



Advisory Committee Update

Date: 7/17/23

Subject: De-Prescribing

Statin De-Prescribing

Should I de-prescribe statins for primary prevention in my elderly patients?

As we review the medication lists of our older patients - especially those on more than five regular medications (the definition of polypharmacy) - we may consider de-prescribing a statin used for primary prevention. Why?

1. *To decrease polypharmacy and associated harm risk*
2. *To comply with a patient's wish to be on fewer meds*
3. *To avoid adverse effects* - muscle pain is the most common, but other adverse effects have been associated with statins. Here is a summary of the UpToDate article on this topic:

What other adverse effects are associated with statins?

- *Diabetes* - high-intensity statins may increase risk for diabetes, but this risk seems confined to patients with risk factors for developing diabetes.
 - *Renal dysfunction* - statins increase proteinuria (especially rosuvastatin and simvastatin) although this is thought to be benign according to UpToDate. There is convincing evidence that statins are associated with improved mortality in chronic kidney disease.
 - *May increase fatigue* - in one randomized study of the effect of statins on energy and fatigue, pravastatin and simvastatin were associated with reduced energy levels and increased fatigue, especially in women.
 - *Do statins cause cognitive decline?* There are rare case reports of severe irritability after starting statins, and case reports of memory loss with lipophilic statins (simvastatin, atorvastatin, lovastatin, fluvastatin). However, some large retrospective studies show statins may lower risk for dementia - possibly due to decreasing amyloid production in the brain, and/or reducing strokes.
4. *To stop a medication whose benefit has not been established with strong evidence*
 - Although there is evidence to support the use of statins for secondary prevention in adults >75, the evidence supporting use for primary prevention in this group is mixed.

- Current studies are underway to evaluate how starting a statin for primary prevention in adults >70-75 affects survival, physical disability, cardiovascular events, and dementia.
- However, the question of whether statins should be started in this group is different from whether statins should be stopped

Are there harms associated with de-prescribing in this situation? What studies have been done to evaluate de-prescribing statins for primary prevention in the elderly?

- **One small RCT** looked at statin discontinuation in patients with life expectancy of <1 year with primary end point of mortality at 60 days. There was no difference in mortality between the two groups. Those who stopped statins had a small increase in quality of life.¹
- **Three observational cohort studies** have shown increased incidence of various negative outcomes associated with stopping statins
 - A retrospective cohort study of 29,000 elderly (average age 76) taking statins with other meds (for diabetes, HTN, antiplatelet) for at least 2 years then followed for another three years. 5800 stopped statins and were matched with a comparator. Compared with the maintaining group, patients in the discontinuing group had increased risk of hospital admissions for heart failure, deaths from any cause, and emergency admissions.²
 - A cohort study of 27,000 elderly taking statins at least 5 years (avg age 79) found increased incidence of adverse cardiovascular events (MI, stroke, TIA, death due to MI/stroke) in those who stopped statins. There was 1 extra major adverse cardiovascular event for every 112 who stopped. Follow-up period was five years.³
 - Population-based cohort study followed 120,000 people aged 75 for 2.5 years. 14% stopped statins and had a 33% increased risk of admission for a cardiovascular event.⁴

The bottom line on the evidence - No evidence currently exists to support stopping statins for primary prevention in older adults with life expectancy >1 year. Existing evidence suggests there may be harms associated with stopping statins and that the increased risk of cardiovascular events may be greatest in the first 6 months after a statin is stopped.

¹ Kutner, J. S., Blatchford, P. J., Taylor, D. H., Jr, Ritchie, C. S., Bull, J. H., Fairclough, D. L., Hanson, L. C., LeBlanc, T. W., Samsa, G. P., Wolf, S., Aziz, N. M., Currow, D. C., Ferrell, B., Wagner-Johnston, N., Zafar, S. Y., Cleary, J. F., Dev, S., Goode, P. S., Kamal, A. H., Kassner, C., ... Abernethy, A. P. (2015). Safety and benefit of discontinuing statin therapy in the setting of advanced, life-limiting illness: a randomized clinical trial. *JAMA internal medicine*, 175(5), 691–700. <https://doi.org/10.1001/jamainternmed.2015.0289>

² Rea F, Biffi A, Ronco R, et al. Cardiovascular Outcomes and Mortality Associated With Discontinuing Statins in Older Patients Receiving Polypharmacy. *JAMA Netw Open*. 2021;4(6):e2113186. doi:10.1001/jamanetworkopen.2021.13186

³ Thompson W, Morin L, Jarbøl DE, et al. Statin Discontinuation and Cardiovascular Events Among Older People in Denmark. *JAMA Netw Open*. 2021;4(12):e2136802. doi:10.1001/jamanetworkopen.2021.36802

⁴ Philippe Giral and others, Cardiovascular effect of discontinuing statins for primary prevention at the age of 75 years: a nationwide population-based cohort study in France, *European Heart Journal*, Volume 40, Issue 43, 14 November 2019, Pages 3516–3525, <https://doi.org/10.1093/eurheartj/ehz458>

However, the existing evidence is limited (only four studies, three of which were cohort studies). In the cohort studies, we do not know why patients stopped statins. Previous data has shown statins are more likely to be discontinued in frail patients. If those who stopped statins were more frail than their matched cohorts, that would explain why they were at higher risk of negative outcomes.

More data to come – an RCT is currently underway to evaluate deprescribing statins for primary prevention in those >75.

My takeaway - at this time, I am not inclined to stop a statin in a patient who is tolerating it well unless there is a compelling reason (such as limited life expectancy or strong patient preference after discussion). If I did stop a statin, I would taper it.

Sarah Tsang, MD

De-prescribing Advisory Committee Member
