PATIENT INFORMATION & CONSENT FORM

BOLD Study

Targeted Pre and Post-operative Blood Pressure Control Reduces Incidence of Type II Endoleak after EVAR: A Randomised, Controlled Trial

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Royal Brisbane and Women's Hospital
Metro North Hospital and Health Service

PARTICIPANT INFORMATION AND CONSENT FORM

The Royal Brisbane and Women's Hospital

Project Title: **B**lood pressure c**O**ntro**L** for en**D**oleak (**BOLD** Study)

Scientific Title: Targeted Pre- and Post-operative Blood Pressure Control Reduces the Incidence of Type II Endoleak post-Endovascular Aneurysm Repair (EVAR)

HREC No: _____

Investigators: Dr Krishna Pattabathula (Registrar Vascular Surgery), Dr J Jenkins (Director of Vascular Surgery, Dr M Ogg (Vascular Surgeon), M Mcgrath (Research CN)

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*This Participant Information and Consent Form is **12** pages. Please check you have all of the pages.

PART 1: INTRODUCTION

1. Invitation

As a patient of the Royal Brisbane and Women's Hospital Vascular Surgery department, you are invited to participate in a research project. Before you decide about being involved, we would like to explain why you're being asked, what we're studying, what we're hoping to prove and importantly, what we need from you. Please remember that, at all times, your decision to participate is voluntary and your consent can be freely revoked. Your decision about participating in this study will not delay your surgery nor change your relationship with the surgeons. Please read the following Information Sheet carefully and feel free to ask any questions about information you would like clarified. There is a Consent Form at the end, a copy of which you will be able to keep.

2. Why am I being asked?

You have an abdominal aortic aneurysm (AAA), which is a dilation (or ballooning-out) in the size of your aorta. Generally speaking, the larger they are, the more likely they are to rupture. Unfortunately, ruptured AAA remains a commonly fatal condition. You and your surgeon have decided that the balance of risks favours you having your aneurysm fixed, and that the most suitable operation is Endovascular Aneurysm Repair (EVAR).

3. What is an EVAR?

EVAR involves the insertion of a stent-graft, which is a polyester fabric supported by a metal framework made of nickel-titinanium alloy (Nitinol) and sutured together with polyester/polyethylene, into the aorta. The surgeon will access your aorta via your femoral arteries (in the groins) and use angiography to place the stent-graft in the right place. EVAR is well-established as a treatment method for AAA for the suitable patient. Generally, without complications, the procedure takes approximately 2-hours and most patients are ready to go home by 2-3 days after surgery. Large, international studies comparing it to the open approach show benefits of EVAR compared to open-surgical repair with overall reduced injury and death to patients, but only in the first few months after the surgery. After that, the longer-term outcomes for patients with EVAR are very similar to patients who had open surgery.

4. What are the problems with EVAR?

EVAR has an Achilles' heel which is *endoleak*. An *endoleak* is when blood flows around the stent-graft and into the aneurysm. There's several types, depending on where the blood is coming from, with the most common (Type II) relating to blood flowing backwards into your aneurysm from surrounding circulation such as from the gut or the spine. In the majority of cases, when we see a small type II endoleak, we don't need to do anything but observe. Though, given this risk exists, we frequently complete a surveillance scans, with CT or ultrasound to (1) check for a leak, and if present, where it's coming from and (2) ensure that the aneurysm isn't still continuing to grow. Usually, we complete these scans at standard intervals such as 6-weeks, 6-months and annually thereafter. If there's anything untoward on these scans, it may prompt repeat surgery to fix the leak. Large studies have estimated the risk of needing repeat surgery, in any fashion, as high as 5%.

5. What are we interested in?

Naturally, Vascular surgeons are very interested in methods that we can develop to reduce how many of our patients experience endoleaks and how many of them require more surgeries. Ideally, we want to find out if there is a way to non-invasively prevent the development of endoleaks. We have hypothesised that if we can reduce a patient's blood-pressure to a specific level before their surgery and maintain it at that level after their surgery, the body will be more capable of blocking off leaks on its own.

6. What do we already know about this?

There have been two studies about this in the past, both of which showed that lower blood pressures do appear to reduce the number of patients who develop endoleaks after EVAR. However, these studies were completed with limited numbers and they did not compare to a group that didn't have blood-pressure control, so their evidence is not as scientifically and statistically strong.

(1) One study, from Italy and published in 2019, showed that pre-operative blood-pressure management with frequent BP checks and reviews with a Cardiologist to start blood-pressure medications, can reduce type II endoleak.
(2) Another study, from Japan and published in 2018, showed that post-operative blood-pressure management with intravenous blood-pressure medication in an intensive care unit (ICU), can reduce type II endoleak.

7. Why aren't we doing this already?

In Medicine, as in all scientific fields, we need a high level of evidence before we can be sure that a certain management/medication/surgery/device etc. will have benefit to patients and will not cause them undue harm. To do this, we need to 'control' the study, that is, we need to compare the outcomes of one group that has the intervention with a group that doesn't. Both of these groups need to have the same surgery and their outcomes need to be identically observed. Further, we need to see that neither group are having adverse outcomes from the management. At present, there are no studies that have done this. Therefore, we haven't been able to safely and ethically practice this approach to-date.

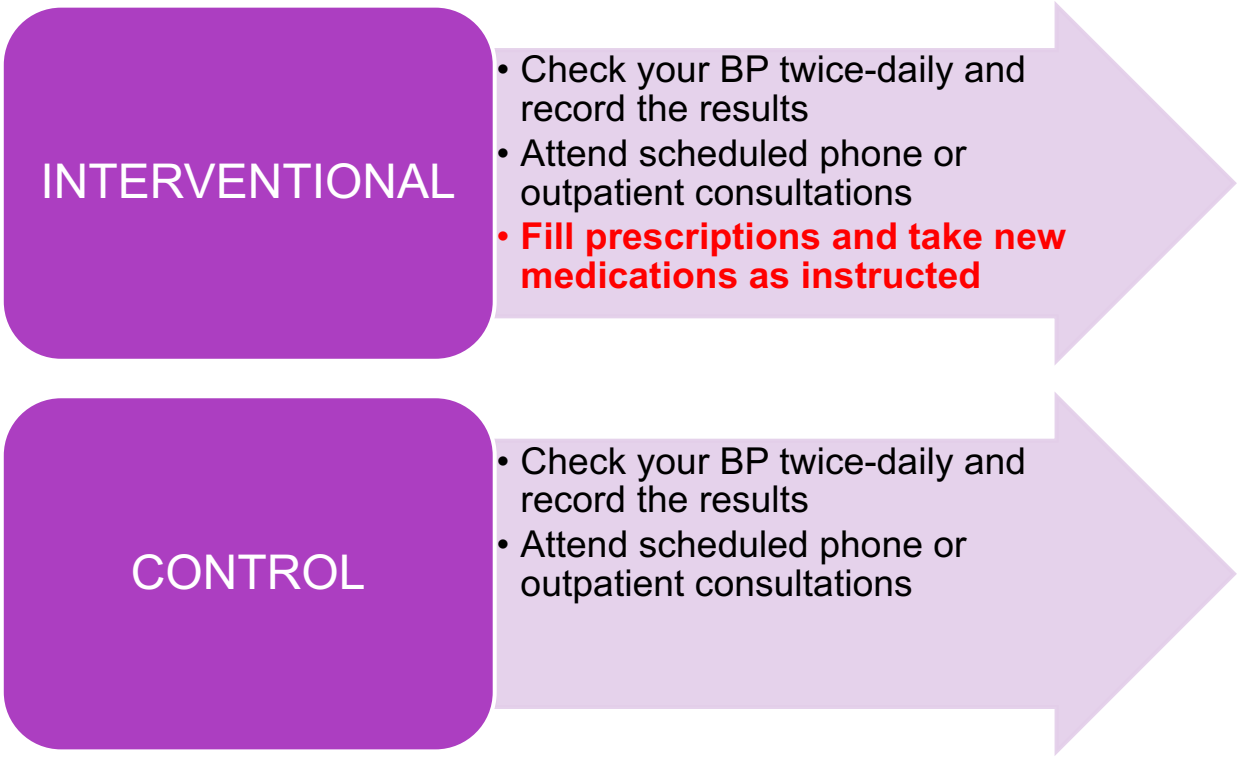
PART 2: THE STUDY

1. Do I have to take part?

Participation in this research project is completely *voluntary* and *opt-in*, and you have the right to choose not to be involved. Your decision will not impact on the timing of your surgery and in the majority of cases, you will have your surgery date before the study starts.

2. What do I have to do?

If you decide to participate in this study, you will be allocated to either an INTERVENTIONAL group or a CONTROL group. The allocation is made randomly, and without any influence by your surgeons. Your job in each group is very similar, but the INTERVENTIONAL group has a little more to do. Both groups have to check their blood-pressure twice a day, and record the results on an online form (which we'll teach you how to do) and on-paper. The INTERVENTIONAL group will be started on new doses or new medications to try and bring their blood-pressure down. If you're allocated to this group, you will very likely have new prescriptions to fill and to start taking. We'll give you a BP machine to take home, and teach you how to use it.



Both groups will have weekly scheduled phone-calls to see how they're going. Specifically, you'll be asked if you're tolerating the new medications well, if there's any unusual side-effects, if you're feeling light-headed/dizzy/faint or you're experiencing chest pain or shortness of breath.

3. How long does the study take?

The study starts at 3-weeks BEFORE your EVAR surgery and lasts for 6-weeks AFTER your EVAR surgery, that's a total of just over 2-months. After that, we'll see how you're going at 6-months and at 12-months with a phone-consultation.

4. Will I be reimbursed for the prescriptions and travel?

If you are a part of the BOLD study, we will cover the costs outright or fully reimburse you for any costs associated with travelling to outpatient appointments, to the pharmacy, to consultations as well as the cost of any prescriptions.

5. What if I decide to withdraw from the study?

If you decide to withdraw, all you have to do is notify one of the Investigators via the contact details at the end of this form. You can withdraw at any time before and during the study. Again, the decision to participate and the decision to withdraw will not affect your surgery date, the outcomes of your surgery nor your relationship with the surgeons.

Once you've withdrawn, the investigators will not collect any further personal or clinical information. You will remain in the care of the surgeon who looks after you and follow the usual process before and after your surgery.

6. Could this research be unexpectedly stopped?

Yes, we may decide to stop the study early for a number of reasons, including:

1. Unacceptable number of patients experiencing side-effects
2. Unacceptable number of complications in either group
3. It being clear that the lowering blood-pressure is leading to adverse outcomes for our patients
4. Decisions made by regulatory authorities such as the Ethics committee

7. How will the Investigators observe my blood-pressures?

As we mentioned, you enter your blood-pressures daily into an easy-to-use online form. We see this on our side and we can observe if your blood-pressure and heart rate are within targets, too high or possibly, too low. We'll act on this as we think is safest for you.

8. Will my normal blood-pressure medications be stopped?

In both groups, we'll keep your blood-pressure medications the same to start with. However, If you're in the INTERVENTIONAL group, we'll slowly increase the dose or change/add new medications to help your blood pressure to get down to around 120mmHg.

9. How will be information and data be stored?

Your information will only be used for this research project, and it will only be disclosed to yourself if you request it or if it is required by law. The information pertains mostly to your health records including your blood-pressure levels and your medications. It will always be stored on a password-secure and encrypted Queensland Health computer. It will remain as secure as your medical information currently is. Following the 5-year period that is required by the National Health and Medical Research Council (NHMRC) for your data to be stored, it will be permanently deleted.

PART 3: BENEFITS & RISKS

1. What are the benefits of taking part?

It can be argued that all patients with abdominal aortic aneurysms, like yourself, should be taking their blood pressure twice daily regardless. This particularly applies to patients who have high blood-pressure and take blood-pressure medications already. For some of you, you won't have to take your blood-pressure any more frequently than you already do.

Your own personal health and outcome from this surgery is very unlikely to change from participation in this study, regardless of which group you are allocated too. However, the fundamental benefit of participating is to help Vascular surgeons find a *preventative* and *non-invasive* way of fixing endoleak. If we're able to prove our hypothesis, we will very likely suggest that all patients who are to have an EVAR, should have their blood-pressure controlled before and

after their surgery. This has worldwide implications and can potentially change outcomes for large numbers of people.

2. What are the risks?

The risks are slightly different, depending on which group you are allocated too:

(1) In the CONTROL group, the primary risk is that you will experience the physical discomfort of twice-daily blood-pressure machine cuff inflation. A secondary risk is the time commitment of entering your blood-pressures in daily.
(2) In the INTERVENTIONAL group, the primary risk is that with changes in your blood-pressure medications, you may experience some understood side-effects. These include having your blood-pressure drop too much and feeling faint/lightheaded/dizzy but can extend to having issues with your kidney function. You will also have the risks of physical discomfort with blood-tests after changes in your blood-pressure and pain associated with any blood-tests that we may request that you have.

3. How are we mitigating these risks?

We'll tell you about the warning signs for any of these concerning symptoms. We have set up a phone-hotline that is contactable during business hours Monday-Friday that you can call if you have any queries/concerns regarding the study. Out of hours, we've given you the numbers for your GP practice, home-doctor service and Emergency services.

PART 4: OTHER INFORMATION AND FREQUENTLY ASKED QUESTIONS (FAQS)

1. Complaints and Compensation

If you have any complaints regarding the study or the participation, we've attached a list of contacts including the Ethics board that you can lodge a complaint too. Your decision to lodge a complaint will not impact the date of your surgery, your outcomes from our care or your relationship with the surgeons.

2. Who is organising and funding the research?

This research projected is being conducted by the investigators listed on the first page. This investigator, nor any member of the research team will receive a financial benefit from your involvement in this research project. No companies will financially benefit from this project. We are seeking numerous grants to help us continue to cover the costs of the study.

3. Who has reviewed this medical project?

All research in Australia involving humans is reviewed by an independent group, who are acreddited by the NHMRC, called the Human Research Ethics Committee (HREC). The ethical aspects of this research project are *pending* approved by the HREC of the Royal Brisbane and Women's Hospital. The project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)* produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

PART 5: CONTACT

Should you have any concerns or complaints about any aspect of the project, the way it is being conducted or any questions about your rights as a research participant, you may contact:

Group: Human Research Ethics Committee

Telephone: (07) 3646 5490

E-mail: RBWH-Ethics@health.qld.gov,au

Address: HREC Office, Executive Suites, Lower Ground Floor, Dr James Mayne Building
Royal Brisbane and Women's Hospital
Butterfield Street, Herston
QLD 4029

Name: Dr Krishna Pattabathula

Position: Principal Investigator, Vascular Surgery Research Registrar

Telephone: (07) 3646 8111

E-mail: Krishna.pattabathula@health.qld.gov.au

Address: Vascular Outpatient Clinic, Level 7, Dr Ned Hanlon Building
Royal Brisbane and Women's Hospital

Name: Dr Jason Jenkins

Position: Director of Vascular Surgery Department

Telephone: (07) 3646 8111

Address: Vascular Outpatient Clinic, Level 7, Dr Ned Hanlon Building
Royal Brisbane and Women's Hospital

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CONSENT FORM

Project Title: Targeted Pre- and Post-operative Blood Pressure Control Reduces the Incidence of Type II Endoleak post-Endovascular Aneurysm Repair (EVAR)

HREC No: KP03422

I, _____, agree to participate in the above named project. In doing so, I acknowledge that:

- I have read the above Participant Information and understand the context, purpose and reasoning for this research project as it is described.
- I have had an opportunity to review all of the material and discuss any questions or concerns with the Investigators. I have been satisfied with the answers given to me.
- I have been informed that my consent to this project can be revoked at any time. I understand that revocation of my consent will not affect the quality of my treatment.
- This study is *pending approval* from the Royal Brisbane and Women's Hospital Human Research Ethics Committee (HREC) and is in accordance with the National Health and Medical Research Council (NHMRC) guidelines.
- I am aware that I will be allocated to either an INTERVENTIONAL or CONTROL group, and that the allocation will be randomised amongst all the study participants. I agree to participate regardless of my allocation.
- I understand that I will be able to keep the Patient Information and a copy of the Consent form for review if required, at any time.
- I will, to the best of my ability, attempt to participate in the study's requirements of myself including blood-pressure monitoring twice-daily and compliance with any blood-pressure medication changes.

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I thereby consent to the following;

1. To be randomized to be in EITHER the INTERVENTIONAL or CONTROL groups prior to my EVAR surgery, and the roles/implications of this allocation	Yes ☐ No ☐
2. To be contacted, for 3-weeks before my surgery, and for 6-weeks after my surgery and attend scheduled outpatient appointments	Yes ☐ No ☐
3. The storage of my clinical information and data at the Royal Brisbane and Women's Hospital for study analysis and use.	Yes ☐ No ☐
4. If in the INTERVENTIONAL group, the inherent risks of changing of blood-pressure medications including symptomatic hypotension, dizziness, fainting, low heart-rate, temporary or permanent kidney damage, pain from blood tests	Yes ☐ No ☐

Declarations

Participant's name (printed): _____

Outcome: **Agree / Disagree to participate in the BOLD study**

Signature: _____

Declaration by Investigator: I have discussed the project, specifically referencing the responsibilities and risks, with the participant. I believe the participant has understood this explanation and is capable of participating in the study.

Investigator's name (printed): _____

Investigator's signature (printed): _____