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

Lani Desaulniers MD, FAAFP
Clinical Consultant - DDTP
July 26, 2023
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.”

- 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.

American Heart Association
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.
Lifestyle Management

• Smoking Cessation
  – 5 A’s: Ask, Advise, Assess, Assist, and Arrange

• Diet
  – DASH-style eating pattern
    ◊ Reducing sodium and increasing potassium
    ◊ Reducing saturated fat and trans fat
    ◊ Increase n-3 fatty acids, viscous fiber, and plant stanols/sterols
  – Weight loss through caloric restriction, as indicated
  – Moderation of alcohol intake (servings: ≤ 2/day men, ≤ 1/day women)

• Exercise
  – Minimum 150 minutes of moderate aerobic or 75 minutes of vigorous activity per week
  – More is better
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.
Hypertension is defined as a systolic blood pressure ≥130 mmHg or a diastolic blood pressure ≥80 mmHg based on an average of ≥2 measurements obtained on ≥2 occasions.

• **Recommendations 10.3** For people with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses cardiovascular risk, potential adverse effects of antihypertensive medications, and patient preferences. B
• **10.4** People with diabetes and hypertension qualify for antihypertensive drug therapy when the blood pressure is persistently elevated ≥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)

<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 - T2DM age 40-79 with known ASCVD or risk factors</td>
<td>Systolic BP target &lt; 120 mmHg achieved mean BP 119/64 mmHg</td>
<td>Systolic BP target 130-140 mmHg achieved mean BP 134/71 mmHg</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</td>
<td>11,140 people - T2DM age &gt;55 with ASCVD or multiple risk factors</td>
<td>Fixed dose ACEI/diuretic achieved mean BP 136/73 mmHg</td>
<td>Control: placebo achieved mean BP 142/75 mmHg</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</td>
<td>Diastolic BP target &lt; 80 mmHg</td>
<td>Diastolic BP target ≤ 90 mmHg</td>
<td>In overall trial, no CV benefit from more intensive targets Decreased CV risk, MACE, CV death in pts with DM with DBP &lt; 80 mmHg vs ≤ 90 mmHg</td>
</tr>
<tr>
<td>SPRINT</td>
<td>9,361 people without diabetes</td>
<td>Systolic BP target &lt; 120 mmHg achieved mean BP 121 mmHg</td>
<td>Systolic BP target &lt; 140 mmHg achieved mean BP 136 mmHg</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>STEP</td>
<td>8,511 people aged 60-80 years - 1,627 with diabetes</td>
<td>Systolic BP target &lt; 130 mm Hg achieved mean BP 127.5 mmHg</td>
<td>Systolic BP target &lt; 150 mmHg achieved mean BP 135.3 mmHg</td>
<td>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</td>
</tr>
</tbody>
</table>
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:
2. Handler J. The Importance of accurate blood pressure measurement. The Permanente Journal/Summer 2009/Vol 13 No. 3 S1

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.
BP Monitoring

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

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

Self-Monitoring Blood Pressure

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

24 hour ambulatory blood pressure monitoring can be helpful.

Other resources to evaluate BP

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

* Self-Measured Blood Pressure Monitoring: Action Steps for Clinicians
## HTN Treatment: Impact of Lifestyle Changes on Systolic BP

<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, &amp; low fat dairy, decreased total and saturated fat</td>
<td>- 11 mm Hg</td>
</tr>
<tr>
<td>Reduce sodium</td>
<td>Goal: less than 1500 mg/day, but at least 1000 mg reduction</td>
<td>- 5 to 6 mm Hg</td>
</tr>
<tr>
<td>Increase potassium</td>
<td>Goal: 3500-5000 mg/day, preferably from dietary sources</td>
<td>- 4 to 5 mm Hg</td>
</tr>
<tr>
<td>Reduce alcohol</td>
<td>Men ≤ 2 drinks/day, Women ≤ 1 drink/day</td>
<td>- 4 mm Hg</td>
</tr>
</tbody>
</table>

2017 ACC/AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults
A Report of the American College of Cardiology/American Heart Association Hypertension. Volume 71, Issue 6, June 2018
AHA/ACC guidelines recommend aerobic & resistance exercise 90-150 minutes/week of moderate to vigorous intensity.

• Effects of aerobic exercise on BP
  ◊ 5-8 mm Hg decrease systolic BP
  ◊ 24 hour duration of effect
  ◊ can lower CVD risk 20-30%

  Effects of isometric or dynamic resistance exercise on BP
  ◊ 4-5 mm Hg decrease systolic BP

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

<table>
<thead>
<tr>
<th></th>
<th>Aerobic</th>
<th>Resistance</th>
<th>Flexibility</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>≥5–7 d · wk⁻¹</td>
<td>≥2–3 d · wk⁻¹</td>
<td>≥2–3 d · wk⁻¹</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>Moderate (i.e., 40%–59% O₂R or HRR; RPE 12–13 on a 6–20 scale)</td>
<td>Moderate (i.e., 60%–70% 1-RM; may progress to 80% 1-RM; for older individuals and novice exercisers, begin with 40%–50% 1-RM)</td>
<td>Stretch to the point of feeling tightness or slight discomfort.</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td>≥30 min · d⁻¹ of continuous or accumulated exercise</td>
<td>2–4 sets of 8–12 repetitions of each of the major muscle groups per session to total ≥20 min per session with rest days interspersed depending on the muscle groups being exercised</td>
<td>Hold static stretch for 10–30 s with 2–4 repetitions of each exercise targeting the major muscle tendon units to total 60 s of total stretching time for each exercise; ≤10 min per session</td>
</tr>
<tr>
<td><strong>Type</strong></td>
<td>Prolonged, rhythmic activities using large muscle groups (e.g., walking, cycling, swimming)</td>
<td>Resistance machines, free weights, resistance bands, and/or functional body weight exercise</td>
<td>Static, dynamic, and/or proprioceptive neuromuscular facilitation</td>
</tr>
</tbody>
</table>

1-RM, one repetition maximum; HRR, heart rate reserve; O₂R, oxygen uptake reserve; RPE, rating of perceived exertion.

**Prefered 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, telesartan, and valsartan.

Calcium Channel Blockers (CCB)

Amlodipine Start 2.5-5mg daily; usually 5-10mg daily.
Other dihydropyridine CCBs include felodipine, lacidipine, lercanidipine, nilvadipine 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 160-240mg 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 chlorothalidone 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
Controlling hypertension (blood pressure ≥130/80 mmHg on two or more visits) reduces the risk of heart attack, stroke, heart failure, and kidney disease. Treatment targets should be individualized based on shared decision making which addresses risks, benefits, and patient preferences.

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

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

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

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

**Initial Medication Therapy**

- **BP ≥130/80 mmHg and <160/100 mmHg**
  - Use ACEi or ARB (preferred)**

- **BP ≥160/100 mmHg**
  - Use 2 agents: ACEi or ARB and CCB or diuretic

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

**Resistant Hypertension***

- **BP ≥140/90 mmHg and treated with ACEi or ARB, CCB, and Diuretic, consider**
  - Mineralocorticoid Receptor Antagonist: Spironolactone or Eplerenone
  - AND/OR
  - Consult or refer to: nephrologist, cardiologist, or endocrinologist

---

* Dietary Approaches to Stop Hypertension (DASH) Consider referral to dietitian. https://www.nhlbi.nih.gov/health-topics/dash-eating-plan
** If unable to tolerate angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), use calcium channel blocker (CCB) or diuretic.
*** Consider evaluation for secondary hypertension.
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
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: $>10$ years T2DM, $>20$ years T1DM
- Albuminuria
- Neuropathy
- PVD (ABI < 0.9)
- Retinopathy

2018 AHA/ACC Guideline on the Management of Blood Cholesterol
Lipid Therapy in Type 2 Diabetes

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

- Obtain a fasting lipid panel in patients with diabetes:
  - at diagnosis of diabetes or initial diabetes visit;
  - at least every 5 years if age <40 years, annually after 40, and
  - at initiation of statin therapy and after dosing changes.
- Provide lifestyle therapy to all patients with diabetes (individualized nutrition therapy, physical activity, and weight loss guidance).
- Evaluate for statin therapy
  - Secondary Prevention:
    - Prescribe high-intensity statin therapy for patients with diabetes and ASCVD.1
  - Primary Prevention:
    - Use the following table to guide statin therapy and dosing for people with diabetes and no ASCVD diagnosis:
      - Evaluate ASCVD risk factors independent of diabetes2

<table>
<thead>
<tr>
<th>Age</th>
<th>ASCVD1 Risk</th>
<th>Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>40-75 years</td>
<td>None or 10-year ASCVD risk &lt;5% Moderate or High Intensity3</td>
<td>Moderate Intensity</td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>Individualized ASCVD risk assessment5 Moderate or High Intensity4</td>
<td></td>
</tr>
</tbody>
</table>

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 include: LDL cholesterol ≥160 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

Lipid & Aspirin Therapy in Type 2 Diabetes

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

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

Contraindications: acute liver disease, pregnancy, nursing mothers

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

Statin intolerance: Usually due to side effect, such as myalgias. 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 (>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 350 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.

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.
# Lipid Therapy in Type 2 Diabetes

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

- Obtain a fasting lipid panel in patients with diabetes
  - at diagnosis of diabetes or initial diabetes visit;
  - at least every 5 years if age <40 years, annually after 40; and
  - at initiation of statin therapy and after dosing changes.

- Provide lifestyle therapy to all patients with diabetes (individualized nutrition therapy, physical activity, and weight loss guidance).

- Evaluate for statin therapy
  - Secondary Prevention: 
    - Prescribe high intensity statin therapy for patients with diabetes and ASCVD\(^1\).
  - Primary Prevention: 
    - Use the following table to guide statin therapy and dosing for people with diabetes and no ASCVD diagnosis.
      - Evaluate ASCVD risk factors independent of diabetes\(^2\).
      - Calculate 10-year ASCVD risk for patients aged 40-75 years using the ASCVD Risk Estimator Plus at [https://tools.acc.org/ASCVD-Risk-Estimator-Plus/](https://tools.acc.org/ASCVD-Risk-Estimator-Plus/)

<table>
<thead>
<tr>
<th>Age</th>
<th>ASCVD(^1) Risk</th>
<th>Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>One or more ASCVD risk factors(^2)</td>
<td>Moderate or High Intensity(^3)</td>
</tr>
<tr>
<td>40-75 years</td>
<td>None or 10-year ASCVD risk &lt;5%</td>
<td>Moderate Intensity</td>
</tr>
<tr>
<td></td>
<td>One or more ASCVD risk factors(^2) or</td>
<td>Moderate or High Intensity(^3)</td>
</tr>
<tr>
<td></td>
<td>10-year ASCVD risk 5-20%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10-year ASCVD risk &gt;20%</td>
<td>High Intensity(^4)</td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>Individualize ASCVD risk assessment(^5)</td>
<td>Moderate or High Intensity</td>
</tr>
</tbody>
</table>

IHS DDTP Lipid & Aspirin Therapy in Type 2 Diabetes Algorithm
### Statin Medications

<table>
<thead>
<tr>
<th>Statin Medications</th>
<th>Moderate Intensity Dose</th>
<th>High Intensity Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>10-20 mg</td>
<td>40-80 mg</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>5-10 mg</td>
<td>20-40 mg</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20-40 mg</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>40-80 mg</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

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 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 (>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).
  - Fenofoibrate 120-160 mg daily
  - Omega 3 fatty acid 2 g bid
  - Icosapent ethyl (*Vascepa*) 2 g bid
Non-statins Medications

<table>
<thead>
<tr>
<th>Ezetimibe</th>
<th>PCSK9 Inhibitors* Evolucumab (Repatha) &amp; Alirocumab (Praluent)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism of Action</strong></td>
<td>Inhibits intestinal absorption of cholesterol</td>
</tr>
<tr>
<td><strong>LDL-C reduction</strong></td>
<td>20-25% reduction</td>
</tr>
<tr>
<td><strong>CVD risk reduction</strong></td>
<td>CVD benefit when added to statin in patients with CVD</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>Oral, daily dosing</td>
</tr>
<tr>
<td><strong>Availability</strong></td>
<td>Generic, on National Core Formulary</td>
</tr>
</tbody>
</table>

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

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.
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

<table>
<thead>
<tr>
<th>Trial</th>
<th>Drug</th>
<th>Relative Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEADER</td>
<td>Liraglutide vs. placebo</td>
<td>13% for major adverse cardiac events (MACE)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13% for heart failure hospitalization</td>
</tr>
<tr>
<td></td>
<td></td>
<td>22% for cardiovascular death</td>
</tr>
<tr>
<td>SUSTAIN-6</td>
<td>Semaglutide (injectable) vs. placebo</td>
<td>26% for MACE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>39% for stroke</td>
</tr>
<tr>
<td>REWIND</td>
<td>Dulaglutide vs. placebo</td>
<td>12% for MACE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24% for stroke</td>
</tr>
</tbody>
</table>
# SGLT-2 Inhibitors in People with Diabetes and CVD or High-Risk for CVD

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

- 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/

• 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)
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

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?
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 

**Million Hearts**  
(Centers for Disease Control and Prevention and Centers for Medicare and Medicaid Services)

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

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.0000000000000065
Questions?