



## To Statin or Not to Statin

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### Background

#### Statins – A Brief Prelude

- Statins entered common use in the 1990s, as a drug that could reduce the risk of heart attack and stroke by 20 to 30 percent.
- Statin therapy is most commonly used for lowering cholesterol and risk reduction of cardiovascular disease.
- Statins also have pleiotropic effects: reduces inflammation, improves endothelial function, and has anti-oxidant and anti-inflammatory properties.

#### Increased Life Expectancy & the Burden Of Atherosclerotic Cardiovascular Disease

- At age 65, life expectancy is currently estimated to be >20 years for women and >17 years for men in most high-income countries.
- The prevalence of coronary heart disease – the most prevalent form of atherosclerotic cardiovascular disease (ASCVD) – in the United States will increase by as much as 43% (about 5 million more) by the year 2030, with an estimated cost of about \$70 billion.
- The burden of atherosclerotic cardiovascular disease (ASCVD) in high-income countries is mostly borne by the elderly.

#### What Is Known?

- Statins make sense for adults of any age who already have heart disease, who have suffered a heart attack or stroke, or who have had arteries unblocked with a procedure like stenting. This is called secondary prevention.
- In 2013, the American College of Cardiology and the American Heart Association issued a series of statin recommendations for primary prevention, relevant to adults up to age 75 who have high cholesterol or diabetes, or who for other reasons face an estimated 7.5 percent risk or greater of developing heart disease within 10 years.
- In 2016, the US Preventive Services Task Force similarly recommended statins for primary prevention in people aged 40 to 75 who had risk factors like high cholesterol, diabetes, high blood pressure or smoking, with a 10- year disease risk of 10 percent or greater. For people over age 75, both panels agreed, there was not sufficient evidence to reach a conclusion.

### **Statin Use In Older Adults**

- With increasing life expectancy, clear guidance on sensible use of statin therapy to prevent a first and potentially devastating ASCVD event is critically important to ensure a healthy aging population.
- There is a great number of studies investigating the effect of statins on CVD morbidity and mortality; however, most of the studies included younger/middle aged subjects, while the elderly were investigated in subgroups analyses. The result - small amounts of data about statin effect on CVD risk in the elderly.
- This data does not allow for the adequate implementation of current guidelines in older patients with multiple CVD risk factors and chronic health conditions. Thus, there are unanswered clinical problems in the management of CVD risk in the elderly.

### **Consider The Side Effects**

- Older adults have a higher incidence of chronic kidney disease (CKD) and some statins are metabolized by the kidneys. Apart from atorvastatin, the other statins cannot be administered or their dose should be adjusted to GFR.
- In 2012, the US FDA issued safety label changes suggesting possible a risk of cognitive impairment after statin treatment. That data does not support cognitive decline as a drug class effect.
- Estimates reveal 30 percent of statin takers experience myalgia – muscle aches sometimes present with fatigue. Myalgia reverses when people stop taking statins. Still, many older people already struggle to remain mobile and perform daily tasks.
- Older adults often take multiple drugs. Statins interact with many of them, including proton pump inhibitors, blood pressure and heart medications and many antibiotics.

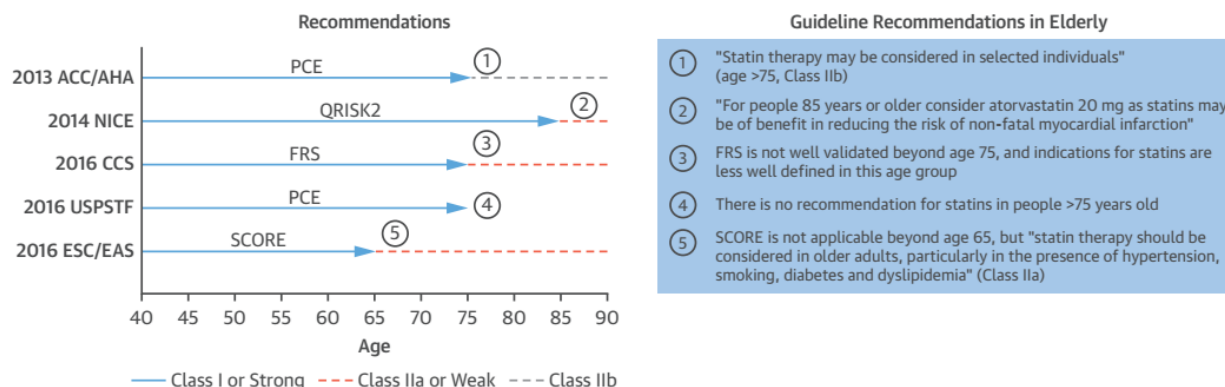
### **Primary Prevention**

- Current guidelines recommend statins for primary prevention — but only for those up to age 75. Yet, almost half of adults aged 75 and older take statins, per Centers for Disease Control and Prevention.
- Since 2013, 5 major North American and European guidelines on statin use in primary prevention of ASCVD have been released by the American College of Cardiology/American Heart Association, the UK National Institute for Health and Care Excellence, the Canadian Cardiovascular Society, U.S. Preventive Services Task Force, and the European Society of Cardiology/European Atherosclerosis Society. Guidance on using statin therapy in primary ASCVD prevention in the growing elderly population (>65 years of age) differs markedly in treatment recommendations and clinical practice.
- Until more evidence is available for those individuals >75 years of age, initiation of primary prevention with statins in this age group must be based on well informed shared decision making.

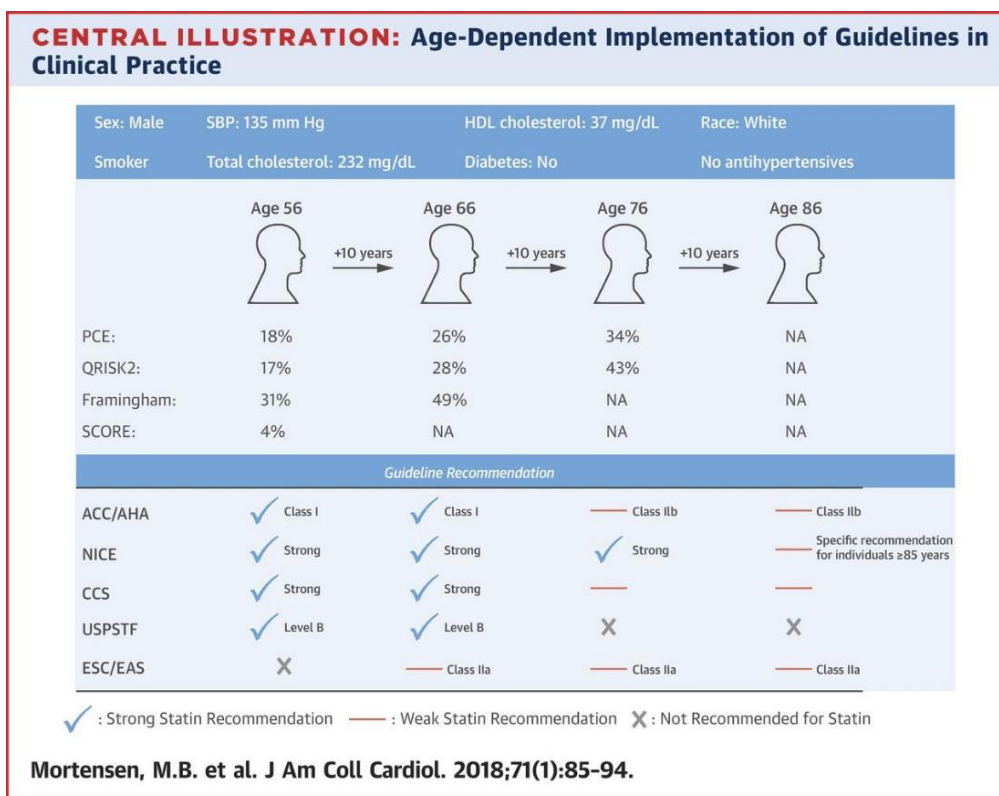
### **Secondary Prevention**

- The first secondary CVD prevention study (patients with or at high-risk of developing CHD or stroke) that included only elderly individuals was the PROspective Study of Pravastatin in the Elderly at Risk (PROSPER) trial, published in 2002.
- The study followed 5,800 patients for three years and found that pravastatin provided secondary, but not primary prevention, against cardiovascular events. These results suggest that statins are beneficial in the elderly for secondary prevention.

**FIGURE 1 Recommendations for Primary Prevention With Statins in Apparently Healthy People**



Handling of individuals >65 years of age differs substantially among contemporary European and North American guidelines, partly because of the performance (applicability) of the risk model used. ACC/AHA = American College of Cardiology/American Heart Association; CCS = Canadian Cardiovascular Society; ESC/EAS = European Society of Cardiology/European Atherosclerosis Society; FRS = Framingham Risk Score for general cardiovascular disease; NICE = National Institute for Health and Care Excellence; PCE = pooled cohort equation; SCORE = Systematic COronary Risk Evaluation; USPSTF = U.S. Preventive Services Task Force.



## The Bottom Line

### Individuals At High Risk Or For Secondary Prevention

- Statins make sense for a select group of people- those who have clinically diagnosed ASCVD or stroke, or who have had arteries unblocked with a procedure like stenting.
- The decision about statin administration in elderly at high CVD risk should be always based on the patient's general health and on the presence of comorbidities or drug interactions that increase the risk of adverse events.
- For nursing home residents, the seriously ill, or for elders who are frail, have life-limiting diseases, or are already on daunting number of prescriptions, statins do not make much clinical sense.

### Statins For Primary Prevention

- For others who merely have high LDL, prescribing statins is dubious, considering comorbidity, polypharmacy, potential side effects, and limited life expectancy.
- In primary prevention, discontinuing statin therapy is reasonable to consider in elderly, frail people with low chance of benefit because of limited life expectancy.
- The main goal of primary prevention with statins is to achieve net-benefit from treatment. As frailty, comorbidity, and polypharmacy may increase the risk for adverse statin-associated symptoms, the "risk-benefit" balance in the elderly could theoretically tip in favor of withholding statin therapy.