Atherosclerotic Cardiovascular Disease (ASCVD) Primary Prevention Guideline

Last guideline approval: April 2018

Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

Major Changes as of April 2018

New	Previous
10-year risk estimates are based on ACC/AHA Pooled Cohort Equation.	5-year risk estimates were based on modified Framingham calculation.
The lipid screening recommendations have been simplified. We now recommend screening with a non-fasting lipid panel for both men and women between ages 40 and 75 at a minimum of every 5 years.	Previously, lipid screening was recommended to begin at age 35 for men and at age 45 for women and to continue through age 79, at a minimum of every 5 years, using a cholesterol screen.
New ASCVD shared decision making tool in Epic.	No shared decision making tool.
Atorvastatin and rosuvastatin are now the preferred statins for primary prevention.	Simvastatin was the preferred statin for primary prevention.
Annual LDL monitoring is no longer required for people on a statin or with diabetes.	Annual LDL monitoring was recommended for all patients on a statin.
Non-fasting lipid panel is now the preferred cholesterol test.	Fasting lipoprotein panel or direct LDL cholesterol were the preferred cholesterol tests.
Updated blood pressure targets: < 140/90 mm Hg for most people < 130/80 mm Hg for patients with ≥10% risk of ASCVD (myocardial infarction or stroke) over 10 years, diabetes, systolic heart failure, or CKD	Previous blood pressure targets: < 140/90 mm Hg for most people < 150/90 mm Hg for patients aged 80 and over
Updated aspirin recommendations: - Aspirin is recommended for patients 50–59 if ≥ 10% risk of ASCVD (myocardial infarction or stroke) over 10 years. - Use shared decision making for patients aged 60–69 if ≥ 10% risk over 10 years. - No recommendation on aspirin for patients under age 50 or over age 70 due to insufficient evidence.	Previous aspirin recommendations: - Aspirin recommended for patients if ≥ 10% risk of ASCVD over 5 years. - Use shared decision if patient has moderate risk (5–10%) over 5 years, LDL cholesterol > 190 mg/dL, or diabetes. - Aspirin not recommended for patients with < 5% risk over 5 years.
Updated statin recommendations 5.0–7.4% 10-year risk of ASCVD (myocardial infarction or stroke): Shared decision making. Consider discussing treatment with a moderate-intensity statin. 7.5–14.9% 10-year risk: Shared decision making. Consider treatment with a moderate- to high-intensity statin. ≥ 7.5% 10-year risk *and* diabetes, age 40–75: Initiate or continue moderate-intensity statin. Consider use of high-intensity statin. - Age 40–75 with diabetes and LDL 70–189 mg/dL, initiate or continue moderate-intensity statins. ≥ 15% 10-year risk: Initiate or continue treatment with a moderate- to high-intensity statin. - LDL ≥ 190 mg/dL: Initiate or continue high-intensity statin.	Previous statin recommendations: - Statins recommended for patients if ≥ 10% 5-year risk of ASCVD or have diabetes and over age 40. - Use shared decision making if patient has moderate ASCVD risk (5–10%) over 5 years, LDL cholesterol > 190 mg/dL. - Statins not recommended for patients with < 5% risk of ASCVD over 5 years.

Definitions

ASCVD, or atherosclerotic cardiovascular disease, is caused by plaque buildup in arterial walls and refers to the following conditions:
- Coronary heart disease (CHD), such as myocardial infarction, angina, and coronary artery stenosis > 50%.
- Cerebrovascular disease, such as transient ischemic attack, ischemic stroke, and carotid artery stenosis > 50%.
- Peripheral artery disease, such as claudication.
- Aortic atherosclerotic disease, such as abdominal aortic aneurysm and descending thoracic aneurysm.

Primary prevention refers to the effort to prevent or delay the onset of ASCVD.

Secondary prevention refers to the effort to treat known, clinically significant ASCVD, and to prevent or delay the onset of disease manifestations.

Goals of Primary Prevention

Modify risk factors or prevent their development with the aim of delaying or preventing new-onset ASCVD. This guideline addresses the primary prevention of ASCVD in general. It does not attempt to address screening or treatment of specific potential manifestations of ASCVD.

Lipid Screening and ASCVD Risk Calculation

Table 1. Lipid screening for patients not already on statins		
Eligible population	**Test**	**Frequency**
Under age 40	Routine screening is not recommended unless patient has a major cardiovascular risk factor (e.g., diabetes, hypertension, family history, smoking).	
Age 40–75	Non-fasting lipid panel	Every 5 years at a minimum [1]
Over age 75	Routine screening is not recommended.	Upon patient request or based on other ASCVD risk factors
[1] Consider re-screening intervals based on ASCVD risk: - Every **5 years** if ASCVD risk < 7.5% over 10 years - Every **2 years** if ASCVD risk 7.5–14.9% over 10 years **Annually** if ASCVD risk ≥ 15% over 10 years and not on statin		

Lipid screening tests

Lipid panel: for most patients

The results of a **lipid panel**—total cholesterol, HDL, LDL, and triglycerides—ordered through Epic include the patient's 10-year risk calculation for cardiovascular disease. It is recommended that the patient be non-fasting for the lipid panel, as this is much easier for the patient and does not require a return visit. Any patient who has a triglyceride level > 400 mg/dL (regardless of LDL level) will need to return for a fasting lipid panel.

hs-CRP: consider for patients at 7.5–14.9% risk

For patients **at 7.5–14.9% ASCVD risk over 10 years,** consider testing with hs-CRP to help confirm elevated risk when deciding whether to recommend statin therapy.

Table 2. Interpreting hs-CRP test results	
Result	**Interpretation**
< 1 mg/L	Risk is lower than the ASCVD risk calculation.
1–3 mg/L	Risk is close to the ASCVD risk calculation.
3.1–9.9 mg/L	Risk is higher than the ASCVD risk calculation.
≥ 10 mg/L	These elevations are associated with a nonspecific inflammatory process. Cardiac risk CRP should be reevaluated after the inflammatory condition has resolved.

Biomarker tests: *not recommended*

Testing for the following biomarkers of inflammation and lipid-related markers is **not** recommended. Although they may be independently associated with cardiovascular disease risk, they have only a minimal prognostic value when added to conventional risk markers:

- Fibrinogen
- Lipoprotein(a)
- Phospholipase A_2
- Apolipoprotein B and A-1 combined

Coronary artery calcium scoring: *not recommended*

Coronary artery calcium scoring generally is **not** recommended because it has not been proven to add significantly to clinical decision making in a way that improves outcomes. See Clinical Review Criteria for CT Angiography and CT Cardiography: Screening & Calcium Scores for more information.

ASCVD risk calculation

Kaiser Foundation Health Plan of Washington is now using the **Pooled Cohort Equation** to estimate a patient's risk of developing an ASCVD event (myocardial infarction or stroke) over the following 10 years. Use of this risk estimate will help determine which patients might benefit from primary prevention interventions. The calculations will be returned with the lipid panel results or by using a SmartLink in Epic.

Note: **ASCVD risk calculators can only *estimate* risk. Interpretation of ASCVD risk calculations should always reflect informed clinical judgment.**

The ASCVD calculator is available:
- On the public website for use by clinicians, contracted providers, and members.
- Through the Epic SmartLink **.ascvdrisk**, which pulls information from a patient's record to calculate the risk.
- In the Health Profile online tool for members.
- In the Clinical Lab's lipid panel results.

Lifestyle Modifications

Tobacco cessation

- Ask patients about tobacco use at every office visit.
- Advise tobacco users to quit.
- Advise patients at every office visit to avoid exposure to environmental tobacco smoke at home, work, and in public places.
- See the Tobacco Use Guideline for additional information.

Healthy diet

All patients should strive to:
- Make smart choices from every food group to meet caloric needs.

- Get the most and best nutrition from the calories consumed.

There is strong evidence that adhering to a Mediterranean-style eating plan reduces the incidence of major cardiovascular events in people at risk for ASCVD. Adhering to a DASH eating plan can be an alternative. Both eating plans provide similar key elements: an emphasis on plant foods (fruits, vegetables, whole-grain breads or other forms of cereals, beans, nuts, and seeds), minimally processed foods, and seasonally fresh foods; inclusion of fish; and minimal intake of red meat. The SmartPhrases **.avsmediterraneandiet**, **.avsdash**, and **.avsnutrition** are available for after-visit summaries.

There is some evidence that consuming an average of two fish servings weekly may reduce CHD mortality.

Moderation of alcohol consumption
- Consider having patients complete the AUDIT-C alcohol use questionnaire.
- See the Unhealthy Drinking in Adults Guideline for additional information.

Physical activity
The American Heart Association recommends the following physical activity goals:
- At least 30 minutes of moderate-intensity aerobic activity 5 or more days per week.
- Moderate- to high-intensity muscle-strengthening activity 2 or more days per week.

An example of moderate-intensity aerobic activity is walking at a pace that makes a patient feel slightly out of breath but still able to maintain a conversation.

For patients who have been inactive for a while, recommend that they start slowly and work up to at least 30 minutes per day at a pace that is comfortable. If they are unable to be active for 30 minutes at one time, suggest accumulating activity over the course of the day in 10- to 15-minute sessions.

Weight management
- Encourage getting to or maintaining a healthy weight through an appropriate balance of caloric intake and physical activity.
- See the Adult Weight Management Guideline for additional information.

Blood pressure management
- The target the blood pressure for the general population is **< 140/90 mm Hg.**
- For patients who are at ≥ 10% 10-year risk of ASCVD, or who have diabetes, systolic heart failure, or chronic kidney disease (CKD), the blood pressure target is **< 130/80 mm Hg.**
- If a patient's blood pressure is higher than goal, see the Hypertension Guideline for management recommendations.

Dietary Supplements

Calcium and vitamin D

- If a patient is taking a calcium supplement for the prevention of osteoporosis, recommend that it be taken in combination with vitamin D and that its dose not exceed 1,200 mg per day.
- There is some evidence that calcium supplementation may be associated with increased risk of cardiovascular events, particularly myocardial infarction. The co-administration of vitamin D with the calcium supplement may weaken the observed adverse effects of calcium supplementation.
- The literature indicates that intake of calcium from whole foods is not associated with an increased ASCVD risk.

Dietary supplements that are *not* recommended

- Multivitamins: There is evidence that daily intake of a multivitamin does not reduce major cardiovascular events, MI, stroke, or ASCVD mortality.
- Folic acid, vitamin B12, and vitamin E: There is evidence of no benefit and/or possible harm with the use of these supplements/vitamins in the primary prevention of ASCVD.
- Beta-carotene: There is good evidence that supplemental doses of beta-carotene do not improve cardiovascular outcome and that they may be associated with increased cardiovascular deaths and overall mortality.
- Vitamin C: There is evidence that vitamin C supplementation has no benefit in the primary prevention of ASCVD.
- Fish oil: There is some evidence that fish oil supplementation has no significant benefit in reducing cardiovascular events or mortality among individuals with no history of ASCVD.

Statin Therapy

Table 3. Overview of statin therapy recommendations for primary prevention of ASCVD	
Population	**Statin therapy**
ASCVD risk 5–7.4% over 10 years	Use shared decision making. Consider treatment with a moderate-intensity statin.
ASCVD risk 7.5–14.9% over 10 years	Use shared decision making. Consider treatment with a moderate- to high-intensity statin.
ASCVD risk ≥ 15% over 10 years	Initiate or continue moderate- to high-intensity statin.
People **with diabetes,** aged 40–75, with ASCVD risk ≥ 7.5% over 10 years	Initiate or continue moderate-intensity statin. Consider use of a high-intensity statin.
People **with diabetes**, aged 40–75, with LDL cholesterol 70–189 mg/dL	Initiate or continue moderate-intensity statin.
LDL cholesterol ≥ 190 mg/dL	Initiate or continue high-intensity statin.

Recommended statin dosing

Most patients who are taking statins for primary prevention of ASCVD should be initiated on moderate-intensity statins, defined as those lowering LDL cholesterol by an average of 30–49%. See Table 4.

Only patients with questionable ability to tolerate moderate-intensity statins—the frail/elderly, those taking interacting drugs, and those with hepatic/renal impairment or untreated hypothyroidism—should be initiated on reduced doses, as given in Table 5.

Table 4. STANDARD (moderate-intensity) statin dosing for primary prevention of ASCVD Standard dosing applies to patients for whom there are no concerns about their ability to tolerate moderate-intensity statin therapy.			
Line	**Medication**	**Initial dose**	**Maximum dose**
1st	Atorvastatin	20 mg daily	80 mg daily
	Rosuvastatin	5–10 mg daily	40 mg daily
2nd	Simvastatin	40 mg daily at bedtime	40 mg [1] daily at bedtime

[1] For patients already on simvastatin 80 mg daily, it is acceptable to maintain the dose if they have been taking the drug for 12 months or longer, are not taking interacting medications, are at LDL goal, and are without myopathy.

Table 5. REDUCED (low-intensity) statin dosing for primary prevention of ASCVD Reduced dosing applies only to patients with questionable ability to tolerate moderate-intensity statin therapy, including those who are elderly/frail, have hepatic/renal impairment or untreated hypothyroidism, or are taking interacting drugs.			
Line	**Medication**	**Initial dose**	**Maximum dose**
1st	Atorvastatin	10 mg daily	80 mg daily
	Rosuvastatin	2.5–5 mg daily	40 mg daily
2nd	Simvastatin	10–20 mg daily at bedtime	40 mg daily at bedtime
3rd	Pravastatin [1] (Alternative in cases of drug interactions or side effects)	20–40 mg daily at bedtime	80 mg daily at bedtime

[1] Pravastatin has about half the potency of simvastatin; however, it is less likely to interact with other medications, particularly medications that are strong CYP3A4 inhibitors.

Cholesterol and lipid goals

LDL levels

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LDL goal < 100 mg/dL

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Generally, LDL is measured only as follow-up for patients on statin therapy to assess response and adjust dose if needed. The LDL goals listed above may not fit all patients. An alternative goal is a 30–40% reduction from the previous LDL measure.

HDL levels

All patients on statins: no specific HDL target for therapy
A low HDL level is an independent risk factor for ASCVD, but there is no evidence to date that increasing HDL levels reduces cardiovascular risk. Encourage patients to increase HDL levels through lifestyle measures, e.g., increased physical activity, weight loss if overweight, and tobacco cessation. Medications generally are not recommended.

Triglycerides and pancreatitis

All patients on statins: triglyceride target < 500 mg/dL
Evidence has shown, at most, a weak association between elevated triglycerides (TGs) and health outcomes. Neither the threshold nor target of therapy is known. Although there is no direct evidence, there is consensus that TG levels of 500 mg/dL or greater warrant treatment to prevent pancreatitis. (See Lowering Triglycerides to Prevent Pancreatitis section on page 13.) Treatment/investigation at > 1,000 mg/dL would also be reasonable; use shared decision making.

Follow-up for patients on statins

Statin therapy should be adjusted if patients are not meeting the LDL goals above. For patients on at least moderate-intensity therapy who are above the LDL goal, consider increasing to high-intensity statin therapy (defined as lowering LDL cholesterol by an average of ≥ 50%). On the other hand, if a patient has achieved a very low LDL level, **do not lower** the intensity of statin therapy. Expert opinion is that no LDL level is too low.

Use clinical judgment before escalating doses or changing or adding medications.

If the statin is not working (patient not achieving LDL goal)

1. First, assess adherence to therapy. Patients often are not taking their medication regularly. Approximately half of patients who start on statin drugs stop them on their own within 1 year.
2. If they are taking their medication regularly, consider increasing dose (if not already at maximum).
3. If the statin is still not working, use shared decision making to decide whether to consider switching to another statin. Consider an e-consult with Cardiology, where available.
4. Consider adding ezetimibe 10 mg for patients who are not able to achieve an LDL < 100 mg/dL on maximally tolerated doses of formulary statins **and** meet at least one of the following criteria:
   o 10-year ASCVD risk ≥ 7.5% based on Pooled Cohort Equation, or
   o Patient aged 40 or older with diabetes, or
   o Any patient with LDL ≥ 190 mg/dL

If the patient *appears* intolerant to statins

1. First, consider decreasing the dose.
2. If the patient is still intolerant, use shared decision making to decide whether to consider switching to another statin. Consider an e-consult with Cardiology, where available.
3. To determine if myalgia symptoms can be attributed to use of the statin, consider using the American College of Cardiology's statin intolerance tool.
4. Consider supplementation with co-enzyme Q10 to relieve statin-induced muscle symptoms. Evidence is conflicting, but some studies suggest a benefit.

If the patient is *still* intolerant or has contraindications to statins

- For patients who are not able to achieve an LDL < 100 mg/dL **and** meet at least one of the following criteria, **stop the statin and consider prescribing ezetimibe:**
  - 10-year ASCVD risk ≥ 7.5% based on Pooled Cohort Equation, or
  - Patient aged 40 or older with diabetes, or
  - Any patient with LDL ≥ 190 mg/dL
- For patients who are not able to achieve an LDL < 100 mg/dL but **do not** meet any of the above criteria*,* **stop the statin** and do not prescribe further medications.

What is statin intolerance?

The National Lipid Association (Guyton 2014) defines statin treatment intolerance as
…a clinical syndrome characterized by the inability to tolerate at least 2 statins: one statin at the lowest starting daily dose AND another statin at any daily dose, due to either objectionable symptoms (real or perceived) or abnormal lab determinations, which are temporally related to statin treatment and reversible upon statin discontinuation, but reproducible by re-challenge with other known determinants being excluded (such as hypothyroidism, interacting drugs, concurrent illnesses, significant changes in physical activity or exercise, and underlying muscle disease). Specifically, the lowest starting statin daily dose, is defined as rosuvastatin 5 mg, atorvastatin 10 mg, simvastatin 10 mg, lovastatin 20 mg, pravastatin 40 mg, fluvastatin 40 mg, and pitavastatin 2 mg.

Shared decision making for statin therapy

To help providers discuss the risks and benefits of taking statins for primary prevention of ASCVD, Kaiser Permanente has developed a shared decision making (SDM) tool that calculates ASCVD risk using pre-populated data from Epic. The SDM tool provides recommendations on aspirin as well as statins.

This tool is available in any Epic encounter and can also be accessed at
https://clm.kp.org/pkc/national/cmi/programs/dyslipidemia/cadrisk/index.html.

ASCVD risks can also be displayed in a format that shows patients how much their risks would do down if they added interventions such as taking a statin or aspirin or quitting smoking:

Risks of statin therapy

For patients who are concerned about the risks of statins, the following evidence summary on potential harms of statin therapy may be helpful.

- *Cognitive impairment:* Per the U.S. Food and Drug Administration (FDA), rare post-marketing reports of cognitive impairment (e.g., memory loss/impairment, forgetfulness, amnesia, confusion) have been reported with statin use, with time to onset ranging from 1 day to years after starting statin therapy (USFDA 2012). The incidence of cognitive-related adverse events reported to the FDA for statins (1.9 per 1 million prescriptions) was similar to those reported for losartan (1.6 per 1 million prescriptions) and clopidogrel (1.9 per 1 million prescriptions) (Richardson 2013). If cognitive impairment occurs, discontinue the statin (median time to symptom resolution was 3 weeks upon statin discontinuation).

- *Diabetes risk:* The FDA added warnings to all statins (except pravastatin) that statin use can increase HbA1c and fasting serum glucose levels. The absolute excess risk of new-onset diabetes is very low, approximately 0.1% per year (number needed to harm [NNH] 255 over 4 years; Sattar 2010). The FDA (2012) also analyzed this data, and stated that the cardiovascular benefits of statins in clinically appropriate patients outweigh this risk. Therefore, statin treatment alone does not constitute an indication to screen for diabetes, but screening should still be considered if other risk factors for diabetes exist.

- *Myalgias/musculoskeletal injuries/decreased benefits of exercise*: In a recent meta-analysis of 55 placebo-controlled RCTs (N=43,531), there was no significant increase in myalgia with statins compared with control (Naci 2013), whereas observational studies have reported myalgia incidence varying from 1 to 25% (Sathasivam 2012, Parker 2013). Keep in mind, however, that many of the RCTs had a "run-in" period of 30 days, where patients who were intolerant of the statins were excluded from the study. A recent retrospective, propensity-matched cohort study (N=13,934) reported a 0.6% per-year risk of dislocation/strain/sprain with statin use (NNH 38 over 4.7 years; Mansi 2013). Other small RCTs have reported conflicting results of whether statin use decreases muscle strength or exercise capacity (Parker 2013, Mikus 2013).

- *Rhabdomyolysis:* Very rare. A large (N=473,343) observational cohort study reported that for commercially available statins, rates of hospitalized rhabdomyolysis events were approximately 0.3–1.6 per 10,000 person-years of statin use (NNH 6,250–33,334 per year) (Cziraky 2013).

- *Acute kidney injury (AKI):* Rare. A large (N=2,067,639) retrospective observational analysis reported that in non-CKD patients on low-dose statins, hospitalizations for acute kidney injury at 6 months ranged from 1.0 to 3.5 per 1,000 patients in those younger than 65 years old and 3.1 to 4.0 per 1,000 patients in those aged 65 years and older (Dormuth 2013). Non-CKD patients on high-potency statins versus low-potency statins were 34% more likely to be hospitalized for acute kidney injury, but incidence remained rare, with NNH 1,700 over 120 days.

- *Hepatotoxicity:* Per the FDA, statins have a very low risk of serious liver injury (reported at a rate of ≤ 2 per 1 million person-years), and routine liver function monitoring is not recommended, as ALT monitoring does not appear to detect or prevent serious liver injury (USFDA 2011).

Antiplatelet Therapy

Initiation of low-dose aspirin (81 mg) is recommended for patients **aged 50–59** at ≥ 10% risk of ASCVD over 10 years.

For patients **aged 60–69** at ≥ 10% risk of ASCVD over 10 years, **shared decision making** is recommended to weigh the individualized risks and benefits of daily low-dose aspirin.

Factors that increase GI bleeding risk (Bhatt 2008):
- Patient has **one** of the following risk factors: history of ulcer disease, history of GI bleeding, current dual antiplatelet therapy (clopidogrel plus daily NSAID/aspirin), or current concomitant anticoagulant therapy (warfarin, enoxaparin, etc.).
- Patient has **more than one** of the following risk factors: aged 60 or older, concomitant systemic corticosteroid use, or dyspepsia or GERD symptoms.

There is insufficient evidence to make recommendations on aspirin use for patients **under age 50 or over age 70** (USPSTF 2016).

Patients with Diabetes: ACE Inhibitor or ARB Therapy

Patients with diabetes who have a ≥ 7.5% risk of ASCVD over 10 years should take an ACE inhibitor or ARB as described in Table 7.

Line	Medication	Initial dose	Maximum dose
Table 7. Patients with diabetes at ≥ 7.5% risk: ACE inhibitor or ARB therapy for primary prevention of ASCVD			
1st	ACE inhibitor		
	Lisinopril **or**	5–10 mg daily	40 mg daily (target dose is 20 mg daily)
	Ramipril	2.5–5 mg daily	20 mg daily (target dose is 10 mg daily)
2nd	ARB [1]		
	Losartan	25–50 mg/day in 1–2 doses	100 mg/day in 1–2 doses

[1] Use an ARB (losartan) for patients who cannot tolerate an ACE inhibitor because of cough, rash, or angioedema (rather than because of renal failure, hyperkalemia, or hypotension). In a patient who previously developed angioedema with an ACE inhibitor, an ARB is less likely to cause angioedema, but there is still a risk of cross-reactivity. In the CHARM-Alternative study, the ARB group had 2.6% ACE-ARB cross-reactivity versus 0% in the placebo group (Granger 2003).

Combination therapy is *not* recommended

ACE inhibitor and ARB combination therapy is **not** recommended. There is evidence that there is harm and no additional benefit in combining an ACE inhibitor and an ARB. Numbers needed to harm (NNH) are 33 for hypotensive symptoms, 1,000 for syncope, 250 for diarrhea, and 250 for renal impairment.

Lowering Triglycerides to Prevent Pancreatitis

Triglycerides do not require investigation or treatment unless they are higher than 500 mg/dL. (Treatment/investigation at higher than 1,000 mg/dL would also be reasonable. Use shared-decision making.) If a patient has elevated triglycerides, consider the following workup:

- HbA1c, TSH, protein/creatinine ratio, and pregnancy test (if applicable).
- Review other items that can cause triglyceride elevations:
  - Obesity (review diet).
  - Alcohol intake.
  - Medications: estrogen replacement, oral contraceptives, tamoxifen, HIV antiretroviral regimens, beta-blockers (excluding carvedilol), retinoids, and immunosuppressive agents such as glucocorticoids and cyclosporine.

Consult with Endocrinology if:

- Cause of elevated triglycerides cannot be identified.
- You are not able to get triglyceride level lower than 500 mg/dL with treatment.
- You have any other questions about elevated triglycerides.

Table 8. Medications for lowering triglyceride levels to prevent possible pancreatitis See also the **prescribing notes** that follow Table 8.			
	Medication	**Initial dose**	**Maximum dose**
Start with:	Atorvastatin	80 mg daily	80 mg daily
	or		
	Rosuvastatin	20 mg daily	40 mg daily
If TG not < 500 mg/dL:	**Add** Fenofibrate	54–160 mg daily	160 mg daily
If TG still not < 500 mg/dL:	**Add** Fish oil (if LDL at goal)	2,000 mg DHA/EPA in divided doses daily	4,000 mg DHA/EPA in divided doses daily

Prescribing notes for Table 8

Atorvastatin and rosuvastatin

Use maximum dose of atorvastatin and rosuvastatin with caution in patients at risk for statin intolerance or adverse effects, such as those who are elderly, have kidney disease (rosuvastatin max dose = 10 mg/day with CrCl < 30 mL/min), have untreated hypothyroidism, or are taking interacting drugs.

Fenofibrate

- For patients with CKD 3 (CrCl 30–59 mL/min), do not exceed fenofibrate 54 mg per day.
- Do not use for patients with CKD 4–5.

Medication Monitoring

Table 9. Medication monitoring		
Eligible population	**Tests**	**Frequency of lab testing**
Patients on statin	Non-fasting lipoprotein panel	4–6 weeks after initiating therapy
Patients on ACE inhibitor or ARB	Potassium **and** Creatinine	At baseline **and** 2 weeks after initiating therapy **and** With each dose increase **and** Annually
Patients on fenofibrate therapy	Creatinine **and**	At baseline **and** 3 months after initiating therapy **and** Every 6 months
	ALT/AST (Only for patients on combo therapy with a statin)	At baseline **and** 4–6 weeks after initiating therapy **and** Annually
Patients on niacin	ALT/AST **and** Fasting blood glucose or HbA1c **and** Uric acid	At baseline **and** 2–4 weeks after increasing dose **and** Every 6 months

Medication monitoring that is *not* recommended

ALT/AST

For patients on statin monotherapy, routine baseline and periodic ALT or AST monitoring are not recommended. Liver function tests are recommended only if clinically indicated to work up symptoms of liver disease. Asymptomatic transaminase elevations with statin use are common but usually mild, transient, and reversible. They do not indicate liver dysfunction. Progression to liver toxicity is exceedingly rare and is likely due to idiosyncratic or immunoallergic reactions. The presence of chronic liver disease other than cirrhosis is not a contraindication for statin use. However, consultation with Gastroenterology first is recommended.

Creatine kinase (CK)

Routine CKs are not helpful and often are misleading. Check creatine kinase only if patient has symptoms of myopathy, an extremely rare side effect.

Evidence Summary

The Primary Prevention of ASCVD Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

As part of our improvement process, the Kaiser Permanente Washington guideline team is working towards updating our clinical guidelines every 2–3 years. To achieve this goal, we are adapting evidence-based recommendations from high-quality external guidelines, if available and appropriate. The external guidelines must meet several quality standards to be considered for adaptation. They must: be developed by a multidisciplinary team with no or minimal conflicts of interest; be evidence-based; address a population that is reasonably similar to the KPWA population; and be transparent about the frequency of updates and the date the current version was completed.

In addition to identifying the recently published guidelines that meet the above standards, a literature search was conducted to identify studies relevant to the key questions that are not addressed by the external guidelines.

External guidelines meeting KPWA criteria for adaptation/adoption

2017   ACC/AHA (and 9 other Professional Societies) Guideline: Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

2017   Focused Update of the 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL: Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular disease.

2017   American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for management of dyslipidemia and prevention of cardiovascular disease (Jellinger 2017)

2017   Update on the use of PCSK9 inhibitors in adults: Recommendations from an Expert Panel of the National Lipid Association (Orringer 2017)

2017   Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults (Leung 2017)

2016   Kaiser Permanente National Integrated Cardiovascular Health Guidelines: Aspirin therapy

2016   ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL: Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular disease. A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents Cardiovascular Disease Risk (Lloyd-Jones 2016)

2016   Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult (Anderson 2016)

2016   European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR) (Piepoli 2016)

2016   ESC/EAS Guidelines for the Management of Dyslipidaemias: The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR) (Catapano 2016)

2016   European Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine Joint Consensus Statement. Fasting Is Not Routinely Required for Determination of a Lipid Profile: Clinical and Laboratory Implications Including Flagging at Desirable Concentration Cutpoints (Nordestgaard 2016)

2016   U.S. Preventive Services Task Force (UPSTF). Aspirin Use to Prevent Cardiovascular Disease and Colorectal Cancer: Preventive Medication. April 2016

2016   USPSTF Statin Use for the Primary Prevention of Cardiovascular Disease in Adults: Preventive Medication. November 2016

2014   Management of dyslipidemia for cardiovascular disease risk reduction: synopsis of the 2014 U.S. Department of Veterans Affairs and U.S. Department of Defense clinical practice guideline (Downs 2015)

| 2014 | National Institute for Health Care Excellence (NICE). Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline [CG181]. Last updated September 2016. |
| 2013 | ACC/AHA Guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults (Goff 2014, Stone 2014) |

Key questions addressed in the KPWA guideline

Key question 1.1

What is the comparative accuracy of the ACC/AHA Pooled Cohort Equation (PCE), the traditional Framingham Risk Scoring, and other cardiovascular risk assessment methods or tools? Are there any other risk calculators derived and validated in population samples similar to our population that may be better predictors of risk than the calculator we currently use in KPWA?

Key question 1.2

Compared with no risk assessment, does using one of the currently recommended risk engines improve the management of dyslipidemia and reduce CVD events in adults?

- The AHA/ACC Guideline (Goff 2014)—and several other studies, including DeFilippis 2017, Muntner 2014, Kavousi 2014, Pursnani 2013, and Ridker 2013—found the Pooled Cohort Equation overestimated risk in independent cohorts.
- DeFilippis (2017) showed that PCE overestimated the risk in men, women, and all race/ethnic groups studied in MESA, including Black Americans, for whom the risk calculator is particularly recommended.
- The published studies and analyses show that the majority of risk calculators used in the U.S.— including FRS-CVD, FRS-CHD, ATPgemfibr-FRS, and the newly developed Pooled Cohort Equations—all overestimate the risk of CV events. Different explanations were provided by the investigators.
- RRS was found to be more accurate than the other calculators, yet it underestimated the risk for women.
- Opponents of the Pooled Cohort Equation argue that:
  - This new risk scoring system shifts treatment recommendations to older individuals at the expense of younger individuals, among whom the benefits might be greater.
  - The equation was developed from decades-old data that do not reflect the decreasing rates of CHD events in the last decades due to the increased awareness of the population, changes in smoking and diet habits, physical activities, blood pressure control, and statin use as well as the use of other modern CVD therapies, including revascularization.
  - The PCE was derived from studies that did not use risk calculators or global risk prediction scores to determine eligibility for the trials.
  - Smoking is a dichotomized variable in all risk score models, which does not consider the intensity and duration of smoking nor the changes to cigarette contents over the years.
  - Five of the work group members had some relationship with the drug industry.
  - As the AHA/ACC guideline authors recognized that the PCE overestimates risk, they increased the 10-year risk threshold for statin therapy from 5% to 7.5%. This may not be optimal if the risk score is used for other purposes, such as the use of aspirin for primary prevention (Ridker 2016).
  - It is essential to have accurate cardiac risk estimation if the risk calculators are used to determine the eligibility of patients for preventive therapies. Overestimation in low-risk participants would expose them unnecessarily to the risks of preventive drugs used for primary prevention of ASCVD (e.g., the bleeding risk associated with aspirin, which has a very narrow benefit-to-risk ratio when used for primary prevention, or the potential side effects of long-term statins as well as their cost to the patient and health system.) Underestimation of risk, on the other hand (as with the RRS in women), would result in undertreatment with preventive therapies.
  - The PCE and other risk calculators do not measure risk factors such as salt and fat intake, environmental pollution, diet, or other factors that have developed and/or changed over the years (DeFilippis 2017).
  - Four placebo-controlled trials (CORONA [Kjekshus 2007], GISSI-HF [Tavazzi 2008], AURORA [Fellström 2009] and the German Diabetes and Dialysis Study [Wanner 2005])

enrolled individuals at high absolute risk in the setting of heart failure or renal failure and found little evidence of event reduction with statin therapy despite the large reduction in LDL-C.

- o Ridker (2015) calculated that 11.1 million (34%) of those recommended to consider treatment using the ACC/AHA 10-year risk of ≥ 7.5 would not have qualified for any major statin trial; many of the individuals in this group had high risk due to hypertension and smoking; and 28.5% had no modifiable risk factors yet were at high 10-year risk because of their age.
- o The PCE, like some other prediction tools, does not include family history; including family history may improve the discrimination accuracy of equations (Ridker 2016).
- o Some investigators advocate for coronary artery calcium (CAC) screening in a primary prevention setting to improve the prediction of risk. However, CAC's limitations include cost, radiation exposure, and potential incidental findings. In addition, repeat measurement of CAC may not be appropriate in patients receiving statins, which are reported to increase coronary artery calcium (Ridker 2016).

- A dynamic tool—the "Million Hearts Longitudinal ASCVD Risk Assessment Tool"—using the PCE has recently been developed to allow for dynamic longitudinal ASCVD prediction in the Medicare population (Lloyd-Jones 2017).
- Two Cochrane systematic reviews with meta-analyses (Dykova 2016, Karmali 2017) assessed the effects of CVD risk assessment and scoring in adults without prevalent CVD on cardiovascular outcomes, risk factor levels, and preventive medication prescribing. Both reviews concluded that low-quality evidence suggests that systematic risk assessment for primary prevention of CVD has no statistically significant effects on clinical endpoints but may slightly reduce CVD risk factor levels and increase preventive medication prescribing.

Key question 2

How accurate is assessing the lipid profile using blood samples collected in the nonfasting state compared to the fasting state for a) calculating ASCVD risk in adults with no previous history of CVD and b) monitoring response to statin therapy?

- There is fair evidence from several prospective studies and an earlier meta-analysis showing no significant difference between measuring lipids in the fasting versus nonfasting state for predicting the risk of CVD among groups of patients. There have been no studies to date that examine the predictive value of lipids measured in the fasting and nonfasting states in the same individual.
- According to several investigators, while more precision is beneficial when lipid profile is used to determine whether to treat dyslipidemia, the minimal variation in total HDL-C and total cholesterol levels would not affect the decision on whether to use lipid-lowering drugs for individuals, especially when this is driven by calculating the individual's overall risk (Gaziano 2012, Naugler 2014).
- There is insufficient evidence to support the use of nonfasting lipid panel to monitor lipid therapy. Major guidelines differ in their recommendations, but it appears that more guidelines recommend fasting lipid profile for monitoring LDL-C in patients taking lipid-lowering medications.
- It is recommended to use fasting lipid samples for monitoring response to lipid-lowering treatment in patients with high triglyceride levels.

Key question 3

In adults on lipid-lowering therapy, does the use of treatment targets reduce CVD events? Should we keep following the treat-to-target approach, and to what targets according to the individual patient risk of CV events?

- To date, there is insufficient evidence to determine an optimal LDL-C target or a threshold beyond which there is no further reduction in CV events or increased harm.
- The following guidelines and pathways recommend a treat-to-target approach in the management of dyslipidemia to diminish CVD risk: 2016 American College of Cardiology (Lloyd-Jones 2016), 2016 Canadian Cardiovascular Society (Anderson 2016), and 2016 ESC/EAS (Catapano 2016).
- There is insufficient evidence to determine the safety profile of achieving very low (< 30 mg/dL) LDL-C. An analysis of IMPROVE-IT trial results (Giugliano 2017) shows no significant differences in long-term safety outcomes with intensive lipid-lowering therapy. On the other hand, a post hoc analysis of the JUPITER trial (Everett 2014) suggests that achieving LDL-C levels < 30 mg/dL with high-intensity statin therapy may be generally well tolerated, but may also be associated with a small but statistically significant increase in the rates of diabetes, hematuria, hepatobiliary disorders, and insomnia when compared to LDL-C levels > 30 mg/dL with rosuvastatin. The FOURIER trial results (Sabatine 2017) that compared the effect of lipid lowering with evolocumab versus a placebo showed no differences between the two groups in the overall rates of adverse events, serious adverse events, or events leading to the discontinuation of the study regimen. There were, however, a statistically significant higher rate of injection site reactions and a statistically insignificant higher rate of adjudicated cases of new-onset diabetes in the evolocumab group.

Key question 4

What is the safety and effectiveness of PCSK9 inhibitors in preventing or reducing CV events in patients at high CV risk who have not reached their LDL-C targets with other lipid-lowering drugs?

- There is evidence that PCSK9 inhibitors may significantly lower LDL-C levels compared to placebo.
- Medium-term follow-up studies suggest that PCSK9 inhibitors may reduce incidence of CV events compared to placebo, but with little or no difference in reducing overall mortality.
- There is insufficient evidence to determine the relative efficacy and safety of PCSK9 inhibitors to active lipid-lowering drugs.
- The FOURIER trial (Sabatine 2017), the first study on PCSK9 inhibitors that had cardiovascular outcomes, shows that the use of evolocumab in selected high-risk individuals reduced the LDL-C to a median of 30 mg/dL and decreased the composite CV outcomes, with an NNT of 67 in an average of 2.2 years. However, this was not associated with a reduction in CV or all-cause mortality, which on the contrary was insignificantly higher in the evolocumab group. This might be due to chance as the study was not powered to detect a difference in mortality, but the early termination of the study does not allow examining the long-term risks or benefits of evolocumab.
- To date, there is no evidence to determine that the addition of PCSK9 inhibitors to the highest tolerable dose of statin with or without ezetimibe is more beneficial than the use of the maximally tolerated dose of statin with or without ezetimibe. Evolocumab was tested against a placebo and not against a statin-plus-ezetimibe combination therapy, which would be the appropriate comparator. In addition, FOURIER study participants were not receiving the maximal tolerated statin therapy at randomization.
- There is insufficient evidence to determine the long-term harms of reducing the LDL-C level to ≤ 30 mg/dL (discussed earlier).
- There is some evidence suggesting that PCSK9 inhibitors may be associated with a significant increase in any adverse events, including neurocognitive events and cataract, compared to placebo.

Key question 5

What is the optimal blood pressure target for the general population and for those at high cardiovascular risk? What are the comparative benefits and harms of intensive treatment of blood pressure to an SBP target of < 120 mm Hg versus standard SBP target of < 140 mm Hg?

- SPRINT results (Wright 2015) provide evidence that intensive blood pressure control targeting an SBP ≤ 120 mm Hg versus < 140 mm Hg among community-dwelling adults aged 50 or older at high risk of CVD with SBP 130–180 mm Hg, significantly lowers the rates of fatal and nonfatal major CV events and death from any cause, but at the expense of higher rates of a number of serious adverse events that may increase ED visits, including hypotension, syncope, electrolyte abnormalities, and acute kidney injury or acute renal failure.
- SPRINT results may not be generalized to patients with diabetes mellitus, history of stroke, symptomatic heart failure, LVEF < 35%, polycystic kidney disease, medical conditions that limit survival to < 3 years, or dementia; nor may they be generalized to individuals living in nursing homes and other population groups excluded from the study.
- SPRINT used programmed automated oscillometric blood pressure meters, which may give BP values 5–10 mm Hg lower than those measured in the office by conventional methods.
- Subanalyses for elderly patients showed similar results and had similar limitations as SPRINT. The elderly patients were analyzed as one group with no categorization or subanalyses according to age. The authors performed an exploratory secondary analysis to examine modification of the treatment effect by frailty status, which was a specified outcome in the trial protocol. The results of the analysis stratified by baseline frailty status showed higher event rates with increasing frailty in both treatment groups. However, within each frailty stratum, absolute event rates were lower for the intensive treatment group. According to the authors and some investigators, frail older SPRINT participants do not represent the entire population of frail older adults.
- Two recent meta-analyses (Ettehad 2016, Xie 2016) provide supporting evidence on the cardiovascular benefits of more intensive blood pressure lowering in individuals, including high-risk patients with SBP < 140 mm Hg.
- During follow-up of patients with no CV disease at baseline who were at intermediate risk, the HOPE-3 trial (Yusuf 2016) showed a decrease in SBP/DBP that was 6.0/3.0 mm Hg greater in the active treatment group versus the placebo group. However, this did not result in a statistically significant difference in the incidence of the first co-primary outcome, second primary outcome, secondary outcome, or components of each in patients receiving BP lowering alone, but it did lead to significantly better clinical outcomes in the group that received both the BP- and lipid-lowering drugs. A pre-specified subgroup analysis showed that participants in the upper third of SBP (> 143.5 mm Hg [mean 154.1±8.9 mm Hg]) receiving active treatment had significantly lower rates of the first and second primary outcomes compared to those in the placebo group.

Key question 6

What is the safety and tolerability of the long-term use of high-intensity statins (e.g., atorvastatin 80 mg)?
- Li and colleagues' 2016 meta-analysis on the safety profile of atorvastatin 80 mg/day suggests that it is less well tolerated than atorvastatin with lower intensity or placebo when used for more than 52 weeks, and is associated with a higher risk of transaminase elevation when used for more than 16 weeks, especially among patients with CAD.
- There is more recent evidence supporting the association of statins in general with the risk of diabetes mellitus. The association appears to be stronger with atorvastatin 80 mg and rosuvastatin compared to lower-intensity atorvastatin and other statins used.

Key question 7

Should we adopt the USPSTF recommendations on the use of aspirin for the primary prevention of ASCVD?

- The U.S. Preventive Services Task Force (Bibbins-Domingo 2016) recommends initiating low-dose aspirin use for the primary prevention of CVD and colon cancer in adults aged 50–59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years. *(B recommendation)*
- The decision to initiate low-dose aspirin use for the primary prevention of CVD and colon cancer in adults aged 60–69 years who have a 10% or greater 10-year CVD risk should be an individual one. Persons who are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years are more likely to benefit. Persons who place a higher value on the potential benefits than the potential harms may choose to initiate low-dose aspirin. *(C recommendation)*
- The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and colon cancer in adults younger than 50 years. *(I statement)*
- The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and colon cancer in adults aged 70 years or older. *(I statement)*

The USPSTF recommendation was based on three systematic reviews and a modeling analysis that incorpatated findings from these reviews to estimate the magnitude of the net benefit of asprin therapy for the primary prevention of CVD and colon cancer. Overall, the systematic reviews included 11 major aspirin primary prevention trials (N=118,445 participants). Four of these studies were published after the 2009 USPSTF review. Participants' mean ages ranged from 55 to 65 years. Aspirin dose ranged between the trials from 50 to 325mg in all but one; eight trials used a dose of ≤ 100 mg/day. The duration of use and follow-up ranged from 4 to 10 years. The trials showed that aspirin use significantly reduced nonfatal MI, CV mortality, and all-cause mortality, but not the risk of nonfatal stroke. The pooled analysis of trials with aspirin dose ≤ 100 mg/day showed a significant reduction in nonfatal MI and coronary events (RR 0.83; 95% CI, 0.74–0.94), nonfatal stroke (RR 0.86; 95% CI, 0.76–0.98), but a nonsignificant reduction in all-cause mortality. The pooled results of 10 studies using any aspirin showed a 22% reduction in nonfatal MI and coronary events.

The reported major risk of bleeding increased by 58% in aspirin users (OR 1.58; 95% CI, 1.29–1.95). Similar results were observed across the the range of aspirin doses. The pooled analysis of nine trials using any dose aspirin showed an increased risk of hemorrhagic stroke (OR 1.33; 95% CI, 1.03–1.71). Trials with low-dose aspirin had OR 1.27 and 95% CI, 0.96–1.68.

Subgroup analysis based on age, sex, and diabetes status suggests that older age groups have greater benefits than younger ages, and that there was insufficient evidence to determine any sex difference.

The more recent trials that evaluated aspirin for primary prevention in patients receiving statins and other preventative therapies did not demonstrate a significant reduction in fatal and nonfatal ASCVD events.

The USPSTF used a microsimulation model to estimate the magnitude of the net benefit. The estimates showed that the benefits were greatest with initiating aspirin at 50–59 years and continuing it unless contraindicated by adverse bleeding events. The net gain in benefits was less if aspirin was inititaed at 60–69 years.

Both the net ASCVD benefit and bleeding risk increased with the increase in the absolute ASCVD risk. The net benefit exceeded the risk of bleeding at baseline 10-year ASCVD risk ≥ 10% (Bibbins-Domingo 2016).

The USPSTF used the Pooled Cohort Equation to predict 10-year risk for hard ASCVD events.

Key question 8

Should we adopt the USPSTF recommendations on the use of statins for the primary prevention of ASCVD?

- The USPSTF recommends initiating the use of low- to moderate-dose statins in adults aged 40–75 years without a history of CVD who have one or more CVD risk factors (dyslipidemia, diabetes, hypertension, or smoking) and a calculated 10-year CVD event risk of 10% or greater. *(B recommendation)*
- The USPSTF recommends that clinicians selectively offer low- to moderate-dose statins to adults aged 40–75 years without a history of CVD who have one or more CVD risk factors and a calculated 10-year CVD event risk of 7.5%–10%. *(C recommendation)*
- The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of initiating statin use in adults 76 years and older. *(I statement)*

The recommendations were based on a systematic review (Chou 2015) of 19 randomized controlled trials (involving 71,344 participants) that evaluated the effects of statins versus placebo or no statins on health outcomes in adults aged 40–75 years without known CVD. Most of the trials enrolled participants based on an elevated LDL-C level, a diabetes diagnosis, or at least one CVD risk factor. The pooled results of the trials showed that the use of low- or moderate-dose statins was associated with a reduced risk of all-cause mortality (RR 0.86; 95% CI, 0.80–0.93), cardiovascular mortality (RR, 0.69; 95% CI, 0.54–0.88), ischemic stroke (RR 0.71; 95% CI, 0.62–0.82), heart attack (RR 0.64; 95% CI, 0.57–0.71), and a composite cardiovascular outcome (RR 0.70; 95% CI, 0.63–0.78).The relative risk reduction was similar across age, sex, race/ethnicity, lipid level, and other risk factors. Trials that stratified participants according to a baseline global cardiovascular risk score showed similar risk reduction estimates in participants at a higher versus lower risk. The task force evidence report estimated that 244 individuals would need to take a statin daily to prevent one death from any cause in 5 years.

The review suggested that statins were not associated with increased risk of withdrawal due to adverse events, serious adverse events, myalgia, cancer, or liver-related harms compared to controls. The pooled analysis showed a higher but statistically insignificant risk of diabetes with statins. There was significant heterogeneity between the studies, and one large trial (JUPITER [Everett 2014]) that evaluated a high-potency statin showed a significant increased risk.

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Guideline Development Process and Team

Development process

The guideline team developed the ASCVD Primary Prevention Guideline using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in April 2018.

Team

The ASCVD Primary Prevention Guideline development team included representatives from the following specialties: cardiology, clinical laboratory, family medicine, nursing, and pharmacy.

Clinician lead: Dave McCulloch, MD, Medical Director, Clinical Improvement
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Disclosure of conflict of interest

Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care–related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the ASCVD Primary Prevention Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.