

Statins provide protective immune benefits for females

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Pill bottle. Credit: CDC/Public domain

Cholesterol tends to get a bad rap through its association with cardiovascular disease. But its role in the body is much more nuanced.

When we have too much cholesterol, it can build up in the walls of our arteries and cause cardiovascular disease. But cholesterol molecules play

a critical role in our cells' structure and signaling pathways, and—as scientists are beginning to understand—[immune function](#).

Catherine Andersen, associate professor of nutritional sciences in the College of Agriculture, Health and Natural Resources, recently published her findings uncovering a new piece of this puzzle in *Frontiers in Medicine*. Andersen found that statins, commonly prescribed [lipid](#)-lowering drugs, provide a protective immune function in females.

Previous studies in cell and animal models showed that lipids play an important role in modulating immune cells, but there was little evidence of this relationship in humans.

To investigate this connection, Andersen looked to see if there was an association between serum lipid levels (which include measures of total cholesterol, HDL- and LDL-cholesterol, and triglycerides) and antinuclear antibodies (ANA). ANA are the most common type of autoantibodies, and serve as diagnostic and predictive markers of current or future autoimmune disease, in addition to cardiovascular disease and death. The presence of ANA can also be an indicator of immune activation or dysfunction in response to cell turnover or pathogens—including SARS-CoV2 infection, as ANA have been detected in COVID-19 patients with worse prognoses.

"We wanted to start out by seeing if there was an association between serum lipids and [antinuclear antibodies](#)," Andersen says. "Having really elevated lipid levels can prime our [immune cells](#) to be more reactive. And there's some evidence in animal studies that really high lipid levels can induce autoimmunity."

Andersen did not find a strong association between serum lipid levels and ANAs, so she considered another variable: statin use.

The effects of statin use in autoimmunity is controversial. While some studies report anti-inflammatory benefits of statins in populations with autoimmune conditions, other studies suggest that statins may promote the development of autoimmune disorders. So, Andersen was surprised to see that statin use had a beneficial effect for women, but not men. Women taking statins were 75% less likely to be ANA+ than those who did not.

Andersen says this finding is especially significant because historically, drug trials have used predominantly male participants. This means females often experience more severe or unexpected side effects.

"I think that's really important because women tend to have more adverse reactions to statins," Andersen says. "Oftentimes, adherence to [statin treatment](#) might not be as strong [among women] because they experience more side effects, and they might not feel as heard when they go to their physician to express their concerns."

Andersen did not find any significant differences in this relationship for women across race/ethnicity and educational level.

"That's something that's as important to include," Andersen says. "Because when we're drawing conclusions and saying that one therapeutic treatment may be beneficial to women, we do want to ensure that we're really basing this on a diverse sample and our conclusion would be applicable to all or as many populations as [possible]."

This study was only looking at the correlation between [statin use](#) and ANAs. Andersen says potential follow-up studies may help identify what causes this sex-specific phenomenon.

"I think, to date, the research has been siloed," Andersen says. "We know that there are sex-specific differences in the immune response. We

know that there are sex-specific differences in [lipid metabolism](#). But the relationship between lipid metabolism and immune response? There has been much more limited investigation, especially in humans, to elucidate how these lipid-immune interactions might be different—or how traditional cardiovascular drugs that are targeting lipid metabolism might confer benefit to males versus females within the context of immunity in different ways. I think it certainly warrants more investigation and our study supports that."

Andersen is now looking to use the same data from the National Health and Nutrition Examination Survey to look at infection outcomes, and if certain dietary patterns can bolster the relationship between lipid metabolism and immunity.

More information: Catherine J. Andersen et al, Sex-Specific Associations Between Serum Lipids, Antinuclear Antibodies, and Statin Use in National Health and Nutrition Examination Surveys 1999–2004, *Frontiers in Medicine* (2022). [DOI: 10.3389/fmed.2022.887741](https://doi.org/10.3389/fmed.2022.887741)

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