

Endovascular treatment for multiple sclerosis: The intersection of science, policy and the public

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Funding: No funding for this commentary was required.

Competing interests: AL is reimbursed by Novartis for his membership on a Data Monitoring Committee that is monitoring studies of the use of 2 drugs, fingolomid and a drug that has not yet been licensed, in patients with MS. AS chairs an Advisory Committee for Rx&D and is compensated for this. Both AL and AS are, or have been, members of CIHR committees and receive funding from the CIHR for their research (none of which is related to MS).

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IT WOULD BE DIFFICULT TO BE A CANADIAN AND BE unaware of the controversy regarding endovascular treatment for multiple sclerosis (MS). Dr. Paolo Zamboni, an Italian physician, has hypothesized that MS is caused by a newly discovered abnormality of venous drainage from the brain that he has called chronic cerebrospinal venous insufficiency (CCSVI), and that endovascular treatment of CCSVI can markedly improve the symptoms of MS.^{1,2} The endovascular treatment has been given the rather sensational name “liberation procedure,” invoking the notion of “setting free.” The overwhelming majority of MS researchers dismiss Dr. Zamboni's findings because they fly in the face of what is known about the etiology of MS, and because of questions about the scientific quality of Dr. Zamboni's work. His studies of the association between CCSVI and MS have not been consistently replicated, and his trial addressing the effectiveness of endovascular treatment

was not randomized. As well, although Zamboni found no serious complications in 65 MS patients undergoing angioplasty of the jugular veins, no large-scale study of complications has been reported. These are important and valid criticisms.

The public profile of CCSVI in Canada was raised in the fall of 2009 by a relatively uncritical article in *The Globe and Mail* (Toronto), and an even more uncritical broadcast on the CTV public affairs program *W5*.^{3,4} Both portrayed Dr. Zamboni as a pioneer whose theories were discounted by conventional medicine and focused relatively little on the criticisms of his studies. Many Canadians with MS, eager for an effective treatment for this miserable disease, have been convinced by Dr. Zamboni's research, and by the testimonials of patients who have travelled to other countries to receive the procedure. They accuse many in the MS scientific community of being narrow minded, obsessed with irrelevant scientific niceties, and/or of being in the clutches of the pharmaceutical industry.⁵ They demand that endovascular treatment be made available in Canada or, at the very least, that a randomized trial of the procedure be started immediately.

Into this perfect storm have marched the Canadian Institutes of Health Research (CIHR) and the Multiple Sclerosis Society of Canada. In September of this year they released a summary of the deliberations of a “Joint Invitational Meeting” of 15 clinical and scientific experts, 5 employees of the CIHR, 3 employees of the MS Society, and one unidentified person with MS. The panel examined the scientific literature relating CCSVI and MS, and decided that the evidence linking CCSVI and MS was so unconvincing that it would be inappropriate at this time to perform a clinical trial examining the benefits and risks of endovascular treatment as a therapy for MS.⁶

Too often, health care interventions are introduced on the basis of poor scientific evidence. Therefore, what the CIHR and MS Society have attempted to do seems admirable to those of us who are proponents of evidence-based health care and evidence-informed policy-making. A review and summary of all research that is relevant to important health policy decisions by unbiased experts can be used by politicians and policy-makers to make policy decisions, in this case whether to fund endovascular treatment for CCSVI, either as part of a randomized trial or through the publicly funded health care system. However, we suggest that there are important lessons to be learned from this panel's experience that should be considered when constituting future panels that address other issues that are at the intersection of science, advocacy and policy-making.

Concerns have been raised about the membership of the expert panel.⁷ No proponents of the liberation procedure participated in the Invitational Meeting, which seems odd. Most scientific experts have some degree of conflict of interest, and these are usually dealt with by publicly declaring them, not by excluding a particular point of view from a panel. Conversely, the potential conflicts of interest of the individuals who were on the panel were not described in the report, thus allowing some to accuse the CIHR of attempting to hide their potential biases.⁸

The panel recommended that no clinical trials of endovascular treatment for CSSVI should be conducted until the association between MS and CCSVI has been firmly established. The rationale for this recommendation is sensible: one should not expose MS patients to the risks of endovascular therapy—which, although rare, can be fatal^{9,10}—if there is no rational scientific reason to think that CCSVI causes MS. However, the panel spent little time either justifying their controversial recommendation or discussing potentially opposing points of view. We believe that both the panel's approach to the problem and its membership were too narrow to completely fulfill its mandate.

It appears to us that the panel addressed three questions. The first question was whether current evidence establishes that patients with MS have a higher frequency of CCSVI than patients without MS. The second was whether current evidence establishes that the benefits of endovascular treatment in patients with MS outweigh the risks. The third was whether a publicly funded randomized trial of endovascular therapy for MS should be initiated now.

The first two questions are largely ones of science, and are best addressed by highly qualified experts who represent the diversity of views in the scientific community. However, we believe that although the third question must be informed by science, it should be addressed using a broader perspective. A clinical trial of endovascular treatment funded by the CIHR or provincial governments would consume public resources, which are clearly limited. Given the controversy, and given the way this issue has galvanized the public, the decision about whether to conduct a clinical trial should be informed by the public. We believe that members of the public, beyond 3 employees of the MS Society and one anonymous person with MS, should have been included on the Joint Invitational Meeting panel. By “members of the public,” we do not mean only patients with multiple sclerosis or advocates for MS patients, but also thoughtful citizens without MS who can consider all points of

view, deliberate about them, and contribute to informed recommendations.

If half a dozen or so such individuals had participated in the deliberations, they might have asked questions about why proponents of the liberation procedure were not members of the panel, and they would have contributed greatly to the discussion about the appropriateness of a clinical trial in the face of poor scientific evidence supporting the CCSVI hypothesis and uncertainty about the risks of endovascular therapy (which appear to vary depending upon whether or not a stent is inserted). They would likely have encouraged the panel to more fully articulate the reasons why a clinical trial should not (or possibly should) be conducted now, and might have had different views about how to balance information about the risks and potential benefits of angioplasty. A number of Canadians are now using their own resources to travel to other countries to undergo endovascular treatment, performed by surgical teams whose quality standards are not always clear. Would these patients be better off, and policy-makers and the public better informed, if a randomized trial were conducted now? If patients are fully informed about current doubts regarding the association of CCSVI and MS, as well as the limitations of Zamboni's non-randomized trial of endovascular treatment, and the potential side-effects of endovascular treatment, should they be given the opportunity of participating in a trial now? Of course, surgeons and interventional radiologists should not participate in the trial if they feel that the current evidence suggests they are likely to do more harm than good to their patients. However, we know of reputable Canadian vascular surgeons who would operate on MS patients in the context of a randomized trial.

Even had greater public membership on the panel not changed the recommendations made in the report at all, or had the committee not been able to come to a consensus, the very fact that members of the public were on the committee would likely have increased the legitimacy of the report in the eyes of the public (although not in everyone's).

The public pays for research funded by the CIHR and the MS Society of Canada, are affected by the findings, and are more likely to be supportive of research in general if they feel that researchers are more in touch with the community. The CIHR has itself, in reference to its Stem Cell Oversight Committee, stated “Technical experts will provide the Committee access to the latest scientific and ethical information, and representatives from the general public will represent the views and values of Canadians potentially affected by the new technologies.”¹¹

We agree with this statement and suggest that, in the future, members of the public should be more actively involved in scientifically based, but patient-relevant and emotionally charged, issues considered by the CIHR, by other Canadian research organizations and by the provincial, territorial and federal governments.

Contributors: AL wrote the first draft, and AS and AL together revised the manuscript numerous times thereafter. AL approved the final copyedited version and is the guarantor of the article.

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Citation: Laupacis A, Slutsky AS. Endovascular treatment for multiple sclerosis: The intersection of science, policy and the public. *Open Med*. 2010;4(4):e197–e199.

Published: 7 December 2010

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