# CoMICS trial

## MiECC vs. CECC

# Aims of the day

- Trial team
- Overview and trial design
- Trial interventions
- Patient screening and recruitment
- Randomisation
- Data collection
- Safety reporting
- Trial database
- Starting the trial

# Overview and trial design

# Trial overview

- CoMICS will compare the effectiveness and cost effectiveness of MiECC versus CECC in patients undergoing cardiac surgery requiring extra corporeal-circulation.

- Why is CoMICS important?
  - Currently, Extra Corporeal Circuit chosen by hospital/perfusion team preference.
  - MiECC is thought to reduce the proportion of patients having one or several serious post-operative complications following surgery.
  - Choice of circuit should be informed by high quality evidence (large Randomised Controlled Trial (RCT) to evaluate the benefits, harms and costs of difference circuits).

AIM:

To inform clinical understanding and influence surgical practice by providing high quality evidence to support **or** refute the use of MiECC for patients undergoing cardiac surgery

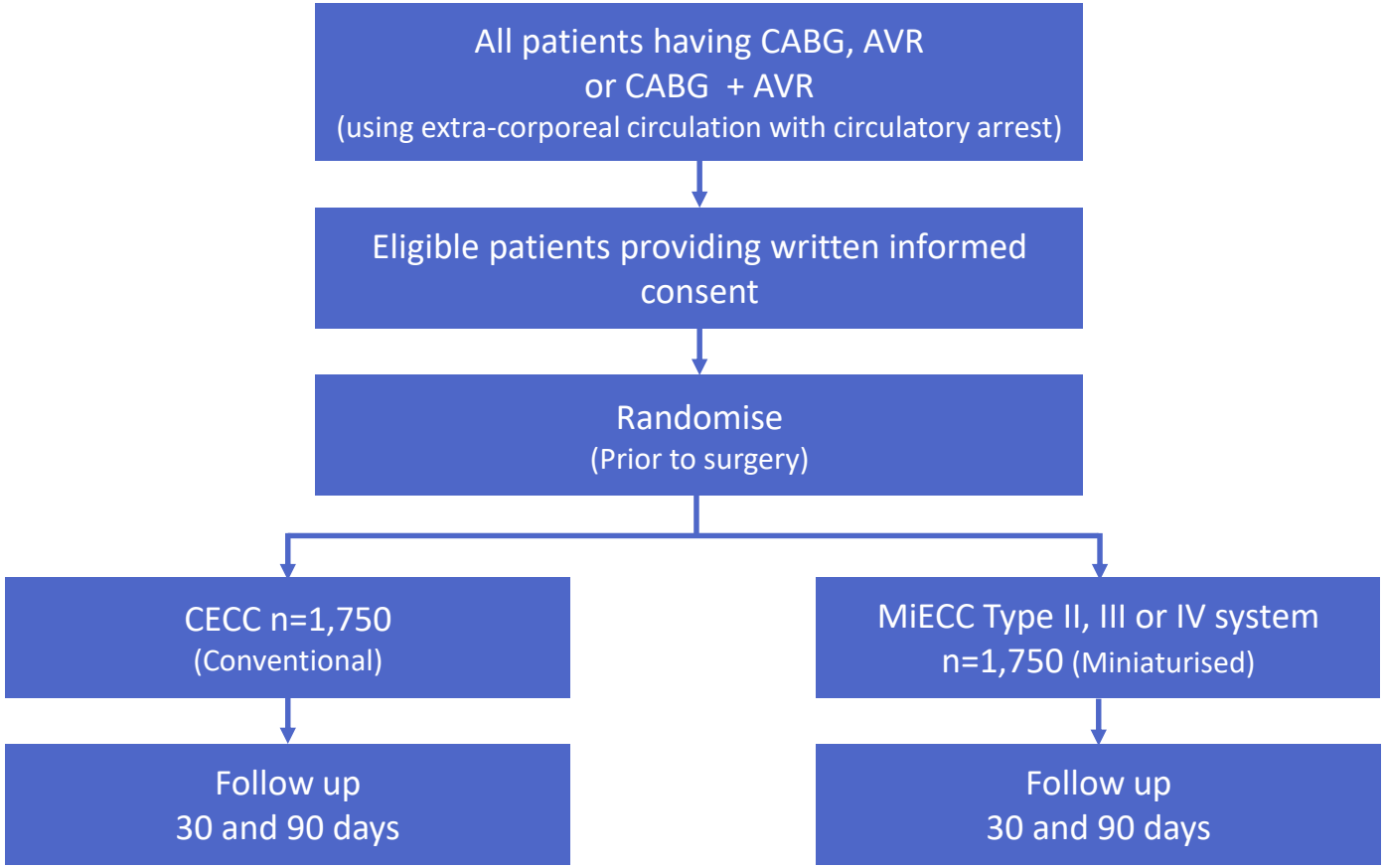
# Trial objectives

- To estimate the difference in the proportion of participants experiencing the primary outcome up to 30 days after randomisation between the MiECC or CECC groups.

- To compare secondary outcomes between the MiECC and CECC groups:
  - serious adverse events not included in the primary outcome,
  - RBC and other blood products transfused,
  - duration of cardiac ICU and hospital stay following the index admission,
  - resource use, generic health-related quality of life (HRQoL).

- To estimate the cost-effectiveness of MiECC versus CECC.

# Trial schema



# Trial design

- Multi-centre
- Two group parallel RCT
- 3,500 patients undergoing CABG, AVR or AVR+CABG
  - Centres (perfusion team) must have used MiECC for >50 operations of the type for which patients are being recruited.
- Randomise to CECC or MiECC
- Follow up to be completed at 30 and 90 days

# Eligibility criteria

- A participant may enter the trial if ALL of the following apply:
  - Age ≥18 and <85 years
  - Undergoing any elective or urgent CABG, AVR surgery, or CABG+AVR surgery, using extra-corporeal circulation without circulatory arrest.
- A patient may not enter trial if ANY of the following apply
  - Requirement for emergency or salvage operation
  - Requirement for major aortic surgery (e.g. aortic root replacement)
  - Contraindication or objection (e.g. Jehovah's Witnesses) to transfusion of blood products.
  - Congenital or acquired platelet, red cell or clotting disorders (patients with iron deficient anaemia will not be excluded)
  - Inability to give informed consent for the trial (e.g. learning or language difficulties).

# Trial interventions

- Minimal invasive ExtraCorporeal circulation (MiECC - Experimental)
  - MiECC systems have evolved in a modular fashion, to address safety, volume and blood management issues.
  - Systems are classified according to their features (Types I, II, II & IV; Anastasiadis *et al*. Perfusion 2015;30(3):195-200.)
  - Centres must use CE marked components which have features consistent with Type II, III or IV – **Type I is excluded for this Trial**
- Conventional ExtraCorporeal Circulation (CECC)
  - Required components
    - standard oxygenator, roller pump, hard-cell reservoir, arterial filter, shed-blood suctions, any of a range of venting options, uncoated tubing, and a cell-saver device.
    - The following optional/alternative components can be integrated (and recorded accordingly): coated oxygenator, coated tubing and centrifugal pump.

# Trial interventions (cont.)

- Aspects common to both CECC and MiECC
  - Centres must use same cardioplegia solution regardless of the assigned group.
  - Surgeons must carry out the particular operation using the same body temperature for MiECC and CECC.

- Operative details will be collected in both groups to characterise and report these variations.

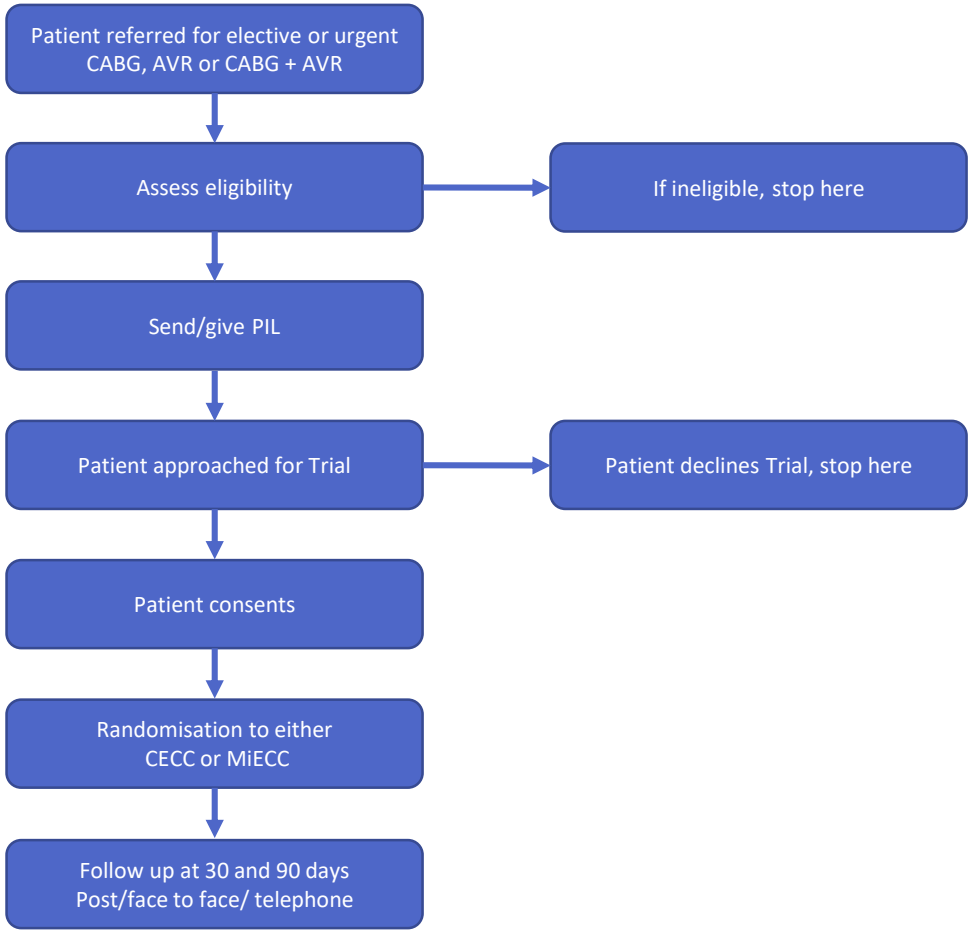
# Outcomes

- Primary outcomes
  - Post-operative SAEs up to 30 days after admission.
  - SAEs that qualify (as follows; documentary evidence will be required).
    - Death, myocardial infarction, stroke, gut infarction, AKI Network criteria for stage 3 AKI, reintubation, tracheostomy, mechanical ventilation for >48 hours, reoperation, percutaneous intervention, sternal wound infection with dehiscence, septicaemia confirmed by microbiology

- Secondary outcomes
  - The following outcomes will qualify up to 30 days post randomisation
    - Mortality, 'other' SAEs, units of RBC transfused, other blood products transfused.
  - The following outcomes will qualify during the hospital stay
    - Discharge times from cardiac ICU and total hospital stay, delirium in ICU up to 5 day post surgery,
  - The following outcomes will be measured up to 90 days after randomisation
    - HRQoL using the EQ-5D-5L, health and social care resources and associated costs

# Patient screening and recruitment

# Patient screening



# Patient screening

- All patients referred for CABG, AVR or CABG + AVR using using extracorporeal circulation without circulatory arrest should be screened for CoMICS.
- Each patient must have a screening log entry (A1) completed and entered onto the database whether they are eligible or not.
- Eligibility must be assessed in full.
- It is anticipated patients will be identified at the following stages:
  - Initial outpatient appointments.
  - Pre-op assessment.
  - Inpatient referrals.
  - Night before surgery (urgent inpatient).

# Data collection

# CRFs – A Forms

- A1 – Trial Eligibility/Screening log
  - Patient details, eligibility and patient questions
    - This is particularly important for Non-UK sites as you will be doing your own 30 and 90 day follow up by phone or post.

- A2 – Trial Allocation
  - This is to be completed by the person responsible for randomising patients and given to the perfusionist (if different)
  - This form does require entering onto the database and can be destroyed after the operation.

# CRFs – B Forms

- B1 – Preoperative details
  - Anthropometrics, NHYA & CCS class, baseline angio/echo details and bloods.
- B2 – Euroscore II
  - This needs to be completed accurately and in full at baseline.
- B3 – Preoperative Medical History
  - Record of medical history and preoperative medications.

# CRFs – C Forms

- C1 – Operation details
  - Basic operation details, blood products used, intraoperative details.

- C2 – Cardiopulmonary bypass details
  - Details of intervention and CPB circuit used
    - THIS FORM CONTAINS DETAILS OF THE RANDOMISATION – IT MUST BE COMPLETED AND ENTERED ONTO THE DATABASE BY THE PERFUSIONIST OR DELEGATED MEMBER OF THE TEAM.

# CRFs – D Forms

- D1 – Post-operative details
  - Ward movements, observations and extubation details.
- D2 – Delirium checklist
  - Derived from the ISDSC checklist. To be completed each day post-operatively.
- D3 – Blood products
  - Record of all blood products transfused during hospital stay.
- D4 – Primary outcomes (up to discharge)
  - Complications that qualify as the primary outcome.

# CRFs – D Forms (cont)

- D5-6 – Post-operative expected complications
  - Expected complications up until discharge (listed in the protocol) that don't require expedited SAE reporting.

- D7 – Admissions within 30 days of surgery
  - Complications that qualify as the primary outcome.

# Safety Reporting

# Safety Reporting

- Data on adverse events will be collected from time of consent and up to 30 days after surgery.
- Adverse events are classified as expected or unexpected.
  - Expected events are listed in the protocol & on the trial CRFs. These do not require an SAE form to be completed
  - Unexpected events are not listed in the protocol or CRFs. These do require reporting but only if they fulfil the serious criteria (below):

| Serious criteria |
| --- |
| Increased length of admission |
| Life threatening |
| Persistent or significant disability |
| Caused death |
| Congenital anomaly/birth defect |

# Expected and unexpected events

| Admission point | Expected (those list in the protocol) | Unexpected |
|---|---|---|
| In hospital period (from consent until discharge) | Report on CRFs D4-D6 | Complete CRFs S1 and S2 |
| At 30 days after surgery | Report on CRF D7 or X1 | Complete CRFs S1 and S2 |
| Deaths | Must be reported using the S1 and S2 form. | |

# Unexpected and serious adverse events

- Reporting procedure
  - Complete S1 and S2 (SAE initial report form)
    - Complete with all available information
    - PI to assign relatedness & sign
    - Fax to CTEU (+44117 342 3288) with coversheet <24 hours
    - Or Email comics-trial@Bristol.ac.uk **ensuring no patient identifiers**
    - If the SAE is 'ongoing', a FU report (S3) should be submitted via fax every 5 days until event resolution unless otherwise agreed with the Bristol CTEU.
  - SAEs forms can be sent incomplete whilst you are waiting for information.