



# When a Statin is Not Enough: the Use of Ezetimibe and PCSK9 Inhibitors in Hyperlipidemia

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## Background

Heart disease remains the leading cause of death worldwide. Statins lower low-density lipoprotein (LDL) cholesterol levels and reduce the risk of cardiovascular events, even in patients without cardiovascular disease.<sup>2</sup> However, many patients currently taking a statin remain at high risk for recurrent cardiovascular events including myocardial infarction, stroke, and death from cardiovascular disease.<sup>2</sup>

Ezetimibe can reduce the risk of cardiovascular events in patients with a history of acute coronary syndrome (ACS) who are already on statin therapy.<sup>2</sup>

The PCSK9 Inhibitors alirocumab and evolocumab can lower the risk of cardiovascular events in patients with a history of ACS or known atherosclerotic cardiovascular risk who are already on high-intensity or maximum tolerated statin therapy.<sup>3,4</sup>

## Objective

Identify research studies that compare statins as monotherapy to statins plus additional lipid lowering agents in people with hyperlipidemia and cardiovascular disease.

Increase the prescribing of ezetimibe and/or PCSK9 inhibitors by primary care providers for people with a high risk of cardiovascular adverse events.

## Methods

Search engines: CINAHL, PubMed, Medline

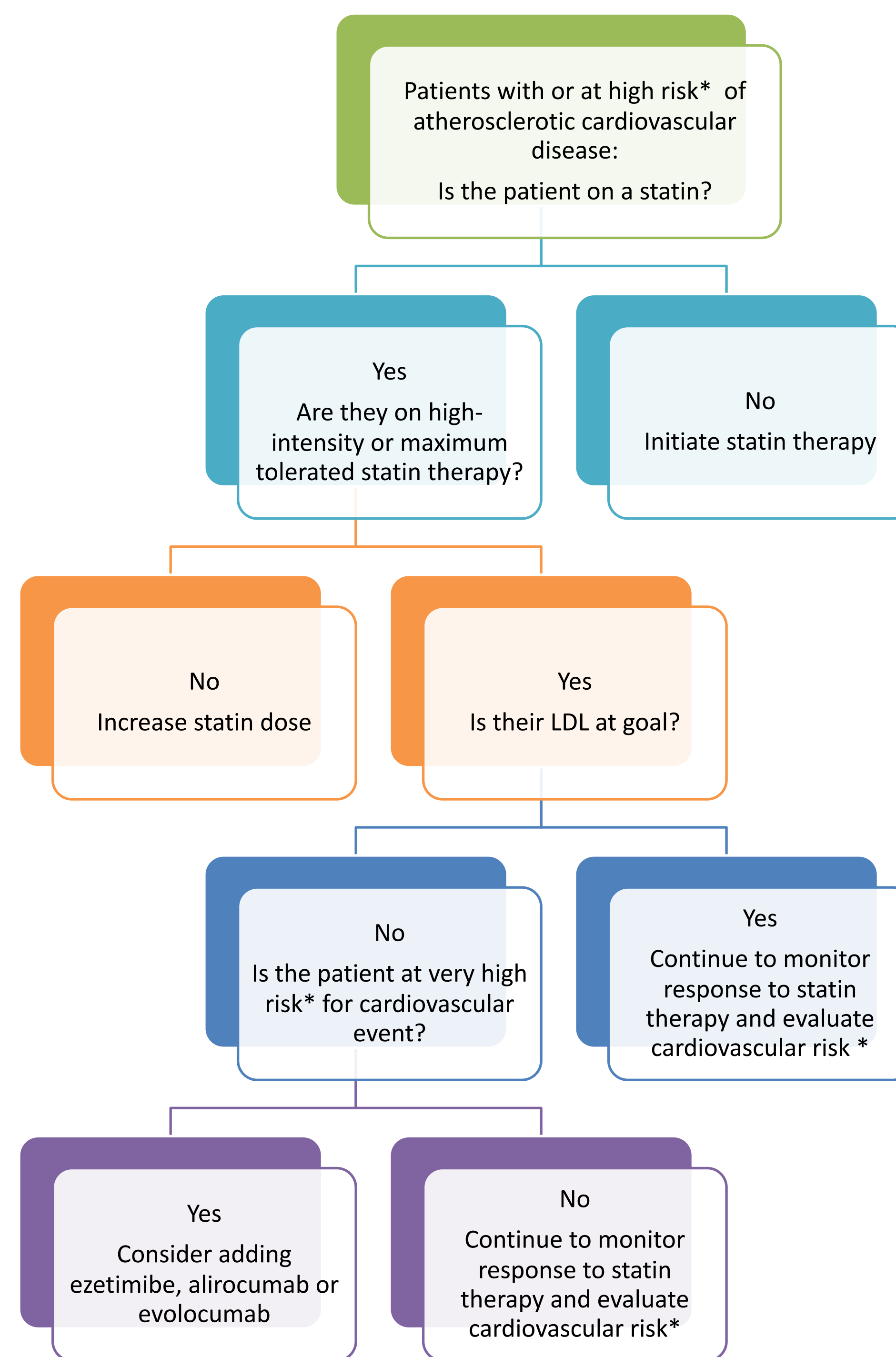
Search terms: hyperlipidemia, statins, ezetimibe, PCSK9 inhibitors

Inclusion criteria: Dates from 2015-2020, adults 18 years or older

Exclusion criteria: Statin intolerant patients, review articles

Results: 5 research articles

## Clinical Decision Making



\*consider patients with 3 or more of the following risk factors: age greater than or equal to 75 years, current smoking, estimated GFR less than 60 ml/min/1.73 m, history of diabetes mellitus, heart failure, hypertension, peripheral artery disease, stroke, or previous coronary artery bypass graft surgery.<sup>1</sup>

## Assessment of Current Practice

Patients at very high risk of recurrent cardiovascular events are most often treated with a high-intensity statin as monotherapy.<sup>5</sup> High-intensity or maximum tolerated statin therapy remains the first-line for patients with atherosclerotic cardiovascular disease.<sup>5</sup>

Primary care providers may not prescribe ezetimibe or PCSK9 inhibitors to high-risk patients on a high-intensity statin because of a lack of awareness of their benefits or due to the high cost of PCSK9 inhibitors in particular.<sup>5</sup>

## Recommendations for Providers

Adding ezetimibe or a PCSK9 Inhibitor to statin therapy provides the greatest benefit to patients at very high-risk of cardiovascular events.<sup>1,5</sup>

Providers should assist patients in finding patient assistance programs, such as GoodRx, to help patients better afford ezetimibe and/or PCSK9 inhibitors.

Further work is needed to assist providers in identifying patients at very high risk of cardiovascular events who would benefit from these additional therapies.<sup>1</sup>

One simple tool has identified high-risk patients who most benefitted from the addition of ezetimibe to statin therapy as those with at least 3 of 9 risk factors\*.<sup>1</sup> If this tool is further validated and effective for the addition of PCSK9 inhibitors as well, it could provide a quick and simple screening tool for clinicians.

## References

1. Bohula, E., Morrow, D., Giugliano, R., Blazing, M., He, P., Park, J., Murphy, S., White, J., Kesaniemi, Y., Pedersen, T., Brady, A., Mitchel, Y., Cannon, C., & Braunwald, E. (2017). Atherothrombotic Risk Stratification and Ezetimibe for Secondary Prevention. *JACC (Journal of the American College of Cardiology)*, 69(8), 911–921.
2. Cannon, C., Blazing, M., Giugliano, R., McCagg, A., White, J., Theroux, P., Darius, H., Lewis, B., Ophuis, T., Jukema, J., De Ferrari, G., Ruzyllo, W., De Lucca, P., Im, K., Bohula, E., Reist, C., Wiviott, S., Tershakovec, A., Musliner, T., ... Califf, R. (2015). Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. *The New England Journal of Medicine*, 372(25), 2387–2397.
3. Sabatine, M. S., Giugliano, R. P., Keech, A. C., Narimon, H., Wiviott, S. D., Murphy, S. A., ... Pedersen, T. R. (2017). Evolocumab and clinical outcomes in patients with cardiovascular disease. *The New England Journal of Medicine*, 376(18), 1713–1722.
4. Schwartz, G., Steg, P., Szarek, M., Bhatt, D., Bittner, V., Diaz, R., Edelberg, J., Goodman, S., Hanotin, C., Harrington, R., Jukema, J., Lecorps, G., Mahaffey, K., Moryusef, A., Pordy, R., Quintero, K., Roe, M., Sasiela, W., Tamby, J., ... Zeiher, A. (2018). Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. *The New England Journal of Medicine*, 379(22), 2097–2107.
5. Toyota, T., Morimoto, T., Yamashita, Y., Shiomi, H., Kato, T., Makiyama, T., Nakagawa, Y., Saito, N., Shizuta, S., Ono, K., & Kimura, T. (2019). More-Versus Less-Intensive Lipid-Lowering Therapy. *Circulation*, 12(8).