



Multiple
Sclerosis
Society of
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en plaques



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CCSVI Phase I/II Clinical Trials Frequently Asked Questions

Who made the decision to proceed with Phase I/Phase II clinical trials?

The recommendation to proceed with Phase I/Phase II clinical trials was based upon a meeting of the CIHR's scientific expert working group, which met June 28th, 2011. The group recommended that CIHR support a Phase I/II interventional trial. As well, the Scientific Expert Working Group will continue to monitor and analyse the data from the seven funded studies and other studies related to CCSVI and MS around the world. The highlights from this meeting are posted on the CIHR [website](#).

What will the study aim to do?

The main objective of the trial is to determine the safety of venous angioplasty and obtain better evidence on patient outcomes.

What does Phase I/Phase II mean?

Clinical trials go through four distinct phases (steps), which are designed to answer specific research questions. Each phase of a clinical trial has a particular goal and the information that is gained is used to build knowledge about the new drug or intervention and support the next phase of the development process.

Phase I Trials

Phase I trials test the experimental treatment in a small group of people (20-80 people). The purpose is to determine a treatment's safety, learn about a safe dosage range and treatment application, identify side-effects and answer a few initial questions about the way the treatment works in the human body. Phase I trials are usually open-label trials (both the researcher and the participant know what the participant is taking as a medication).

Phase II Trials

Phase II trials look more closely at safety and efficacy, and how a treatment affects the human body. They are a smaller version of a definitive phase III trial and a major purpose of a phase II study is to provide a rough estimate of how effective a treatment is so that a properly sized phase III trial can occur. Phase II trials usually involve a slightly larger number of people (100-200) who have the disease or condition for which the treatment was developed. Most phase II trials have a control group. The control group does not receive the treatment which is being evaluated. Rather they are subject to a placebo or sham procedure. In terms of CCSVI, a sham procedure might mean inserting a catheter without using the balloon, so the person does not know whether or not they have actually

undergone the procedure. Phase II trials are often double-blind, meaning, neither the person taking the treatment nor the researcher supplying it knows whether it's the real treatment or not. This way neither the patients' nor the doctors' expectations about the experimental treatment can influence the observations and results.

Phase III Trials

Phase III trials are the last step before a treatment is submitted to Health Canada. Because of the natural history of the disease, phase III trials in multiple sclerosis are conducted on large populations of study participants (1,000), and can last up to several years. Phase III trials are large, *multi-centre* (at many different geographic locations), *randomized* (subjects randomly chosen to receive one treatment or another), *double-blind* (patient and evaluating clinician do not know what treatment was received) and *controlled* (there are comparison groups such as a group receiving a placebo or another competing treatment). The purpose is to confirm the new treatment's efficacy, monitor side effects and safety, and compare it to commonly used treatments.

Health Canada Review

The results from the Phase I to Phase III studies are compiled and the data assessed and presented as an application (with the goal of approving the treatment) to Canada's health regulatory agency, Health Canada. The process of data analysis can take many months. The review process by Health Canada likewise takes many months.

Phase IV Trials

Once a treatment has received approval from Health Canada, a phase IV study is often done. These post-marketing trials seek to identify further information about the treatment's risks, benefits, side-effects and optimal use. Several hundred to several thousand people may take part in a phase IV study. Read more about [clinical trials](#).

What are the next steps in terms of the clinical trial design and launch?

In November 2011, the Government of Canada and the Canadian Institutes of Health Research (CIHR), announced that it was ready to accept research proposals for the Phase I/II clinical trial on chronic cerebrospinal venous insufficiency (CCSVI). The request for research proposals, available on CIHR's website in November 2011, is a collaborative initiative between the CIHR and the MS Society of Canada. CIHR will also continue to work with the provinces and territories as it moves forward with this initiative. The MS Society of Canada has [committed funding](#) towards the financial cost of a clinical trial.

CIHR announced in April 2012 that a research team has been selected for consideration through a rigorous peer review process to undertake an interventional Phase I/II clinical trial for Chronic Cerebrospinal Venous Insufficiency (CCSVI) in persons with multiple sclerosis. The main objective of the trial is to determine the safety of venous angioplasty and obtain better evidence on patient outcomes. This selected team now has to obtain ethics approval from relevant institutional research ethics board(s). The names of the research team's members and institutions involved will be announced once REB approval is complete. In addition, the funds will be released and the study will begin as soon as

ethics approval is granted. These are all usual steps in conducting clinical research. In the meantime, the CIHR Scientific Expert Working Group continues to review and analyze any new research evidence on CCSVI.

What are the usual steps to launching a clinical trial?

The involvement of people in research is highly regulated by the Canadian government and requires a number of additional steps over a laboratory study. These steps frequently add to the length of time it takes for a study to begin or to be completed. Some of the main steps include:

- Defining the overall purpose of the study, ensuring financial resources and/or finalizing funding agreements to support the study, and seeking out new collaborations with various experts who haven't necessarily worked together before.
- Developing a detailed protocol or blueprint of the study's design including exactly what to study, how, with what number of participants and for how long. This step is particularly important as a poorly designed study has no scientific value and is therefore a misuse of time and funds. The specific step by step procedures for each part of the study are essential to ensure that each participant undergoes the same protocol and that the information obtained is scientifically useful.
- Developing one or more "Informed Consent" documents. These describe the study in detail, including what will be done at each step and the risks and benefits of participation in the study. Patients must be fully informed of all of this information, have the opportunity to ask questions, be free from coercion regarding participation and sign the consent form if they wish to participate.
- Applying for approval to begin the study from a Research Ethics Board (Canada), including approval of the Consent Form and other plans. This step is required by the government to ensure adherence to guidelines related to the protection of human subjects in research.
- Hiring staff needed to conduct the study, and ensuring staff are trained in the protocol and any relevant techniques to be used.
- Buying or renting equipment, clinic time, and/or extra space, as needed.
- Establishing a data and safety monitoring committee to provide oversight and feedback on any research or safety issues encountered.
- Recruiting and screening participants that meet the study's criteria and obtaining their informed consent.
- Conducting the study, including performing scanning, clinical evaluations and other data collection. Some protocols require repeated scans or additional scans, meaning additional clinic visits.
- Gathering, merging and evaluating the data from all participants.
- Communicating and publishing results.

When and where will the trials begin? Can I become a part of the clinical trial?

Specific details about the study design, timing, location and enrollment process have not yet been determined. The MS Society will post information about the clinical trial as it becomes available.

What role will the seven studies funded by the MS Society of Canada and the U.S. National MS Society play in the clinical trial process?

All seven funded studies have made good progress. Read more about the studies [here](#).

The CIHR's Scientific Expert Working Group will continue to monitor and analyze the data from these studies and other studies related to CCSVI and MS around the world.

How will the clinical trials be funded?

The Phase I/II clinical trials will very likely be funded by a number of partners potentially including federal and provincial governments and the MS Society of Canada.

The MS Society of Canada has already committed \$1 million towards the cost of a nationwide clinical trial. More details about funding and design will become available in the coming weeks and months.

What will the MS Society's role be with respect to the clinical trials?

The request for research proposals is a collaborative initiative between the CIHR and the MS Society of Canada. The MS Society of Canada has also committed funding towards the cost of a nationwide clinical trial. We are closely monitoring the developments and will provide updates to the MS community whenever further information is available.