

# Low Right Care

## Reducing Overuse and Underuse

### Overuse of Statins in Older Adults

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#### Case Scenario

Mr. G is an 83-year-old man who lives alone with some assistance from family members. He has well-controlled hypertension, hyperlipidemia, and arthritis. His maximum low-density lipoprotein (LDL) cholesterol level is around 135 mg per dL (3.50 mmol per L). He uses a walker and has fallen several times in the past year, sustaining a wrist fracture. He had a coronary stent placed 15 years ago for asymptomatic coronary artery disease (CAD) that was detected after an exercise stress test. He has visited a cardiologist since the stent placement and is taking 80 mg of atorvastatin (Lipitor) per day to reduce his LDL cholesterol to below 80 mg per dL (2.07 mmol per L). His family physician is uncertain if Mr. G benefits from the high-dose statin because his primary two symptoms are fatigue and muscle weakness. Mr. G's cardiologist feels that the dose is appropriate, and that his symptoms are not related to the statin. Mr. G's family physician plans to keep him on a statin indefinitely, because statins are required for anyone older than 21 years with a diagnosis of CAD according to the Centers for Medicare and Medicaid Services quality indicator #438.

#### Clinical Commentary

The 2018 American College of Cardiology/American Heart Association guideline states that it may be reasonable to initiate or continue moderate- to high-dose statin therapy for secondary prevention and initiate moderate-dose statin therapy for primary prevention in people older than 75 years if they have an LDL cholesterol level of 70 to 189 mg per dL (1.81 to 4.90 mmol per L). For primary prevention, this means that 18 million older adults could be eligible for

a statin.<sup>1</sup> However, there are few data about the impact of statins on longevity, cardiac outcomes, and muscle strength in adults older than 75 years.

#### PRIMARY PREVENTION IN PATIENTS WITHOUT RISK FACTORS FOR CAD

No study has shown an impact of statins on cardiovascular outcomes among older adults without preexisting CAD or significant risk factors. The U.S. Preventive Services Task Force guideline states that current evidence is insufficient to assess the balance of benefits and harms of statins in people older than 75 years who have no history of stroke or heart attack.<sup>2</sup> For people 65 to 75 years of age with one or more risk factors, the U.S. Preventive Services Task Force recommends that clinicians selectively prescribe statins for those with at least one risk factor and a 7.5% to 10% risk of a cardiovascular event in 10 years.<sup>3</sup> The ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) evaluated the use of pravastatin (Pravachol) for primary prevention in adults older than 65 years who had high cholesterol.<sup>3</sup> The study found no improvement in CAD or mortality in the pravastatin arm despite decreases in LDL cholesterol. There was also a trend toward higher mortality with statins in those older than 75 years. Subgroup analyses of people older than 75 in other studies have shown variable benefits of statins on cardiovascular outcomes and no reductions in mortality.<sup>4</sup>

Many older people are prescribed statins for primary prevention despite potential adverse effects and no evidence of effectiveness. In a study of patients older than 80 years in an integrated health system, 22% of them received a statin, 71% of whom were at low risk of CAD (primary prevention), and most of whom were treated to LDL levels of 90 mg per dL (2.33 mmol per L) or lower.<sup>5</sup> A national survey showed that the percentage of older people treated with statins for primary prevention increased from 8.8% in 2000 to 34% in 2012.<sup>4</sup>

#### SECONDARY PREVENTION

There is some evidence that statins can reduce cardiac events without necessarily improving longevity for older people with a history of CAD or at very high risk of CAD. The 2002 PROSPER (Pravastatin in Elderly Individuals at Risk of Vascular Disease) study is the only randomized prospective analysis of secondary prevention in older persons.<sup>6</sup> A total

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**CME** This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 738.

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## TAKE-HOME MESSAGES FOR RIGHT CARE

No study has shown an impact of statins on cardiovascular outcomes among older adults without preexisting CAD or significant risk factors.

The U.S. Preventive Services Task Force guideline states that current evidence is insufficient to assess the balance of benefits and harms of statins in people older than 75 years who have no history of stroke or heart attack.

There is no definitive evidence that statins can prevent future CAD or death for people with CAD who are older than 80 years.

Statins may cause muscle pain or weakness and increase fall and fracture risk in older persons.

CAD = coronary artery disease.

of 5,804 patients 70 to 82 years of age with a history of CAD were randomized to 40 mg of pravastatin per day or placebo and were followed for three years. The primary endpoint (composite of cardiovascular death, myocardial infarction, and stroke) occurred in 21 out of 1,000 fewer pravastatin users compared with those using placebo (number needed to treat [NNT] = 48); however, there was no reduction in overall mortality.<sup>7</sup> When patients in the PROSPER study were followed for eight years, those taking pravastatin had no reduction in cardiovascular mortality, myocardial infarction, or death compared with those taking placebo.<sup>8</sup>

A recent retrospective cohort study that researched the impact of statins on older people with diabetes mellitus showed a small statin benefit in those 75 to 85 years of age.<sup>9</sup> Over 10 years, 1.8 out of 1,000 fewer statin users developed CAD compared with those using placebo (NNT = 556), and 13 out of 1,000 fewer statin users died (NNT = 77). There was no benefit for people older than 85 years.

A Bayesian meta-analysis of people older than 65 who had an active diagnosis of CAD also showed a small statin benefit over five years (NNT = 385 to prevent one CAD diagnosis; NNT = 323 to prevent one death).<sup>10</sup> However, few people in this study were older than 80 years.

### ADVERSE EFFECTS

The most commonly reported adverse effect of statins is muscle pain. Although the PROSPER study reported a 1% incidence of myalgia,<sup>11</sup> other studies have reported that muscle pain significantly impacts about five out of 100 more statin users than those not on statins (number needed to harm = 20).<sup>12-14</sup> Reports of muscle pain in clinical studies tend to be less common compared with experiences in community practice. There is some evidence that people who exercise experience more myalgias, and that women, the very old, and people with renal or hepatic abnormalities are underrepresented in most studies and experience more myopathy.<sup>11,15</sup> Statins can cause increased fatigue<sup>16</sup> and muscle weakness, which are adverse effects rarely reported in the literature. One analysis reported more falls and fractures in those taking statins who were older than 80 years.<sup>17</sup> A meta-analysis of 13 statin trials found that statins slightly increase the risk of incident diabetes, although the clinical significance of this finding for older adults is unclear.<sup>18</sup>

### Resolution of Case

Although the Centers for Medicare and Medicaid Services guidelines mandate the use of a statin for Mr. G because of his distant history of CAD, the evidence does not support a benefit from continuing a high-dose statin, which could increase his risk of adverse effects. In addition, although Mr. G has no muscle pain, he has muscle weakness and fatigue. After a shared decision-making discussion, Mr. G and his family decide that the uncertain, but likely small, potential benefit of

atorvastatin use does not outweigh the potential harms given his clinical situation. He chooses to stop taking the drug.

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