



Can statins cause harm?

There is research evidence that when patients describe adverse effects, doctors often don't recognize that certain harms are caused by statins. This can put patients at greater risk. Here is some of what is currently known about the harms that statins can cause:

Miscarriages, birth defects and infant developmental delays

Statin use has been linked to miscarriages and birth defects, as well as to problems in infant development for breastfed babies whose mothers were taking statins. Since almost half of all pregnancies are unplanned, women of reproductive age who are taking statins need to be very cautious.

Health Canada warns that women intending to get pregnant, those who are already pregnant, those nursing, and those intending to nurse, as well as all women of potential childbearing age, *should not take statins* unless they consult with their physicians. Recent research from the U.K. warns that all types of statins are equally risky during pregnancy.

Muscle and cognitive problems

In 2001, the statin Baycol was withdrawn from the market after it was linked to at least 50 deaths worldwide from rhabdomyolysis—a serious and potentially fatal muscle disorder. In 2005, Health Canada notified health practitioners and health consumers that *all statins* may increase the risk for rhabdomyolysis. Crestor, in particular, poses a risk for rhabdomyolysis, particularly for Asians taking the medication. Health Canada further advises that those on Crestor should take the lowest possible dosage.

Additional research, summarized in a 2008 overview, indicates problems with chronic muscle pain and cognitive functions, difficulty walking, weakness, and exercise intolerance.

Recent warnings from health regulators in New Zealand, Australia, and the U.K. have linked statin exposure to sleep disturbances, memory problems, depression, lung problems, and variations in mood, including severe irritability and aggressive behaviour.

Other effects

A 2008 trial indicated an increase in diabetes among statin users. Other pancreatic problems have also been noted.

Hormone therapy and oral contraceptives

Most research on statin use has not examined the effect of taking statins in combination with other pharmaceutical drugs. This is significant because many women taking statins are post-menopausal and may also be taking hormone therapy.

Hormone therapy, like statins, has been shown to lower cholesterol levels in women. But recent studies have shown that it may actually increase the risk for heart disease. For this reason, hormone therapy is no longer recommended for the prevention of heart disease and only the smallest dosage for the shortest duration is recommended to relieve

menopausal symptoms, such as hot flashes. Some researchers have expressed concern about an increase in breast cancer risk associated with the combination of hormone therapy and statins.

We also do not know if there are risks associated with taking statins at the same time as oral contraceptives (birth control pills). Since women typically take both drugs for many years, this is an area where more research is needed.

Other risks remain unknown

Most studies to date have only reported on rates of death from heart disease, but not other illnesses or causes of deaths that may or may not be related to statin use. In other words, we do not yet have enough published evidence to know if there are other risks or harms associated with long-term use of statins.

Health Canada keeps a database of health problems that are believed to be caused by pharmaceutical drugs. As of November 2006, there were almost 6,000 reports (half from women) of health problems believed to be linked to statin use; 195 of these reports linked statin use with premature death.

Evidence for caution What women need to know about statins

Statins are a class of prescription drugs that lower cholesterol. The statins currently available in Canada include Lipitor, Crestor, Mevacor, Pravacol, Zocor and Lescol. Approximately three million Canadians take statins daily, and the statin Lipitor is the top selling pharmaceutical in the country.

Doctors recommend statins to lower the risk of heart disease for primary prevention (where patients have not experienced a heart attack or stroke, but are thought to be at risk) and secondary prevention (where patients have already survived a heart attack or stroke).

Statins are one of the most common drugs prescribed *to women* for the prevention of heart disease. Yet most of the clinical trials to assess their benefits and safety have focused *on men*. In fact, for women who have no history of heart disease, *there is no substantial clinical trial evidence that statins reduce the number of heart events or deaths in women of any age.*

In addition, the safety profile of statin use in women is disturbing, with links to higher risks for miscarriages, birth defects and infant development problems in women of childbearing age, and a possibility that statin use may increase the risk of breast cancer. Health Canada has warned that all statins may increase the risk for rhabdomyolysis—a rare, but serious and potentially fatal muscle disorder. And there is not yet enough evidence to know if there are other risks or harms associated with long-term use of statins.

In sum, there is no high quality clinical trial evidence that cholesterol lowering through statin use will benefit the majority of women who are now taking these drugs. And we know that statins carry potentially dangerous risks, particularly for

women of reproductive age. While some say that statins are so safe they should be in our drinking water, there is mounting evidence that a very cautious approach is more appropriate.

Here are some facts to consider....

Cholesterol: The new 'disease'

Cholesterol has received much negative press in the last few decades. Health information sources tell us that to prevent heart disease, it is important to keep our 'bad' cholesterol (LDL or low-density lipoprotein) low and our 'good cholesterol' (HDL or high-density lipoprotein) high.

But cholesterol levels are only one of many risk factors for heart disease. Factors such as poverty, stress, and exposure to environmental and occupational pollutants all play a major role as well. Even prescription drugs—such as hormone therapy and some pain-killers—have been shown to have a negative effect on heart health. Other risk factors include smoking, diet, weight, and family history.

Because there has been so much emphasis on a single risk factor—cholesterol—it has almost come to be seen as a ►

FOR MORE INFORMATION ...

Evidence for Caution: Women and Statin Use (2007) by Harriet Rosenberg and Danielle Allard for Women and Health Protection.
Available at: www.whp-apsf.ca

More information on reporting an adverse drug reaction is available at:
www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/reporting-declaration-eng.php#a1

Based on *Evidence for Caution: Women and Statin Use* (2007) by Harriet Rosenberg and Danielle Allard. Written by Women and Health Protection.

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Recovering from statin exposure

Depending on a person's symptoms, and how long they were taking the drug, people who stop taking statins respond differently. Some see a complete reversal of their symptoms. For others, some of the harms caused by statins may not go away when statin use is stopped.

Are there alternatives to statins?

The good news is that some research suggests regular, moderate exercise, a healthy diet and quitting smoking may have much bigger benefits for preventing heart disease than lowering cholesterol levels by taking statins or other cholesterol-lowering medication.

If you are taking statins and want to stop...

Consult your health practitioner if you are considering discontinuing your statin medication. It is important not to stop taking a statin drug abruptly.

disease in itself. This is based on the notion that high levels of so-called 'bad cholesterol' cause an increase in the amount of plaque formation in our arteries, which can lead to a blockage causing a heart attack or stroke. The so-called 'good cholesterol', on the other hand, reduces plaque build-up in the arteries and, therefore, may reduce the risk for heart disease.

But this is an over-simplified model that does not fully explain the very complex role of cholesterol and related processes in the body. We are rarely told that cholesterol and lipoproteins are not the same thing and that cholesterol is vital to the body and essential for normal brain function, hormone development, cell wall structure, immune system function, nerve-muscle communication, and Vitamin D synthesis. It is also critical during pregnancy and breastfeeding to ensure healthy foetal and infant development.

In other words, *lower cholesterol is not always better.*

"Behind the scenes" on the cause of heart disease

U.S. research on hospital admissions indicates that the majority of people hospitalized for heart disease have what is now considered normal, or even low, cholesterol levels. While some researchers think this means that guidelines for acceptable cholesterol levels are still too high, others argue that there are other, more important causes of heart disease related to inflammation. We don't know yet whether inflammation affects women and men differently, but some studies suggest that it does and that inflammation may be a better predictor of cardiovascular problems in women. Another puzzle that the research has not yet solved is whether taking medication is more or less effective than other approaches to treatment.

One size does not fit all: Heart disease in women and men

We often hear that heart disease is the number one killer of women in Canada. This is true. But this

statement hides the real risks for *specific age groups of women*. It is only when women reach their 80s that heart disease becomes the number one killer. Men, on the other hand, are much more likely to experience heart disease at an earlier age. And research already shows us that women experience different and a wider range of symptoms for heart disease than men. Because women, and their doctors, may not recognize the symptoms, women may face more serious consequences because of a faulty diagnosis.

Women are physically different from men and often have different social responsibilities, expectations and lived experiences. Women's bodies also process drugs differently. This may be due to their hormone levels, distributions of body fat, or ways they metabolize enzymes. All of these factors play an important role in a woman's health status, and in her health risks, including her risk of heart disease.

Yet findings from studies that include only or mostly men have been reported as if the results applied equally to women. This does not make for good science. No gold standard clinical trial on the benefits and risks of statins has ever been undertaken specifically for women.

What do we know about statin use for women?

The Framingham study of the 1950s was the first significant research to highlight a relationship between cholesterol levels and heart disease. But the study focused only on young and middle-aged men, and the study authors themselves state that their findings do not apply to people over age 65.

Since then, many studies have examined the relationship between cholesterol levels and heart health, and looked specifically at statins and other cholesterol-lowering drugs. But again, the findings are often not relevant to women, or to women of all ages, since many of the studies focus solely on male participants, or do not provide data separately

for women and men.

More recent community-based research has found that there is *no benefit to lowering LDL cholesterol in older women, and that for women over the age of 50, high cholesterol levels are not linked to heart disease*. Some of these same studies indicate that lower cholesterol levels in women over 50 are actually linked to higher levels of cancer, liver disease, mental illness and early death.

For women under the age of 50, studies have suggested a link between high cholesterol levels and heart disease, but more research is needed to determine if cholesterol-lowering drugs, such as statins, are of any benefit.

For women who did not already have heart disease, independent reviews of clinical trial evidence in 2003, 2004, 2007, and 2008 found no proof that statin use reduces deaths from heart problems or that the number of heart attacks or other heart events was lowered. Some information from trials even suggests an increased risk of heart problems for some women.

For women with a history of heart disease, reviews of clinical trials did find that women taking statins had fewer deaths from heart attacks and fewer heart events, but the advantage was small, and there were not actually fewer deaths overall.

What to look for when reading media accounts of statin research:

- **Are women specifically addressed? Does the research reflect a woman like you (your age group, social situation, etc.)?**
- **Are the benefits of statins expressed in terms of how many people have to take the drug in order to see an overall benefit?**
- **Is there any discussion of side effects in the story?**
- **Is there information about the authors and any potential conflicts of interest? Who paid for the research?**

If the findings seem too good to be true, they just might be!

Do you think you have experienced a negative reaction as a result of taking statins?

- **Inform yourself by reading independent research on harms caused by statins. (See *For more information, over*)**
- **Discuss with your doctor how to safely taper off the drug.**
- **Ask your doctor to report your concerns to Health Canada's adverse drug reaction database; or consider reporting your concerns directly to Health Canada. This can be done by phoning 1-866-234-2345.**