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

Lani Desaulniers, MD, FAAFP
Clinical Consultant
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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

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

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

<table>
<thead>
<tr>
<th>Trial</th>
<th>Population</th>
<th>Intensive</th>
<th>Standard</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACCORD BP</td>
<td>4,733 people with T2DM age 40–79 with known ASCVD or risk factors (mean 4.7 year follow up)</td>
<td>Systolic BP target &lt; 120 mm Hg achieved mean BP 119/64 mm Hg</td>
<td>Systolic BP target 130–140 mm Hg achieved mean BP 134/71 mm Hg</td>
<td>MACE similar in both groups, 41% risk reduction for stroke, Greater risk of adverse drug events 3.3% vs 1.3%</td>
</tr>
<tr>
<td>ADVANCE BP</td>
<td>11,140 people with T2DM age &gt; 55 with ASCVD or multiple risk factors (mean 4.3 year follow up)</td>
<td>Fixed dose ACEI/diuretic achieved mean BP 136/73 mm Hg</td>
<td>Control: placebo achieved mean BP 142/75 mm Hg</td>
<td>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</td>
</tr>
<tr>
<td>HOT</td>
<td>18,790 people -1,501 with diabetes (mean 3.8 year follow up)</td>
<td>Diastolic BP target ≤ 80 mm Hg</td>
<td>Diastolic BP target ≤ 90 mm Hg</td>
<td>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</td>
</tr>
<tr>
<td>SPRINT</td>
<td>9,361 people without diabetes (mean 3.3 year follow up)</td>
<td>Systolic BP target &lt; 120 mm Hg achieved mean 121 mm Hg</td>
<td>Systolic BP target &lt; 140 mm Hg achieved mean 136 mm Hg</td>
<td>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</td>
</tr>
<tr>
<td>UKPDS-38</td>
<td>1,148 people with T2DM and HTN (mean 8.4 year follow up)</td>
<td>Tight BP control &lt; 150/85 mm Hg</td>
<td>Less tight BP control &lt; 180/105 mm Hg</td>
<td>24% RRR in DM related endpoints, 23% in DM related deaths, 37% in microvascular endpoints</td>
</tr>
</tbody>
</table>
### Hypertension Targets

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

<table>
<thead>
<tr>
<th>Class</th>
<th>SBP</th>
<th>DBP</th>
<th>10 Year ASCVD Risk &lt;10%</th>
<th>10 Year ASCVD Risk ≥ 10%</th>
<th>ASCVD Secondary Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 120 mmHg</td>
<td>and &lt; 80 mmHg</td>
<td>Reassess 1 year</td>
<td>Lifestyle modification</td>
<td>Lifestyle modification</td>
</tr>
<tr>
<td>Elevated</td>
<td>120–129 mmHg</td>
<td>and &lt; 80 mmHg</td>
<td>Non-pharmacologic intervention</td>
<td>Non-pharmacologic intervention</td>
<td>Non-pharmacologic intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reassess 3–6 months</td>
<td>Reassess 3–6 months</td>
<td>Reassess 3–6 months</td>
</tr>
<tr>
<td>Stage 1</td>
<td>130–139 mmHg</td>
<td>or 80–89 mmHg</td>
<td>Non-pharmacologic intervention</td>
<td>Medical therapy and Non-pharmacologic intervention</td>
<td>Medical therapy and Non-pharmacologic intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reassess 3–6 months</td>
<td>Reassess 1 month</td>
<td>Reassess 1 month</td>
</tr>
<tr>
<td>Stage 2</td>
<td>≥ 140 mmHg</td>
<td>or ≥ 90 mmHg</td>
<td>Medical therapy and Non-pharmacologic intervention</td>
<td>Medical therapy and Non-pharmacologic intervention</td>
<td>Medical therapy and Non-pharmacologic intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reassess 1 month</td>
<td>Reassess 1 month</td>
<td>Reassess 1 month</td>
</tr>
</tbody>
</table>
Hypertension Therapy in Type 2 Diabetes

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

** Consider using a CVD risk calculator such as the ASCVD PLUS risk calculator.
  https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/
Lifestyle Management
# HTN Treatment: Impact of Lifestyle Changes on Systolic BP

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Dose</th>
<th>Approximate Effect on SBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>Goal: ideal body weight, but can expect 1 mm Hg decrease per 1 kg of weight loss</td>
<td>-5 mm Hg</td>
</tr>
<tr>
<td>DASH-style Diet</td>
<td>Diet rich in whole grains, fruits, vegetables, and low-fat dairy, decreased total and saturated fat</td>
<td>-11 mm Hg</td>
</tr>
<tr>
<td>Reduce sodium</td>
<td>Goal: less than 1,500 mg/day, but at least 1,000 mg reduction</td>
<td>-5 to 6 mm Hg</td>
</tr>
<tr>
<td>Increase potassium</td>
<td>Goal: 3,500–5,000 mg/day, preferably from dietary sources</td>
<td>-4 to 5 mm Hg</td>
</tr>
</tbody>
</table>
| 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)

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**: Chlorothalidone, HCTZ
- **Calcium Channel Blocker**: Amlodipine, Diltiazem, Nifedipine

- **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

--- 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 240-300mg daily; max 480mg daily.**
- **Nifedipine XL**: Start 30mg daily; max dose 120mg daily.
  - **May cause edema.**

Diuretics
- **HCTZ or chlorothalidone**: 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. Titrates 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.
  - **Titrates 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.
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 ≥ 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 ≥ 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 ≥ 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


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

**ASCVD Risk Factors**: None, 1 or more

**ASCVD** risk factors include: LDL ≥100mg/dL, smoking, hypertension, chronic kidney disease, albuminuria, and family history of premature ASCVD

**ASCVD** is atherothrombosis 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 ≥55 years**

**Statin Medications**

- **Aspirin (Lipitor®)**
  - Moderate Intensity: 10-20 mg
  - High Intensity: 40-60 mg
- **Rosuvastatin (Crestor®)**
  - Moderate Intensity: 5-10 mg
  - High Intensity: 20-40 mg
- **Simvastatin (Zocor®)**
  - Moderate Intensity: 20-40 mg
  - High Intensity: NA
- **Pravastatin (Pravachol®)**
  - Moderate Intensity: 40 mg
  - High Intensity: NA

**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., ≥500 mg/dL) to reduce risk of pancreatitis.

- **Gemfibrozil (Lopid®)** (930mg BID)
  - Fenofibrate (TriCor®, others) 145mg Daily
  - Fish Oil (Omega-3, others) 2-4g Daily

**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 able to aspirin, consider clopidogrel 75mg daily.

**Primary Prevention**

Consider aspirin 75-162mg daily in patients with increased risk of ASCVD, (e.g., age ≥55 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.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMPROVE-IT</td>
<td>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)</td>
<td>Randomized to simvastatin 40mg/placebo vs. simvastatin 40mg/ezetimibe 10 mg, Median LDL-C lower with combination 53.7 vs. 69.5 mg/dl</td>
<td>Decreased composite CVD outcomes (32.7% vs 34.7%) — ARR 2 % Decreased myocardial infarction and stroke No cardiovascular or overall mortality benefit</td>
</tr>
<tr>
<td>FOURIER</td>
<td>27,564 patients with ASCVD and LDL &gt; 70 mg/dl on max tolerated statin (median 26 month follow up)</td>
<td>Added evolucumab, comparison with placebo control group, Median LDL lowered from 92 to 30 mg/dl</td>
<td>Decreased composite CVD outcomes (9.8% vs 11.3%) — ARR 1.5 %, No cardiovascular or overall mortality benefit</td>
</tr>
<tr>
<td>ODYSSEY OUTCOMES</td>
<td>18,924 patients with recent ACS, on max tolerated statin (median 34-month follow-up)</td>
<td>Added alirocumab, comparison with placebo control group, Median LDL-C lowered from 92 to 53 mg/dl</td>
<td>Decreased composite CVD outcomes (9.5% vs 11.1%) - ARR 1.6% Decreased all cause mortality – ARR 0.6%</td>
</tr>
</tbody>
</table>
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 ≥ 70 mg/dL
  • Once daily dosing, generally well tolerated
  • Now on National Core Formulary, generic in U.S.
Non-statins: PCSK9 Inhibitors

- Evolucumab (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

<table>
<thead>
<tr>
<th>Intentional</th>
<th>Unintentional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mistrust</td>
<td>Forgets</td>
</tr>
<tr>
<td>Side effects</td>
<td>Confusion</td>
</tr>
<tr>
<td>Concern about possible side effects</td>
<td>Work schedule issues</td>
</tr>
<tr>
<td>Fear of harm</td>
<td>Psychiatric illness</td>
</tr>
<tr>
<td>Unsure about benefit</td>
<td></td>
</tr>
<tr>
<td>Cost</td>
<td></td>
</tr>
</tbody>
</table>
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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• **Overcoming Barriers to Statin Adherence**
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
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