

# A study for investigating organ complications in preeclampsia

<b>Submission date</b> 10/06/2020	<b>Recruitment status</b> Recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 16/07/2020	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 04/08/2025	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Pre-eclampsia, one of the most serious complications of pregnancy, is associated with severe morbidity and mortality for the mother and baby. There is an urgent need to better understand this devastating disease.

Pre-eclampsia affects 3-8 % of pregnancies worldwide. It is a multi-system disorder involving maternal blood vessels, the kidneys, the liver, the lungs, and the fetus. In its most severe form, it affects the brain, causing seizures (eclampsia), cerebrovascular events and even death. It is a leading cause of maternal and fetal/neonatal morbidity.

Globally, pre-eclampsia is responsible for > 60,000 maternal deaths annually, and in South Africa the hypertensive disorders of pregnancy are responsible for 14% of maternal deaths. The pathophysiology of pre-eclampsia is not completely understood but the leading hypothesis is based on placental dysfunction.

Unfortunately, pre-eclampsia is a disease that is seen only in humans and there are no convincing animal models of pre-eclampsia. This makes it imperative that critical laboratory observations are made on human tissues.

### Study aims

We propose establishing an ethically responsible biobank to facilitate quicker access to clinical information, special investigations and biological samples to undertake research in the field of pre-eclampsia. It is modelled on many tissue banks currently in existence.

### Who can participate?

Women with pre-eclampsia (cases) and women with healthy pregnancies (controls) between the ages of 16-45 and in gestational week 20-42 will be eligible. As this is a biobank there will be no limit to the number of participants included.

### What does the study involve?

Our research team will be notified by attending clinicians when there is a possible candidate for the biobank. A member of the research team will then see the candidate and will give them an information and consent sheet and explain the project. If they decide to participate and after consent has been obtained, clinical information will be collected, samples may be collected, and special investigations may be done. The participants will be seen daily and will be contacted

again after discharge. All information will be kept confidential and the participants may withdraw at any stage.

#### Possible risks and benefits of participating

The risk of adverse events is unlikely. There are no added risks associated with being involved in the study. Any publications arising from projects that utilised the biobank will need to acknowledge the participants.

All information collected will be stored in a locked office in the principal researcher or research midwife's office. The medical data will be recorded in a REDCap database and only the biobank investigators and research midwives will have access to the identification codes. All information used for follow-up projects will be pseudonymised. Samples stored in the biobank will be given an identifying code and will not contain any identifying information. Samples will not be used for a genetic register.

#### Where is the study run from?

The study is run from Tygerberg Hospital, Cape Town, South Africa

#### When is the study starting and how long is it expected to run for?

The study started in April 2018 and is expected to run until December 2030

#### Who is funding the study?

This study is supported by STINT; The Swedish foundation of International Cooperation in Research and Higher Education, Preeclampsia foundation, Märta Lundqvist's foundation, Ester Åsberg's foundation, Jane and Dan Olsson's foundation, Center for Clinical research Dalarna and the Swedish Society of Medicine.

#### Who is the main contact?

Dr Catherine Cluver, [cathycluver@hotmail.com](mailto:cathycluver@hotmail.com)

Dr Lina Bergman, [lina.bergman.2@gu.se](mailto:lina.bergman.2@gu.se)

## Contact information

#### Type(s)

Scientific

#### Contact name

Prof Catherine Cluver

#### ORCID ID

<https://orcid.org/0000-0002-0406-8964>

#### Contact details

Department of Obstetrics and Gynaecology

Faculty of Health Sciences

Stellenbosch University

Francie van Zyl Drive

Tygerberg

Cape Town

South Africa

7505  
+27 823210298  
cathycluver@hotmail.com

### **Type(s)**

Public

### **Contact name**

Dr Lina Bergman

### **ORCID ID**

<https://orcid.org/0000-0001-5202-9428>

### **Contact details**

Sankt Sigfridsgatan 46  
Gothenburg  
Sweden  
41266  
+46 707920780  
lina.bergman.2@gu.se

## **Additional identifiers**

### **Clinical Trials Information System (CTIS)**

Nil known

### **ClinicalTrials.gov (NCT)**

Nil known

### **Protocol serial number**

Nil known

## **Study information**

### **Scientific Title**

PROVE: PReeclampsia Obstetric adVerse Events

### **Acronym**

PROVE

### **Study objectives**

To set up a preeclampsia biobank at Tygerberg Hospital, Stellenbosch University, to facilitate clinical and laboratory based research in preeclampsia.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 28/02/2018, Regional ethical board at Stellenbosch University (PO Box 241, Cape Town 8000, South Africa; +27 (0)21 9389677; no email provided), ref: N17/05/048

## **Study design**

Single center prospectively collected database and biobank of women with severe preeclampsia

## **Primary study design**

Observational

## **Study type(s)**

Diagnostic

## **Health condition(s) or problem(s) studied**

Preeclampsia

## **Interventions**

Our research team will be notified by attending clinicians when there is a possible candidate for the biobank. A member of the research team will then see the candidate and will give them an information and consent sheet and explain the project. If they decide to participate and after consent has been obtained, clinical information will be collected, samples may be collected, and special investigations may be done. The participants will be seen daily and will be contacted again after discharge. All information will be kept confidential and the participants may withdraw at any stage.

When a project arises that involves the use of information or samples from the biobank, an independent proposal to HREC will be obtained and approval from the Preeclampsia biobank will be requested. Once this is done, deidentified information and samples will be released. The outcomes of updates will be reported annually to the ethics committee. We will collect information on the pregnancy and outcomes of the pregnancy. We may perform cognitive function assessments and questionnaires on symptoms and signs of preeclampsia. Special investigations could include MRI examinations of the brain, studies using ultrasound, ophthalmological examinations and non-invasive endothelial function assessment.

The sample collection includes the following

- Specimens usually discarded during clinical care: E.g. placenta, placental membranes, umbilical cord, cord blood, urine, stool and cerebrospinal fluid (CSF). The CSF (maximum volume of 0.5 ml) will only be collected in women who are having spinal anaesthesia. We will collect the fluid that is usually discarded before the anaesthetic is injected.
- Blood samples: maximum of 12 ml at each collection time (usually only a single test tube of 5 ml). We will only collect samples if the patient is having blood taken for a clinical indication. We will collect blood up to a maximum of 6 times per participant.
- Saliva: This will be collected once in a 3 cc cup, 1-2 ml for freezing.

## **Intervention Type**

Other

## **Primary outcome(s)**

The items collected for the biobank include:

1. Specimens usually discarded during clinical care: E.g. placenta, placental membranes, umbilical cord, cord blood, urine, stool and cerebrospinal fluid (CSF). The CSF (maximum volume of 0.5 ml) will only be collected in women who are having spinal anaesthesia. We will collect the fluid that is usually discarded before the anaesthetic is injected
2. Blood samples: maximum of 12 ml at each collection time (usually only a single test tube of 5 ml). We will only collect samples if the patient is having blood taken for a clinical indication. We

will collect blood up to a maximum of 6 times per participant  
3. Saliva: This will be collected once in a 3 cc cup, 1-2 ml for freezing

### **Key secondary outcome(s)**

There are no secondary outcome measures

### **Completion date**

31/12/2030

## **Eligibility**

### **Key inclusion criteria**

1. Cases:

1.1. Women with a diagnosis of preeclampsia or severe preeclampsia in gestational week 20-42

1.2. Admitted to Tygerberg hospital

Severe preeclampsia is defined as preeclampsia with an organ complication such as renal failure, pulmonary oedema, eclampsia, intracerebral hemorrhage, cerebral oedema, heart failure or disseminated intravascular coagulation

2. Controls:

2.1. Women with healthy pregnancies matched for gestational age admitted for delivery at Tygerberg hospital

Both primiparous and parous women are included

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

All

### **Sex**

Female

### **Key exclusion criteria**

1. Cases: If the woman is not able to give informed consent

1.1. For women with pulmonary edema: Existing cardiac disease

1.2. For women with eclampsia: Existing neurological disease

2. Normotensive controls:

2.1. Pre-existing hypertension

2.2. Diabetes mellitus before or during pregnancy

2.3. Pre-existing cardiovascular, renal or cerebral disease

2.4. Chronic medication

### **Date of first enrolment**

12/04/2018

**Date of final enrolment**

31/12/2029

## Locations

**Countries of recruitment**

South Africa

**Study participating centre**

**Tygerberg Hospital**

Stellenbosch University

Francie van Zijl Drive

Cape Town

South Africa

7505

## Sponsor information

**Organisation**

Stellenbosch University

**ROR**

<https://ror.org/05bk57929>

## Funder(s)

**Funder type**

Hospital/treatment centre

**Funder Name**

Mercy Perinatal

**Funder Name**

Svenska Läkaresällskapet

**Alternative Name(s)**

Swedish Society of Medicine, Swedish Medical Society, SLS

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

Sweden

**Funder Name**

Märta Lundqvists Stiftelse

**Alternative Name(s)**

Märta Lundqvists Foundation

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

Sweden

**Funder Name**

Swedish Foundation for International Cooperation in Research and Higher Education

**Alternative Name(s)**

Stiftelsen för internationalisering av högre utbildning och forskning, The Swedish Foundation for International Cooperation in Research and Higher Education, STINT

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

Sweden

**Funder Name**

Preeclampsia Foundation

**Alternative Name(s)**

The Preeclampsia Foundation, Preeclampsia Fndn, Preeklampsie Stigting, Fondacioni i Preeklampsisë, , , PF

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

United States of America

**Funder Name**

Ester Åsbergs Stiftelse

**Funder Name**

Center for Clinical research, Dalarna, Sweden

**Funder Name**

Jane och Dan Olssons Stiftelse

**Alternative Name(s)**

Jane and Dan Olssons Foundation

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

Sweden

## Results and Publications

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
-------------	---------	--------------	------------	----------------	-----------------

<a href="#">Protocol article</a>	PROVE-Pre-Eclampsia Obstetric Adverse Events: Establishment of a Biobank and Database for Pre-Eclampsia	20/04/2021	22/10/2021	Yes	No
<a href="#">Other publications</a>	Blood pressure as a risk factor for eclampsia and pulmonary oedema in pre-eclampsia	23/07/2021	22/10/2021	Yes	No
<a href="#">Other publications</a>	Cerebral perfusion pressure and autoregulation in eclampsia-a case control study	17/03/2021	22/10/2021	Yes	No
<a href="#">Other publications</a>	Cognitive impairment in preeclampsia complicated by eclampsia and pulmonary edema after delivery	16/02/2021	22/10/2021	Yes	No
<a href="#">Other publications</a>	Associations Between Soluble fms-Like Tyrosine Kinase-1 and Placental Growth Factor and Disease Severity Among Women With Preterm Eclampsia and Preeclampsia	16/08/2022	02/11/2023	Yes	No
<a href="#">Other publications</a>	Cardiac magnetic resonance imaging in preeclampsia complicated by pulmonary edema shows myocardial edema with normal left ventricular systolic function	01/08/2022	02/11/2023	Yes	No
<a href="#">Other publications</a>	Cerebral biomarkers in neurologic complications of preeclampsia	01/08/2022	02/11/2023	Yes	No
<a href="#">Other publications</a>	Circulating Chemerin Is Elevated in Women With Preeclampsia	13/03/2023	02/11/2023	Yes	No
<a href="#">Other publications</a>	Circulating Growth Differentiation Factor 15 Is Increased Preceding Preeclampsia Diagnosis: Implications as a Disease Biomarker	17/08/2021	02/11/2023	Yes	No
<a href="#">Other publications</a>	Circulating concentrations of glyocalyx degradation products in preeclampsia	13/10/2022	02/11/2023	Yes	No
<a href="#">Other publications</a>	Correlation between cognitive assessment scores and circulating cerebral biomarkers in women with pre-eclampsia and eclampsia	01/03/2023	02/11/2023	Yes	No
<a href="#">Other publications</a>	Evidence of Neuroinflammation and Blood-Brain Barrier Disruption in Women with Preeclampsia and Eclampsia	05/11/2021	02/11/2023	Yes	No
<a href="#">Other publications</a>	PSG7 and 9 (Pregnancy-Specific $\beta$ -1 Glycoproteins 7 and 9): Novel Biomarkers for Preeclampsia	05/04/2022	02/11/2023	Yes	No
<a href="#">Other publications</a>	Blood-brain barrier injury and neuroinflammation in pre-eclampsia and eclampsia	01/06/2025	04/08/2025	Yes	No
<a href="#">Other publications</a>	Cerebral infarcts, edema, hypoperfusion, and vasospasm in preeclampsia and eclampsia	01/06/2025	04/08/2025	Yes	No
<a href="#">Other publications</a>	Reduced circulating NrCAM as a biomarker for fetal growth restriction	21/07/2021	04/08/2025	Yes	No
<a href="#">Other publications</a>	The association between circulating SIGLEC6 and preeclampsia: observational studies of seven cohorts	29/07/2025	04/08/2025	Yes	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes