



Division of Diabetes  
Treatment and Prevention

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

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# 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 33-35% of individuals in the IHS Diabetes Care and Outcomes Audit report over last 8 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)

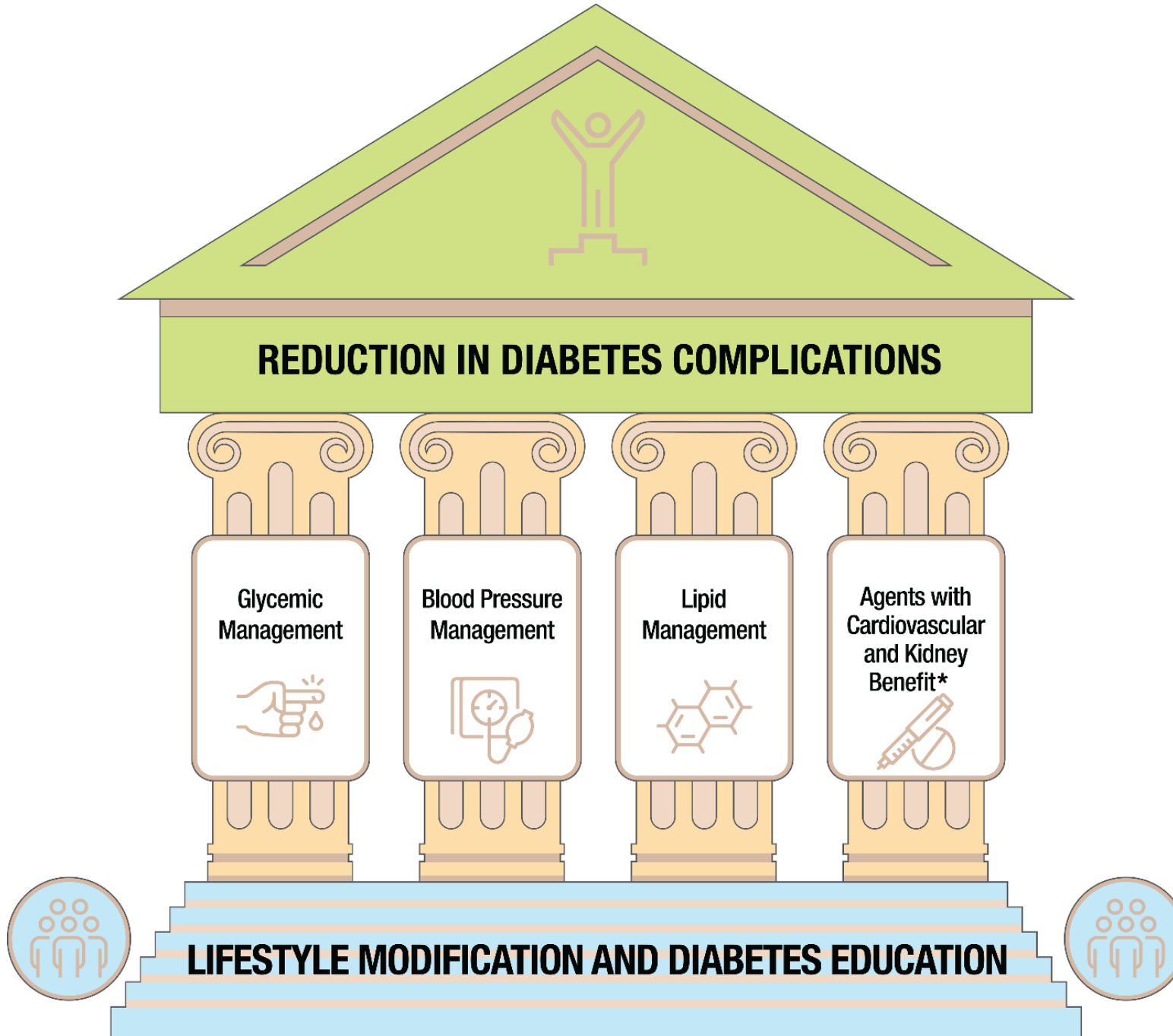


# Cardiovascular Disease Congestive Heart Failure

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)

Multifactorial approach to reduction in risk of diabetes complications.  
\*Risk reduction interventions to be applied as individually appropriate.



From: 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes --2023  
Diabetes Care.  
2023;46(Supplement\_1):S158-S190.  
doi:10.2337/dc23-S010



# 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:  $\leq 2$ /day men,  $\leq 1$ /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 -2023 (Update)

Hypertension is defined as a systolic blood pressure  $\geq 130$  mmHg or a diastolic blood pressure  $\geq 80$  mmHg based on an average of  $\geq 2$  measurements obtained on  $\geq 2$  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 patient preferences. **B**
- **10.4** People with diabetes and hypertension qualify for antihypertensive drug therapy when the blood pressure is persistently elevated  $\geq 130/80$  mmHg. The on-treatment target blood pressure goal is  $< 130/80$  mmHg, if it can be safely attained. **B**

# BP Control – the Evidence

(from Diabetes Care 2023;46(Suppl. 1):S158–S190)

Trial	Population	Intensive	Standard	Outcomes
ACCORD BP	4,733 people - T2DM age 40-79 with known ASCVD or risk factors	Systolic BP target < 120 mmHg achieved mean BP 119/64 mmHg	Systolic BP target 130-140 mmHg achieved mean BP 134/71 mmHg	MACE similar in both groups, 41% risk reduction for stroke, Greater risk of adverse drug events 3.3% vs 1.3%
ADVANCE	11,140 people -T2DM age >55 with ASCVD or multiple risk factors	Fixed dose ACEI/diuretic achieved mean BP 136/73 mmHg	Control: placebo achieved mean BP 142/75 mm Hg	Composite endpoints: CV death, nonfatal MI, nonfatal stroke, worsening retinopathy or nephropathy 9% RRR in MACE, 14 % RRR in total mortality, 18% RRR CVD death
HOT	18,790 people - 1,501 with diabetes	Diastolic BP target ≤ 80 mmHg	Diastolic BP target ≤ 90 mmHg	In overall trial, no CV benefit from more intensive targets Decreased CV risk, MACE, CV death in pts with DM with DBP ≤ 80 mmHg vs ≤ 90 mmHg
SPRINT	9,361 people without diabetes	Systolic BP target < 120 mmHg achieved mean BP 121 mmHg	Systolic BP target < 140 mmHg achieved mean BP 136 mmHg	Lower MACE in intensive treatment 1.65% vs 2.19% HR 0.75 All cause mortality lower in intensive treatment HR 0.73 Adverse events, not including falls, higher in intensive treatment
STEP	8,511 people aged 60-80 years - 1,627 with diabetes	Systolic BP target < 130 mm Hg achieved mean BP 127.5 mmHg	Systolic BP target < 150 mmHg achieved mean BP 135.3 mmHg	Intensive treatment: 26 % RRR in composite outcome (stroke, ACS, acute decompensated heart failure, coronary revascularization, atrial fibrillation, or CVD death) 28% RRR in CVD death Increased hypotension risk



## 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](http://www.ama-assn.org/ama-johns-hopkins-blood-pressure-resources).



# BP Monitoring

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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





# HTN 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

## FITT. FITT Recommendations For Individuals With Hypertension



	Aerobic	Resistance	Flexibility
Frequency	$\geq 5-7 \text{ d} \cdot \text{wk}^{-1}$	$\geq 2-3 \text{ d} \cdot \text{wk}^{-1}$	$\geq 2-3 \text{ d} \cdot \text{wk}^{-1}$
Intensity	Moderate ( <i>i.e.</i> , 40%–59% $\text{O}_2\text{R}$ or HRR; RPE 12–13 on a 6–20 scale)	Moderate ( <i>i.e.</i> , 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	$\geq 30 \text{ min} \cdot \text{d}^{-1}$ of continuous or accumulated exercise	2–4 sets of 8–12 repetitions of each of the major muscle groups per session to total $\geq 20 \text{ min}$ 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; $\leq 10 \text{ min}$ per session
Type	Prolonged, rhythmic activities using large muscle groups ( <i>e.g.</i> , 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;  $\text{O}_2\text{R}$ , oxygen uptake reserve; RPE, rating of perceived exertion.

**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  $\geq 130/80$  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  $\geq 130/80$  mmHg  
 and  $< 160/100$  mmHg



Use ACEi or ARB (preferred)\*\*

BP  $\geq 160/100$  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  $\geq 140/90$  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



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**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  $\geq$ 130/80 mmHg  
and <160/100 mmHg



Use ACEi or ARB (preferred)\*\*

BP  $\geq$ 160/100 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.

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Mineralocorticoid Receptor  
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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.



# Hyperlipidemia in Diabetes - 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.
- Statin use is contraindicated in pregnancy.

## Current Questions

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



# Key Points

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

### Secondary Prevention

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

### 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  $\geq 20\%$  consider addition of non-statin therapy.
- Assess adherence and LDL response, check lipids in 1-3 months and periodically.



# ASCVD Risk Estimator Plus (American College of Cardiology)

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



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



# Consideration of Other CVD Risk Enhancers

Family history of premature ASCVD

LDL persistently  $\geq 160$  mg/dL, Elevated TG  $\geq 175$  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:  $\geq 10$  years T2DM,  $\geq 20$  years T1DM
- Albuminuria
- Neuropathy
- PVD (ABI  $< 0.9$ )
- Retinopathy

## 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<sup>1</sup>.**
  - 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<sup>2</sup>.**
    - 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 <sup>1</sup> Risk	Statin Therapy
<40 years	None	None
	One or more ASCVD risk factors <sup>2</sup>	Moderate or High Intensity <sup>3</sup>
40-75 years	None or 10-year ASCVD risk <5%	Moderate Intensity
	One or more ASCVD risk factors <sup>2</sup> or 10-year ASCVD risk 5-20%	Moderate or High Intensity <sup>3</sup>
	10-year ASCVD risk >20%	High Intensity <sup>4</sup>
>75 years	Individualize ASCVD risk assessment <sup>5</sup>	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
<b>Atorvastatin</b>	10-20 mg	40-80 mg
<b>Rosuvastatin</b>	5-10 mg	20-40 mg
<b>Simvastatin</b>	20-40 mg	Not applicable
<b>Pravastatin</b>	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. Consider trying a different statin. If unable to tolerate daily statin, there may still be benefit from a lower dose or less frequent dosing.

**Combination therapy:** In patients with ASCVD and very high risk with an LDL cholesterol ≥70 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 (&gt;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 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.

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- ▶ 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<sup>1</sup>.**
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[IHS DDTP Lipid & Aspirin Therapy in Type 2 Diabetes Algorithm](#)



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# 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 Agents

- LDL-lowering
  - Inclisiran (Leqvio)
  - Bempedoic Acid (Nexletol)
- Triglyceride-lowering
  - Icosopent-ethyl
    - 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

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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.



# 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

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.





# 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



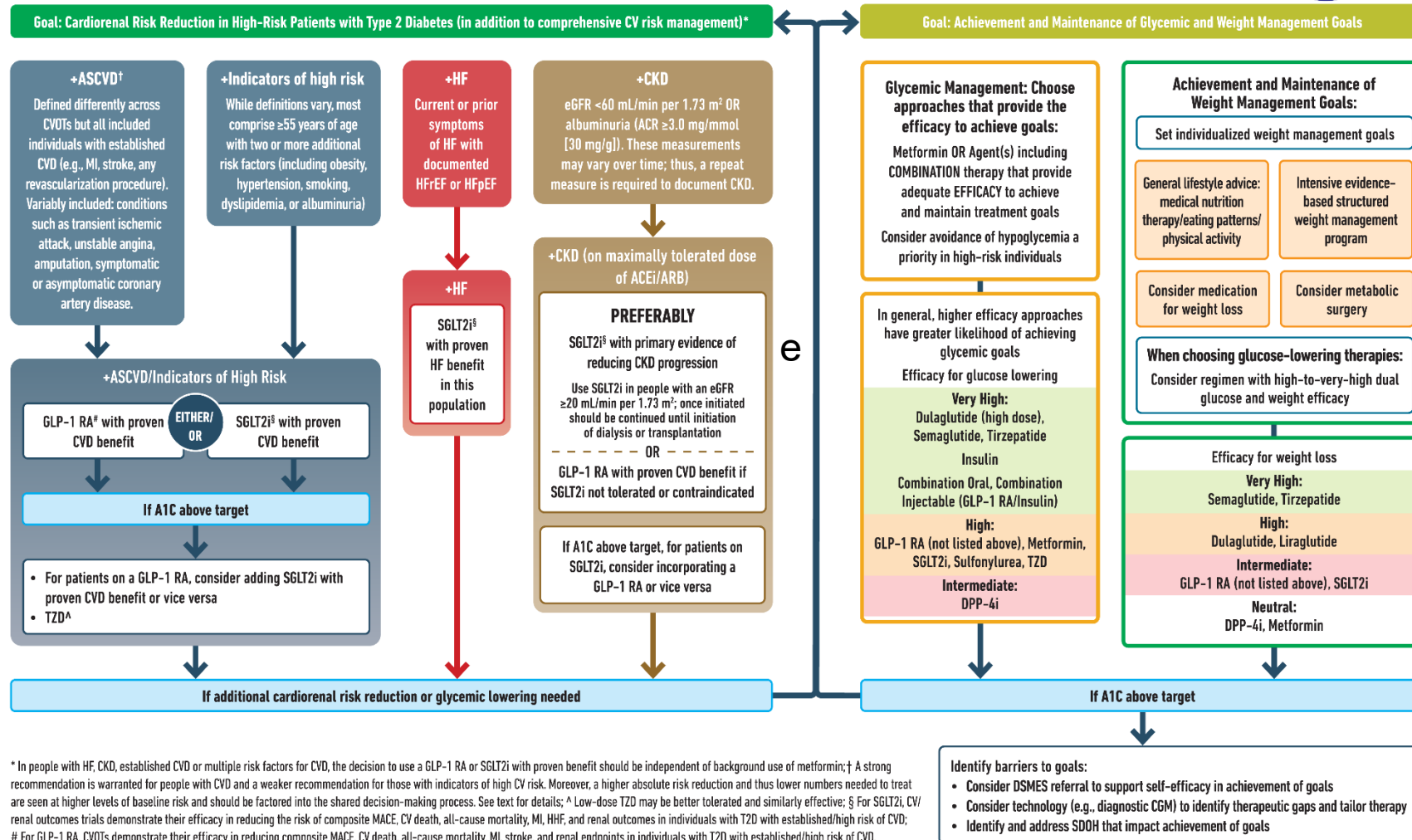
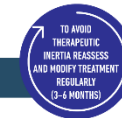
## SGLT-2 Inhibitors in People with Diabetes and CVD or High-Risk for CVD

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



## 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)



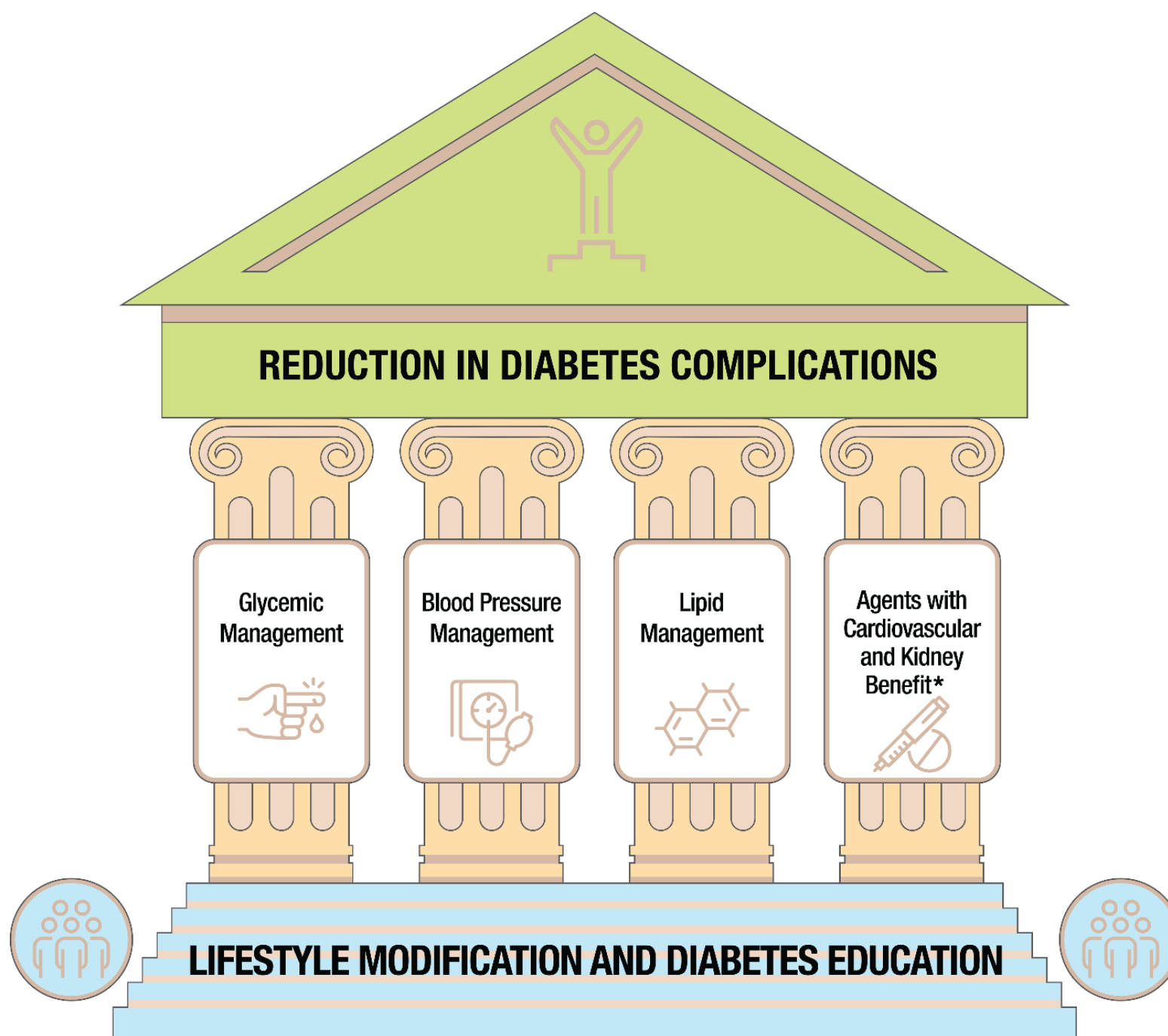


# ADA Recommendations for Cardiovascular and Renal Protection

**9.8** A person-centered approach should guide the choice of pharmacologic agents. Consider the effects on cardiovascular and renal comorbidities, efficacy, hypoglycemia risk, impact on weight, cost and access, risk for side effects, and individual preferences. **E**

**9.9** Among individuals with type 2 diabetes who have established atherosclerotic cardiovascular disease or indicators of high cardiovascular risk, established kidney disease, or heart failure, a sodium–glucose cotransporter 2 inhibitor and/or glucagon-like peptide 1 receptor agonist with demonstrated cardiovascular disease benefit is recommended as part of the glucose-lowering regimen and comprehensive cardiovascular risk reduction, independent of A1C and in consideration of person-specific factors. **A**

Multifactorial approach to reduction in risk of diabetes complications.  
\*Risk reduction interventions to be applied as individually appropriate.



From: 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes --2023 Diabetes Care. 2023;46(Supplement\_1):S158-S190. doi:10.2337/dc23-S010



# Patient Centered/ Shared Decision Making

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- Patient 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 for 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/>

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- Online Catalog: new handouts
  - Blood Pressure and Diabetes
  - Fats and Heart Health
  - More to come.....
- Clinical Resources
  - Algorithms
    - » Hypertension in Type 2 Diabetes (new)
    - » Lipid and Aspirin Therapy in Type 2 Diabetes
  - Standards of Care
    - » Lipid Management
    - » Blood Pressure (new)
- SDPI Healthy Heart Toolkit
- On-line Recorded Trainings (Free CME Credit)





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# Case studies





# Case Study #1

46 year old female with T2DM x 6 years

- 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: T2 DM, HTN, CVA – father, deceased age 62
- 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

- Current medications:
  - Metformin ER 1 gm daily

**Her ASCVD risk is 8%**

- 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, age 64)
- 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, A/C ratio 300 mg/g

- Current medications:
  - Metformin ER 1 gm daily
  - Alogliptin 25 mg daily
  - Lisinopril 20 mg daily
  - Atorvastatin 20 mg daily

**His 10 year ASCVD risk is 7.5%**

- **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, 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%**

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



# Case Study #4

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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, no CHF
- 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, A/C ratio 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?



# References

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**Cardiovascular Disease and Risk Management: *Standards of Medical Care in Diabetes—2023*** American Diabetes Association; Diabetes Care 2023 Jan; 46(Supplement 1): S158-190.

<https://doi.org/10.2337/dc23-2010>

**Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2023**

Diabetes Care. 2023;46(Supplement\_1):S140-S157. <https://doi:10.2337/dc23-S009>

## **Million Hearts**

(Centers for Disease Control and Prevention and Centers for Medicare and Medicaid Services)

**2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines**

Grundy SM, et al. Circulation. 2019; Volume 139, Issue 25

<https://www.ahajournals.org/doi/suppl/10.1161/CIR.0000000000000625>

**2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA 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

<https://www.ahajournals.org/doi/10.1161/HYP.000000000000065>



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# Questions?