**Study Title**

The 2nd Sprint National Anaesthesia Project (SNAP-2): Epidemiology of Critical Care provision after Surgery

Short title / Acronym:

EPICCS

Chief Investigator

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Protocol details

Version number: 1.6

Date: 02 February 2017

DECLARATIONS

The undersigned confirm that the following protocol has been agreed and accepted and that the investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the Research Governance Framework 2005 (as amended thereafter), the Trust Data & Information policy, Sponsor and other relevant SOPs and applicable Trust policies and legal frameworks.

I (investigator) agree to ensure that the confidential information contained in this document will not be used for any other purposes other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I (investigator) also confirm that an honest accurate and transparent account of the study will be given; and that any deviations from the study as planned in this protocol will be explained and reported accordingly.

**Chief Investigator:**

**Signature:..................................................................................... Date....../....../.......**

**Print Name(in full):.......................................................................**

**Position:.......................................................................................**

**On behalf of the Study Sponsor:**

**Signature:..................................................................................... Date....../....../.......**

**Print Name(in full):.......................................................................**

**Position:.......................................................................................**

Study summary

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| **Identifiers** |  |
| IRAS Number | **154486** |
| REC Reference No | **16/SC/0349** |
| Sponsor Reference No | **15/0671** |
| Other research reference number(s) (if applicable) |  |
| NIHR CPMS ID | **31913** |
| Full (Scientific) title | **The Second UK Sprint National Anaesthesia Project: Epidemiology of Critical Care provision after Surgery (SNAP-2: EpiCCS)** |
| Health condition(s) or problem(s) studied | **Anaesthesia, Perioperative Medicine and Critical Care** |
| Study Type i.e. Cohort etc | **Prospective Observational Cohort Study** |
| Target sample size | **8,177** |
|  |  |
| **STUDY TIMELINES** |  |
| Study Duration/length | **10 years, 2 months** |
| Expected Start Date | **March 2017** |
| End of Study definition and anticipated date | **February 2027** following completion of 10-year mortality follow-up obtained via data-linkage with the Health and Social Care Information Centre / Office of National Statistics mortality database. |
| Key Study milestones  | **26 February – 30 April 2016**: Submission for Sponsorship Review, application for Regulatory Reviews and Health Research Authority assessment**May – 1 March 2016**: Health Research Authority approval and local R&D approvals for individual hospitals and study sites**17 – 24 January 2017:** pilot study in two hospitals**21 – 27 March 2017**: Cohort recruitment week and study commencing**28 March – 3 April 2017**: 7-day Post-Operative Morbidity Survey follow-up completion across all sites**3 May 2017 – 1 July 2017**: 30-day mortality data linkage with HSCIC/ONS mortality database **3 July – 1 September 2017**: 90-day mortality data linkage with HSCIC/ONS mortality database**27 March 2018 – 3 April 2018**: 1-year mortality data linkage with HSCIC/ONS mortality database**27 March 2027 – 3 April 2027**: 10-year mortality data linkage with HSCIC/ONS mortality database and study completion |
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| **STORAGE of SAMPLES** **(if applicable)** |  |
| Data collected / Storage | Data custodian: **Sharon Drake**, Director of Research and Education, Royal College of Anaesthetists (sdrake@rcoa.ac.uk) |
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**KEY ROLES AND RESPONSIBILITIES**

**SPONSOR:** The sponsor is responsible for ensuring before a study begins that arrangements are in place for the research team to access resources and support to deliver the research as proposed and allocate responsibilities for the management, monitoring and reporting of the research. The Sponsor also has to be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds, and approve any modifications to the design.

**FUNDER:** The funder is the entity that will provide the funds (financial support) for the conduction of the study. Funders are expected to provide assistance to any enquiry, audit or investigation related to the funded work.

**CHIEF INVESTIGATOR (CI):** The person who takes overall responsibility for the design, conduct and reporting of a study. If the study involves researchers at more than once site, the CI takes on the primary responsibility whether or not he/she is an investigator at any particular site.

The CI role is to complete and to ensure that all relevant regulatory approvals are in place before the study begins. Ensure arrangements are in place for good study conduct, robust monitoring and reporting, including prompt reporting of incidents, this includes putting in place adequate training for study staff to conduct the study as per the protocol and relevant standards.

The Chief Investigator is responsible for submission of annual reports as required. The Chief Investigator will notify the RE of the end of the study, including the reasons for the premature termination. Within one year after the end of study, the Chief Investigator will submit a final report with the results, including any publications/abstracts to the REC.

**PRINCIPAL INVESTIGATOR (PI):** Individually or as leader of the researchers at a site; ensuring that the study is conducted as per the approved study protocol, and report/notify the relevant parties – this includes the CI of any breaches or incidents related to the study.

**KEY WORDS**

Anaesthesia, surgery, critical care, epidemiology, perioperative medicine

**LIST OF ABBREVIATIONS**

|  |  |
| --- | --- |
| AE | Adverse Event |
| AR | Adverse Reaction |
| CCU | Critical Care Unit |
| CI | Chief Investigator |
| CRF | Case Report Form |
| CRO | Contract Research Organisation |
| DMC | Data Monitoring Committee |
| EPICCS | Epidemiology of Critical Care after Surgery study |
| GAfREC | Governance Arrangement for NHS Research Ethics |
| HSCIC | Health & Social Care Information Centre |
| HSRC | Health Services Research Centre |
| IB | Investigator Brochure |
| ICF | Informed Consent Form |
| NIAA | National Institute for Academic Anaesthesia |
| NIHR | National Institute for Health Research |
| PI | Principal Investigator |
| PIS | Participant Information Sheet |
| POMS | Post Operative Morbidity Survey |
| QuARCS | Quality Audit and Research Coordinators |
| RCoA | Royal College of Anaesthetists |
| REC | Research Ethics committee |
| SAR | Serious Adverse Reaction |
| SAE | Serious Adverse Event |
| SDV | Source Data Verification |
| SOP | Standard Operating Procedure |
| SNAP | Sprint National Anaesthesia Project |
| SSI | Site Specific Information |
| TMF | Trial Master File |
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# 1. Summary

EpiCCS will describe the epidemiology of perioperative risk and outcome, and critical care referral and admission after inpatient surgery in the UK. A secondary aim is to estimate the clinical effectiveness of planned postoperative critical care admission as an intervention to reduce postoperative morbidity.

EpiCCS will be a prospective observational cohort study.

Data will be collected by perioperative anaesthetists on all patients undergoing inpatient surgery in participating UK hospitals for one week. Postoperative morbidity will be recorded for patients who remain in hospital on Day 7 after surgery. Mortality data will be collected through linkage facilitated by the HSCIC. The dataset will also include patient risk factors, and questions about clinical decision-making and resource availability related to critical care referral and admission.

Additionally, an organizational questionnaire for each hospital will be completed to describe structure and process in those institutions, the number and reasons for any cancellations of surgery during the study, and critical care unit occupancy at regular time-intervals throughout the one-week data collection period.

The epidemiology of perioperative risk stratification, postoperative care and patient outcome will be described. Multivariable regression, instrumental variable and propensity score matched analyses will be conducted to ascertain the clinical effectiveness of postoperative critical care admission in reducing adverse outcomes after inpatient surgery.

# 2. Background and Rationale

### 2.1 Background

Surgical morbidity and mortality is a well-described public health issue. An estimated 313 million operations take place world-wide each year. [1] In the UK, inpatient surgical mortality has been estimated to be as high as 3.6% in one study; [2] particularly high risk procedures such as emergency laparotomy have a population mortality of between 11 and 15%. [3] [4] Morbidity or complications after surgery occur up to ten times more frequently than short-term mortality and are associated with reduced long-term survival, even after accounting for known preoperative patient-related risk factors. [5] The potential to improve the quality of surgical healthcare is shown by studies demonstrating variation in postoperative outcomes between institutions and countries. [2] [4]

Planned postoperative critical care admission is recommended for the "high risk surgical patient". [6] [7] Cohort studies reveal that despite this, the majority of patients undergoing non-cardiac, non-neurological surgery who die before hospital discharge do not have planned critical care admission after surgery. [2] [3] This implies that a substantial proportion of high risk patients are not admitted to postoperative critical care and we do not know the reasons for the failure to adhere to our national standards.

### 2.2 Justification

EpiCCS will explore the referral patterns and resource limitations which may be responsible for patients not being admitted to critical care, despite being high risk according to national guidelines. In particular, we will explore these areas:

1. *Quality and accuracy of risk stratification*

Recent data have shown that the majority of surgical patients who die before hospital discharge do not fall into an easily defined high-risk population based on solely on surgical urgency or magnitude. [2] The highest proportions of deaths occur in patients having emergency surgery; however, as a result of the much larger volume of elective surgery, the absolute numbers of patients who die postoperatively may be greatest in these categories. This observation, known as the “Prevention Paradox”, is well-described throughout medicine. [8, 9]

Thus, for the surgical population in its entirety, we propose that individualized risk assessment to help determine the optimal postoperative destination and management plan may improve outcome. EpiCCS will help develop an understanding of if and how clinicians risk stratify patients prior to surgery and how accurate their methods are.

1. *Critical care bed capacity*

We do not know whether there is capacity to meet recommendations that high-risk patients should receive critical care postoperatively. The UK has a much smaller proportion of critical care beds per hospital bed than other high-income nations; [10] however, clinical experience tells us that patient may also be admitted postoperatively to units which may not be classed as critical care beds according to the standards set by the Faculty of Intensive Care Medicine. [11] EpiCCS will investigate the reasons for failing to admit high-risk patients to critical care, including lack of capacity.

1. *Clinical uncertainty that critical care admission would be of benefit*

The hypothesis that critical care benefits high-risk patients has not been tested in a major multi-centre randomised controlled trial. Despite this, national recommendations state that critical care admission should be a standard of care for high-risk patients (>5% predicted mortality) [7] Therefore, it is possible that some clinicians feel justified in not sending their patients to CCU postoperatively (because of equipoise) while others may believe that it would be unethical not to do so (because of guidelines).

# 3. Aims and objectives

### 3.1 Research Questions (RQ)

1. How do clinicians determine the risk of postoperative mortality in clinical practice?
2. Do previously validated risk stratification tools accurately predict postoperative mortality?
3. On what basis do clinicians refer patients for planned postoperative critical care?
4. What factors influence whether patients actually receive planned postoperative critical care?
5. Does immediate critical care admission reduce postoperative morbidity and mortality?

### 3.2 Objectives

1. To collect data on all patients undergoing inpatient surgery for one week in UK NHS hospitals (RQ1,2,4,5)
2. To measure and analyse patient-level estimates of perioperative risk using previously validated risk prediction tools to determine their accuracy (discrimination and calibration) in a comprehensive national sample (RQ2,3)
3. To use three different analytic techniques (regression, instrumental variable and propensity score matched analyses) to measure the relationship between patient risk factors, postoperative critical care admission and patient outcomes (morbidity and mortality) (RQ5)
4. To survey anaesthetists and surgeons on their attitudes and behaviours regarding risk prediction and postoperative critical care admission (RQ3)

# 4. Study design

EpiCCS will be a one-week, prospective observational cohort study of patients and anaesthetists in NHS hospitals

# 5. Study schedule

### 5.1 Enrolment process

Main EPICCS patient study

All patients undergoing inpatient surgery (elective or emergency) during the study week will be enrolled onto the main EPICCS study.

Clinician perception sub-study

All anaesthetists and surgeons who undertake perioperative care for inpatient surgery during the study period will be invited to participate, and a participation information leaflet provided. If they decline, they will be asked to provide the reason why. If they agree and complete the questionnaire, this will be taken as evidence of implied consent.

### 5.2 Follow-up

Main EPICCS study

Inpatient follow up will be completed on discharge from hospital or death. Follow-up via the Office of National Statistics mortality tracking system will continue for 10 years.

Clinician perception sub-study

No follow-up beyond the initial questionnaire will be required

### 5.3 Participant withdrawal

Main EPICCS study

Although this will be a non-consenting study, all participating hospitals will be provided with posters and patient information leaflets explaining that the study is ongoing and providing information on how to withdraw if they would like to (see appendix 1). Patient information leaflets will be supplied preoperatively to each patient undergoing surgery that week. Posters will be displayed prominently in perioperative hospital areas.

We have included a 1% drop-out rate in our sample size calculation in order to account for the risk that data linkage with HSCIC mortality data registry may not be possible (because of incorrect patient identifiable data being entered).

Clinician perception sub-study

If a clinician wishes to withdraw their consent from participation in the study, they will need to contact the local principle investigator who will contact the study team and the relevant data will be removed from analysis. We do not expect this to be a problem.

### 5.4 Study closure

Study recruitment will end after one week (168 hours) of recruitment has been completed in all participating sites.

### 5.5 Study management

The project team is chaired by the Chief Investigator and is meeting monthly to deliver the day-to-day organization of the study. A study steering committee with an independent chair (Professor Mike Grocott, University of Southampton) is meeting quarter annually and is advising on study design and conduct; this consists of multi-disciplinary, professional and lay representation.

# Consent

This study will have two types of participant: patients recruited to the EpiCCS patient study and the clinicians’ perceptions sub-study. The approach to consent for each type of participant is listed below.

Main EpiCCS patient study: Section 251 exemption to be sought

To be able to collect patient data without consent, we will apply for Section 251 exemption. The reason for a non-consenting approach is an attempt to avoid sampling bias. It is likely that patients who are of higher perioperative risk will be unable or unwilling to provide consent – we have data to support this assertion from a study we conducted in 2014 [12] which followed a similar methodology of trying to achieve participation from 100% of eligible UK hospitals for a short-term study. There are also data from other settings which support the notion that the requirement for informed consent can introduce bias into studies where the target population may be critically unwell, and therefore jeopardise the results. [13] This therefore poses the risk that we may not have data on exactly the group of patients who may most benefit from critical care admission, hence introducing bias into our analyses.

Clinician perception sub-study: implied consent approach

We propose an implied consent approach, with completion of the questionnaire as evidence of consent. The implied consent approach was used for collection of data in the SNAP-1 study undertaken by this project team in 2014. [12]

Every perioperative anaesthetist and surgeon during the study week will be asked to complete a questionnaire which explores their approach to risk stratification and postoperative care (e.g. which risk prediction measures used, if any; what they estimate to be the risk of postoperative death or complications, where they proposed the patient should be cared for postoperatively). Given that there are national guidelines regarding these questions, we are keen to provide reassurance to perioperative anaesthetists and surgeons that their responses will be used in confidence, without risk of litigation or reprisal. We will provide an explanation of this on the front page of the questionnaire, including the fact that their information will be non-identifiable at the analysis stage. If anaesthetists or surgeons choose not to answer the questionnaire, then they will be asked to provide a reason why, for the purposes of analysis.

# 7. Eligibility criteria

### 7.1 Hospital level

All NHS hospitals which undertake inpatient surgery will be eligible to take part. The main EPICCS study will be piloted in two hospitals prior to the main study.

### 7.2 Patient level

Inclusion criteria:

Adult (>=18 years) patients undergoing surgery or other interventions who are expected to require overnight stay in hospital which require the support of an anaesthetist. These would include all procedures taking place in an operating theatre, radiology suite, endoscopy suite or catheter laboratory for which inpatient (overnight) stay is planned, including both planned and emergency/urgent surgery of all types, Caesarean section, surgery for complications of childbirth, endoscopy and interventional radiology procedures.

Exclusion criteria:

Patients who indicate they do not want to participate in the study; Ambulatory surgery; children (<18 years); non-surgical obstetrics; ASA-PS grade VI; non-interventional diagnostic imaging (e.g. CT or MRI scanning without interventions); emergency department or critical care interventions requiring anaesthesia or sedation but no interventional procedure

# 8. Recruitment

#### Hospital recruitment

Hospitals will be recruited using the NIAA HSRC’s Quality Audit and Research Coordinator (QuARC) network, aiming for 100% coverage across the UK.

#### Participant recruitment

There will be two sets of participants in this study: hospital clinicians (perioperative anaesthetists and surgeons) and patients undergoing inpatient surgery during our one-week study recruitment window. All patients who meet our inclusion and exclusion criteria will be enrolled. Patients in the main EPICCS study will not be approached for consent (see below).

Main EpiCCS patient study

All patients who meet our inclusion criteria in participating hospitals will be included. We have received approval from the Confidentiality Advisory Group (CAG) for a non-consenting approach to patient data collection. This is important because of the risk of selection bias if patients who are too unwell to consent are excluded from our study, especially as it is possible that the very unwell patients are those who are most likely to benefit from critical care admission after surgery. All patients will be given the opportunity to opt out of the study. Perioperative anaesthetists will complete a CRF for every patients undergoing surgery during the study week, unless the patient has indicated that they would like to opt out of the study.

As there is the possibility particularly in high-risk or emergency cases, that perioperative anaesthetists may be unable to complete the CRF at the time of surgery, local investigators will compare the patient CRFs completed against local records of patients undergoing surgery on a daily basis to ensure that all eligible patients are included. If a patient is found not to have a form completed, local investigators will be responsible for completing the patient data retrospectively, through accessing the patient notes / hospital results system. The sections on risk stratification will be left blank (see Appendix 1). All patients who opt out will be recorded in a site log so that local investigators ensure that their data is not subsequently collected. Patients who have their surgical procedures cancelled during the study will not be enrolled onto the study, but reasons for cancellations of surgery will be collected in aggregate by local investigators.

Clinician perception sub-study

All anaesthetists and surgeons who are delivering care for patients who are eligible by our study criteria, will be asked to complete a single questionnaire about their practice related to risk stratification and postoperative critical care referral. Implied consent will be taken by completion of this questionnaire.

# 9. Statistical methods

### 9.1 Analysis plan

The descriptive epidemiology of decision making, referral and admission to critical care after surgery will be reported. Logistic regression will determine independent predictors for critical care referral and admission, including both patient risk factors and structure / process level indicators with attention being paid to the hierarchical structure of the data (patients nested within hospitals). The discrimination and calibration of four previously validated risk stratification tools (the ASA-PS, the P-POSSUM score, the Surgical Risk Scale and the Surgical Outcome Risk Tool) [14, 15] will be compared using receiver-operator-characteristic curves and using the Hosmer-Lemeshow Chi-squared statistic. The accuracy of these tools will be compared with clinician estimates of postoperative mortality.

### 9.2 Analysis to determine clinical effectiveness of postoperative critical care admission for high-risk surgical patients

We propose to conduct both propensity score matched and instrumental variable analyses to answer the question: Does immediate postoperative critical care admission improve outcome after surgery?

Our primary outcome will be Day 7 inpatient morbidity as measured by the Post Operative Morbidity Survey (POMS).

Secondary outcome measures will be mortality at 30 days, 90 days and 1 year; longer term survival (up to 10 years); cost analysis of planned critical care vs. planned ward care; length of hospital stay.

##### Propensity score matched analysis

Propensity score matching is a well-established method for taking into account selection bias in observational settings. Our dataset draws on the existing literature [14, 15] and previous propensity score matched studies of surgical outcome to include a comprehensive list of variables which should be considered in analyses.

##### Instrumental variable analysis

Evaluating the effect of direct admission to critical care following surgery in an observational study is difficult because of indication bias. The most unwell patients are most likely to be admitted, and we rely on risk adjustment to compare the outcome of these patients to those not admitted directly. Such comparisons assume that the measurements used to adjust for risk, completely capture all the factors that go into the clinical assessment that was used to allocate treatment. This is equivalent to saying that there is no added value in the ‘end of the bed’ clinical assessment beyond that captured in the preoperative risk score. Unsurprisingly, most clinicians would dispute this.

One solution is to substitute the link between allocation by indication with allocation by randomisation in a controlled trial. Where randomisation is not possible, Instrumental Variable (IV) analysis is an alternative technique widely used in the econometric and social sciences literature. IV analysis is a method of estimating the effect of a natural randomisation procedure. An example of this is the effect of class size on educational achievement. In Israeli schools, class size is capped at 40 students, beyond which the class is split. Comparisons are then made between schools with an intake of 40 students versus those with an intake of 41 students who must hire a second teacher. One assumes that the number of students born in a particular year in a particular school district should not have an effect on educational achievement other than through class size.

There is evidence that because critical care units run at near capacity, that occupancy affects access. This is unlikely to be an issue for the most unwell who would be admitted directly regardless. However, for others, then IV analysis would argue that the number of beds occupied on the CCU at the time of surgery should not affect the outcome of that surgery except through altering the chances of being directly admitted to critical care. This is of particular relevance in the UK where critical care to hospital bed ratios are low.

Therefore, information will be collected on occupancy of the critical care unit at the time of surgery. Both physical occupancy, and the available staffing will be considered. The first stage model will examine how occupancy affects the decision making by clinicians, and the delivery of direct admission to critical care. Attention will be paid to the structural factors that affect this, in particular, the size of critical care units. Two IV models will be investigated.

1. A linear IV model, which ignores the non-linearity of the dependent variable (mortality), will be used to estimate the Local Average Treatment Effect (LATE). This is the effect of direct admission on morbidity for the sub-population of patients that would have been treated if an ICU bed been available.
2. A bivariate probit model, in which mortality is represented as a latent linear variable, will be used to estimate the effect measure on the complete population of eligible patients.

##### Sample size calculation

Our sample size calculation is based on the EpiCCS patient study.

There are no realistic estimates available to guide us on the potential effect which critical care admission may have on reducing postoperative morbidity. This issue is further complicated by the likelihood that critical care admission may have a different effect on postoperative outcome depending on the patient and surgical risk factors, and that there is unlikely to be a linear relationship between risk and benefit.

We have used previous studies to guide the allocation proportions and estimates of baseline morbidity. Based on a morbidity rate of 30% on Day 7 in patients admitted postoperatively to the general ward and a 15% relative risk reduction for patients electively admitted to critical care, an allocation ratio of 1:10 (ICU: ward care), R-squared (multiple correlation between the exposure and other covariates) =10 % and a dropout rate of 1%, the minimum sample size (n) required is 8,177. In one week, based on data from the SNAP-1 study, we estimate that we should be able to recruit at least 12,000 patients therefore comfortably achieving our sample size.

# 10. Patient and public involvement (PPI)

We have had patient and public involvement from inception of this study. Our patient representative is Mr. Richard Shawyer, who has had several major surgical procedures and has also been a patient representative on a previous NIHR funded study sponsored by UCLH. He has commented on the study design, was a co-applicant on the grant, is a member of the study steering committee and will provide input to all aspects of the study including dissemination. We have had further review of the patient information sheets by Ms Elspeth Evans, representing the Royal College of Anaesthetists’ Lay Representation Committee.

# 11. Funding

The study funding has been reviewed by the UCL/UCLH Research Office, and deemed sufficient to cover the requirements of the study. NHS costs will be supported via UCLH and the Local Clinical Research Network.

The research costs for the study have been supported by the National Institute for Academic Anaesthesia (AAGBI Project grant), the Royal College of Anaesthetists and the UCLH NIHR Biomedical Research Centre.

Insurance for all participating sites will be provided through NHS Indemnity.

# 12. Data handling and management

### 12.1 Patient level data

The CRFs are included in Appendices 1 and 2.

Data will be collected on all patients who meet inclusion criteria in participating hospitals for one week. Each hospital taking part will have nominated staff who will be responsible for data collection and postoperative follow up.

Perioperative anaesthetists will be asked to complete a case report form (CRF) for each patient they anaesthetise. The information which the anaesthetist will be asked to complete, will comprise questions regarding patient risk factors (e.g. age, type of surgery, type of anaesthesia) and the anaesthetists’ views of the perioperative risk associated with each patient. Where there is more than one anaesthetist responsible during a case, the most senior anaesthetist will be asked to complete the questionnaire. Where a patient is handed over between anaesthetists, the most senior anaesthetist present at the end of surgery will be asked to review the responses to the questionnaire and amend if necessary (see Appendix 1).

The completed questionnaires will be taken directly to a secure location accessible by the local PI and other named members of the study team. On Day 7 postoperatively, local investigators will check the patient status (remains inpatient, vs. discharged from hospital, vs. died). If the patient remains alive in hospital, the Post Operative Morbidity Survey (POMS) will be completed for this patient, through review of the patient record (medical notes, nursing charts and clinical / laboratory investigations). The POMS is a validated measure of postoperative morbidity [16] which has been used in multiple studies. [16] [5] If the patient has been discharged from hospital or has died, this will be recorded on the CRF.

Inpatient stay will be censored at 60 days post-surgery. Therefore, the final entry in the CRF will be whichever of the following three options is the chronologically earliest date: date of discharge from hospital, date of death while in hospital, or 60 days post-surgery if the patient remains in hospital on that date.

### 12.2 Critical Care occupancy data

The Principle Investigator at each site will be responsible for documenting critical care occupancy twice daily on a structured data entry form (see Appendix 3).

#### 12.3 Data handling and record keeping

In the study, data will be collected in accordance with the patient consent form, participant information sheet and sections 5,6,7,8 and 12 of this protocol.

At individual hospital level, the completed CRFs will be held in a secure location accessible by the local PI and other named members of the study team in accordance with GCP guidelines and local information and research governance frameworks. Information from the paper CRF will be entered via a secure web-based portal onto the study database. The website and database are being developed by Netsolving Ltd (www.netsolving.com) who have a strong track record in delivering secure websites / databases for NHS based medical research and audits, e.g. the National Emergency Laparotomy Audit; (<http://www.nela.org.uk/>) and SNAP-1 (<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4422533/> ) The database will be hosted on servers managed by the Royal College of Anaesthetists purchased from UK Fast). The minimum amount of patient identifiable data will be extracted from the study database by the central investigation team, onto a password protected Excel spreadsheet, and emailed securely to the Health and Social Care Information Centre, to facilitate linkage to central held mortality data. Mortality will be tracked for all patients with a final censure date of 10 years after participant recruitment.

These fields will be used to ensure individual patient records within the EpiCCS system are managed correctly, keeping distinct treatment episodes linked to the correct patient. Four patient identifiers will be used: patient name, date of birth, NHS number and postcode.

These identifiers will also be used to link the EpiCCS dataset to one other routine dataset, the HSCIC mortality tracking system. The NHS number is not completely populated in the HSCIC system and the other patient identifiers are used when the NHS number is absent. In addition, by using these four identifiers in combination, possible erroneous record linkages are flagged.

Among the patient identifiers, only sex will used for analysis. An anonymised dataset will be used by the central EPICCS study team for analysis.

In this dataset:

• The NHS number will be replaced by a unique study patient identifier.

• Date of Birth will be converted to Age on date of surgery, and trimmed to month and year of birth

• Postcode will be converted to PCT, SHA of residence, and the Office for National Statistics Lower Super Output Area, which allows the allocation of the Index of Multiple Deprivation.

The data items will be retained in their original format in the identifiable dataset which is retained within the EpiCCS IT system.

The following paragraphs describe the process of linkage to the HSCIC mortality tracking system. The same process will be applied for linkage to HES data.

A file (P) containing patient identifiers only will be extracted from the full dataset hosted in the webtool, and will be sent securely to a trusted Data Linkage Service. For both mortality tracking data and HES data, this would be the Health and Social Care Information Centre (HSCIC). File (P) will contain the following identifiers:

• EpiCCS anonymised identifier

• NHS number

• Date of Birth

• Sex

• Postcode

For each patient in the file, the HSCIC will identify the matching ONS ID. The HSCIC will return to the RCoA a ‘look-up’ file (L) containing only the EpiCCS identifier and the HESID identifiers, and a MATCH\_RANK field which indicates the strength of the match.

An extract of anonymised ONS mortality data will then be requested from the HSCIC for all the list of ONS IDs contained in file (L).

The file (L) will be placed in the secure RCoA server accessible only to the project data manager. It will then be used to link the anonymised ONS data to the anonymised EPICCS data for analysis. The anonymised EpiCCS extract will not contain NHS number, postcode or date of birth. Patients will be labeled with the EpiCCS identifier only.

The electronic patient datasets will be appropriately sent to Dr Ramani Moonesinghe, Dr Danny Wong and Dr Steve Harris; the RCoA (Ms Sharon Drake) will act as the data controller for the study. These individuals are all based at one or more of the following organisations:

* University College London Hospitals NHS Foundation Trust (Surgical Outcomes Research Centre)
* University College London (Department of Applied Health Research)
* Royal College of Anaesthetists (Health Services Research Centre)

The RCoA will process, store and dispose of all participant datasets in accordance with all applicable legal and regulatory requirements, including the Data Protection Act 1998 and any amendments thereto.

# 13. Peer and regulatory review

The study has been peer reviewed in accordance with the requirements outlined by UCL/UCLH

The Sponsor considers the procedure for obtaining funding from the National Institute for Academic Anaesthesia (which is an NIHR portfolio partner) to be of sufficient rigour and independence to be considered an adequate peer review.

# 14. Assessment and management of risk

We do not consider this observational study to carry any significant risks to participants or investigators.

# 15. Indemnity arrangements

University College London holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, if this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the clinical study. University College London does not accept liability for any breach in the hospital’s duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

# 16. Archiving

UCL and each participating site recognise that there is an obligation to archive study related documents at the end of the study (as such end is defined within this protocol) and in line with all relevant legal and statutory requirements. The Chief Investigator confirms that she will archive the study master file at UCLH for 10 years from the end of participant recruitment. The Principal Investigator at each participating site agrees to archive his/her respective site’s study documents for 10 years from the end of participant recruitment and in line with all relevant legal and statutory requirements.

# 17. Publication and dissemination policy

We intend to present the results online via the study website, in peer reviewed scientific journals and in the form of conference presentations. In addition to academic publications we will provide specific summary reports for the following groups:

Healthcare policy makers – this will include medical and nursing Royal Colleges, specialist societies, Department of Health, NHS England, NHS Wales, NHS Scotland and Health and Social Care Ireland.

Patients and the Public – our lay representative and the Lay representative group at the Royal College of Anaesthetists will provide support in our dissemination to the non-medical audience

Participating NHS Trusts and Health Boards – all NHS Chief executives of participating organisations will be sent a summary of the key findings.

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# Appendices

* 1. Patient dataset
	2. Quality of Recovery dataset (This has now been removed from the study)
	3. Critical Care Occupancy dataset
	4. Clinicians’ Perceptions dataset
	5. Participant information leaflet –main EPICCS study
	6. Quality of Recovery telephone interview script (This has now been removed from the study)
	7. Patient information poster