

Long-Term Use of Statins and Postmenopausal Breast Cancer Risk, By Subtype

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Approximately 25% of US women over the age of 45 currently use statins to prevent stroke and heart disease. Statins are highly effective in treating hyperlipidemia, or high levels of lipids in the blood, a risk factor for cardiovascular disease. However, some studies have suggested that they may be linked to breast cancer risk. Statins have only recently begun to be used on a broad scale, and although multiple meta-analyses have observed no association between statins and breast cancer, these analyses were limited in their ability to assess the effects of long-term statin use. Almost all previous studies of this question were conducted in populations with a very low frequency of long-term statin use (less than 3% of women had used statins for 5 or more years). The potential association with long-term use in particular is important, as statins are generally prescribed as a long-term treatment. Furthermore, little is known about the association between statins and the specific types of breast cancer.

Drs. Jean McDougall, Christopher Li, and colleagues in PHS addressed these questions among 1,984 invasive breast cancer cases (including 1,068 lobular and 916 ductal cases) and 902 controls ages 50-74 years in the Puget Sound region. Cases and controls were interviewed to ascertain detailed histories of lipid-lowering drug use prior to diagnosis (or prior to a similar assigned reference date among controls). Extra measures were taken to maximize recall accuracy, including asking women to bring bottles of their medications, and to identify past medications from photos of pills and bottles. Participants also provided information on breast cancer risk factors and on history of hyperlipidemia.

Women who reported using statins for the past 10 or more years had an 83% higher risk of invasive ductal breast cancer (95% confidence interval (CI) 1.1-2.9) and a doubled risk of invasive lobular breast cancer (95% CI 1.3-3.1) compared to women who had never used statins, after adjusting for age (5-year age categories), reference year, county, and use of menopausal hormone therapy. These associations were stronger when analyses were limited to cases and controls with hyperlipidemia, with a doubled risk of ductal (95% CI 1.2-3.6) and a 2.4-fold risk of lobular breast cancer (95% CI 1.4-4.2), compared to never-users. When analyses included all statin users (i.e. not

just long-term users), there was little evidence of an association, suggesting that if statins do increase the risk of breast cancer, they may only do so after a longer period of use. Analyses of the risk of specific types of breast cancer suggested that long-term statin use (10 or more years) is associated with a doubled risk of estrogen receptor (ER)-positive breast cancers (both ductal and lobular, 95% CIs 1.2-3.2 and 1.3-3.2, respectively) but not with ER-negative ductal breast cancer. This could be due to limited statistical power in the ER-negative ductal breast cancer analyses, or it may be that statins increase breast cancer via a hormonally mediated pathway.

Dr. McDougall commented that, if future studies also observe an increased risk of invasive ductal and lobular breast cancers associated with long-term statin use, this would “warrant further study [into] the biologic mechanism by which long term statin use could impact breast cancer risk.” She also cited a need for additional research, in order to determine “whether the excess risk of breast cancer could outweigh the benefits of statins for lowering cholesterol and reducing cardiovascular disease risk in some women.”

[McDougall JA, Malone KE, Daling JR, Cushing-Haugen KL, Porter PL, Li CI](#). 2013. Long-Term Statin Use and Risk of Ductal and Lobular Breast Cancer among Women 55 to 74 Years of Age. *Cancer Epidemiol Biomarkers Prev*. Aug 21. [Epub ahead of print]