

# Propofol in cardiac surgery: ProMPT-2

<b>Submission date</b>	<b>Recruitment status</b>	<input type="checkbox"/> Prospectively registered
11/03/2019	No longer recruiting	<input checked="" type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input checked="" type="checkbox"/> Statistical analysis plan
26/03/2019	Completed	<input type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
30/12/2025	Circulatory System	<input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Almost 2.3 million people in the UK are living heart disease and > 36,000 cardiac surgery operations are carried out each year. During surgery the heart is isolated from the rest of the circulation and a heart-lung machine is used to supply oxygen to the blood and pump it around the body. The heart is stopped and provided with nutrients by a cardioplegic solution that is injected directly into the heart arteries. This allows the surgeon to operate on the heart while it is still and not filled with blood, but looking after the heart in this way during surgery is not ideal. The heart muscle can become short of oxygen, and when the heart is restarted, and blood starts to flow again the muscle can be harmed.

The damage is believed to be caused mainly by the formation of highly reactive molecules known as 'free radicals' in the heart muscle during the time it is short of oxygen. Propofol is a general anaesthetic widely used in cardiac surgery and research suggests that propofol could protect the heart muscle against damage from free radicals. We want to investigate whether adding propofol to the cardioplegic solution in patients having isolated coronary artery bypass grafting (CABG) surgery using the heart-lung machine is beneficial and if the benefit is greater the more propofol that is used.

### Who can participate?

Anyone having elective or urgent isolated CABG with cardiopulmonary bypass (CPB)

### What does the study involve?

During heart surgery, it is important that the heart be kept still while the surgical team are working on it. This is done by injecting a solution called cardioplegia. We believe that adding propofol to this solution will protect the heart muscle during its period of inactivity, and this in turn may lead to fewer complications after the operation.

The purpose of this study is to compare the results from three different approaches: adding a low dose of propofol to the cardioplegia solution, adding a higher dose, and not adding any at all. Propofol is widely used as an anaesthetic, and you will receive this anyway as part of usual general anaesthesia.

### What are the possible benefits and risks of participating?

Whilst we cannot promise taking part in this study will help you, the information gained will help us make decisions which could potentially improve the treatment of heart surgery patients in the future.

Patients in all groups are at risk of operative and postoperative complications, your doctor will discuss this with you prior to your operation and inform you of the possible side effects of propofol as part of routine care. However, no extra complications are expected due to adding the propofol to the cardioplegia solution with propofol, but if you would like further information, please ask a member of the research team.

Where is the study run from?

The University of Bristol is the sponsor for this study and has overall responsibility for the study. The study is managed by the Bristol Trials Centre (CTEU).

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

August 2018 to March 2024

Who is funding the study?

NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

Who is the main contact?

Beth Fitzgerald, [Prompt2-trial@bristol.ac.uk](mailto:Prompt2-trial@bristol.ac.uk)

## Contact information

**Type(s)**

Public

**Contact name**

Ms Beth Fitzgerald

**Contact details**

Bristol Trials Centre

University of Bristol

1-5 Whiteladies Road

Bristol

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BS8 1NU

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[Prompt2-trial@bristol.ac.uk](mailto:Prompt2-trial@bristol.ac.uk)

## Additional identifiers

**Clinical Trials Information System (CTIS)**

2018-000169-35

**ClinicalTrials.gov (NCT)**

Nil known

**Protocol serial number**

CPMS 37464

## Study information

**Scientific Title**

Efficacy of propofol-supplemented cardioplegia on biomarkers of organ injury in patients having cardiac surgery using cardiopulmonary bypass: Propofol cardioplegia for myocardial protection randomised controlled trial: the PROMPT2 Study

**Acronym**

ProMPT 2

**Study objectives**

Adding propofol to the cardioplegic solution used during cardiac surgery reduces organ damage

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 12/10/2018, South Central - Berkshire B Research Ethics Committee (Whitefriars, Level 3, Block B Lewins Mead, Bristol BS1 2NT; nrescommittee.southcentral-berkshire@nhs.net; +44 (0)207 104 8059), ref: 18/SC/0472

**Study design**

Interventional randomized controlled trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

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

Reperfusion injury of the heart following coronary artery bypass grafting (CABG) surgery

**Interventions**

Study patients will be randomly allocated in a 1:1:1 ratio to one of the following:

Placebo: Blood cardioplegia with sham supplementation (normal saline 0.9% weight/volume sodium chloride, NaCl),

Propofol - LD: Blood cardioplegia with low dose (6mcg/ml) propofol supplementation

Propofol - HD: Blood cardioplegia with high dose (12mcg/ml) propofol supplementation

The total duration of treatment is for as long as the cardiac surgery takes.

The follow-up period is at 3 and 12 months, by QoL questionnaires.

Randomisation will be carried out as close to the planned operation as possible, after eligibility has been confirmed and written informed consent given. Randomisation will be performed by a member of the research team not involved in data collection using a secure internet-based randomisation system ensuring allocation concealment. Randomisation will take place as soon as it is confirmed the surgery will go ahead, which is typically 30 minutes before the patient is taken to theatre. Patients will be allocated in a 1:1:1 ratio to either i) high dose propofol supplementation or ii) low dose propofol supplementation or iii) sham supplementation. The allocation will be computer-generated and stratified by centre. Baseline quality of life (QoL) will be collected from the patients prior to randomisation.

**Intervention Type**

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Propofol

**Primary outcome(s)**

Myocardial injury, assessed by serial measurements of cTnT in serum from blood samples collected pre-operatively and during the first 48-hours post chest closure.

**Key secondary outcome(s)**

Current secondary outcome measures as of 06/06/2023:

1. Systemic metabolic stress as measured by blood lactate at pre-op, 10 mins post cross clamp, 1, 6, 12, 24, 48 hours post chest closure
2. Renal function, as measured by creatinine in serum at pre-op, 1, 6, 12, 24, 48 hours post chest closure
3. Markers of Inflammation and oxidative stress as measured by tumour necrosis factor (TNF)-alpha, interleukin (IL)-10, IL-8, IL-6 and myeloperoxidase (MPO) in serum (Bristol cohort only) at pre-op, 1, 6, 12, 24, 48 hours post chest closure
4. Blood pH at pre-op, 1, 6, 12, 24, 48 hours post chest closure
5. Length of intensive care unit (ICU) stay
6. Length of postoperative hospital stay
7. Clinical outcomes and serious adverse events, i.e. serious post-operative complications (e.g. MI, permanent stroke, acute kidney injury) and death from any cause
8. QoL measured using the Coronary Revascularisation Outcome Questionnaire (CROQ) and the EQ-5D-5L questionnaire at baseline, 3 months and 12 months

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Previous secondary outcome measures as of 27/05/2022:

1. Systemic metabolic stress as measured by blood lactate at pre-op, 10 mins post cross clamp, 1, 6, 12, 24, 48 hours post chest closure
2. Renal function, as measured by creatinine in serum at pre-op, 1, 6, 12, 24, 48 hours post chest closure
3. Markers of Inflammation and oxidative stress as measured by tumour necrosis factor (TNF)-alpha, interleukin (IL)-10, IL-8, IL-6 and myeloperoxidase (MPO) in serum (Bristol cohort only) at pre-op, 1, 6, 12, 24, 48 hours post chest closure
4. Blood pH at pre-op, 1, 6, 12, 24, 48 hours post chest closure
5. Investigate the association between cTnT and circulating level of cardiac-released microRNA-1 and exosomal microRNA-1 content at pre-op, 1, 6, 12, 24, 48 hours post chest closure (Bristol cohort only)
6. Examine whether the association between cTnT and microRNA and exosomal microRNA-1 content differs between groups (i.e. differs with the propofol supplementation received) at pre-op, 1, 6, 12, 24, 48 hours post chest closure (Bristol cohort only)
7. Length of intensive care unit (ICU) stay
8. Length of postoperative hospital stay
9. Clinical outcomes and serious adverse events, i.e. serious post-operative complications (e.g.

MI, permanent stroke, acute kidney injury) and death from any cause

10. QoL measured using the Coronary Revascularisation Outcome Questionnaire (CROQ) and the EQ-5D-5L questionnaire at baseline, 3 months and 12 months

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4. Blood pH at pre-op, 1, 6, 12, 24, 48 hours post chest closure
5. Investigate the association between cTnT and circulating level of cardiac -released microRNA-1 and exosomal microRNA-1 content at pre-op, 1, 6, 12, 24, 48 hours post chest closure.
6. Examine whether the association between cTnT and microRNA and exosomal microRNA-1 content differs between groups (i.e. differs with the propofol supplementation received) at pre-op, 1, 6, 12, 24, 48 hours post chest closure.
7. Length of intensive care unit (ICU) stay
8. Length of postoperative hospital stay
9. Clinical outcomes and serious adverse events, i.e. serious post-operative complications (e.g. MI, permanent stroke, acute kidney injury) and death from any cause.
10. QoL measured using the Coronary Revascularisation Outcome Questionnaire (CROQ) and the EQ-5D-5L questionnaire at baseline, 3-months and 12-months.

#### Completion date

31/03/2024

## Eligibility

#### Key inclusion criteria

1. Aged >= 18 years
2. Having elective or urgent isolated CABG with CPB
3. Ability to give informed consent

Women only:

4. Negative pregnancy test, or be surgically or post-menopausal for >12 months

#### Participant type(s)

Patient

#### Healthy volunteers allowed

No

#### Age group

Mixed

#### Lower age limit

18 years

**Upper age limit**

100 years

**Sex**

All

**Total final enrolment**

240

### **Key exclusion criteria**

Current participant exclusion criteria as of 20/05/2020:

1. Previous cardiac surgery
2. Planned concomitant procedure
3. Emergency or salvage operation
4. Long-term steroid therapy (taking tablets on a daily basis for at least 1 month prior to surgery)
5. Pre-operative estimated glomerular filtration rate  $\leq$  30 ml/min/1.73m<sup>2</sup>
6. Current congestive heart failure
7. Left ventricular (LV) ejection fraction <30% (i.e. poor LV function)
8. Allergy to peanuts, eggs, egg products, soybeans or soy products
9. Already participating in another interventional clinical study
10. Prisoners
11. Patients taking immunosuppressants (e.g. methotrexate or azathioprine)
12. Patients known to have cTnT level >500 ng/l (or cTnI level >600 ng/l) in the last 4 days (prior to eligibility check)

Women only:

13. Breast feeding

Previous participant exclusion criteria:

1. Previous cardiac surgery
2. Planned concomitant procedure
3. Emergency or salvage operation
4. Long-term steroid therapy
5. Pre-operative estimated glomerular filtration rate  $\leq$  60 mls/min/1.73m<sup>2</sup>
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8. Allergy to peanuts, eggs, egg products, soybeans or soy products
9. Already participating in another interventional clinical study
10. Prisoners

Women only:

11. Breastfeeding

**Date of first enrolment**

31/08/2018

**Date of final enrolment**

07/11/2022

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Bristol Heart Institute**

Marlborough Street

Bristol

England

BS2 8HW

**Study participating centre**

**National Heart and Lung Institute**

Hammersmith Hospital

Du Cane Road

London

England

W12 0HS

**Study participating centre**

**Glenfield Hospital**

Groby Road

Leicester

England

LE3 9QP

**Study participating centre**

**Harefield Hospital**

Hill End Road

Harefield

England

UB9 6JH

**Study participating centre**

**Wythenshawe Hospital**

Southmoor Rd

Roundthorn Industrial Estate

Wythenshawe

England

M23 9LT

**Study participating centre**

**Royal United Hospitals Bath NHS Foundation Trust**  
Combe Park  
Bath  
England  
BA1 3NG

**Study participating centre**

**Musgrove Park Hospital (taunton)**  
Musgrove Park Hospital  
Taunton  
England  
TA1 5DA

## **Sponsor information**

**Organisation**

University of Bristol

**ROR**

<https://ror.org/0524sp257>

## **Funder(s)**

**Funder type**

Government

**Funder Name**

NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 15/180/55

## **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.

Anonymised individual patient data (baseline, intervention, outcome data and adverse events) will be made available for secondary research, conditional on assurance from the secondary

researcher that the proposed use of the data is compliant with the with the UK Policy Framework for Health and Social Care Research and MRC Policy on Data Preservation and Sharing regarding scientific quality, ethical requirements and value for money. Please contact Prof. Chris Rogers (prompt2-trial@bristol.ac.uk ) to discuss any data requests. Data will be made available after the study has been closed and the primary publication is out. It will be made available indefinitely. Only data from patients who have consented for their data to be shared with other researchers will be provided.

## 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>		16/02/2023	17/02/2023	Yes	No
<a href="#">HRA research summary</a>			26/07/2023	No	No
<a href="#">Plain English results</a>			30/12/2025	No	Yes
<a href="#">Statistical Analysis Plan</a>		29/02/2024	01/03/2024	Yes	No