**Participant Information and Consent Form**

**Interventional Trial**-*Adult providing own consent*

**Title**: An international, multicentre, prospective randomised outcome-blinded study of the effects of the use of a single antiplatelet agent versus no antiplatelet agent in patients with a history of stroke due to intracerebral haemorrhage

**Short Title**: **A**ntiplatelet **S**econdary **P**revention **I**nternational **R**andomised trial after **IN**tracerebral haemorrhage (ASPIRING)

**Protocol Number: Version 1, December 16, 2020**

**Project Sponsor: Sir Charles Gairdner Hospital**

**Investigator: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Location: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Invitation**

You are invited to take part in this research project. This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don’t understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend, or your local doctor.

**Why am I invited?**

You are being invited because you have had a stroke due to a bleed in the brain, known as an intracerebral (inside the brain) haemorrhage, which has been caused by a burst blood vessel in the brain.

People who experience a spontaneous (non- traumatic) stroke due to brain haemorrhage are also commonly affected by, or at risk of, vaso-occlusive diseases that cause blood to clot in blood vessels (e.g. atherosclerosis, or hardening of the arteries) and block (occlude) the supply of blood to the brain or heart, causing an ischaemic stroke (stroke caused by a blood clot in the brain) or heart attack.

These vaso-occlusive events (ischaemic stroke and heart attack) occur as frequently as recurrent brain haemorrhage in patients with a history of prior brain haemorrhage. One reason for this is that more than half of the adults with stroke due to brain haemorrhage have past histories of high blood pressure, smoking and diabetes mellitus, which cause them to be at risk of occlusive blood vessel diseases.

After a brain haemorrhage, patients and their doctors are often uncertain about whether it is beneficial to take blood-thinning (antiplatelet) medications, such as aspirin or clopidogrel, to prevent future blood clots occurring in diseased blood vessels, or whether to avoid them in case they increase the risk of bleeding.

The research project is testing whether taking or avoiding a blood-thinning medication (aspirin or clopidogrel) once daily is best for your overall health after brain haemorrhage.

**What is the purpose of this research?**

The purpose of this research project is to determine if blood-thinning medication following a brain haemorrhage is of overall net benefit in reducing the occurrence of all serious vascular events (medical events caused by blood clots forming in blood vessels, or bleeding from them).

At the moment, some people choose to take medication to prevent clots occurring after a brain haemorrhage, while others do not: both policies are used in clinical practice but nobody is certain as to the most appropriate action to provide health benefits.

Where there is this uncertainty among patients and their doctors (about whether it is best to treat with blood-thinning medication or to avoid treatment with blood-thinning medication), it is ethical and appropriate to try and find out the best treatment option by comparing the treatment options in a randomised controlled trial (RCT).

In a RCT, participants are randomly allocated into two groups – one group receives the active treatment and one group avoids the active treatment. The two groups are followed up over the next few years and the long-term health outcomes of the two groups are compared against each other.

A recent RCT, in the UK, called RESTART (REstart or STop Antithrombotics Randomised Trial), recruited 537 brain haemorrhage participants with previous occlusive diseases, and found that those who were allocated to take blood-thinning medicine had half as many recurrent brain haemorrhages and fewer major vascular events (such as ischaemic stroke, heart attack or death from any cardiovascular cause) compared to avoiding blood-thinning medicine over two years. This result was reassuring about the safety of blood-thinning medicine after brain haemorrhage. However, it remains uncertain whether this result is robust and applies to all types of patients with brain haemorrhage and in other countries.

In this trial, the ASPIRING trial, we are using a similar design to RESTART to find out whether blood-thinning medication benefits people like you who have had a brain haemorrhage. The ASPIRING trial will include about 4000 people with previous brain haemorrhage in Australia, China, New Zealand, Vietnam and possibly other countries.

**Do I have to take part?**

It is up to you to decide if you wish to participate in the trial. We will describe the aim and procedures, and go through this information sheet with you. If you decide to take part and later change your mind, you are free to withdraw from any or all parts of this trial at any time, without giving a reason. You will receive the best possible care whether or not you take part.

**What will happen if I take part?**

If you decide to participate, you will be asked to sign this consent form before any trial specific assessments are done. By signing it you are telling us that you:

* Understand what you have read
* Consent to take part in the research project
* Consent to have the tests and treatments that are described
* Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

Please keep your copy in a safe place.

At the first (baseline) visit, various examinations will be performed in order to determine if you are eligible to participate. These examinations will include:

* Collection of demographic data (e.g. age, sex, education, and occupation)
* Your medical history and previous medications, including over-the-counter and herbal medications
* A urine pregnancy test (if you are of childbearing potential)
* Your home address and telephone numbers, and those of your next-of-kin or other close personal contacts, will be recorded to enable the members of the project team to contact you later to find out about your health.

A member of the team will complete a health questionnaire with you to explore your independence in activities of daily living (what you can and cannot do). This initial assessment will take approximately 45 to 60 minutes.

You will be allocated at random to take one type of blood-thinning medicine once daily or to avoid blood-thinning medicine altogether.

This means that, overall you will have a 50:50 chance of being allocated to either group. If you are randomised to receive blood-thinning medication once daily, your doctor will decide which is the most appropriate blood-thinning medication to be prescribed to you from one of aspirin or clopidogrel.

If you develop any symptoms which you think might be due to the trial medication you should inform the doctors or nurses responsible for your care.

If you decide to participate in this trial, the study doctor will inform your local doctor.

*Follow-up assessments at hospital discharge or 1 month (whichever is earlier) and then at 3 and 6 months, and then every 6 months thereafter over the next 4 years.*

Participation in the trial involves up to 9 follow-up visits:

* The first around the time of your discharge from hospital or 1 month (whichever is earlier) by the doctors who entered you in the trial; and then

at 3 and 6 months, and

* 6-monthly thereafter (i.e.12, 18, 24, 30, 36, 42 and 48 months) until the end of the trial, either by the doctors at your hospital or the trial coordinating centre at the QEII Medical Centre in Perth, Western Australia by telephone or postal questionnaire.

We will ask you:

* How you are, and specifically about any recurrent strokes, heart condition or other health-related issues you may have
* Whether you are still taking blood-thinning medication
* Whether you have had any side-effects from the medication
* Other current medications
* Your blood pressure
* Your independence in activities of daily living (what you can and cannot do).

The discharge or 1-month (whichever is earlier) follow-up will take about 30 minutes. At this follow-up, your doctors will ensure that your contact details are complete and correct and forward these to the trial coordinating centre in Perth, Western Australia to enable them to contact you to complete your remaining follow-up assessments. At this time, a letter of introduction will be sent to you from the trial coordinating centre, with their contact details to enable you to contact them if the need arises.

The 3, 6, 12, 18, 24, 30, 36, 42 and 48 month follow-ups will take approximately 15 to 30 minutes. At these follow-up visits, we will remind you of the importance of keeping your blood pressure well controlled. You may be asked to go and see your general practitioner if necessary, to check and monitor your blood pressure and provide some detailed information and medical records if applicable.

**Other medication:** At the start of the trial, your trial doctor will advise you about medications (including over-the-counter and herbal medicines) that you should NOT take. Please do not take any new medications without consulting your doctor. You will also be asked to keep a record of the name and date your started taking all new medications and, if applicable, the date you stopped taking it. You will be asked about your current medications at each follow-up assessment.

**Adherence to treatment:**

It is important that you adhere to the blood-thinning medication policy allocated to you. However, if you are allocated to take blood-thinning medication, and you experience a side-effect on the medication, you should let us know and discuss whether to continue the medication with your doctor.

**Adverse effects of blood-thinning medication can include the following:**

Aspirin

* Stomach discomfort, indigestion, heartburn, nausea
* Ringing in the ears
* Allergic reactions (hives, facial swelling, wheezing, and asthma)
* Bruising
* Bleeding (e.g. nose bleeds, black bowel motions).

Clopidogrel

* Skin rash
* Diarrhoea
* Bruising
* Bleeding (e.g. nose bleeds, black bowel motions).

All blood-thinning medications can cause increased bleeding (your blood taking longer to clot – for example, when you cut yourself), or easy bruising.

**What happens after the final assessment?**

When you have completed the final follow-up assessment, you will be referred back to your General Practitioner for your on-going care and management.

If you are agreeable, we may like to contact you again in the future, after the study has completed, if there are further research questions or studies to discuss with you.

**Are there any risks?**

The main risk of starting blood-thinning medication after a brain haemorrhage is that it could increase the risk of another (recurrent) brain haemorrhage. However, RESTART did not find that blood-thinning medicine increased the risk of recurrent brain haemorrhage. Instead, RESTART found that blood-thinning medicine might have halved the risk of recurrent brain haemorrhage.

It could also increase the risk of bleeding elsewhere in the body, such as from an existing ulcer, or in the event of trauma.

**Are there any benefits?**

*Possibility of benefit*

The results of the RESTART trial were promising; in showing that blood-thinning medicine might halve the risk of recurrent brain haemorrhage. As blood-thinning medicine is also known to reduce the risk of clotting problems, we anticipate that blood-thinning medicine will be of overall net benefit in helping people with brain haemorrhage by reducing the risk of future heart attacks and strokes due to blood clots without increasing the future risk of another bleed into the brain.

*Participation in a clinical trial*

Individuals who participate in clinical trials tend to have better outcomes than individuals who don’t. One explanation may be that trial participants are regularly followed-up by health care professionals who are interested not only in documenting their health, but also in providing support.

*Contribution to medical knowledge and the health of future generations*

This trial aims to further medical knowledge about the longer-term outcome of survivors of brain haemorrhage and whether the outcome is improved by long-term blood-thinning medication.

**Pregnancy and contraception**

It is important that womenparticipating in this trial are not pregnant and do not become pregnant during thetrial as it is possible that the trial drug may damage an unborn baby. The effect of the trial drug on an unborn baby is unknown. If you are a woman of childbearing age and there is any possibility that you are pregnant, the researchers will need to perform a urine pregnancy test before you start in the trial.

If necessary, you should use reliable contraception (such as oral or implanted contraception, an IUD or have had a tubal ligation if you are female, or condoms if you are male) during the course of the trial. If at any time you think that you, or your sexual partner may be pregnant, it is important to let the researchers know immediately. If this should occur, all usual follow-up will continue as per the trial protocol and the pregnancy will also be followed.

Females should continue to take contraception for at least two weeks after ceasing trial medication.

**Confidentiality / Privacy**

Of the people treating you, only the ASPIRING researchers or necessary others (e.g. allnursing staff involved in your care)will know whether or not you are participating inthis trial. Any identifiable information that is collected about you in connectionwith this trial will remain confidential and will be disclosed only with yourpermission, or except as required by law. Only the researchers, trial monitor and representatives of regulatory authorities and the ethics committee will have access to your details.

Your data will be stored in locked filing cabinets at \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_and at the ASPIRING trial coordinating centre located:

QE II Medical Centre

Harry Perkins Institute of Medical Research Building

QQ Block, Level 2

6 Verdun Street

Nedlands, WA, 6009, Australia

Once the trial has been completed your data will be de-identified and archived at both these locations for a minimum of 15 years as per regulatory requirements and then destroyed by incineration.

**Data sharing**

The study results may be presented at a conference or in a scientific publication. You will not be personally identified in any reports or publications resulting from this study.

Some de-identifiable data (information about you, after removing all identifying details) may be shared with other researchers to improve knowledge about brain haemorrhage and blood-thinning therapy. However, this will only occur as part of data-sharing research (individual patient data meta-analysis) that follows strict standards and only aims to improve understanding about how different people are affected by brain haemorrhage, how they respond to treatment and how their outcomes can be improved.

**Compensation**

If you suffer any injuries or complications as a result of this trial, you should contact the trial doctor as soon as possible, who will assist you in arranging appropriate medical treatment. If you are eligible for health insurance (e.g. Medicare), then you can receive any medical treatment required for your injury or complication free of charge as a public patient in any public hospital.

You do not give up any legal rights to compensation by participating in this trial and you may have a right to take legal action to obtain compensation for any injuries or complications resulting from the trial. Compensation may be available if your injury or complication is sufficiently serious and caused by unsafe drugs or equipment, or by the negligence of one of the parties involved in the trial (e.g. the researcher, the hospital, or the treating doctor). If you receive compensation that includes an amount for medical expenses, you will be required to pay for your medical treatment from those compensation monies.

**Will taking part in this trial cost me anything, and will I be paid?**

The blood-thinning medications being used in this trial are not new medications; they are approved medications already available on the market and widely prescribed for the prevention of blood clots. If you are allocated to take blood-thinning medication, you will be asked to visit your usual doctor (i.e. GP) for your ongoing prescriptions at your own expense.

You will not be paid for your participation in this trial.

**What happens with the results?**

If you give us your permission by signing the consent document, we plan to discuss/publish the results of the trial in medical journals. In any publication, information will be provided in such a way that you cannot be identified (see data sharing section above). Results of the trial will be provided to you, if you wish.

**Who is running this research?**

This research project has been designed and is being conducted by doctors and medical research scientists at Sir Charles Gairdner Hospital, The University of Western Australia, The George Institute for Global Health (Australia and China) and the University of Edinburgh, United Kingdom.

The trial will be conducted at centres around Australia, China, New Zealand and Vietnam, and possibly other countries.

**Who is funding this research project?**

*The Pilot Phase*

* The National Health and Medical Research Council (NHMRC), Australia; project grants to The University of Western Australia (Chair of Neurology Start Up fund); and The George Institute for Global Health, Australia.

*Main Phase*

* A Clinical Trials project grant application will be made to the National Health and Medical Research Council (NHMRC), Australia for the funding period 2022-2026 is planned to be submitted in 2021. If application is successful, the main phase of the trial will proceed.

Complaints

This trial has been approved by \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_The trial has been approved on the basis (amongst others) that the reported risk of an adverse event is either small or acceptable in terms of the risk you face as a result of your current illness, or the benefit that is possible with the new treatment being tested. If you have any concerns about the conduct of the trial, or your rights as a trial participant, you may contact: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Contact details**

When you have read this information, the researcher will discuss it with you and any queries you may have. If you would like to know more at any stage, please do not hesitate to contact him/her.

**Dr** *\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_*

**Working hours Telephone No –** *\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_*

**After hours Telephone No –** (via switchboard for clinical trials or mobile for other studies) *\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_*

If you have any problems while on the trial, please contact:

The ASPIRING Trial Coordinating Centre:

* Tel: +61 8 6151 1061
* Fax: +61 8 6151 1028
* Email: ASPIRING@health.wa.gov.au

**Thank you for taking the time to consider this trial.**

**If you wish to take part in it, please sign the attached consent form.**

**This information sheet is for you to keep.**

**CONSENT TO PARTICIPATE IN RESEARCH**

**Chief Investigator:** *\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_*

1. I understand that the researcher named above will conduct this trial in a manner conforming to ethical and scientific principles set out by the National Health and Medical Research Council of Australia and the Good Clinical Research Practice Guidelines of the Therapeutic Goods Administration.
2. I acknowledge that I have read, or have had read to me the Participant Information Sheet relating to this trial, and that I understand the Participant Information Sheet.
3. I acknowledge that the general purposes, methods, demands and possible risks and inconveniences which may occur to me during the trial have been explained to me by \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_(“the researcher”) and I, being over the age of 18 acknowledge that I understand the general purposes, methods, demands and possible risks and inconveniences which may occur during the trial.
4. I acknowledge that I have been given time to consider the information and seek advice.
5. I acknowledge that declining to take part in this trial will not affect the usual treatment of my condition.
6. I acknowledge that I am volunteering to take part in this trial and may withdraw at any time.
7. I acknowledge that the study results may be presented at a scientific conference or in publication(s) and that some de-identified data about me may be shared with other researchers as part of data-sharing research, but I will not be personally identified in any presentations, reports or publications.
8. I acknowledge that I may be contacted by the research team after the study has completed, with enquires about further research questions or participation in studies that may arise.
9. I acknowledge that this research has been approved by \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
10. I acknowledge that I have received a copy of this form and the Participant Information Sheet, which I have signed.
11. I acknowledge that any regulatory authorities may have access to my medical records *relevant to this trial* to monitor the research in which I am agreeing to participate. However, my identity will not be disclosed.

Name of participant \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date of Birth \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Address of participant \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature of participant \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature of researcher \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature of witness \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

*Note: This consent should only be signed by a participant who is over the age of 18 years.*