ASSESS AND ADDRESS RISK OF CARDIOVASCULAR DISEASE

Care teams systematically evaluate each patient's risk for cardiovascular disease, using a trusted risk assessment tool. For patients at risk, treatment plans include primary and secondary prevention in accordance with American Diabetes Association (ADA) recommendations for lifestyle, lipid-lowering and antihypertensive medications, and aspirin.

Heart diseases and stroke are the top causes of death and disability among people with Type 2 diabetes. In fact, at least 65 percent of people with diabetes die from some form of heart disease or stroke. To reverse these trends, care teams must assess risk of cardiovascular disease for people with Type 2 diabetes and intervene in order to prevent these major health events.

TIPS TO INCORPORATE CARDIOVASCULAR RISK ASSESSMENT

- Use the ACC/AHA ASCVD Risk Calculator (refer to Appendix E: Suggested Readings for a link) for all patients with Type 2 diabetes over 40 years old annually, but including those who are newly diagnosed with the condition.
- Develop a workflow to facilitate ease of adoption. This workflow may incorporate:
  - Inclusion of point-of-care alerts,
  - Delegation of this responsibility (e.g., to a medical assistant or care coordinator),
  - Development of automated tools built into the EHR, and
  - Utilization monitoring of these tools (e.g., Did a point-of-care alert appear and was statin ordered, if appropriate? Did medication reconciliation include statin adherence over 80%?).
- Ensure the results are entered into the EHR and/or your diabetes registry in a discrete, searchable field.
- Educate clinicians and care team members about the importance of cardiovascular risk assessment for patients with Type 2 diabetes, the approved workflow, and appropriate management per your organization's treatment algorithms (refer to Adopt Treatment Algorithm plank).
- Develop or adopt treatment guidelines that include use of moderate- or high-intensity statins, lifestyle changes, antihypertensive medications, and aspirin for at-risk patients.
- Establish a process to assess medication adherence such as patient questionnaires, self-reports, pill counts, and pharmacy refills.
- Offer patient education materials and self-management tools that are culturally appropriate and accessible to audiences with low literacy.
- Monitor use of the risk calculator and adherence to the workflow and report back to the Accountable Diabetes Team at your organization (refer to Build an Accountable Diabetes Team plank).
- Leverage the work previously completed in your organization with Measure Up/Pressure Down® or other related efforts.

TOOL: CARDIOVASCULAR DISEASE ALGORITHM

INTERMOUNTAIN HEALTHCARE

PREVENTION AND MANAGEMENT OF RELATED CONDITIONS

Patients with diabetes are likely to have related conditions such as:

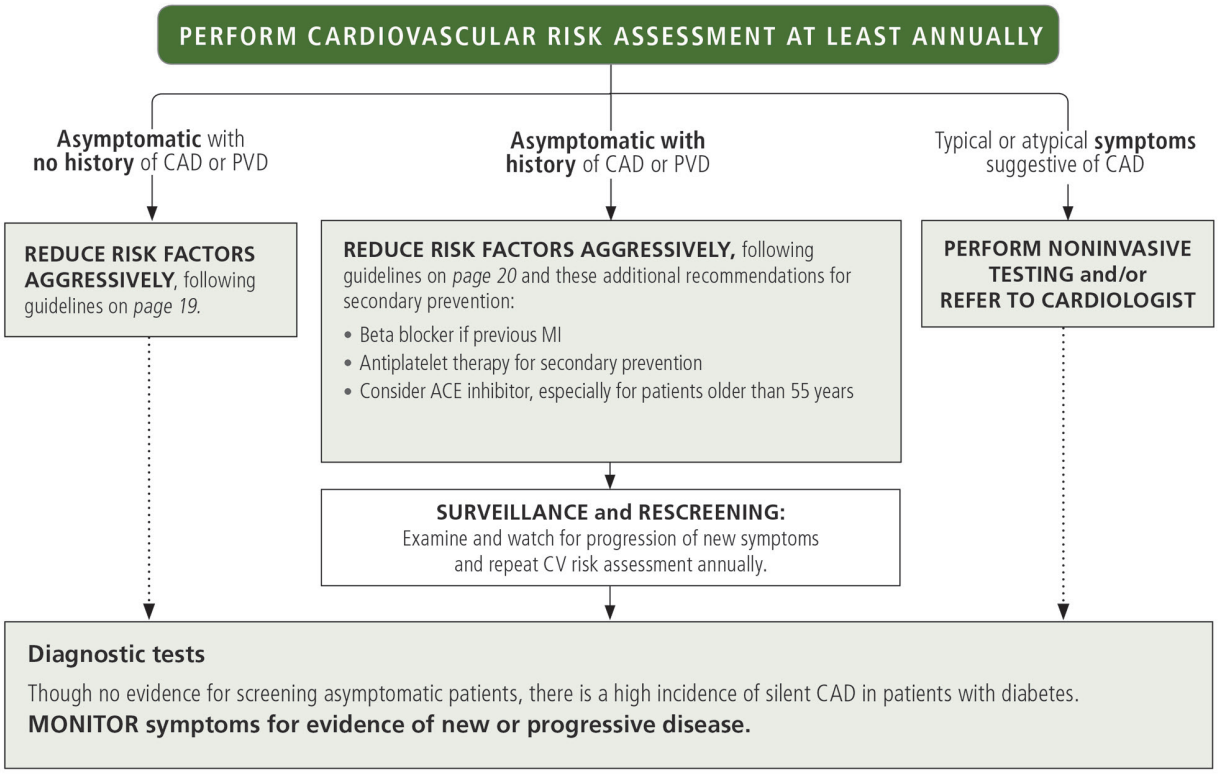
- Cardiovascular disease *(p. 18)*
- High cholesterol *(p. 20)*
- High blood pressure *(p. 22)*
- Kidney disease *(p. 24)*
- Retinopathy *(p. 25)*
- Low testosterone in men *(p. 25)*
- Foot problems *(p. 26)*
- Obstructive sleep apnea *(p. 28)*
- Conditions associated with type 1 diabetes *(p. 28)*

This section gives an overview of risks, goals, and management options for these conditions that often accompany or result from diabetes.

Cardiovascular disease

Diabetes is considered a cardiovascular disease equivalent, and patients with diabetes have a 2 to 8 times higher prevalence of, incidence of, and mortality from all forms of cardiovascular disease than those without diabetes.[GRU] All patients with diabetes should be assessed annually for cardiovascular risk. Treat all risk factors aggressively, and perform further screening and diagnostic testing as suggested in the algorithm below.

ALGORITHM: RISK ASSESSMENT & SCREENING FOR CARDIOVASCULAR DISEASE



CAD = coronary artery disease; PVD = peripheral vascular disease; ECG = echocardiogram

Multifactorial risk reduction for cardiovascular disease

In patients with diabetes, risk factors for cardiovascular disease and cardiovascular events are similar to those in patients without diabetes. However, the magnitude of risk may be greater. Research suggests that long-term control of blood glucose, blood pressure, and lipids can substantially reduce these risks in all patients, but that patients with diabetes may benefit to an even greater extent.[ADA1,GAE]

We recommend helping patients lower their cardiovascular risk by promoting lifestyle modifications as needed (smoking cessation, weight loss, etc.) and following the guidelines in this CPM for good management of glucose, lipids, and blood pressure. **Also consider using proven medications in appropriate patients; see the discussion below.**

ACE inhibitors

Several studies have shown that ACE inhibitors can reduce cardiovascular complications even more than can be explained by blood pressure reduction alone. For example, the HOPE trial showed a reduction in cardiovascular events in diabetes patients over 55 years of age with normal blood pressure. If not contraindicated, consider an ACE inhibitor in all patients over 55 years of age, with or without hypertension, with any additional risk factor such as history of cardiovascular disease, dyslipidemia, increased urinary albumin, or smoking.[DAG]

Beta blockers

Patients with diabetes and significant coronary artery disease may benefit from beta blockers, especially those who have had a coronary event within the previous 2 years.

Aspirin therapy[UTA]

For secondary prevention in people with atherosclerotic vascular disease, low-dose aspirin provides a substantial 20% relative risk reduction (RRR) and 1.5% per year absolute risk reduction (ARR) in recurrent cardiovascular disease (CVD) events. However, for primary prevention the relative and absolute benefits of aspirin are much lower — just 12% RRR and 0.06% per year ARR in CVD events. For primary prevention in people with diabetes, recent randomized trials and meta-analyses of available trials have found a similar 10% RRR in CVD events. Given the uncertain efficacy of aspirin for primary prevention of CVD in adults with diabetes and its recognized risk for upper gastrointestinal bleeds and hemorrhagic stroke, a **2010 expert consensus document suggested that for primary prevention, aspirin therapy should be guided by a combined assessment of either age, sex, and other CVD risk factors or by an estimate of absolute 10-year CVD risk.** Risk can be calculated via the resources noted at right.

For patients with no history of CVD who are not at increased risk for bleeding (no history of prior gastrointestinal bleeding, no prior peptic ulcer disease, no concurrent warfarin or NSAID therapy), **we recommend aspirin at a dose of 75 to 162 mg/day following the guidelines below.**

Aspirin is ***recommended*** for:	Aspirin may be ***considered*** for:	Aspirin is ***not recommended*** for:
• Adults with >10% 10-year CVD risk* ***or for*** • Most men >50 years and women >60 years with any of these **risk factors:** ❑ Smoking ❑ High cholesterol ❑ High blood pressure ❑ Family history of premature CVD ❑ Albuminuria	• Adults with 5–10% 10-year CVD risk* ***or for*** • Men >50 years or women >60 years with none of the risk factors noted in the first column ***or for*** • Men ≤50 years or women ≤60 years with one or more risk factors noted in the first column	• Adults with < 5% 10-year CVD risk* ***or for*** • Men < 50 years and women < 60 years with none of the risk factors noted in the first column

BEYOND CVD

In addition to heart disease, many complex factors contribute to reduced cardiopulmonary function in patients with diabetes, including:

- Obstructive sleep apnea
- Diastolic dysfunction
- Reduced pulmonary diffusing capacity
- Functional restrictive lung disease

These conditions are commonly underdiagnosed in patients with diabetes. However, they can aggravate hypertension, cause fatigue, and reduce exercise capacity. The cornerstones of therapy are:

- Tight blood pressure control
- Blood glucose control
- Weight loss

Calculate 10-year CVD risk

The American Heart Association and American College of Cardiology[ACC] recommend the new Pooled Cohort Risk Equation to evaluate 10-year and lifetime risk of ASCVD. It is available at:

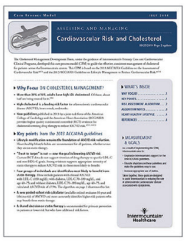
tools.cardiosource.org/ASCVD-Risk-Estimator

TOOL: CHOLESTEROL ALGORITHM

INTERMOUNTAIN HEALTHCARE

CARDIOVASCULAR RISK AND CHOLESTEROL CPM

The 2014 *Cardiovascular Risk and Cholesterol CPM* provides further guidance on treating dyslipidemia.



Click the image to open the document, or see page 31 for ordering information.

DIABETES AND AGE 20–39 OR OVER 75: INTERMOUNTAIN RECOMMENDATIONS

For patients with diabetes who are outside the 40–75 age range, the AHA/ACC did not have enough data to make clear recommendations. Intermountain experts in cardiology and primary care recommend shared decision making with patients in these categories, considering the patient's cumulative risk factors and patient preference in making the final decision:

- For nonpregnant patients age 20–39
  - If lifetime ASCVD risk is 30% to 40%, consider a low-intensity statin.
  - If lifetime ASCVD risk is >40%, consider a moderate-intensity statin.
- For patients older than 75, consider a moderate-intensity statin.

STATIN INTOLERANCE

Statin intolerance may occur in 5% to 15% of patients:

- Symptoms include myalgias, proximal and symmetrical, often in the thighs.
- Symptoms typically occur 1 month after statin start or change, and are often dose-dependent. Confirmation of intolerance may require a 2 to 6 week trial off statin.
- **Treatment options** include lowering statin dose by 50%; reducing frequency to every other day or less often; and trials of other statins, e.g., pravastatin or rosuvastatin.

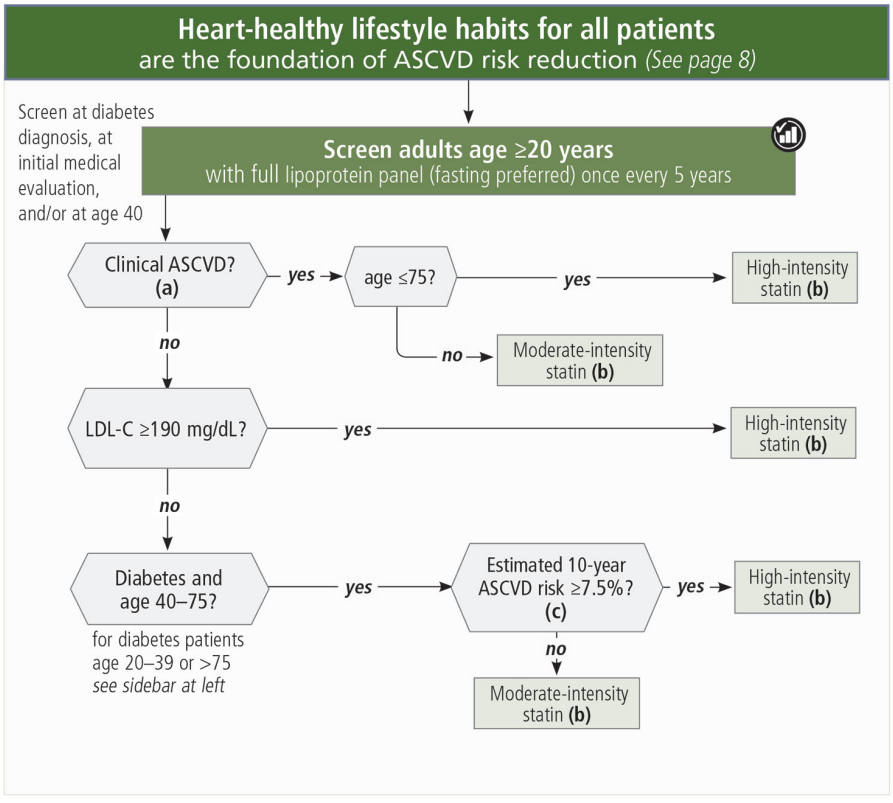
High cholesterol

Diabetes mellitus is associated with multiple lipid abnormalities, most typically hypertriglyceridemia, low HDL cholesterol, and increased numbers of small, dense LDL cholesterol particles. Insulin resistance, insulin deficiency, hyperglycemia, and obesity are common contributing factors for dyslipidemia in people with diabetes. Multiple studies have demonstrated that treating dyslipidemia can improve cardiovascular disease outcomes in people with diabetes.[COLH,HEA,SEV]

Recommendations on cholesterol management have recently changed. In 2013 the American Heart Association and American College of Cardiology revised their cholesterol treatment guidelines to recommend that **treatment initiation and initial statin dose be driven primarily by risk status, not by LDL cholesterol level.** The 2015 ADA Standards recommend following this guideline for diabetes treatment.[ADAA] The algorithm below is taken directly from Intermountain's Cardiovascular Risk and Cholesterol CPM.

Some controversy exists around the new recommendations. The National Lipid Association (NLA) continues to recommend initiation of statin therapy based on lipid targets. For a detailed comparison of AHA and NLA recommendations, visit **www.lipid.org/recommendations**.

▸ ALGORITHM: ASSESSING AND MANAGING CHOLESTEROL LEVELS AND ASCVD RISK



Indicates an Intermountain measure

TOOL: CHOLESTEROL ALGORITHM (CONTINUED)

INTERMOUNTAIN HEALTHCARE

ALGORITHM NOTES

(a) Clinical ASCVD

Clinical ASCVD is defined as one or more of the following:

- Acute coronary syndromes
- History of MI
- Stable or unstable angina
- Coronary or other arterial revascularization
- Atherosclerotic stroke
- Atherosclerotic TIA
- Atherosclerotic peripheral artery disease
- Abdominal aortic aneurysm

Treatment fundamentals for patients with clinical ASCVD:

A — Aspirin/antiplatelet therapy

B — Blood pressure control

C — Cholesterol control and Cigarette smoking cessation

D — Diet and weight management and Diabetes and blood glucose control

E — Exercise

(b) Statin Therapy[ACC] *(Do not prescribe if patient is pregnant or lactating)*

High-intensity statin therapy (For patients with clinical ASCVD and age <75, LDL-C >190, diabetes and age 40 to 75 with other risk factors, or >7.5% 10-year ASCVD risk)	Moderate-intensity statin therapy (For patients with clinical ASCVD and age >75, diabetes and age 40 to 75 without other risk factors, or 5%–7.5% 10-year ASCVD risk)	Low-intensity statin therapy (For patients with < 5% 10-year ASCVD risk and other risk factors)
Daily dose lowers LDL-C on average by approximately 50% or more*	Daily dose lowers LDL-C on average by approximately 30% to 50%*	Daily dose lowers LDL-C on average by up to 30%*
• **Atorvastatin (40†)–80 mg** • Rosuvastatin 20 (40) mg	• **Atorvastatin 10** *(20)* **mg** • **Simvastatin 20 mg–40 mg**‡ • **Pravastatin 40** *(80)* **mg** • **Lovastatin 40 mg** • Fluvastatin XL 80 mg • Fluvastatin 40 mg bid • Pitavastatin 2 mg–4 mg • Rosuvastatin (5) 10 mg	• **Pravastatin 10 mg–20 mg** • **Lovastatin 20 mg** • Simvastatin 10 mg • Fluvastatin 20 mg–40 mg • Pitavastatin 1 mg

Bold text indicates preferred drug.

(c) New Pooled-Cohort Risk Calculator

The American Heart Association and American College of Cardiology[ACC] recommend the new Pooled Cohort Risk Equation to evaluate 10-year and lifetime risk of ASCVD and more accurately identify higher-risk patients who may benefit from statin therapy.

Available at: tools.cardiosource.org/ASCVD-Risk-Estimator

OTHER ISSUES

Triglycerides: If triglycerides are over 500 mg/dL, treat to reduce risk of pancreatitis. There is no evidence of cardiovascular risk reduction from treatment.

Blood glucose: The impact of statins on blood glucose is small and should not influence the decision to prescribe.

Other classes of lipid-lowering medications:

- **Fibrates.** Gemfibrozil should not be initiated in patients on statin therapy because of an increased risk for muscle symptoms and rhabdomyolysis. Fenofibrates may be considered concurrent with low- or moderate-intensity statin only if benefits are judged to outweigh risks.
- **Ezetimibe.** May show some benefit. Make shared decision with patient.
- **Omega-3 fatty acids** (fish oil supplements). Not recommended.
- **Bile acid sequestrants.** Consider using colesevelam for statin-intolerant patients.

TOOL: HYPERTENSION ALGORITHM

INTERMOUNTAIN HEALTHCARE

HIGH BLOOD PRESSURE CPM

The 2014 *High Blood Pressure CPM* provides further guidance on treating high blood pressure. It recommends a standardized medication cascade for most patients.

Click the image to open the document, or see page 31 for ordering information.

High blood pressure

High blood pressure affects most patients with diabetes. Aggressive treatment of high blood pressure has been convincingly shown to reduce cardiovascular risk in these patients **to an extent equal to or greater than the effect of glucose control.**[UKPD,JAM] The 2015 ADA Standards of Medical Care in Diabetes changed the recommended goal for diastolic blood pressure in most patients with diabetes from 80 mm Hg to 90 mm Hg, reflecting the clearest evidence from randomized clinical trials.

The algorithm below is a shortened version of the algorithm in the High Blood Pressure CPM and is consistent with the recommendations in the ADA Standards. Using the same treatment protocol across the system has been shown to facilitate consistent team-based care.

ALGORITHM: MANAGEMENT OF HYPERTENSION

General approach for most patients under 80 years old

Check BP at each office visit (a)

Systolic ≥140 *or* Diastolic ≥90? — *No* → back to Check BP

Yes

RECHECK to confirm high BP (b)
- Follow-up office visit
- Home BP readings

High BP confirmed? — *No* → back to Check BP

Yes

TREAT high BP to management target: <140/<90 (c)
- Consider individualized target as needed based on patient's clinical circumstances.
- Consider secondary causes of high BP **(g)**

INITIATE therapeutic lifestyle changes (TLC) (d)
- Start meds concurrently with TLC.
- Maintain TLC throughout course of treatment.

ACEI *(or ARB)*: **lisinopril** *(or losartan)* **(e)**
Lisinopril titration: 10 mg daily ➔ 20 mg daily

For patients who require additional medications to manage high blood pressure, refer to the High Blood Pressure CPM.

Treatment process:

- **Evaluate BP every 2 weeks** while titrating or switching medications. **(d)**
- **Order BMP 2–3 weeks** after initiation or dose changes of lisinopril or HCTZ.
- **Consider divided dosing** (AM/PM) when patient is on more than one medication.
- **When BP is at target**, maintain current therapy and evaluate BP every 6 months.

Special populations:

See note ***(f)*** for options in treating high blood pressure in the following:
- Prediabetes
- Coronary artery disease
- Heart failure
- Chronic kidney disease
- Black patients (African descent)
- Older patients (≥80 years)
- Pregnancy

Indicates an Intermountain measure

TOOL: HYPERTENSION ALGORITHM (CONTINUED)

INTERMOUNTAIN HEALTHCARE

ALGORITHM NOTES

(a) Check BP at Each Office Visit

Best practices for consistent BP readings:

- Patient should be seated with feet on the floor, back supported, and arm supported at heart level
- Rest for 5 minutes, empty bladder if necessary, and wait at least 30 minutes since last heavy meal, heavy exercise, or intake of caffeine, alcohol, or nicotine
- Use appropriate size cuff (not too small)
- Avoid talking with the patient or asking questions while taking BP

See the High Blood Pressure CPM for more detail.

(b) Confirming High BP

Methods

Follow-up office visit	High BP can be confirmed through 2 office visits total, with 2 BP checks in each visit.
Home BP monitoring	• Train patient on checking BP at home and make sure patient has appropriate home BP monitor. • Patient takes at least 6–10 home BP readings over 2 weeks or more. Make sure patient brings monitor to office visit to verify consistency of readings.

(c) Blood Pressure Targets

Most patients	The 2015 ADA Standards recommend management to **<140/<90** for most patients with diabetes, but allow for individualized targets for patients with chronic kidney disease or other risk factors.
Younger or at risk for stroke	Consider a target of **<130/<80** for some patients, including younger patients, if the burden of more aggressive therapy is not excessive.
Elderly	In elderly patients, avoid reducing diastolic BP below an average of 60. Lower diastolic BP may cause symptoms of hypotension and increase risk of myocardial infarction and stroke.

(d) Therapeutic Lifestyle Changes (TLC)

TLC elements include weight reduction, the DASH eating plan, sodium reduction, regular physical activity, limiting alcohol, and smoking cessation. *For more information on the effects of TLC on blood pressure, see page 10 of the High Blood Pressure CPM.*

(g) Secondary Causes of Uncontrolled BP

If a patient is on multiple medications and still not meeting BP goals, explore these possible secondary causes: Primary aldosteronism, sleep apnea, chronic kidney disease, coarctation of aorta, Cushing's syndrome or steroid therapy, drug-induced hypertension, pheochromocytoma, renovascular disease, thyroid/parathyroid disease, alcohol use.

(e) Medication Notes

- **Consider nonadherence.** Ask how many doses were missed since the last visit.
- **Consider interfering agents,** such as NSAIDs.

Medications in the algorithm

lisinopril/ losartan	• Either drug class is acceptable as a first-line choice. • If dry cough with lisinopril, switch to losartan. • Avoid all ACEI or ARB medications in pregnancy. • Do NOT combine an ACEI or an ARB. • Avoid the direct renin inhibitor aliskiren.

Other preferred blood pressure medications

amlodipine	• Monitor for peripheral edema. • If patient is on simvastatin >20 mg daily, consider alternative statin due to drug interaction. • Consider starting with 2.5 mg daily in elderly patients. Maximum therapeutic effect can take up to 3 weeks.
HCTZ	• Prescribe as single combination with an ACEI/ARB.
carvedilol	• Monitor for bradycardia (keep HR >55 BPM).

(f) Special Populations

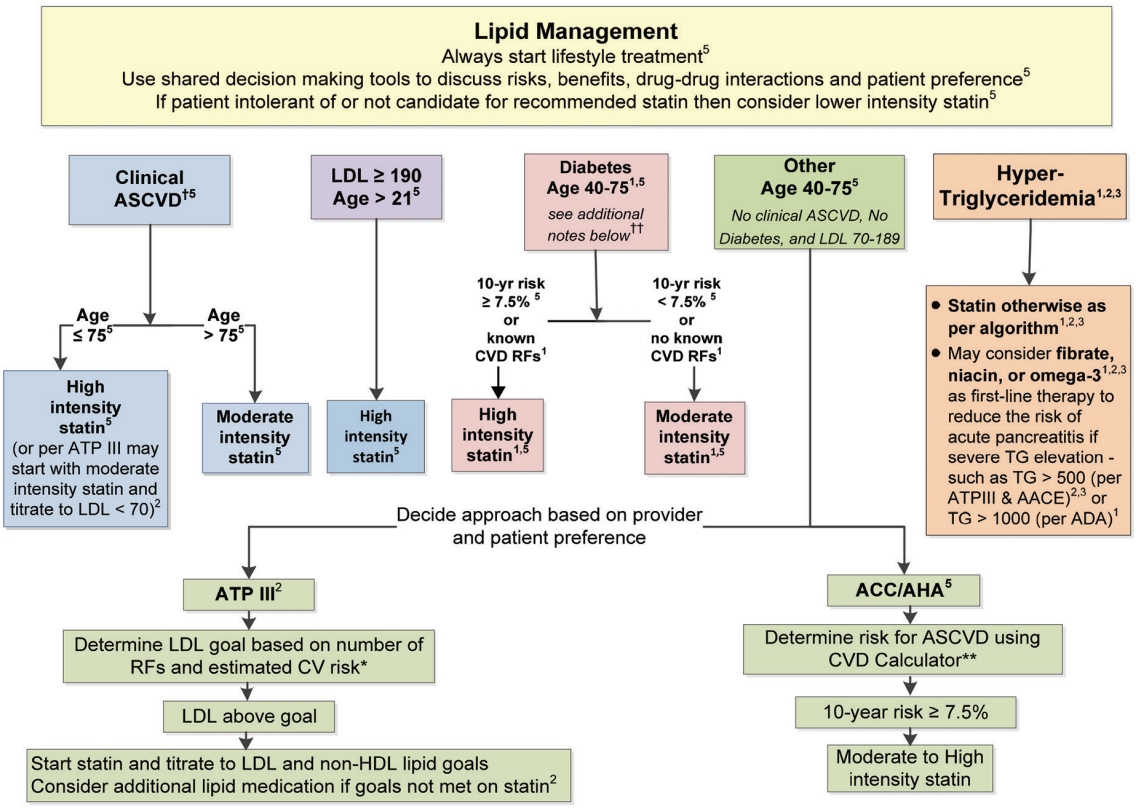
Prediabetes	Consider avoiding thiazides and beta blockers, as they can increase blood glucose. However, if a beta blocker is used, carvedilol is preferred as it may help with insulin resistance.

The recommendations below are for patients with both diabetes and the condition listed

Coronary artery disease	Consider adding carvedilol (preferred) or metoprolol succinate to ACEI/ARB. As needed, add amlodipine and then a diuretic.
Heart failure	If ejection fraction ≤40%, ACEI/ARB, *plus* carvedilol (preferred) or metoprolol succinate, *plus* spironolactone (if not contraindicated). If needed for BP, add amlodipine
Kidney disease	Treat to <140/<90; consider <130/80 if ACR >300. Monitor K+ and creatinine with ACEI/ARBs.
Black (African ancestry)	Consider starting with CCB or thiazide, then add thiazide or CCB as 2nd line.
Age >80 years	Consider target of <150/<90 and individualized approach; consider starting with CCB or thiazide.
Pregnancy	Avoid ACEI/ARB medications. Consider labetalol, CCB (nifedipine preferred), hydralazine, or methyldopa.

TOOL: ADULT LIPID GUIDELINES

SUTTER HEALTH



***ATP III (2002)**
LDL Goal Determination[2]

1. If 0-1 Major Risk Factors (RFs): LDL goal <160[2]
2. If 2+ Major Risk Factors (RFs) then determine LDL goal based on Framingham Risk Assessment tool[2] (http://cvdrisk.nhlbi.nih.gov/calculator.asp) or Reynolds Risk score (http://www.reynoldsriskscore.org)
   a. 10-year risk >20%: LDL goal <100
   b. 10-year risk 10-20%: LDL goal <130
   c. 10-year risk <10%: LDL goal <130
3. Major Risk Factors:
   a. Cigarette Smoking,[2,3]
   b. Hypertension (BP ≥ 140/90 or on anti-hypertension medication), [2,3]
   c. FH of premature CHD2,3 (CHD in male first degree relative < 55 years, CHD in female first degree relative < 65 years),
   d. Advancing Age[2,3] (men ≥ 45 years, women ≥ 55 years),
   e. Low HDL cholesterol, [2,3] (Note High HDL-cholesterol (≥ 60) is a negative risk factor and can be subtracted)
4. Additional risk factors to consider: obesity, truncal obesity, family history of hyperlipidemia, fasting/postprandial hypertriglyceridemia, PCOS, dyslipidemic triad (low HDL, high TG, small dense LDL)[3]

**** ACC/AHA Guideline (2013)**
CVD Risk Calculation[5]

1. Calculate patient's 10-year risk for ASCVD[5] http://my.americanheart.org/professional/StatementsGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp[5]
2. Additional risk factors (RFs) may consider in selected patients for informed decision making[5]:
   a. Evidence of genetic hyperlipidemias
   b. Family history of premature ASCVD with onset <55 years of age in a first degree male relative or <65 years of age in a first degree female relative
   c. High-sensitivity C-reactive protein >2 mg/L
   d. CAC score ≥300 Agatston units or ≥75 percentile for age, sex, and ethnicity,
   e. Ankle-brachial index <0.9
   f. Elevated lifetime risk of ASCVD (such high risk patients < 40 who have high lifetime ASCVD risk)

[†] **Clinical ASCVD:** acute coronary syndromes, history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin.

[††] **Additional Diabetes Notes**

1. The ACC/AHA guideline emphasizes treatment by above algorithm for patients with diabetes if LDL 70-189.[5]
2. The ADA guideline also recommends moderate or high intensity statin for diabetes patients age < 40 or > 75 with known additional CVD RFs or moderate dose statin if age > 75 even if no known additional CVD RFs.[1] (Additional RFs include: LDL ≥100, HTN, smoking, overweight/obesity.)[1]

I. Determining statin type and dose:

1. Determine statin intensity according to algorithm above. See table below for specific type and dose.
2. Note: used reduced doses of statin if below[5]:
   a. Multiple or serious comorbidities, including impaired renal or hepatic function. [5]
   b. History of previous statin intolerance or muscle disorders. [5]
   c. Unexplained ALT elevations >3 times ULN. [5]
   d. Patient characteristics or concomitant use of drugs affecting statin metabolism.[5]
   e. >75 years of age. [5]
   f. History of hemorrhagic stroke. [5]
   g. Asian ancestry. [5]

Table 1: Statin Intensity

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C on average, by approximately ≥50%	**Daily dose lowers LDL-C on average, by approximately** 30-50%	**Daily dose lowers LDL-C on average, by approximately** <30%
Atorvastatin *(40)*[ii] 80mg[i] PO daily* Rosuvastatin 20mg[i] (40)[ii] PO daily	Atorvastatin 10 mg[i] *(20)*[ii] PO daily* Rosuvastatin *(5*[ii]*)*10 mg[i] PO daily Simvastatin 20-40 mg[i] PO daily* Pravastatin 40[i] *(80)*[ii]mg PO daily* Lovastatin 40 mg[i] PO daily* Fluvastatin 40mg[i] PO BID* *Fluvastatin XL 80 mg*[ii] *Pitavastatin 2-4 mg*[ii]	Pravastatin 10-20 mg[i] PO daily* Lovastatin [i]20 mg[i] PO daily* *Fluvastatin 20-40 mg*[ii] *PO daily** *Pitavastatin 1 mg*[ii] *PO daily* *Simvastatin 10mg*[ii] *PO daily*

(*) indicates generic availability

[i] Based on ASCVD risk reduction demonstrated from randomized controlled trials
[ii] FDA-approved for dyslipidemia, but its effect on ASCVD risk is not studied in randomized controlled trials

II. Laboratory screening and monitoring

1. Who to screen
   i. ATP III and AACE: recommend screen all adults every 5 years if low risk, 1-2 years if high risk[2, 3]
   ii. AHA/ACC: Calculate patients risk score every 4-6 years[5]
   iii. USPSTF recommends screen all adults ≥ 20 at increased risk for CVD and all men ≥ 35 years old[6]
2. Evaluate at baseline, prior to initiating therapy
   i. Fasting lipid panel (if initially non-fasting, repeat as fasting if TG > 500)[1,2,3,5]
   ii. Serum alanine transaminase (ALT)[5,7]
   iii. A1C (diabetes screen) if diabetes status unknown[5]
   iv. Serum creatine kinase (CK) if increased risk for developing adverse muscle effects[5]
3. Evaluate in 4-12 weeks, after initiating therapy and then every 3-12 months as indicated[5]
   i. Lipid panel
      1. Check LDL to monitor for adherence (and possible titration).[5] Note: individual response may be variable based on inherent biologic differences.[5]
      2. Expect therapeutic response below.
         a. ≥ 50% LDL reduction for high intensity statin.[5]
         b. 30-50% LDL reduction for low intensity statin.[5]
      3. If therapeutic response not attained
         a. Reinforce adherence.[5]
         b. Consider titrate statin dose or add non-statin medication to reach therapeutic goal (esp if very high risk such as clinical ASCVD and < 75 yo, baseline LDL > 190, or diabetes). [5]

c. Exclude secondary causes of hyperlipidemia (see section III below) [5]

4. If LDL < 40 twice in a row may consider lower statin dose[5]

ii. Diabetes

1. Screen for diabetes in patients treated with statins.[1,5]
2. Statin use is associated with risk of new onset diabetes. The increased risk appears to be confined to those with risk factors for diabetes.[1,5]
3. If patient develops diabetes while on statin, encourage heart healthy lifestyle and continue statin to reduce ASCVD risk. [1,5]

iii. Muscle symptoms

1. Pain, tenderness, stiffness, cramping, weakness, generalized fatigue[5]
2. Check CK[5] (CK > 10 times the upper limit of normal is indication to stop medication[8])
3. Management - Compare to baseline pre-statin symptoms for comparison[5]
   a. Severe muscle pain or fatigue[5]
      i. Discontinue statin therapy[5]
      ii. Measure creatinine and urinalysis to evaluate for rhabdomyolysis[5]
   b. Mild to moderate symptoms[5]
      i. Evaluate possible etiology of symptoms[5]
      ii. May consider trial discontinue statin therapy[5]
         1. If no alternate etiology and muscle symptoms resolve, re-challenge with same or lower statin dose of therap[5] or try a different class of statin[5]
         2. If alternate etiology of muscle pain discovered, OK to restart statin[5]

iv. Hepatotoxicity

1. Fatigue, weakness, loss of appetite, abdominal pain, dark-colored urine, yellowing of the skin or sclera[5]
2. If present measure ALT[5]
3. LFTs > 3 time the upper limit of normal is indication to change or stop medication[7]

v. Memory Impairment[5]

1. Look for other non-statin cause or consider possibility of adverse effect associated with statin therapy[5]

vi. Pregnancy - Statin use is contraindicated during pregnancy[5]

III. Evaluation for possible secondary dyslipidemia

1. Consider evaluate for secondary causes if LDL > 190 or TG > 500[5]
   i. Familial hyperlipidemia[5]
   ii. Medications[5] (such as progestins, anabolic steroids, and corticosteroids)
   iii. Diseases/conditions: Diabetes, [5] Obesity, [5] Hypothyroidism,[5] Obstructive liver disease,[5] Chronic renal failure,[5] nephrotic syndrome,[5] pregnancy[5]
   iv. Diet[5]

IV. Lifestyle modifications[9]

1. Heart healthy diet (adapt to appropriate calorie requirements, personal and cultural food preferences and nutritional therapy for other conditions)
   i. Consisting of vegetables, fruits, and whole grains, low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils and nuts
   ii. Limit intake of sweets, sugar-sweetened beverages and red meats
   iii. Limit calories from saturated fats to 5-6% of total caloric intake
   iv. Eliminate trans fat in diet.
   v. Examples of heart healthy diets include: DASH diet, USDA Food Pattern, and AHA diet
2. Regular exercise habits
   i. Physical activity that is moderately to highly vigorous in intensity

ii. Three to four sessions per week, lasting approximately 40 minutes each

3. Tobacco cessation
4. Achieve and maintain healthy weight

Table 2: Statin-Drug Interactions

Drug	Drug/Food Interactions (not all inclusive)[4]
Atorvastatin	Cyp3A4 inducers and inhibitors, Grapefruit Juice, St John's Wort **Dose modification:** Clarithromycin, Colchicine, Daptomycin, Diltiazem, Niacin, Phenytoin, Protease Inhibitors, Rifamycin, Rivaroxaban, Sildenafil, Telithromycin, Verapamil **Avoid:** Cyclosporine, Gemfibrozil, Pimozide
Rosuvastatin (Crestor)	**Dose Modification:** Amiodarone, Colchicine, Cyclosporine, Daptomycin, Niacin, Protease Inhibitors **Avoid:** Gemfibrozil, Ledipasvir
Simvastatin	Cyp3A4 inducers and inhibitors, Grapefruit Juice, St John's Wort **Dose modification:** Amiodarone, Amlodipine, Colchicine, Daptomycin, Diltiazem, Dronedarone, Niacin, Phenytoin, Rifamycin, Sildenafil, Verapamil **Avoid:** Clarithromycin, Cyclosporine, Erythromycin, Gemfibrozil, Protease Inhibitors, Telithromycin
Pravastatin	**Dose modification:** Bile Acid Sequestrants, Clarithromycin, Colchicine, Cyclosporine, Daptomycin, Niacin, Phenytoin, Rifamycin **Avoid:** Gemfibrozil, Pimozide
Lovastatin	Cyp3A4 inducers and inhibitors, Grapefruit Juice, St John's Wort **Dose modification:** Amiodarone, Colchicine, Daptomycin, Diltiazem, Dronedarone, Niacin, Phenytoin, Rifamycin, Sildenafil, Tigrelor, Verapamil **Avoid:** Clarithromycin, Cyclosporine, Erythromycin, Gemfibrozil, Pimozide, Protease Inhibitors, Telithromycin
Fluvastatin	Cyp2C9 substrates **Dose modification:** Amiodarone, Cholestyramine Resin, Colchicine, Cyclosporine, Daptomycin, Fluconazole, Niacin, Phenytoin, Rifamycin **Avoid:** Gemfibrozil, Pimozide
Pitavastatin (Livalo)	**Dose modification:** Colchicine, Daptomycin, Erythromycin, Niacin, Rifamycin, Sildenafil, **Avoid:** Cyclosporine, Gemfibrozil

Table 3: Non-Statin Therapy[4]

Drug Class & Lipid Effects	Agent and Dosage (not all inclusive)	Common Adverse Reactions	Comments & Precautions
Fibric Acid Derivatives LDL↓ 5-30% TG ↓30-60% HDL ↑ 10-20%	**Fenofibrate (TriCor)*** • 48-145 mg daily **Fenofibrate (Trilipix)*** • 45-135 mg daily **Gemfibrozil (Lopid)*** • 600 mg BID	• Dyspepsia • Cholelithiasis • Myopathy/ rhabdomyolysis • Headache • ↑ transaminases • ↑ SCr	• Fenofibrate is contraindicated in active liver disease, severe renal dysfunction, pre-existing gallbladder disease, and nursing mothers. • SCr and eGFR should be evaluated before fenofibrate initiation, within 3 months after initiation, and every 6 months thereafter.
Nicotinic Acid LDL↓ 5-25% TG ↓20-50% HDL ↑15-35 %	**Niacin (Niacor)*** • Initial: 100 mg TID • ↑ gradually as tolerated to 3 g daily divided in 2-3 doses **Niacin, extended release (Niaspan)*** • Initial: 500 mg daily • ↑ gradually (not more frequently than weekly) over 4-8 weeks as tolerated to a maximum dose of 2 g daily	• Flushing/pruritus • GI effects • ↑ prothrombin time • Hepatotoxicity • Hypophosphatemia • ↑ blood sugar • Hyperuricemia • Hypotension • Atrial fibrillation • Edema • Dizziness • Headache	• Different formulations of niacin are not interchangeable. • Niacin should not be used if: ○ Transaminase ↑ >2-3x ULN ○ Persistent severe cutaneous symptoms, persistent hyperglycemia, acute gout, or unexplained abdominal pain or GI symptoms occur ○ New- onset atrial fibrillation or weight loss occurs • Baseline hepatic transaminases, fasting blood glucose or A1c, and uric acid should be obtained before niacin initiation, during up titration, and every 6 months thereafter. • Take with food or premedicate with aspirin 325 mg 30 minutes before niacin dosing to alleviate flushing symptoms.

Cholesterol Absorption Inhibitors LDL↓15-20 % (Additional 25-40% w/ statin) TG ↓5-8% HDL ↑ 1-4%	**Ezetimibe (Zetia)** • 10 mg daily	• Fatigue • Diarrhea • Arthralgia • Upper respiratory tract infection • ↑ transaminases with statins	• When coadministered with a statin, monitor transaminase levels as clinically indicated, and discontinue if persistent ALT ↑ >3x ULN occur.
Bile Acid Sequestrants LDL↓15-30% TG ↑0-20% HDL ↑ 3-5%	**Cholestyramine Resin (Questran, Prevalite)*** • Initial: 4 g 1-2 times/day • ↑ gradually (not more frequently than monthly) • Maintenance: 8-16 g daily divided in 2 doses • Maximum: 24 g daily **Colestipol (Colestid)*** • Granules: ○ Initial: 5 g 1-2 times/day ○ ↑ by 5 g/day at 1-2 month intervals ○ Maintenance: 5-30 g daily or in divided doses • Tablets: ○ Initial: 2 g 1-2 times/day ○ ↑ by 2 g 1-2 times/day at 1-2 month intervals ○ Maintenance: 2-16 g daily or in divided doses **Colesevelam (Welchol)** • 3.75g daily or 1.875g BID	• Bleeding • Constipation • GI effects • Hypothyroidism • Hypertriglyceridemia	• Bile acid sequestrants should not be used in patients with: ○ Baseline fasting triglyceride levels ≥300mg/dL ○ Type III hyperlipoproteinemia • Fasting lipid panel should be obtained before bile acid sequestrant initiation, 3 months after initiation, and every 6-12 months thereafter. • Bile acid sequestrants can decrease the absorption of certain other drugs and vitamins.
Omega-3 fatty acids LDL ↑44% TG ↓26-47% HDL ↑9%	**Lovaza*** • 4 g daily or 2 g BID **Vascepa*** • 2 g BID with meals **Fish Oil Supplement*** (EPA and DHA) daily	• GI effects • ↑ transaminases • ↑LDL • Arthralgia • Fatigue	• If EPA and/or DHA are used for severe hypertriglyceridemia (≥500mg/dL), it is reasonable to evaluate patient for GI disturbances, skin changes, and bleeding. • Omega-3 fatty acids should be used as an adjunct to diet/exercise and only if triglyceride levels ≥500 mg/dl.

(*) indicates generic availability

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[4]Lexicomp Online 2012-2013 http://online.lexi.com/crlsql/servlet/crlonline

[5]2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Stone NJ, et al American College of Cardiology/American Heart Association Task Force on Practice Guidelines.J Am Coll Cardiol. 2014 Jul 1;63(25 Pt B):2889-934

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[7]FDA Drug Safety Communication: Important safety label changes to cholesterol-lowering statin drugs 07/03/2012 http://www.fda.gov/Drugs/DrugSafety/ucm293101.htm

[8]2013 UpToDate, Inc Statins: Actions, side effects, and administration, Robert S Rosenson, MD. Approach to the patient with hypertriglyceridemia, Robert S Rosenson, MD

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