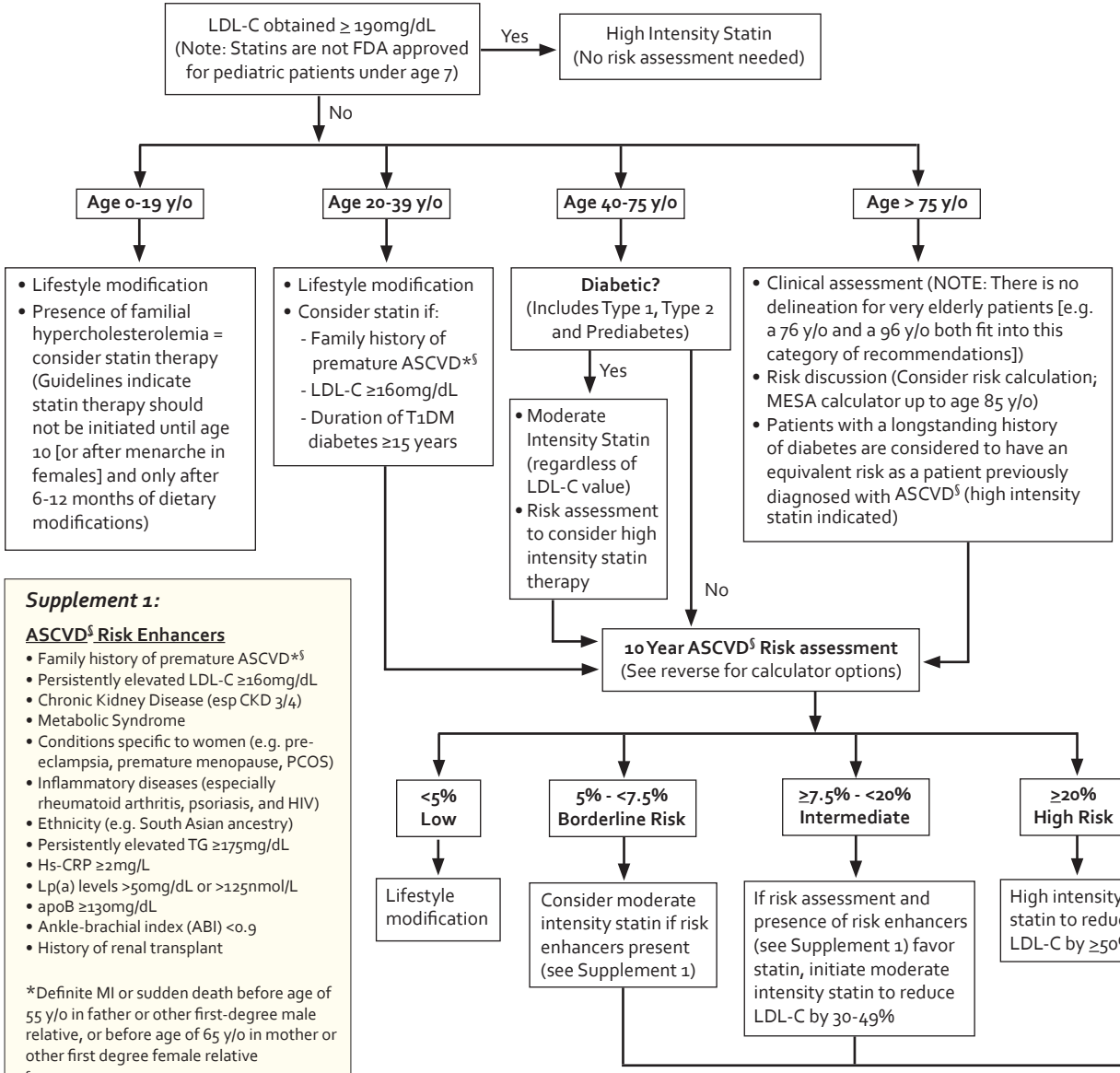
Utilization of Statin Therapy

Bryan HEALTH CONNECT

Figure 1: HMG-CoA Reductase Inhibitor Therapy (for Primary Prevention)

NOTE: Lifestyle modification is an integral addition to any statin regimen (e.g. smoking cessation, weight loss, etc.)



Supplement 1:

ASCVD§ Risk Enhancers

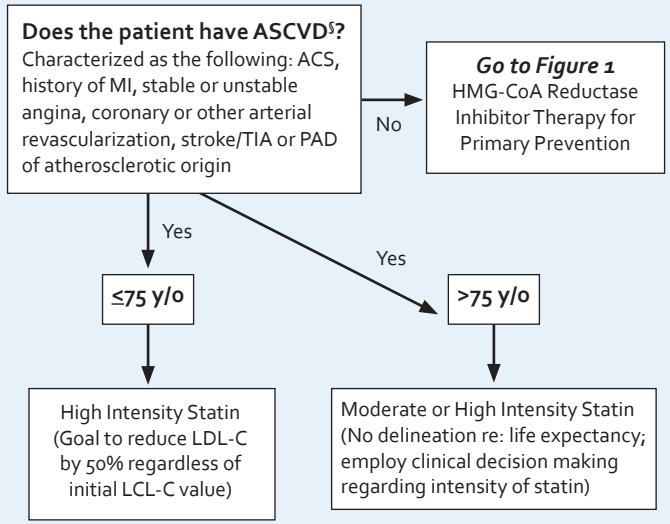
- Family history of premature ASCVD*§
- Persistently elevated LDL-C ≥160mg/dL
- Chronic Kidney Disease (esp CKD 3/4)
- Metabolic Syndrome
- Conditions specific to women (e.g. pre-eclampsia, premature menopause, PCOS)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, and HIV)
- Ethnicity (e.g. South Asian ancestry)
- Persistently elevated TG ≥175mg/dL
- Hs-CRP ≥2mg/L
- Lp(a) levels >50mg/dL or >125nmol/L
- apoB ≥130mg/dL
- Ankle-brachial index (ABI) <0.9
- History of renal transplant

*Definite MI or sudden death before age of 55 y/o in father or other first-degree male relative, or before age of 65 y/o in mother or other first degree female relative

§ Atherosclerotic Cardiovascular Disease

Figure 2: Utilization of Statin (HMG-CoA Reductase Inhibitor) Therapy for Secondary Prevention

NOTE: Lifestyle modification is an integral addition to any statin regimen (e.g. smoking cessation, weight loss, etc.)



Supplement 2
Cardiovascular Disease (ASCVD[§]) Risk Calculators

****UTILIZE FOR PRIMARY PREVENTION ONLY****

- **Framingham Heart Study:** Ages 30-74 y/o w/o CVD at baseline.
  - https://framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease- 10-year-risk/#
- **ACC/AHA Risk Estimator:** Ages 40-79 y/o w/o CVD at baseline.
  - http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/
- **MESA (multi-ethnic study of atherosclerosis):** Ages 45-85 y/o and in the following racial/ethnic groups- Caucasian, Chinese American, African American or Hispanic.
  - https://mesa-nhlbi.org?MESACHDRisk/MesaRiskScore/RiskScore.aspx
- **Reynolds Risk Score for Cardiovascular Risk:** Appropriate for women 45-80 y/o.
  - http://www.reynoldsriskscore.org (CAVEAT – asks for a hsCRP)
- **UK Prospective Diabetes Study (UKPDS) Risk:** Scoring System for Type 2 Diabetes.
  - https://www.dtu.ox.ac.uk/riskengine/

Supplement 3
Lab Monitoring

Prior to initiating statin therapy
- Lipid panel (fasting or non-fasting): consider fasting if family history of hypercholesterolemia or premature ASCVD[§]), LFTs, A1c (if DM status unknown), CK (if indicated).

Upon initiation of statin therapy
- FLP 4-12 weeks after initiation and every 3-12 months thereafter.

Utilization of lipid panel (in particular LDL-C)
- To make an assessment regarding when to initiate statin therapy for primary prevention (see Table 1).
- To make an assessment regarding appropriateness of statin dosing and necessity of adjunct therapy with other non-statin lipid-lowering agents (see Supplement 6).

Supplement 4
General LDL-C Goals

- Primary Prevention: <70-<130mg/dL (NOTE: Diabetic patient with risk assessment of >20% OR a patient with a history of familial hypercholesterolemia would have an LDL-C goal at the lower end of the range [<70mg/dL]).
- Secondary Prevention (lower risk of repeat event): <70mg/dL
- Secondary Prevention (higher risk of repeat event) – e.g. progressive ASCVD[§] including unstable angina after achieving an LDL-C <70mg/dL OR hx of premature ASCVD[§] [<55 male, <65 female]): <55mg/dL.

Supplement 5
Relative Statin Equipotency

Low Intensity
- Simvastatin 10 mg PO HS
- Pravastatin 10-20 mg PO HS
- Lovastatin 20 mg PO HS
- Fluvastatin 20-40 mg PO HS
- Atorvastatin 5 mg PO daily

Moderate Intensity
- Atorvastatin 10-20 mg PO daily
- Rosuvastatin 5-10 mg PO daily
- Simvastatin 20-40 mg PO HS*
- Pravastatin 40-80 mg PO HS
- Lovastatin 40-80 mg PO HS
- Fluvastatin XL 80 mg PO daily
- Fluvastatin 40 mg PO BID
- Pitavastatin 1-4 mg PO daily

High Intensity
- Atorvastatin 40-80 mg PO daily
- Rosuvastatin 20-40 mg PO daily

*Simvastatin doses above 40 mg/day are not recommended due to increased risk of myopathy/rhabdomyolysis. Patients who have been maintained on simvastatin 80 mg/day for more than 12 consecutive months without evidence of myopathy and are not currently taking or initiating a medication that interacts with simvastatin may continue 80 mg/day dosing.

Supplement 6
Alternative Therapy/Augmenting Therapy to Reach Treatment Goals

- TG (goal <150mg/dL): If persistently elevated after initiating statin therapy, consider adding a fibrate and/or initiating omega-3.
- LDL: If still above goal after a trial of the highest tolerated dose of high-intensity statin, consider ezetimibe and/or a PCSK9i (Praulent® or Repatha®).
- HDL (desired >40mg/dL in males; >50mg/dL in females):
  - Do not target specifically with pharmacotherapy; consider dietary modifications. HDL can also be increased by statin, fibrate, and/or ezetimibe therapy.

Caveats for Niacin therapy
- Proposed to have pleiotropic effects on cholesterol (NOT endorsed by current ACC/AHA guidelines as an adjunct to statin therapy).
- If a patient is wanting to utilize a niacin product; he/she needs to use nicotinic acid OR niacin only (niacinamide and other OTC "flush-free" formulations have no activity on lipids but act as vitamin B3 supplementation only).

Caveats for CoQ10
- Some literature suggests benefit to adding CoQ10 to statin therapy to help ameliorate statin-induced myopathies (increase tolerability).
- Studies examining the ability of CoQ10 to actually lower lipid levels are inconclusive.

Supplement 7
Alternative Dosing Strategies/Techniques to Mitigate Statin Intolerance

- Dose with maximum tolerated statin intensity every other day, 3x/week, or as frequently as tolerated.
- Consider a drug holiday (stop statin therapy and restart at a lower dose).
- Change statin (hydrophilic vs lipophilic. See Supplement 8).
- Correct underlying medication issues (potential medication source of lipid abnormalities?)
- Evaluate non-statin medications for propensity to cause muscle weakness/pain and change to alternative therapies if possible.

Supplement 8:
Hydrophilic vs Lipophilic Statin Therapy

Hydrophilic = pravastatin, rosuvastatin and pitavastatin
- Potential lower risk of myalgias due to reduced tissue absorption.
- Lower liver dependence for metabolism (theoretically FEWER drug-drug interactions).

Lipophilic = atorvastatin, fluvastatin, lovastatin and simvastatin
- Potential higher risk of myalgias due to greater tissue absorption (less risk of injury with lower doses).
- Higher liver dependence for metabolism (theoretically MORE drug-drug interactions).

Supplement 9
Patient Counseling Points

- Statins significantly reduce mortality.
- Statins significantly reduce ASCVD[§] risk
- Relatively low incidence of statin ADRs
  - 9-20% incidence of myopathy
  - Statin muscle pain typically generalized and accompanied by lab abnormalities (e.g. CK elevated 10x ULN)
- Any statin usage is better than avoiding completely (see Supplement 7).
- Take lower intensity statins at bedtime for maximum benefit (see Supplement 5).

Sources

Arnett, D. et al. Clinical Practice Guideline: 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease. Journal of the American College of Cardiology, 74(10): e177-e232. doi:10.1016/j.jack.2019.03.010

Awad, K, et al. Efficacy and Safety of Alternate-Day Versus Daily Dosing of Statins: a Systematic Review and Meta-Analysis. Cardiovascular Drugs and Therapy. doi: 10.1007/s10557-017-6743-0

Brinton, E. Understanding Patient Adherence and Concerns with Statins and Medication Discussion with Physicians (ACTION): A survey on the patient perspective of dialogue with healthcare providers regarding statin therapy. Clinical Cardiology, 41:710-720, doi: 10.1002/clc.22975

Driver, S. et al. Fasting or Nonfasting Lipid Measurements: It Depends on the Question. Journal of the American College of Cardiology. doi: https://doi.org/10.1016/j.jacc.2015.12.047

Grundy SM, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation, 139: e1082-e1143. doi:10.1161/cir.0000000000000625

Grundy, SM, et al. 2018 Guideline on the Management of Blood Cholesterol: Guidelines Made Simple (a selection of tables and figures). J Am Coll Cardiology. doi: 10.1016/j.jacc.2018.11.003

Jellinger, P. et al. AACE 2017 Clinical Practice Guidelines for Managing Dyslipidemia & Prevention of CVD. Endocrine Practice, 23 (2). doi: 10.4158/ep171764.appgl

Konstantinos, A. et al. Summarizing the Current State and Evidence on Efficacy and Safety of Statin Therapy. American College of Cardiology. https://acc.org/latest-in-cardiology/articles/2016/11/17/09/03/summarizing-the-current-state-and-evidence-on-efficacy-and-safety-of-statin-therapy. Accessed 1/29/2019

Qu, H, et al. Effects of Coenzyme Q10 on Statin-Induced Myopathy: An Updated Meta-Analysis of Randomized Controlled Trials. Journal of the American Heart Association. doi: https://doi.org/10.1161/JAHA.118.009835

Riddle, M, et al. Diabetes Care, Vol 42, S1. doi: 10.2337/dc19-sint01