Don't be so quick to ban medications

Although evidence-based medicine has caught on among physicians, it seems that regulatory agencies persist in generating hysteria-based blanket recommendations.

Donald Farquhar[1] wrote a clinical update for *CMAJ* on a case–control study showing that, mainly when it is used repeatedly for appetite suppresion, phenylpropanolamine is associated with increased risk of hemorrhagic stroke primarily in women who smoke cigarettes and are black, hypertensive and less well educated.[2] This population also seems to be at some risk even at first use of phenylpropanolamine-containing cough or cold remedies. On this basis the US Food and Drug Administration and Health Canada announced they were taking steps to remove phenylpropanolamine from all drug products and requested that all drug companies stop marketing products containing phenylpropanolamine.

Why? How many millions of patients find relief from using these medications each year, and what is their risk of stroke? The risk is not distributed evenly, because among men there was no increased risk of hemorrhagic stroke with use of phenylpropanolamine-containing products.[2]

What is the number needed to harm? Since 1969, only 60 cases of hemorrhagic stroke associated with the use of products containing phenylpropanolamine have been reported to the US Food and Drug Administration, or about 2 reported strokes per year.[2]

This isn't the first time good medicines have been killed because regulatory agencies have overreacted. Cisapride was removed from the market after the deaths of fewer than a dozen people with identifiable risk factors. However, these agencies are somewhat inconsistent: dozens of men have accepted the well-publicized risk of death associated with use of sildenafil and died, yet this drug remains on the market.

We place appropriate warning signs concerning the risk of stroke on cigarette packages. Why not do the same with medications? When risk factors for serious harm become known they should be placed in bold type on the drug packaging and made well known to health care workers. Products containing phenylpropanolamine should probably be placed behind the counter so pharmacists can advise those patients identifiably at increased risk to use other products; they shouldn't be banned from the marketplace.

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Troponin assays for coronary syndrome diagnosis

I read with interest the article by David Fitchett and colleagues in *CMAJ*'s series on the management of acute coronary syndromes.[1] From a laboratory point of view, the reader should bear in mind several points, especially as troponins are now the arbiter par excellence of coronary syndrome diagnosis.[2] The first is that a low-sensitivity test (CK MB [creatine kinase – MB isoenzyme activity or mass] level) should not be used to clarify the results of a high-sensitivity test (troponin).[3,4] Laboratories are often asked for a CK MB level when a patient has an elevated troponin level in an unclear clinical situation; the results of the test for the CK MB level may be falsely negative. Secondly, the troponin I value considered "normal" is assay dependent and can differ among manufacturers. The clinician should be aware of the reference limits and the coefficient of variation at the lower limits of the troponin assay used at his or her institution. Both troponin and CK MB levels are proportional to myocardial damage, but the relationship between troponin and CK MB levels is more complex; one has to gain experience with each to know what to expect with, for example, a massive myocardial infarction. Lastly, risk stratification may become more complex and, one would hope, more exact with the use of additional markers such as C-reactive protein and homocysteine.

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[The authors respond:]

Cardiac troponin I and T assays are indeed highly sensitive for the detection of myocardial injury. Approximately 30% of patients previously diagnosed with unstable angina with no increase in creatine kinase (CK) or its MB isoenzyme (CK MB) are found to have elevated levels of circulating cardiac troponin.[1] Today these patients are considered to have minor degrees of myocardial injury; by American College

of Cardiology and European Society of Cardiology criteria[2] their diagnosis would be reclassified as myocardial infarction. We therefore agree that it makes no sense to use CK or CK MB levels to "clarify" the results of troponin assays. It is likely that troponin will eventually replace CK MB as the gold standard for the diagnosis of myocardial infarction. However, because of persistence of circulating troponin for up to 14 days after an acute myocardial infarction, CK MB may remain the preferred marker for the diagnosis of reinfarction.

The limitations of the currently available troponin assays, such as limited diagnostic accuracy at low levels and not-infrequent analytical errors,[3–5] reduce confidence in troponin as a perfect biomarker for myocardial injury. Furthermore, circulating cardiac troponin may be detectable in patients with conditions other than acute coronary syndromes.[6–12] Repeating the troponin measurement and electrocardiogram is often helpful in assessing the patient with a possible acute coronary syndrome and borderline troponin elevation.

Circulating cardiac troponin should be undetectable in healthy people. As Brian Gilfix correctly indicates, it is important that the clinician be aware of the locally measured reference value of the assay as well as the variability of the measurement at these low levels and not depend on the manufacturer's "normal" value.

Risk stratification of patients with acute coronary syndromes is facilitated by measuring the cardiac troponin level. Outcomes relate directly to both the level at presentation and the maximal level in the first 24 hours.[13] High and low risk stratification by clinical criteria is unchanged by a finding of either borderline or clearly elevated troponin levels. However, patients stratified to an intermediate risk by clinical criteria are at high risk of adverse outcomes if they have high levels of troponin.

Cardiac troponin measurements have been an important advance in the diagnosis and risk stratification of acute coronary syndromes. However, limitations of the currently available assays require clinicians to also carefully evaluate all of the clinical information.

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Cell phone regulation

It is difficult to understand why Emile Therien, President of the Canada Safety Council, is so vigorously opposed to cell phone regulation.[1] His objections appear to be based on 2 reports not published in peer-reviewed journals, to which he attaches the same weight as the report in the *New England Journal of Medicine*[2] that prompted *CMAJ*'s editorial on the subject.[3]

Therien implies that the report by Claire Laberge-Nadeau[4] reached conclusions that "contrast" with those in the *CMAJ* editorial and that it is more credible than the *New England Journal of Medicine* report because it had a larger sample. Apart from the fact that more subjects do not necessarily mean better science, Therien provides no data from the Laberge-Nadeau study to help readers draw their own conclusions. Instead, taking a page out of the National Rifle Association's book, Therien concludes that it is not the phone that is the problem, but the user.

The other report he uses to support his position showed that over 10% of crashes caused by distracted drivers involved the use of cell phones.[5] Therien glosses over this startling finding by focusing on the 11.4% of crashes in which the driver was distracted by adjusting a radio or cassette and the 30% that involved distraction by "an outside person, object or event." Unfortunately, we cannot regulate all possible sources of distraction, but we can do something about a device whose lethal effects may reach epidemic proportions when it becomes as ubiquitous as radios or cassette players.

This is not the first time the Canada Safety Council has taken a position that runs contrary to the evidence; it also did so when it opposed changing the permissible blood alcohol limit for drivers from 0.08 to 0.05. One cannot help, therefore, but wonder what would moti-