

# Findings

## Review Questions Evidence on Statins for Non-CVD Outcomes

There is a “dearth of convincing evidence” that lipid-lowering treatment with statin drugs plays any major role in improving outcomes other than cardiovascular disease (CVD), concludes a review and meta-analysis in *Annals of Internal Medicine*.

The researchers report an “umbrella” review of 268 previous meta-analyses of data on non-CVD outcomes of statin treatment. Their review identified 144 papers reporting 297 meta-analyses of randomized controlled trials (RCTs) and 112 papers reporting 268 meta-analyses of observational studies. The analysis examined a total of 278 unique non-CVD outcomes. It included credibility assessments incorporating summary effect sizes, study heterogeneity, 95% prediction intervals, study size, and significance bias.

On analysis of RCT data, there was only one significant statin-related non-CVD outcome with a sufficient amount of evidence and no sign of bias: reduced all-cause mortality in patients with chronic kidney disease. Analysis of observational data found no “convincing” associations and two “suggestive” associations: decreased cancer mortality in patients with cancer and decreased exacerbation rate in patients with chronic obstructive pulmonary disease. The observational data also showed “weak” associations for 42 additional non-CVD outcomes.

Analysis of adverse events in the RCT data found no effects of statins on risks for myopathy, myalgia, or rhabdomyolysis. For the observational studies, there was “suggestive” evidence for increased risks of diabetes and myopathy.

Statins have well-demonstrated benefits in reducing the risk of heart disease and stroke. Although many studies have suggested that statins can improve various non-CVD outcomes, the evidence supporting these benefits is less clear.

Only a few of the reported effects of statins on non-CVD outcomes show convincing evidence of a credible association, according to the umbrella review of existing meta-analyses. Even the reduction in all-cause mortality in chronic kidney disease might be attributable to CVD events, the authors suggest. They conclude that their findings “do not support any change in the existing clinical recommendations regarding statin use for non-CVD conditions” [He Y, et al. Statins and multiple noncardiovascular outcomes: umbrella review of meta-analyses of observational studies and randomized controlled trials. *Ann Intern Med* 2018; 169:543–553]. ■

## No Increase in CKD Risk with Allopurinol for Gout

For patients with gout, starting urate-lowering therapy with allopurinol does not appear to lead to an increased risk of developing stage 3 or higher chronic kidney disease (CKD), reports a study in *JAMA Internal Medicine*.

Using a UK general practice database, the researchers identified two propensity-score matched groups of patients with newly diagnosed gout. One group of 4760 patients initiated urate-lowering treatment with allopurinol. The comparison group included the same number of patients who did not receive allopurinol. About 83% of patients in both groups were men. Mean age was 57 years and mean body mass index was 30. All patients had initially normal or

near-normal kidney function.

The main outcome of interest was the development of stage 3 or higher CKD. Mean follow-up was 5 years in patients who initiated allopurinol and 4 years in the comparison group.

Patients starting allopurinol at a dose of at least 300 mg/d were less likely to develop stage 3 or higher CKD: adjusted hazard ratio 0.87. There was little or no difference in the association after additional adjustment for the covariates included in the propensity score. At initial doses of less than 300 mg/d, allopurinol therapy showed no association with decline in renal function.

Only one-third of patients with gout receive urate-lowering therapy; the problem of undertreatment is compounded by frequent comorbidity with CKD. Physicians

are cautious about using allopurinol in patients with gout, especially those with declining renal function. There is a lack of data on the renal effects of allopurinol in gout patients with normal renal function.

This large study analysis of primary care data finds a reduced risk of stage 3 CKD among newly diagnosed gout patients starting on allopurinol, 300 mg/d or higher. The researchers discuss their findings in the context of the ongoing suboptimal treatment of gout. They conclude: “Because allopurinol does not appear to be associated with renal function decline, clinicians should consider evaluating other potential causes when patients with gout experience renal function decline” [Vargas-Santos AB, et al. Association of chronic kidney disease with allopurinol use in gout treatment. *JAMA Intern Med* 2018; 178:1526–1533]. ■

