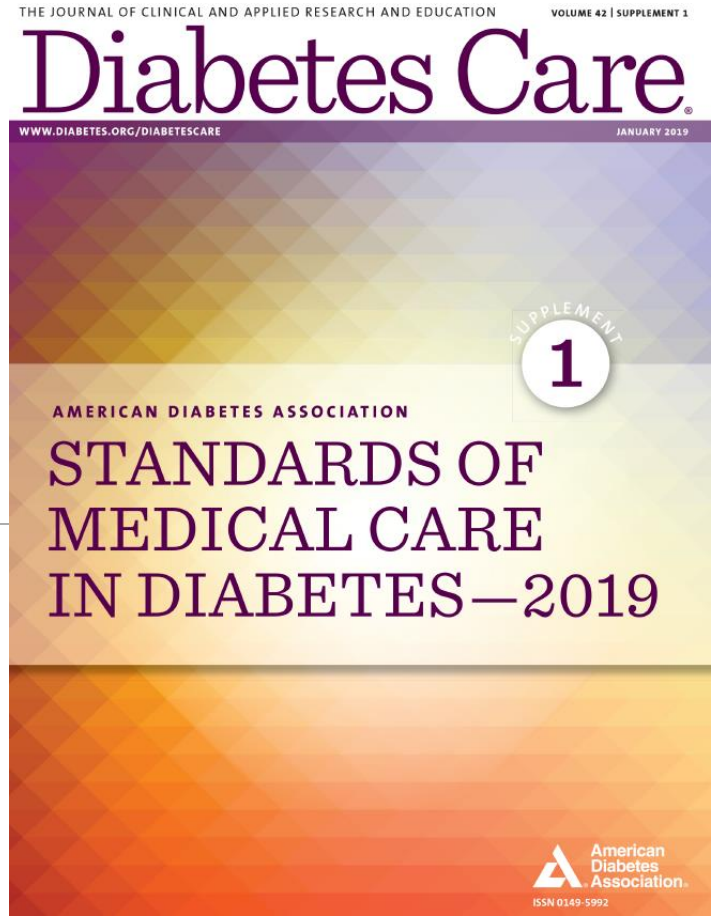
Standards of Medical Care in Diabetes - 2019

AI-LING LIN, DO
ALASKA NATIVE TRIBAL HEALTH CONSORTIUM
DIABETES PROGRAM
JUNE 2019



Objectives:

Diagnosis of Diabetes and Pre-Diabetes

Review Goals of Care from Standards of Medical Care in Diabetes 2019 from ADA

Review of 2019 ADA pharmacologic recommendations of glycemic treatment for type 2 diabetes

Other Maintenance Care for Diabetes

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

PRE-diabetes

	Prediabetes
A1C	5.7–6.4%*
FPG	100–125 mg/dL (5.6–6.9 mmol/L)*
OGTT	140–199 mg/dL (7.8–11.0 mmol/L)*

TABLE 1. Criteria for Testing for Diabetes or Prediabetes in Asymptomatic Adults

1. Testing should be considered in overweight or obese (BMI ≥25 kg/m^2 or ≥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 (≥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 ≥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.

IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

ADA 2019

Screening

TABLE 2. Risk-Based Screening for Type 2 Diabetes or Prediabetes in Asymptomatic Children and Adolescents in a Clinical Setting

Testing should be considered in youth* who are overweight (≥85% percentile) or obese (≥95 percentile) A and who have one or more additional risk factors based on the strength of their association with diabetes:

- Maternal history of diabetes or GDM during the child's gestation A
- Family history of type 2 diabetes in first- or second-degree relative A
- Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander) A
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight) B

**After the onset of puberty or after 10 years of age, whichever occurs earlier. If tests are normal, repeat testing at a minimum of 3-year intervals, or more frequently if BMI is increasing, is recommended.*

ADA 2019

Diagnosis of Diabetes

2. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes—2019*

Diabetes Care 2019;42(Suppl. 1):S13–S28 | https://doi.org/10.2337/dc19-S002

TABLE 3. Criteria for the Screening and Diagnosis of Diabetes

	Prediabetes	Diabetes
A1C	5.7–6.4%*	≥6.5%†
FPG	100–125 mg/dL (5.6–6.9 mmol/L)*	≥126 mg/dL (7.0 mmol/L)†
OGTT	140–199 mg/dL (7.8–11.0 mmol/L)*	≥200 mg/dL (11.1 mmol/L)†
RPG		≥200 mg/dL (11.1 mmol/L)‡

**For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range. †In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate samples. ‡Only diagnostic in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis. RPG, random plasma glucose.*

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)

Features Suggestive of MODY

Strong family history (typically 2-3 generations affected)

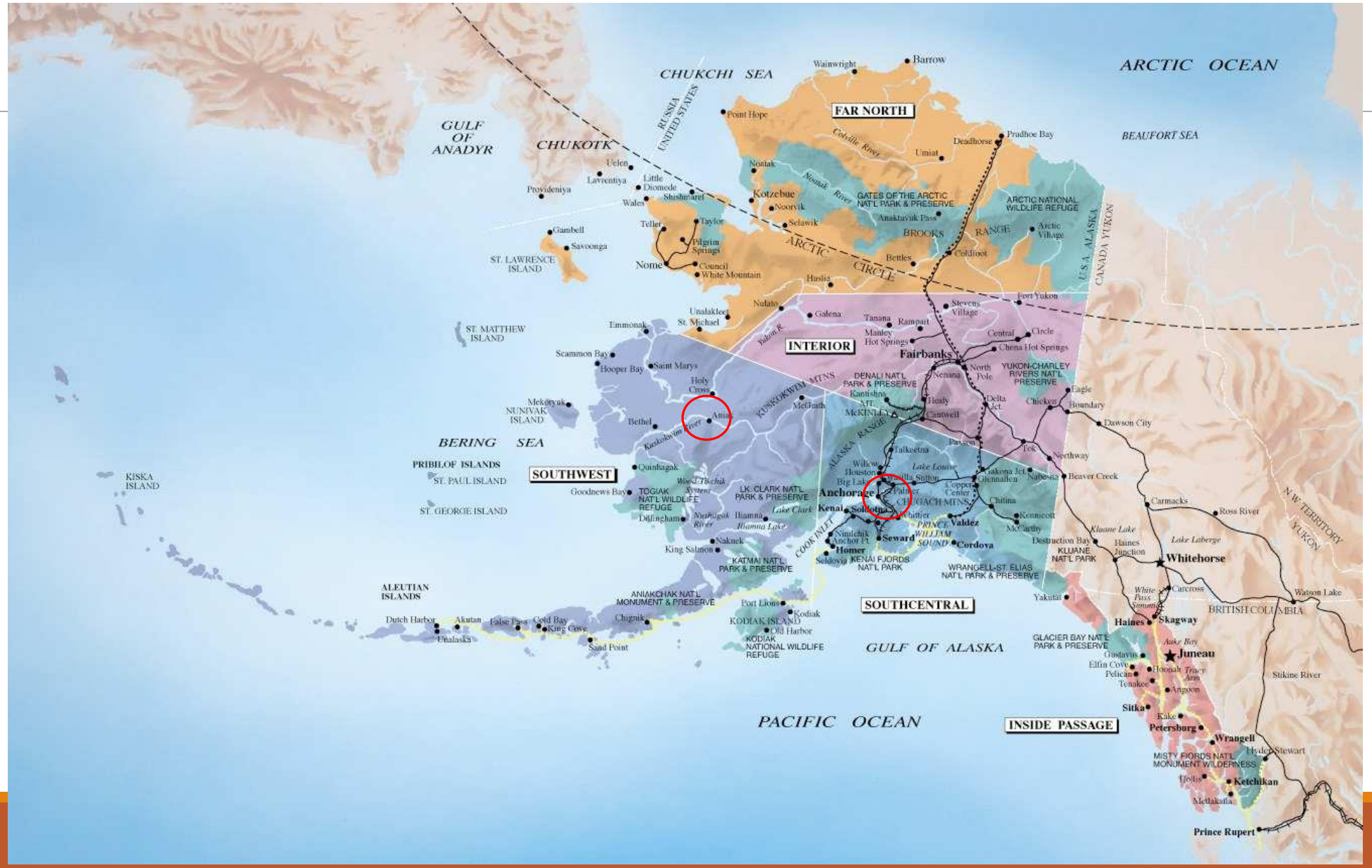
Young onset of diabetes (<25 years of age)

Sulfonylurea sensitivity

Absence of insulin resistant features

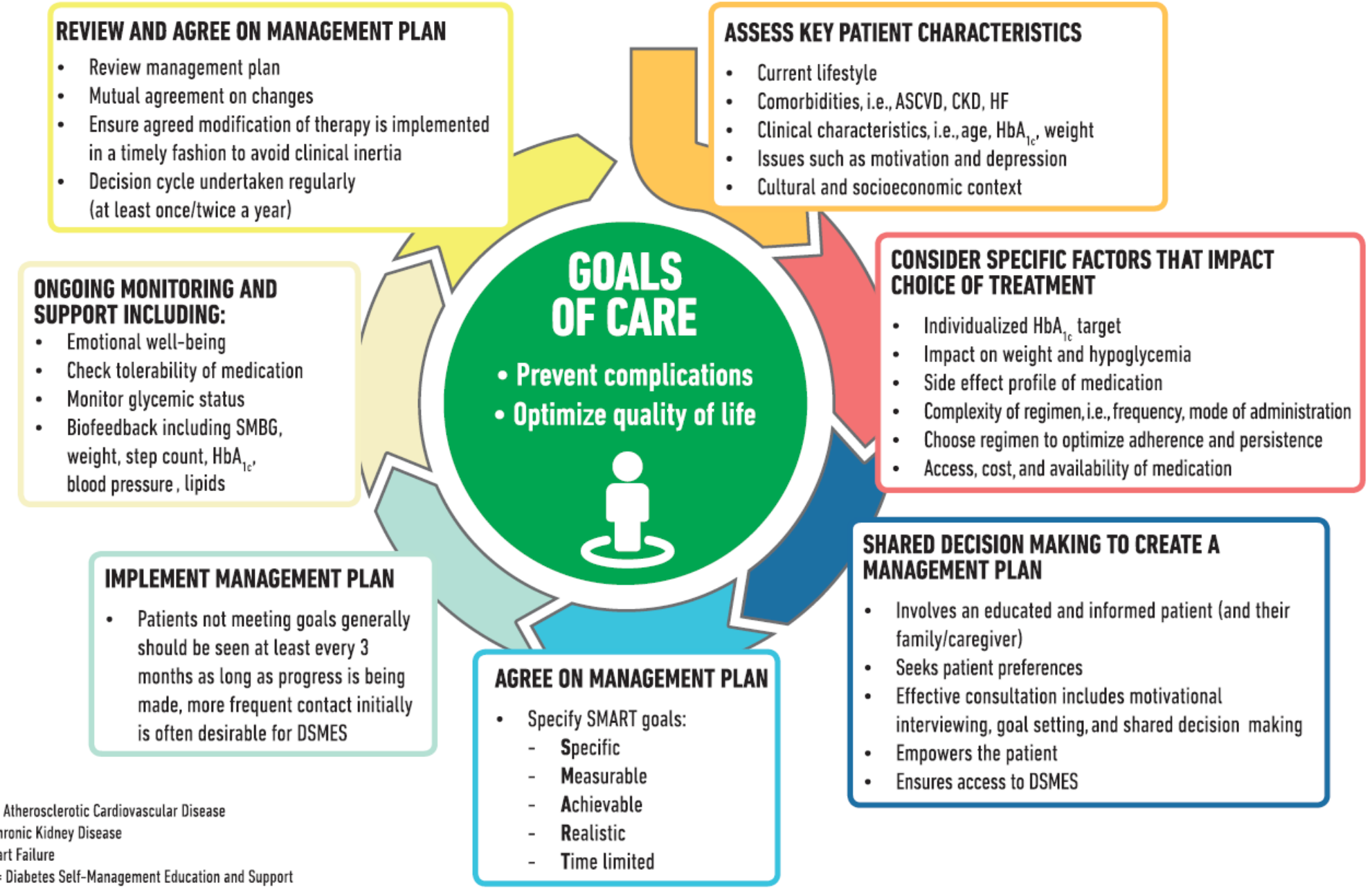
Absence of Beta cell automimmunity

Why do we care



Features	Type 1 diabetes	Type 2 diabetes	HNF1A/4A-Mody
Typical age of diagnosis	10-30	>25	15-45
Diabetic ketoacidosis	Common	Rare	Rare
Insulin dependent	Yes	No	No
Parental history of diabetes	<15%	>50% in young onset Type 2 DM	60-90%
Obesity	Uncommon	Common	Uncommon
Insulin resistance	Uncommon	Common	Uncommon
Presence of B cell antibodies	>90%	Negative	Rare
C-peptide concentration	Undetectable/low	Normal/high	Normal
Optimal first line treatment	Insulin	Metformin	Sulfonylurea

Diagnosis and management of maturity onset diabetes of the young. BMJ 2011;343:d6044



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

Individualized Care

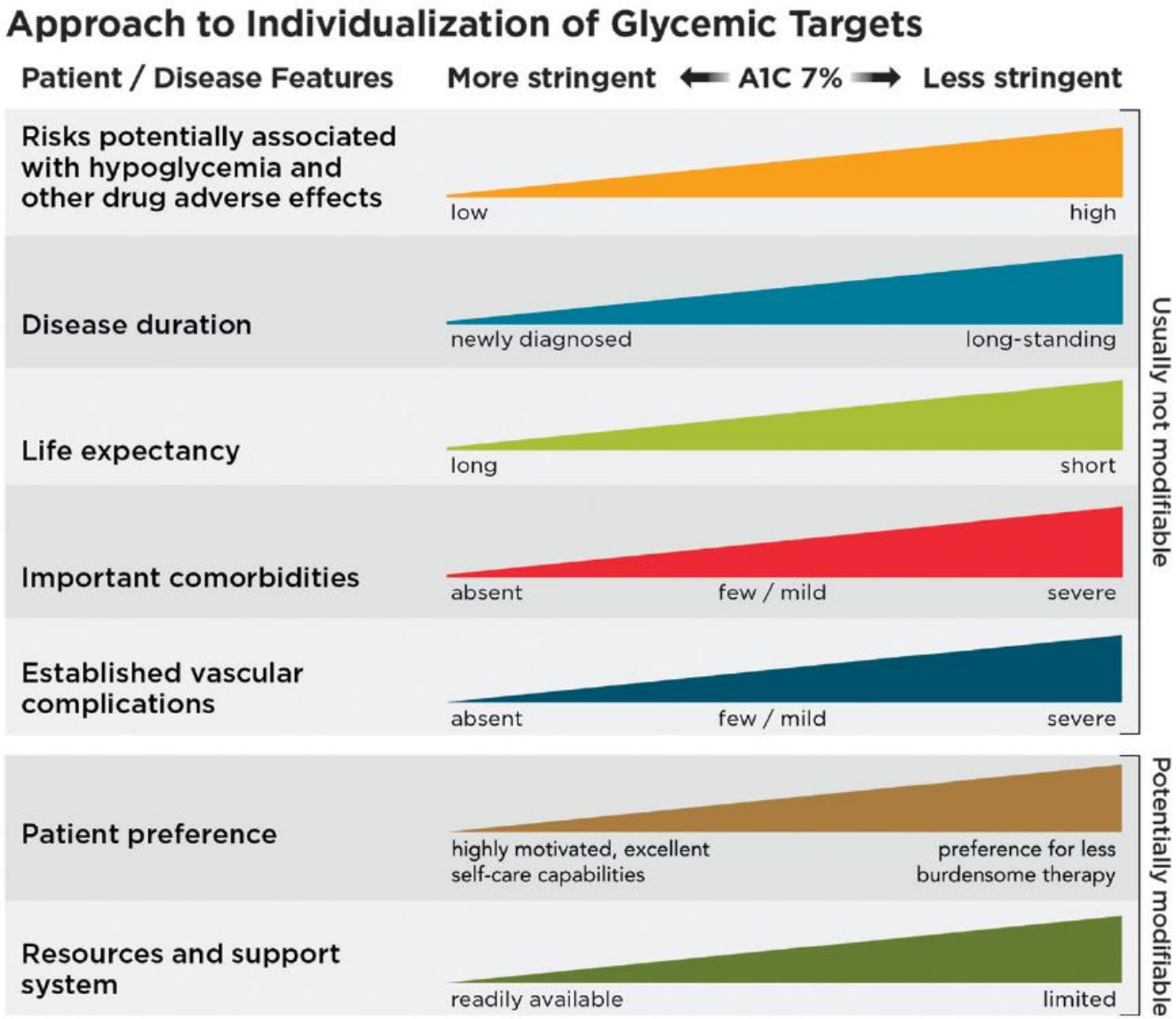
New diagnosis?

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?



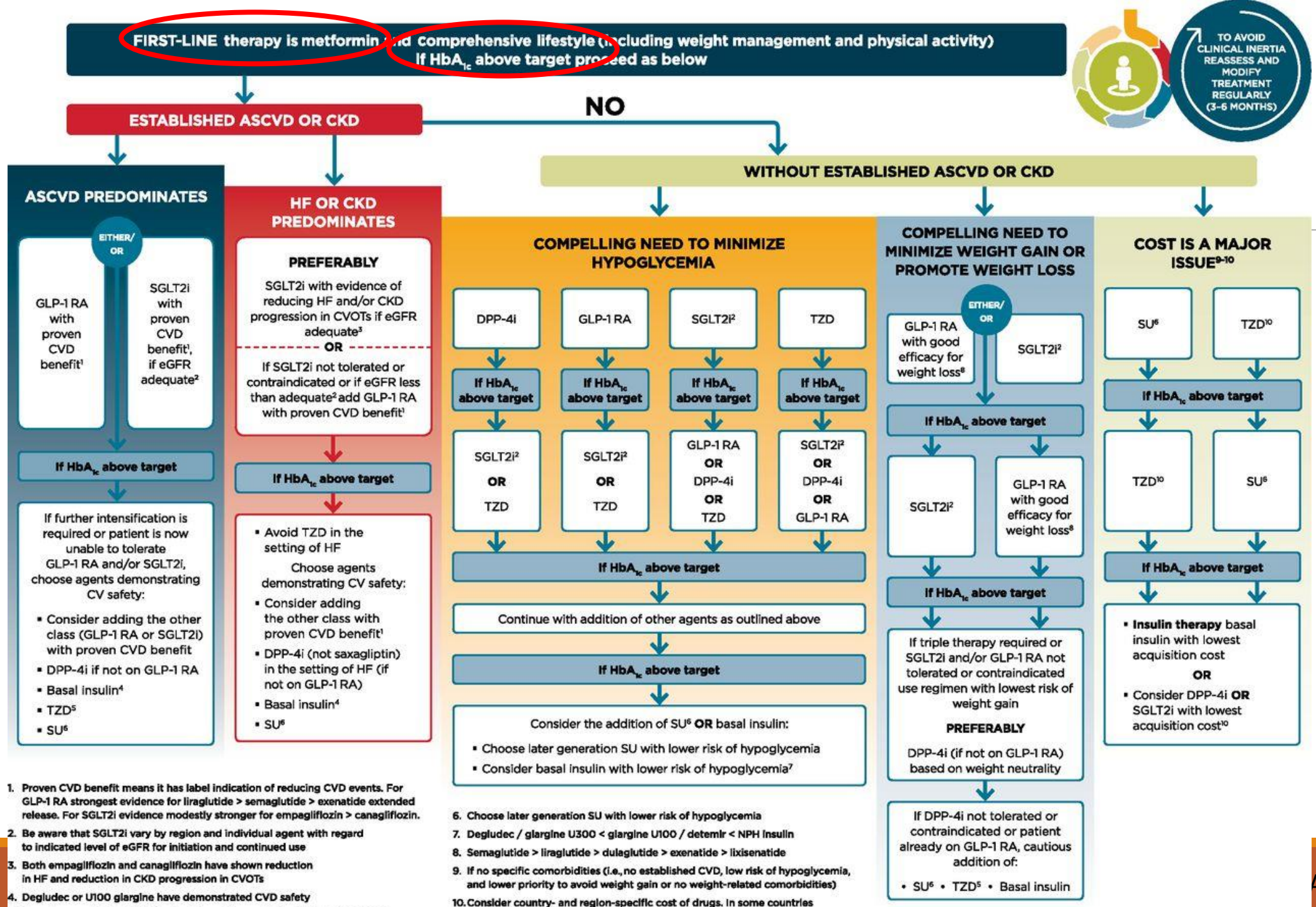
ADA 2019

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 2019



1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U100 glargine have demonstrated CVD safety
6. Choose later generation SU with lower risk of hypoglycemia
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

ASCVD+ or CKD

Liraglutide

Semaglutide

1. **Contraindication: HX pancreatitis, medullary thyroid cancer or MEN syndrome, caution with gastroparesis, gall bladder disease**
2. No dosage adjustment in renal or liver disease

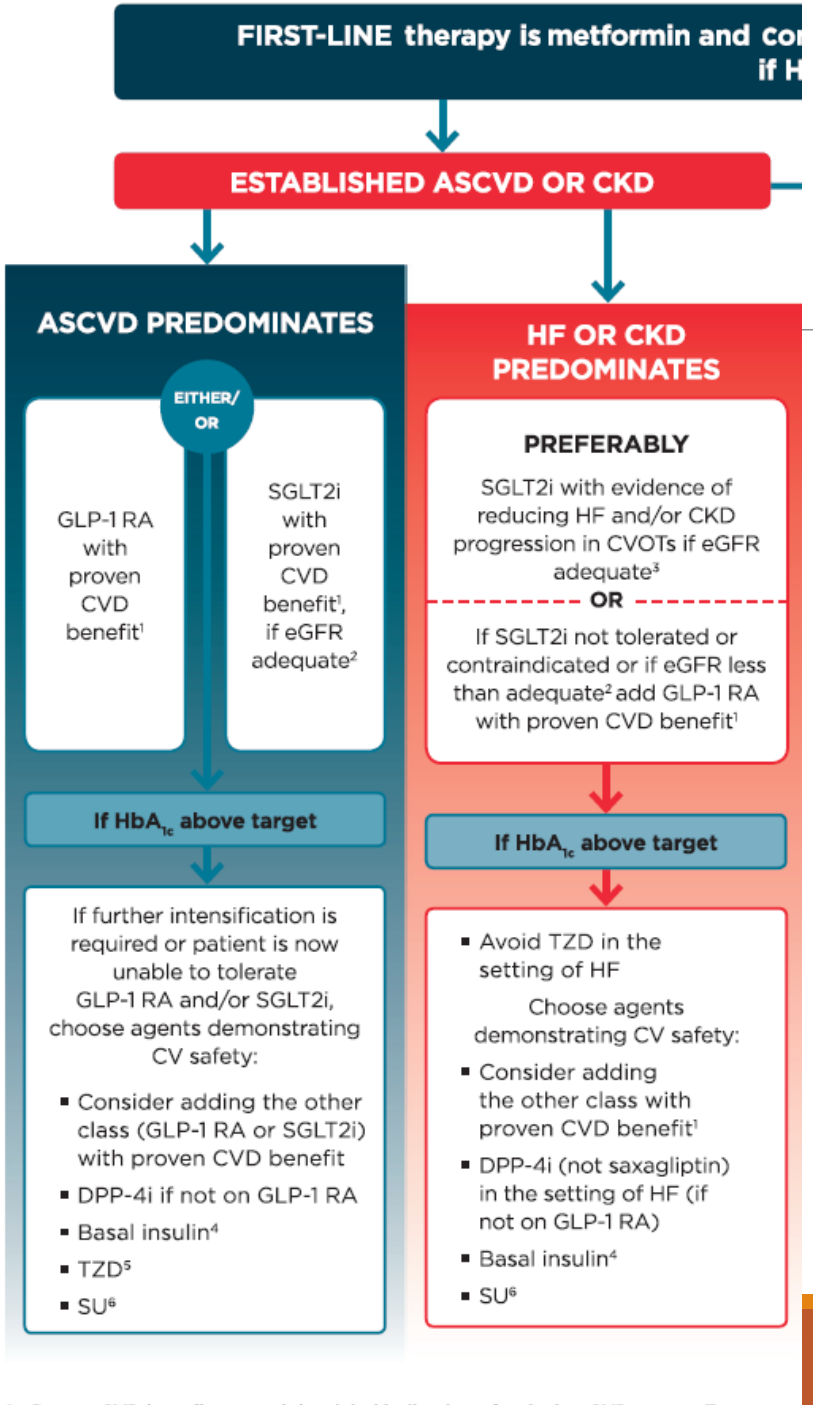
Empagliflozin

- CrCl <45 mL/min use not recommended

Canagliflozin

- **CrCl 45 to <60 mL/min = 100 mg**
- **CrCl < 45 mL/min contraindicated**

1. **Side-effects: UTI, mycotic infections, vulvovaginitis, dehydration**



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CVOT:	EMPA-REG
SGLT2-i	Empagliflozin
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
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)

Inzucchi, S. ADA Post-Grad Course. 2019

CREDENCE: NEJM April 2019

N=4401

Time: 2.62year

Relative Risk Reduction 30% in ESRD, doubling serum creatinine level, death from renal or CV causes

CV death, renal complication reduction: NNT: 22 in 2.6 years

CVOT	CANVAS
SGLT2-i	Canagliflozin (34% 1°P)
3-P MACE	14% RRR (HR=0.86; 0.75-0.97)
CV Death	NS (HR=0.87; 0.72-1.06)
CV Death *or* HHF	22% RRR (HR=0.78; 0.67-0.91)
All-cause death	
Non-fatal MI	NS (HR=0.85; 0.69-1.05)
Non-fatal Stroke	NS (HR=0.90; 0.71-1.15)
HHF	33% RRR (HR=0.67; 0.52-0.87)
CKD Progression	40% RRR (HR=0.60; 0.47-0.77)

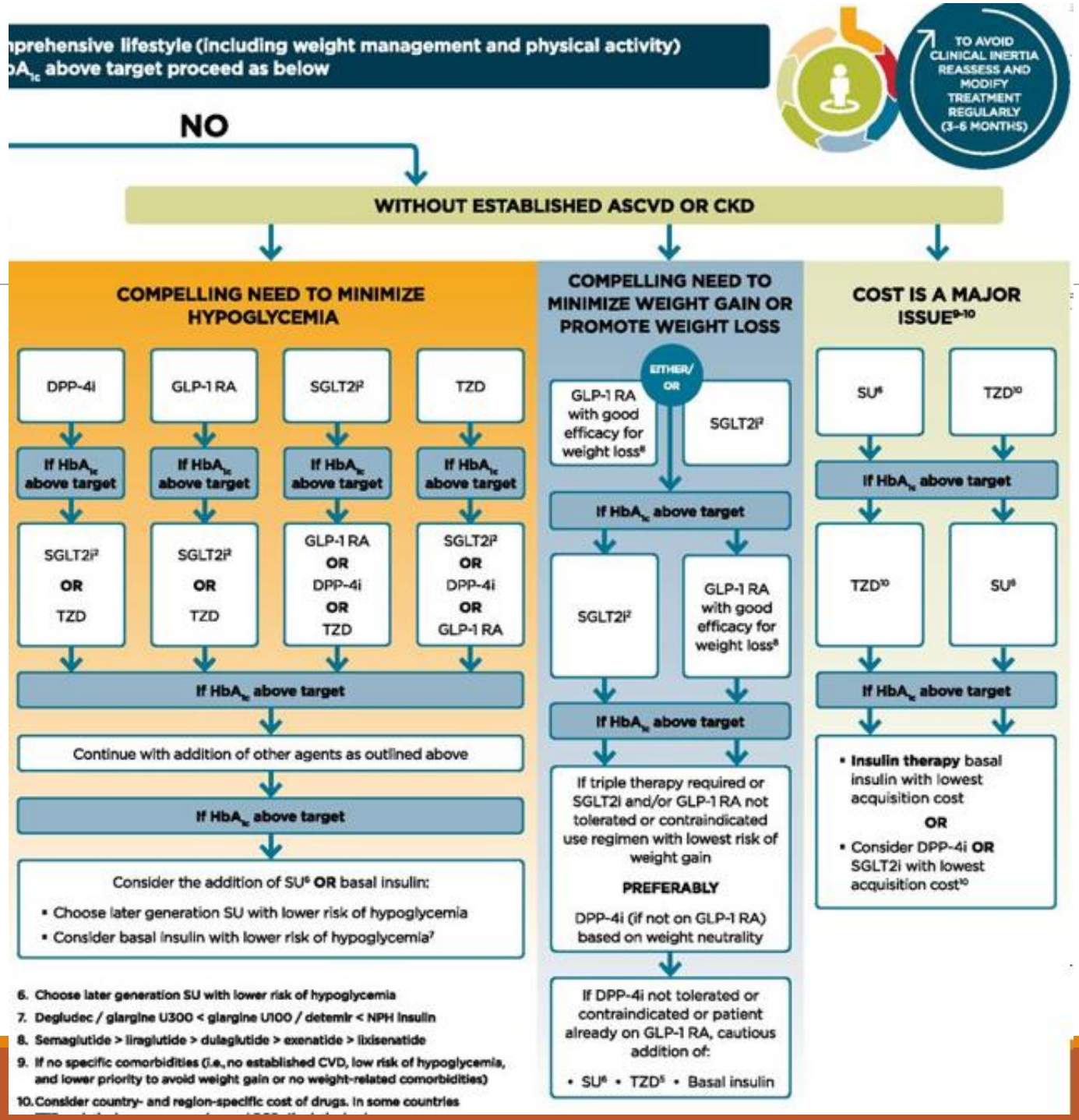
https://www.nejm.org/doi/full/10.1056/NEJMoa1811744

GLP-1 (Do not use together with DDP4)

Generic Name	Brand Name	Usual Dosing	Benefits
Liraglutide	Victoza Saxenda (if high dose)	1.2-1.8mg sc daily 3mg sc daily	Reduction in CV events Weight loss
Semaglutide	Ozempic	1mg-2mg sc weekly	Reduction in CV events
Delaglutide	Trulicity	0.75mg – 1.5mg weekly	Weekly dosing

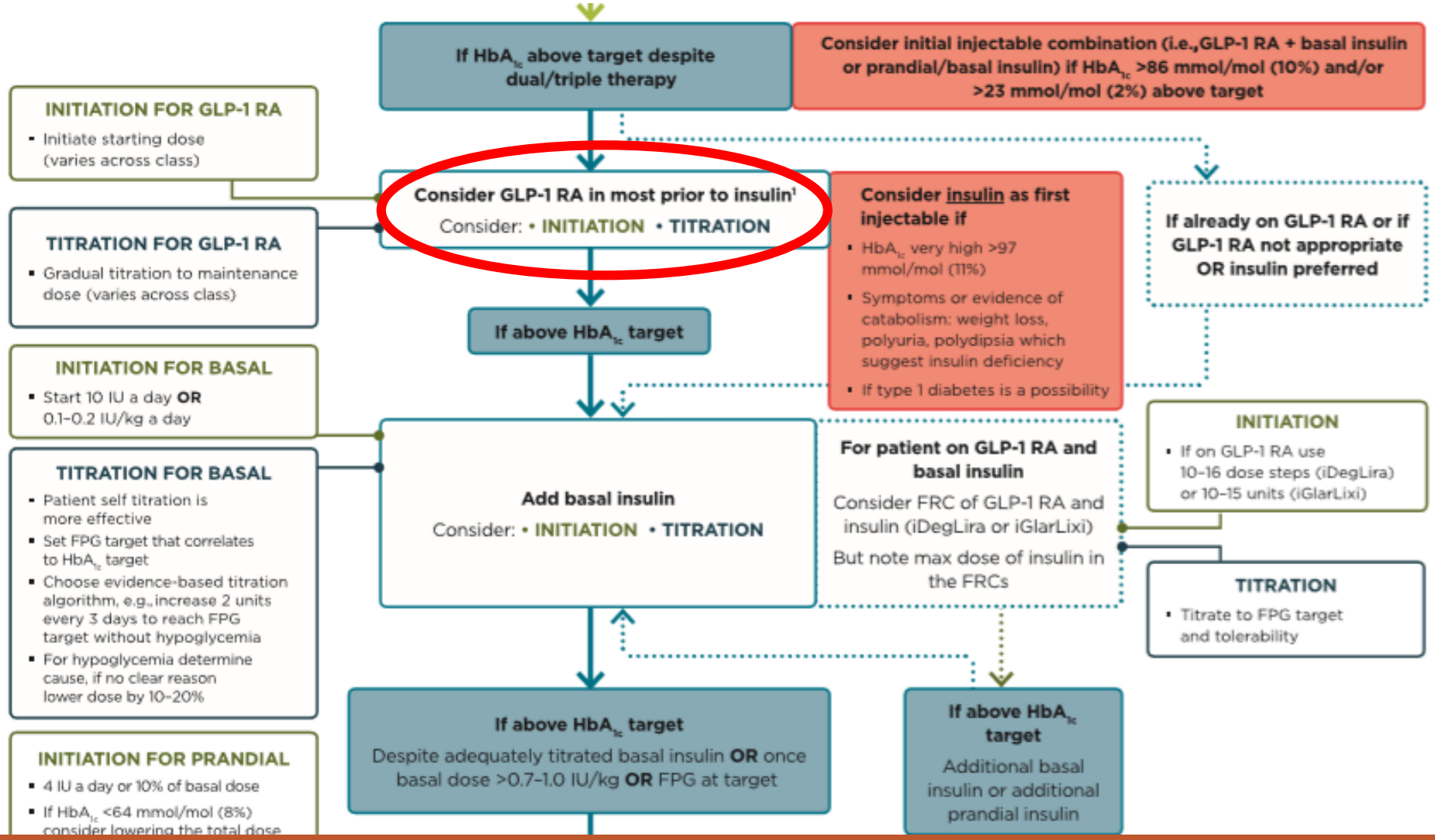
SGLT2-I (reduce other diuretics by half, know CrCl)

Generic Name	Brand Name	Usual Dosing	Cautions	Benefit
Canagliflozin	Invokana®	100-300 mg once daily	**CrCl 45 to <60 mL/min = 100 mg** CrCl < 45 mL/min contraindicated	Reduction in albuminuria & HF hospitalization
Dapagliflozin	Farxiga®	5-10 mg once daily	CrCl <60 mL/min contraindicated	
Empagliflozin	Jardiance®	10-25 mg once daily	CrCl <45 mL/min use not recommended	Reduction in albuminuria & CV death


prehensive lifestyle (including weight management and physical activity)
A_{1c} above target proceed as below
NO
TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)
WITHOUT ESTABLISHED ASCVD OR CKD
COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA
DPP-4i
GLP-1 RA
SGLT2i[2]
TZD
If HbA_{1c} 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 HbA_{1c} above target
Continue with addition of other agents as outlined above
If HbA_{1c} 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 HbA_{1c} above target
SGLT2i[2]
GLP-1 RA with good efficacy for weight loss[8]
If HbA_{1c} above target
If triple 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 HbA_{1c} above target
TZD[10]
SU[6]
If HbA_{1c} 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 with lower risk of hypoglycemia
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

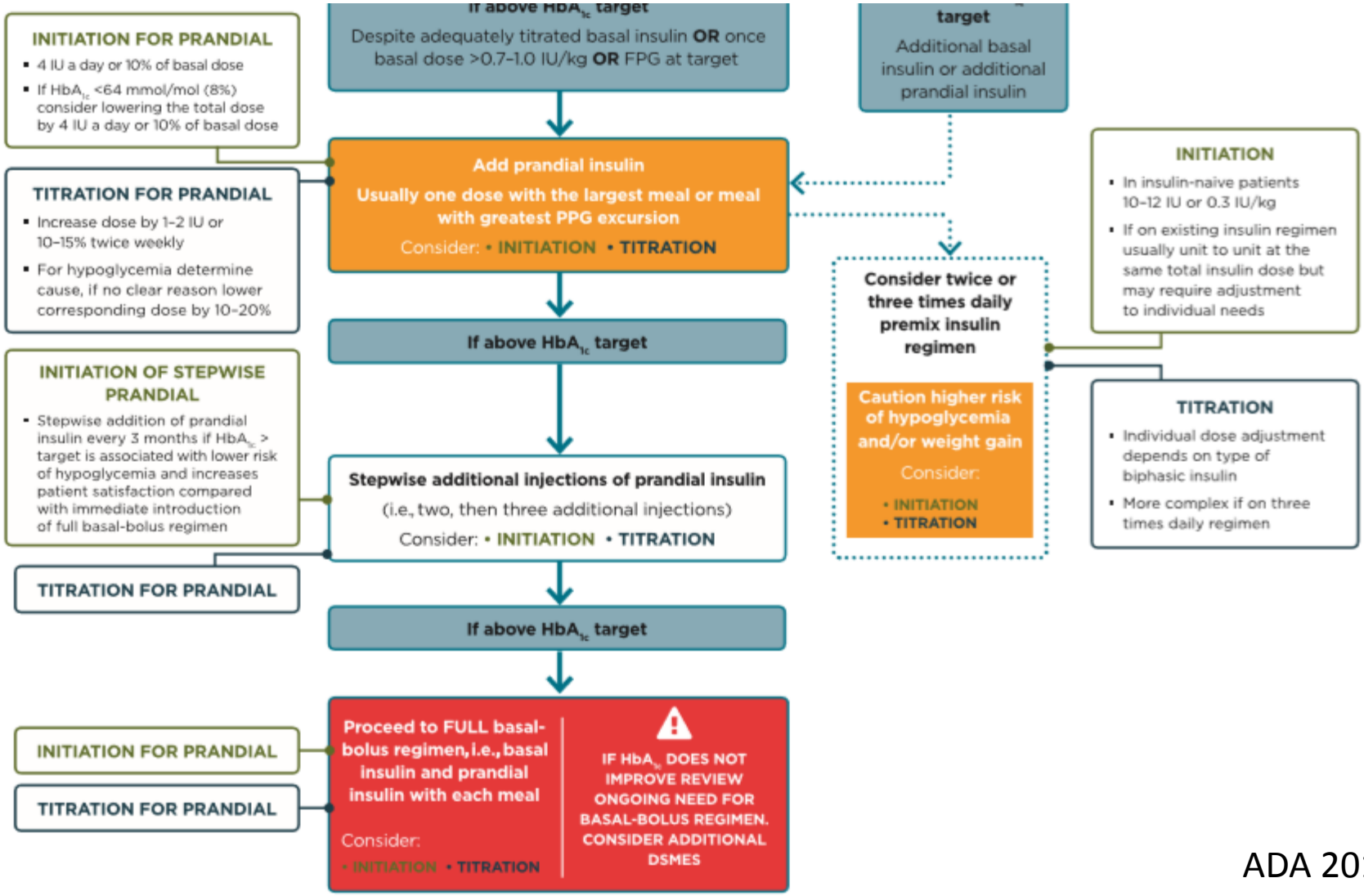
ADA 2019

Insulin - Basal



ADA 2019

Insulin - Prandial



ADA 2019

Blood Pressure

Using ASCVD 10-yr risk

- >15%
- <15%

Per Dr. Trowbridge…. ??

- individualized care

- as close to ‘normal’ blood pressure as possible

preferences. C

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**

LDL

10.19 For patients of all ages with diabetes and atherosclerotic cardiovascular disease or 10-year atherosclerotic cardiovascular disease risk >20%, high-intensity statin therapy should be added to lifestyle therapy. **A**

10.20 For patients with diabetes aged <40 years with additional atherosclerotic cardiovascular disease risk factors, the patient and provider should consider using moderate-intensity statin in addition to lifestyle therapy. **C**

Table 10.2—Recommendations for statin and combination treatment in adults with diabetes

Age	ASCVD or 10-year ASCVD risk >20%	Recommended statin intensity^ and combination treatment*
<40 years	No	None†
	Yes	High • In patients with ASCVD, if LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)#
≥40 years	No	Moderate‡
	Yes	High • In patients with ASCVD, if LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)

ADA 2019

AMERICAN COLLEGE of CARDIOLOGY

ASCVD Risk Estimator Plus

Estimate Risk | Therapy Impact

App should be used for primary prevention patients (those without ASCVD) only.

Current Age *
Age must be between 20-79

Sex *
Male | Female

Race *
White | African American | Other

Systolic Blood Pressure (mm Hg) *
Value must be between 90-200

Diastolic Blood Pressure (mm Hg)
Value must be between 60-130

Total Cholesterol (mg/dL) *
Value must be between 130 - 320

HDL Cholesterol (mg/dL) *
Value must be between 20 - 100

LDL Cholesterol (mg/dL)
Value must be between 30-300

History of Diabetes? *
Yes | No

Smoker? *
Current | Former | Never

On Hypertension Treatment? *
Yes | No

On a Statin?
Yes | No

On Aspirin Therapy?
Yes | No

http://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/

	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

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 for medical nutrition therapy
- Diabetes self-management education and support
- Dentist for comprehensive dental and periodontal examination
- Mental health professional, if indicated

4.6 The 10-year risk of a first atherosclerotic cardiovascular disease event should be assessed using the race- and sex-specific Pooled Cohort Equations to better stratify atherosclerotic cardiovascular disease risk. **B**

Maintenance Care

Annual:

- Foot exam
- Eye exam
- Dental exam
- Microalbumin/cr ratio
- 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: Pneumovax23
- After 65yo: PCV13 then PCV23 (1 year apart)

Other:

- TB screening
- HCV screening
- Routine vaccines as regular population: annual flu vaccine, tetanus vaccine q10yr, etc

Resources

AHA/ACC Hypertension Guideline 2017. AHA/ACC 2017. https://www.ahajournals.org/doi/10.1161/HYP.0000000000000065

Standards of Medical Care in Diabetes - 2019. American Diabetes Association. January 01 2019; volume 42 issue Supplement 1. http://care.diabetesjournals.org/content/42/Supplement_1

Vaccinations for Adults with Diabetes. http://www.immunize.org/catg.d/p4043.pdf

Tuberculosis and Diabetes. WHO. 2016. https://www.who.int/tb/publications/diabetes_tb.pdf

BP Thresholds for and Goals of Pharmacologic Therapy in Patients with Hypertension According to Clinical Conditions

Clinical Condition (s)	BP Threshold mm Hg	BP Goal mm Hg
General		
Clinical CVD or 10 year ASCVD risk ≥ 10%	≥130/80	<130/80
No clinical CVD and 10 year ASCVD risk <10%	≥140/90	<130/80
Older persons (≥65 years of age; non-institutionalized, ambulatory, community-living adults)	≥130 (SBP)	<130 (SBP)
Speci c Comorbidities		
Diabetes mellitus	≥130/80	<130/80
Chronic kidney disease	≥130/80	<130/80
Chronic kidney disease post-renal transplantation	≥130/80	<130/80
Heart failure	≥130/80	<130/80
Stable ischemic heart disease	≥130/80	<130/80
Secondary stroke prevention	≥140/90	<130/80
Peripheral arterial disease	≥130/80	<130/80

AHA/ACC Hypertension Guideline 2017

ASCVD Risk Categories and LDL-C Treatment Goals

Risk category	Risk factors/10-year risk	Treatment goals		
		LDL-C (mg/dL)	Non-HDL-C (mg/dL)	Apo B (mg/dL)
Extreme risk	– Progressive ASCVD including unstable angina in individuals after achieving an LDL-C <70 mg/dL – Established clinical cardiovascular disease in individuals with DM, stage 3 or 4 CKD, or HeFH – History of premature ASCVD (<55 male, <65 female)	<55	<80	<70
Very high risk	– Established or recent hospitalization for ACS, coronary, carotid or peripheral vascular disease, 10-year risk >20% – DM or stage 3 or 4 CKD with 1 or more risk factor(s) – HeFH	<70	<100	<80
High risk	– ≥2 risk factors and 10-year risk 10%-20% – DM or stage 3 or 4 CKD with no other risk factors	<100	<130	<90
Moderate risk	≤2 risk factors and 10-year risk <10%	<100	<130	<90
Low risk	0 risk factors	<130	<160	NR

AACE/ACE 2018

Major Atherosclerotic Cardiovascular Disease Risk Factors

Major risk factors	Additional risk factors	Nontraditional risk factors
Advancing age	Obesity, abdominal obesity	⇧ Lipoprotein (a)
⇧ Total serum cholesterol level	Family history of hyperlipidemia	⇧ Clotting factors
⇧ Non–HDL-C	⇧ Small, dense LDL-C	⇧ Inflammation markers
⇧ LDL-C	⇧ Apo B	(hsCRP; Lp-PLA_2)
Low HDL-C	⇧ LDL particle concentration	⇧ Homocysteine levels
Diabetes mellitus	Fasting/postprandial	Apo E4 isoform
Hypertension	hypertriglyceridemia	⇧ Uric acid
Stage 3 or 4 chronic kidney disease	PCOS	⇧ TG-rich remnants
Cigarette smoking	Dyslipidemic triad	
Family history of ASCVD		

Abbreviations: apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; hsCRP, highly sensitive C-reactive protein; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; Lp-PLA2, lipoprotein-associated phospholipase; PCOS, polycystic ovary syndrome.