



Call for 'liberation': a November 2010 rally in Edmonton, Canada, for a multiple-sclerosis treatment.

The rise of people power

Calls in Canada for trials of a contentious treatment for multiple sclerosis illustrate how social media can affect research priorities, say **Roger Chafe** and his colleagues.

In 2008, Paolo Zamboni, a vascular surgeon from the University of Ferrara in Italy, hypothesized a new cause of multiple sclerosis (MS). He pointed to abnormalities in the veins draining the brain and spinal cord, a condition he called chronic cerebrospinal venous insufficiency (CCSVI). Zamboni proposed that unblocking the veins by mechanically widening them can improve the symptoms of the disease. He termed his treatment 'the liberation procedure'.

Zamboni's hypothesis is a radical departure from the prevailing view that MS is mainly an autoimmune disorder. In most countries, it has received little attention. In Canada, however, a national debate is under way about whether publicly funded clinical trials should be conducted on the treatment of CCSVI, or even whether patients with MS should have immediate, publicly funded access to a vein-widening procedure called venoplasty. This is despite the fact that virtually none of the country's MS physicians and researchers, and not even the Multiple Sclerosis Society of Canada — the nation's largest support organization for patients — have advocated for either.

What is fascinating here is the extraordinary mobilizing power of the media and the Internet. More than 500 Facebook groups, pages and events dedicated to promoting vascular treatment for MS have emerged in less than two years and amassed tens of thousands of participants. Indeed, the case indicates the unprecedented pressures that politicians and funders worldwide can now face to alter research priorities even in the absence of credible scientific evidence.

In this new social-media environment, researchers and clinicians need to engage more actively with the public to articulate the science validating, or debunking, novel treatments — and to ensure that patients' concerns and priorities are heard.

HIGH HOPES

MS is a chronic neurological disease that causes a variety of symptoms — including weakness, loss of balance or vision, and memory loss — and can be functionally disabling. In the 'relapsing–remitting' form of the disease, symptoms can improve for months or years before worsening again. Currently there is no cure.

Zamboni proposed that obstructions in veins lead to a build-up of iron deposits in the central nervous system, which triggers an autoimmune response¹. In a non-randomized, non-blinded study of 65 patients, he found that those with the relapsing–remitting form of the disease had fewer relapses after venoplasty. Patients with progressive forms of MS showed little improvement². On the basis of these findings, Zamboni has called for randomized trials to assess the effects of venoplasty more rigorously.

Most neurologists and other physicians who treat patients with MS say that a non-randomized, non-blinded trial is poor evidence that venoplasty is beneficial, especially given the variable nature of some forms of the disease. Moreover, several studies^{3,4} have failed to replicate Zamboni's original findings. Nonetheless, in Canada, CCSVI has garnered an extraordinary amount of attention.

In November 2009, *The Globe and Mail* — one of the country's leading national newspapers — and the Canadian Television Network's news programme *W5*, featured stories about Zamboni and CCSVI. Both stories described patients with MS, including Zamboni's wife, as experiencing dramatic improvements after venoplasty. The *W5* programme described it as "a revolutionary treatment for a most debilitating disease [that] could free MS patients from a lifetime of suffering"⁵. Reports in the Canadian media about Zamboni and 'the liberation procedure' have appeared almost weekly since.

The reluctance of the Multiple Sclerosis Society of Canada, clinicians and researchers to advocate for patients' immediate access to venoplasty or even for clinical trials to test its efficacy has led hundreds of patients and their supporters to form advocacy organizations. These groups have used the Internet and social media to share information and testimonials about positive responses to the therapy, to attack the credibility of those advocating caution and to organize campaigns and demonstrations. Some have even accused the MS society and MS physicians of being swayed by conflicts of interest as "when CCSVI is introduced, the number of MS patients will drop".

Partly in response to pressure from such groups, Canada's largest public funder of health research, the Canadian Institutes of Health Research, in partnership with the MS society, convened an expert panel in August last year to assess the CCSVI–MS hypothesis. The panel concluded that more observational studies — for instance, comparing the frequency of abnormal venous blood flow in people with MS with that in individuals who do not have the disease — should be performed, but "in the absence of clear and convincing evidence for CCSVI, the performance of an interventional venous angioplasty trial with its attendant risk to MS

patients is not appropriate at this time”⁶.

Yet the issue rumbles on. Whether a clinical trial that subjects patients to an invasive and potentially risky procedure ought to be conducted was one of the main focuses of the 2010 annual meeting of the country's federal and provincial health ministers. In December last year, Michael Ignatieff, the leader of Canada's largest federal opposition party, stated his support for clinical trials of endovascular treatment of MS. Meanwhile, hundreds of Canadian patients are travelling, at their own expense, to receive treatment from private clinics around the world now offering venoplasty and in some cases stenting (in which a small tube is placed in a vein to help it stay open) to treat CCSVI.

Although severe adverse events from these procedures are rare, at least two patients have reportedly died after receiving treatment⁷. Complications include clotting, serious bleeding, stents moving to a different part of the body and abnormal heart rhythms.

FACEBOOK EQUIPOISE

What lessons should scientists take from the Canadian CCSVI experience?

A recent poll found that about half of Canadians are now familiar with the use of venoplasty to treat MS. Canada does have a higher prevalence of MS than many other countries. But seemingly unique to Canada are the initial extremely positive news stories about Zamboni and CCSVI, the effective use of social media by patients, and ongoing media interest. We searched 2 leading newspapers in each of 7 countries between November 2009 and January 2011, and found 83 articles on Zamboni and CCSVI in Canadian papers, 16 in Italian papers, and 6 articles in total in the newspapers from the other 5 countries (see ‘Hot topic’).

Unproven treatments have long been proposed, and tried, for diseases. Tools such

as Facebook and YouTube make it considerably more likely that patients will learn about such therapies, without necessarily learning about their potential limitations. Similarly, the mobilizing power of social networking means that unprecedented pressures can be applied to politicians and research funders to expand access to procedures for which there is little scientific support.

A clear lesson is that the traditional approaches for communicating scientific findings to the public and to policy advisers (reports, briefing notes, press releases and news conferences) are insufficient. When patient groups are using social media to advocate and mobilize, scientists must use similarly effective tools to communicate.

Scientists and research funders also need to avoid adopting an ‘us versus them’ mentality. Many researchers have been frustrated by the lack of impact that science often has on public debates, but new models for engagement are emerging. For instance, the James Lind Alliance in Oxford, UK, brings together patients and clinicians to identify questions that have not received adequate attention from industry or academia. The patients and clinicians then jointly identify priorities for research.

A thornier issue is whether patient pressure and social media should affect the design and timing of clinical studies.

The dominant paradigm is that an interventional trial is not justified unless there is a strong biological rationale supported by observational studies, and ‘clinical equipoise’ regarding its efficacy — that is, a lack of consensus between researchers and clinicians about whether the treatment is preferable to others that are already available. This strategy is logical and defensible. But in today's era of ‘Facebook equipoise’, it may make sense in rare cases to conduct a clinical trial before the desired weight of scientific evidence

accumulates; for instance, if thousands of patients are exposing themselves to risks and costs of unevaluated medical procedures.

The Multiple Sclerosis Society of Canada and the National Multiple Sclerosis Society in the United States are funding seven studies to evaluate the association between CCSVI and MS. If these studies consistently show no association, this may be enough to convince most people with MS that venoplasty is not worth trying. If the results are delayed, or are unconvincing to many patients, we believe

“Traditional approaches for communicating scientific findings to the public are insufficient.”

that the benefits of a double-blinded randomized trial would outweigh the costs — including the diversion of resources from other priorities. Such a study would involve giving one group of patients a vein-widening procedure and another a sham procedure, and having the assessor being unaware of which patients received which procedure.

Rigorous evaluation has previously been important in helping to refute unproven medical claims, such as the purported benefits of the drug Laetrile (amygdalin) for cancer⁸, or the alleged dangers of the measles, mumps, rubella (MMR) vaccine in causing autism.

In the long term, to prevent an increasing proportion of public resources being diverted to testing what will probably turn out to be ineffective or harmful therapies, more effort needs to be devoted to improving the scientific literacy of the public, politicians and the media — and to engaging with a public that is no longer deferential to experts. ■

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HOT TOPIC

A measure of the number of Google searches for the term CCSVI (chronic cerebrospinal venous insufficiency) reveals that public interest in Canada soared in just one year.

