CASCADE Protocol v2.8
14/11/2021

Student Audit and Research in Surgery (STARSurg) Collaborative

EuroSurg Collaborative

CArdiovaSCuIAr outcomes after major abDominal surgEry

CASCADE

A student-led observational prospective audit of postoperative cardiovascular complication after major abdominal surgery

Study protocol v2.8
14 November 2021

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### STARSurg Steering Committee

*Members listed alphabetically by surname*

<table>
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<th>Name</th>
<th>Training stage</th>
<th>Twitter</th>
</tr>
</thead>
<tbody>
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<td>Samuel Brown</td>
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</tbody>
</table>
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*Members listed alphabetically by surname*

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<th>Name</th>
<th>Training stage</th>
<th>Twitter</th>
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<th>Name</th>
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<tbody>
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<td><strong>Anaesthesia and Critical Care</strong></td>
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</tr>
</tbody>
</table>
## Project Timeline

<table>
<thead>
<tr>
<th>Dates</th>
<th>Description</th>
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<tbody>
<tr>
<td>6&lt;sup&gt;th&lt;/sup&gt; Aug 2021</td>
<td>CASCADE Regional Lead recruitment opens</td>
</tr>
<tr>
<td>27&lt;sup&gt;th&lt;/sup&gt; Aug 2021</td>
<td>Recruitment for CASCADE Regional Leads closes</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Oct 2021</td>
<td>Online launch of CASCADE Protocol</td>
</tr>
<tr>
<td>Mid Oct 2021</td>
<td>Virtual conference for CASCADE Study Launch</td>
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<tr>
<td>24&lt;sup&gt;th&lt;/sup&gt; Jan - 6&lt;sup&gt;th&lt;/sup&gt; Feb 2022</td>
<td>Start of data collection period 1 (30-day follow-up ends 8&lt;sup&gt;th&lt;/sup&gt; Mar 2022)</td>
</tr>
<tr>
<td>7&lt;sup&gt;th&lt;/sup&gt; Feb - 20&lt;sup&gt;th&lt;/sup&gt; Feb 2022</td>
<td>Start of data collection period 2 (30-day follow-up ends 22&lt;sup&gt;nd&lt;/sup&gt; Mar 2022)</td>
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<tr>
<td>21&lt;sup&gt;st&lt;/sup&gt; Feb - 6&lt;sup&gt;th&lt;/sup&gt; Mar 2022</td>
<td>Start of data collection period 3 (30-day follow-up ends 5&lt;sup&gt;th&lt;/sup&gt; Apr 2022)</td>
</tr>
<tr>
<td>7&lt;sup&gt;th&lt;/sup&gt; Mar - 20&lt;sup&gt;th&lt;/sup&gt; Mar 2022</td>
<td>Start of data collection period 4 (30-day follow-up ends 19&lt;sup&gt;th&lt;/sup&gt; Apr 2022)</td>
</tr>
<tr>
<td>21&lt;sup&gt;st&lt;/sup&gt; Mar - 3&lt;sup&gt;rd&lt;/sup&gt; Apr 2022</td>
<td>Start of data collection period 5 (30-day follow-up ends 3&lt;sup&gt;rd&lt;/sup&gt; May 2022)</td>
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<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; July 2022</td>
<td>REDCap database locked, final data submission deadline</td>
</tr>
<tr>
<td>Mid-2022</td>
<td>CASCADE results presented to ESCP &amp; AAGBI</td>
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About STARSurg

Student Audit and Research in Surgery (STARSurg) is a student-led, national research collaborative empowering medical students and junior doctors to conduct high-quality, protocol-driven audit and research in a multicentre setting. Students contribute data to national studies whilst gaining an understanding of clinical academia, audit and research methodology, and ethical considerations in research1.

The ‘collaborative’ trainee-led model for ‘snapshot’ audit has been pioneered from the West Midlands, developing from regional networks of surgical registrars to national and international groups across specialties and around the world2. These networks have delivered major multicentre projects including cohort studies and randomised controlled trials. In accordance with National Research Collaborative (NRC) authorship guidelines3, these studies typically use a single corporate author model, where all publications are listed under a single collaborative name with all contributing authors listed as PubMed-citable collaborators4. This seeks to democratise the publication process and flatten traditional research hierarchies.

STARSurg has now delivered seven national audits of surgical and perioperative practice: STARSurg-15, Determining Surgical Complications in the Overweight (DISCOVER)6, Outcomes after kidney injury in surgery (OAKS)-14, OAKS-2, Ileus Management International (IMAGINE)7, REspiratory COmplications after abdomiNal Surgery (RECON)8, and COMPlieAted intra-abdominal collectionS after colorectal Surgery (COMPASS)9. To date, we have engaged over 7,500 collaborators in our projects from over 170 centres in the UK and Ireland, with data collected on more than 32,000 patients. This has resulted in 25 peer reviewed papers published within high impact journals, including the British Journal of Surgery (BJS), British Journal of Anaesthesia and Anaesthesia. Members of the steering committee and Regional Leads have given over 80 presentations at regional, national and international conferences (see www.starsurg.org).

STARSurg is proud partners of the BJS Society who provide invaluable support for the day-to-day running of STARSurg activities and our infrastructure.
About EuroSurg

The EuroSurg collaborative is an international research group led by students and surgical trainee.\textsuperscript{10} Founded at the European Society of Coloproctology (ESCP) 2015 meeting, it has since expanded rapidly with active members in Czech Republic, France, Germany, Italy, Netherlands, Spain, Turkey, Portugal, Ireland and the United Kingdom (eurosurg.org). In our most recent study, COMPASS\textsuperscript{9} which explored international drain placement practices in colorectal surgery, centres from South Africa, Australia and New Zealand took part as well.

Collaboration across international surgical communities produces transferable results which may inform the design of future RCTs and changes in clinical practice. Through participating in the EuroSurg project, students will acquire essential skills in surgical audit and research methodology.\textsuperscript{11} EuroSurg will replicate previous groups’ successful authorship policy, which designates all student and trainee collaborators as PubMed-citable “Collaborators”. An example of this authorship model can be seen here: EuroSurg Collaborative (doi: 10.1002/bjs.11326).\textsuperscript{12}
Introduction

Postoperative cardiovascular complications are increasingly common after major non-cardiac surgery, with a spectrum of severity from minor complications, such as supraventricular arrhythmias, to life-threatening complications, such as myocardial infarction, pulmonary embolism and cardiac arrest.\textsuperscript{13} Incidence of postoperative cardiovascular complications varies across published studies, owing to variation in definitions use, and can be as high as 33%.\textsuperscript{14} Various risk factors for postoperative cardiovascular complications are recognised such as revised cardiac risk index.\textsuperscript{15,16} With an increasing ageing population, the prevalence of various cardiovascular diseases in patients undergoing non-cardiac surgery ranges from 5% to 70%.\textsuperscript{15} Mitigating risks of postoperative cardiovascular complications is important, since these complications are associated with increased healthcare costs, disability, and morbidity and mortality.\textsuperscript{17-19} This is especially relevant in patients undergoing major abdominal and pelvic surgery where rates are as high as 25%.\textsuperscript{20}

To date, there remains a paucity of robust evidence regarding the risk factors, incidence, and outcomes in major abdominal surgery. Firstly, there is a lack of contemporary data on cardiovascular outcomes with the recent consensus definitions for the Standardized Endpoints in Perioperative Medicine (StEP) initiative.\textsuperscript{13} New data assessing rates of these new composite cardiovascular endpoints would provide benchmarking data for future randomised controlled trials. Secondly, there are limited European guidelines regarding the prevention (i.e. perioperative beta-blocker therapy) and/or management of cardiovascular complications. Royal College of Anaesthetists Guidelines for the Provision of Anaesthesia Services (GPAS) provide a number of risk reduction strategies and standards within the pre-, intra- and post-operative periods. In addition, relevant Enhanced Recovery After Surgery (ERAS) protocols exist to minimise postoperative cardiovascular complication.\textsuperscript{21} Further, risk modification (i.e. anaemia, frailty) on postoperative cardiovascular complications remain an area of uncertainty.\textsuperscript{22}

CASCADE (CArdiovaSCulAr outcomes after major abDominal surgEry) aims to increase our understanding of variability and adherence to risk reduction measures for postoperative cardiovascular complications following major abdominal surgery through an international, multicentre study across Europe.
### Audit Standards

* Relevant audit standards from selected American College of Cardiology (ACC) / American Heart Association (AHA), Enhanced Recovery after Surgery, National Institute of Clinical Excellence guidelines

<table>
<thead>
<tr>
<th>Pre-operative Standards</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Weight and body mass index should be recorded.</td>
<td><strong>Royal College of Anaesthetists: Guidelines for the Provision of Anaesthesia Services 2021</strong>(^{23})</td>
</tr>
<tr>
<td></td>
<td>• <strong>Pre-operative Assessment and Preparation Recommendation 12.44</strong>: Medical records should include the</td>
</tr>
<tr>
<td></td>
<td>patient’s weight and body mass index (BMI)</td>
</tr>
<tr>
<td>2. Preoperative scoring tools should be used to risk stratify patients</td>
<td><strong>ERAS for gastrointestinal surgery: consensus statement for anaesthesia practice</strong>(^{24})</td>
</tr>
<tr>
<td></td>
<td>• <strong>Preoperative risk scoring</strong>: Preoperative scoring tools and functional capacity tests can be used to</td>
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<tr>
<td></td>
<td>identify patients at risk of complications and to stratify perioperative risk</td>
</tr>
<tr>
<td></td>
<td><strong>American College of Cardiology (ACC) / American Heart Association (AHA) Clinical Practice Guideline</strong>(^{22})</td>
</tr>
<tr>
<td></td>
<td>• <strong>Preoperative risk scoring</strong>: A validated risk-prediction tool can be useful in predicting the risk of</td>
</tr>
<tr>
<td></td>
<td>perioperative major adverse cardiovascular events in patients undergoing noncardiac surgery</td>
</tr>
<tr>
<td>3. Pre-operative Electrocardiogram (ECG)</td>
<td><strong>American College of Cardiology (ACC) / American Heart Association (AHA) Clinical Practice Guideline</strong>(^{22})</td>
</tr>
<tr>
<td></td>
<td>• <strong>Preoperative ECG</strong>: Pre-operative ECG is recommended for patients who have risk factor(s)d and are</td>
</tr>
<tr>
<td></td>
<td>scheduled for intermediate- or high-risk surgery</td>
</tr>
<tr>
<td>4. Cardiopulmonary exercise testing for high-risk patients</td>
<td><strong>Royal College of Anaesthetists: Guidelines for the Provision of Anaesthesia Services 2021</strong>(^{23})</td>
</tr>
<tr>
<td></td>
<td>• <strong>Pre-operative Assessment and Preparation Recommendation 2.2</strong>: Cardiopulmonary exercise testing or</td>
</tr>
<tr>
<td></td>
<td>functional assessment for high-risk patients should be carried out.</td>
</tr>
<tr>
<td>5. Preoperative iron supplementation in iron-deficiency anaemia</td>
<td><strong>National Institute of Clinical Excellence: Blood Transfusion Quality Standard (QS138) 2016</strong></td>
</tr>
<tr>
<td></td>
<td>• <strong>Iron supplementation</strong>: People with iron-deficiency anaemia who are having surgery are offered iron</td>
</tr>
<tr>
<td></td>
<td>supplementation before and after surgery.</td>
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</table>
### Intra-operative Standards

1. **WHO Surgical Safety Checklist** should be used for all procedures.
   - Royal College of Anaesthetists: Guidelines for the Provision of Anaesthesia Services 2021
     - **Pre-operative Assessment and Preparation Recommendation 12.50**: The WHO’s Surgical Safety Checklist should be used and is fully endorsed by the RCoA as the instrument for promoting team working and patient safety.

### Post-operative Standards

1. **Early recognition of patients needing specialist postoperative input**
   - Royal College of Anaesthetists: Guidelines for the Provision of Anaesthesia Services 2019
     - **Provision of Postoperative Care Recommendation 3.23**: Mechanisms for the early recognition of patients requiring specialist postoperative input from geriatrician-led services and/or critical care should be developed. These should include patients at risk of or presenting with delirium, multiple medical complications, functional decline or complex discharge planning.

2. **Postoperative intravenous iron therapy** is indicated in patients with iron deficiency anaemia
   - International consensus statement on Postoperative Anaemia after Major Surgery 2018
     - **Postoperative iron therapy**: Should postoperative iron therapy be indicated, i.v. formulations are recommended

3. **Extended pharmacological VTE prophylaxis** is indicated in patients at high VTE risk after major abdominal or pelvic surgery
   - National Institute of Clinical Excellence: Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism (NG89) 2018
     - Consider extending pharmacological VTE prophylaxis to 28 days postoperatively for people who have had major cancer surgery in the abdomen.
Methods

1. Summary
A prospective, multicentre, study will be delivered by STARSurg Collaborative & EuroSurg Collaborative across Europe. Mini-teams of up to four collaborators (medical students and at least one doctor) per speciality group per data collection period will prospectively collect data over a continuous 14-day period at each participating centre. This will be on consecutive patients undergoing major abdominal surgery, with follow-up to 30 postoperative days. All mini-teams should be supervised by a consultant in surgery.

2. Study Aims:

- **Primary Aim:** To audit compliance to pre-, intra-, and postoperative audit standards in reducing risk of postoperative cardiovascular complication.

- **Secondary Aims**
  - To characterise rates and risk factors associated with postoperative cardiovascular complications following major abdominal surgery in Europe.
  - To explore the association of pre-operative and postoperative anaemia with postoperative cardiovascular complications and short-term outcomes (length of stay, readmission and 30-day mortality).
  - To characterise the efficacy and safety profile of extended pharmacological thromboprophylaxis in patients at high risk for VTE.

3. Project Timeline:
- The suggested overall data collection periods will be Monday 24th January 2022 to 3rd April 2022. Each mini-team will collect data over a 14-day, consecutive period with subsequent 30-day follow-up:
  - Period 1: 00:00 24th Jan 2022 - 23:59 06th Feb 2022 (+ 30 Day Follow-up)
  - Period 2: 00:00 07th Feb 2022 - 23:59 20th Feb 2022 (+ 30 Day Follow-up)
  - Period 3: 00:00 21st Feb 2022 - 23:59 06th Mar 2022 (+ 30 Day Follow-up).
  - Period 4: 00:00 07th Mar 2022 - 23:59 20th Mar 2022 (+ 30 Day Follow-up).
  - Period 5: 00:00 21st Mar 2022 - 23:59 03rd Apr 2022 (+ 30 Day Follow-up).
- Patients should be included if their operation started (defined as 'knife-to-skin' time) within
the time period during the data collection periods as specified above.
- Additional data collection periods may be added later in the study, to give flexibility to include further centres, who have had logistical difficulties in study start up.

4. Centre Eligibility:
- CASCADE is open to any hospital in UK and Europe that routinely performs either elective and emergency major abdominal surgery.
- All participating centres are required to register the CASCADE audit according to local regulations. In the UK, CASCADE has been confirmed by the NHS East of Scotland REC Committee that it does not need NHS ethical review under the terms of the Governance Arrangements for Research Ethics Committees (Appendix F).
- Internationally, individual study investigators are responsible for ensuring the correct audit, ethical or departmental approval has been achieved prior to commencing data collection (this can be registered as an audit or service evaluation, if appropriate).
- Evidence of successful audit registration must be sent to study management team (or the appropriate regional lead for UK centres) prior to commencement of data collection. Centres will not be allowed to upload patients’ data onto REDCap without evidence of successful registration of the study.
- Following completion of the CASCADE audit, it is a requirement of participation that mini-teams should present the audit findings to the surgery and/or audit departments at each centre.

Providing feedback on the audit’s findings to your department’s clinicians is an essential step in the audit loop. Presenting local results will help collaborators develop analytical and presentation skills and will boost their CVs.

5. Patient Eligibility:
**Summary**: Consecutive adult patients undergoing emergency or elective abdominal and/or pelvic visceral resection, formation or reversal of stoma, open vascular surgery, anterior abdominal wall hernia repair, or transplant surgery through any operative approach.

**Inclusion criteria**:
- **Age**: Adult, 18 years or above.
- **Procedure**: Major abdominal surgery, including one or more of the following:
  - Visceral resection, defined as complete transection and removal of a segment of the oesophagus, stomach, small bowel, liver, pancreas, gallbladder, colon, appendix, rectum, kidney, bladder, ovary and/or uterus, including multivisceral resections.
  - Formation and reversal of stoma (ileostomy, colostomy or urostomy).
  - Open repair of abdominal aortic aneurysm or vascular bypass procedure with abdominal component.
  - Anterior abdominal wall incisional hernia or parastomal hernia repair.
  - Transplant surgery, including renal, liver or pancreas surgery.

- **Approach**: Open, laparoscopic, laparoscopic assisted, laparoscopic converted, robotic, robotic converted procedures are all eligible.

- **Urgency**: Patients undergoing planned (elective or expedited) or unplanned (emergency) surgery.

**Exclusion criteria:**

**Procedures:**

- Groin (femoral, inguinal), umbilical or paraumbilical hernia repairs and other abdominal and/or pelvic surgeries without resection (e.g. anti-reflux surgery, rectopexy, sterilisation) are excluded.
- Caesarean sections (C-sections) are excluded.
- Bariatric procedures (i.e., sleeve gastrectomy, gastric bypass) are excluded.
- Diagnostic laparoscopy or laparotomy without resection are excluded.
- Transanal, transurethral, transvaginal procedures without an abdominal incision are excluded.

- **Indication**: Procedures performed for a trauma indication (blunt or penetrating) are excluded.

- **Pregnancy**: pregnant patients (positive urine or blood hCG test prior to surgery) are excluded.

- **Minor surgery**: Planned day case procedures (discharge home on the same day as surgery) are excluded.

- **Extent of surgery**: We will exclude operations that are either:
  - Staged with a planned return for reoperation (such as but not limited to damage control laparotomy or burns surgery) OR
- Change in operative plan such that during the first procedure it is determined that a reoperation is necessary, even if the patient was enrolled preoperatively

- **Return to theatre**: Each individual patient should only be included in the study once. Patients returning to theatre due to complications following earlier surgery can be included, as long as their indexed procedure has not already been included in the CASCADE audit.

You should collect data on consecutive patients operated at your centre during the data collection period. This means that all eligible patients should be included.

*Strategies to identify consecutive eligible patients could include:*

- **Daily review of elective theatre lists.**
- **Daily review of handover sheets/ emergency admission and ward lists.**
- **Daily review of theatre logbooks (both elective and emergency).**

6. **Covariates:**

Data will be collected on audit standards and confounding factors for risk-adjusted analyses. These include age, sex, ethnicity, body mass index, American Society of Anaesthesiologists (ASA) grade, relevant comorbidities, smoking status, anticoagulant or antiplatelet use, preoperative blood test values, and preoperative anaemia management. Variables including operative urgency, operative procedure, operative contamination, use of tranexamic acid, intraoperative blood transfusions used, haemoglobin level at transfusion, duration of procedure and post-operative iron therapy will also be collected. Without appropriately adjusting for risk factors, it is likely that any findings would be biased and unable to be appropriately analysed on a national scale. A full list of required data fields is available in Appendix B, and on the REDCap database.

7. **Outcome Measures and Follow-up:**

**Primary outcome measure:**

- Rates of compliance to pre-, intra-, and postoperative audit standards in reducing risk of postoperative cardiovascular complication.

**Secondary outcome measures:**

- Incidence of postoperative cardiovascular complications within 30-days of surgery
according to the Standardized Endpoints for Perioperative Medicine (StEP) cardiovascular.13 (see Appendix D: Definitions of Key Outcomes).

- 30-day postoperative blood transfusion rates
- 30-day complication rates defined according to the Clavien-Dindo classification (see Appendix D: Definitions of Key Outcomes)
- 30-day reoperation rates
- Critical care bed days up to 30 days postoperatively
- Length of in-patient stay (days) up to 30 days postoperatively
- 30-day readmission rates
- 30-day bleeding event rates (see Appendix D: Definitions of Key Outcomes)
- Length of pharmacological VTE prophylaxis (days) up to 30 days postoperatively.

Follow-up should be performed in line with current routine practice within each hospital settings. No additional telephone, in-person or questionnaire-based follow-up is required. Source data may be acquired from hospital in-patient notes, clinical electronic systems, or outpatient letters.

Prior to collecting data, all collaborators will be required complete the mandatory e-learning modules available from the CASCADE project online hub: https://incept.ac.uk/course/view.php?id=7

These include: (1) CASCADE Patient selection; (2) Clavien-Dindo classification (3) Postoperative cardiovascular complications; (4) Postoperative bleeding complications; (5) VTE pharmacological prophylaxis; (6) Data safety governance; (7) Quiz

8. Data Governance:
Data will be collected and stored online through a secure server running the Research Electronic Data Capture (REDCap) web application,27,28 and allows safe anonymised data storage by collaborators across Europe. The service is managed by the Birmingham Surgical Trials Consortium (BiSTC) REDCap system hosted at the University of Birmingham, United Kingdom. The security of the study database system is governed by the policies of the University of Birmingham. Data management and data security within the BiSTC REDCap will abide by the requirements of the General Data Protection Regulations (GDPR) and any subsequent
amendments. Collaborators will be given secure REDCap project server login details, allowing secure data storage on the REDCap system.

No patient data will be uploaded or stored on the REDCap database without prior local permissions. All data should be handled in accordance with local data governance policies, and all paper copies of any data should be destroyed as confidential waste within the centre once uploaded to REDCap. Data collected during the CASCADE study can be used for future analyses at the Study Management Group's discretion.

9. Data Analysis & Sample Size:
Based on previous STARSurg and EuroSurg studies, CASCADE is anticipated to include around 300 centres in Europe. With consideration to recent figures provided by previous STARSurg and EuroSurg studies, it has been estimated that, on average, ten patients will undergo surgery per week at each participating centre. Therefore, a sample of approximately 6000 patients is anticipated. No surgeon-, hospital- or country-specific comparisons will be performed. Further secondary analyses may be performed at the Study Management Group discretion.

10. Local Project Registration:
At European centres, if the option is available, this project may be registered as clinical audit or service evaluation. Alternatively, it may be necessary to obtain formal ethical approval. It is the responsibility of the local mini-team at each site to ensure that the study is registered appropriately, according to local regulations. CASCADE should be registered in the UK and ROI as a clinical audit. It is the responsibility of the local mini-team at each site to identify a local consultant in surgery, anaesthesia or critical care to supervise them and ensure registration.

Confirmation that ethical review is not required for CASCADE within the UK is available in Appendix F. Examples of audit registration forms can be found at the online project hub. When registering CASCADE as a clinical audit you can emphasis that:

- CASCADE is a national audit, and all data collected will measure current practice.
- No changes to normal patient pathways/treatment will be made.
- All CASCADE data will be collected and stored online through a secure server running the Research Electronic Data Capture (REDCap) web application. REDCap allows collaborators to enter and store data in a secure system. Collaborators will be given secure REDCap project server login details, allowing secure data storage on the REDCap system.
Collaborators in the UK should seek their trust’s Caldicott Guardian’s permission to submit data to the REDCap system. **No data should be uploaded to REDCap prior to written approval from the Caldicott Guardian.** No patient identifiable information (e.g. NHS numbers) should be uploaded or stored on the REDCap database without explicit permission from the trust’s Caldicott Guardian. All data should be handled in accordance with national and local data governance policies.

**REDCap accounts will not be issued until evidence is sent to your university’s regional lead that the following approvals are in place at your centre:**

- Successful registration of CASCADE with the audit department.
- Caldicott Guardian permission for data to be submitted to REDCap.

**11. Quality assurance:**

**Design:** This protocol was written with guidance from an expert cross-speciality advisory group.

**Training:** CASCADE Regional Leads are encouraged to hold local meetings with collaborating teams at their medical school to brief them on the protocol, and to feedback any local issues or questions raised. To ensure collaborators understand the study topic, inclusion criteria, primary outcomes, application of the Clavien-Dindo classification and the principles of data governance, they will all be asked to complete online **e-learning** on these (pass mark is 100%) prior to starting data collection (online at: [https://incept.ac.uk/course/view.php?id=7](https://incept.ac.uk/course/view.php?id=7)).

**Project team structure:** Medical students will take the lead in disseminating and delivering this study alongside junior doctors. These ‘mini-teams’ should be supervised by up to two consultants (two surgeons or anaesthetists) at each site (**Figure 1**). Each team should include at least one qualified doctor to provide additional local support for participating medical students.
Data completeness: Following data collection, only data sets with >95% data completeness will be accepted for pooled national analysis. To emphasise the importance of data completeness to collaborators, data collection periods with >5% missing data points will be excluded from the study and collaborators from those periods withdrawn from the published list of citable collaborators.

Validation: This methodology for student-driven snapshot audit has been widely validated across multiple datasets, both nationally in the UK and Ireland and internationally, demonstrating high levels of case ascertainment (typically greater than 90 to 95%) and data accuracy (greater than 96 to 98%).

12. Authorship:
In accordance with National Research Collaborative (NRC) authorship guidelines, all research outputs from CASCADE will be listed under a single corporate authorship (“STARSurg Collaborative & EuroSurg Collaborative”).

All collaborators will be listed as PubMed-citable collaborators in accordance with the roles defined below (so long as the minimum requirements for authorship are met).

- **Writing Group:** A group of medical students, junior doctors and external advisory board members responsible for the overall scientific content, data analysis, and preparation of
research manuscripts.

- **Steering Committee**: A core group of medical students and junior doctors who have overall responsibility for protocol design, project co-ordination, and data handling.

- **Statistical Analysis**: A small team of dedicated statisticians who take overall responsibility for the statistical analysis plan and quality assurance of data analysis.

- **Regional Leads**: A network of medical students across all medical schools. They are responsible for co-ordinating mini-teams at local hospitals, and act as a link between mini-teams / hospital leads, and the steering committee. Requirements for authorship on CASCADE outputs include:
  - Active engagement with dissemination of CASCADE and other STARSurg activities at their local medical school.
  - Effective and responsive communication with the STARSurg steering committee, and with local collaborators throughout their time as Regional Leads.
  - Recruitment of at least two mini-teams at each centre where students from their medical school have surgical placements, with a minimum of one centre meeting the criteria for inclusion within the CASCADE dataset.
  - Responsible for representing STARSurg at regional educational and research meetings.

- **Local (Hospital) Leads**: A single lead point of contact for data collection at each site who has overall responsibility for site governance registration and coordinating handover between local collaborator teams. Local Leads should be prospectively identified by Regional Leads (although remain an optional role), and these are recommended to be the junior doctor or a senior medical student within the mini-team, and only one person can fulfil this role. Minimum requirements for authorship on CASCADE outputs include:
  - Primary person responsible in obtaining local approvals for conduct of the CASCADE audit (e.g. registration of the audit, seeking Caldicott guardian permission to upload data to REDCap).
  - Active involvement in a mini-team during a data collection period at the centre which meets the criteria for inclusion within the CASCADE dataset.
  - Co-ordination of handover between all local collaborator teams at the centre, and involvement in local dissemination of CASCADE and other STARSurg & EuroSurg activities.
  - Presentation of local results at their centre from the CASCADE audit (or otherwise arranges another collaborator to present on their behalf).
• **Local collaborators (data collectors):** A team of up to 3 people responsible for data collection per specialty group over a specific 2-week period at a particular centre. This should ideally be formed by 1-2 medical students collaborating with a junior doctor (FY1 to senior registrar grade). Reflecting the cross-specialty nature of the CASCADE audit, one mini-team (3 members) will be permitted *per specialty group*, defined as: (1) gastrointestinal and liver surgery; (2) vascular and transplant surgery; (3) urological surgery; (4) gynaecological surgery (a maximum of 12 collaborators per data period per hospital). Minimum requirements for authorship on CASCADE outputs include:
  - Compliance with local audit approval processes and data governance policies.
  - Active involvement in data collection over at least one data collection period at a centre which meets the criteria for inclusion within the CASCADE dataset (below).
  - While assistance with other teams is encouraged, collaborator status will only be assessed based on successful completion of the allocated period.
  - Collaboration with the regional / local lead to ensure that the audit results are reported back to the audit office / clinical teams.

• **Supervising Consultant:** Data collection in each hospital must be supervised by up to two consultants (at least one in a surgical or anaesthetic specialty). Minimum requirements for authorship on CASCADE outputs include:
  - Sponsorship of local audit registration, and responsible to ensure local collaborators act in accordance with local governance guidelines.
  - Inclusion of at least one data collection period at their centre which meets the criteria for inclusion within the CASCADE dataset.
  - Facilitation of local audit results presentation and support of appropriate post-audit interventions.
  - Completion of workplace-based assessments for students or trainees (ePortfolio/ISCP), if requested.

**Criteria for centre inclusion within CASCADE:**
- Obtain of all appropriate local approvals for conduct of the CASCADE audit.
- Successful completion of at least one data collection period at the centre (with a minimum of one eligible patient per period included). Individual data collection periods will only be included when:
  - >95% data completeness has been achieved.
ii. All data for the period has been uploaded within the specified deadlines.

Please note if these criteria are not met, then the contributing mini-team and/or the centre may be removed from the dataset and authorship list (please get in contact as soon as potential issues arise so we can support as many centres to be included as possible). See Appendix F for advice to help ensure for successful inclusion of your centre in the CASCADE audit.
## Appendix A: Summary of data fields (CRF)

### Use with Data Dictionary to aid data collection.

#### Section 1: Pre-operative data fields

<table>
<thead>
<tr>
<th>REDCap Unique ID</th>
<th>Age (years)</th>
<th>Gender</th>
<th>ASA grade</th>
<th>BMI (2dp)</th>
<th>Smoking status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Current E-smoker (&lt;6 weeks)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ex-smoker (6 weeks -1 year)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ex-smoker (&gt;1 year)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>□ I</td>
<td>□ II</td>
<td>□ III</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>□ IV</td>
<td>□ V</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** *Never smoked* (if smoker/ex-smoker: □ Tobacco cigarettes □ E-cigarettes or vapes)

**Clinical Frailty Scale:** □ 1-3 □ 4-6 □ 7-9


### History (Hx) of cardiovascular disease (Tick all that apply)

- MI
- Angina
- TIA/stroke
- Hypertension
- Atrial Fibrillation
- Deep vein thrombosis
- Pulmonary Embolism
- Congestive Heart Failure (CHF)

- Exertional dyspnoea or chest x-ray (CRX): mild COPD
- Exertional dyspnoea <1 flight or CRX: moderate COPD
- Dyspnoea at rest/rate >30 at rest or CRX: fibrosis or consolidation

**Hx of COPD:** □ Yes □ No

**Hx of respiratory disease (best describing respiratory signs and chest x-ray appearance):** □ None

- □ NYHA: □ I □ II □ III □ IV

### Management of iron-deficiency anaemia (IDA)

- □ None
- □ Iron (Oral / IV ?)
- □ Tranexamic acid (TXA)
- □ RBC transfusion

**IF POD:** □ Yes □ No

### Hx of chronic kidney disease

- □ I □ II □ IIIa □ IIIb □ IV □ V
- □ None

- □ Yes

**Hx of liver cirrhosis:** □ None

**Hx of diabetes mellitus:** □ None

**Type I:** □ Yes □ No

**Active cancer and/or cancer treatment:** □ None □ Yes

**Hx of IBD:** □ None □ Yes

### Pre-admission therapeutic anticoagulation

- □ LMWH □ Warfarin □ Direct oral anticoagulant (DOACs)

**IF elective:** □ Yes □ No

**IF yes:** Did this include pre-operative cardiologymphasic exercise testing?

- □ Yes (VO2 peak _ _ _ ml/min kg^-1 / AT _ _ _ ml/min kg^-1)

- □ No

**IF emergency:** Yes (inpatient perioperative or elderly medicine)

**ECG (normal/AF rate 60-90/AF rate >90 or any other abnormal rhythm?):** □ None

**ECHO (LVEF _ _ _ %):** □ Coronary angiogram □ None

### Admission blood tests* (Please complete all) *Include first blood test results from this admission*

- □ Hb _ _ _ g/L
- □ Albumin _ _ _ g/L
- □ Creatinine _ _ _ umol/L

**Pre-admission blood tests* (Please complete all) *Include most recent blood tests within the 90 days prior to operation**

- □ Hb _ _ _ g/L
- □ Albumin _ _ _ g/L
- □ Sodium _ _ _ mmol/L
- □ Potassium _ _ _ mmol/L
- □ Urea _ _ _ mmol/L
- □ Creatinine _ _ _ umol/L

### Admission observations

- □ Pulse _ _ _ bpm
- □ Systolic BP _ _ _ mmHg
- □ GCS _ _ _ (15)

**Pre-operative assessment**

### Preoperative investigations (Tick all that apply)

**If (elective):** □ Yes (pre-admission anaesthetic assessment clinic)

**If yes:** Did this include pre-operative cardiologymphasic exercise testing?

- □ Yes (VO2 peak _ _ _ ml/min kg^-1 / AT _ _ _ ml/min kg^-1)

- □ No

**If emergency:** Yes (inpatient perioperative or elderly medicine)

**ECG (normal/AF rate 60-90/AF rate >90 or any other abnormal rhythm?):** □ None

**ECHO (LVEF _ _ _ %):** □ Coronary angiogram □ None

**Duration of operation:** _ _ _ mins

**Estimated blood loss:** _ _ _ ml

**Intra-operative interventions:** □ TXA □ RBC □ None

**If RBC, how many units?:** □ 1 □ 2 □ 3 □ 4 □ 5

**If RBC, Hb at transfusion:** □ _ _ _ g/L □ Not available

### Section 2: Intra-operative data fields

#### Prior abdo operations

- □ 1 □ 2 □ >2

**Urgency (NCEPOD):** □ Elective □ Urgent

**Primary diagnosis:** □ Benign □ Primary Malignancy only

**Primary indication:** □ Benign □ Primary Malignancy only

**WHO checklist:** □ Yes □ No

### Operation

**Approach:** □ Open □ Laparoscopic □ Laparoscopic-assisted

**Operative Contamination:** □ Clean □ Clean-contaminated □ Contaminated □ Dirty

**Peritoneal soiling:** □ Yes □ No

**Serosal fluid:** □ Localised pus □ Free content □ None

**WHO checklist:** □ Yes □ No

### Duration of operation

- _ _ _ mins

**Estimated blood loss:** _ _ _ ml

### Intra-operative interventions

**If RBC, how many units?:** □ 1 □ 2 □ 3 □ 4 □ 5

**If RBC, Hb at transfusion:** □ _ _ _ g/L □ Not available

### Section 3: Post-operative data fields

#### Critical care admission

- □ Yes, planned from theatre
- □ Yes, unplanned from theatre
- □ Yes, unplanned from ward

**If yes, cvc inserted?** □ Yes □ No

**Critical care bed days:** _ _ _ days

**Postop Hb (lowest):** _ _ _ g/L

**If RBC, how many units?:** □ 1 □ 2 □ 3 □ 4 □ 5

**IDA mx (Tick all that apply):** □ None

**Bleeding complication within 30 days (Tick all that apply):** □ Non-major bleeding (POD _ _ _)

**Major bleeding (POD _ _ _):** □ None

**Post-operative length of stay:** _ _ _ days

**Highest 30-day complication grade:** _ _ _

**30-day Reoperation:** □ Yes □ No

**30-day readmission:** □ Yes □ No (planned/unplanned?)

CASCADE Protocol v2.8 14/11/2021
<table>
<thead>
<tr>
<th>Postoperative outpatient VTE prophylaxis duration</th>
<th>None</th>
<th>If readmission, what was Hb (include the first blood test results on readmission)</th>
<th>If readmission, anaemia intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ None □ Yes, preop (≤ 7 days prior op) □ Yes, preop (8-42 days prior op) □ Yes, postop (POD_ _)</td>
<td>□ _ _ g/L □ Not available</td>
<td>□ None □ Iron (Oral / IV ?) □ RBC transfusion</td>
<td></td>
</tr>
<tr>
<td>If preop: Symptomatic? □ Yes □ No</td>
<td></td>
<td>(if RBC: □ 1 □ 2 □ 3 □ 4 □ ≥ 5 units)</td>
<td></td>
</tr>
<tr>
<td>If preop or postop: Vaccinated? □ Partial □ Full □ No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Postoperative outpatient VTE prophylaxis duration _ _ days

Discharged home on therapeutic anticoagulation (e.g. inpatient diagnosis of PE and/or DVT, or restarted on the therapeutic anticoagulation the patient was on prior to admission) (if DOAC: □ dabigatran □ rivaroxaban □ apixaban □ edoxaban □ betrixaban)
### Appendix B: Data Dictionary

#### Pre-operative Data Fields

<table>
<thead>
<tr>
<th></th>
<th>Required data (definition / comment)</th>
<th>Suggested source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Patient age (whole years at the time of operation)</td>
<td>Clinical letters / notes</td>
</tr>
<tr>
<td>2.</td>
<td>Patient sex</td>
<td>Clinical letters / notes</td>
</tr>
<tr>
<td>3.</td>
<td>Patient body mass index (BMI) (record to two decimal places)</td>
<td>Drug charts</td>
</tr>
<tr>
<td>4.</td>
<td>Patient ASA grade (Full ASA classification available at: <a href="https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system">https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system</a>)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>5.</td>
<td>Smoking status (Current, Previous (stopped smoking &lt;6 weeks), Previous (stopped smoking &gt;1 year), Never smoked)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>6.</td>
<td>Mode of smoking (Tobacco cigarettes, Electronic cigarettes or vapes, unknown)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>7.</td>
<td>Clinical Frailty scale (Full Clinical frailty scale available at: <a href="https://www.dal.ca/sites/gmr/our-tools/clinical-frailty-scale.html">https://www.dal.ca/sites/gmr/our-tools/clinical-frailty-scale.html</a>)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>8.</td>
<td>History of cardiovascular disease (myocardial infarction, angina, congestive cardiac failure, TIA/stroke, hypertension, peripheral vascular disease, atrial fibrillation, Deep vein thrombosis, pulmonary embolism)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>9.</td>
<td>History of respiratory disease (select option that best describes the patient's respiratory signs and chest x-ray (CXR) appearance)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>10.</td>
<td>History of COPD (Low Molecular Weight Heparin (LMWH), Warfarin, Direct acting oral anticoagulants (DOACs))</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>11.</td>
<td>History of chronic kidney disease (diet controlled, tablet controlled, insulin controlled)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>12.</td>
<td>History of liver cirrhosis</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>13.</td>
<td>History of diabetes mellitus (Type I / Type II)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>14.</td>
<td>Active cancer and/or cancer treatment (diet controlled, tablet controlled, insulin controlled)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>15.</td>
<td>Inflammatory bowel disease</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>16.</td>
<td>Management of iron-deficiency anaemia (oral or IV?) (Tranexamic acid / RBC transfusion) (If yes: 1, 2, 3, 4, 5 units)</td>
<td>Admissions clerking</td>
</tr>
<tr>
<td>17.</td>
<td>Pre-admission treatment (Aspirin, ACEi/ARB, β-blocker, α₂ agonist, rate controlling CCB, DHP CCB)</td>
<td>Clinical letters / notes PACS software</td>
</tr>
<tr>
<td>18.</td>
<td>Pre-admission therapeutic anticoagulation (Low Molecular Weight Heparin (LMWH), Warfarin, Direct acting oral anticoagulants (DOACs))</td>
<td>Clinical letters / notes PACS software</td>
</tr>
<tr>
<td>19.</td>
<td>Pre-admission blood tests (Haemoglobin (grams / litre) / Albumin (grams / litre) / Creatinine (umol/L))</td>
<td>Pathology systems</td>
</tr>
</tbody>
</table>

---

**Notes:**
- **Preoperative Data:**
  - **Patient age:** Years (whole years at the time of operation)
  - **Patient sex:** Male / Female
  - **Patient body mass index (BMI):** kg/m² (record to two decimal places)
  - **Patient ASA grade:** Grade I-V (Full ASA classification available at: https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system)
  - **Smoking status:** Current, Previous (stopped smoking <6 weeks), Previous (stopped smoking 6 weeks – 1 year), Never smoked
  - **Mode of smoking:** Tobacco cigarettes, Electronic cigarettes or vapes, unknown
  - **Clinical Frailty scale:** 1-3 / 4-6 / 7-9 (Full Clinical frailty scale available at: https://www.dal.ca/sites/gmr/our-tools/clinical-frailty-scale.html)
  - **History of cardiovascular disease:** Yes (myocardial infarction, angina, congestive cardiac failure, TIA/stroke, hypertension, peripheral vascular disease, atrial fibrillation, Deep vein thrombosis, pulmonary embolism) / No
  - **History of respiratory disease:** None / Dyspnoea on exertion or CXR: mild COPD / Dyspnoea limiting exertion to <1 flight or CXR: moderate COPD / Dyspnoea at rest/rate >30 at rest or CXR: fibrosis or consolidation
  - **History of COPD:** Yes / No
  - **History of chronic kidney disease:** Yes (I / II / IIIA / IIIB / IV / V) / No
  - **History of liver cirrhosis:** Yes / No
  - **History of diabetes mellitus:** Yes - Type I / Yes - Type II (diabetes controlled, insulin controlled) / No
  - **Active cancer and/or cancer treatment:** Yes / No
  - **Inflammatory bowel disease:** Yes / No

---

**Suggested sources:**
- **Clinical letters / notes**
- **Drug charts**
- **Anaesthetic notes**
- **Admissions clerking**
- **Clinical notes**
- **Admissions clerking**
- **Admissions clerking**
- **Admissions clerking**
- **Clinical notes**
- **Clinical notes**
- **Clinical notes**
- **Clinical notes**
- **Clinical notes**
- **Pathology systems**
<table>
<thead>
<tr>
<th>Intra-operative Data Fields</th>
<th>Required data (definition / comment)</th>
<th>Suggested source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Including this operation, how many abdominal operations has the patient had in the 30 day period prior to this procedure?</td>
<td>1 / 2 / &gt;2</td>
<td>– Operative note – Admissions clerking</td>
</tr>
<tr>
<td>2. Operative urgency (NCEPOD Classification of Intervention) (available at: <a href="https://www.ncepod.org.uk/classification.html">https://www.ncepod.org.uk/classification.html</a>)</td>
<td>Immediate (Immediate life, limb or organ-saving intervention - resuscitation simultaneous with intervention. Normally within minutes of decision to operate). Urgent (Intervention for acute onset or clinical deterioration of potentially life-threatening conditions, for those conditions that may threaten the survival of limb or organ, for fixation of many fractures and for relief of pain or other distressing symptoms. Normally within hours of decision to operate). Expedited (requiring early treatment where the condition is not an immediate threat to life, limb or organ survival. Normally within days of decision to operate). Elective (Intervention planned in advance of routine admission to hospital).</td>
<td>– Operative note – Admissions clerking</td>
</tr>
<tr>
<td>3. Primary indication</td>
<td>Malignant / Benign</td>
<td>– Operative note – Clinical notes – Theatre records</td>
</tr>
<tr>
<td>4. Operative procedure</td>
<td>Select main procedure from Appendix C (closest option from the drop-down list or enter as free text by selecting “other”).</td>
<td>– Operative note</td>
</tr>
<tr>
<td>5. Operative approach</td>
<td>Open (performed exclusively using instruments inserted into the abdomen through a surgical incision). Laparoscopic (performed exclusively using instruments inserted into the abdomen through small ports) or Laparoscopic-assisted (laparoscopic surgery in which an incision is enlarged to deliver a specimen or to insert a gloved hand into the abdomen). Laparoscopic converted to open (surgery planned to be performed laparoscopically but for unforeseen reasons the decision was made to change to an open approach). Robotic (robot-assisted surgery with no conversion to either laparoscopic or open approaches). Robotic converted to open (surgery planned to be performed robotically but for unforeseen reasons the decision was made to change to an open approach).</td>
<td>– Operative note</td>
</tr>
<tr>
<td>6. Operative contamination</td>
<td>Clean (Gastrointestinal (GI) and genitourinary (GU) tract not entered). Clean-Contaminated (GI or GU tracts entered but no gross contamination). Contaminated (GI or GU tracts entered with gross spillage or major break in sterile technique).</td>
<td>– Operative note</td>
</tr>
</tbody>
</table>

**Abbreviations:** ASA = American Society of Anaesthesiologists; Hb = Haemoglobin; LVEF = Left Ventricular Ejection Fraction PACS = Picture Archiving and Communication.
Dirty (There is already contamination prior to operation, e.g. faeces or bile).

<table>
<thead>
<tr>
<th>7. Peritoneal soiling</th>
<th>None / Serous Fluid / Localised Pus / Free bowel content (i.e. pus or blood)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Was the WHO checklist used?</td>
<td>Yes / No</td>
</tr>
<tr>
<td>9. Duration of operation</td>
<td>(mins)</td>
</tr>
<tr>
<td>10. Estimated blood loss</td>
<td>(Millilitres)</td>
</tr>
<tr>
<td>11. Intra-operative interventions</td>
<td>No / Tranexamic acid use / RBC transfusion (If yes: 1, 2, 3, 4, 5 units)</td>
</tr>
<tr>
<td>12. Haemoglobin at transfusion</td>
<td>Not available / Available</td>
</tr>
</tbody>
</table>

If available, please state value in grams/litre

Abbreviations: NCEPOD: National Confidential Enquiry into Patient Outcome and Death, RBC = Red Blood Cell, WHO = World Health Organisation

<table>
<thead>
<tr>
<th>Post-operative Data Fields</th>
<th>Required data (definition / comment)</th>
<th>Suggested sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Critical care admission (including intensive care and high dependency units)</td>
<td>Yes, planned admission from theatre / Yes, unplanned admission from theatre / Yes, unplanned admission from ward / No If yes, was a central venous catheter inserted?</td>
<td></td>
</tr>
<tr>
<td>2. Critical care bed days (if yes)</td>
<td>Number (days from first post-operative day to day of discharge from critical care. If the patient has not been discharged prior to the end of 30-day follow-up, enter ‘31’).</td>
<td></td>
</tr>
<tr>
<td>3. Postoperative haemoglobin</td>
<td>Not applicable / Available (day 0-1, day 2-3, day 4-6, last prior to discharge) If available, please state value in grams/litre Please record lowest Hb</td>
<td></td>
</tr>
<tr>
<td>4. Postoperative interventions for anaemia</td>
<td>None / iron supplementation (oral or IV?) / Tranexamic acid / RBC transfusion (If yes: 1, 2, 3, 4, 5 units)</td>
<td></td>
</tr>
<tr>
<td>5. Cardiovascular complications within 30 days (select all that apply)</td>
<td>None / Myocardial infarction / Myocardial injury / Non-fatal cardiac arrest / Coronary revascularisation / Pulmonary embolism (symptomatic non-fatal / asymptomatic) / Deep venous thrombosis (proximal / distal? symptomatic / asymptomatic?) / New onset Atrial fibrillation / Stroke *see Appendix D for definitions Please indicate the Post-operative day of the event(s) selected (0 if the same day of operation)</td>
<td></td>
</tr>
<tr>
<td>6. Bleeding complications within 30 days</td>
<td>None / Major bleeding / Clinically relevant non-major bleeding *see Appendix D for definitions Please indicate the Post-operative day occurred (0 if the same day of operation)</td>
<td></td>
</tr>
<tr>
<td>7. Post-operative length of stay</td>
<td>Number (days between from the first post-operative day to day of discharge. If the patient has not been discharged prior to the end of 30-day follow-up, enter ‘31’).</td>
<td></td>
</tr>
<tr>
<td>8. Highest 30-day complication grade</td>
<td>None / Clavien-Dindo Grade I-V (see Appendix D for the full 7-point Clavien-Dindo scale). If grade V, was death cardiac, PE or non-cardiac? If grade V, please indicate postoperative day death occurred (see Appendix D for definitions)</td>
<td></td>
</tr>
</tbody>
</table>

*see Appendix D for definitions
<table>
<thead>
<tr>
<th></th>
<th>9. 30-day Reoperation</th>
<th>Yes / No</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.</td>
<td>30-day Readmission</td>
<td>Yes - planned / Yes-unplanned / No (this applies if patient had died during initial admission)</td>
</tr>
</tbody>
</table>
| 11. | 30-day postoperative COVID status (COVID Must be diagnosed via SARS-CoV-2 swab (PCR) test or Rapid antigen test (e.g. lateral flow test)) | None / Preoperative (≤7 days prior operation) / Preoperative 8-42 days prior operation) / Postoperative (i.e., within 30 days postop)  
If postoperative: what day were they COVID positive postoperatively?  
If preoperative: are you still symptomatic (yes/no)?  
If preoperative or postoperative: were you vaccinated (no / partial / full)? |
| 12. | Haemoglobin on readmission | Not available / Available  
If available, please state value in grams/litre |
| 13. | Interventions for anaemia at readmission | None / iron supplementation (Oral / Intravenous?), blood transfusion (If yes: 1, 2, 3, 4, ≥5 units) |
| 14. | Postoperative outpatient VTE prophylaxis duration | Number (days of pharmacological VTE prophylaxis the patient was discharged home with) |
| 15. | Postoperative outpatient VTE prophylaxis | None / Low molecular weight heparin / Direct oral anticoagulants (dabigatran, rivaroxaban, apixaban, edoxaban or betrixaban?) / Warfarin  
Was the patient discharged home on therapeutic anticoagulation (e.g. inpatient diagnosis of PE and/or DVT, or restarted on the therapeutic anticoagulation the patient was on prior to admission)? |
## Appendix C: Included Operative Procedures

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Gastrointestinal</td>
<td>• Oesophagogastrectomy (excision of oesophagus and stomach)</td>
</tr>
<tr>
<td></td>
<td>• Oesophagectomy (excision of oesophagus).</td>
</tr>
<tr>
<td></td>
<td>• Gastrectomy (excision of stomach).</td>
</tr>
<tr>
<td></td>
<td>• Duodenectomy / Small bowel resection (excision of small bowel).</td>
</tr>
<tr>
<td>Hepatopancreatobilary</td>
<td>• Cholecystectomy (total or partial excision of gallbladder).</td>
</tr>
<tr>
<td></td>
<td>• Hepatectomy (segmental or partial excision of liver)</td>
</tr>
<tr>
<td></td>
<td>• Excision of bile</td>
</tr>
<tr>
<td></td>
<td>• Pancreatectomy (total or partial excision of pancreas, including Whipple’s procedure).</td>
</tr>
<tr>
<td></td>
<td>• Splenectomy (total or partial excision of spleen).</td>
</tr>
<tr>
<td>Lower gastrointestinal</td>
<td>• Appendicectomy (Total or partial excision of appendix).</td>
</tr>
<tr>
<td></td>
<td>• Panproctocolectomy (total excision of colon and rectum).</td>
</tr>
<tr>
<td></td>
<td>• Completion proctectomy</td>
</tr>
<tr>
<td></td>
<td>• Pancolectomy (total excision of colon).</td>
</tr>
<tr>
<td></td>
<td>• Subtotal colectomy</td>
</tr>
<tr>
<td></td>
<td>• Ileocaecal resection</td>
</tr>
<tr>
<td></td>
<td>• Right colectomy (excision of right colon; including extended).</td>
</tr>
<tr>
<td></td>
<td>• Transverse colectomy (excision of transverse colon).</td>
</tr>
<tr>
<td></td>
<td>• Left colectomy (excision of left colon; including extended).</td>
</tr>
<tr>
<td></td>
<td>• Sigmoid colectomy (excision of sigmoid colon).</td>
</tr>
<tr>
<td></td>
<td>• Excision of rectum (including abdominoperineal resection, anterior resection or Hartmann's procedure).</td>
</tr>
<tr>
<td>Stoma</td>
<td>• Formation, reversal or closure of ileostomy.</td>
</tr>
<tr>
<td></td>
<td>• Formation, reversal or closure of colostomy (include reversal of Hartmann’s).</td>
</tr>
<tr>
<td></td>
<td>• Formation of urostomy (including ileal conduit, Kock pouch, Indiana pouch, Mitrofanoff procedure and ileal neobladder).</td>
</tr>
<tr>
<td>Vascular</td>
<td>• Open replacement or repair of aneurysmal segment of aorta.</td>
</tr>
<tr>
<td></td>
<td>• Vascular bypass surgery including abdominal component (e.g. aortobifemoral or aortounifemoral bypass)</td>
</tr>
<tr>
<td>Endocrine</td>
<td>• Adrenalectomy (excision of adrenal gland).</td>
</tr>
<tr>
<td>Transplant</td>
<td>• Transplantation of liver</td>
</tr>
<tr>
<td></td>
<td>• Transplantation of pancreas (or islet cell transplantation)</td>
</tr>
<tr>
<td></td>
<td>• Transplantation of kidney</td>
</tr>
<tr>
<td></td>
<td>• Live donor nephrectomy (excision of kidney for transplant indication)</td>
</tr>
<tr>
<td></td>
<td>• Transplantation of bowel</td>
</tr>
<tr>
<td>Gynaecology</td>
<td>• Trachelectomy or cervicectomy (excision of cervix uteri).</td>
</tr>
<tr>
<td></td>
<td>• Hysterectomy (total or partial excision of uterus).</td>
</tr>
<tr>
<td></td>
<td>• Salpingo-oophorectomy (total or partial excision of fallopian tube or ovary).</td>
</tr>
<tr>
<td>Category</td>
<td>Description</td>
</tr>
<tr>
<td>------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Urology</td>
<td>- Nephrectomy (total or partial excision of kidney).</td>
</tr>
<tr>
<td></td>
<td>- Ureterectomy (excision of ureter).</td>
</tr>
<tr>
<td></td>
<td>- Cystectomy (total or partial excision of bladder).</td>
</tr>
<tr>
<td></td>
<td>- Prostatectomy (total or partial excision of prostate).</td>
</tr>
<tr>
<td>Hernia</td>
<td>- Anterior abdominal wall incisional hernia repair.</td>
</tr>
<tr>
<td></td>
<td>- Parastomal hernia repair.</td>
</tr>
<tr>
<td>Other</td>
<td>- Multivisceral resection (resection of several viscera in combination, including pelvic exenteration)</td>
</tr>
<tr>
<td></td>
<td>- Other (free text)</td>
</tr>
</tbody>
</table>
Appendix D: Definitions of Key Outcomes

A. Cardiovascular complications:
There are several factors which can increase the risk of postoperative cardiovascular complications in the perioperative content, particularly in patients with pre-existing cardiac disease.

There are heterogenous definitions with the medical literature regarding which conditions should be considered postoperative cardiovascular complications (and how these should be defined). This makes it difficult to interpret new studies in the context of the existing literature, and so means it often is not possible to pool the data within systematic reviews.

A recent systematic review and international consensus process\textsuperscript{13} recommended redefining postoperative cardiovascular outcomes that can be used in future trials to measure the effectiveness of perioperative interventions. The following outcomes are included within the new definition of perioperative cardiovascular adverse events:

1. **Atrial fibrillation:** New onset of irregularly irregular heart rate in the absence of P wave lasting at least 30 s or for the duration of the ECG recording (if <30 s)

2. **Myocardial infarction:** Acute myocardial injury with clinical evidence of acute myocardial ischaemia and with detection of an increase or decrease in cardiac troponin (cTn) values with at least one value above the 99th percentile upper reference limit (URL) and at least one of the following:
   a. Symptoms of myocardial ischaemia
   b. New ischaemic ECG changes
   c. Development of pathological Q waves
   d. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology
   e. Identification of a coronary thrombus by angiography or autopsy - Post-mortem demonstration of acute atherothrombosis in the artery supplying the infarcted myocardium.

Cardiac death in patients with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes before cTn values become available.
3. **Myocardial injury**: Detection of an elevated cTn value above the 99th percentile URL is defined as myocardial injury. The injury is considered acute if there is an increase or decrease in cTn values
   a. Note: it is not clinically possible to distinguish which increases of cTn levels are attributable to which mechanisms
   b. A diagnosis of myocardial infarction requires an increase of cTn values and evidence of myocardial ischaemia that may be evident from the peri- and postoperative period (e.g. ST segment changes on telemetry/ECG, repeated episodes of hypoxia, hypotension, tachycardia, or imaging evidence of myocardial injury)
   c. In the absence of evidence for acute myocardial ischaemia, the diagnosis is acute myocardial injury

4. **Coronary revascularisation**: Cardiac revascularisation procedure was defined as percutaneous coronary intervention or coronary artery bypass graft surgery within 30 days of the index surgery.

5. **Cardiac death**: Death with a vascular cause and included those deaths after a myocardial infarction, cardiac arrest, and cardiac revascularisation procedure.
   a. Excludes:
      i. Death after pulmonary embolism
      ii. Death after haemorrhage
      iii. Death after multi-organ failure
      iv. Cause of deaths unknown

6. **Non-fatal cardiac arrest**: Successful resuscitation from either documented or presumed ventricular fibrillation, sustained ventricular tachycardia, asystole, or pulseless electrical activity requiring cardiopulmonary resuscitation, pharmacological therapy, or cardiac defibrillation

7. **Major adverse cardiac event**: A composite outcome that should include:
   a. Cardiac death (as defined previously)
   b. Myocardial infarction (as defined previously)
c. Non-fatal cardiac arrest (as defined previously)
d. Coronary revascularisation (as defined previously) within 30 days of index surgery
e. *Excludes* - Pulmonary embolism, haemorrhage, deep venous thrombosis, all-cause mortality

8. **Pulmonary embolism may present as sudden death, breathlessness, faintness, collapse or chest pain.** Diagnosis of pulmonary embolism requires any one of the following:
   a. A high probability ventilation/perfusion lung scan
   b. An intraluminal filling defect of segmental or larger artery on a helical CT scan
   c. An intraluminal filling defect on pulmonary angiography
d. A positive diagnostic test for deep venous thrombosis (e.g. positive compression ultrasound) and one of the following:
   i. Non-diagnostic (i.e. low or intermediate probability) ventilation/perfusion lung scan
   ii. Non-diagnostic (i.e. sub-segmental defects or technically inadequate study) helical CT scan

9. **Deep vein thrombosis (DVT) is defined as the formation of a thrombus (blood clot) in a deep vein.**
   a. Diagnosis of DVT requires any one of the following:
      i. A persistent intraluminal filling defect on contrast venography
      ii. Non-compressibility of one or more venous segments on B-mode compression ultrasonography
      iii. A clearly defined intraluminal filling defect on contrast enhanced CT
   b. DVT can be divided in proximal and distal\(^3\):
      i. Proximal DVT is defined as DVT in the popliteal vein and/or higher (femoral vein, common femoral vein, iliac vein, vena cava).
      ii. Distal DVT (calf DVT) is defined as DVT in at least 1 of the 3 major paired veins (posterior tibial, anterior tibial, peroneal) in the calf, below the popliteal vein.
   c. DVT can be also divided in symptomatic and asymptomatic\(^3\):
      i. Symptomatic DVT is defined as leg pain and swelling resulting from thrombotic occlusion of a major leg vein. It requires specific investigation and treatment.
ii. Asymptomatic DVT is defined as DVT detected by screening with ultrasound or ascending venography, and with no associated symptoms (leg pain and swelling).

10. **Stroke**: Embolic, thrombotic, or haemorrhagic event lasting at least 30 min with or without persistent residual motor, sensory, or cognitive dysfunction; if the neurological symptoms continue for >24hrs, a person is diagnosed with stroke, and if lasting <24 h the event is defined as a transient ischaemic attack.\textsuperscript{32}
B. Bleeding outcomes

Bleeding is an important safety outcome in studies exploring the use of anticoagulation pharmacological therapies. To ensure consistency across research studies, a validated and clinically relevant classification should be used. In the CASCADE study, we have adopted the definitions of bleeding outcomes recommended by the European Medicines Agency.

**Major bleeding**\(^{33}\) is defined as a bleeding event that meets at least one of the following criteria:

- fatal bleeding
- critical bleeding (intracranial, intraocular, intraspinal, pericardial, retroperitoneal, in a non-operated joint, or intramuscular with compartment syndrome)
- clinically overt bleeding (at surgical or extrasurgical site) associated with a decrease in the haemoglobin level of more than 2 g/dL (20 g/l; 1.24 mmol/L) compared with the pre-operative level
- clinically overt bleeding (at surgical or extrasurgical site) leading to transfusion of two or more units of whole blood or packed cells
- bleeding located at the surgical site and leading to re-operation or to any unusual medical intervention or procedure for relief (e.g. draining or puncture of an haematoma at the surgical site, transfer to an ICU or emergency room).

**Clinically relevant non-major bleeding**\(^{33,34}\) is defined as any clinically overt bleeding that:

- does not meet the criteria for major bleeding BUT
- requires medical attention (e.g.: hospitalisation, medical treatment for bleeding) AND/OR
  a change in antithrombotic therapy (including discontinuation or down-titration) AND/OR
  any other bleeding type considered to have clinical consequences for a patient.

Examples of clinically relevant non-major bleeding are:

- multiple-source bleeding;
- spontaneous haematoma >25 cm\(^2\), or > 100 cm\(^2\) if there was a traumatic cause;
- intramuscular haematoma documented by ultrasonography without compartment syndrome;
- excessive wound haematoma not requiring draining or puncture;
- macroscopic haematuria (spontaneous or lasting >24 h if associated with an intervention);
- epistaxis or gingival bleeding that requires tamponade or other medical intervention;
haemoptysis, haematemesis or spontaneous rectal bleeding requiring endoscopy or other medical intervention.
C. Clavien-Dindo Classification System:

Adverse post-operative events may be classified in different ways:

- **Failure of treatment** - This occurs when the original surgery fails to achieve its intended benefits; for example, persistent pain following laparoscopic cholecystectomy or tumour recurrence following cancer surgery.

- **Sequelae**: The recognised consequences of a given procedure; for example, gut malabsorption following a large small bowel resection or immune deficiency following splenectomy.

- **Complication**: Any deviation from the normal post-operative course that has an adverse effect on the patient and is not either a treatment failure or sequel.

In the Clavien-Dindo classification 35, the factor determining the severity of a complication is the treatment required. Consequently, a given complication may be graded differently depending on how it has been managed. For example, an anastomotic leak may be managed just with antibiotics if it is contained (grade II) or it may require re-operation under anaesthetic (grade IIIb).

Some other considerations:

- Intra-operative complications are not considered unless they have an adverse effect on the patient post-operatively. The only exception to this is intra-operative death; this is classified as grade V.

- All post-operative adverse events are included, even when there is no direct relationship to the surgery.

- All adverse events within the follow-up period (30 days) are included, even after following discharge.

- Diagnostic procedures are not included. For example, a diagnostic oesophagoduodenoscopy (OGD) to look for a source of bleeding without any intervention would not be considered a complication, but a therapeutic OGD with clipping of a bleeding vessel would be considered a grade IIIa complication. Since negative exploratory laparotomies are considered to be diagnostic procedures, they should not be recorded as complications.
<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition (examples listed in italics)</th>
</tr>
</thead>
</table>
| I     | Any deviation from the normal postoperative course without the need for pharmacological (other than “allowed therapeutic regimens”), surgical, endoscopic or radiological intervention. Allowed therapeutic regimens are: selected drugs (antiemetics, antipyretics, analgesics, diuretics and electrolyte replacement), physiotherapy and wound infections opened at the bedside but not treated with antibiotics.  
**Examples:** Ileus (deviation from the norm); hypokalaemia treated with K; nausea treated with cyclizine; acute kidney injury treated with intravenous fluids. |
| II    | Requiring pharmacological treatment with drugs beyond those allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.  
**Examples:** Surgical site infection treated with antibiotics; myocardial infarction treated medically; deep venous thrombosis treated with enoxaparin; pneumonia or urinary tract infection treated with antibiotics; blood transfusion for anaemia. |
| IIIa  | Requiring surgical, endoscopic or radiological intervention, not under general Anaesthetic (GA).  
**Examples:** Therapeutic endoscopic therapy (do not include diagnostic procedures); interventional radiology procedures. |
| IIIb  | Requiring surgical, endoscopic or radiological intervention, under GA.  
**Examples:** Return to theatre for any reason. |
| IVa   | Life-threatening complications requiring critical care management with single organ dysfunction, or neurological complications including brain haemorrhage and ischemic stroke (excluding TIA).  
**Examples:** Single organ dysfunction requiring critical care management, e.g. pneumonia with ventilator support, renal failure with filtration; SAH; stroke |
| IVb   | Life-threatening complications requiring critical care management with multi-organ dysfunction. |
Appendix E: Steps for successful inclusion of your centre

1. Contact your local lead about participation in the CASCADE study. They will connect you to any other interested medical students and foundation doctors.

2. Form a mini-team of up to three collaborators. A medical student should be co-ordinating the team and leading audit registration and data collection. The student should be supported by at least one motivated doctor. This can be any doctor from junior doctor to consultant grade. The collaborating doctor could be:
   - A junior (e.g. FY1, FY2, CT1, CT2) you know on rotation in the surgical department.
   - If you don’t know any juniors working in the surgical teams, try walking onto the ward to find an FY1 to ask who the best FY1/2 to help the audit is; this approach often succeeds. If there is an FY1/2 on an academic rotation, they may be well placed to help you.
   - The consultant who will be supervising your surgical placement.
   - The consultant lead for audit in the department of surgery.
   - A member of your local registrar-led research collaborative (http://www.asit.org/resources/collaboratives).

3. Up to four teams of students can cover consecutive 2-week periods, working together to deliver 30-day follow-up. Discuss with your regional lead to establish a 14-day consecutive data collection period from below to suit your availability:
   - Period 1: 00:00 24th Jan 2022 - 23:59 06th Feb 2022 (+ 30 Day Follow-up)
   - Period 2: 00:00 07th Feb 2022 - 23:59 20th Feb 2022 (+ 30 Day Follow-up)
   - Period 3: 00:00 21st Feb 2022 - 23:59 06th Mar 2022 (+ 30 Day Follow-up).
   - Period 4: 00:00 07th Mar 2022 - 23:59 20th Mar 2022 (+ 30 Day Follow-up).
   - Period 5: 00:00 21st Mar 2022 - 23:59 03rd Apr 2022 (+ 30 Day Follow-up).

4. Ensure that you secure formal audit approval from your hospital’s clinical audit department prior to commencing data collection. This may seem daunting at first but is in fact quite straightforward. Every hospital has an audit department and it is a simple case of approaching them with the information we have prepared in this protocol and applying this to the local audit registration form. You will need a local consultant to support you and sign the hospital’s audit form (this should be the same consultant which is supervising the mini-teams). Ensure that the audit department know that this is part of a national project and that you will enter data on REDCap.
It is essential that you begin this process immediately; approval can take up to a month or more. You may have to contact or even visit the hospital before your placement starts to ensure that you will be ready. If you have any difficulties contact your regional lead, your supervising junior doctor/consultant or the steering committee.

5. Contact your hospital’s Caldicott Guardian (often the medical director - the audit department can help you find out who this is) to request permission to submit data to REDCap. You need additional permission from the Caldicott Guardian to store any patient numbers on REDCap.

6. Agree with your audit office and Caldicott Guardian how you will facilitate 30-day follow-up. You will require the hospital number for each patient to undertake follow-up, and so this needs to be stored in a safe and secure manner until accessed for 30-day follow-up, in line with local and national data governance guidance. This can be within the hospital site (paper or computer), or on REDCap (if permission from the Caldicott Guardian has been obtained).

7. Once the audit is registered and you have Caldicott Guardian approval, please forward evidence of this to your regional lead. REDCap accounts will not be issued until proof of audit registration AND Caldicott approval has been received.

8. Arrange to meet with the other members of your mini-team, including the junior doctor and, if possible, supervising consultant. If possible, it is also highly recommended to meet with the preceding mini-team at your centre (this would ideally include a period of shadowing):
   - They will have a lot of helpful advice regarding what worked well. In your mini-team, agree in advance who will be responsible for each stage of the project (e.g. identifying patients, collecting baseline data, completing follow-up, data entry to REDCap).
   - Talk through how you will identify patients and collect required data, it will be particularly helpful if the consultant is present to offer guidance regarding this. Agree who will access blood test results; will students have a login or will the junior doctor check the results?

9. Identify all patients fitting the inclusion criteria within your specified two-week window. Contact your regional lead with any questions or issues that may arise over your data collection period.

10. Regularly follow-up for information on complications over the 30-day post-operative period. This study is prospective, so you should not wait until the end of the post-operative period to
follow-up patients (this would be retrospective). Discuss the best way to follow up patients with the consultant supervising your audit, as this will vary from centre to centre.

Be proactive in identifying post-operative adverse events, as this will prevent under-estimation of true complication rates. Remember that in this audit no changes to normal patient follow-up should be made.

Strategies for identifying complications in the follow-up period include:

- Regularly reviewing patient notes to identify in-hospital complications.
- Reviewing clinic notes and clinic letters, if seen in clinic by 30 days.
- Checking electronic systems and handover lists for re-admissions.
- Checking for A&E re-attendances.

If case notes are reviewed shortly prior to discharge they do not be need to be requested/retrieved again for follow-up at 30-days, but do check electronic records for discharge letters, clinic letters, re-admissions.

11. Ensure all data has been uploaded to the REDCap system by the data collection deadline, and you have completed all fields, avoiding missing data points. If more than 5% of patients at your centre have missing data, your centre cannot be included in the CASCADE dataset and your name will be withdrawn from the author list.

12. It is a condition of participation in CASCADE that following completion of the audit at your centre you must ensure that your local results are presented to your hospital’s surgical department and/or reported back to the audit department. You may also like to return to present again at a later date, when the final national results of CASCADE become available.
Appendix F: Confirmation of Audit Status

South East Scotland Research Ethics Service

Date: 09/05/2021
Your Ref: NR/161A56
Email: Helen.Newbery@nhslothian.scot.nhs.uk

Dr. Aya Riad,
STARSurg,
The University of Edinburgh.

Dear Dr. Riad,

Project Title: CArdiovaSCulAr outcomes after major abDominal surgery (CASCADE)

You have sought advice from the South East Scotland Research Ethics Service on the above project. This has been considered by the Scientific Officer and you are advised that, based on the submitted documentation it does not need NHS ethical review under the terms of the Governance Arrangements for Research Ethics Committees (A Harmonised Edition).

The advice is based on the following:

- The project is limited to using data obtained as part of usual care, but note the requirement for Caldicott Guardian approval for the use or transfer of person-identifiable information within or from an organisation

If the project is considered to be health-related research you will require a sponsor and ethical approval as outlined in The Research Governance Framework for Health and Community Care. You may wish to contact your employer or professional body to arrange this. You may also require NHS management permission (R&D approval). You should contact the relevant NHS R&D departments to organise this.

For projects that are not research and will be conducted within the NHS you should contact the relevant local clinical governance team who will inform you of the relevant governance procedures required before the project commences.

This letter should not be interpreted as giving a form of ethical approval or any endorsement of the project, but it may be provided to a journal or other body as evidence that NHS ethical approval is not required. However, if you, your sponsor/funder feel that the project requires ethical review by an NHS REC, please write setting out your reasons and we will be pleased to consider further. You should retain a copy of this letter with your project file as evidence that you have sought advice from the South East Scotland Research Ethics Service.

Yours sincerely,

Helen Newbery
Scientific Officer
South East Scotland Research Ethics Service

CASCADE Protocol v2.8 14/11/2021
Appendix G: References

https://rcoa.ac.uk/gpas/chapter-2
https://www.rcoa.ac.uk/gpas/chapter-4

