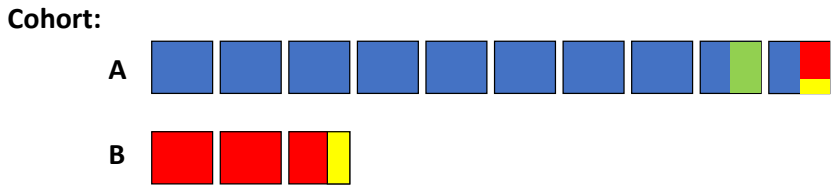
FAQ for eCRFs

Which bits do I complete for my patient?

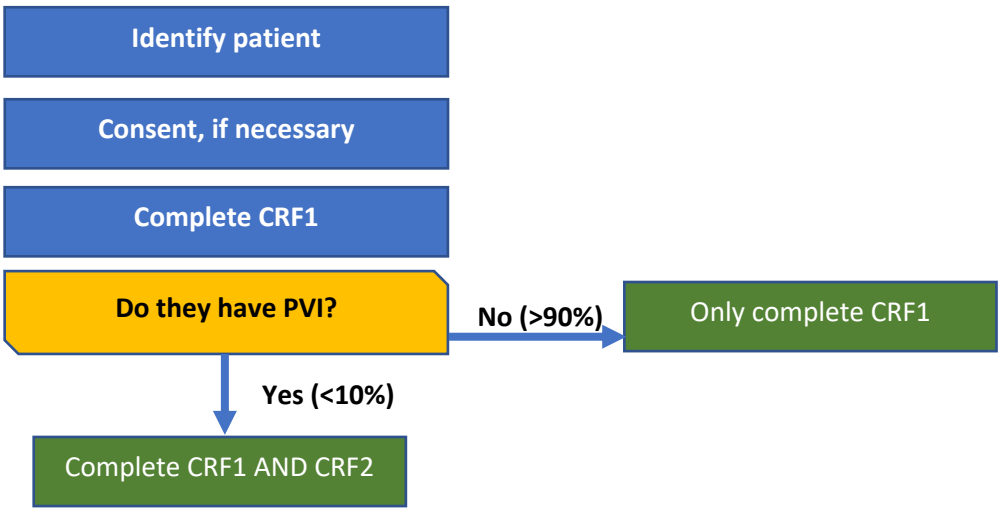
As defined in the protocol there are two cohorts. One cohort is recruited over one week. In this cohort only a minority of patients are anticipated to receive PVI. In the second we recruit only patients receiving PVI. This cohort is recruited over a one-year period. Demonstrated diagrammatically:



Legend:

	Complete CRF: 1	2	3
Patient without postoperative vasopressor infusion	☑		
Patient **with** postoperative vasopressor infusion (PVI)	☑	☑	
Patient **with** postoperative Atrial Fibrillation (AF)	☑		☑
Patient **with** PVI and POAF	☑	☑	☑

<u>During the one week of recruitment</u>



During the one year of recruitment

Identify patient with PVI

Consent, if necessary

Complete CRF1 AND CRF2

CRF 3 should be completed for all patients who develop NEW atrial fibrillation.

To see a video about common mistakes, click on this link: https://we.tl/t-Znisdwgd1X

CRF1

Please use your judgement, any queries should be resolved by the site PI.

(Pages 1-7 of PDF export of eCRF)

"Patient information" section

1.1. Year of birth (mandatory)

It is not necessary for us to know a date of birth, just the year of birth.

1.2./1.3. Weight and Height (mandatory)

Estimated if necessary.

1.4. Clinical Frailty Scale (Rockwood)

This is easiest to do after reading clinical notes and having a brief chat with the patient about their lives. It does not need to be done by a specialist like a geriatrician or occupational therapist.

If it is impossible to find out this information then there is an option for "don't know".

1.5.-1.20. Previous medical history (mandatory)

A series of 15 Yes/No questions about co-morbid conditions. These can be previously confirmed diagnoses or concluded from available data.

Chronic liver disease should include conditions characterised by impairment of liver function, or a significant predisposition to failure of liver function. Cirrhosis of any extent would be a 'Yes'. A single hepatic metastasis would be 'No', whereas a large number of metastases without significant remaining liver would be a 'Yes'.

Chronic respiratory disease includes Chronic Obstructive Pulmonary Disease (COPD), emphysema and chronic bronchitis.

Thyroid dysfunction includes both patients with known hyperthyroidism and patients with hypothyroidism who take thyroxine replacement (i.e. levothyroxine).

Alcohol excess for women is >3 units/day or >21 units/week; and for men >4.5 units/ day or >31.5 units/ week. Where it is unclear whether a patient's alcohol intake is excessive, the decision will be left to the local PI.

Current smoker is someone who has smoked >100 cigarettes/cigars in their lifetime and has smoked within the last 28 days.

History of DVT/PE is any previous history of deep vein thrombosis or pulmonary embolism.

History of bleeding disorder is a known history of haemophilia or a previous major bleed, defined as intracranial bleeding, bleeding requiring hospitalisation, a haemoglobin decrease of more than 2 g/dL, or the need for transfusion secondary to bleeding.

Eight questions about chronic medication use, for seven of them if they are selected then a further question is asked to determine if the medication was taken on the day of surgery or not.

The medication questions are about drug classes. A low dose aspirin (75mg, for example) does not count as an NSAID. Inhaled corticosteroids do not count as long-term steroid use.

Ideally, we'd like to know if the medication was taken on the day of surgery but if it's impossible to know this then it can be indicated.

1.21.-1.26. Haemodynamics

1.16-1.18. Recent blood pressure and heart rate, if available. If not available, leave blank.

1.19.-1.21. Blood pressure and heart rate immediately before anaesthesia, should be present in most cases. In rare circumstances, where there is no information available, this can be left blank.

1.27.-1.29. Laboratory

Creatinine, Albumin and Haemoglobin concentration, if available. Use values closest to time of anaesthesia.

"Surgery" section

2.1.-2.2 Reason for surgery and category of surgical procedure.

Please choose the option that fits best.

We will analyse the data using the reason for surgery and the type of surgery. Please do select a reason or category whenever possible to avoid entering text into a free text box or discrepancy note. This will help to reduce data queries and the speed up data cleaning.

For example, for laparoscopic cholecystectomy being done for episodes of cholecystitis – please select "infection" and "upper GI surgery". Do not select "other" and "other" in order to tell us that it was a laparoscopic cholecystectomy.

2.3. Severity of surgery (minor/intermediate/major).

Please choose the option that fits best.

- Minor: Procedure of less than 30 minutes duration performed in a dedicated operating room which would often involve extremities or body surface or brief diagnostic and therapeutic procedures. Examples include: arthroscopy without intervention, removal of small cutaneous tumour, diagnostic proctology procedures, biopsy or excision biopsy of small lesions, etc
- Intermediate: More prolonged or complex procedure performed in a dedicated operating room that may pose the risk of significant complications or tissue injury. Examples include: laparoscopic cholecystectomy, arthroscopy with intervention, bilateral varicose vein removal, tonsillectomy, inguinal hernia repair, breast lump resection, haemorrhoidectomy, appendicectomy, partial thyroidectomy, cataract surgery, uvuloplasty, minimally invasive repair of vaginal prolapse, vaginal hysterectomy, tendon repair of hand, fixation of mandibular fracture, etc
- Major: Any surgical procedure that requires anaesthesia, performed in a dedicated operating room and is expected to last more than 90 minutes. Examples include: major gut resection, major joint replacement, mastectomy, extensive head and neck tumour resection, abdominal aortic aneurysm repair, major vascular bypass procedure, procedures involving free flap to repair tissue defect, amputation, total thyroidectomy, cystectomy, trans-urethral resection of prostate, resection of liver tumour, carotid endarterectomy, nephrectomy, total abdominal hysterectomy, spinal discectomy, etc

2.4. ASA-PS

'American Society of Anaesthesiology Physical status' use the value attributed by the anaesthetist. We do not include ASA VI in our list since organ donors are not included in SQUEEZE.

ASA grade	
I	Normal healthy patient
II	Patient with mild systemic disease
III	Patient with severe systemic disease
IV	Patient with severe systemic disease that is constant threat to life
V	Moribund patient who is not expected to survive without the operation
VI	Declared brain-dead patient whose organs are being removed for donor purposes

2.5. Urgency

Urgent (includes emergency, expedited, urgent and immediate)
Non-urgent (also known as planned or elective)

"Operative" section

3.1.-3.2. Date and time of anaesthesia induction (mandatory)

3.3.-3.4. Date and time of end of the surgery (mandatory)

Different hospitals use different definitions for start and finish of anaesthesia, therefore we do not provide a single definition – please use what your hospital records routinely. The date is necessary for the unusual occurrences of surgeries that span one day to the next.

3.5. Estimated blood loss (mandatory)

3.6-3.7. Lowest systolic and lowest diastolic (mandatory)

Values taken at the same time, selected based on the systolic. For example:

	09:05	09:10	09:15	09:20	09:25
Systolic (SBP)	120	100	90	85	92
Diastolic (DBP)	80	70	60	65	70

The lowest SBP is 85, at this time the diastolic is 65 – so these are the values we want. We do not want SBP 85 and DBP of 60 as these values were not taken at the same time.

3.8. Anaesthesia

More than one type can be selected. TIVA refers to total intravenous anaesthesia but this is not restricted to use of specific pumps or dosing systems.

We are specifically interested in maintenance of anaesthesia not induction. For example, if the induction of anaesthesia is volatile and then TIVA is used for maintenance – please just select TIVA. If induction is with IV and then volatile is used for maintenance – please just select volatile.

Details about the epidural including level of insertion, the height of the block and the drugs given are not required. Equally, details about any spinal are not required.

3.9. Airway

Please check the most appropriate one. More than one can be selected.

3.10. Arterial line

Is there a cannula/catheter in a peripheral artery for the purposes of monitoring?

3.11. Central Venous Line

Is there a cannula/catheter in a central vein? It may be newly sited or already present for monitoring or therapy.

Please exclude peripherally inserted central cannulae (PICC), midlines or long term central venous lines for dialysis, parenteral nutrition or chemotherapy unless they are being used perioperatively for vasopressors.

3.12.1-2. Intra-operative drugs via infusion or bolus

This is a list of vasoactive medications and/or anti-arrhythmic medications that the patient receives during surgery. The dosing is not recorded. Please check all that apply.

Please note that this only relates to drugs given INTRA-operatively.

3.13. Was the patient receiving a vasopressor infusion prior to anaesthesia?

We anticipate that this is rare occurrence.

3.14. Fluids and blood products received during surgery

For each of six types of fluids, please enter the volume in millilitres. If the records only indicate how many units of a product, please estimate the volumes based on your local experience.

"Post-operative" section

4. Questions about post-operative vasopressors:

1. Yes/No question about **post-operative** receipt of **enteral** vasopressors.
2. Yes/No question about **post-operative** receipt of **boluses** of vasopressors (different to earlier question about intra-operative).
3. Yes/No question about **post-operative** receipt of **infusions** of vasopressors (different to earlier question about intra-operative).
4. Yes/No question about if a post-operative infusion of vasopressors continued for more than 1 hour after the end of surgery.
5. Yes/No question about if a post-operative infusion of vasopressors started within 24 hours of the end of surgery.

These questions are to determine if the patient in question fulfils the criteria for PVI, which would mean that additional questions (CRF2) need to be completed. From the protocol:

> **Definition**: Postoperative Vasopressor Infusion (PVI) is defined, for the purposes of this study, as the continuous intravenous infusion of a drug with a predominant vasoconstrictor effect (vasopressor). Therefore, repeated dosing of intravenous boluses is excluded, and infusion of a drug that is predominantly a positive inotrope (without concurrent vasopressor) is excluded. Additionally, we are not interested in vasopressor infusions that are used intra-operatively to counter the effect of general anaesthesia (or regional anaesthesia) and because this effect can take time to resolve, any infusion of vasopressor in the first hour following surgery is excluded – unless it continues after one hour following surgery. Infusions of vasopressor that are started more than 24 hours after the end of surgery is also excluded from this definition. Infusions of vasopressor that start before surgery will only be included if they also meet the above criteria.

"Outcomes" section

5.1. Intrahospital, post-operative complications

<u>During the patient's 30 days following the date of surgery:</u>

- Ventilation: No, NIV, IMV.

If the patient received invasive mechanical ventilation (IMV, via endotracheal tube or tracheostomy) that started after the end of surgery, then please select this. If the patient *continued to receive* invasive mechanical ventilation that *started prior* to surgery, then please do NOT select this.

On the day of surgery there will often have been invasive mechanical ventilation and if that is completed (i.e. the patient was extubated) within 4 hours of the end of surgery then this would not count as a day of IMV. If IMV continues for more than 4 hours after the end of surgery then this should count as a day of postoperative IMV.

If the patient received non-invasive ventilation (NIV, including BiPAP and CPAP) via a facemask (any duration) then please select this. For the purposes of this study high flow oxygen delivered via nasal cannulae is not considered NIV.

If neither IMV nor NIV are provided then please select No.

5.2 Acute Myocardial Infarction: No/Yes

If the clinician believes that the patient has an acute Myocardial Infarction then please select Yes. If you are not sure (e.g. there is a troponin rise) then please ask your principal investigator to adjudicate.

5.3. New onset Atrial Fibrillation: No/Yes

If the clinicians believe that the patient has atrial fibrillation that was not present prior to the operation (i.e. no history of chronic or paroxysmal AF) and is more than briefly present, then please select yes.

5.4. New onset of dysrhythmia other than AF: No/Yes

If the clinicians believe that patient has any new dysrhythmia (includes SVT, VF and VT) that was not present prior to the operation and is more than briefly present, then please select yes.

5.5. Highest creatinine within the first week.

This will allow us to determine if the patient met criteria for acute kidney injury (AKI). Leave blank if you do not have measured creatinine postoperatively.

5.6. Renal replacement therapy: No/Yes.

If the patient received at least one episode of renal replacement therapy (including haemodialysis, haemofiltration, haemodiafiltration, peritoneal dialysis) and this isn't a usual occurrence for them (i.e. they don't usually require any form of renal replacement therapy, RRT) then please select Yes. It is not important if they received the RRT intermittently or continuously.

If they have chronic RRT or did not receive any RRT then please select No.

5.7. Parenteral nutrition: No/Yes.

If the patient received at least one bag of parenteral nutrition (PN) and this isn't a usual occurrence for them (i.e. they don't have chronic intestinal failure) then please select Yes. If they have chronic intestinal failure or did not receive any PN then please select No.

Parenteral nutrition does not include simple dextrose infusions.

5.8. Antibiotics for a newly diagnosed infection:

If the clinicians believe that patient has an infection and they have started some antibiotics then please select yes. A further selection will appear and please select the most appropriate of: skin (or soft tissue), respiratory, urinary, abdominal, lines, other. During their postoperative recovery they may have multiple infections – please select all that apply.

5.9. Severity of surgical complication

This is the Accordion classification of surgical complication. Choose one of the following:

1. None
2. Mild complication: Requires only minor invasive procedures that can be done at the bedside such as insertion of intravenous lines, urinary catheters, and nasogastric tubes, and drainage of wound infections. Physiotherapy and the following drugs are allowed-antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy.
3. Moderate complication: Requires pharmacologic treatment with drugs other than such allowed for minor complications, for instance antibiotics. Blood transfusions and total parenteral nutrition are also included.
4. Severe complication: All complications requiring endoscopic or interventional radiologic procedures or re-operation as well as complications resulting in failure of one or more organ systems.
5. Death

5.10. Survival to hospital discharge: No/Yes. (mandatory)

If you answer Yes, then "Date of hospital discharge"

If you answer No, then "Date of death"

5.11. Stayed an inpatient for more than 30 days: No/Yes. (mandatory)

Please monitor the patient's status until day 30 or hospital discharge. If they are alive at day 30 but die on day 31 (or later) then, for the purposes of this CRF and study, their 30-day mortality status is alive.

For most patients during the recruitment of cohort A this is all that will be required.

For those patients in cohort who have PVI, and all those in cohort B (who by definition have PVI), they also need CRF2 completed about them.

CRF2

PVI

6.1. Did this patient have an infusion of vasopressors either started or continued at least 1hr after surgery? (Mandatory)

This question aims to double-check that this form is being completed only in appropriate patients.

6.2-6.5. Characterising the patient with PVI (Mandatory)

These three questions that aim to further characterise the patient with PVI, at one after the completion of surgery:

- Are they receiving a continuous infusion of neuraxial anaesthesia/analgesia i.e. epidural infusion: Yes/No.
- Are they receiving a continuous infusion of sedative drug i.e. propofol or midazolam or similar: Yes/No.
- Does the patient have an airway in place (endotracheal tube, tracheostomy or supraglottic airway): Yes/No.

6.6. HOW was it determined that the patient should be receiving PVI?

The investigator needs to determine how the clinical team decided to use a PVI. There is a choice of two options:

Either “Already receiving a vasopressor infusion and attempts to lower the infusion rate produced unacceptable hypotension”

Or “It was decided that the patient would no longer benefit from further attempts to increase the cardiac output through administration of IV fluids and the blood pressure was unacceptably low.”

If the second choice is selected that the investigator must choose an option that helps us understand why this was decided, one of the following options must be chosen:

- Clinical assessment alone (vital signs-examination-lab results)
- Clinical assessment AND a measurement of preload responsiveness using cardiac output monitoring (or some direct surrogate of)
- Clinical assessment AND a measurement of preload responsiveness using echocardiography
- Clinical assessment AND a previously established maximum for IV fluid administration has been met i.e. 2L or 20ml/kg etc...
- Other
- Unknown

It may be difficult to determine this solely from the documentation and we would like to avoid too many patients where “other” or “unknown” is selected as it’s not useful information. Please talk to your clinicians and politely enquire which of the options is most suitable.

"MAPS and vasopressors" section

7.1 SOFA score

This is the sequential organ failure score. It is widely used in critical care and can simply be determined. There is a link to an online calculator.

We are interested in the *highest* score in the first 24 hours after surgery.

Calculating the SOFA score

Healthy person scores 0

Maximally sick person scores 24

Respiratory

If an Arterial Blood Gas is available then please use the values taken at the same time for PaO2 (partial pressure of oxygen in arterial blood) and FiO2 (fraction of inspired oxygen 0.21 = 21% = air)

PaO_2/FiO_2 (kPa)	SOFA score
≥ 53.3	0
< 53.3	+1
< 40	+2
< 26.7 **and** mechanically ventilated	+3
< 13.3 **and** mechanically ventilated	+4

If Arterial Blood gases have NOT been done in the 6 hours prior to enrolment, then use the values taken at the same time for SpO2 (Saturations of oxygen in arterial blood, from pulse oximetry) and FiO2 (fraction of inspired oxygen 0.21 = 21% = air)

SpO_2/FiO_2	SOFA score
≥ 512	0
< 512	+1
< 357	+2
< 214	+3
< 89	+4

Reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3776410/

Nervous system

Glasgow coma scale	SOFA score
15	0
13–14 (delirium)	+1
10–12 (obtunded)	+2
6–9 (semi-comatose)	+3
< 6 (comatose)	+4

Cardiovascular

If MAP hasn't been recorded or charted by Systolic and Diastolic have been, then calculate the MAP using this formula: MAP = 1/3 (SBP – DBP) + DBP

norepinephrine = noradrenaline

Mean arterial pressure OR administration of vasopressors required	SOFA score
MAP ≥ 70 mmHg	0
MAP < 70 mmHg	+1
dopamine ≤ 5 µg/kg/min or dobutamine (any dose)	+2
dopamine > 5 µg/kg/min OR epinephrine ≤ 0.1 µg/kg/min OR norepinephrine ≤ 0.1 µg/kg/min	+3
dopamine > 15 µg/kg/min OR epinephrine > 0.1 µg/kg/min OR norepinephrine > 0.1 µg/kg/min	+4

Liver

Bilirubin µmol/L	SOFA score
< 20, or not measured	0
20-32	+1
33-101	+2
102-204	+3
> 204	+4

Coagulation

Platelets ×10³/µl	SOFA score
≥ 150, or not measured	0
< 150	+1
< 100	+2
< 50	+3
< 20	+4

Renal

Creatinine µmol/L (or urine output)	SOFA score
< 110	0
110-170	+1
171-299	+2
300-440 or < 500 ml/d	+3
> 440 or < 200 ml/d	+4

7.2 -7.8 MAP target

Typically, in patients receiving PVI there is a target blood pressure and most commonly it is a target for the mean arterial pressure (MAP).

We are interested in the MAP target for each of day 0, 1, 2, 3, 4, 5 and 6.

If it is unknown then this can be indicated.

7.9-7.24 Blood pressure

For each day we would ask you to identify the highest and the lowest paired BP (systolic and diastolic) during that calendar day. Please leave blank if you have no available data.

7.25-7.34 Vasoactive drug infusions = vasopressors and/or inotropes

For each day we would ask you to indicate the maximum dose of vasoactive drugs the patient is receiving as an infusion.

7.35-7.39 Outcomes

In the first 30 days following surgery, how many days (in total, not necessarily serially) was there:

1. Receipt of ventilation (IMV or NIV)
2. Vasopressor infusion
3. Parenteral nutrition
4. Renal replacement therapy
5. Time spent on the ICU/HDU/PACU.

The definitions for these are unchanged from earlier.

7.40 COVID questions

Testing for the presence of virus, **not** antibodies to the virus.

The perioperative period is considered to be one week before surgery and anytime during the hospital stay after.

CRF 3

This CRF is for all patients who develop NEW perioperative atrial fibrillation (AF).

Patients who develop AF will be followed up for 48 hours from the onset of AF.

8.1-8.9. Within the first 4 hours of the onset of new AF

Please indicate if the heart rate was documented as being over 110 bpm at any point during the first four hours following the onset of AF.

There are seven Yes/No options for treatments administered to treat the new atrial fibrillation within the first four hours of its onset.

Calcium channel blockers/antagonists that may be used to treat AF include diltiazem or verapamil.

If there is uncertainty as to whether administration of fluids counts as a fluid bolus, this should be discussed with the local PI.

8.10. Between 4- and 24-hours following onset of new AF

Select any additional medications that were given to treat the atrial fibrillation between 4- and 24-hours after its onset.

Calcium channel blockers/antagonists that may be used to treat AF include diltiazem or verapamil.

8.11-8.21. Between 24- and 48-hours after the onset of new AF

Indicate if any blood results during the period 24-48hrs after onset of new atrial fibrillation fulfil the criteria listed.

We would like you to indicate which anticoagulation the patient received within the first 48hrs following onset of new atrial fibrillation. For example, a patient might receive both prophylactic low molecular weight heparin (LMWH) and a novel oral anticoagulation (NOAC) or direct oral anticoagulant (DOAC) within the 48-hour period following onset of AF.

If an ‘intermediate’ dose of LMWH is used, this should be considered a ‘prophylactic dose LMWH’.

NOAC/DOAC drugs may include but are not limited to rivaroxaban, dabigatran, apixaban and edoxaban.

8.22-8.24. At 48-hours following onset of new AF

Data for these three questions about the rhythm, rate and ongoing antiarrhythmic therapy can be taken from 48 to 72 hours after the onset of new atrial fibrillation.

Calcium channel blockers/antagonists that may be used to treat atrial fibrillation include diltiazem or verapamil.