



Division of Diabetes
Treatment and Prevention

Hypertension and Lipid Management: A Patient-Centered Approach to CVD Risk Reduction

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Objectives

- Examine key evidence supporting current guidelines for hypertension (HTN) and lipid management in people with diabetes.
- Individualize treatment strategies for management of blood pressure (BP) and lipids.
- Name three common barriers to adherence to treatment regimens and discuss approaches to addressing them.

Cardiovascular Disease

Atherosclerotic Cardiovascular Disease (ASCVD) — includes coronary heart disease, cerebrovascular disease, and peripheral artery disease

- Common in people with diabetes
- Leading cause of morbidity and mortality — 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 Risk Assessment (1)

ASCVD Plus Risk Calculator (American College of Cardiology)

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

Cardiovascular Risk Assessment (2)

Calculator used in people without ASCVD

- Generates 10-year risk estimate of cardiovascular disease
- Low risk < 5%; Borderline risk 5%–7.4%;
- Intermediate risk 7.5%–19.9%; High risk > 20%

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

Hypertension

Hypertension and Diabetes: Overview

- **General Consensus**

- Proper measurement of blood pressure is important
- Controlling blood pressure can decrease risk of cardiovascular disease
 - (heart disease, stroke), kidney disease, and retinopathy
- Treatment strategies
 - Lifestyle management
 - Medications: ACEI/ARB as first line agents
 - Particularly in patients with albuminuria and CKD (if tolerated)
 - People commonly require more than one medication to achieve BP control
 - Pregnant women
 - BP targets higher due to adverse fetal effects of lowering BP
 - Medication restrictions (no ACEI, ARB, spironolactone, diuretics)

- **Current Questions**

- BP targets in diabetes (different guidelines)
- BP targets in pregnancy

BP Measurement: 7 Steps for Accurate Readings

Step	Source of Error	Effect on Systolic BP
Use proper cuff size	Cuff too small Cuff too large	+ 2–10 mm Hg - 1–5 mm Hg
Place cuff on bare arm	Over clothing	+ 5–50 mm Hg
Arm supported at heart level	Unsupported arm	+ 10 mm Hg
Empty bladder prior to BP measurement	Full bladder	+ 10 mm Hg
No conversation during measurement	Talking or active listening	+ 10 mm Hg
Back supported, feet on floor	Unsupported back, feet	+ 6 mm Hg

AMA Target BP Infographic:

https://targetbp.org/tools_downloads/mbp/

Out-of-Office BP Monitoring

- **Ambulatory 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
 - Patient engagement
 - Monitor treatment
 - Allows assessment of pattern of BP elevation
- **Home BP monitors**
 - Instructions for use
 - Encourage patients to bring to office — to evaluate technique, readings
- **Other resources to evaluate BP**
 - PHN/CHR/Wellness Centers
 - Pharmacy, drug store, other locations

BP Control: The Evidence

Trial	Population	Intensive	Standard	Outcomes
ACCORD BP	4,733 people with T2DM age 40–79 with known ASCVD or risk factors (mean 4.7 year follow up)	Systolic BP target < 120 mm Hg achieved mean BP 119/64 mm Hg	Systolic BP target 130- 140 mm Hg achieved mean BP 134/71 mm Hg	MACE similar in both groups, 41% risk reduction for stroke, Greater risk of adverse drug events 3.3% vs 1.3%
ADVANCE BP	11,140 people with T2DM age > 55 with ASCVD or multiple risk factors (mean 4.3 year follow up)	Fixed dose ACEI/diuretic achieved mean BP 136/73 mm Hg	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 (mean 3.8 year follow up)	Diastolic BP target ≤ 80 mm Hg	Diastolic BP target ≤ 90 mm Hg	In overall trial, no CV benefit from more intensive targets Decreased CV risk, MACE, CV death in patients with DM with DBP ≤ 80 vs ≤ 90
SPRINT	9,361 people without diabetes (mean 3.3 year follow up)	Systolic BP target < 120 mm Hg achieved mean 121 mm Hg	Systolic BP target < 140 mm Hg achieved mean 136 mm Hg	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
UKPDS -38	1,148 people with T2DM and HTN (mean 8.4 year follow up)	Tight BP control < 150/85 mm Hg	Less tight BP control < 180/105 mm Hg	24% RRR in DM related endpoints, 23% in DM related deaths, 37% in microvascular endpoints

Hypertension Targets

Guideline	Systolic BP Targets	Diastolic BP Target	Rationale
American Diabetes Association (2013–2020)	< 140 mm Hg (grade A) < 130 mm Hg (grade C)	< 90 mm Hg (grade A) < 80 mm Hg (grade C)	SBP target raised because evidence that SBP greater than (>) 140 is harmful, but for some patients, a target closer to 130 is appropriate. DBP target raised because strong evidence from RCTs support DBP less than (<) 90, but a target less than (<) 80 may still be appropriate for patients with long life expectancy, CKD, CVD, or additional risk factors
American College of Cardiology /American Heart Association (2017)	< 130 mm Hg (grade A)	< 80 mm Hg (grade A)	SBP and DBP targets of 130/80 recommended for based on meta-analyses of RCTs demonstrating CVD risk reduction
JNC 8 (2013)	< 140 mm Hg (grade E)	< 90 mm Hg (grade E)	SBP & DBP targets raised b/c no RCTs have addressed whether treatment to < 140 and < 90 improved health outcomes or mortality compared to higher goals

ACC 2017 Hypertension Summary Table

Class	SBP	DBP	10 Year ASCVD Risk <10%	10 Year ASCVD Risk ≥ 10%	ASCVD Secondary Prevention
Normal	< 120 mmHg	and < 80 mmHg	Reassess 1 year	Lifestyle modification	Lifestyle modification
Elevated	120–129 mmHg	and < 80 mmHg	Non-pharmacologic intervention Reassess 3–6 months	Non-pharmacologic intervention Reassess 3–6 months	Non-pharmacologic intervention Reassess 3-6 months
Stage 1	130–139 mmHg	or 80–89 mmHg	Non-pharmacologic intervention Reassess 3–6 months	Medical therapy and Non-pharmacologic intervention Reassess 1 month	Medical therapy and Non- pharmacologic intervention Reassess 1 month
Stage 2	≥ 140 mmHg	or ≥ 90 mmHg	Medical therapy and Non-pharmacologic intervention Reassess 1 month	Medical therapy and Non-pharmacologic intervention Reassess 1 month	Medical therapy and Non- pharmacologic intervention Reassess 1 month

Hypertension Therapy in Type 2 Diabetes

https://www.ihs.gov/sites/diabetes/themes/responsive2017/display_objects/documents/algorithms/AlgorithmHypertension.pdf

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.

Therapeutic Lifestyle Changes
DASH-style diet*, limit sodium intake, increase physical activity, tobacco cessation, weight loss if overweight, and limit alcohol consumption

First-Line Medication Classes

ACEI: Lisinopril or, ARB: Losartan	Diuretic: Chlorthalidone, HCTZ	Calcium Channel Blocker: Amlodipine, Diltiazem, Nifedipine
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- If BP not at goal in one month, consider titrating dose up and/or adding medication from a different class above.
- Consider ACEI or ARB for patients with chronic kidney disease (CKD).
- Utilize these 3 classes before considering additional medication classes; however, base treatment selection on individual patient's indications and comorbidities.

Consider Additional Medication Classes
If BP not at goal or unable to tolerate the first-line medication classes above, consider adding medications from additional drug classes.

Mineralocorticoid: Spironolactone	Beta Blocker: Metoprolol, Atenolol	Centrally Acting: Clonidine	Alpha Blocker: Prazosin, Doxazosin
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Treatment Target: < 140/90 for Most Patients

Consider < 130/80 if:

- Younger Age
- Healthier
- CKD
- Low risk for hypotension
- Higher cardiovascular disease risk**
- Target is achievable without burdensome side effects

Consider < 150/90 if:

- Older Age/Frail
- Polypharmacy
- Multiple advanced comorbidities
- High risk for hypotension
- Lower targets are unachievable due to side effects

* Dietary Approaches to Stop Hypertension (DASH) - consider referral to dietitian <https://www.nhlbi.nih.gov/health-topics/dash-eating-plan>

** Consider using a CVD risk calculator such as the ASCVD PLUS risk calculator. <https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#/calculate/estimate/>

– First-Line Medication Classes –

ACE Inhibitors (ACEI) / Angiotensin Receptor Blockers (ARBs)
Lisinopril Start 2.5-5mg daily; usually 20-40mg daily; max 60mg daily.
Losartan Start 25-50mg daily; max 100mg daily. Consider if intolerant to ACEI.
• First line choice for patients with CKD. Can increase potassium and creatinine.
• May cause cough (with ACEI) and rarely angioedema.
• Do not use an ACEI and an ARB together in the same patient.

Calcium Channel Blockers
Amlodipine Start 2.5-5mg daily; usually 5-10mg daily.
• Consider in patients with angina or CHF.
Diltiazem Multiple formulations exist:
• Sustained Release (BID), Controlled Delivery (daily), and Long Acting (daily)
• Consult your local formulary to assure appropriate selection and dosing.
• Diltiazem CD start 180-240mg daily; usually 240-360mg daily; max 480mg daily
Nifedipine XL Start 30mg daily; max dose 120mg daily.
• May cause edema.

Diuretics
HCTZ or chlorthalidone Start 12.5mg daily; usually 25-50mg daily.
• Higher doses may be used for other indications (e.g., edema).
• Can decrease potassium.

Additional Medication Classes

Mineralocorticoid
Spironolactone Start 25mg daily; usually 50-100mg daily in 1-2 divided doses.
• Can increase potassium. May take 2 weeks for treatment response.

Beta Blockers
Atenolol Start 25-50mg daily in 1-2 divided doses; usually 50-100mg/day.
Metoprolol Start 50-100mg daily in 1-2 divided doses; usually 100-200mg/day; max 450mg daily. XR formulation dosed once daily.
Carvedilol Start 6.25mg BID; usually 12.5-25mg BID. CR formulation dosed once daily. Also indicated for heart failure (start 3.125mg BID)
• Do not use if bradycardia or 2nd/3rd degree block. Caution in severe CHF, asthma or renal dysfunction. Do not stop abruptly.

Centrally Acting
Clonidine Start 0.1mg BID (first dose at bedtime); usually 0.1-0.3mg BID; max 1.2mg BID. Titrate up slowly. Can cause sedation, dizziness, and weakness. Do not stop abruptly.

Alpha Blockers
Doxazosin start 1mg immediate release at bedtime; max 16mg daily.
Prazosin Start 1mg BID-TID (first dose at bedtime); max 15mg daily.
• Titrate up slowly. Can cause dizziness, drowsiness, and weakness.

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

Target Treatment: < 140/90 for Most Patients

- Consider 130/80 if:
 - Younger Age
 - Healthier
 - CKD
 - Low risk for hypertension
 - Higher cardiovascular risk**
 - Target is achievable without burdensome side effects
- Consider < 150/90 if:
 - Older Age/Frail
 - Polypharmacy
 - Multiple advanced comorbidities
 - High risk for hypotension
 - Lower targets are unachievable due to side effects

* Dietary Approached to Stop Hypertension (DASH) — consider referral to dietitian
<https://www.nhlbi.nih.gov/health-topics/dash-eating-plan>

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Lifestyle Management

HTN Treatment:

Impact of Lifestyle Changes on Systolic BP

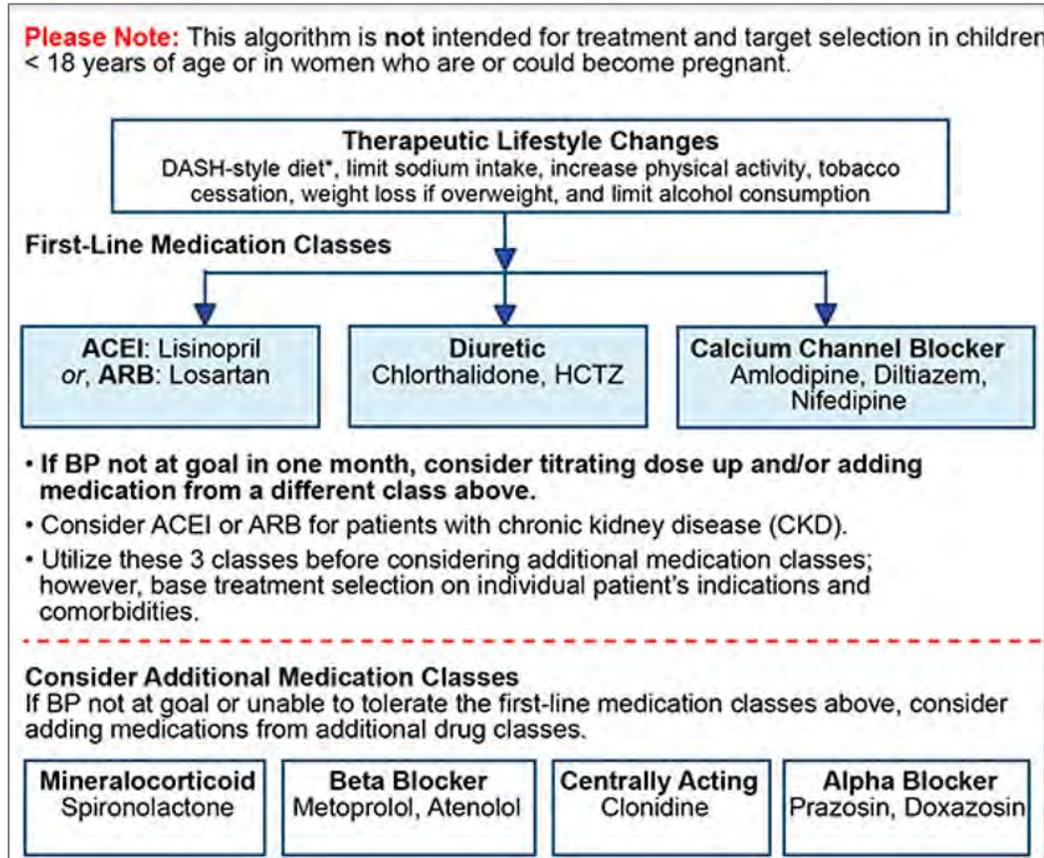
Intervention	Dose	Approximate Effect on SBP
Weight loss	Goal: ideal body weight, but can expect 1 mm Hg decrease per 1 kg of weight loss	-5 mm Hg
DASH-style Diet	Diet rich in whole grains, fruits, vegetables, and low-fat dairy, decreased total and saturated fat	-11 mm Hg
Reduce sodium	Goal: less than 1,500 mg/day, but at least 1,000 mg reduction	-5 to 6 mm Hg
Increase potassium	Goal: 3,500–5,000 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 and resistance exercise 90–150 minutes/week of moderate to vigorous intensity
- Effects of aerobic exercise:
 - 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
 - 4–5 mm Hg decrease systolic BP

Medications

Medications (2)



-- First-Line Medication Classes --

ACE Inhibitors (ACEI) / Angiotensin Receptor Blockers (ARBs)

Lisinopril Start 2.5-5mg daily; usually 20-40mg daily; max 80mg daily.

Losartan Start 25-50mg daily; max 100mg daily. Consider if intolerant to ACEI.

- First line choice for patients with CKD. Can increase potassium and creatinine.
- May cause cough (with ACEI) and rarely angioedema.
- Do not use an ACEI and an ARB together in the same patient.

Calcium Channel Blockers

Amlodipine Start 2.5-5mg daily; usually 5-10mg daily.

- Consider in patients with angina or CHF.

Diltiazem Multiple formulations exist:

- Sustained Release (BID), Controlled Delivery (daily), and Long Acting (daily).
- Consult your local formulary to assure appropriate selection and dosing.
- Diltiazem CD start 180-240mg daily; usually 240-360mg daily; max 480mg daily.

Nifedipine XL Start 30mg daily; max dose 120mg daily.

- May cause edema.

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Additional Medication Classes

Mineralocorticoid

Spironolactone Start 25mg daily; usually 50-100mg daily in 1-2 divided doses.

- Can increase potassium. May take 2 weeks for treatment response.

Beta Blockers

Atenolol Start 25-50mg daily in 1-2 divided doses; usually 50-100mg/day.

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- Do not use if bradycardia or 2nd/3rd degree block. Caution in severe CHF, asthma, or renal dysfunction. Do not stop abruptly.

Centrally Acting

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Please consult a complete prescribing reference for more detailed information.
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Hyperlipidemia

Hyperlipidemia in Diabetes: Overview

General Consensus

- Hyperlipidemia contributes to cardiovascular disease
- Statins: cornerstone therapy for primary and secondary prevention
- Lowering LDL reduces risk of cardiovascular events
 - One meta-analysis 170,000 patients primary and secondary prevention
Each 1 mmol/l (39 mg/dl) reduction in LDL-C associated with 22% reduction in major vascular events and 10% reduction in all cause mortality
- Statin intolerance and statin adherence issues pose clinical challenges
- Avoid statins in pregnancy due to teratogenic risk (X)

Current Questions

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

Lipid Measurement: To Fast or Not to Fast

- Fasting lipid panel: Total cholesterol, triglycerides, HDL, LDL-C
- LDL-C is calculated by Friedewald formula:
 - **Total Chol-HDL – TG/5 = LDL-C**
- Elevated TG can result in lower reported LDL-C value
 - Most labs will not report LDL for TG > 400 mg/dl
 - Lesser TG elevations will impact LDL value
- Calculated LDL-C is less accurate in lower range < 70 mg/dl
- Baseline assessment should be fasting
- Follow up testing — may be performed in non-fasting state, in absence of hypertriglyceridemia

Key Points

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
- Very high-risk group with LDL-C over threshold ≥ 70 mg/dl — consider adding
 - non-statin (ezetimibe or PCSK9 inhibitor)
 - defined very high risk — patients with ASCVD, or patients with 10-year risk $\geq 20\%$

Primary Prevention:

- Clinician-patient discussion before starting statin
- Calculate 10-year ASCVD risk, assess risk-enhancing factors, lifestyle modification, risk/benefit of statin or other therapies, patient preferences, 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 Plus (American College of Cardiology)

- Age *
- Sex
- Race (white, African American, other)
- BP (systolic and 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 ≥ 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, ≥ 20 years T1DM
 - Albuminuria
 - Neuropathy
 - PVD (ABI < 0.9)
 - Retinopathy

Lipid and Aspirin Therapy in Type 2 Diabetes

https://www.ihs.gov/sites/diabetes/themes/responsive2017/display_objects/documents/algorithms/AspirinLipid_Therapy.pdf

Lipid Panel Screening
 Order a lipid panel:
 - at diagnosis of diabetes
 - if < 40 years old and not on a statin, consider annual lipid panel
 - at age 40 if not yet on a statin to establish treatment baseline
 - as needed every 1-5 years (e.g. to evaluate adherence to lipid therapy)

For all patients with diabetes, initiate lifestyle therapy, then:

Age	ASCVD Risk Factors*	Statin Therapy
<40 years	None	None
	1 or more	Moderate or High Intensity
	ASCVD**	High Intensity
40-75 years	None	Moderate Intensity
	1 or more	High Intensity
	ASCVD**	High Intensity
>75 years	None	Moderate Intensity
	1 or more	Moderate or High Intensity
	ASCVD**	High Intensity

* ASCVD (Atherosclerotic Cardiovascular Disease) Risk Factors include: LDL \geq 100mg/dL, smoking hypertension, chronic kidney disease, albuminuria, and family history of premature ASCVD

** ASCVD is atherosclerosis affecting the vasculature of any of the following: heart, periphery (e.g., legs, carotids), and brain (e.g., stroke, transient ischemic attack)

Statin intolerance: Consider trying a different statin. If unable to tolerate daily statin, there may still be benefit from less than daily dosing. There is little evidence of ASCVD benefit from monotherapy with non-statin lipid medications.

Combination therapy (statin plus non-statin lipid medication): There is little evidence of ASCVD benefit with combination therapy.***

*** Limited data suggests ezetimibe 10mg daily plus moderate intensity statin (when high intensity statin is not tolerated) may provide a small reduction in risk of ASCVD events over moderate intensity statin therapy alone if initiated within 10 days of an acute coronary event in patients age \geq 50 years

Statin Medications	Moderate Intensity Dose	High Intensity Dose
Atorvastatin (Lipitor®)****	10-20 mg	40-80 mg
Rosuvastatin (Crestor®)	5-10 mg	20-40 mg
Simvastatin (Zocor®)	20-40 mg	NA
Pravastatin (Pravachol®)	40 mg	NA

**** Note: Only atorvastatin 40-80mg is on the IHS National Core Formulary

Contraindications: acute liver disease, pregnancy, nursing mothers
Statin drug interactions: consult package insert prior to prescribing
 All statins - Caution or contraindication with gemfibrozil, cyclosporine, or danazole.
 Simvastatin - Caution or contraindication with strong CYP3A4 inhibitors (e.g., azole antifungals, erythromycins, HIV protease inhibitors, nefazodone)
 Decrease dose of simvastatin with niacin, amiodarone, diltiazem, amlodipine, grapefruit
 Check ALT before initiating therapy; Routine monitoring not necessary

Elevated Triglycerides: Ensure blood sugar control and identify any secondary causes (e.g., high fat and/or high carbohydrate diet, hypothyroidism, excessive alcohol use, medications). Consider triglyceride lowering therapy if severely elevated (e.g. \geq 1,000 mg/dL) to reduce risk of pancreatitis.
 - Gemfibrozil (Lopid®) 600mg BID
 - Fenofibrate (Tricor®, others) 145mg Daily
 - Fish Oil (Lovaza®, others) 2-4g Daily

Note: Medications in green are not on the IHS National Core Formulary

Aspirin Therapy for ASCVD

Secondary Prevention:
 Patients with a history of ASCVD should receive aspirin 75-162mg daily if they are not at increased risk of bleeding.
 If allergic to aspirin, consider clopidogrel 75mg daily.

Primary Prevention:
 Consider aspirin 75-162mg daily in patients with increased risk of ASCVD, (e.g., age \geq 50 years and 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 major ASCVD risk factors*).

Consult a complete prescribing reference for more detailed information. This algorithm is not intended for treatment selection in children or in women who are or could become pregnant.

Ref: ADA Clinical Practice Recommendations, Diabetes Care 2017; 40, Supplement 1. ACC/AHA Cholesterol Guideline, J Am Coll Cardiol 2014; 63:2689-934.

Non-statin Medications: The Evidence

Trial	Population	Intervention	Outcomes
IMPROVE-IT	18,144 patients with ACS (within 10 days) and LDL-C 50-100 mg/dl if on lipid Rx, or 50-125 mg/dl if not on lipid Rx (median follow-up 6 years)	Randomized to simvastatin 40mg/placebo vs. simvastatin 40mg/ezetimibe 10 mg Median LDL-C lower with combination 53.7 vs. 69.5 mg/dl	Decreased composite CVD outcomes (32.7% vs 34.7%) — ARR 2 % Decreased myocardial infarction and stroke No cardiovascular or overall mortality benefit
FOURIER	27,564 patients with ASCVD and LDL > 70 mg/dl on max tolerated statin (median 26 month follow up)	Added evolucumab, comparison with placebo control group Median LDL lowered from 92 to 30 mg/dl	Decreased composite CVD outcomes (9.8% vs 11.3%)— ARR 1.5 %, No cardiovascular or overall mortality benefit
ODYSSEY OUTCOMES	18,924 patients with recent ACS, on max tolerated statin (median 34-month follow-up)	Added alirocumab, comparison with placebo control group Median LDL-C lowered from 92 to 53 mg/dl	Decreased composite CVD outcomes (9.5% vs 11.1%) - ARR 1.6% Decreased all cause mortality – ARR 0.6%

Non-statins: Ezetimibe

- Ezetimibe (Zetia)
 - Inhibits intestinal absorption of cholesterol
 - 20%–25% LDL-C reduction
 - When added to statin, CVD benefit seen in patients with CVD
 - Lipid guidelines recommend use in patients with ASCVD and elevated LDL \geq 70 mg/dl
 - Once daily dosing, generally well tolerated
 - Now on National Core Formulary, generic in U.S.

Non-statins: PCSK9 Inhibitors

- Evolocumab (Repatha) and Alirocumab (Praluent) licensed in the U.S. in 2015
- Monoclonal antibodies which bind to proprotein convertase subtilisin/kexin type 9 (PCSK9)
- Prevents PCSK9 attachment to LDL receptors, so more receptors are available to clear LDL in the liver
- Result in 50%–60% LDL-C reduction
- CVD benefit (ARR 1.5%–1.6%) in patients with known CVD on max tolerated statin
- AHA/ACC/ADA Lipid guidelines recommend use in **very high-risk patients** (with CVD) who are not at LDL target < 70 mg/dl
- Injected every 2–4 weeks, generally well tolerated
- Expensive, not on National Core Formulary, most insurance requires PA
- Recommend consultation with cardiologist or lipidologist before prescribing

Medication Adherence

Medication Adherence: Statins

Nonadherence

- Several large population studies have estimated 50%–54% continuation rate
- Continuation associated with improved outcomes
 - For each 10% decrease in MPR (medication possession ratio), 5% increase in risk for CVD-related hospitalizations
 - 2 large retrospective analyses of persons with CVD increased adherence to statins, decreased mortality in VA population HR 1.3 and Medicare populations HR 1.26
 - Retrospective study in Israeli HMO of statin use in persons with and without CHD: primary prevention HR 1.46, secondary prevention HR 1.53
- **Statin intolerance**
 - Muscle aches, myositis, rhabdomyolysis, CNS side effects
 - Change to hydrophilic (non-lipophilic) statin e.g., rosuvastatin, pravastatin
 - Change dosing schedule, alternate days, lower dose, agent with long half life

Medication Adherence: Challenges

Intentional

- Mistrust
- Side effects
- Concern about possible side effects
- Fear of harm
- Unsure about benefit
- Cost

Unintentional

- Forgets
- Confusion
- Work schedule issues
- Psychiatric illness

Medication Adherence – Strategies for Improvement

- **Encourage patients to bring all meds to office visits**
 - Might include additional message with reminder call
- **Patient centered conversation about meds** — questions, concerns
- **Problem solve** — with individual patient or family, if appropriate
- Attention to literacy issues, visual or cognitive impairment
- Address traditional and cultural beliefs
- Simplify regimen, schedule
- Encourage at-home BP-monitoring for people with hypertension
- **Team involvement** in medication education, review, and reconciliation — nursing staff, clinical pharmacist, pharmacy clinician, dietitians, educators, case managers

Patient Centered/ Shared Decision Making

- **Patient goals, health concerns, and health beliefs**
- **ASCVD risk assessment**
- **Address lifestyle management, potential benefit lifestyle modification**
- **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
 - Collaborative plan
 - Involve care team, other resources



Case Studies

Case Study #1

46-year-old female with T2DM x 4 years

- Office job, frequent required overtime, single mother of 2 teen boys
- Zumba class after work 1–2 days week, no other exercise
- Cooks on weekends, fast food 3–4 nights/week, tries to limit fried foods
- History of GDM, preeclampsia with last pregnancy 14 years ago
- PMH: otherwise unremarkable
- Fam Hx: T2 DM, HTN, CVA — father, deceased age 70
- Occ. ETOH, no h/o tobacco or illicit substance use
- BP 135/85, last A1C 7.2, BMI 31, Total Chol 220, LDL-C 90, HDL 55 mg/dl
- Current medications:
 - Metformin ER 1 gm daily

Her ASCVD risk is 2.2%

- What should her BP target be?
- What might you recommend as an initial treatment plan?
- What about her lipids?
- Is she a statin candidate?

Case Study #2

74-year-old male with type 2 DM x 20 years

- Jogs 2 miles, 5 days/week, lifts weights at fitness center 1 hour 3 days/week
- Eats a “traditional” diet, has a small farm: grows corn, squash, melons, and chile
- PMH: HTN, elevated cholesterol, mild DJD B knees, otherwise unremarkable
- Fam Hx: T2 DM, HTN, CVA — father, deceased age 90, mother age 96 in “good health”
- Former heavy ETOH (sober x 20 years) no h/o tobacco or illicit substance use
- BP 148/89, last A1C 7.8, BMI 26
- Total Chol 220 mg/dl, LDL-C 120 mg/dl, HDL 42 mg/dl, A/C ratio 200 mg/g
- Current medications:
 - Metformin ER 1 gm daily
 - Levemir 10 units at bedtime
 - Lisinopril 20 mg daily
 - Atorvastatin 20 mg daily

His 10-year ASCVD risk is 58%

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

Case Study #3

73-year-old female with T2DM for 20 years, had MI 3 years ago, 2 stents placed

- Walks 20–30 minutes 3–4 days/week, cooks for husband — 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 135/89, last A1c 7.9, BMI 28, Total Chol 200 mg/dl, LDL-C 85 mg/dl, HDL 35 mg/dl
- Current medications:
 - Metformin ER 1 gm daily
 - Levemir 10 units at bedtime
 - Lisinopril 10 mg daily
 - Metoprolol 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?

Case Study #4

68-year-old female with T2DM for 30 years

- Lives alone, some family support, mild depression, occasional forgetfulness
- PMH: CKD, HTN, DJD, neuropathy, osteoporosis, hyperlipidemia, COPD on O2
- Fam Hx: T2DM, HTN, CVA, ESRD — mother, deceased age 65; father, lung cancer, deceased
- Nonsmoker, no alcohol or illicit substance use
- BP 145/95, last A1c 8.2, BMI 26, Total Chol 240 mg/dl, LDL-C 110 mg/dl, HDL 35 mg/dl, eGFR 45
- Current medications:
 - Metformin ER 1 gm daily
 - Levemir 20 units at bedtime
 - Lisinopril 40 mg daily
 - HCTZ 12.5 mg daily
 - Amlodipine 5 mg daily
 - Atorvastatin 20 mg daily
 - Aspirin 81 mg daily

Her 10-year ASCVD risk is 34.8%

- What should her BP target be?
- What about her lipids?
- What questions might you have for her prior to changing medications?

Questions?

References

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Resources from IHS Division of Diabetes Treatment and Prevention

<https://www.ihs.gov/Diabetes/>

- Online Catalog: educational materials
- Clinical Resources
 - Algorithms
 - Standards of Care
- SDPI Healthy Heart Program Toolkit
- Online Recorded Training (Free CME Credit)