

## COMMENTARY

### Evidence for Caution: Women and Statin Use

by Harriet G. Rosenberg and Danielle Allard

Statins – cholesterol-lowering drugs – are the most widely prescribed drugs in the world and about half of all individuals taking them are women. Women are commonly prescribed statins to protect against cardiovascular diseases, but for women without previous heart problems, there is little evidence to suggest that lowering cholesterol actually reduces a woman’s risk of experiencing cardiovascular events, such as heart attack, stroke or even death.<sup>[1-4]</sup> In fact, there has never been a clinical trial showing the benefits of statin use among women who have not previously experienced cardiovascular health issues,<sup>[5]</sup> yet 75 percent of women taking statins fall into this category. For women who already have heart problems, statins do reduce the risk of heart attacks, the need for angioplasty, bypass surgery and coronary heart disease-related deaths, but do not reduce overall mortality.<sup>[1,6]</sup> At the same time, there is growing evidence linking statins to breast cancer,<sup>[7,8]</sup> miscarriage,<sup>[9]</sup> and birth defects.<sup>[9-11]</sup> Thus, statin therapy seems to have no effect on preventing overall deaths among women with or without previous heart disease,<sup>[1,3,12,13]</sup> raising concern that we may be trading off heart disease deaths for other causes of death, such as cancer. As well, statin use has been related to depression<sup>[14-15]</sup> and muscle impairments<sup>[16]</sup> in both women and men. It is difficult for women and their doctors to make informed choices about statins or understand normal life course increases in cholesterol levels during pregnancy or menopause because of a lack of sex- and gender-based analysis in this area. To increase knowledge about the effects of statin use, public funding should be made available for randomized clinical trials exclusively for women. Additionally, information detailing crucial adverse events for both women and men must be gathered and fully disclosed. Further research is also needed on the gender dimensions of diagnosis and treatment for cardiovascular diseases, including prescription of statins.

#### References

1. Walsh JME, Pignone M. Drug treatment of hyperlipidemia in women. *J Med Am Assoc.* 2004;291(18):243-52.
2. Do statins have a role in primary prevention? Therapeutic Letter [serial online]. 2003 [cited 2007 Apr 10] April-June;1-2. Available from [www.ti.ubc.ca/PDF/48.pdf](http://www.ti.ubc.ca/PDF/48.pdf)
3. Abramson J. *Overdosed America: the broken promises of American medicine.* New York: Harper Collins; 2004.
4. Hayward RA, Hofer TP, Vijan S. Narrative review: lack of evidence for recommended low-density lipoprotein treatment targets: a solvable problem. *Ann Intern Med.* 2006;145(7):520-30.

### What Policies Currently Exist to Address Mercury Pollution? Are These Policies Effective?

To date, the standard governmental response – both federally and provincially – to the issue of mercury contamination has been to issue retail and sport fish consumption advisories, which distinguish between dangerous and non-dangerous levels of fish consumption.<sup>[1]</sup> Given the established risks associated with mercury exposure, this action is wholly inadequate. It neglects to consider the danger of compounding effects as well as the regularity with which some populations consume fish high in mercury.<sup>[10]</sup> In the case of First Nations and coastal communities, for example, there are important socio-cultural, economic and nutritional benefits associated with fish, shellfish and marine mammal consumption that must be weighed against the health risks associated with the consumption of mercury. At the same time, fish and shellfish consumption advisories neglect the role of industry and the obligations of governments to regulate industries in order to prevent mercury pollution.<sup>[3]</sup>

Although less mercury is being released into the environment by individuals and industries<sup>[2]</sup> (as established and measured through federal standards on industrial emissions and mercury containing lamps and dental amalgams<sup>a</sup>) and there is growing recognition of the need for risk management tools and pollution prevention planning, we still need emissions control standards and protocols that are binding.<sup>[2]</sup> Tighter controls on emissions are the most direct way to diminish mercury contamination and to reduce the dangers of fish and shellfish consumption, which many people living in Canada currently have to weigh against the health benefits of eating such animals.

Alongside efforts to reduce mercury contamination, it is also important that policy initiatives include a gendered approach and an awareness that mercury does not have a uniform impact across communities. For example, pregnant women currently receive mixed messages about fish and shellfish consumption, with health educators

a The Canada-wide Standards (CWSs) for mercury emissions refer specifically to smelters and waste incinerators as well as emissions from lamps and waste.

simultaneously praising their benefits (e.g., protein, unsaturated fatty acids, omega-3 fatty acids) while warning against their dangers (e.g., contaminants, methyl mercury).<sup>[11]</sup> For many women living in coastal communities, food that comes from the sea is a primary source of diet, making mixed messages and the threat of mercury contamination increasingly stressful for pregnant women in those communities. In addition, better tools are needed to measure mercury contamination as well as data that are disaggregated by sex, age, ethnicity, geography and other determinants of health. Ultimately, a thorough and effective approach to the issue of mercury contamination requires involvement at all levels of government as well as collaboration from Native leaders and public health units.

## Conclusion

Sex- and gender-based analysis helps us to better understand the ways in which environmental contaminants pose different biological risks for women and men. It also encourages us to consider the health impacts of pollution for different populations of women and men. This study of mercury demonstrates the importance of sex-disaggregated data in ascertaining cause and effect. In this case, the acknowledgement that mercury contamination presents unique risks for women, particularly in First Nations and coastal communities, is an important platform from which to assess and anticipate future policy on mercury and highlights the issues of bioaccumulation, chronic low-level exposure and in-utero contamination.

5. Wright J, Abramson J. Are lipid-lowering guidelines evidence based? *J Lancet*. 2007;369(9557):168-9.
6. Criqui MH, Golomb BA. Low and lowered cholesterol and total mortality. *J Am Coll Cardiol*. 2004;44(5):1009-10.
7. Shepard J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomized controlled trial. *J Lancet*. 2002;360(23):1623-30.
8. Lewis SJ, Sacks FM, Mitchell JS, East C, Glasser S, Kell S, et al. Effect of pravastatin on cardiovascular events in women after myocardial infarction: the cholesterol and recurrent events (CARE) trial. *J Am Coll Cardiol*. 1998;32(1):140-6.
9. Kenis I, Tartakover-Matalon S, Cherepin N, Drucker L, Fishman A, Pomeranz M, et al. Simvastatin has deleterious effects on human first trimester placental explants. *Hum Reprod*. 2005;20(10):2866-72.
10. Edison RJ, Muenke M. Mechanistic and epidemiological considerations in the evaluation of adverse birth outcomes following gestational exposure to statins. *Am J Med Genet*. 2004;131A:287-98.
11. Forbes K, Hurst LM, Gibson JM, Aplin JD, Westwood M. Statins are detrimental to human placental development and function: use of statins during early pregnancy is inadvisable. *J Cell Mol Med*. Forthcoming 2008.
12. Eisenberg T, Wells MT. Statins and adverse cardiovascular events in moderate-risk females: a statistical and legal analysis with implications for FDA pre-emption claims. *J Empirical Legal Stud*. 2008;5(3):507-50.
13. Petretta M, Costanzo P, Perrone-Filardi P, Chiariello M. Impact of gender in primary prevention of coronary heart disease with statin therapy: a meta-analysis. *Int J Cardiol*. 2008 Sept 13 [epub ahead of print]. Available from National Centre of Biotechnology Information.
14. Adverse Drug Reactions Advisory Committee, Adverse Drug Reactions Unit of the Therapeutic Goods Administration. Ezetimibe and depression - a possible signal. *Australian Adverse Drug Reactions Bulletin* [serial online]. 2006 [cited 2008 Dec 10]; 5(5). Available from [www.tga.gov.au/adrb/aadr0610.htm#a3](http://www.tga.gov.au/adrb/aadr0610.htm#a3).
15. Medicines and Healthcare Products Regulatory Agency (MHRA) and the Commission on Human Medicines (CHM). Statins: class effects identified. *Drug Safety Update*. 2008;1(7):2.
16. Radcliffe K, Campbell WW. Statin myopathy. *Curr Neurol Neurosci Rep*. 2008;8(11):66-72.