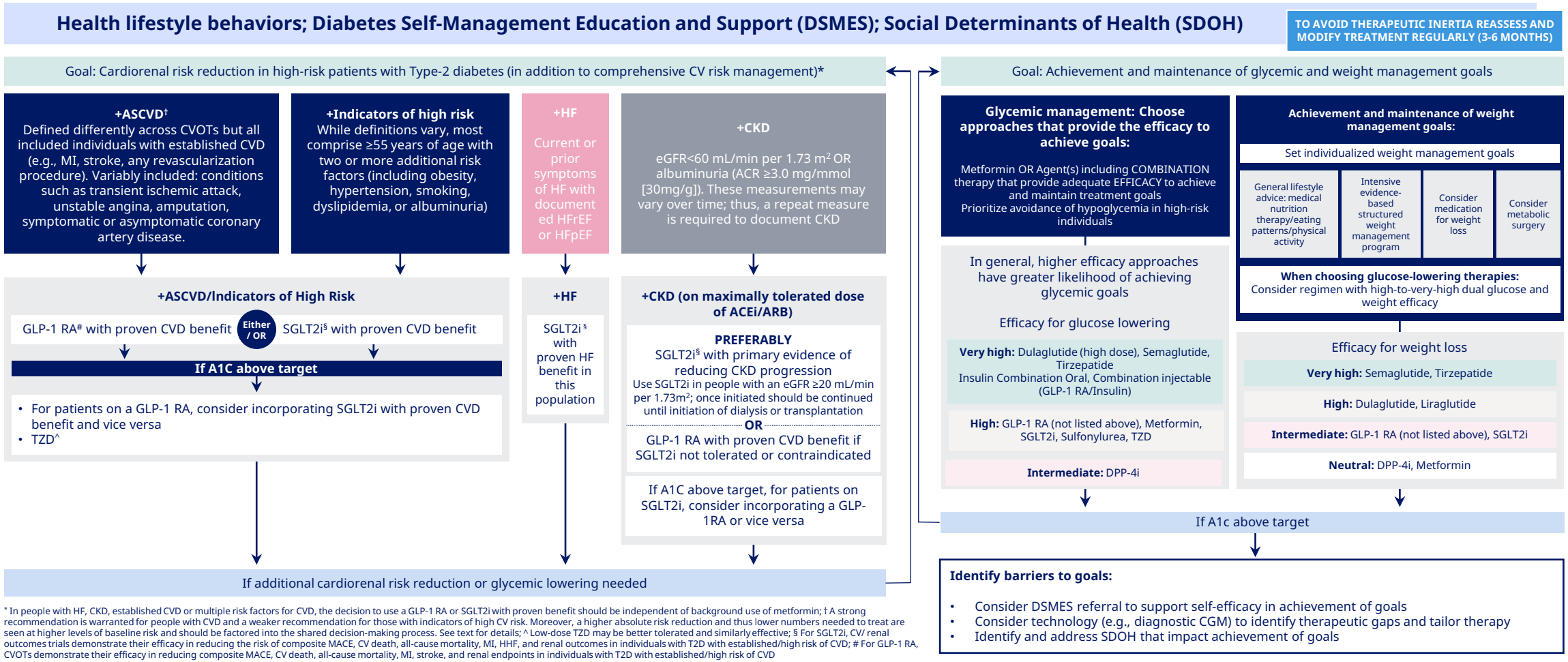
Guideline Directed Management of Diabetes Comorbidities

August 2024

ADA STANDARDS OF MEDICAL CARE IN DIABETES – 2024

2024 ADA: Use of Glucose- lowering medications in the management of T2D *(Figure 9.3; S166)*



* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/ renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD

A1C, glycated hemoglobin; ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; CVOT, cardiovascular outcomes trial; DPP-4i, dipeptidyl peptidase 4 inhibitor; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular events; MI, myocardial infarction; SDOH, social determinants of health; SGLT2i, sodium-glucose cotransporter 2 inhibitor; T2D, type 2 diabetes; TZD, thiazolidinedione.
Adapted from Davies et al. (84).
American Diabetes Association (ADA). Diabetes Care 2024;47(Supplement_1):S158–S178

DCRM 2.0 MULTISPECIALTY PRACTICE RECOMMENDATIONS

Antihyperglycemic therapy in Type 2 Diabetes

Lifestyle Therapy

Cardiorenal Track

Prevent ASCVD/HF/CKD Events Independent of Glycemic Status

ASCVD	HFpEF	HFrEF/HFmrEF	CKD	Stoke/TIA
GLP1-Ra[a,b]	SGLT2i[b]	SGLT2i[b]	SGLT2i[b]	GLP1-RA[a]
SGLT2i[b]	GLP1-RA[a,b]		GLP1-Ra[a,b]	Pio
Pio				

Proven benefits in CVOTs Hypoglycemia and/or HF risk

a. GLP-1 RA with proven benefit.
b. Combining GLP-1 RA and SGLT2i is encouraged to improve outcomes.
c. GLP-1 RA or GIP/GLP-1 RA.
d. If CKD, efficacy may be lower; consider using SGLT2i later in glucose hierarchy.
e. Glycated albumin or fructosamine may also be considered for evaluation of glycemic control.
f. Do not combine incretin classes (GLP-1 RA, GIP/GLP-1 RA, DPP4i). Use caution when combining insulin + SU, insulin + SGLT2i, or insulin + TZD.

Hyperglycemia Track

Manage Hyperglycemia to Individualized Goal

Recently diagnosed, healthier, few to no comorbidities

A1C: **6.0%** — **6.5%** — **7.0%** — **7.5%**

Limited life expectancy,, frail, complex comorbidities

Most patients

Glucose Hierarchy

Preferred	GLP1-RA-based
	Metformin
	SGLT2i
	TZD
	Insulin
	DPP4i
	SU
Less used	Glinide
	Colesevelam
	AGI
	Bromocriptine QR
	Pramlintide

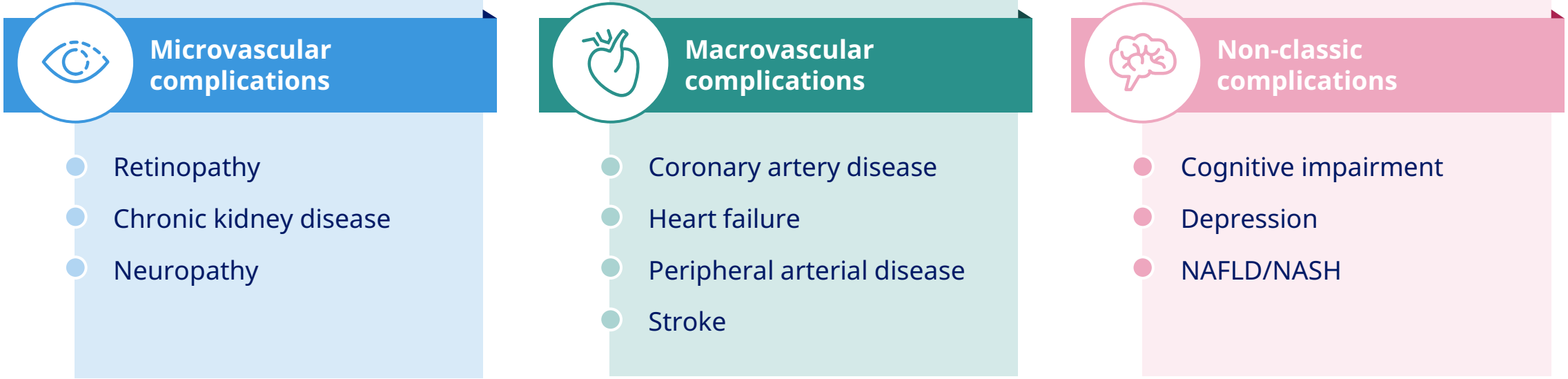
- **Generally, use initial combination therapy for patients with A1C >1–2% above individualized goal**
- Lower A1C goals can be achieved safely provided there is no hypoglycemia
- Assess glucose control with A1C plus CGM or SMBG and intensify therapy until goal achieved[e]
- Add agents with complementary MOA to maintain glucose control at goal[f]
- Choose agents according to recommended hierarchy, based on individual patient's risks and benefits, preferences, and access to therapies
- Consider initial insulin therapy in severe hyperglycemia/metabolic decompensation

AGI, alpha glucosidase inhibitor; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CVOT, cardiovascular outcome trial; DPP4i, dipeptidyl peptide 4 inhibitor; GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MOA, mechanism of action; Pio, pioglitazone; QR, quick release; SGLT2i, sodium glucose cotransporter 2 inhibitor; SMBG, self-monitored blood glucose; SU, sulfonylurea; TIA, transient ischemic attack; TZD, thiazolidinedione.

Handelsman Y et al. Metabolism. 2024 Jun 4:155931. doi: 10.1016/j.metabol.2024.155931

ADA STANDARDS OF MEDICAL CARE IN DIABETES – 2024: T2D AND ITS COMPLICATIONS

Diabetes-related complications affect multiple organs

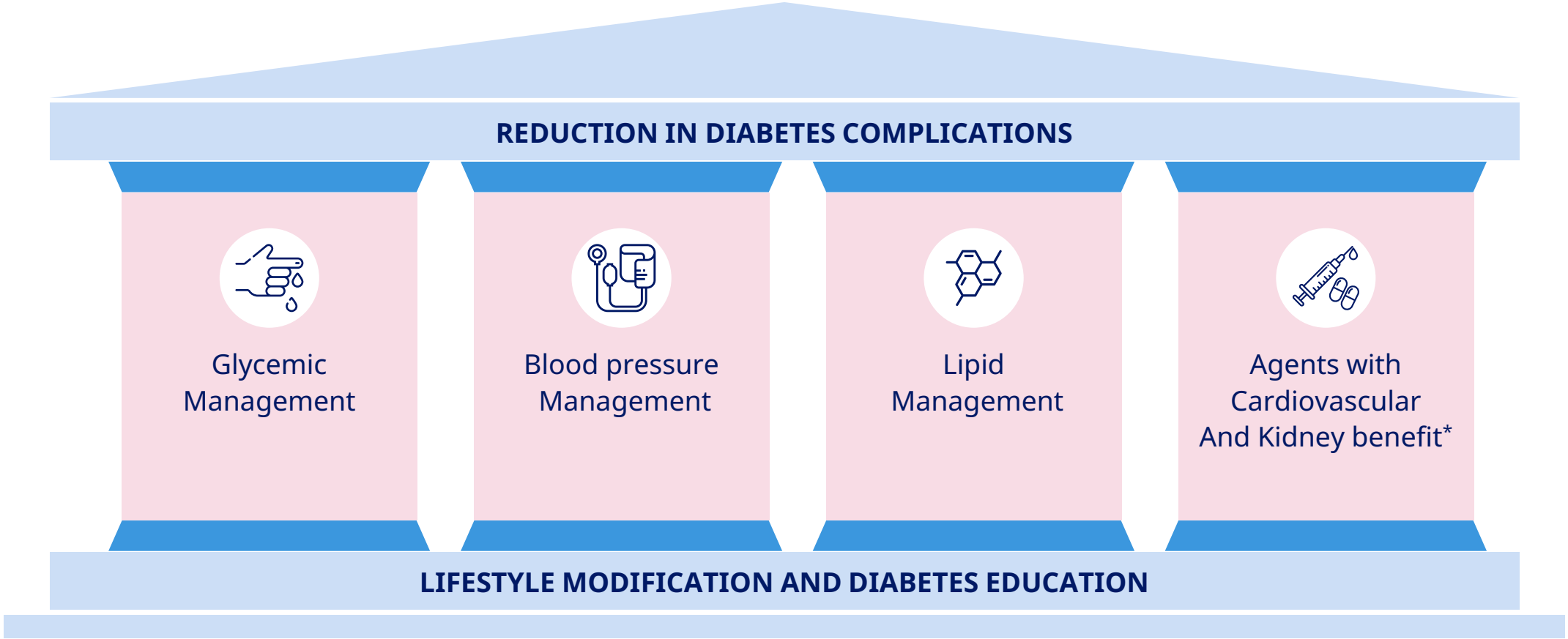


NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis

1. American Diabetes Association (ADA). Diabetes Care 2022 Jan; 45(Supplement 1);

ADA STANDARDS OF MEDICAL CARE IN DIABETES – 2024

2024 ADA: Multifactorial approach to reduction in risk of diabetes complications *(Figure 10.1; S180)*



**Risk reduction interventions to be applied as individually appropriate*

American Diabetes Association (ADA). Diabetes Care 2024;47(Supplement_1):):S179–S218

AHA/ACC TREATMENT GUIDELINES

Recommendations for prevention and treatment of ASCVD

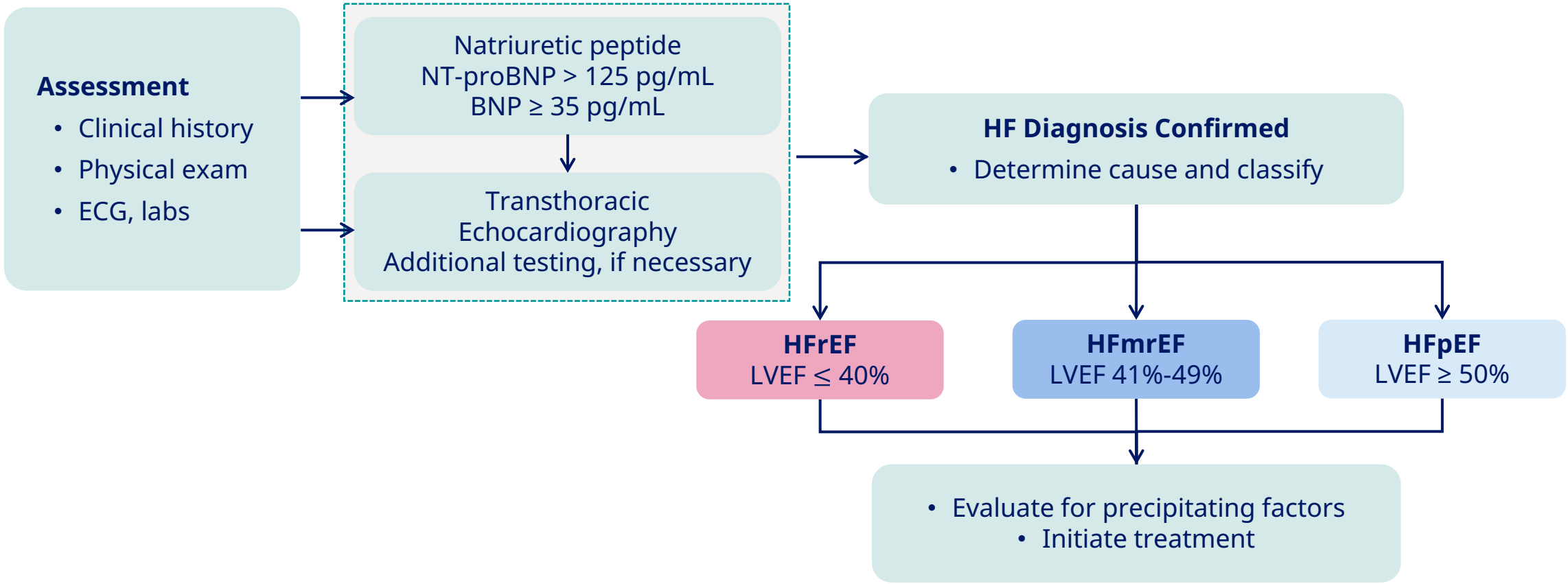
	Primary prevention	Secondary prevention
Treatment goals[1,2,5]	Lifestyle/smoking interventions SBP <130 mmHg DBP <80 mmHg) + LDL-C: No specific guidance‡ Intensify treatment based on CV risk and other patient factors	Lifestyle/smoking interventions SBP <130 mmHg DBP <80 mmHg) + LDL-C: ≥50% reduction from baseline ≥1.8 mmol/L (≥ 70 mg/dL)† Intensify treatment based on CV risk and other patient factors Use SGLT2 inhibitor or GLP-1 RA with proven CV benefit in patients with CCD and T2D and SGLT2 inhibitor in patients with CCD and HF
Lifestyle/smoking interventions[1,2.5]	Physical activity Diet & alcohol consumption	Body weight/composition Smoking Cessation
Lipid-lowering agents[1,2.5]	Initiate/intensify statin	2 Add ezetimibe 3 Add PCSK9i Bempedoic acid or inclisiran may be added in place of PCSK9i
Anti-hypertensive agents[3,5]	1 First-line agents include beta-blockers, thiazide diuretics, calcium channel blockers, and ACE inhibitors or ARBs	2 Intensification: Combination therapy and/or MRA to optimize BP control
Anti-thrombotic agents[1,4,5]	Low-dose aspirin (75–100 mg daily) in select adults (40–70 years); not routinely administered in adults >70 years	Aspirin in patients with CAD → DAPT to intensify* in patients ≤1 y post-ACS or stable IHD >1 y post-PCI Initiate proton pump inhibitor¥

*‡ Specific recommendations are depending on risk factors; † Both for patients with clinical ASCVD and very high-risk ASCVD with multiple risk factors; * Intensification of antithrombotic therapy should always account for individual patient bleeding risk;*
¥ In patients with history/ currently increased risk of gastrointestinal bleeding.
ACC/AHA, American college of Cardiology/ American heart association; ACEi, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; DBP, diastolic blood pressure; CAD, coronary artery disease; CCD, chronic coronary disease; CV, cardiovascular; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HF, heart failure; IHD, ischemic heart disease; LDL-C, low-density lipoprotein cholesterol; MRA, mineralocorticoid receptor antagonists; PCI, percutaneous coronary intervention; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; SBP, systolic blood pressure; SGLT2i, sodium–glucose cotransporter 2 inhibitor; T2D, type 2 diabetes

1. Arnett DK et al. Circulation 2019;140:e596–e646; 2. Grundy SM et al. Circulation. 2019;139:e1046–e1081; 3.Whelton PK et al. Hypertension 2018;71:e13–e115; 4. Levine GN et al. J Am Coll Cardiol 2016;68:1082–1115; 5. Virani SS et al. J Am Coll Cardiol. 2023;S0735-1097(23)05281-6

2022 AHA/ACC/HFSA GUIDELINE

Diagnostic Algorithm for HF and EF-Based Classification



BNP indicates B-type natriuretic peptide; ECG, electrocardiogram; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LV, left ventricle; LVEF, left ventricular ejection fraction; and NT-proBNP, N-terminal pro-B type natriuretic peptide.

Heidenreich, P. A. et al. (2022). 2022 AHA/ACC/HFSA Guideline for Heart Failure. Circulation.

DCRM 2.0 MULTISPECIALTY PRACTICE RECOMMENDATIONS

Heart Failure Prevention and Management

Initial and Longitudinal Clinical Assessment

Serially assess for signs or symptoms of congestion/volume overload or inadequate perfusion

Prevention of Heart Failure

General Recommendations	
All	• Lifestyle intervention (low-salt diet, smoking cessation, physical activity, maintaining healthy weight) • BP control; target SBP <130 mm Hg • ASCVD interventions as indicated
T2D	Natriuretic peptide screening followed by team-based care, including cardiology referral, can be useful in preventing HF
High HF risk	

Medication Recommendations	
T2D + high CV risk or established CVD	SGLT2i
CKD with or without T2D	SGLT2i
T2D + CKD	Nonsteroidal MRA

a. ARNI preferred over ACE or ARB.
b. Steroidal MRA.
c. Select agent with proven benefits; recommended to improve symptoms and physical limitations
d. If T2D + CKD, consider nonsteroidal MRA.

Strongly recommended | Reasonable to use | May be considered

Treatment of Heart Failure

Heart failure defined as:

- Signs and/or symptoms of HF caused by structural/functional cardiac abnormality
  -plus-
- Elevated natriuretic peptides or objective evidence of congestion (e.g. echocardiograph evidence, right heart catheterization)

HFrEF (EF ≤40%)

Diuretic (if congested) + quadruple therapy

ARNI (or ACEi/ARB) + β-blocker + SGLTi + MRA[b]

Follow HF guidelines for device and Class II therapy recommendations

HFmrEF (EF=41-49%)

Diuretic (if congested) + SGLTi + Consider additional therapies

GLP-1 RA[c] (if BMI ≥30 kg/m² and EF ≥45%) + ARNI or ACEi or ARB[a] + β-blocker + MRA[b,d]

HFpEF (EF ≥50%)

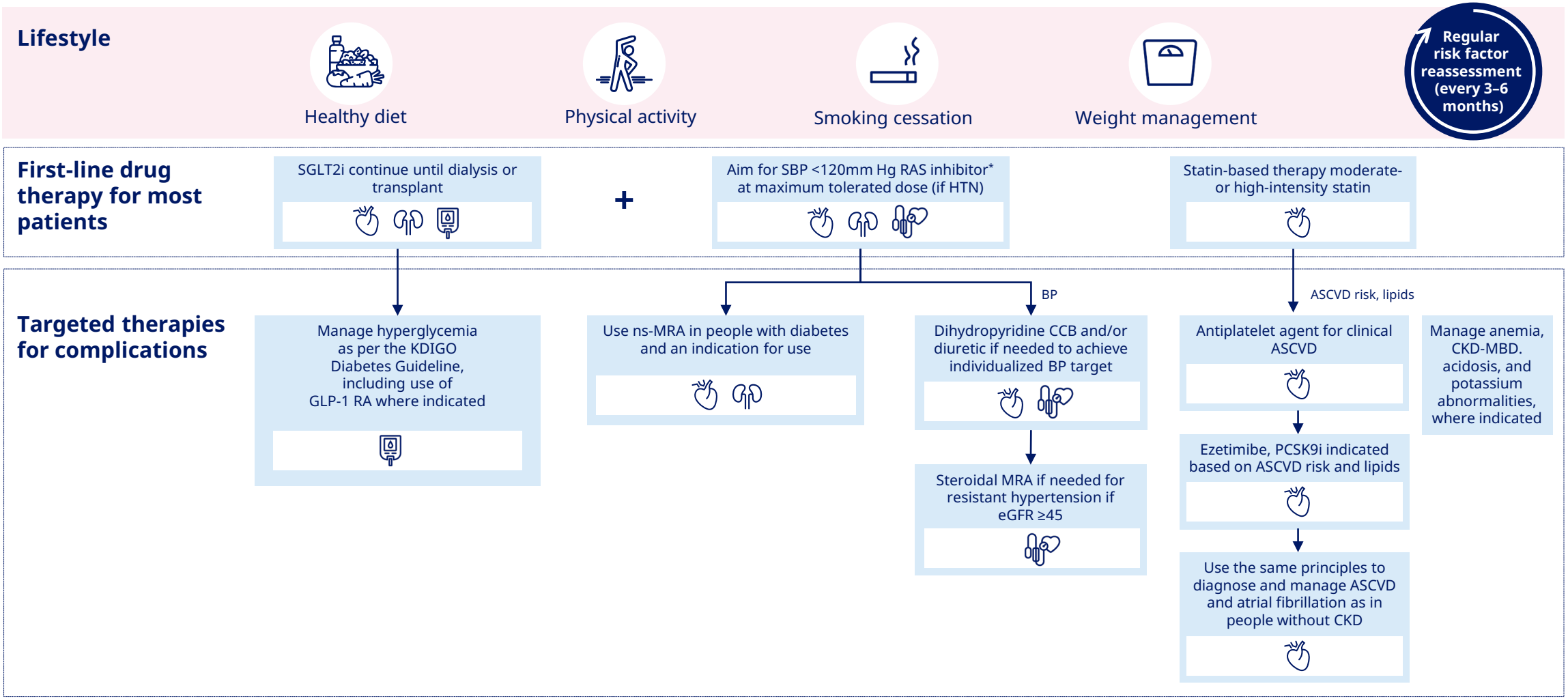
Diuretic (if congested) + SGLTi + Consider additional therapies

GLP-1 RA[c] (if BMI ≥30 kg/m²) + ARNI or ARB[a] (EF up to 55-60%) + MRA[b,d] (EF up to 55-60%)

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; CVD, CV disease; EF, ejection fraction; GLP-1 RA, glucagon-like receptor agonist; HFmrEF, HF with mildly reduced EF; HFpEF, HF with preserved EF; HFrEF, HF with reduced EF; MRA, mineralocorticoid receptor agonist; SBP, systolic blood pressure; SGLT2i, sodium glucose cotransporter 2 inhibitor; T2D, type 2 diabetes.

Handelsman Y et al. Metabolism. 2024 Jun 4:155931. doi: 10.1016/j.metabol.2024.155931

Holistic approach to chronic kidney disease (CKD) treatment and risk modification



**Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker should be first-line therapy for blood pressure (BP) control when albuminuria is present; otherwise dihydropyridine calcium channel blocker (CCB) or diuretic can also be considered. All 3 classes are often needed to attain BP targets..*

ASCVD, atherosclerotic cardiovascular disease; CKD-MBD, chronic kidney disease-mineral and bone disorder; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HTN hypertension; KDIGO, Kidney Disease: Improving Global Outcomes; MRA, mineralocorticoid receptor antagonist; ns-MRA, nonsteroidal mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAS, renin-angiotensin system; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter-2 inhibitor

Kidney Int. 2024 Apr;105(4S):S117-S314. doi: 10.1016/j.kint.2023.10.018.

DCRM 2.0 MULTISPECIALTY PRACTICE RECOMMENDATIONS

CKD Prevention and Management

Prevention

Risk Assessment

CKD associated with:

- ▲ Mortality
- ▲ ASCVD (increased risk if UACR ≥30 mg/g /≥3 mg/mmol
- ▲ HF
- ▲ ESKD
- ▲ Hypertension
- ▲ Arrhythmia
- ▲ Hypoglycemia

Lifestyle Therapy *Plus* Goal-Directed Pharmacotherapy

- BP control (<130/80 mm Hg)
- Glucose control (A1C <7.0% / <53 mmol/mol)
- Lipid control (max dose statin ± other lipid-lowering agents)
- Albuminuria reduction (RASi + SGLT2i)

Management

Screening and Diagnosis

Assess:

- UACR
  -and-
- eGFR

Diagnose CKD if:

- Persistent UACR ≥30 mg/g / ≥3 kg/mmol
  -and/or-
- Persistent eGFR <60 mL/min/1.73 m^2

CKD with diabetes	**Max tolerated RASi[a]**	+	**SGLT2i**	+	**Nonsteroidal MRA**	+ **GLP-1 RA**
CKD without diabetes	**Max tolerated RASi[a]**	+	**SGLT2i**			

[a] Avoid down-titration or cessation if hyperkalemic

A1C, hemoglobin A1C (HbA1c); ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HF, heart failure; GLP-1 RA, glucagon-like peptide 1 receptor agonist with proven benefit; MRA, mineralocorticoid receptor agonist; RASi, renin angiotensin system inhibitor; SGLT2i, sodium glucose cotransporter 2 inhibitor; UACR, urine albumin-creatinine ratio.

Handelsman Y et al. Metabolism. 2024 Jun 4:155931. doi: 10.1016/j.metabol.2024.155931

ADA STANDARDS OF MEDICAL CARE IN DIABETES 2024 AND KDIGO: TREATMENT GUIDELINES FOR MANAGEMENT OF CKD

Glycemic control in CKD

Factors guiding individualized glycemic target[1,2]

<6.5%	HbA_{1c}	<8.0%
CKD G1	Severity of CKD	CKD G5
Absent/minor	Macrovascular complications	Present/severe
Few	Comorbidities	Many
Long	Life expectancy	Short
Present	Hypoglycemia awareness	Impaired
Available	Resources for hypoglycemia management	Scarce
Low	Propensity of treatment to cause hypoglycemia	High

KDIGO 2020[1], 2022[2]

Patients with diabetes and CKD not treated with dialysis[1,2]
<6.5% to <8.0%
Patients for whom prevention of complications is the key goal[1]
<6.5% or <7.0%
Patients with multiple comorbidities or increased hypoglycemia[1]
<7.5% or <8.0%

ADA 2024[3]

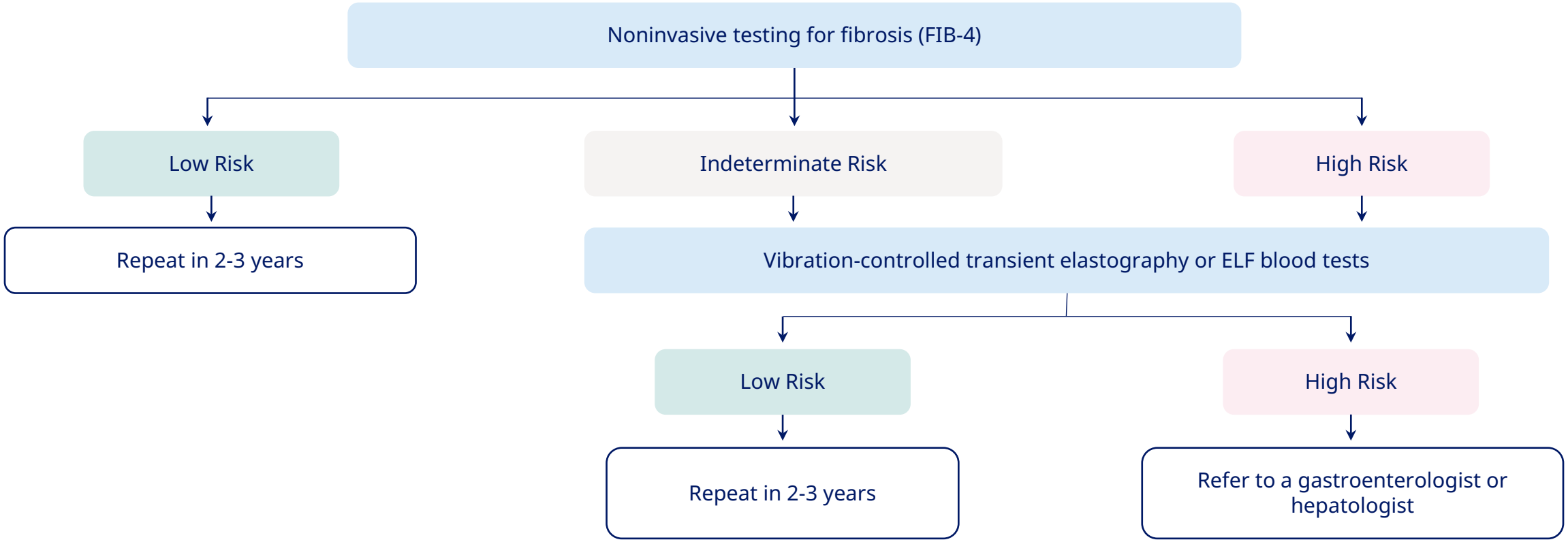
- Lowering blood glucose itself helps prevent CKD and its progression
- For people with T2D and established CKD, special considerations for the selection of glucose-lowering medications include
  - Comorbidity and CKD stage
  - Individual patient's risk (cardiovascular and renal in addition to glucose)
  - Drug dosing modification with eGFR <60 mL/min/1.73 m^2
  - Convenience and cost

ADA, American diabetes association; CKD, chronic kidney disease; G1, eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated hemoglobin; KDIGO, Kidney Disease Improving Global Outcome

1. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. Kidney Int. 2020;98(4S):S1–S115; 2. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2022;102(5S):S1-S127 3. American Diabetes Association (ADA). Diabetes Care 2024;47(Supplement_1)

ADA STANDARDS OF MEDICAL CARE IN DIABETES – 2024

2024 ADA: A proposed algorithm for risk stratification in individuals with nonalcoholic fatty liver disease (NAFLD) or nonalcoholic steatohepatitis (NASH). *(Figure 4.2; S67)*



ELF, enhanced liver fibrosis; FIB-4, fibrosis 4 index Adapted from Kanwal et al (174)
American Diabetes Association (ADA). Diabetes Care 2024;47(Supplement_1):S52–S76

MASLD/MASH (NAFLD/NASH) Prevention and Management

Screen for MASLD

Identify patients at risk:

- ≥2 metabolic risk factors[a]
- T2D
- Steatosis on imaging or ▲ aminotransferases

Exclude other conditions

- Alcohol intake history: women, ≥14 drinks/week; men, ≥21 drinks/week
- HCV antibody + HCV RNA reflex testing
- Consider HBsAg, HBsAb, HBcAb,
- Consider ANA, AMA, ASMA, immunoglobulins, ferritin, A1At
- Check for clinical signs of advanced liver disease/cirrhosis
- Consider genetic causes and endocrinopathies

Test results consistent with other forms of liver disease or cirrhosis → **Refer to hepatologist**

Negative for other forms of liver disease

Risk Stratification

FIB-4 <1.3 or (<2.0 if ≥65 years of age)

- **Yes**
  - **No T2D or <2 metabolic risk factors**
  - **T2D or ≥2 metabolic risk factors**
- **No**

Reassess every year

Secondary Assessment

Risk level	ELF	VCTE	MRE
Low	<7.7	≤8.0	<2.6
Intermediate	7.7-9.8	8.1-12	2.6-3.6
High	>9.8	>12	>3.6
Cirrhosis or Portal HTN	>11.3	>15	>4.6

Across all risk levels, consider liver biopsy whenever NITs are discordant

- Intermediate → **Annual monitoring with VCTE or MRE Consider referring to hepatologist**
- High / Cirrhosis or Portal HTN → **Refer to hepatologist Monitor and screen for HCC and esophageal varices**

F0-F1	F2-F3	F4
Lifestyle modification	Lifestyle modification Consider pharmacotherapy	Lifestyle modification Cirrhosis-based management
	← Refer to hepatologist and monitor →	

[a] Hyperglycemia, ↑ TG, ↑ BP, ↓ HDL-C, abdominal obesity.

- Achieve ≥10% weight reduction with lifestyle, with intensification to pharmacologic or surgical interventions if necessary
- Risk factor reduction: optimal lipid and BP control and appropriate therapy for obesity, diabetes, ASCVD, CKD, HF
- Consider resmetirom if appropriate for subjects with F2–F3 fibrosis
- Consider pioglitazone, SGLT2is, or GLP-1 RAs if indicated for other comorbidities such as T2D
- Consider leptin and pioglitazone for persons with lipodystrophy

A1At, alpha-1 antitrypsin deficiency AMA, antimitochondrial antibodies; ANA, antinuclear antibodies; ASCVD, atherosclerotic cardiovascular disease; ASMA, anti-smooth muscle antibodies; BP, blood pressure; cAb, core antibody; CKD, chronic kidney disease; ELF, enhanced liver fibrosis Fn, fibrosis stage (0–4);FIB-4, fibrosis 4 calculation; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HB, hepatitis B; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDL-C, high-density lipoprotein cholesterol; HF, heart failure; HTN, hypertension; MASLD, metabolic dysfunction–associated steatotic liver disease; MASH, metabolic dysfunction–associated steatohepatitis; MRE, magnetic resonance elastography; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; NIT, noninvasive test; sAb, surface antibody; sAg, surface antigen; SGLT2i = sodium glucose cotransporter 2 inhibitor; T2D, type 2 diabetes; TG, triglyceride; VCTE, vibration-controlled transient elastography.

Handelsman Y et al. Metabolism. 2024 Jun 4:155931. doi: 10.1016/j.metabol.2024.155931

ADA STANDARDS OF MEDICAL CARE IN DIABETES – 2024

Peripheral Artery Disease (PAD)

ADA recommends screening for asymptomatic PAD using ankle brachial index in people with diabetes at high risk for PAD, including any of the following:

age ≥ 50 years

diabetes with duration ≥ 10 years

comorbid microvascular disease

clinical evidence of foot complications

or any end-organ damage from diabetes.

Initial screening for PAD should include:

- Assessment of lower-extremity pulses, capillary refill time
- Rubor on dependency
- Pallor on elevation, and venous filling time
- Individuals with a history of leg fatigue, claudication, and rest pain relieved with dependency or decreased or absent pedal pulses should be referred for ankle-brachial index with toe pressures and for further vascular assessment as appropriate

PAD, peripheral arterial disease
American Diabetes Association (ADA). Diabetes Care 2024;47(Supplement_1)

Medical Therapy and Foot Care for PAD (1/2)

Class1: Strong | Class2a: Moderate | Class2b: Weak

Asymptomatic PAD

- Cardiovascular risk reduction (lipid-lowering, anti hypertensive therapy, diabetes management*)
- Smoking cessation
- Preventive foot care
- Influenza and SARS-CoV-2 vaccination
- SAPT

Symptomatic PAD (Chronic symptomatic, including claudication, and CLTI)

Antiplatelet and antithrombotic therapy

No recent revascularization

- **SAPT**
  - **Clopidogrel** 75 mg daily
  - **Aspirin** 75-325 mg daily
- Low-dose **aspirin + rivaroxaban** 2.5 mg BID

Recent revascularization (endovascular or surgical)

- **Antiplatelet** and **antithrombotic** therapy
  - Low-dose **aspirin + rivaroxaban** 2.5 mg BID
  - APT: low-dose **aspirin + P2Y12 inhibitor** after endovascular revascularizaton
  - APT: low-dose **aspirin + P2Y12 inhibitor** after surgical revascularization with a **prosthetic graft**
  - **SAPT** with full intensity anticoagulation (if needed for AFIB,VTE, or other indication)

** In patients with PAD and T2D use of GLP-1RA (liraglutide and semaglutide) and SGLT2i (canagliflozin, dapagliflozin and empagliflozin are effective to reduce the risk of MACE (section 5.5)*

Afib, atrial fibrillation; BID, 2 times daily; CLTI, chronic limb-threatening ischemia; DAPT, dual antiplatelet therapy; PAD, peripheral artery disease; SAPT, single antiplatelet therapy; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2;VTE, venous thromboembolism

Gornik HL, et al. 2024 Circulation. 2024 Jun 11;149(24):e1313-e1410. doi: 10.1161/CIR.0000000000001251.

Medical Therapy and Foot Care for PAD (2/2)

Class1: Strong | Class2a: Moderate | Class2b: Weak

Symptomatic PAD (Chronic symptomatic, including claudication, and CLTI)

- Cardiovascular risk reduction (lipid-lowering, anti hypertensive therapy, diabetes management)
- Smoking cessation
- Structured exercise (chronic symptomatic PAD)
- Cilostazol (chronic symptomatic PAD)
- Preventive foot care (chronic symptomatic PAD)
- Wound care, pressure offloading, management of infection (CLTI)
- Influenza and SARS-CoV-2 vaccination

CLTI, chronic limb-threatening ischemia; DAPT, dual antiplatelet therapy; PAD, peripheral artery disease; SAPT, single antiplatelet therapy; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2;VTE, venous thromboembolism
Gornik HL, et al. 2024 Circulation. 2024 Jun 11;149(24):e1313-e1410. doi: 10.1161/CIR.0000000000001251.

DCRM 2.0 MULTISPECIALTY PRACTICE RECOMMENDATIONS

Inflammation

Evaluating Inflammation in ASCVD Risk Assessment

Assessments

hsCRP	>2.0 mg/L / >1.9 mmol/L (>1 measurement if asymptomatic)
UACR	>30 mg/g / >3 mg/mmol

Setting – Evaluate if:

Primary prevention	• ASCVD risk unclear
Secondary prevention	• Recurrent CV events despite optimal CV risk factor control • Unclear attributable CV risk in known ASCVD
All	• Patient preference/choice in shared decision making • Potential for residual risk reduction • Potential contributor to CV risk in rheumatologic and other chronic inflammatory conditions

If hsCRP >2.0 mg/L / >1.9 mmol/L, Consider

- CT-CAC, CTA for CV risk stratification in primary prevention
- Other potential causes of increased hsCRP

Managing Inflammation

Lifestyle Therapy

Weight Reduction

- If overweight or prediabetes, ≥5% - 10% weight reduction with lifestyle
- If obesity, intensify to pharmacotherapy or other interventions as indicated

Treatment options

Positive CVOT Benefits + Known hsCRP-Lowering Effect[a]	
ASCVD	Statin
	Ezetimibe
	Bempedoic acid
Hypertriglyceridemia	IPE
Overweight/obesity	GLP-1 RA-based[b]
T2D	GLP-1 RA-based[b]
	Pioglitazone
	SGLT2i
Direct Anti-inflammatory Medication	
ASCVD	Colchicine
Chronic inflammation	

[a]Residual CV risk reduction; no specific hsCRP indication.

[b]GLP-1 RA or GIP/GLP-1 RA

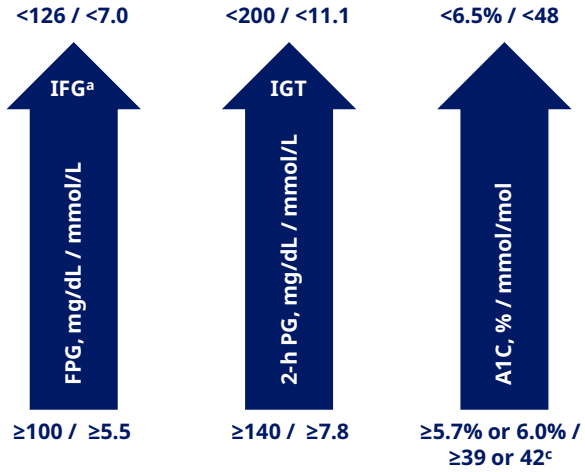
ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; CT, computed tomography; CTA, computed tomography angiography; CV, cardiovascular; CVOT, cardiovascular outcome trial; GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist; hsCRP, high-sensitivity C-reactive protein; IPE, cosapent ethyl; LDL-C, low-density lipoprotein cholesterol; SGLT2i, sodium glucose cotransporter 2 inhibitor; T2D, type 2 diabetes; UACR, urine-albumin creatinine ratio.

Handelsman Y et al. Metabolism. 2024 Jun 4:155931. doi: 10.1016/j.metabol.2024.155931

DCRM 2.0 MULTISPECIALTY PRACTICE RECOMMENDATIONS

Prediabetes

Prediabetes Glucose Ranges



Risk for CVD and CKD

- All with prediabetes are at risk of CKD, ASCVD, HF
- Risk of progression to T2D increases as prediabetes advances

Lifestyle Intervention for All ≥7% Weight Reduction for Most Persons

CVD Therapies

Start as needed/indicated:

- Lipid-control agents[d]
- BP-reducing agents
- GLP-1 RA
- SGLT2i
- Pioglitazone[e]
- Other CVD therapies[f]

Weight Reduction Therapies

Start if obesity present and ≥7% weight reduction not achieved with lifestyle alone:

1. GLP-1 RA based[g]
2. Phentermine-topiramate
3. Endoscopic or surgical interventions

Antihyperglycemic Therapies

Start if hyperglycemia progresses:

1. GLP-1 RA based[g]
2. Pioglitazone
3. Metformin
4. SGLT2i
5. Acarbose

Goals

Prevent progression of hyperglycemia and reduce CVD/CKD risk

Achieve normoglycemia with lifestyle and reduce CVD risk factors

- Even short-term regression to normal glucose tolerance with lifestyle may have durable benefits

Initiation of guideline-directed medical therapy for those with CVD, CKD, HF, or progression to T2D

Initiate and intensify treatment based on risk of CVD and progression to T2D

[a]WHO definition:110 to <126 mg/dL / 6.1 to <7.0 mmol/L.
[b]Caution with A1C diagnosis of prediabetes in African American, Latinx, and other ethnic groups.
[c]US, 5.7% / ≥39 mmol/mol; Europe, 6.0% / ≥42 mmol/mol; CV risk elevated at ≥6.0% / ≥42 mmol/mol.
[d]CVD benefit from stains more important than potential A1C increases.
[e]Do not use in HF.
[f]Antiplatelet therapies, MRAs, etc.
[g]GLP-1 RA or GIP/GLP-1 RA.

(HbA1c; hemoglobin A1C) ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; FPG, fasting plasma glucose; GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist with proven benefit in indicated population; HF, heart failure; IFG, impaired fasting glucose; IGT, mpaired glucose tolerance; MRA, mineralocorticoid receptor agonist; PG, plasma glucose; SGLT2i, sodium glucose cotransporter 2 inhibitor; T2D, type 2 diabetes; WHO, World Health Organization.
Handelsman Y et al. Metabolism. 2024 Jun 4:155931. doi: 10.1016/j.metabol.2024.155931