Indian Health Service

Division of Diabetes
Treatment and Prevention

A Patient Centered Approach to CVD Risk Reduction in People with Diabetes

Lani Desaulniers MD, FAAFP

Clinical Consultant - DDTP

May 23, 2024

Objectives

- Employ a multifactorial approach to cardiovascular risk reduction in the care of people with diabetes
- Examine the new ADA guidelines for management of hypertension in people with diabetes
- Explain the rationale for the use of pharmacologic agents which provide cardiovascular benefit to people with diabetes

Diabetes and Cardiovascular Disease

"People living with Type 2 diabetes are two times more likely to develop and die from cardiovascular disease, such as heart attacks, strokes, and heart failure, than people who don't have diabetes." American Heart Association

- Risk is related to co-existing conditions, such as hypertension and hyperlipidemia, in addition to diabetes.
- A diagnosis of CVD has been noted in 33-36% of individuals in the IHS Diabetes Care and Outcomes Audit report over last 9 years.
- Evidence supports significant benefit from cardiovascular risk reduction in preventing or slowing atherosclerotic cardiovascular disease.

Cardiovascular Disease
Atherosclerotic Cardiovascular Disease (ASCVD)

- Includes coronary heart disease, cerebrovascular disease, and peripheral artery disease
- Leading cause of morbidity and mortality in people with diabetes (heart attack, stroke, heart failure, limb ischemia)
- ASCVD risk reduction includes strategies to
  - Prevent ASCVD (Primary Prevention)
  - Prevent further cardiovascular complications in people with known ASCVD (Secondary Prevention)

Cardiovascular Disease
Congestive Heart Failure

Major cause of morbidity and mortality in people with diabetes

- Rates of heart failure hospitalization 2x higher
- Both types may be seen:
  - HFpEF (heart failure with preserved ejection fraction)
  - HFrEF (heart failure with reduced ejection fraction)
- Causative factors
  - Hypertension
  - ASCVD (particularly myocardial infarction)

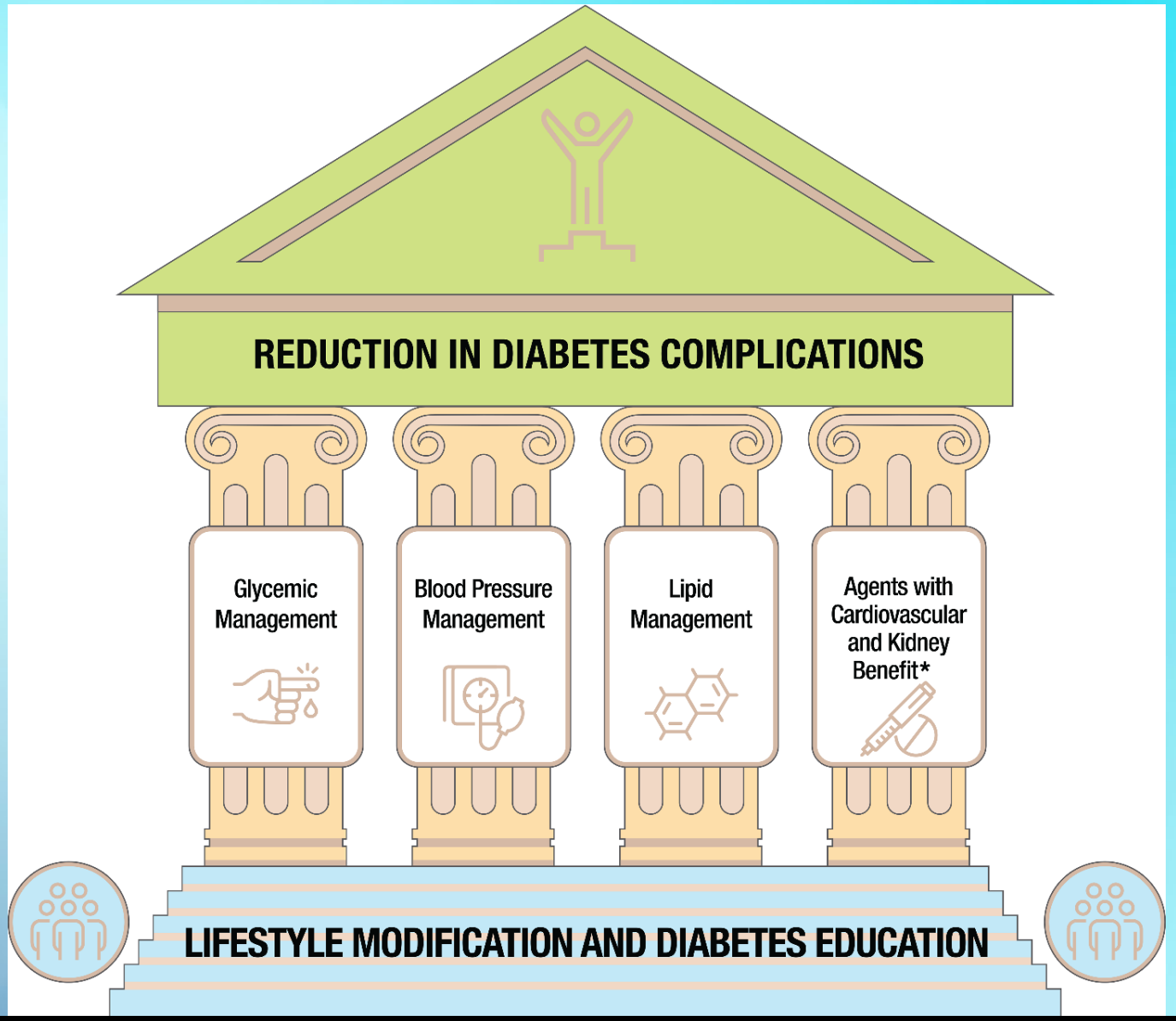
Congestive Heart Failure

- Symptoms include shortness of breath, chest pain, palpitations, fatigue with exertion, dry cough, swelling of legs, ankles, abdomen
- American Diabetes Association and AHA/ACC screening recommendations for asymptomatic people with type 2 diabetes

10.39a Adults with diabetes are at increased risk for the development of asymptomatic cardiac structural or functional abnormalities (stage B heart failure) or symptomatic (stage C) heart failure. Consider screening adults with diabetes by measuring a natriuretic peptide (B-type natriuretic peptide [BNP] or N-terminal pro-BNP [NT-proBNP]) to facilitate prevention of stage C heart failure. **B**

10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes --2024 Diabetes Care. 2024;47(Supplement_1):S179-S218

Multifactorial approach to reduction in risk of diabetes complications.



From: 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes --2024 Diabetes Care. 2024;47(Supplement_1):S179-S218. doi:10.2337/dc24-S010

*Risk reduction interventions to be applied as individually appropriate.

Lifestyle Management

- Smoking Cessation
  - 5 A's: Ask, Advise, Assess, Assist, and Arrange
- Diet
  - DASH-style eating pattern
    - Reducing sodium and increasing potassium
    - Reducing saturated fat and trans fat
    - Increase n-3 fatty acids, viscous fiber, and plant stanols/sterols
    - Weight loss through caloric restriction, as indicated
    - Moderation of alcohol intake (servings: ≤2/day men, ≤1/day women)
- Exercise
  - Minimum 150 minutes of moderate aerobic or 75 minutes of vigorous activity per week
  - More is better

Hypertension and Diabetes
General Principles

- Proper measurement of blood pressure is important.
- Controlling blood pressure can decrease risk of heart disease, stroke, kidney disease, and retinopathy.
- Target BP <130/<80 mm Hg for most patients, but should be individualized.

American Diabetes Association Standards of Care in Diabetes -2024

Hypertension is defined as a systolic blood pressure ≥130 mmHg or a diastolic blood pressure ≥80 mmHg based on an average of ≥2 measurements obtained on ≥2 occasions.

Recommendations

- **10.3** For people with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses cardiovascular risk, potential adverse effects of antihypertensive medications, and individual preferences. **B**
- **10.4** The on-treatment target blood pressure goal is <130/80 mmHg, if it can be safely attained. **A**

10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes --2024 Diabetes Care. 2024;47(Supplement_1):S179-S218.

TARGET:BP | American Heart Association. | AMA

7 SIMPLE TIPS TO GET AN ACCURATE BLOOD PRESSURE READING

The common positioning errors can result in inaccurate blood pressure measurement. Figures shown are estimates of how improper positioning can potentially impact blood pressure readings.

Sources:

1. *Pickering, et al.* Recommendations for Blood Pressure Measurement in Humans and Experimental Animals Part 1: Blood Pressure Measurement in Humans. *Circulation.* 2005;111: 697-716.
2. *Handler J.* The Importance of accurate blood pressure measurement. *The Permanente Journal*/Summer 2009/Volume 13 No. 3 51

This 7 simple tips to get an accurate blood pressure reading was adapted with permission of the American Medical Association and The Johns Hopkins University. The original copyrighted content can be found at www.ama-assn.org/ama-johns-hopkins-blood-pressure-resources.

Content provided by AMA | MAPBP™

This resource is part of AMA MAP BP™, a quality improvement program. Using a single or subset of AMA MAP BP tools or resources does not constitute implementing this program. AMA MAP BP includes guidance from AMA hypertension experts and has been shown to improve BP control rates by 10 percentage points and sustain results.

BP Monitoring

ADA recommends all persons with DM and HTN monitor home BP.

- "White coat hypertension" – BP may be elevated in office setting
- "Masked hypertension" – office BP may be lower than home readings
- Monitor treatment, assessment of pattern of BP elevation

Self-Monitoring Blood Pressure

- Instructions for use (Million Hearts Resource*)
- Encourage pts to bring to office – to evaluate technique, readings

24 hour ambulatory blood pressure monitoring can be helpful.

Other resources to evaluate BP

- PHN/CHR/Wellness Centers
- Pharmacy, drug stores, other locations

* Self-Measured Blood Pressure Monitoring: Action Steps for Clinicians

HTN Treatment:
Impact of Lifestyle Changes on Systolic BP

Intervention	Dose	Approximate Effect on SBP
Weight loss	Goal: ideal body weight, but can expect 1 mm Hg decrease per 1 kg of weight loss	- 5 mm Hg
DASH-style diet	Diet rich in whole grains, fruits, vegetables, & low fat dairy, decreased total and saturated fat	- 11 mm Hg
Reduce sodium	Goal: less than 1500 mg/day, but at least 1000 mg reduction	- 5 to 6 mm Hg
Increase potassium	Goal: 3500-5000 mg/day, preferably from dietary sources	- 4 to 5 mm Hg
Reduce alcohol consumption	Men $\leq$ 2 drinks/day Women $\leq$ 1 drink/day	- 4 mm Hg

2017 ACC/AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults
A Report of the American College of Cardiology/American Heart Association Hypertension. Volume 71, Issue 6, June 2018.

Hypertension Treatment: Impact of Exercise

AHA/ACC guidelines recommend aerobic & resistance exercise
90-150 minutes/week of moderate to vigorous intensity.

- Effects of aerobic exercise on BP
  - 5-8 mm Hg decrease systolic BP
  - 24 hour duration of effect
  - can lower CVD risk 20-30%
- Effects of isometric or dynamic resistance exercise on BP
  - 4-5 mm Hg decrease systolic BP

2017 ACC/AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults
A Report of the American College of Cardiology/American Heart Association Hypertension. Volume 71, Issue 6, June 2018

FITT. FITT Recommendations For Individuals With Hypertension

	Aerobic	Resistance	Flexibility
Frequency	≥5–7 d · wk^{-1}	≥2–3 d · wk^{-1}	≥2–3 d · wk^{-1}
Intensity	Moderate (*i.e.*, 40%–59% O_2R or HRR; RPE 12–13 on a 6–20 scale)	Moderate (*i.e.*, 60%–70% 1-RM; may progress to 80% 1-RM; for older individuals and novice exercisers, begin with 40%–50% 1-RM)	Stretch to the point of feeling tightness or slight discomfort.
Time	≥30 min · d^{-1} of continuous or accumulated exercise	2–4 sets of 8–12 repetitions of each of the major muscle groups per session to total ≥20 min per session with rest days interspersed depending on the muscle groups being exercised	Hold static stretch for 10–30 s with 2–4 repetitions of each exercise targeting the major muscle tendon units to total 60 s of total stretching time for each exercise; ≤10 min per session
Type	Prolonged, rhythmic activities using large muscle groups (*e.g.*, walking, cycling, swimming)	Resistance machines, free weights, resistance bands, and/or functional body weight exercise	Static, dynamic, and/or proprioceptive neuromuscular facilitation

1-RM, one repetition maximum; HRR, heart rate reserve; O_2R, oxygen uptake reserve; RPE, rating of perceived exertion.

Source: American College of Sports Medicine's Guidelines for Exercise Testing and Prescription, 11th Edition (2022)

Hypertension Therapy in Type 2 Diabetes

Hypertension Therapy in Type 2 Diabetes

Please Note: This algorithm is **not** intended for treatment and target selection in children or in women who are, or could become, pregnant.

Controlling hypertension (blood pressure ≥130/80 mmHg on two or more visits) reduces the risk of heart attack, stroke, heart failure, and kidney disease.Treatment targets should be individualized based on shared decision making which addresses risks, benefits, and patient preferences.

Blood Pressure (BP) Treatment Target:
<130/80 mmHg for most patients

Consider less stringent BP target: older age, frail, or advanced comorbidities
Consider more stringent BP target: high risk for kidney disease progression

Measuring and Monitoring Blood Pressure

- Follow established procedures for measuring BP including proper positioning and appropriate cuff size and placement (See In-Office Measuring Blood Pressure Infographic).
- Measure BP at diabetes diagnosis and at every visit.
- Prescribe home BP monitor and encourage patient to measure and record blood pressure particularly prior to provider visits or with medication changes.

Treatment of Hypertension

Recommend Therapeutic Lifestyle Changes for BP >120/80 mmHg
DASH diet*, limit sodium intake, increase physical activity, tobacco cessation, weight loss if overweight, and limit alcohol consumption

Initial Medication Therapy

BP ≥130/80 mmHg and <150/90 mmHg	→	**Use ACEi or ARB (preferred)****
BP ≥150/90 mmHg	→	**Use 2 agents: ACEi *or* ARB and CCB or diuretic**

Followup BP in one month
Review home BP records, if available. If BP not at goal, consider titrating dose up and/or adding medication from a different class. Work with patient to address any medication concerns or adherence issues. Combine ACEi or ARB with CCB and diuretic for triple medication therapy, as needed.

Resistant Hypertension***

BP ≥140/90 mmHg and treated with ACEi or ARB, CCB, and Diuretic, consider

Mineralocorticoid Receptor Antagonist: Spironolactone or Eplerenone **AND/OR** **Consult or refer to: nephrologist, cardiologist, or endocrinologist**

*Dietary Approaches to Stop Hypertension (DASH) Consider referral to dietitian. https://www.nhlbi.nih.gov/health-topics/dash-eating-plan
**If unable to tolerate angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), use calcium channel blocker (CCB) or diuretic.
***Consider evaluation for secondary hypertension.

Preferred Medication Classes

Angiotensin Converting Enzyme Inhibitors (ACEi) or Angiotensin Receptor Blockers (ARB)

- May increase potassium and creatinine, especially in patients with CKD
- Do not use an ACEi and an ARB together in the same patient.

Lisinopril Start 2.5-5mg daily; usually 20-40mg daily; max 80mg daily.
Other ACEi include benazepril, captopril, enalapril, fosinopril, moexipril, perindopril, quinapril, ramipril, and trandolapril.

- May cause cough, and rarely angioedema

Losartan Start 25-50mg daily; max 100mg daily. Consider if intolerant to ACEi.
Other ARBs include azilsartan, candesartan, eprosartan, irbesartan, olmesartan, telmisartan, and valsartan.

Calcium Channel Blockers (CCB)

Amlodipine Start 2.5-5mg daily; usually 5-10mg daily.
Other dihydropyridine CCBs include felodipine, lacidipine, levamlodipine, nifedipine XL, and nisoldipine.

- May cause edema

Diltiazem and **Verapamil** (non-dihydropyridine CCBs) are available in multiple formulations: consult your local formulary to assure appropriate selection and dosing.
Diltiazem CD Start 180-240mg daily; usually 240-360mg daily; max 480mg daily.
Verapamil ER Start 180mg daily; usually 240-360mg daily; max 360-480mg daily.

- May reduce proteinuria and heart rate in patients

Thiazide Diuretics

Hydrochlorothiazide (HCTZ) **or** **chlorthalidone** Start 12.5mg daily; max 50mg daily.
Indapamide Start 1.25mg daily; max 5mg daily.

- Higher doses may worsen hyperglycemia
- Monitor for hypokalemia

Note: Multiple combination formulations of medications listed above are available.

Mineralocorticoid Receptor Antagonists

Spironolactone Start 25mg daily; usually 50-100mg daily in 1-2 divided doses; max 200mg daily.
Eplerenone Start 50mg daily; may increase to 50mg twice daily after 4 weeks; max 100mg daily.

- Assess for hyperkalemia
- May cause gynecomastia and/or impotence in men

Medications on the **IHS National Core Formulary** are in **BOLD** above. Please consult a complete prescribing reference for more detailed information. No endorsement of specific products is implied.

Reference: American Diabetes Association Standards of Care

IHS DDTP Hypertension in Type 2 Diabetes Algorithm

Controlling hypertension (blood pressure ≥130/80 mmHg on two or more visits) reduces the risk of heart attack, stroke, heart failure, and kidney disease.Treatment targets should be individualized based on shared decision making which addresses risks, benefits, and patient preferences.

Blood Pressure (BP) Treatment Target: <130/80 mmHg for most patients

Consider less stringent BP target: older age, frail, or advanced comorbidities
Consider more stringent BP target: high risk for kidney disease progression

Measuring and Monitoring Blood Pressure

- Follow established procedures for measuring BP including proper positioning and appropriate cuff size and placement (See In-Office Measuring Blood Pressure Infographic).
- Measure BP at diabetes diagnosis and at every visit.
- Prescribe home BP monitor and encourage patient to measure and record blood pressure particularly prior to provider visits or with medication changes.

IHS DDTP Hypertension in Type 2 Diabetes Algorithm

Treatment of Hypertension

Recommend Therapeutic Lifestyle Changes for BP >120/80 mmHg

DASH diet*, limit sodium intake, increase physical activity, tobacco cessation, weight loss if overweight, and limit alcohol consumption

Initial Medication Therapy

BP ≥130/80 mmHg and <150/90 mmHg	→	**Use ACEi or ARB (preferred)****
BP ≥150/90 mmHg	→	**Use 2 agents: ACEi *or* ARB and CCB or diuretic**

Followup BP in one month

Review home BP records, if available. If BP not at goal, consider titrating dose up and/or adding medication from a different class. Work with patient to address any medication concerns or adherence issues. Combine ACEi or ARB with CCB and diuretic for triple medication therapy, as needed.

Resistant Hypertension***

BP ≥140/90 mmHg and treated with ACEi or ARB, CCB, and Diuretic, consider

Mineralocorticoid Receptor Antagonist: Spironolactone or Eplerenone	**AND/OR**	**Consult or refer to: nephrologist, cardiologist, or endocrinologist**

*Dietary Approaches to Stop Hypertension (DASH) Consider referral to dietitian.
https://www.nhlbi.nih.gov/health-topics/dash-eating-plan
**If unable to tolerate angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), use calcium channel blocker (CCB) or diuretic.
***Consider evaluation for secondary hypertension.

IHS DDTP Hypertension in Type 2 Diabetes Algorithm

Hypertension Therapy in Type 2 Diabetes

Preferred Medication Classes

Angiotensin Converting Enzyme Inhibitors (ACEi) or Angiotensin Receptor Blockers (ARB)

- May increase potassium and creatinine, especially in patients with CKD
- Do not use an ACEi and an ARB together in the same patient.

Lisinopril Start 2.5-5mg daily; usually 20-40mg daily; max 80mg daily.
Other ACEi include benazepril, captopril, enalapril, fosinopril, moexipril, perindopril, quinapril, ramipril, and trandolapril.

- May cause cough, and rarely angioedema

Losartan Start 25-50mg daily; max 100mg daily. Consider if intolerant to ACEi.
Other ARBs include azilsartan, candesartan, eprosartan, irbesartan, olmesartan, telmisartan, and valsartan.

Calcium Channel Blockers (CCB)

Amlodipine Start 2.5-5mg daily; usually 5-10mg daily.
Other dihydropyridine CCBs include felodipine, lacidipine, levamlodipine, nifedipine XL, and nisoldipine.

- May cause edema

Diltiazem and **Verapamil** (non-dihydropyridine CCBs) are available in multiple formulations: consult your local formulary to assure appropriate selection and dosing.
Diltiazem CD Start 180-240mg daily; usually 240-360mg daily; max 480mg daily.
Verapamil ER Start 180mg daily; usually 240-360mg daily; max 360-480mg daily.

- May reduce proteinuria and heart rate in patients

Thiazide Diuretics

Hydrochlorothiazide (HCTZ) **or** **chlorthalidone** Start 12.5mg daily; max 50mg daily.
Indapamide Start 1.25mg daily; max 5mg daily.

- Higher doses may worsen hyperglycemia
- Monitor for hypokalemia

Note: Multiple combination formulations of medications listed above are available.

Mineralocorticoid Receptor Antagonists

Spironolactone Start 25mg daily; usually 50-100mg daily in 1-2 divided doses; max 200mg daily.
Eplerenone Start 50mg daily; may increase to 50mg twice daily after 4 weeks; max 100mg daily.

- Assess for hyperkalemia
- May cause gynecomastia and/or impotence in men

Medications on the **IHS National Core Formulary** are in **BOLD** above. Please consult a complete prescribing reference for more detailed information. No endorsement of specific products is implied.

Reference: American Diabetes Association Standards of Care

Last updated March 2024

IHS DDTP Hypertension in Type 2 Diabetes Algorithm

Hyperlipidemia in Diabetes – an Overview

General Consensus

- Hyperlipidemia contributes to cardiovascular disease.
- Lowering LDL reduces risk of cardiovascular events.
- Statins are the cornerstone therapy for primary and secondary prevention.
- Statin intolerance and statin adherence issues pose clinical challenges.

Current Questions

- Statin use in primary prevention
  - Who, when, how much, and how long?
- Role of non-statin therapies

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/ AGS/APhA/ASPC/NLA/PCNA Lipid Guidelines

Secondary Prevention

- In clinical ASCVD, reduce LDL-C by ≥ 50% with high intensity or maximum tolerated statin.
- For very high risk group [pts with ASCVD, or pts with 10 year risk ≥ 20%] with LDL-C over threshold ≥70 mg/dL, consider adding non-statin (ezetimibe or PCSK9 inhibitor).

Primary prevention:

- Clinician-patient discussion advised before starting statin.
- Calculate 10 year ASCVD risk, assess risk-enhancing factors, lifestyle modification, risk/benefit of statin or other therapies, patient preferences, and engage in shared decision making.
- In adults ages 40-75 with DM, use moderate intensity statin, regardless of risk, but if ASCVD risk is high, or multiple risk-enhancing factors, use high intensity statin
- If ASCVD risk ≥ 20% consider addition of non-statin therapy.
- Assess adherence and LDL response, check lipids in 1-3 months and periodically.

2018 AHA/ACC Guideline on the Management of Blood Cholesterol Grundy SM, et al. Circulation. 2019; Volume 139, Issue 25

ASCVD Risk Estimator Plus (American College of Cardiology)

- Age
- Sex
- Race (white, African American, other)
- Diagnosis of diabetes
- BP (systolic & diastolic)
- Cholesterol results (total, HDL, LDL)
- Smoking (current, former, never)
- On HTN treatment?
- On statin?
- On ASA?

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

PREVENT™ Online Calculator
(American Heart Association)

- Age
- Sex
- Diagnosis of diabetes
- BP (systolic)
- BMI
- Cholesterol results (total, HDL)
- eGFR
- Smoking (current, former, never)
- On HTN treatment?
- On lipid treatment?
- Optional
  - A1C
  - UACR
  - Zip code

https://professional.heart.org/en/guidelines-and-statements/prevent-calculator

Other CVD Risk Enhancers

- Neuropathy
- Family history of premature ASCVD
- LDL persistently ≥160 mg/dL, Elevated TG ≥175 mg/dL
- Chronic kidney disease
- Metabolic syndrome
- History of preeclampsia, premature menopause
- Inflammatory diseases (e.g. Rheumatoid Arthritis)
- Risk enhancers specific to diabetes
  - Long duration: ≥10 years T2DM or ≥20 years T1DM
  - Albuminuria
  - PVD (ABI < 0.9)
  - Retinopathy

2018 AHA/ACC Guideline on the Management of Blood Cholesterol
Grundy SM, et al. Circulation. 2019; Volume 139, Issue 25

Lipid & Aspirin Therapy in Type 2 Diabetes

Lipid & Aspirin Therapy in Type 2 Diabetes

Lipid Therapy in Type 2 Diabetes

Please Note: This algorithm is **not** intended for treatment and target selection in children <18 years of age or in women who are or could become pregnant.

- ► Obtain a fasting lipid panel in patients with diabetes
  - at diagnosis of diabetes or initial diabetes visit;
  - at least every 5 years if age <40 years, annually after 40; and
  - at initiation of statin therapy and after dosing changes.
- ► Provide lifestyle therapy to all patients with diabetes (individualized nutrition therapy, physical activity, and weight loss guidance).
- ► Evaluate for statin therapy
  - Secondary Prevention:
    Prescribe high intensity statin therapy for patients with diabetes and ASCVD[1].
  - Primary Prevention:
    Use the following table to guide statin therapy and dosing for people with diabetes and no ASCVD diagnosis.
    - Evaluate ASCVD risk factors **independent of diabetes**[2].
    - Calculate 10-year ASCVD risk for patients aged 40-75 years using the ASCVD Risk Estimator Plus at https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/.

Age	ASCVD[1] Risk	Statin Therapy
<40 years	None	None
	One or more ASCVD risk factors[2]	Moderate or High Intensity[3]
40-75 years	None or 10-year ASCVD risk <5%	Moderate Intensity
	One or more ASCVD risk factors[2] or 10-year ASCVD risk 5-20%	Moderate or High Intensity[3]
	10-year ASCVD risk >20%	High Intensity[4]
>75 years	Individualize ASCVD risk assessment[5]	Moderate or High Intensity

1 ASCVD (atherosclerotic cardiovascular disease) is atherosclerosis affecting the vasculature that results in diseases of any of the following: heart (e.g. myocardial infarction, angina), the brain (e.g., stroke, transient ischemic attack), and the lower extremities (e.g peripheral artery disease, limb ischemia).

2 ASCVD Risk Factors **independent of diabetes** include: LDL cholesterol ≥100 mg/dL, smoking, hypertension, chronic kidney disease, albuminuria, or family history of premature ASCVD.

3 Consider high intensity statin therapy if multiple ASCVD risk factors.

4 Consider adding ezetimibe to maximally tolerated statin if ASCVD risk >20% to reduce LDL cholesterol by 50% or more from baseline.

5 Use of statin therapy for primary prevention of ASCVD in patients aged >75 years should include careful consideration of the potential risks of adverse drug events versus benefit of therapy.

Reference: American Diabetes Association Clinical Practice Recommendations

Statin Medications	Moderate Intensity Dose	High Intensity Dose
Atorvastatin	10-20 mg	40-80 mg
Rosuvastatin	5-10 mg	20-40 mg
Simvastatin	20-40 mg	Not applicable
Pravastatin	40-80 mg	Not applicable

Note: All statins are dosed daily.
Other statins include fluvastatin, lovastatin, pitavastatin (*Livalo*).

Contraindications: acute liver disease, pregnancy, nursing mothers

Safety and monitoring: Check liver function tests before initiating therapy; routine monitoring not necessary.

Statin intolerance: Usually due to side effect, such as myalgias. If unable to tolerate daily statin, there may still be benefit from a lower dose or less frequent dosing, may also consider bempedoic acid (*Nexletol*) 180 mg daily.

Combination therapy: In patients with ASCVD and very high risk with an LDL cholesterol ≥55 mg/dL on a maximally tolerated statin, consider the addition of **ezetimibe** 10 mg daily and/or a PCSK9 inhibitor to further reduce the risk of cardiovascular events.

- Evolocumab (*Repatha*) 140 mg SC every two weeks or 420 mg SC monthly
- Alirocumab (*Praluent*) 75-150 mg SC every two weeks or 300 mg SC monthly

Managing Elevated Triglycerides (>150 mg/dL)

- Ensure optimal blood glucose control; identify and address any secondary causes (e.g., high fat and/or high carbohydrate diet, hypothyroidism, excessive alcohol use, and medications).
- Consider initiating or increasing statin therapy when triglyceride levels >150 mg/dL to ≤500 mg/dL.
- Consider additional lipid lowering medications to reduce risk of pancreatitis if triglycerides ≥500 mg/dL (especially if ≥1,000 mg/dL).
  - Fenofibrate 120-160 mg daily
  - Omega 3 fatty acid 2 g bid
  - Icosapent ethyl (*Vascepa*) 2 g bid

Aspirin Therapy in Type 2 Diabetes

Secondary Prevention: Patients with a history of ASCVD should receive **aspirin** 75-162 mg daily if it is not contraindicated. If allergic to aspirin, consider **clopidogrel** 75 mg daily.

Primary Prevention: Consider **aspirin** 75-162 mg daily in patients with diabetes aged 50-70 years and an increased risk of ASCVD (e.g., one or more risk factors) if they are not at increased risk of bleeding.

Aspirin is not recommended in patients at lower risk of ASCVD (e.g., age <50 years with no other ASCVD risk factors). Aspirin is not generally recommended in those aged >70 years due to increased bleeding risk.

Medications on the **IHS National Core Formulary** are in **BOLD** above.
Please consult a complete prescribing reference for more detailed information.
No endorsement of specific products is implied.

IHS DDTP Lipid & Aspirin Therapy in Type 2 Diabetes Algorithm

Lipid Therapy in Type 2 Diabetes

Please Note: This algorithm is **not** intended for treatment and target selection in children <18 years of age or in women who are or could become pregnant.

- ▶ Obtain a fasting lipid panel in patients with diabetes
  - at diagnosis of diabetes or initial diabetes visit;
  - at least every 5 years if age <40 years, annually after 40; and
  - at initiation of statin therapy and after dosing changes.
- ▶ Provide lifestyle therapy to all patients with diabetes (individualized nutrition therapy, physical activity, and weight loss guidance).
- ▶ Evaluate for statin therapy
  - Secondary Prevention:
    Prescribe high intensity statin therapy for patients with diabetes and ASCVD[1].
  - Primary Prevention:
    Use the following table to guide statin therapy and dosing for people with diabetes and no ASCVD diagnosis.
    - Evaluate ASCVD risk factors **independent of diabetes**[2].
    - Calculate 10-year ASCVD risk for patients aged 40-75 years using the ASCVD Risk Estimator Plus at https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/.

Age	ASCVD[1] Risk	Statin Therapy
<40 years	None	None
	One or more ASCVD risk factors[2]	Moderate or High Intensity[3]
40-75 years	None or 10-year ASCVD risk <5%	Moderate Intensity
	One or more ASCVD risk factors[2] or 10-year ASCVD risk 5-20%	Moderate or High Intensity[3]
	10-year ASCVD risk >20%	High Intensity[4]
>75 years	Individualize ASCVD risk assessment[5]	Moderate or High Intensity

IHS DDTP Lipid & Aspirin Therapy in Type 2 Diabetes Algorithm

Statin Medications	Moderate Intensity Dose	High Intensity Dose
Atorvastatin	10-20 mg	40-80 mg
Rosuvastatin	5-10 mg	20-40 mg
Simvastatin	20-40 mg	Not applicable
Pravastatin	40-80 mg	Not applicable

Note: All statins are dosed daily.
Other statins include fluvastatin, lovastatin, pitavastatin (*Livalo*).

Contraindications: acute liver disease, pregnancy, nursing mothers

Safety and monitoring: Check liver function tests before initiating therapy; routine monitoring not necessary.

Statin intolerance: Usually due to side effect, such as myalgias. If unable to tolerate daily statin, there may still be benefit from a lower dose or less frequent dosing, may also consider bempedoic acid (*Nexletol*) 180 mg daily.

Combination therapy: In patients with ASCVD and very high risk with an LDL cholesterol ≥55 mg/dL on a maximally tolerated statin, consider the addition of **ezetimibe** 10 mg daily and/or a PCSK9 inhibitor to further reduce the risk of cardiovascular events.

- Evolocumab (*Repatha*) 140 mg SC every two weeks or 420 mg SC monthly
- Alirocumab (*Praluent*) 75-150 mg SC every two weeks or 300 mg SC monthly

Managing Elevated Triglycerides (>150 mg/dL)

- Ensure optimal blood glucose control; identify and address any secondary causes (e.g., high fat and/or high carbohydrate diet, hypothyroidism, excessive alcohol use, and medications).
- Consider initiating or increasing statin therapy when triglyceride levels >150 mg/dL to ≤500 mg/dL.
- Consider additional lipid lowering medications to reduce risk of pancreatitis if triglycerides ≥500 mg/dL (especially if ≥1,000 mg/dL).
  - Fenofibrate 120-160 mg daily
  - Omega 3 fatty acid 2 g bid
  - Icosapent ethyl (*Vascepa*) 2 g bid

IHS DDTP Lipid & Aspirin Therapy in Type 2 Diabetes Algorithm

Non-statin Medications

	Ezetimibe	PCSK9 Inhibitors* Evolucumab (Repatha) & Alirocumab (Praluent)
Mechanism of Action	Inhibits intestinal absorption of cholesterol	Monoclonal antibodies bind to PCSK9, preventing PCSK9 from attaching to LDL receptors, allowing increased LDL clearance
LDL- C reduction	20-25% reduction	50-60% reduction
CVD risk reduction	CVD benefit when added to statin in patients with CVD	~ 30% risk reduction when added to statin in patients with CVD
Dosing	Oral, daily dosing	Injected, every 2-4 weeks
Availability	Generic, on National Core Formulary	Brand name only, expensive, not on National Core Formulary (most insurance requires prior authorization)

* Proprotein convertase subtilisin/kexin type 9 (PCSK9) Inhibitors

Other Non-statin Medications

- Inclisiran (*Leqvio*)
  - Small interfering mRNA directed at PCSK9 mRNA
  - 50% LDL – C reduction when used with statin
  - Subcutaneous injection (by healthcare provider); repeat at 3 months, then every 6 months thereafter
- Bempedoic acid (*Nexletol*)
  - Adenosine Triphosphate-Citrate Lyase inhibitor – decreases cholesterol synthesis
  - Decreases LDL
  - Evidence for CVD benefit in people with statin intolerance

Triglyceride-lowering Medications

- Icosopent-ethyl (*Vascepa,* other generics)
  - Evidence for CVD risk reduction
- Omega-3 fatty acids & fenofibrate
  - Treatment of severe hypertriglyceridemia to prevent pancreatitis
  - May be used individually, or in combination
  - Risk of myopathy, if fibrate combined with statin

CVD Risk Reduction: Recommendations for Aspirin and Antiplatelet Therapy

Aspirin Therapy in Type 2 Diabetes

Secondary Prevention: Patients with a history of ASCVD should receive **aspirin** 75-162 mg daily if it is not contraindicated. If allergic to aspirin, consider **clopidogrel** 75 mg daily.

Primary Prevention: Consider **aspirin** 75-162 mg daily in patients with increased risk of ASCVD (e.g., age 50-70 years and one or more ASCVD risk factors) if they are not at increased risk of bleeding.

Aspirin is not recommended in patients at lower risk of ASCVD (e.g., age <50 years with no other ASCVD risk factors). Aspirin is not generally recommended in those aged >70 years due to increased bleeding risk.

IHS DDTP Lipid & Aspirin Therapy in Type 2 Diabetes Algorithm

Glycemic Control

- Earlier glycemic control and cardiovascular outcomes trials [DCCT (Type 1), UKPDS (Type 2 DM), ACCORD, ADVANCE, VADT] provided heterogeneous findings regarding macrovascular outcomes.
- Hypoglycemia risk was observed with intensive treatment.
  - Particular concern in people with underlying CVD and other comorbidities (ACCORD)
- Intensive glucose control may be of more benefit to younger, more recently diagnosed people (UKPDS).

Glycemic Control Agents and CVD Risk

In response to concern regarding rosiglitazone and cardiovascular events, the FDA required cardiovascular outcomes trials for new diabetes drugs beginning in 2008.

- SGLT-2 inhibitors and GLP-1 receptor agonists were shown to have proven cardiovascular benefit in people with CVD.
- SGLT-2 inhibitors are now a recommended treatment for congestive heart failure.
- SGLT-2 inhibitors have been found to have renal protective effects.

SGLT-2 Inhibitors in People with Diabetes and CVD or High-Risk for CVD

Trial	Drug	Relative Risk Reduction
EMPA-REG OUTCOME	Empagliflozin vs. placebo	14% for major adverse cardiac events (MACE) 35% for hospitalization for heart failure (HHF) 38% for cardiovascular death
CANVAS Program	Canagliflozin vs. placebo	14% for MACE 27% for HHF
DECLARE-TIMI 58	Dapagliflozin vs. placebo	17% for cardiovascular death or HHF 27% for HHF

GLP-1 Receptor Agonists in People with Diabetes and CVD or High-Risk for CVD

Trial	Drug	Relative Risk Reduction
LEADER	Liraglutide vs. placebo	13% for major adverse cardiac events (MACE) 13% for heart failure hospitalization 22% for cardiovascular death
SUSTAIN-6	Semaglutide (injectable) vs. placebo	26% for MACE 39% for stroke
REWIND	Dulaglutide vs. placebo	12% for MACE 24% for stroke

American Diabetes Association®

From: **9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2024**

Diabetes Care. 2023;47(Supplement_1):S158-S178. doi:10.2337/dc24-S009

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

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

Goal: Cardiorenal Risk Reduction in High-Risk Individuals with Type 2 Diabetes (in addition to comprehensive CV risk management)*

+ASCVD†
Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, any revascularization procedure). Variably included: conditions such as transient ischemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk
While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria)

+HF
Current or prior symptoms of HF with documented HFrEF or HFpEF

+CKD
eGFR <60 mL/min per 1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). These measurements may vary over time; thus, a repeat measure is required to document CKD.

+ASCVD/Indicators of High Risk

GLP-1 RA# with proven CVD benefit — EITHER/OR — SGLT2i§ with proven CVD benefit

If A1C above target

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit or vice versa
- TZD^

+HF

SGLT2i§ with proven HF benefit in this population

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY
SGLT2i§ with primary evidence of reducing CKD progression
Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation

OR

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiorenal risk reduction or glycemic lowering needed

Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

Glycemic Management: Choose approaches that provide the efficacy to achieve goals:
Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals
Prioritize avoidance of hypoglycemia in high-risk individuals

In general, higher efficacy approaches have greater likelihood of achieving glycemic goals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide
Insulin
Combination Oral, Combination Injectable (GLP-1 RA/Insulin)

High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD

Intermediate:
DPP-4i

Achievement and Maintenance of Weight Management Goals:

Set individualized weight management goals

- General lifestyle advice: medical nutrition therapy/eating patterns/physical activity
- Intensive evidence-based structured weight management program
- Consider medication for weight loss
- Consider metabolic surgery

When choosing glucose-lowering therapies:
Consider regimen with high-to-very-high dual glucose and weight efficacy

Efficacy for weight loss

Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1 RA (not listed above), SGLT2i

Neutral:
DPP-4i, Metformin

If A1C above target

Identify barriers to goals:
- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g., diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of goals

* 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.

Figure Legend:
Use of glucose-lowering medications in the management of type 2 diabetes. 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 2 inhibitor; T2D, type 2 diabetes; TZD, thiazoheart failure; MACE, major adverse cardiovascular events; MI, myocardial infarction; SDOH, social determinants of health; SGLT2i, sodium-glucose cotransporter lidinedione. Adapted from Davies et al. (84).

ADA Recommendations for Type 2 Diabetes Treatment

9.9 A person-centered shared decision-making approach should guide the choice of pharmacologic agents for adults with type 2 diabetes. Consider the effects on cardiovascular and renal comorbidities; effectiveness; hypoglycemia risk; impact on weight, cost and access; risk for adverse reactions and tolerability; and individual preference. E

9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2024 Diabetes Care. 2024;47(Supplement_1):S158-S178. doi:10.2337/dc24-S009

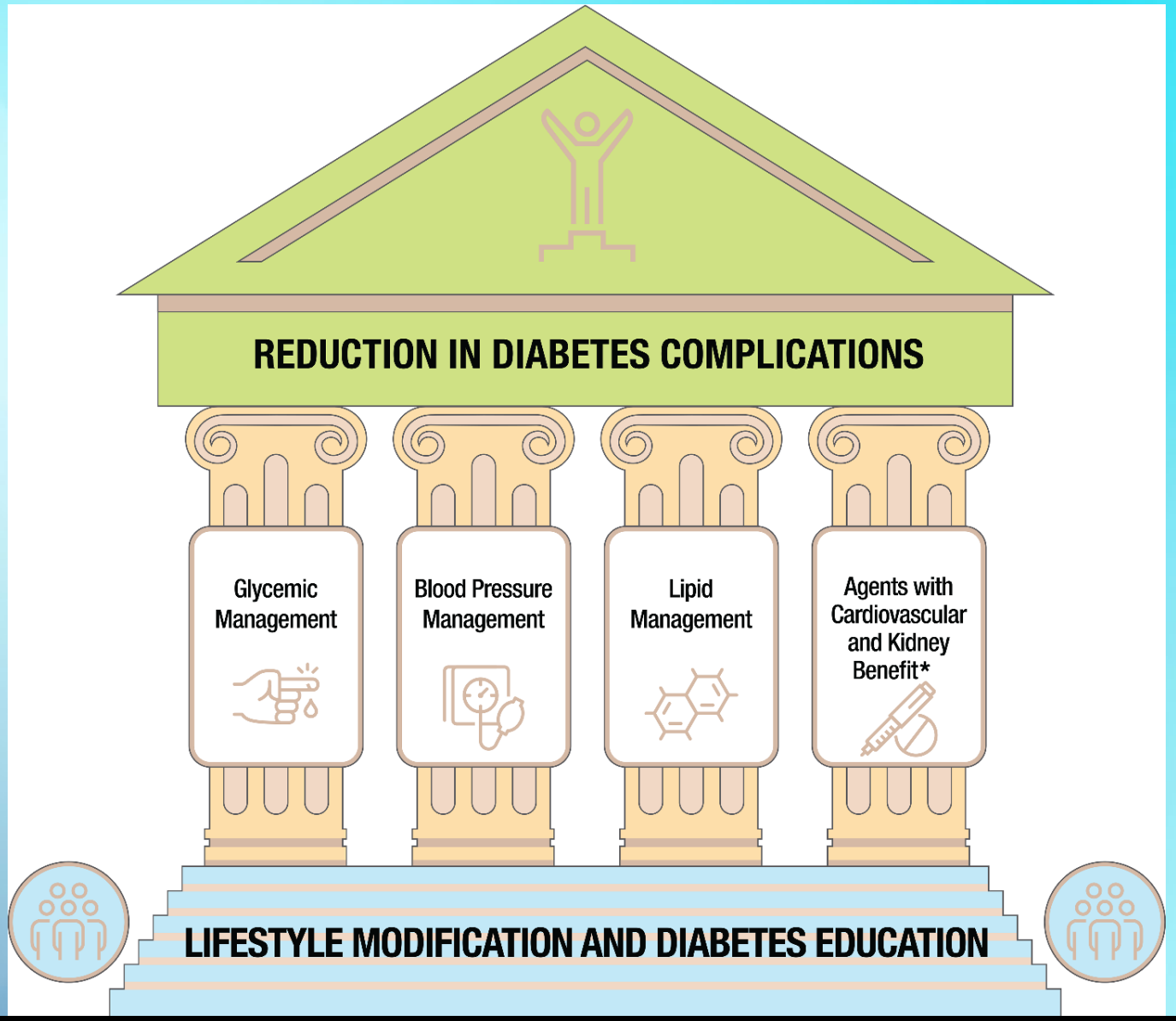
ADA Recommendations for Cardiovascular Protection

9.18 In adults with type 2 diabetes and established or high risk of atherosclerotic cardiovascular disease, heart failure (HF), and/or chronic kidney disease (CKD), the treatment plan should include agent(s) that reduce cardiovascular and kidney disease risk (e.g., sodium–glucose cotransporter 2 inhibitor [SGLT2] and/or glucagon-like peptide 1 receptor agonist [GLP-1 RA…. for glycemic management and comprehensive cardiovascular risk reduction, independent of A1C and in consideration of person-specific factors. **A**

9.19 In adults with type 2 diabetes who have HF (with either reduced or preserved ejection fraction), an SGLT2 inhibitor is recommended, for glycemic management and prevention of HF hospitalizations. **A**

9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2024 Diabetes Care. 2024;47(Supplement_1):S158-S178. doi:10.2337/dc24-S009

Multifactorial approach to reduction in risk of diabetes complications.



From: 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes --2024 Diabetes Care. 2024;47(Supplement_1):S179-S218. doi:10.2337/dc24-S010

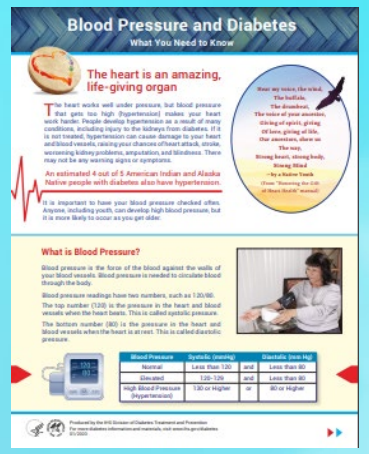
*Risk reduction interventions to be applied as individually appropriate.

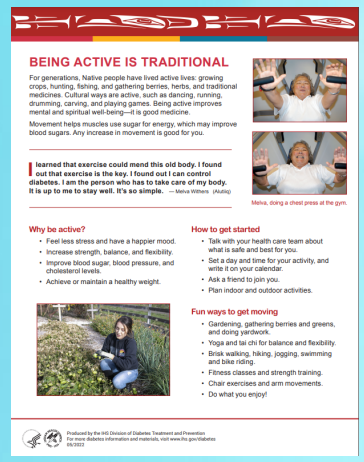
Person-centered/Shared Decision-making

- Person's goals, health concerns, and health beliefs
- CVD, CKD Diagnosis? If not, assess ASCVD risk
- Address lifestyle management, potential benefits of lifestyle modification
  - Consult with care team, providers for guidance on exercise Rx
- Identify resources for education, assistance, and support
- Review risks/benefits of medication use
  - Potential risk reduction from BP and lipid medications
  - Possible adverse effects, polypharmacy
  - Costs (if a consideration)
- Shared decision-making
  - Encourage questions, address concerns, develop collaborative plan
  - Involve care team, other resources

Resources from DDTP https://www.ihs.gov/Diabetes/

- Educational Materials and Resources Handouts
  - Blood Pressure and Diabetes
  - Sodium and Your Health
  - Fats and Heart Health
  - Keeping Your Heart Healthy
  - Understanding Your Cholesterol
  - Being Active is Traditional





More Resources from DDTP https://www.ihs.gov/Diabetes/

- Clinical Resources
  - Algorithms
    - Hypertension in Type 2 Diabetes
    - Lipid and Aspirin Therapy in Type 2 Diabetes
  - Standards of Care
    - Lipid Management
    - Blood Pressure
- SDPI Healthy Heart Toolkit
- On-line Recorded Trainings (free CME)

Indian Health Service

Division of Diabetes
Treatment and Prevention

Case Studies

Case Study #1

44 year old female with T2DM x 6 years

- Sedentary office job, frequent mandatory overtime, single mother teenage son
- Zumba class after work 1 or 2 days week
- Cooks on weekends, fast food 3-4 nights/week, trying to eat more salad
- History of GDM, preeclampsia with pregnancy 15 years ago
- Fam Hx: T2DM, HTN, CVA – father, deceased age 58
- Occ ETOH, light smoking when visiting casinos
- BP 135/82, last A1C 7.2, BMI 30

  Total Chol 220 mg/dL, LDL 85 mg/dL, HDL 55 mg/dL,

  eGFR >60, UACR 20 mg/g
- Current medications:
  - Metformin ER 1 gm daily

Her ASCVD risk is 6.2% (ACC)

5.7 % (PREVENT)

- What is the first step she might consider to decrease her CVD risk?
- What should her BP target be?
- What might you recommend as an initial treatment plan?
- Is she a statin candidate?

Case Study #2

42 year old male with Type 2 DM x 10 years

- Works out of town in construction 4 days/week
- Married, 3 children, wife cooks when he is home but he eats fast food and convenience foods during week
- PMH: HTN, elevated cholesterol
- Fam Hx: T2DM, HTN, CVD, end stage kidney disease (father)
- No h/o tobacco, ETOH, or illicit substance use
- BP 150/89, last A1C 7.7, BMI 29

  Total Chol 240 mg/dL, LDL 120 mg/dL, HDL 42 mg/dL, eGFR >60, UACR 300 mg/g
- Current medications:
  - Metformin ER 1 gm daily
  - Sitagliptin 100 mg daily
  - Lisinopril 10 mg daily
  - Atorvastatin 20 mg daily

His 10 year ASCVD risk is 7.5% (ACC)
10.8% (PREVENT)

- What should his BP target be?
- What about his lipids?
- Are there any changes you would suggest for his meds?

Case Study #3

70 year old male with Type 2 DM x 20 years

- Retired, has small farm - grows corn, squash, chile, gourds, and hay
- Eats “traditional” diet
- PMH: HTN, elevated cholesterol
- Fam Hx: T2 DM, HTN, CVA – father, deceased at age 90;
  mother age 98 in ”good health”
- Former heavy ETOH (sober x 20 years) no h/o tobacco or illicit substance use
- BP 139/89, last A1C 7.8, BMI 27

  Total Chol 200 mg/dL, LDL 110 mg/dL, HDL 45 mg/dL, eGFR 55, A/C ratio < 30 mg/g
- Current medications:
  - Metformin ER 1 gm daily
  - Lantus 20 units at bedtime
  - Lisinopril 20 mg daily
  - Atorvastatin 20 mg daily

His 10 year ASCVD risk is 42% (ACC)
27% (PREVENT)

- What about his lipids?
- What should his BP target be?
- Are there any changes you would suggest for his meds?

Case Study #4

78 year old female with T2DM for 30 years, had MI 8 years ago, 2 stents placed

- Walks 20-30 minutes 3-4 days/wk, Cooks for family: meat, stews, oven bread
- PMH: CVD, HTN, elevated cholesterol
- Fam Hx: T2DM, HTN, CVA – mother, deceased age 80
- Nonsmoker, no alcohol or illicit substance use
- BP 135/85, last A1C 7.9, BMI 26
- Total Chol 200 mg/dL, LDL 85 mg/dL, HDL 35 mg/dL, UACR 60 mg/g
- Current medications:
  - Metformin ER 1 gm daily
  - Lantus 15 units at bedtime
  - Lisinopril 10 mg daily
  - Metoprolol XL 25 mg daily
  - Atorvastatin 20 mg daily
  - Aspirin 81 mg daily

- What should her BP target be?
- What about her lipids?
- Are there any treatments that you might recommend?
- Any changes to her medication regimen?

Indian Health Service

Division of Diabetes
Treatment and Prevention

Questions?