



CCSVI and MS Information Session English Webcast Transcript April 07, 2010

MO: Good afternoon, and on behalf of the Multiple Sclerosis Society of Canada, I'd like to welcome you to the CCSVI and MS information session. My name is Marlane Oliver. I am the co-anchor of the 680 News morning show, 680 News, all-news radio. And I'm privileged to be your host this afternoon.

On a personal note, the MS Society had a choice to hold a media conference, a news conference about the issue of CCSVI in the MS Society, and they decided not to do that. They wanted to make this about you, and to make it as open and as accessible as possible to people right across this country in a number of different forums and formats, and I applaud them for that. Information is very important in this day and age, and correct and vital and accurate information is most important above all.

So it's wonderful to be part of this session. My role is to guide the discussion and to ensure that this afternoon moves along at a good pace. So we are going to try to make sure as many questions as possible get answered.

We have a couple of housekeeping items. First of all, please turn off all cell phones. Number two, no one is going to be filmed in any way, and for the media who are here, please do not take any shots or footage of anyone without their permission. And also, for those who wish to, there are washrooms just outside of the door, and we have attendants here who are just outside the door. Feel free to use the washrooms any time and assistance will be provided for you.

The topic of CCSVI has electrified the MS community. Since the CCSVI theory became widely publicized last November, it's been the talk of online forums, of Facebook, to say nothing of the follow-up media coverage that has been generated. The MS community, including the MS Society and the research and clinical community, have seen an unprecedented response in their interactions with their own stakeholders.

Questions that have been particularly highlighted these past few months include: Is this a cure? How available are the scans for CCSVI, and is the treatment? And how do we move this research forward? These and many more questions have been part of an important dialogue that continues today. So now, more than four months later, there remains an unparalleled interest in this topic and a strong desire for more information. The desire is evidenced by the unprecedented response the MS Society had when it made this information session available coast to coast. As of today there are 800 registrations, and these registrations, there(?) can be many groups and many people who are at each registration. They're watching us live. We also have over 900 others

who've asked to be notified when this session is going to be posted on YouTube.

We have an excellent panel and they are here to answer your questions. So many of these questions, we've had close to 300 that have been submitted during the registration process. We will also take questions from the room, and anyone who has a question, please raise your hand, and we have Randy on this side of the room, and we have Ashley over here, all right? And they're going to come to you and we're going to circulate around the room and answer as many questions as possible.

For those who are watching our live webstream, you can also post your questions using Twitter. Use the mention @mssocietycanada or you can post a question on Facebook. Go to our wall at facebook.com/mssocietycanada.

Because of time constraints we won't be able to answer every single question asked, but we do hope to answer as many as possible. So please keep an eye on the MS Society's ccsvi.ca website for more updates in the FAQ; that's the frequently asked questions section. MS Society will also make this session available on YouTube and post a transcript of today's conversation in the next couple of days for those who are unable to watch it live.

And on a final note, before I introduce the speakers, the nature of this conference is to be as broadly interesting and relevant as possible. So with this in mind, and because diagnosis and treatment of MS requires a detailed case history, we won't be able to address questions that are related to an individual diagnosis or case of MS.

So I'm very pleased to introduce our panel. On my left, Yves Savoie, President and Chief Executive Officer of the MS Society of Canada. Since 2007, Yves has played the dual role of President and CEO of both the MS Society at a national level as well as the MS Society's Ontario division. And it's nice to have you here.

YS: Thank you, Marlane.

MO: Next to him we have Dr. Jock Murray, who is the founding director of the Dalhousie MS Clinic in Nova Scotia. He is considered worldwide as an expert in the field of multiple sclerosis. He has over 200 publications in his name, several books on MS and neurology, and he has many awards to his name, including Officer of the Order of Canada. And we are very privileged to have Dr. Murray with us today.

JM: Thank you, Marlane.

MO: And we also have Karen Torrie-Racine, who is a volunteer for the MS Society in two capacities: She is a member of the Ontario Board of Directors and is a member of the Cornwallin District chapter, and Karen has lived with MS since 1985. And Karen, we're very pleased to have you with us.

KTR: Thank you.

MO: Okay. To begin with, some introductory questions for each of our panelists. So Yves, if I may ask you, by way of introduction, can you tell us why the MS Society is having this session and what you hope to achieve this afternoon?

YS: Thank you, Marlane. First, let me thank you, and thank you to who you are here and online for joining us for this good conversation.

You've noted that since November there's really been an unprecedented interest in the idea that CCSVI could be associated with MS. This has generated tremendous hope for us at the MS Society and for everyone throughout the world living with MS or who has a loved one living with MS. It has also triggered a tremendous hunger for information, for clarity, for good information. And it's really in that context that we thought it was important to create an opportunity so that Canadians from coast to coast, wherever they hail from, could join in a dialogue about CCSVI and its relevance. And as you have noted, there are a lot of questions. In fact, many more that we'll be able to answer today.

But I think CCSVI, for me, has reminded me in very compelling ways of the role of the Society, the role that way play in accelerating the process of research/discovery. The CCSVI research competition is just one example of that. And the role that we play in providing accurate, timely information to people with MS so that they can make their own decisions. It's important to underscore that our role is not to make the decisions for people with MS but to support them and to honor those decisions. And it's really in that context that we thought this kind of framework was the best for a good conversation.

MO: Thank you, Yves. Now, Dr. Murray, I think we'd benefit from having an overview of where we are so far and an indication of what's coming up next. And I understand you have some slides.

JM: I do. I want to give a brief introduction just to tell you what we know at the present time. We know that there are lots of questions that we can't answer, but at least we can tell you what it is that we know.

Now, the first thing that I think increases the interest in all of this is that the idea of MS as a vascular disease is actually not a new one. And if you look, in 1848, which is many years before MS even had a name, the process was known by a number of people. And Reinfleisch(?), who is one of the early people who published about multiple sclerosis, felt that it was probably related to something about the vascular system. So the theory is actually quite old.

It resurfaced again in 1939 when anticoagulants were discovered. And when anticoagulants were discovered, they were applied to MS patients and they were used quite widely in treating MS. And that went on for almost 20 years. It was before the advent of the randomized clinical trial, so there were no clear studies to see whether or not it was any benefit. But after about 20 years, it

eventually faded and then disappeared because it appeared not to have any benefit. But for 20 years, anticoagulants were used on the basis that it might be a vascular disease.

Now, some of you know about Roy Swank's(?) diet. Roy Swank was a neurologist, originally at the Montreal Neurological Institute in Montreal, and he devised a diet for MS, and it was based on the idea that MS had a vascular basis. And so a low animal fat diet might decrease the obstruction in arteries in people with MS. And so that diet, which is still used by many today, was based on the idea that it was a vascular problem.

And then in 2007, Dr. Zamboni first postulated this idea of CCSVI, the possibility that it was a vascular problem in MS, but not in the arterial system; in the venous system.

Now, this is one of the demonstrations just to simply the process, and if you can look at the blue in the diagram, it just shows that the venous system, which drains down to the heart, is draining away from the brain. And his concept was that an obstruction in the venous outflow from the brain would increase pressure back into the brain and that that might cause the deposit of iron, and then the reaction in the brain would be to both the pressure and the iron deposits occurring within the brain. The logic then would be to decrease the obstruction in some way.

But initially he postulated that process, and then the thing that got a great deal of attention was the publication, just a matter of months ago, of a small group of patients by MS trial standards—only 68 patients—who were treated for the obstruction in their neck, and that's what in fact got a great deal of attention. When he published this, he indicated that 91% of the patients with MS appear to have some obstruction in their venous system in their neck. But looking at people who didn't have MS, nobody seemed to have this. So that's quite a dramatic appearance.

However, a subsequent study done in Buffalo indicated that actually only a little over half of the MS patients had it. So almost half of MS patients don't have that problem. And also 26%, depending on how you count the patients that they studied, 26% of people without MS had these problems in their neck. So it made it a little less clear that the relationship with MS was an overwhelming one.

And he emphasized in his paper, and for those who really want to know what the information from Dr. Zamboni was, it's worth reading the paper and seeing what's in the paper. He finishes by saying that the work is preliminary and requires further study.

In his paper he indicated that the relapse rate, the number of relapses that patients had, was improved in the 18 months after having the procedure, but only for the people who had relapsing/remitting MS, and only in those with

relapsing/remitting MS whose veins stayed open after they had the procedure. Because one group of patients who commonly had the azygos vein, they often stayed open. Those who had the internal jugular vein with an obstruction, a high percentage of them, over half of them, the veins collapsed again. And those with relapsing/remitting MS in whom the veins collapsed didn't show any benefit. So, and if you took them all together, there wasn't any overall statistical benefit. The group of patients who had secondary progressive MS didn't show any benefit. The patients who had primary progressive MS did not show any benefit.

It was difficult, as he pointed out himself, to differentiate the response in therapy because all patients were taking the accepted drug therapy for MS. So they were also on one of the, at least one of the four drugs for MS. And so it made that interpretation difficult. And although the MRIs appeared to improve, Dr. Zamboni indicated that it was difficult to interpret the MRI data because different MRIs were used, different standards were used, and the way the MRIs were done in the different patients were different. So the MRI data wasn't overly helpful.

What we don't know is, because this was an open trial of treating a group of 65 patients, what we don't have is an ethical, randomized control study, which is the standard way to differentiate treatment against non-treatment. And you could do that by short-term measures. Short-term measures are to apply a therapy and then look at whether the MRI changes or whether the relapse rate changes. That's in the short term. What people really want to know, however, is the long term. The long term is if I take this treatment, whatever the treatment may be, am I going to be better than I otherwise would in five years, ten years, or for the rest of my life? Those are the long-term questions about any particular therapy. But needless to say, it takes a long time to know that.

And we also need to know if the benefits of the therapy outweigh the risks. We do have therapies in MS that have some substantial risk. They have benefits and there has to be a balance between the risk you take and the benefit that you will get from the therapy. And also the governments and others want to know that therapies are cost effective; in other words, that the amount that the therapy costs is worth the benefit that it proves. Because benefits, some therapies are very expensive but the benefit is very little. And there is a way of determining what the cost benefit of therapies is, and governments are very involved in that at the present time.

So that is a brief overview of the things we know, the results that occurred in Dr. Zamboni's research, the initial results that came from Buffalo, and the questions and the way that we need to answer some of these questions in the future. But it will rely on the standard, accepted way of determining how much benefit there is from this therapy. And some of the things we will know in the short term, very quickly. For instance, the questions about the veins in the neck, the MRI, the relapse changes with therapy(?). You can answer those fairly quickly in the short term and those are being addressed now. Long-term

questions—what's the benefit in two or three or five years? Obviously take large trials of a large number of people followed for a very long time.

MO: Thank you, Dr. Murray. Karen, you're living with MS. You've been living with MS. You've heard all of this over the last couple of months. What has this been like? This must be such a roller coaster for you.

KTR: It has been. I was diagnosed in 1985, as you mentioned, Marlane, and for 25 years it's been pretty much a roller coaster for me because MS, as everyone knows, is a very uncertain disease. So you never know how you're going to be when you wake up in the morning. And that's a challenge, for sure.

My biggest challenges personally were pretty much between 1985 and 1990, when—1990 was my worst exacerbation and I was in hospital for eleven weeks, moving nothing from my neck down. I had a one-year-old son and when going home with him, had home care for over two years to be able to take care of him on my own. So that was a huge challenge.

And since then, as I said, the uncertainty is very clear in my everyday life. I can wake up some days and not be able to get out of bed, and some days I'm fine. Obviously today that's one of those days that I'm fine, but I'm either 0% or 100%; there's no in-between for me. That's not always the same for all MSers, but it is for me.

And the roller coaster of CCSVI, when I head towards that roller coaster, is it was so exciting to first of all get the first e-mail in October, I believe, announcing, you know, the study and that sort of thing. And then when it was on, you know, when it hit the media and they spoke about the benefits and that sort of thing, it was very exciting. It was a challenge as well, though, because many MSers thought at the time, "Okay, this is it!" because the appearance of CCSVI was so easy to understand. So that roller coaster has been a challenge because it's really not that easy to understand, but compared to an autoimmune disease or the brain and the central nervous system and that sort of thing, this particular study was very easy to understand. So I think a lot of people jumped on the bandwagon and said, "Okay, this is it! I get it, I understand it, so it's got to be it." And all of us are hoping that any of the MS research that's going on right now is it because we want a cure.

MO: Thank you. All right. We're going to turn now to the question and answer segment. And as you know, as I mentioned, we've had hundreds of questions submitted across the country on the Web, so we'll start with some of those. And if you're in the audience, start to think of what question you'd like to ask as well, all right?

So the first question comes to us from Brian, and he submitted it as a Web question: "Why are neurologists so reluctant to write consults for individuals who wish to be tested for indications of CCSVI in private clinics? The tests pose no danger, far less than Tysabri, which is the drug which can be very

dangerous. The costs for the tests are borne by the individual taking the tests, since they are done in private clinics.” Dr. Murray, that falls to you.

JM: Yes. I can understand the question clearly. It's interesting. Tysabri, which does have risks, it's true; however, it also has a number of randomized clinical trials to show that it actually does have benefit. But it does have risks, and that's true.

It isn't true, however, to say that the procedures don't have risk because they are invasive procedures in most cases. There is an attempt to see whether or not external Doppler(?) studies can be done, but the transluminal studies that were done by Dr. Zamboni and by many of the other clinics, and then the procedure itself does have risk. And we've already, I think, heard publicity about some of the complications that have occurred to patients from having the procedure.

So the reluctance is an interesting one. And that's, I think, because physicians are not used to the idea of prescribing experimental therapies. And they know, if they speak to their local radiology department, they're not used to doing these procedures, nor are they set up to do it. And very often they don't have the equipment that the very specialized units, such as the one in Italy, had to study. It was a vascular unit doing this kind of research.

So you had two aspects: The local hospitals are not set up to do this kind of procedure, nor would they likely have permission from their hospital to do, again, an experimental kind of process. So I think the reluctance to some extent was about suddenly being pressured to give something for which there is not a lot of evidence and then talk to the radiologist who is very uncomfortable about the idea of doing the procedures.

MO: Right, you can't have guinea pigs.

JM: You can have—I hate the term, but you can have if you establish a protocol which says, “It's experimental, but this is the way we will do it.” And when you do that you have to go through an ethics committee, and the ethics committee, if it's going to be done in a hospital, will be looked at by the hospital ethics committee, who will evaluate why this is being done and the care and the protocol and the other things. You can't just go ahead and do those things. Now, you could set up a private clinic and do all sorts of things.

MO: Our next question comes on the Web from Francine in Quebec: “Why is the MS Society of Canada only contributing a mere”—these are her words—“\$100,000 per year for a total of two years toward research in CCSVI? What about the \$62 million it has received through fundraising for research to find a cure? To me,” quote, “you are killing the study with this ridiculous amount of money.” Again, from Francine in Quebec. Yves?

YS: Thank you. This is a very important question. I think it's important to ensure that people understand that the \$200,000 over two years per project is in fact

per project. It's not the total sum that will be allocated. We have, quite happily, a good number of applications as a result of the CCSVI competition.

In fact, we let good science drive the total amount of money that is going to be invested in CCSVI research as we do in all of our competitions. The applications are currently being reviewed by a panel of experts from Europe, the United States, and Canada. They include neurologists, radiologists, vascular surgeons, imaging specialists who are themselves not applicants, so they're not in a position of conflict. And they will make independent recommendations about those applications that are good science. We will fund all of the proposals that are good science. What—and those announcements will be available on our website in mid-June.

I think it's important to put this competition in the context of the entire panoply of the society's research activities. The CCSVI competition is itself unprecedented. We opened a special request for proposals on CCSVI in November because our most popular competition has a deadline date of October. It had just closed. Which would have meant, if we hadn't opened this competition, the most natural way to seek funding to answer important questions—for instance, questions about what is the reliable way to image the blockage in the vein so that you don't get the false positives or false negatives; those kinds of questions—and the size of the studies was determined by the medical advisory committee of the society to be appropriate.

The reality is that all of our competitions are open to CCSVI business, if you wish. We did a special one because of the public interest, and it's important to acknowledge that the mobilization of people with MS in support of CCSVI research caused the society to respond because we wanted definitive answers quickly and we couldn't wait until October of 2010, which would have been the next occurring natural timeline. But let me just give you another example: Before June we will open the annual call for proposals for our most significant research projects. They're valued at actually between \$4 million and \$5 million a pop. Those research applications require that a number of institutions come together and collaborate in putting an application forward. We've funded stem cell clinical trials, for instance, or research on the genetics of MS, where Canada has made very important discoveries. And that call is also open to CCSVI.

So the society's contributions to research, which are valued at more than \$120 million over its history, and at more than \$10 million a year, have to be seen in a context of what appears to be relatively modest amounts. And I think it's for that reason that we need to make sure that we don't mistake the \$200,000 per grant as the total sum of dollars that the society will be investing in CCSVI research.

I should also point out that the society was first in launching a competition specifically for CCSVI research. And we're very proud that our American partner organization, the National MS Society based on the US, mirrored our

competition just after the holiday season. And we're actually doing the review together. The panel of reviewers, who are the experts that are going to make these tests, are doing it jointly across all of these applications drawn from the US and the Canadian competition. And together in mid-June we'll make those announcements of the successful projects, so I would just invite you to stay tuned. And it's at that time that we'll be very pleased to communicate the totals of both the US commitments and the Canadian commitments to CCSVI research in this first competition. It won't be the last because we look forward to other applications through our regular and many offerings. All of those, or(?) information about our various competitions are available on the website.

MO: Good. All right. We'll stay tuned for that.

Our next question comes from Tessa in Alberta: "Is it worthwhile to get the appropriate testing done now even though the procedure to remedy the situation is not yet available in my area?" Now, Karen, I just want to ask—we're going to ask Dr. Murray here too, but we've just heard about the testing, that it's not that simple, that there are potentially unclear results. What do you think? Have you thought of getting tested?

KTR: I haven't personally, but I do know people that are very interested in getting it done and have looked into going to Buffalo and that sort of thing. I haven't personally only because it's a personal choice. When this becomes a clinical trial I'll have my hand up first to definitely join. I've taken part in clinical trials in the past. I think it's very important, you know, to study the disease, of course, because that's the only that, you know, to find the cause and to find ultimately the cure. So I have taken part in clinical studies in the past and I'll be jumping on board if this becomes a clinical study for sure. But I haven't as of yet, no.

MO: Dr. Murray, then, about the testing issue?

JM: I don't think so, because there isn't a set protocol now to tell how the testing should be done or what's the accepted procedure. Also, if a person were thinking about having the testing done and perhaps in a year or later having the treatment given, there is no way that a surgeon is going to do the procedure relying on a test that was done a year or two before. So you'd have to have the test repeated again.

And again, your point, Karen, is that once there's a clinical trial, then they'll set up a protocol that says, "This is the way the test is done and this is the appropriate way to deal with the results." Just to get a test now probably wouldn't be very helpful.

MO: Okay. We've had some of those questions submitted on the Web. Now we are inviting the questions from Facebook and from Twitter as well, and also any questions that we have from the room so far. Randy has a question.

Sheila: Hi, my name is Sheila and I have been diagnosed since '87, so I've had MS a long time. Basically I've not heard anything about—let's say my veins are

blocked. Let's say I get the test. It says my veins are severely blocked. But I decide not to get the treatment or go any further. What are the risks for me to live life with blocked veins?

MO: Right. I'm just going to repeat that question. That is from Sheila, who's been living with MS since 1987, and she is asking our panel, if she underwent just a form of a test to find out if her veins were blocked but then decided not to have any procedures done, what are her risks, what's her situation just from having the testing done and finding out that her veins are blocked? Dr. Murray?

JM: I'm not sure we know the answer to that. We do know partial answers. One is that we want to know what the relationship is; in other words, if you have blocked veins, what the relationship is to MS. But the second thing, we know from the Buffalo study that 25% of the people who don't have MS have blocked veins and it doesn't seem to cause them any trouble. So having the blocked veins, we're not certain about it.

We also know that there are some MS experts who are doing studies on this now who wonder whether we're dealing with a secondary result rather than a primary one; in other words, something that's associated with MS but not a cause. One of the things we do not know is is this the cause of MS? But that will be addressed.

If you think of it in terms of whether or not it's the cause of MS, you have to explain then why half the people with MS don't have it.

MO: All right. Do we have another—we have another question in the room, Randy, from your side.

Wendy: Hi, my name's Wendy. I was diagnosed in 2004. You've indicated that the imaging processes, there's different processes, I gather, and different types of equipment. Did the Buffalo study use exactly the same equipment that Dr. Zamboni used? Because you're comparing his results with the Buffalo results yet ...

JM: Yeah.

Wendy: ... potentially there's a difference in the actual imaging equipment which could explain some of the differences in the results.

JM: That's a good point, but in fact they did. And they had Dr. Zamboni as one of their, one of the people who in fact visited and spoke and helped them with their project.

MO: And again, that was a question about the testing that was done in Buffalo as compared to the testing that Dr. Zamboni is—we have a question coming to us from Teresa in Ontario via Facebook: "Can a person who's diagnosed with relapsing/remitting MS for over ten years have both CCSVI and too much iron

in the brain, and still have an ordinary blood test that shows their iron levels are low, too low, almost anemic?" Dr. Murray?

JM: Yes. In fact, there's no relationship between your blood level of iron and this hypothesis that iron deposits in the brain might be an issue here. So treating or non-treating your iron level in your blood has nothing to do with this particular question.

And the issue is not specific to MS. It has been noted that in neurological diseases that have inflammation as part of their process may accumulate more iron in the area of damage than normally seen. Now, we don't know whether, again, that's a secondary effect or whether the iron is causing part of the problem, but in Dr. Zamboni's hypothesis, it is a separate hypothesis. You have the vein issue and then there's this issue of iron. But in the last decade there's been increasing interest in a number of inflammatory diseases of the nervous system, to see what the role is of what appears to be a slight increase in iron in many of the areas.

So you don't need to evoke the iron concept to deal with the venous one, but he has related the two. But altering your blood level of iron has nothing to do with the deposits in the brain.

MO: We have a question in the room, Ashley.

Female: Sorry, hi. To the lady who had that question, Dr. Zavadonov(?) himself said that in his previous study he did not have the proper equipment and he did not follow the full protocol procedures that Dr. Zamboni had for his study, and that could explain the difference in the results. And he said for his next trials he would have the proper equipment and follow the proper protocol.

And, you know, I saw online that the MS Society of Canada has advised that, quote, "for safety reasons the MS Society does not recommend that people with MS be examined or treated for CCSVI outside of an established research protocol." As a longtime supporter of the MS Society, I'm really disappointed in the stance that you've taken towards CCSVI. Given the concerns about CCSVI expressed by the MS Society and its medical advisors, various neurologists, to MS patients, the government, media, medical community, imaging labs, etc., I want to know will the MS Society and its medical advisors now exercise the same concerns with respect to the latest news of another study's results that made the news on March 29?

For safety reasons, have the MS Society of Canada and the neurologist medical advisors begun advising patients to stop their drug treatments until scientists and researchers can replicate the study that revealed there might be two types of MS, and certain drugs that are effective for one type have actually proven harmful to patients with the other type of MS, making their condition in fact worse? Have the MS Society and the neurologist medical advisors begun, and if not, when will they begin actively advocating for the prescribing of these

drugs to cease immediately until larger studies which they want for CCSVI have confirmed or refuted these latest results so as not to put patients at risk of being placed on a drug harmful to their type of MS, as we know now has been done to countless patients for the past many years? Are newly diagnosed patients being advised not to begin any of these drug treatments?

You're stopping testing and treatment of CCSVI because you say further work needs to be done. Clearly further work needs to be done regarding drug treatments currently in use. Are you stopping them as well?

MO: All right, I'm going to just break that down. You have quite a few questions that are in there, and for the purposes of those who are watching us online, just in case they weren't able to pick that up, and later on YouTube. I'm going to, if it's all right with you, break that down into two questions. And the first one, dealing with the statement from the MS Society, Yves, if I can refer that to you, concerning the CCSVI testing that is being done outside of established clinics and protocols, Yves?

YS: Thank you for the question. Let me start by answering—by explaining that the society's role in this context is to provide guidance information based on timely, accurate, hopefully relevant information, but to ensure that our role is as a provider of the information and that we have as a value to honor the right of people with MS to make their own decisions, so I want to make sure that that's clearly understood.

In the context of CCSVI we are, as Dr. Zamboni himself noted in his conclusions, at a very early stage, very preliminary stage in the process of discovery. And the reason we recommend that experimental treatments be sought in the context of clinical trials is really twofold: One is that a clinical trial provides appropriate safeguards for the participants, for the patients, through things like ethical approvals, consent. And secondly, clinical trials provide the appropriate protocols for the information that flows from the patients' response to the therapy in a way that can be rolled up and that becomes data that is, that provides the answers that we need very urgently.

So the reality of our position is that it balances the role that we play in serving the interests of people with MS who want discoveries today, therapies today. We understand that. Living with MS is not easy. MS changes, progresses. It can be very debilitating. But we also want to combine that with the role that we play in racing to those answers that are important in adding to the arsenal of therapies that help us in managing the disease, in slowing its progression, and obviously eventually in bringing us to a cure.

MO: Dr. Murray, I'm throwing this one out there for you. This again is from our question. This is referring to, I believe it was, a study or a news report that was released on March 29 concerning medications.

JM: Yes.

MO: I don't know if you're familiar with that.

JM: But again, that's an initial study which will require validation. But it is suggesting that there may be a marker that could identify people who would be responsive to the therapies as opposed to those who might not be responsive.

The idea that we should recommend that people not take the therapies because of this initial report isn't in keeping with the results. In other words, we have good evidence that patients treated with these therapies, particularly early and when they're relapsed and remitting, get substantial short-term and long-term benefit. So we would not discontinue those therapies.

What would be interesting from that study is if they can develop a marker that can be validated, that it can separate patients. Then you could decide that some patients go on those therapies and others not. At the present time, even as a group patient, there is substantial evidence of benefit in those patients. And the results with those therapies is better now than it was initially in the trials, because in the trials patients who had the disease quite a long time were(?) included in the trials. Now almost everybody who goes on the therapies goes on them early as relapsing/remitting. And so the benefits now are even greater than they were shown in the trials.

MO: All right, we have a question coming to us from Bobby in Ontario. "Thank you for doing this webcast. CCSVI appears to provide a novel explanation for MS. My question is about timing. How long before CCSVI is assessed and, assuming approval, how long before treatment is available to MS patients?" Now, Dr. Murray, I know you've touched on this a little bit before.

JM: Yes. Asking about how long, the initial report from Dr. Zamboni was in 2007, reporting on the observation about the neck problem. As I mentioned, there's a long history of talking about the vascular system and examination of the vascular system in MS. But this venous issue from Dr. Zamboni's 2007 and 2009 reported on the assessment of 65 patients and the therapy, which showed benefit in the relapsing/remitting patients. So that's about the timing of that.

In terms of the assessment further, there are centers now that are evaluating, again, this venous problem, including in Vancouver, but Buffalo is doing that. They're going to be doing 1,600 patients. They've already announced the results in their first 500. And there are a number of centers now who are looking at what can only be the short-term assessments; things like how many patients have the obstruction, what kind of obstruction, what will they then use as an indication of what's an important obstruction as opposed to one that probably is not? So those short-term things are already being studied in a number of centers. So we'll know a lot about that aspect of it in the short term.

MO: We have a question coming to us from Facebook, but also, Randy, you have a question from the floor.

Kathy: Hi, my name is Kathy and I've had MS, relapsing/remitting, for 16 years. I'm really miffed because whenever it was(?) on W5 last year, I immediately e-mailed the doctor down in the States and I got a response. I'd said I'd even pay for it, but they said, "We don't have any money yet. We're not doing anything." And a couple of months later, here there's 300 people chosen to do it! And I'm thinking, "How do you get chosen? How do you get into these studies?" I mean, I'd die to do it because I want to! I mean, and, you know, it's frustrating for me too because I might go into secondary progressive and it won't work, period. So I'm really anxious to get it done now. And everybody I talk to, that's the one question they come up with: Why are these people chosen and not us? So that's my question.

MO: Kathy's question from the floor is about clinical trials: Who gets chosen, who doesn't get chosen? Karen, you had been talking before about, should there be a clinical trial come available, I don't know if you've had any experience at all but you said you have been part of other clinical trials. How did you get chosen?

KTR: I was simply asked at my annual appointment from my neurologist if I was interested in taking part, and he gave me sort of a list of clinical trials that, if I was interested in any. And I did, I chose two or three at the time. I was chosen for one and then the next, over about five or six years, another neurologist that I had at the time did the same thing. And so that's how, I mean, they just ask if you're interested and it's sort of a, I think it's a hit and miss. I really do.

MO: So it's communication with your own physician and the physician has the clinical trials that he or she is accessing, and then they know whether or not you fit.

KTR: That's right.

MO: It's not the other way around.

KTR: And they say, "Are you interested?" And I may not be chosen, though, but they ask if I'm interested, yes or no? And that's how I've been chosen in the past.

MO: All right.

Kathy(?): (Inaudible).

MO: All right. Dr. Murray, going back to the—maybe you can explain too a little bit about clinical trials, and that is Kathy's question.

JM: It's an important question. Each trial will in fact, and one of the things that's required when you go to an ethics committee is you indicate who are the candidates for this particular trial. Now, they can vary. One assessment may be purely by a questionnaire, and so almost anybody is available to fill out a questionnaire. Others, though, if there's a study, may indicate repeated visits.

It's then that(?) indicates the only people who can continue to report to the clinic for assessments or regular MRIs or whatever can be in the trial. And it also says what kind of MS and also the extent of MS. That's always defined. And it indicates whether or not, you usually have to have a balance of patients of various types, and they also indicate things like you can't be pregnant, and there's a whole list of things that are exclusions.

But every trial has a printed list of these. And that's why, when you go to a clinic, they will often indicate what is available and people can indicate whether they're interested in taking part in any of these trials.

MO: Yves, can I ask you, are clinical trials a matter of geography? In other words, it depends where you live and who your physician is? Is that a factor? Could it be a factor?

YS: It is in one important way: People who are treated by neurologists who are in teaching hospitals where a larger number of trials are based will be more likely to be asked this kind of question than if you're treated by a neurologist who works in a community setting and may not be taking part in clinical trials. That's a generalization but I think it's a fair one.

I think it's important to acknowledge we know, at the society, that in the context of the CCSVI trials that are taking place, like Buffalo, or in the process of being launched—i.e., seeking ethical approval—the lists of applicants or people who are interested in those trials are very, very, very large. That is a result of the excitement that we have seen.

In some trials geography will really play a role because you'll want a large trial to not have all of the participants in one geography because if their MS is related, say, to environmental factors, you want to make sure that you're not looking at this only with people who live in very northern climates.

The other thing that's true is that if you want a trial for an MS treatment, a drug like the family of drugs that are currently approved, and you need to have a group of people who are going to be on a placebo, those trials are hard to implement today in places like Canada where those treatments are funded by our governments. Because it is not ethical to exclude a group of patients who should be on a proven therapy just for the purposes of advancing science. So those kinds of trials are moving to parts of the world where those therapies are not refunded(?) by governments, like the Ukraine or the Czech Republic or Russia.

So geography does play a factor, but I think the significant factor to the question that's been asked in the context of CCSVI is one of the unprecedented level of interest more than anything, I would say. And it's really unprecedented. Many thousands of requests, when people are looking to involve in that trial, hundreds or maybe just 1,000 or so participants in a trial.

MO: Thank you. Thank you very much for your question. I'm just going to get this question here from Facebook, from Ricardo, who's contacting us from British Columbia: "With a blockage of veins from the head, why don't we see people with MS with purple lips, red faces, bloodshot eyes, some of the more basic and seemingly obvious side effects of a restricted blood flow?" And then he adds, "To my knowledge, MS is still considered a neurological disease. How does this relate? If CCSVI is proven will this change the classification of multiple sclerosis or perhaps broaden it?" Dr. Murray?

JM: Well, there are two very interesting questions here. We don't know why patients, if they have obstruction in their neck veins that is substantial and producing something like MS perhaps, why patients don't get other symptoms from obstruction to veins. But we apparently don't. And also, why is it that normal people can have obstruction and have no symptoms or evidence of MS? So I'm not sure why there's no other symptoms or problems from this, but there isn't.

But there is something interesting about some of the patients who have had the vein blockage undone, and some of them have said they could tell that it was helpful because they felt that their hands and feet got warmer. That's interesting but it's hard anatomically to figure out how that works, why an obstruction from veins coming from your brain would make your hands and feet warmer, but it is something that they did mention.

About MS being a neurological disease, MS *is* a neurological disease. No matter what they find out about its causation or whatever, it'll still be classified as a neurological disease. But the interesting aspect of that question I think is about the changing frame about how we think about MS. Over the years, our understanding of MS has changed and increased as time has gone on. You used to hear, for instance, that it was a demyelinating disease. Well, we now know that that's a very limited concept. It's not just the myelin; it's the axons that perhaps even more important. So it's not just a demyelinating disease, so our thinking about that has changed.

We talked about it as being a white matter disease that occurs within the white matter of the nervous system. We now know that in fact it involves the gray matter just as much as the white. You just don't see it. When you do an MRI you don't see any changes in the gray matter. And so, but that's very important because it produces a lot of the problems that occur in MS, and so there's a great interest now in looking at the gray matter in MS.

So our concepts are changing. Not that it changes from being a neurological disease, but the way we think of and understand the disease has changed. And that may be one of the things that this whole discussion has assisted, and that is it's making us question whether or not we should think of this disease in another way. We know we don't understand MS entirely and we do enjoy seeing new ideas and new concepts that may change our thinking and that may lead to better answers. But we still have to—every hypothesis has to be

tested, and that's the nature of science: Make a hypothesis, develop a way of examining and experimenting and finding the answer. The hypothesis isn't the answer; it is a possible answer. There are ways to find the answers.

MO: Right. Randy, we have another question from the floor.

Trevor: Hi, my name's Trevor and I've had primary progressive since 2004. My question or questions are directed to Yves. You said earlier in your statement that the MS Society is here to support and provide information for people with MS. My question is since the MS Society was aware of Zamboni's paper that was released in 2007, why is that the MS Society will not provide any information about CCSVI at all to any of its members, nor did it bring to anybody's attention as a possibility or anything(?) for the future?

Also, Yves, you mentioned too about the grants for \$200,000 over two years, so \$100,000 a year. That's only based on the fact if the people that are providing these suggestions meet certain criteria. Who determines what criteria and if it's met or not to go ahead with the study?

MO: I'm just going to repeat those questions from George [sic]. The question is concerning, is directed at Yves of the MS Society concerning Dr. Zamboni's first publications which came out in 2007, and the MS Society's response at that time concerning CCSVI. And then also regarding, the second part of the question, regarding the \$200,000 project going toward CCSVI research right now, who determines exactly what the criteria are for that research? Yves?

YS: To the first question, the MS Society has actually, through its website mainly, had information about CCSVI including before CTV and the *Globe and Mail* brought this story to the major media in November. In October, through our medical update memos, we provided a summary of Professor Zamboni's papers. You can find the medical update memos on our websites. They're not on the front page but there is a collection of them, and they are in fact short summaries of what's happening in the academic publications about MS research. They're very interesting and they cover a broad range, obviously, of different pathways to discovery in MS.

There has been since November a lot of information about CCSVI, again through our website, and the MS Society, through its 120 chapters across the country, have done information sessions. Our provincial divisions have also done information sessions. And the Web has provided links to media stories, links to other resources about CCSVI where we've sought permission from colleagues—whether in hospitals or in the research world—to make available through our gateway any(?) information that is developed by the MS Society itself.

I think the most useful piece of information is probably the series of frequently asked questions. And by the way, they continue to evolve and change as we receive questions from you through all channels. Without identifying those

asking the questions, we develop answers that are easily available in English and French on our website.

To the second question, and it's a very important one about who makes the decision, who makes the decision as to who gets funded, the first step in that process is the process that is the process of peer review, which is that a group of experts in the field, numbering about 15, and in this context, for this competition, they've been gathered in the US, in Canada, and in Europe, who are not themselves applicants and who are not in labs where their colleagues are applicants. They're completely without a conflict or without a personal interest in the results of the determination. And they give us of their time to actually review the proposals. And in this context they're going to be interested in the hypothesis, whether it was clearly articulated, whether the team and the resources that have been proposed is actually appropriate to answer the hypothesis, and whether in fact the study does have relevance to MS.

We're interested in the connection between CCSVI and MS. We've established some criteria; for instance, we want to make sure that in all of the studies there are experts in imaging because of the discussion that we've just had, and neurologists that are connected to the projects. But the projects can involve teams of researchers in different areas. That panel will make recommendations based on that peer review using, by the way, a system that is very, very robust because it's used by governments, foundations, and health charities such as ours worldwide. This is a very, very common approach to making decisions about funding good science.

And those recommendations will then be brought forward to the board of the MS Society of Canada, which is made up of volunteers. It's made up of people who have MS and people who have loved ones with MS, who give of their time to provide really the last stage of oversight. And with the medical advisory committee that advises the board, their concern at the final stage will be to make sure that the process was honored at every stage. They're meeting in the first ten days of June and it's at that time that they will make the final decision, and those will be communicated in mid-June.

MO: Yves, we have another question concerning research. This is coming to us from Steve in Manitoba, and he's asking "How does the MS Society of Canada feel about the negative response of some who are in the research community who actually do receive funding from the MS Society of Canada concerning CCSVI treatments and Dr. Zamboni? I mean, they think that there is nothing to it."

YS: We've been clear: CCSVI represents a very exciting new pathway for discovery. It's like adding a lane in the highway to the eventual cure for MS. We are very clear also that we're driving on a highway with many lanes. Stem cell research, genetics, environmental factors. We actually don't have a policy ever of putting all of our eggs in one basket. CCSVI opened another lane and we're working to make it a fast lane. That's very clear.

There is very clearly a debate, but I think debate is a good thing. Professor Zamboni himself acknowledges that his findings are preliminary. In fact, in his conclusion to his paper in the fall, he concludes by saying that his own data are possibly at risk of bias and therefore need replication. They need to be challenged in larger studies. So this debate is, I think, a healthy thing.

The reality of people engaged(?), like people who are listening today, is also a very healthy thing. When citizens get excited, get mobilized, I have confidence that in fact that will accelerate the process of research discovery. But that process will require debate and at the end of the day, I think we're clear that the debate and the research are required to make sure that this pathway to discovery is confirmed as a valid one and is a promising one for new therapies for people with MS.

MO: Thank you. Yes, Karen?

KTR: I just wanted to mention that that debate as well is happening amongst my fellow MSers, people with MS across the country, in Ontario, within my community. It's happening and I think it's healthy because we all learn from debate. We all learn from the more information that we share. So I think it's healthy.

MO: We have a question, Ashley, from the floor.

Sandy: Hi, my name is Sandy and my husband has MS, and has since—diagnosed in 1982. I have a copy here of the results from the second phase of the Buffalo study that have been done. And what the results was that all of the MS patients that were tested for CCSVI all tested, all 100% tested that they had CCSVI and none of the normal controls had it. So I'm excited about this because it looks like we're moving forward and seeing the connection between CCSVI and MS.

Now, I'm not taking here about a cure. My husband is in end stage(?). He has a G-tube(?) and he has a ventilator for breathing. So what we're looking at is just to have his CCSVI, to be tested for CCSVI to see if he has it, and if he does, to be treated so his blood flow is, you know, the damage that's being done by the iron accumulation in the brain, affecting the blood-brain barrier and crossing over from the circulatory system into the immune system, causing that damage that results in MS, just to have it stop the progression of the disease, to maybe buy him some time. Because I think further research is, as you are stating, there is going to be further research to look into this.

But I'm not really looking at that right now because time is of essence here. I'm looking at testing. Can he be tested for CCSVI? So what I'd like to ask is what is the MS Society, considering you said earlier today that you were here to inform us and to let people with MS make their decisions, what are you doing to help in that decision for the people who want testing for CCSVI and treatment if necessary? Not connecting it to being a cure or a cause; excluding

that. Just let's do this much of it to get the equipment, protocol done, opening up a clinic. The MS Society has funds for doing that. And just what can be done to move forward on this front?

MO: Thank you, Sandy. I just want to recap just briefly, again, for our live streaming audience. Sandy's question is concerning MS—her husband has MS—and the CCSVI testing that can be done for MS. And I'm going to break this into two parts if I may. First of all, I guess Dr. Murray, because we're maybe talking about perhaps some more specific situation here, Sandy's question is concerning her husband who has end-stage MS, whether any kind of testing is worthwhile. I mean, that's a difficult question that I know that I'm posing for you, considering you don't know this patient individually.

JM: No. And I can understand the concern. All we know is that in the results coming from Dr. Zamboni's small open trial was that people with early relapsing/remitting whose veins stayed open appeared to get some short-term benefit. But that none of the other groups did get any benefit. At the end of 18 months, when they looked at the other groups, there was no measurable benefit.

The other difficulty, I think, that the local hospital or clinic or whatever would have difficulty dealing with is if the idea is that anybody who felt they wanted testing, there are over 50,000 MS patients in Canada. And I'm not sure how that would be dealt with. And so the principle has tended to be to provide that kind of testing or therapy in the context of a clinical trial in which you will learn some information.

MO: And also as you mentioned, too, there are still some questions as to what kind of actual testing should be done.

JM: Yes.

MO: The format of the testing.

JM: That will be a problem for any center that decides that they're going to do this. They have to decide what protocol, what procedures they're going to do and how they would judge abnormalities.

MO: Okay. I'm just going to take one quick question here from Facebook. Alex is sending us a question on Facebook: "Why doesn't the MS Society publish the Michigan results or get on television and explain to people that the Zamboni story that was played on TV was in fact not a complete picture of success? I believe a more balanced report would shed a lot of light on the CCSVI and clear up a lot of confusion. I'm tired of the society always being a reactive machine. Good or bad news, report it. At least then we can judge the information ourselves." Well, Yves, I would say that's exactly what we're doing today.

YS: That is the genesis of this conversation. Thank you, Alex. It's significant to say that on our website we provide links or summaries of research results. So that the Buffalo results, which to some appear to contrast the early, very preliminary results from Dr. Zamboni in Italy, that contrasting picture, there's a summary of that available on our website. It's also important to note that on our website will be available, there will be information available about a webcast taking place on April 14 the context of the meeting of the American Academy of Neurology, which meeting is taking place here in Toronto. This is a webcast-only invitation where the results of the Buffalo trial that is led by Dr. Zavadonov will be discussed in a panel presentation that will in fact include Dr. Zamboni and others. So if you want to participate in that webcast the very same way that you registered in this one, come to our website in the next few days and you will find the tips and information about how to register in that panel.

I think at the heart, the MS Society attempts to play a balanced role in providing information. That is the role that we play in the context of CCSVI. It's also the role that we play in the context of other kinds of important decisions, whether it be pregnancy or nutrition or adapting an exercise regimen to different stages of MS. All of those kinds of decisions that are important every day for people living with MS. And I understand the urgency for someone who has a progressive form or is in an advanced stage of the disease's progression to know right now what this testing might offer me. But in this context I think the society has pressed on the accelerator via the research route because we need very definitive answers. And that's the arena in which we can have the most impact.

As Canadian trials get underway, trials that have been subject to the appropriate ethical approvals, those, the information about those trials will be published on our website. So, again, for people who want to register with Institution X or Y will be able to find the information on our website to guide them to the website of the particular institution.

MO: All right. We have just one more question here I'm just going to take from Robin, who's just sent us a question here from Ontario again. It's concerning MS research, and he—Robin says, “I want to contribute to MS research. I feel that CCSVI has the greatest potential. Can I, as a long-term participant in MS walks, direct my contributions specifically to CCSVI?”

YS: Marlane, the answer is an easy yes. But there is an important note, which is that we are asking those who want to do that to contact us and to request that. If you go to our website to support anyone who's participating in the walk, and our walks are starting in mid-April and will continue until early June, and you can do that by going to www.mswalks.ca, you won't be offered that option automatically on the Web. You'll actually have to seek it out and make a phone call to reach one of my colleagues on the staff or a volunteer at one of the MS walk sites.

And I think it's important for me to answer why it is that we're asking people to go through that extra step. It's because the MS walks funds very significantly the important work of our chapters and provincial divisions in providing the first line of support to people with MS. And the excitement about CCSVI has been unprecedented. If we had made this available to everyone, the risk would have been that we would have dried up the resources that are required to pick up the phone in local chapters and talk to someone who's been newly diagnosed, who's calling to support with requests for information about CCSVI and about other things. So it is possible subject to the inquiry of the walker or the donor.

MO: And we're just going to get a question from Randy's side of the room in just a moment, but I just want to go back to something actually that we talked about before we went live on the webcast, as to why the response to the whole CCSVI issue has been so unprecedented. And from a media standpoint I guess part of it comes from the fact—and Dr. Murray, you were talking about this—that it seems simple. And I think because of that it translates well into the world of not even 15-second sound clips anymore but five-second sound clips. And this is not a simple disease. This is not a simple set of circumstances. There is no simple “flick the light on and off” cure. Karen?

JM(?): That was your point.

KTR: Yeah. And I just said that because a lot of clients that I've talked to during my debates have said that it just seems so easy. It seems so simple. They understand it because of heart issues and, you know, diabetes in the legs and that sort of thing, putting stints in. So they just, they seem to understand that. And so they just, they got excited because it's, “Okay, it's not the brain, it's not the autoimmune system, it's not—I get this. So I'm going to look into it.”

MO: And it's a very emotional set of circumstances.

KTR: Oh, of course.

MO: If you think it's that simple.

KTR: Exactly.

JM: It's also, if I may, Marlane, it's also important to underscore that there's been some discussion about Dr. Zamboni's hypothesis as replacing the immune theory of MS. When you read his research it's very clear that he doesn't talk about replacing. He talks about the blockage and the iron deposits that the blockage causes as the trigger. So what one might do is remove the “auto” before “autoimmune,” because then you would have the immune attack explained by the iron deposits that flow from the blockage. But the immune system remains involved in Dr. Zamboni's theory, so we need to be clear about that understanding. It's not a replacement. It's not a substitution for the immune explanation or theory of MS.

MO: Dr. Murray, it sounds as if we're opening the door but we don't know which way the path ahead of us is going to lead just yet.

JM: Yeah. And the normal pattern in science, including in the direction for MS over the last particularly 50 years, has been, as Yves said, is to go down a number of different roads or different hypotheses, examining, questioning, challenging at all times. It's not to drop a whole area of research and invest only in one belief. Because until you prove something it is a belief, and beliefs are open to challenge, and that's what science is about.

So we are going down different directions. I mean, there are teams all over the world doing different kinds of research on MS. This will just be another. And it reflects back on the point of why this got so much attention. Because there are lots of other things; for instance, there are, I can think offhand of five new therapies for which there are randomized clinical trials showing great benefit that got no attention at the time that this one, which doesn't have a randomized clinical trial to substantiate it, got a huge amount. And there are a number of things. The simplicity of understanding it.

Secondly, it was a new way. It wasn't pharmaceutical. It wasn't a drug. It wasn't something that you injected. And that had appeal.

Thirdly, it was the kind of words used around it, because even though the paper, if you read Dr. Zamboni's paper, he's very clear about the fact that this is a preliminary study, it needs to be studied further in randomized trials, many of the aspects of his trial he indicates, as you point out, there is the possibility of bias in how they did it. So he's clear on that. But he wasn't so clear when he was doing interviews. He was using words like "cure." And they were showing some patients who talked about dramatic results. But if you read the results in the paper, you didn't see that. You didn't see that people were getting dramatically better; you saw some very small statistical improvements only in one of the four groups.

So then you say, "Well, why did he get all the attention?" Well, I think for a number of different factors, but I suspect that had the Buffalo paper come out first and Zamboni's second, you wouldn't have heard any of that.

MO: Okay. We have a question from this side of the room. Randy, there you are.

Laura: Hi, my name's Laura. I was diagnosed with MS in 2007. First of all, I'd like to thank the MS Society for sort of jumping on the bandwagon with CCSVI so quickly. I know for a lot of people it doesn't look that way, but I worked in pharmaceutical research and I understand how much it takes to start something like this, so thank you for starting it so quickly.

Is it possible to speculate how long it will be before there's a protocol available to start a clinical trial?

MO: The question is from Laura, who is asking Yves of the MS Society about the CCSVI protocol.

YS: So the—if I speak only to the two competitions that have been launched, one by the MS Society here and then our sister organization in the US, the applications that we invited are for clinical studies or trials. And in the proposals those protocols have to be presented because in fact knowing that part of the review will involve “Are you doing or using the right kind of imaging? Are you using the right kind of processes to actually get us to confirmatory answers, or to answers that are reliable?” And the moment funding flows in late June, early July, from both the US and Canadian societies, will cause those institutions to in fact get on with implementing the trials.

Some of them have in fact started the process of getting the internal ethics approval. Because, as you know, the moment humans are involved in health research, the institutions require appropriate ethical, an appropriate ethical framework. And that process has been engaged already by some of the sites that have applied for funding. So I think this speaks, I think, to the acceleration of the process of discovery. It is happening very quickly.

There are other trials—the one in Buffalo is a good example—which is taking place at this time. Data is being, data is going to be released at 8:00 AM on April 14. They're speaking to the media about those results in a more definitive way. So that is how quickly this is changing our world.

MO: And Yves, if I can just follow up on that, how prepared or excited or ready are Canadian research facilities to embark on CCSVI research?

YS: Marlane, we issued the, we made the announcement that we would launch the competition just two days after the *Globe and Mail* and *W5* articles on the weekend of November 20 or so. And we launched that competition in early January. So effectively, for many researchers, they had notice for five weeks, two of which were the weeks of the holiday season. And I tell you, we had a good number of applications. And three weeks later, those who made the initial test—because it was a two-stage application process—all had their very detailed applications—and when I mean applications, they're an inch thick—those applications in time for the February 9 deadline.

So the response has been tremendous. And you have to understand that preparing the application means coordinating with different specialists in your institution and university because you have to have an imaging specialist, you have to have a neurologist. So all of those partnerships had to be developed. And in many cases, it meant speaking to people in your university or hospital setting with whom you hadn't been having these conversations. People who are interventional radiologists and vascular surgeons. So that, I think, just shows the level of excitement that we see everywhere in the country.

MO: Right. We have a question coming to us from British Columbia, from Eleanor: "If indeed I have a collapsed jugular or vein, why should these not be treated? Why should I have to live with collapsed veins?" Dr. Murray?

JM: Well, we don't actually know the answer. We know that half the patients appear not to have collapsed veins, and we don't know what the difference between those two groups is. And we know that normal people may have collapsed veins and don't appear to have any symptoms. So I don't know that we can answer the question.

MO: Okay. We have another question, Ashley.

Male: Good afternoon. This, my question is directed to Dr. Murray. Dr. Murray, you mentioned earlier that in Dr. Zamboni's study that some or all of his patients, this particular group of patients, have experienced a warming of the hands and feet after the procedure was done. Is that an indicator that if an MS who has severe lack of feeling or of coldness in the extremities, is that an indicator that they have a collapsed vein?

And I have a second part: Even if CCSVI and the procedure might not be MS or a cure for MS, could that be a solution to some of the problems, some of the symptoms of coldness of the extremities?

MO: I'm just going to read the question for our national broadcast. It is, again, a question concerning Dr. Zamboni's research and the warming of the hands and feet that took place after people had their collapsed veins reopened. And then the second part of that question, again, was is there perhaps, outside of MS, just the possibility that CCSVI could help people with warmer extremity circulation? Dr. Murray?

JM: Yes. The observation about this feeling in the hands and feet was mostly on the Internet by some people who had the procedure and were on the Internet talking about this. The question of coldness in the hands and feet that occurs in MS patients, it's referred to as Raynaud's phenomenon. And Raynaud's phenomenon is actually very common. If you go around a room of people and shake everybody's hand, you'll notice that some people have cold hands, and if you ask them, they'll tell you they probably also have cold feet, and also most of the people in their families probably have, because there is a genetic relationship. So the phenomenon of Raynaud's phenomenon is extremely common.

In MS it's actually increased, and part of it is related to the less use of muscles. If you use your muscles extensively, your limbs, hands, feet warm up. You'll notice that many people, if they sit in a wheelchair with their feet down, not using the muscles, that their feet get cold. They even appear to turn blue or even purple. And that's Raynaud's phenomenon. And if you touch the skin it feels cold.

Now, people often get very concerned about it, but it's actually just an annoyance. It doesn't actually—there are vascular diseases that are important, but Raynaud's phenomenon tends to be mostly an annoyance. I suspect that the phenomenon that some of the people have reported after having the veins done and Raynaud's phenomenon, I'm not sure whether it's related or not, but Raynaud's is extremely common.

MO: Is there a connection between cold hands—going back to the second part of your question—cold hands and cold feet and blocked veins? Do we know that?

JM: No. In fact, if you study, what you'll find is that it's an exaggeration of a normal reaction. If you go out in the cold, your hand, the vessels in your hands tend to constrict. If you go into a warm area they tend to dilate. People with Raynaud's phenomenon get an exaggeration of that. So they're often individuals who, when they go out in the winter they always put their gloves on because their hands get so cold, whereas many other people, they don't mind, they don't put gloves on because they don't have Raynaud's phenomenon.

I guess the other question is if you have cold hands, do you have a warm heart?

MO: Karen, what's your experience?

JM: Another research question for us.

KTR: Yes, to that question.

I just wanted to mention that when I've had MS flare-ups in the past and I have numb hands and numb feet, I feel that they're cold and they're actually not. I have, my husband, "Are my feet cold? Are my hands cold?" And I feel that they're cold from the inside but they're not actually cold.

MO: That's a good observation.

KTR: Exactly. It's very weird.

JM: And that's another phenomenon. That's related to the change in sensation. It feels like it's cold.

KTR: Exactly.

MO: All right. We have a question coming to us from Laurie: "How will you respond to pressure from the pharmaceutical industry which may not want current drug therapies to be replaced with CCSVI therapy due to the financial impact they're bound to feel? They carry a lot of weight, pharmaceutical companies, and can slow down or even stall progress that negatively impacts them financially." And Yves, you were talking about this before. This is going down our highway.

YS: Well, I think it's important, actually, to put in context the work of the pharmaceutical industry in terms of developing therapies and other actors in the research arena. Health charities like the MS Society, governments; the federal government is a very major contributor of dollars to health research through the Canadian Institutes of Health Research. And institutions; teaching hospitals and universities do a lot of science with funding that is not linked to the pharmaceutical industry.

In fact, when you think of the MS Society, less than 2% of our revenues in any year comes from the pharmaceutical industry and none of that is intended for a research program. No representative of the pharmaceutical industry has any say in any aspect of the MS Society's business. We have a policy that is very clear that when we accept their funding, it has to be without restriction. They cannot seek through their funding to control what we say, for instance. It's very, very critical.

The bulk of our funding comes from individuals. About a million Canadians from coast to coast contribute of their hard-earned dollars through the walks and carnation sales and through the mail. And I say thank you to all of you. A small number of very generous corporations that are not in the pharmaceutical industry—RONA, Royal Bank, A&W(?) are among very important corporate partners of the society.

So at the end of the day I hope I can dispel the linkage there and tell you, personally, for our members, 30,000 people who are members of the society who are eventually making the ultimate decisions of electing my bosses, the volunteers who sit on the board of directors, everyone at the MS Society is very clear that the day there is a cure and there is no requirement for treatment will be a great day, will be the end of MS, and we'll celebrate that. It will be a great honor for me to put the lock on the door, I tell you. And I just want to dispel this notion that pharmas have some particular lever to control that destiny.

MO: Okay. Is that more of an American—I mean, I know you can't speak of the American health care system, but that may be where we get the impression from.

YS: No, I think in fact, if I may, what I said holds true and I'll just say another piece. The MS Society has a very clear and forceful position that our federal government should almost double its level of investments of public tax dollars in health research. We spend as taxpayers through the federal government about \$1 billion a year, and the MS Society wants that to be \$1.8 billion. And by the way, we're not alone. That's the position of a coalition of health charities; the cancer societies and heart and stroke.

In the US the level of public funding for health research, the stuff that is done in institutions, universities, and hospitals that is not linked to a commercial agenda, is actually much higher than it is in Canada, proportionately to the size of our economies and the size of our governments. So while the federal

government plays a very important, critical role, it needs to play an even greater role in the area of what I would call public benefit research. The kind of work that is not commercially tied: health charities, granting foundations, Bill and Linda Gates, or the National Institutes of Health, which is the federal government arm for health research in the US. They're very, very important institutions that fund the kind of research that is not linked to the pharma industry.

That's not to say that the work of the pharma industry is not important. I want to be clear. But it is a part of the whole and very complex approach, and they certainly don't control the other parts.

MO: All right. We have another question to us coming from Don in Alberta: "Does the MS Society support having testing, MRI and ultrasound testing, done by provincial health care systems?"

YS: Thank you, Don, for the question. It's a very important one. The MS Society plays a very important role in advocating for therapies to be delivered quickly by our health system, our provincial health system. But it's important to understand that our health system in Canada is founded on the notion that there needs to be evidence about the efficacy of a treatment before it's going to be funded. And we have been very active players with available evidence, as in the case of the therapies that are available in MS treatments, to advocate for quickly making those available to Canadians.

At the moment, if we knock at the door of governments, provincial or federal governments, we're going to be met with a response that we would expect, which is "Show us the evidence." So I think it's not—it is appropriate to keep elected officials informed, to share the excitement, but it's important to know that they will look to the evidence before it is funded through our tax dollars.

MO: Okay. From this side of the room, Randy. Yes?

Female: If I didn't have MS and it was—a vascular surgeon today can operate on veins. They do it regularly in legs and all the rest. If I didn't have MS today and they discovered that I had a blockage in the two veins that are being tested right now, could that surgeon or that specialist work with those veins without having to go through clinical trials or procedures?

MO: All right, the question is concerning if there was a situation where there was a blockage of veins that was separate and had nothing to do with MS, is it available, medically speaking today, Dr. Murray, that those veins could be blocked—could be unblocked?

JM: It's a very interesting question because you noticed in the Buffalo study, 25% of the people without MS had problems in their neck. I presume none of them are going to have those operated on.

The other aspect that has to be understood is it's not normal to study the neck veins. So it's very unusual to have an assessment done on patients to look at the patency of their neck veins.

Female: (Inaudible).

JM: Yeah.

Female: (Inaudible).

MO: In other words, you're asking in Canada, is such a procedure available anywhere under any circumstances to unblock neck veins?

Female: (Inaudible).

MO: Do you know of circumstances where that's done?

JM: No. I suspect, though, that to justify doing a procedure in that hospital, it would be questioned if the person had no symptoms and no problems but was going to have surgery. You see, one of the problems with that question is a person without any problems or symptoms, you can't make them better.

Female: (Inaudible).

JM: That's true.

Female: My husband has prostate cancer right now. He had absolutely no symptoms!

MO: As Dr. Murray was saying, there are quite a few people who walk around—I mean, maybe you could explain that part of it a little bit more. How can people walk around with blocked veins and still be perfectly normal and healthy?

JM: See, this is all new information to us. All we know is that the Buffalo study, when it looked at non-MS patients, found that about 25% of them had problems in their neck.

Female: (Inaudible).

JM: No, although you'd find they have no experience in doing it.

MO: Okay. Just, I have a question coming to us from Angela on Facebook: "Dr. Murray, do you think it is unethical that Dr. Zamboni's treatment is being done by neurologists now in Europe? I don't know to the extent to which they are." This is the question from Angela.

JM: Yeah, well, it's an interesting question because there are two contexts. If you look at what's developing in a number of centers, particularly the Italian centers, they're developing research protocols and studying it so we get some information. What is also happening is that in some countries, in Romania and India and in Poland, people are just setting up private clinics and doing the procedure.

Is it unethical? Well, it depends on two things: Whether you think that giving experimental therapy is unethical; secondly, whether the local processes determine that it's unethical. But often private clinics set up to do all sorts of things and if there are no legal restrictions, then there's nothing that says they can't do it. It is, for instance, around the world you can go to places and get all sorts of very unusual therapies. The question of whether it's unethical for people to offer therapies that you think are probably useless is an open question because they may think they're useful. You can go to the Philippines and have some very strange therapies done. You can go to Florida and get snake venom. You can go to Florida and hyperbaric oxygen therapy at great expense, which there are clinical trials showing is of no value in MS. But you can still do it. Is it unethical for those people to do it? I think that it's an open question. It depends to some extent whether their motivation is making patients better because they believe it or they're just trying to make money.

MO: We have a question coming to us from Robin in Manitoba: "As we know, there are children who are diagnosed with MS. Has there been any testing, any connection with CCSVI in children?"

JM: We don't have any information as yet, but in fact a lot of the information we have about children with MS comes from Canada, and the numbers were involved in doing a study many years ago to show that in fact MS does occur in many people in childhood. And now here in Toronto there is a very good unit that assesses and is a world leader in the issues about learning about MS in children. And there's a collaboration around the world about that.

But in terms of this particular question, we don't yet have any information. But in the process as it unravels, I suspect that children will be examined for this as well.

MO: Ashley has a question here from the back. Yes?

Susan: Hi, my name is Susan and I've had MS since 1989, so I appreciate the support of the MS Society, who I have supported for many years, in bringing CCSVI to the forefront, certainly in the research here.

The question I have is surrounding the research competitions, and I'm just wondering, I know that the research results—or the competition results, pardon me, will be released in early June. I'm just wondering if the next phase of your research competition, if those studies, I know there's been lots of discussion about the number, amount of moneys being released being quite small, really. In terms of the scheme of research it's a drop in the bucket. Will those studies be able to be preliminary research for larger studies for the next phase of your competition, perhaps?

And part two of the question is at the table of international experts deciding what gets the award and what doesn't, where's the patient voice? I know that we do need to have the medical experts there and I'm happy to hear there's

vascular and interventional radiologists, but I always think about the patient. I think they have a lot to offer and perhaps some of the hype about this comes from the patients. Some of us kind of have feeling for a number of reasons, and I'd like to see the patient at the table.

MO: All right. Susan has a two-part question. The first part is concerning the CCSVI research competition that Yves was talking about before, that is going to reach its next level in June. I'll simplify that. And she's also talking about whether that is a first round of research that's going to lead to perhaps further, more expanded research. And then the second part is, in this entire process of the research grants, where is the patient's voice? Yves?

YS: Thank you for both questions. The results of the initial competitions will be available in mid-June, and we in fact don't know what it will mean in terms of the results for subsequent competitions. Let me just offer to you, our competitions are driven by the investigators. So they're not—it's not the MS Society that decides what the competitions, what should be prioritized. It's the curiosity of the investigator that drives the demand. They prepare the applications and they come forward with them. And for the largest of the grants that we make, which range between \$4 million and \$5 million, those kinds of studies require in fact that the building block hypothesis already be answered, and those building blocks are answered through research that is done via operating grants, totaling about \$200,000 a project.

But we have a stream of competition that is actually a pilot grant for \$25,000, when someone wants to collect a set of data to actually just do the first part, which is frame the hypothesis. And our competitions are numerous. They happen at different stage(?) of the calendar with opening dates almost in every quarter of the year. Some are for people who are in the training stages, advanced training of their career. Others are for very established researchers, like the largest grants. I can't anticipate for you what will be the level of demand for CCSVI research.

But the second part that I couldn't anticipate, which gets to your second question, is that even if I knew what the demand would be, I couldn't tell you which of those proposals are going to be deemed to be best science. So you could have one in genetics and one in stem cell and one in CCSVI and in fact the team of researchers in one case may have missed a building block that is really important in the development of their hypothesis, and the reviewers might send them back to the drafting table.

The importance of the society's work in funding research is really that process of review because that's the process that assures us that we fund the research that is well designed, well resourced, and that's going to get us to the answers more quickly.

To the second part of your question, which is a very important one, you're absolutely right that the patient voice is important. We have at the society for

our regular competition just started the process, a very important one, of engaging a patient, a person with MS, to bring that perspective to the debates that happen around the table of, the expert review table. So that you combine, obviously, the person's view, the person who stands to benefit, with the experts' view.

And in the context just of CCSVI, because of the speed with which we developed the partnership with the American association to actually form the expert review team, we don't have a patient voice at that table. And for that I can only say I'm sorry, that really our commitment is that in the review process, the person with MS should be present and that voice should be present in those processes of adjudication.

MO: Dr. Murray?

JM: I just wanted to emphasize something Yves actually said earlier because I get a sense from some of the questions that occurred during the afternoon, and some of the ones that came in over the Internet, that there is a sense that the allocation of funds was a limiting factor. The investigators in the field don't feel there's any great limit. They have access to all of the funding that comes from the MS Society for this research. If they put forward a grant, a really superb, outstanding grant, for half a million dollars, that goes into the request for funding from the MS Society.

The unusual thing here is that the MS Society has designated a very specific area to make sure it got some encouragement and funding. But investigators will regard the ability of the MS to fund research is(?) all that's potentially available for CCSVI, if they have the allocations. Isn't that right?

YS: Absolutely. All of the competitions.

JM: So there's nothing limiting about \$200,000.

MO: It's just a first step.

JM: Right. It's specifically allocated but you could submit for all of the funding given by the MS Society if you have good science. That didn't limit the amount that will go to CCSVI.

MO: I just, I want to ask one question before we get—Terry from Manitoba has another question coming up, but just one question for the three of you: We're doing this session the first time. It's the first time publicly, national talking about CCSVI in this kind of a forum. A year from now, next April, Yves, where are we going to be?

YS: Next April we'll have a lot more data. We'll have clinical studies that will have enrolled patients and people with MS participating in the process of discovery.

I think the story of CCSVI is also a story about the Internet and the power of the Internet. And this webcast is also an expression of that. To be able to communicate with people from coast to coast, people in small and large towns, people who are far away from a neurologist and people in downtown Toronto is really tremendous. And I think, I celebrate that. The reality that people have been able to use Facebook to share information around the world very quickly. So I would say that kind of communication that really engages the person with MS and the voice in mobilizing our governments and our researchers and the society to act quickly is, I think, very exciting.

So I think it would be really exciting to look forward to a repeat of this kind of dialogue once we've traveled down the fast lane of the highway on the path to new therapies in MS.

MO: Dr. Murray? A year from now.

JM: A year from now? I think a year from now, in fact, we'll have more information, particularly related to the short-term questions. How extensive is this neck problem, both in non-MS patients and in MS patients. We'll have a lot more information about trials that are currently underway. We'll know more about the Buffalo study, which will be up to 1,600 patients. We will start to see, I think, clinical trial information begin, even though it will be very preliminary, and we'll see a lot more of the reality of the discussion. And I would emphasize you've got an opportunity to listen in on that discussion that's going to go on at the American Academy of Neurology here in Toronto later in the month.

MO: April 14.

JM: April 14. You'll hear the major players. You'll hear the major players talking about it, and I think you'll get a sense of what the reality is about all of this. So I think things will be a lot calmer, clearer, in a year's time, even though at that time we still won't know the answers to the long-term benefit, which is really the issue. What we really want to know is what is going to be the benefit of this as a form of therapy? That will take longer, but I think in a year you're still going to know a lot more.

MO: Karen?

KTR: I think it's very helpful(?) and exciting, and I think in a year from now, Dr. Zamboni started the process and in layman's terms he's taking the baby steps. And I think that as we move forward and clinical studies begin with our researchers, that it's going to be very helpful in that we'll see some results from the clinical studies.

MO: Right. We do have this question from Terry in Manitoba: "I'd like to know if the treatment for CCSVI will benefit those patients with primary progressive MS or mostly benefit those with relapsing/remitting MS." Dr. Murray, what do we know about this so far?

JM: Well, the only information we have so far is the brief treatment trial done by Dr. Zamboni, and the benefit there occurred only in those with relapsing/remitting MS. And those with the relapsing/remitting MS whose veins collapsed again after the procedure was done didn't get any benefit. So they have to have relapsing/remitting MS and the veins stayed open. Those with secondary progressive MS, those with primary progressive MS at the end of 18 months didn't show any benefit.

MO: All right. And we have another question, Ashley.

Male: Actually, I was exactly relating to that. Is there any speculation whatsoever why there was no success or possible effects on patients with progressive MS?

JM: No, except that we found similar things with some of the other treatments for MS. And it may relate to the extent of the disease so that if enough nerves and axons were damaged over the course of many years, then it couldn't be improved or benefit from any form of therapy, and that the benefits really might occur early in the disease, which you can then protect the person against the changes occurring. But that, again, is a postulate.

And having said that, even though so far we have not found substantial benefits, particularly for the primary progressive MS, with one exception, it doesn't mean that it can't occur. And I'll give the other example: For a long time it was thought that you could never reverse Parkinson's disease when it was very advanced. But in fact that occurred in very advanced Parkinson's disease, in so-called idiopathic Parkinson's disease, when the drugs were discovered for Parkinson's. So it is possible in what appears to be irreversible, that changes can still occur.

Now, when I say that there's an exception, there is a new medication that was released in the United States within the past year which is now being fast-tracked in Canada that does show some benefit to some of the symptoms, and particularly the walking, in patients with primary progressive MS. So keep tuned for that one. ... It's called Fampridine.

Male: Sorry?

JM: Fampridine.

MO: All right. We have time just for one more question and then we'll have our summary and our closing taking place. And we have Ashley.

Nada: My name is Nada and I'm talking on behalf of my sister, who is primary progressive. We had a chance actually to do the tests in Buffalo, in a private clinic. We did MRI(?) and ultrasound on her azygos vein, and actually it was done only(?) CT on her—on jugular(?) and CT on her azygos vein. Unfortunately they didn't find anything. I'm not trying to be discouraging but she was that case they couldn't find.

Now, the question is how much we can trust that test, and further to that, I would like to know if there is a place and what kind of test is done to measure deposit of iron in brain which could perhaps indicate something to us?

MO: Nada, I'm just going to shorten up that a bit just because we have to be careful of the time that we have for our national broadcast. If Dr. Murray, if that's all right if I go to the second part of that question which was concerning the iron in the brain. What kind of testing is available?

JM: It takes a very specialized form of MRI examination which is not done with a normal machine to look at that. But there are, that research has been going on for some time around the world, looking at this question of iron in the brain. But the results that occurred in your sister occurred in almost half of the Buffalo studies. So that's a whole issue that requires further examination.

MO: All right.

Nada: (Inaudible).

JM: No, it has to be a research facility that has a specialized MRI that's designed and has the computer hardware and software to look for iron deposits.

MO: Nada was asking if that type of testing was done in Canada, and as far as you know it is not. It's not available.

JM: I can't say whether it is or not. I don't know.

MO: Okay. As we come to the end of our session this afternoon, I want to let you know that the Toronto chapter staff of the MS Society is going to be available. I know we could ask many, many more questions and go on for quite a while, but they are just outside the door. So if you have specific information that you want to pass along, you have specific questions, the staff is there to take down your information and they'll make sure that you get your questions answered. Yves, Dr. Murray, and Karen are going to be borrowed by the national media in just a few moments, so unfortunately they're not going to be available to answer your individual questions right now, all right?

I'd like to thank you very much for participating today. It's been an extremely informative session, and thank you to everyone who is in the room and also to those who are nationally listening and Twittering and Facebooking with us. And Yves, you have some final comments?

YS: Marlane, I want to say thank you to you for giving of your time, to my colleagues on the panel, to all of you who are in the audience. I think this is a very interesting time for those people who have loved ones, with friends, with family members, or who live with MS. CCSVI has opened a new laneway, a fast laneway towards potential new therapeutic avenues in MS. And this builds on 15 years of the development of an arsenal of new therapies in MS.

I think one of the things that also really excites me about the story of the last four or five months is the extent to which people with MS have become mobilized, have become active, are participants in the debate, are turning to Facebook and to events such as these to ask questions, to probe, to challenge, to challenge each other. And I think that it speaks to me very much to the society's role; our role to mobilize volunteers, to mobilize walkers, to mobilize donors. Because at the end of the day, our work, the work that we do on your behalf in investing hard-earned money in good science, in research, and in helping people with MS have the confidence to live with the disease, a difficult disease, and to make decisions every day, that work is made possible through your own work. So to each and every one of you who've taken part here, to those of you who care every day for a person with MS, to those of you who'll be walking in the MS walks or making a contribution, I say thank you.

MO: And we also just want to remind you as well about the webcasts that are coming up on April 14. There are going to be two different sessions that day. One is the French language Web session, and then as you mentioned earlier, we also do have the special neurological, American Association Neurological session is taking place in Toronto.

YS: That second panel—the first one is a repeat of this one in the French language, and the registration, you're welcome to it. It will be held in Montreal, physically, but, again, it's available. It will be exclusively in French, and it takes place at 1:00 on April 14. And the other one takes place at 12:00 on the same day. They'll overlap very slightly. The American Academy of Neurology is the association of neurologists. They will be meeting in Toronto. Dr. Zamboni, Dr. Zavadonov, and Dr. Erin(?) Miller, who's the Chief Medical Officer of the American MS Society will be on a panel and they'll be commenting on the Buffalo trial data.

MO: Right. Again, to Dr. Murray, to Karen Torrie-Racine, and to Yves Savoie, thank you very much. Thank you. Thank you for doing this. If you require any assistance at all, please let us know. We have volunteers here who are able to help you.