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# Optimisation of perioperative cardiovascular management to improve surgical outcome II

**Submission date**
15/11/2016

**Recruitment status**
No longer recruiting

**Registration date**
23/11/2016

**Overall study status**
Completed

**Last Edited**
04/12/2024

**Condition category**
Surgery

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
Around 40,000 NHS patients aged 65 years and over undergo major planned gut surgery each year. After surgery, more than 12,000 patients develop an infection while they are in hospital (hospital acquired infection), and 3,600 die within 180 days. Patients who survive complications to leave hospital commonly suffer a loss of mobility, independence and reduced long-term survival. Hospital acquired infections in this patient group cost the NHS more than £80 million each year. Complications after surgery are more likely if patients receive too much or too little fluid through a drip. The use of small doses of drugs that increase heart function (inotropic drugs) is also important. Currently, the type and dose of these drug treatments is decided by a doctor based on opinion-based assessment of the patient. Advanced heart monitoring technologies may provide a more reliable guide to the use of these treatments. However, only one third of eligible patients currently receive this treatment because many doctors are concerned this approach is more aggressive and may therefore harm some patients by causing small heart attacks. Only a large study can resolve this uncertainty, to find out whether giving this treatment to all eligible patients is beneficial, or ineffective or harmful. The aim of this study is to find out the effect of this treatment on the number of patients who develop hospital acquired infection within 30 days after major planned gastrointestinal (gut) surgery.

Who can participate?
Adults over 65 years old who are undergoing planned major gastrointestinal (gut) surgery.

What does the study involve?
Participants are randomly allocated to one of two groups. Both treatments begin at the start of surgery and finish four hours after this has ended. The two treatments involve slightly different ways of deciding the amount of fluid and drugs given through a drip to improve heart function. If participants receive standard care the doctor uses measurements such as heart rate and blood pressure measurements to guide these treatments. If participants receive the new trial treatment doctors also measure the amount of blood the heart pumps each minute using an extra monitor. These extra measurements should help the doctor to decide how much fluid and drugs they should give to improve heart function. After the treatment is over, the study team reviews the participant's medical records and may talk to the doctors to collect information about their recovery. Participants are also contacted by telephone in one month and again in six

months' time to ask some simple questions about their wellbeing. The phone call lasts for around five minutes. With the participant's permission or if it is not possible to contact the participant, the study team may also contact their General Practitioner for further information.

What are the possible benefits and risks of participating?
There are no direct benefits of participating. Previous research suggests that the treatment we are investigating is very safe and should benefit most patients. However, there is a very small risk of a minor heart attack for some patients. For this reason, patients taking part in the study will be closely monitored throughout the trial period and, if necessary, the research team will make adjustments to the treatment to ensure patient safety.

Where is the study run from?
Hospitals in Australia, Canada, Germany, Spain, Sweden, United Kingdom and United States of America.

When is the study starting and how long is it expected to run for?
August 2016 to March 2023

Who is funding the study?
1. National Institute for Health Research (UK)
2. Edwards Lifesciences Corporation (UK)

Who is the main contact?
1. Dr Priyanthi Dias (scientific and public)
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### Study website
http://optimiseii.org/

# Contact information

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## Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
011560

## Study information

### Scientific Title
Open, multi-centre, randomised controlled trial of cardiac output-guided fluid therapy with low dose inotrope infusion compared to usual care in patients undergoing major elective gastrointestinal surgery

## Acronym
OPTIMISE II

## Study objectives
The aim of the study is to establish whether the use of minimally invasive cardiac output monitoring to guide protocolised administration of intravenous fluid, combined with low dose inotrope infusion for patients undergoing major elective surgery involving the gastrointestinal tract will reduce the incidence of postoperative infection within 30 days of randomisation.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
London - Brent Research Ethics Committee, 28/11/2016, ref: 16/LO/2067

## Study design
International open multi-centre randomized controlled trial

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Hospital

## Study type(s)
Treatment

## Participant information sheet
http://optimiseii.org/documents

## Health condition(s) or problem(s) studied
Major elective gastrointestinal surgery

## Interventions
Following provision of informed consent, participants will be randomly allocated to one of two groups (1:1) using a computer generated dynamic procedure (minimisation) with a random component. Minimisation will be performed by country and surgical procedure category.

Intervention group: The intervention will commence from the induction of general anaesthesia and continue for four hours following surgery. Cardiac output and stroke volume will be measured by cardiac output monitor. Investigators may only use commercially available cardiac output monitoring equipment provided by Edwards Lifesciences in this trial. No more than 500ml of intra-venous fluid will be administered prior to commencing cardiac output monitoring. In addition to the maintenance fluid and blood products, patients will receive 250ml fluid challenges with a recommended solution as required in order to achieve a maximal value of stroke volume. The absence of fluid responsiveness will be defined as the absence of a sustained rise in stroke volume of at least 10% for 20 minutes or more. In addition, patients will receive a

low dose inotrope infusion at a fixed rate which will be commenced after fluid replacement has been initiated. The choice of inotrope will be made at the discretion of the local investigator, according to local preference and availability. The options are dobutamine at a dose/rate of 2.5 µg/kg/min and dopexamine at an equipotent dose/rate of 0.5 µg/kg/min. The infusion rate will be reduced and/or discontinued if the patient develops a tachycardia (heart rate greater than 100bpm) for more than 30 minutes despite adequate anaesthesia and analgesia. Data collection and follow-up for such patients will be performed as normal. All other management decisions will be taken by clinical staff.

Control group: Patients in the control group will be managed by clinical staff according to usual practice. This will include 250ml fluid challenges with a recommended intra-venous fluid administered at the discretion of the clinician guided by pulse rate, arterial pressure, urine output, core-peripheral temperature gradient, serum lactate and base excess. If a specific haemodynamic end-point for fluid challenges is to be used, the most appropriate would usually be a sustained rise in central venous pressure of at least 2 mmHg for 20 minutes or more. Patients should not be randomised if the clinician intends to use cardiac output monitoring regardless of study group allocation; this is considered 'clinician refusal' and is a specific exclusion criteria. However, clinical staff are free to request cardiac output monitoring if this is required to inform the treatment of a patient who becomes critically ill (e.g. because of severe haemorrhage) during the trial intervention period. In this situation a protocol deviation form will be completed.

All participants will be followed for 180 days after randomization.

## Intervention Type
Other

## Primary outcome measure
Postoperative infection rate within 30 days of randomisation. This is defined as one or more of the following infections of Clavien-Dindo grade II or greater:
1. Superficial surgical site infection
2. Deep surgical site infection
3. Organ space surgical site infection
4. Pneumonia
5. Urinary tract infection
6. Laboratory confirmed blood stream infection
7. Infection, source uncertain; this is defined as an infection which could be more than one of the above but it is unclear which

The primary outcome will be assessed using information from a patient's medical notes. Patients discharged from hospital before day 30 will be contacted shortly after day 30 to ascertain whether they have received any new treatment since discharge, or if they have been re-admitted to hospital or seen a doctor since discharge. For patients who have received further treatment or seen a health professional since discharge, further details will be collected directly from the hospital/doctor or from the patient's health records.

## Secondary outcome measures
1. Mortality, assessed by a patient medical record review or data from national databases, within 180 days of randomisation
2. Acute kidney injury of Clavien-Dindo grade II or greater, assessed using a patient medical note review and telephone interview in the same way as primary outcome, within 30 days from

randomisation.
3. Acute cardiac event of Clavien-Dindo grade II or greater, assessed by a review of the patient's medical notes, within 24 hours of randomisation
4. Acute cardiac event of Clavien-Dindo grade II or greater, assessed using a patient medical note review and telephone interview in the same way as primary outcome, within 30 days of randomisation.

Process measures:
1. Duration of hospital stay (number of days from randomisation until hospital discharge), assessed by a review of the patient's medical records.
2. Number of critical care free days*, assessed by a review of the patient's medical records, up to 30 days from randomisation.

*A critical care free day is defined as a day in which the patient is alive and is not in a level 2 or level 3 critical care bed.

### Overall study start date
30/08/2016

### Completion date
31/03/2023

## Eligibility

### Key inclusion criteria
1. Age 65 years and over
2. Patients undergoing major elective surgery involving the gastrointestinal tract that is expected to take longer than 90 minutes

### Participant type(s)
Patient

### Age group
Senior

### Lower age limit
65 Years

### Sex
Both

### Target number of participants
2502 (1251 per arm)

### Total final enrolment
2502

### Key exclusion criteria
1. Inability or refusal to provide patient consent
2. Clinician refusal (including intention to monitor cardiac output from the start of surgery

regardless of study group allocation)
3. American Society of Anesthesiologists (ASA) score of I
4. Patients expected to die within 30 days
5. Acute myocardial ischaemia within 30 days prior to randomisation
6. Acute pulmonary oedema within 30 days prior to randomisation
7. Contra-indication to low-dose inotropic medication
8. Pregnancy at time of enrolment
9. Previous enrolment in the OPTIMISE II trial
10. Current participation in another clinical trial of a treatment with a similar biological mechanism or primary outcome measure

### Date of first enrolment
31/12/2016

### Date of final enrolment
13/09/2022

## Locations

### Countries of recruitment
Australia

Canada

England

Germany

Scotland

Spain

Sweden

United Kingdom

United States of America

Wales

### Study participating centre
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**Study participating centre**
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**Study participating centre**
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**Study participating centre**
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**Sponsor type**
University/education

**Website**
http://bartshealth.nhs.uk/research/about-us/contact-us/

**ROR**
https://ror.org/026zzn846

# Funder(s)

**Funder type**
Government

**Funder Name**
National Institute for Health Research

**Alternative Name(s)**
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
United Kingdom

**Funder Name**
Edwards Lifesciences Corporation

# Results and Publications

**Publication and dissemination plan**
Planned publication in a peer reviewed journal, conference presentations and webcasts. Intent to publish the main paper as soon as possible after completion of the trial.

**Intention to publish date**
31/10/2023

**Individual participant data (IPD) sharing plan**
The datasets generated and analysed during the current study will be available upon request from pctu-data-sharing@qmul.ac.uk. The Pragmatic Clinical Trials Unit (PCTU) shares data via a data-sharing agreement which is submitted to a panel. Enquiries can be sent to the data sharing email address pctu-data-sharing@qmul.ac.uk. Ideally, the Chief Investigator (CI), Professor Rupert Pearse, should be contacted first with the enquiry at admin@optimiseii.org for CI approval. Data would typically only be available to share at the end of the study. Please see the following page for further details regarding PCTU data sharing: https://www.qmul.ac.uk/pctu/collaborate-with-us/data-sharing.

**IPD sharing plan summary**
Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol article | protocol | 15/01/2019 | 12/02/2020 | Yes | No |
| Statistical Analysis Plan | version 3.0 | 17/01/2023 | 24/02/2023 | No | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Results article | | 03/12/2024 | 04/12/2024 | Yes | No |