Statin Therapy Guidelines and Patient Adherence

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Overview

- Part I: Statin Medication Adherence
- Part II: 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk
- Part III: Non-Statin Therapies for LDL-Cholesterol
- Part IV: Statin Intolerance App

Part I: Statin Medication Adherence

Statin Medication Adherence: Issues

- Although the benefits of statin therapy have been evident from a number of randomized clinical trials, their effectiveness can be seen in the real patient population only if there is adequate adherence to the medication regimen.
- Despite well-publicized guidelines and the availability of potentially effective therapies, many patients do not achieve their lipid goals and remain at high risk for cardiac events because of poor adherence.
- The common barriers that could lead to non-adherence can be patient related, physician related or healthcare system related.
- Non-adherence to statin medications is an area of growing concern that can result in increased costs of healthcare, greater hospitalizations, and patient mortality.

Statin Medication Adherence: Previous research

- Statin non-adherence has been associated with around 25% increased hazard for mortality following hospitalization in patients with acute myocardial infarction [1].
- In a study of patients discharged for myocardial infarction, 10% of patients failed to fill their lipid lowering agent one week after discharge [2].
- Physician follow-up and continuity of care combined with increased follow-up and cholesterol testing could promote long term adherence by shortening long gaps in statin use [3].
- One year after dissemination of the 2013 cholesterol guideline, overall treatment rates with statins among patients with ASCVD and diabetes did not change appreciably, and many patients remained either untreated or undertreated [4].

Patient Data on Statin Medication Adherence: Methods

• Patients enrolled in Medicare Advantage Plan (MAPD) who were non-adherent (PDC ≤ 50%) to statins 17% of patients).

 Among the non-adherent patients, 51 patients (PDC ≤ 50%) were randomly selected and contacted via phone by pharmacy students trained in motivational interviewing.

• Identification of potential barriers to statin adherence

Patient Data on Statin Medication Adherence: Results

Frequency distribution of patient demographics

Assessing and a processing and a group		
Patient Characteristic	N	
Age (years)		
<50	5	
50-60	6	
60-70	22	
>70	18	
Gender		
Female	27	
Male	24	
Name of prescribed statin		
Atorvastatin	25	
Simvastatin	14	
Rosuvastatin	6	
Pravastatin	5	
Lovastatin	1	
Proportion of days covered (PDC)		
<30%	6	
30-40%	9	
40-50%	36	

Barriers to statin medication adherence in elderly non-adherent patients

No.	Barriers	N
1	Denial of barrier	27
2	Forgetfulness	8
3	Adverse events	6
4	Cost	5
5	Lack of knowledge	3
6	Discontinued by provider	1
7	Pill burden	1
8	Transportation	1

Patient Data on Statin Medication Adherence: Results

Most commonly reported barriers to statin medication adherence

Forgetfulness

- Health issues
- Too busy to remember

Adverse Events

- Experienced migraines
- Sleepiness

Cost

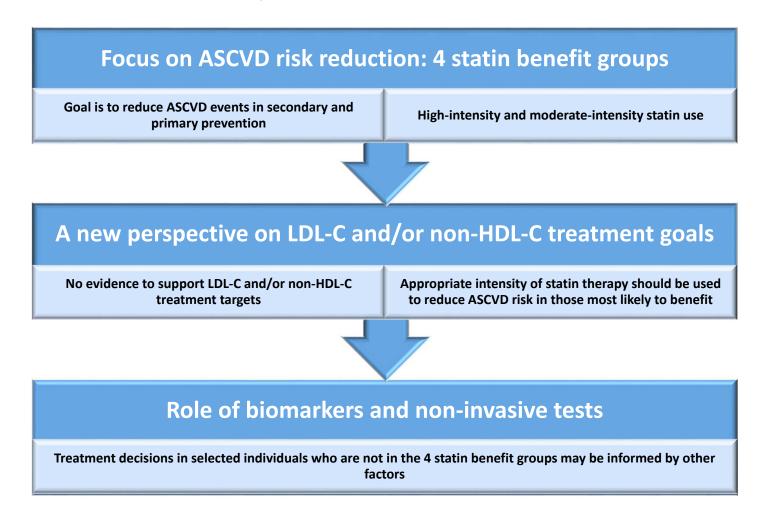
- Getting samples
- Brand-only medication

Lack of Knowledge

- Denies the need for medication
- Patient selfstopped

Part II: 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk⁵

2013 ACC/AHA Guideline: What's New?



2013 ACC/AHA Guideline: What's New?

Global risk assessment for primary prevention

Recommends use of the new Pooled Cohort Equations to estimate 10-year ASCVD risk in both white and black men and women

Recommends a discussion between clinicians and patients before initiation of statin therapy

Indicates, on the basis of RCT data, those highrisk groups that might not benefit Focuses statin therapy on those most likely to benefit by more accurately identifying higher-risk individuals



Safety recommendations

Provides expert guidance on management of statinassociated adverse effects, including muscle symptoms Used RCTs to identify important safety considerations of statins and provides expert guidance on management of adverse effects

2013 ACC/AHA Guideline: 4 Statin Benefit Groups



Individuals with clinical ASCVD – acute coronary syndromes, or a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin – without New York Heart Association (NYHA) class II-IV heart failure or receiving hemodialysis.



Individuals with primary elevations of low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dL.

2013 ACC/AHA Guideline: 4 Statin Benefit Groups



Individuals 40-75 years of age with diabetes, and LDL-C 70-189 mg/dL without clinical ASCVD.



Individuals without clinical ASCVD or diabetes, who are 40-75 years of age with LDL-C 70-189 mg/dL, and have an estimated 10-year ASCVD risk of 7.5% or higher.

Use of Statin Therapy

1

 Acceptable margin of safety when used in properly selected individuals with appropriate monitoring 2

 Recommended for primary and secondary prevention of ASCVD 3

 Reduced morbidity and mortality associated with ASCVD (based on RCTs) 4

 Cost-effective: generic forms available

2013 ACC/AHA Guideline: Intensity of Statin Therapy

Statin Therapy

High-Intensity

Daily dose lowers LDL-C, on average, by approximately ≥50% Atorvastatin (40†)–80 mg Rosuvastatin 20 (40) mg

- † down titrate if 80 mg not tolerated (IDEAL study)
- ‡ 80 mg may have increased risk of myopathy & rhabdomyolysis

Moderate-Intensity

Daily dose lowers LDL-C, on average, by approximately 30% to <50%

Atorvastatin 10 (20) mg

Rosuvastatin (5) 10 mg

Simvastatin 20-40 mg‡

Pravastatin 40 (80) mg

Lovastatin 40 mg

Fluvastatin XL 80 mg

Fluvastatin 40 mg BID

Pitavastatin 2–4 mg

Low-Intensity

Daily dose lowers LDL-C, on average, by <30% Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg Pitavastatin 1 mg

2013 ACC/AHA Guideline: Statin Therapy Recommendations



Known ASCVD

Age ≤ 75 years: High-intensity statin

Age > 75 years: Moderate-intensity statin



LDL ≥ 190 mg/dL

High-intensity statin

2013 ACC/AHA Guideline: Statin Therapy Recommendations



Diabetes without known ASCVD

10-year risk ≥ 7.5%: High-intensity statin

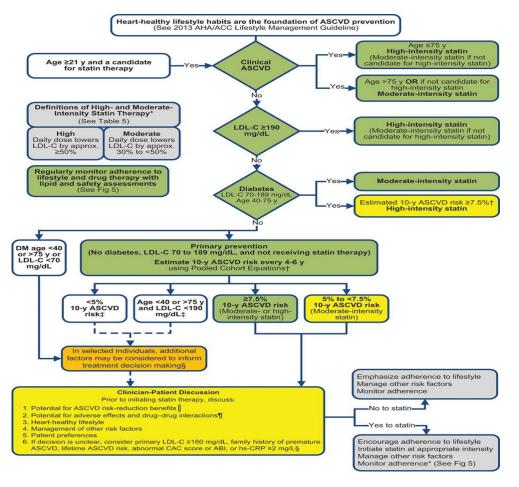
10-year risk < 7.5%: Moderate-intensity statin



ASCVD 10 yr. Risk ≥ 7.5%

Moderate to high-intensity statin

Summary of Statin Initiation Recommendations for the Treatment of Blood Cholesterol to Reduce ASCVD Risk in Adults



Lifestyle Modification as the Foundation for ASCVD Risk-Reduction Efforts

(Both prior to and in concert to cholesterol lowering drug therapies)

- ➤ Lifestyle modification critical components:
- adhering to a heart healthy diet
- regular exercise habits
- avoidance of tobacco products
- maintenance of a healthy weight







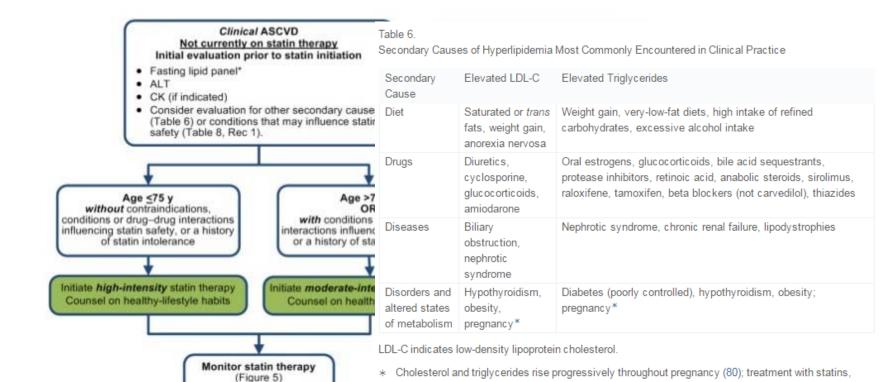
2013 ACC/AHA Guideline: Statin Therapy

- RCT evidence shows that ASCVD events are reduced by using the maximum tolerated statin intensity in those groups shown to benefit.
- In secondary prevention, evidence supports high intensity statin therapy to maximally lower LDL-C.
- For primary prevention, use of the new Pooled Cohort Equations to estimate 10year ASCVD risk.
- Guideline is "patient centered" Potential for risk reduction benefit, adverse effects, and drug-drug interactions, along with patient preferences, must be considered before statins are prescribed for the primary prevention of ASCVD.

2013 ACC/AHA Guideline: Shared Decision Making

- Shared Decision Making (SDM) when appropriate
- Engage in a clinician—patient discussion before initiating statin therapy, especially for primary prevention in patients with lower ASCVD risk.
- The cholesterol guidelines recommend not only the risk calculation, but also the clinician—patient review of the risk and the decision to take a statin.
- Age is a major contributor to the ASCVD risk calculation.
- Clinical judgment, statin safety issues, and consideration of patient preferences inform the treatment plan.
- Treatment plan is a comprehensive approach to risk reduction that begins with the use of the ASCVD risk calculator and incorporates addressing of the modifiable risk factors.

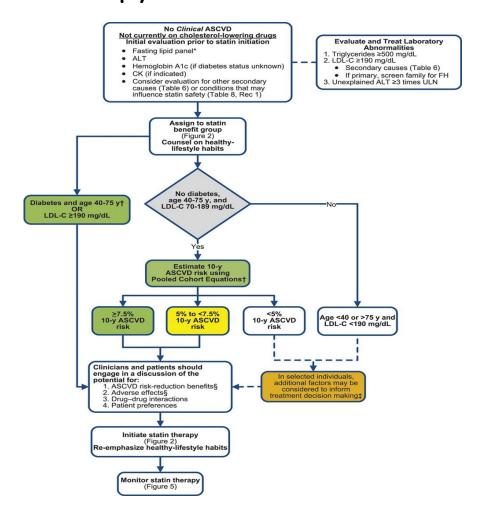
Initiating Statin Therapy in Individuals With Clinical ASCVD



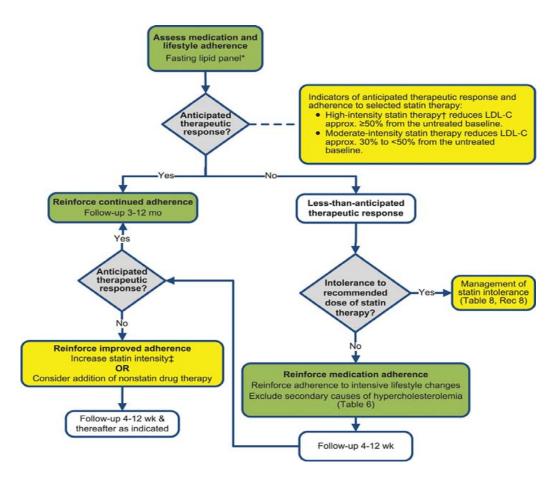
Adapted with permission from Stone et al (80).

niacin, and ezetimibe are contraindicated during pregnancy and lactation.

Initiating Statin Therapy in Individuals Without Clinical ASCVD



Statin Therapy: Monitoring Therapeutic Response and Adherence



2013 ACC/AHA Guideline: Monitoring Statin Therapy

- A baseline lipid panel should be obtained followed by a second lipid panel 4 to 12 weeks after initiation of statin therapy to determine patient's adherence.
- Thereafter, assessments should be every 3 to 12 months as clinically indicated.
- LDL-C levels and per cent reduction are to be used only to assess response to therapy and adherence.

2013 ACC/AHA Guideline: Statin Safety Recommendations

- Use moderate-intensity statin therapy in patients who are predisposed to statinassociated adverse effects.
- Multiple or serious comorbidities, including impaired renal or hepatic function
- History of previous statin intolerance or muscle disorders
- Unexplained ALT elevations > 3 times ULN
- Concomitant use of drugs affecting statin metabolism ⁷
- > 75 years of age
- History of hemorrhagic stroke
- Asian ancestry
- CK should not be routinely measured, although it is reasonable to measure baseline CK in persons at increased risk for adverse muscle events

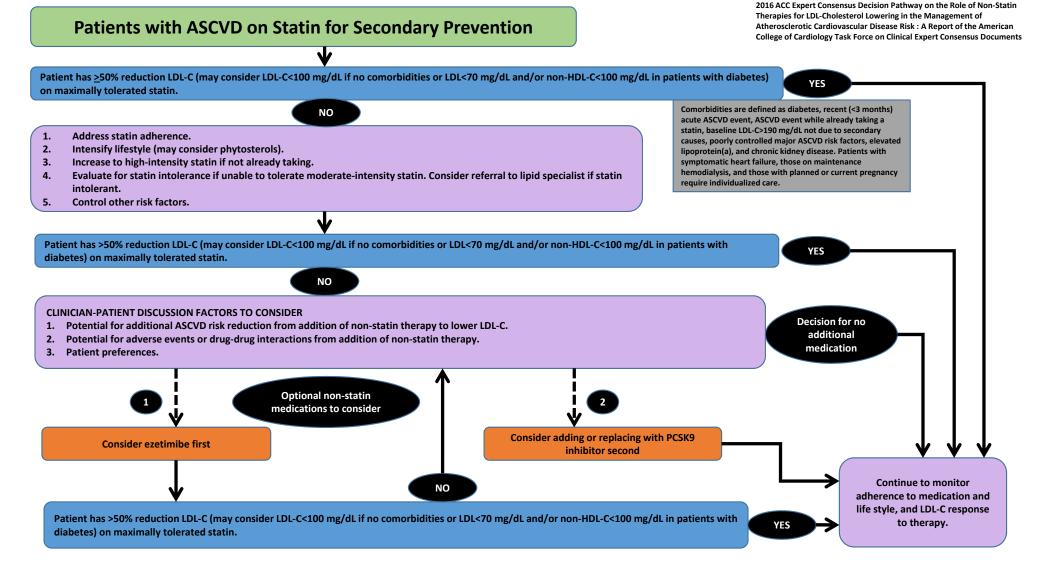
2013 ACC/AHA Guideline: Statin Safety Recommendations

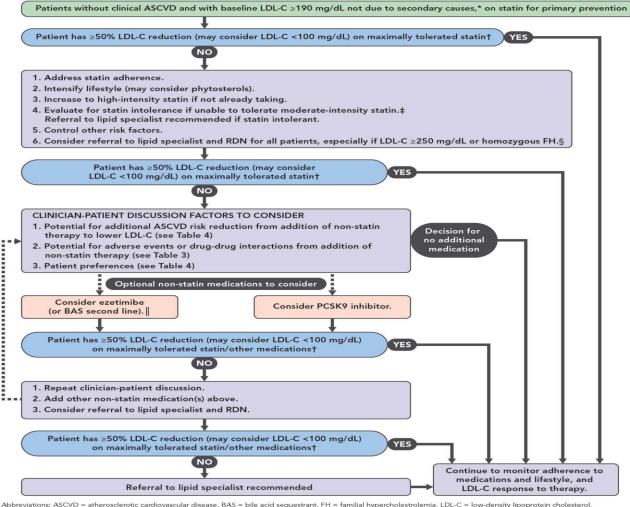
- Individuals on statin therapy should be evaluated for new onset DM . Those
 who develop DM should be counselled on a heart-healthy diet, physical activity,
 healthy body weight, stopping tobacco use. Statin therapy should be continued to
 reduce their risk of ASCVD events.
- Use caution in individuals > 75 years of age, persons taking concomitant meds that alter drug metabolism, taking multiple drugs, taking drugs for conditions that required complex medication regimens (transplant patients or patients with HIV).
 Review prescribing information before initiating any cholesterol-lowering drug.

2013 ACC/AHA Guideline: Insufficient Response to Statin Therapy

- In persons with a less-than-anticipated response to statin therapy or are intolerant to the recommended intensity of statin therapy:
 - Reinforce adherence to medication and lifestyle changes
 - Exclude secondary causes of hyperlipidemia
 - Investigate statin intolerance
- In persons at high ASCVD risk receiving the maximum tolerated statin who have a less-than-anticipated therapeutic response, addition of a nonstatin LDL lowering agent may be considered if the benefits outweigh the potential for adverse effects
 - Individuals with clinical ASCVD < 75 years of age
 - Individuals with baseline LDL-C ≥ 190 mg/dL
 - Individuals 40 to 75 years of age with diabetes

Part III: Non-Statin Therapies for LDL-Cholesterol





Abbreviations: ASCVD = atherosclerotic cardiovascular disease, BAS = bile acid sequestrant, FH = familial hypercholestrolemia, LDL-C = low-density lipoprotein cholesterol, PCSK9 = proprotein convertase subtilisin/kexin 9, RDN = registered dietitian nutritionist.

§May consider mipomersen, lomitapide, or LDL apheresis for appropriate patients.

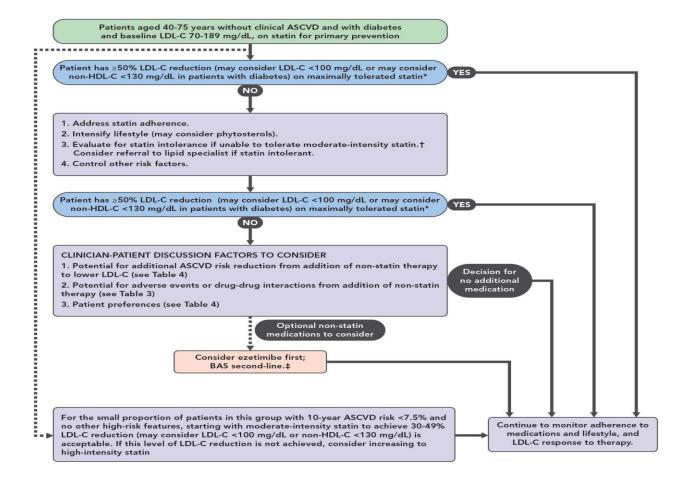
Consider BAS if ezetimibe intolerant and triglycerides <300 mg/dL

Patients ≥21 Years of Age without Clinical ASCVD and with baseline LDL-C ≥190 mg/dL. Not Due To Secondary Causes, on Statin for Primary Prevention

^{*}e.g., hypothyroidism, nephrosis, extreme dietary patterns

[†]The Expert Panel emphasizes that these are not firm triggers for adding medication, but they are factors that may be considered within the broader context of an individual patient's clinical situation.

[‡]See section on strategy for assessment and management of statin intolerance.



Patients Aged 40-75
years without Clinical
ASCVD and with
Diabetes and Baseline
LDL-C 70-189 mg/dL,
on Statin for Primary
Prevention

Abbreviations: ASCVD = atherosclerotic cardiovascular disease, BAS = bile acid sequestrant, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, RDN = registered dietitian nutritionist.

*The Expert Panel emphasizes that these are not firm triggers for adding medication, but they are factors that may be considered within the broader context of an individual patient's clinical situation. Due to increase in triglycerides often present in diabetes, may also consider combination therapy if non-HDL-C ≥ 130 mg/dL. †See section on strategy for assessment and management of statin intolerance.

‡Consider BAS if ezetimibe intolerant and triglycerides <300 mg/dL. Colesevelam may have modest salutary effects on HbA1c and may worsen hypertriglyceridemia.

Part IV: Statin Intolerance App

ACC Statin Intolerance App⁶

- Guides clinicians through the process of managing and treating patients who report muscle symptoms while on statin therapy.
- Clinicians can use the app to:
- Answer questions to evaluate possible intolerance to a patient's current statin prescription.
- Follow steps to manage and treat a patient who reports muscle symptoms on a statin.
- Compare statin characteristics and drug interactions to inform management of LDL-related risk.
- App does not discuss intermittent statin therapy with gradual increases to optimize tolerance.

ACC Statin Intolerance App

- The information and recommendations in this app are derived from the 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults, and the prescribing information for each statin.
- It was developed as part of the American College of Cardiology "LDL: Address the Risk"
 Initiative and further refined and vetted by physicians, physician assistants, nurse
 practitioners, pharmacists and other relevant specialties; and through user testing in care
 settings with patients.
- The Statin Intolerance App is also part of a larger and ongoing effort of the American College of Cardiology to help its members and other clinicians translate guidelines and other clinical policy statements into practice at the point of care.

ACC Statin Intolerance App: How to Download

 This app is available for free in the iTunes and Google Play app stores. You do not have to be an ACC member to download the app.



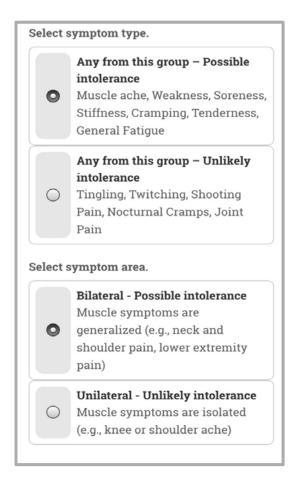
- Search "ACC Statin Intolerance" on the web or in your app store to download.
- Can use one the links below to download the app.

Download the App from iTunes

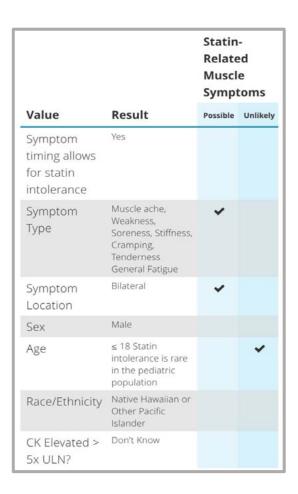
Download the App from Google Play

Launch the Web Version

ACC Statin Intolerance App: Steps to use



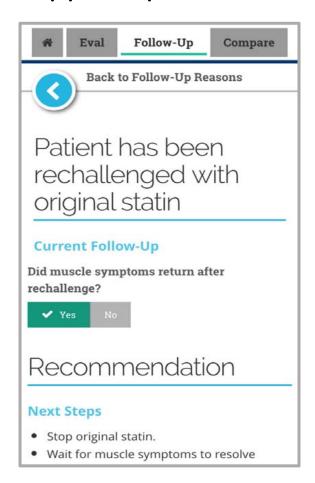
Answer questions to evaluate possible intolerance to a patient's current statin prescription



ACC Statin Intolerance App: Steps to use

STEP 2:

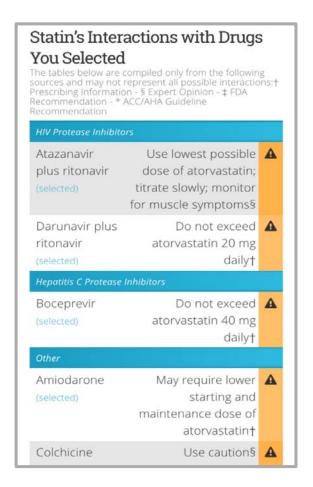
Follow steps to manage and treat a patient who reports muscle symptoms on a statin.



ACC Statin Intolerance App: Steps to use

STEP 3:

Compare statin characteristics and drug interactions to inform management of LDL-related risk.



ACC Statin Intolerance App: FAQs

Who is the intended audience for the App?

The App is targeted to clinicians who care for patients with or at risk for atherosclerotic cardiovascular disease. While the app is not intended for patient use, it is freely available online and in the app stores to all users.

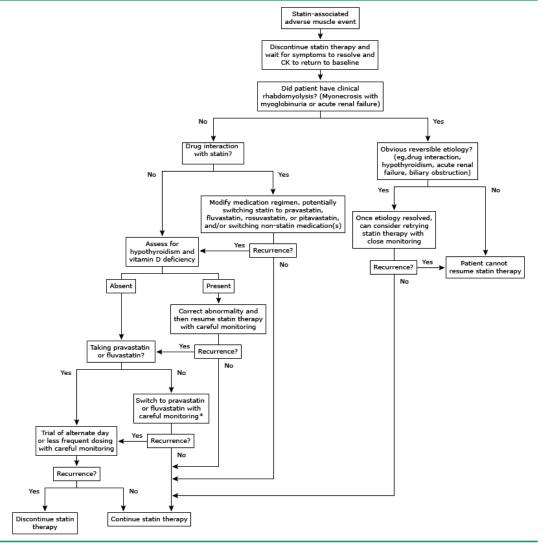
• Will any personal or patient information be collected by the ACC Statin Intolerance App?

The Statin Intolerance App includes some patient demographic questions such as age, sex, race/ethnicity, and statin prescription. This information can be emailed anonymously from the app during the course of an app session to the user's personal email. The app does not record or store any of this information.

Are there any plans to link outputs from the App to EHRs?

Version 1 of the Statin Intolerance App does not currently have the capability for EHR integration. However, the ACC is actively exploring EHR integration as one way to increase the utility of our Apps in the future.

Management of statin myopathy



CK: creatine kinase.

Statin Myopathy from Up-To-Date. Wolters Kluwer. Accessed on line November 23, 2016.

^{*} Pravastatin and fluvastatin appear to be less likely to cause muscle toxicity than other statins.

Recommendations for PCPs

- Think statin therapy as part of your preventive management process as you do vaccinations, cancer screening, etc.
- Emphasize the lifestyle changes that underlie the recommendations.
- Explore the patient preferences and barriers in preventive therapy.
- Consider these key articles for your review and reference:
 - Stone NJ et at. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. J Am Coll Cardiol. 2014;63(25):2889-934.
 - Lloyd-Jones DM et al. 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. J Am Coll Cardiol. 2016;68(1):92-125.
 - US Preventive Task Force. Statin Use for the Primary Prevention of Cardiovascular Disease in Adults. JAMA. 2016:316(19):1997-2007.

Case Study

Patient is a 55 year old African-American male with no history of ASCVD and not being treated for hypertension. He is a non-smoker. His sister suffered a myocardial infarction at age 60. His BP = 135/80, HgbA1C=5.7, total cholesterol=210 with HDL=40.

What would you prescribe for this patient?

Using the pooled cohort calculator, this patient's 10 year risk is 7.9% with a 46% lifetime risk. He would fall in the category of moderate to high dose statins.

Although the Preventive Services Task Force recommendations might be less aggressive. By age 60 if nothing changes his risk would calculate at 9.7%

A frank discussion with the patient about his family history and an initial life style modification approach would be in order with repeat testing.

If repeat testing does not effect change, consider institution of statin.

If patient reluctant, consider CAC for additional data.

Results might also help moderate vs. high dose statin decision.

References

- 1. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. Rasmussen JN, Chong A, Alter DA, JAMA. 2007 Jan 10; 297(2):177-86.
- 2. Prevalence, predictors, and outcomes of primary nonadherence after acute myocardial infarction. Jackevicius CA, Li P, Tu JV Circulation. 2008 Feb 26; 117(8):1028-36.
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