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Outcome Monitoring After Cardiac Surgery (OMACS): a single-centre prospective cohort study of cardiac surgery patients

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ABSTRACT

Introduction More than 30 000 cardiac surgery procedures are performed in the UK each year, however, postoperative complications and long-term failure of interventions are common, leading to repeated surgeries. This represents a significant burden on the patient and health service. Routinely, patients are discharged to their general practitioner 6 weeks postoperatively and research studies typically only report short-term outcomes up to 1 year after surgery, together this makes long-term outcomes of cardiac surgery difficult to monitor. Further, traditional research methods have yet to advance understanding of what causes early complications and why surgical interventions fail.

Methods and analysis This prospective cohort study will characterise participants undergoing cardiac surgery at baseline, describe short-term, medium-term and long-term health outcomes postoperatively and collect tissue samples. All eligible adult patients undergoing cardiac surgery at the Bristol Heart Institute, UK will be approached for consent. Recruitment is expected to continue for up to 10 years resulting in the largest cohort of cardiac patients reported to date. Blood, urine and waste tissue samples will be collected during admission. Samples, along with anonymised data, will be used to investigate outcomes and inform predictive models of complications associated with cardiac surgery.

Data about the surgical admission will be obtained from hospital databases and medical notes. Participants may be monitored up to 5 years postoperatively using data obtained from NHS digital. Participants will complete health questionnaires 3 months and 12 months postoperatively.

The analysis of data and tissue samples to address specific research questions will require separate research protocols and ethical approval.

Ethics and dissemination This study was approved by the East Midlands Nottingham 2 Research Ethics Committee.

Findings will be disseminated through peer-reviewed publications and presentation at national and international meetings. Participants will be informed of results in annual newsletters.

Trial registration number ISRCTN90204321.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A prospective observational cohort study based in a research active cardiac centre in the UK which aims to create a novel dataset of short-term, medium-term and long-term complication outcomes after cardiac surgery.
⇒ High-quality follow-up data will be coupled with preoperative and early postoperative biological sampling, to facilitate future studies linking perioperative markers with outcomes.
⇒ This large ongoing study has the potential to incorporate multiple Studies Within A Trial, which will inform the conduct of future cardiac research studies.
⇒ This study is an efficient and cost-effective method of obtaining information that can be used to evaluate promising interventions in the longer term.
⇒ The requirement for sponsorship and ethical approval for each study analysing the samples can cause slight delays but also ensures all studies using the samples are high quality.

INTRODUCTION

Cardiac surgery is a common procedure in the UK, with the National Adult Cardiac Surgery Audit reporting 31 046 cases carried out in 2019/2020. The most common procedure by far is coronary artery bypass grafting (CABG), accounting for almost 50% of all cardiac surgery cases. This is followed by Aortic Valve Replacements (AVR) or a combination of AVR with another procedure.[1] Cardiac surgery is associated with a high rate of complications in the short term and long term, and surgical interventions may fail over time leading to repeated surgeries. This results in a high burden on patients and the health service.

The risk of developing postoperative complications is dependent on numerous factors including surgery type, patient age and underlying comorbidities. Broadly, acute

kidney injury (AKI) is reported to occur in up to 40% of cases[2–4] with 1%–2% of cases requiring dialysis,[3] atrial fibrillation (AF) in up to 65% of cases depending on surgery type,[2 5] myocardial infarction (MI) in up to 10% of cases[2] and stroke in up to 3% of cases.[1 2 6]

In the longer term, patients may experience recurrence of symptoms as the surgical intervention fails. For example, saphenous vein graft occlusion after CABG occurs in 12% of cases in the first 6 months and up to 40%–50% of cases within 10–15 years.[7 8]

There is currently no mechanism to monitor rates of long-term surgical complications or failures of surgical interventions. Typically, cardiac surgery research studies report short-term outcomes such as mortality and major adverse cardiovascular events (MACE) up to 1 year postoperatively . In addition, patients are routinely discharged to the care of their general practitioner 6 weeks postoperatively and no longer receive care from, nor are followed up by, the cardiac surgery team.

The Outcome Monitoring After Cardiac Surgery (OMACS) study will enable us to record long-term outcomes from patients undergoing cardiac surgery at the Bristol Heart Institute (BHI). The BHI is a large tertiary cardiac centre located in the UK, performing up to 1600 cardiac surgery cases a year. Participants will be monitored during the immediate postoperative period, with follow-up questionnaires at 3 and 12 months and passive follow-up for up to 5 years after their cardiac surgery. This will provide high-quality data to answer questions about complications and return of symptoms after surgery, and help examine why interventions fail. Data will be collected to characterise the demographic and clinical profile of participants undergoing cardiac surgery, the frequencies of in-hospital complications after surgery and long-term outcomes.

Traditional research methods such as modelling or biomarker analysis have not yet been successful in advancing an understanding of early complications or failure of cardiac surgery interventions, and the mechanisms of how they develop. This study will allow the application of large-scale genomic[9] and metabolomic[10 11] approaches to predict complications and applied epidemiological techniques to investigate causality[12–14] and has the potential to advance mechanistic understanding and streamline therapeutic development.[15]

This protocol describes an efficient and cost-effective method of obtaining information that can be used to evaluate evolving clinical practice in the longer term. The information will support the studies of the cardiovascular theme of the National Institute for Health and Care Research (NIHR) Bristol Biomedical Research Centre (BRC-CV) and will provide a bank of quality, ready-to-use data with linked biological samples for use in observational studies and to inform the design of future prospective studies. A further benefit of this study design and long recruitment period is that it will enable multiple Studies Within A Trial (SWATs) to be incorporated. These will provide high-quality evidence for the assessment of measures designed to improve recruitment and retention to future clinical studies.

METHODS AND ANALYSIS

The primary objective of this study is to create a bank of samples and data that may be used by secondary researchers. The research questions and outcomes will be described in an analysis plan or protocol for each secondary study.

Some specific outcomes will be described as part of the OMACS protocol and these are as follows: occurrence of MACE (defined as cardiovascular death, non-fatal MI and non-fatal stroke), all-cause mortality, incidence of postoperative complications including the components of MACE and including but not limited to AKI, AF, infection and reoperation rates. We will also analyse quality of life at 3 and 12 months measured by the Coronary Revascularisation Outcome Questionnaire (CROQ) or Short-Form-12 (SF-12) questionnaire, treatments/investigations undertaken during course of usual care and National Health Service (NHS) resource use.

Study design

This single-centre prospective cohort study will characterise the cohort at baseline, use in-hospital and Hospital Episode Statistics (HES) data provided by NHS Digital to describe short-term, medium-term and long-term health outcomes and collect biological samples from consenting participants who have had cardiac surgery. The study will follow participants for up to 5 years using HES data.

Figure 1 shows the participant pathway through the study.

Study population

Eligible patients over the age of 18 undergoing cardiac surgery at the BHI (University Hospitals Bristol and Weston NHS Foundation Trust) will be approached for consent to take part in the study.

The only exclusion criteria are as follows: patients whose main residence is outside of the UK, patients lacking capacity to give informed consent and prisoners.

Recruitment is expected to continue for up to 10 years, subject to funding. The majority of patients will be approached preoperatively for consent by a research nurse. Alternatively, consent for data collection postoperatively may be obtained in person or by post. Participants can consent to data collection only with no active participation; consent to give biological samples and consent to participation in follow-up in addition to data collection.

Research procedures

If consent is given for biological samples, participants will have blood, urine and waste samples taken during their hospital admission. Samples will be collected preoperatively at induction of anaesthesia and at 2 and 24 hours postoperatively. The maximum amount of blood taken during the study will be 100 mL, however, the exact

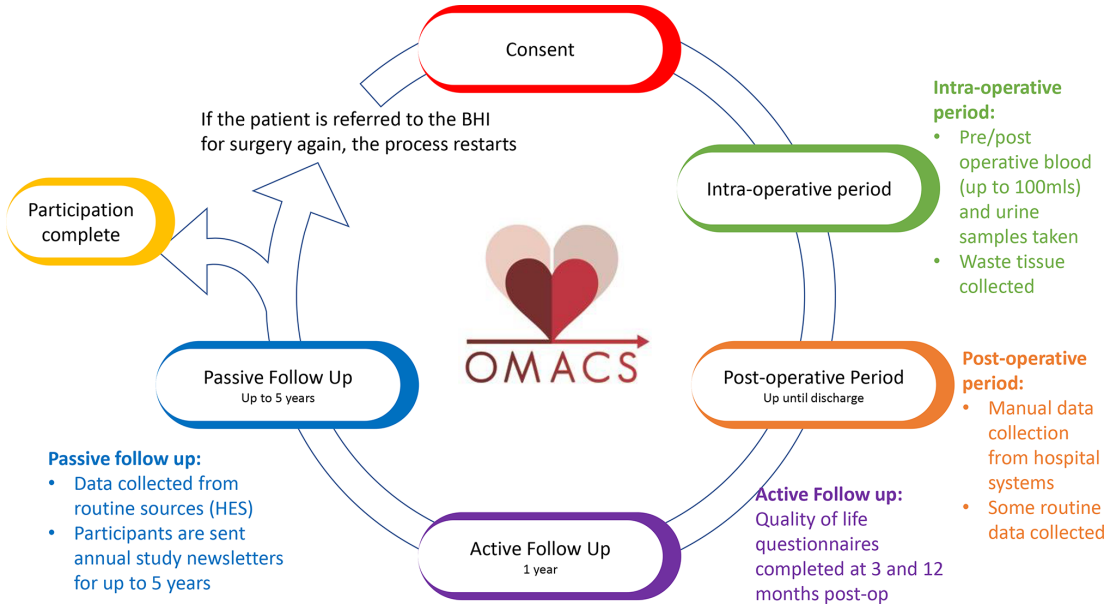

Figure 1 Participant pathway for the Outcome Monitoring After Cardiac Surgery (OMACS) study. Participants remain in the OMACS study for up to 5 years. In-hospital data will be collected from hospital data systems and entered into a bespoke study database. Patients will be actively followed up for 12 months postsurgery using quality of life questionnaires relevant to their surgery, completed at 3 and 12 months postoperatively. Participants will be further monitored passively up to 5 years using data from National Health Service (NHS) digital.

timing and volume of sampling may vary dependent on the requirements of the specific analysis the samples are designated for. In addition, tissue and fluids that are routinely removed as part of the operation will be kept (and not discarded as per routine care). Waste tissue samples will include, but not be limited to, pericardial fluid, pieces of heart tissue and saphenous vein removed during the operation.

Samples may be analysed immediately but the majority will be frozen for future analyses as part of secondary studies. Samples will be stored long term in a licensed biobank.

Data collection

In-hospital data from the participant's admission will be obtained from medical records, in bulk from hospital systems including Medway (the patient administration database used by the University Hospitals Bristol and Weston NHS Foundation Trust), electronic cardiac intensive care unit records, outcome data from Patient Administration and Tracing System or haematology and biochemistry systems. Data on in-hospital complications will be collected on specifically designed case report forms (CRFs) from paper and electronic medical notes and entered onto the specially designed and user-restricted OMACS database. The bespoke database is programmed to automatically validate data, ensuring consistency and quality. Data quality will be monitored on an ongoing basis.

Long-term outcome data up to 5 years postoperatively will be obtained from HES. An advantage of HES is that we will be able to record admissions to other hospitals in England.

Participants will be asked to complete short health questionnaires at 3 months and 12 months postoperatively. Participants undergoing CABG surgery, including those having CABG surgery alongside another procedure will receive the validated CROQ.[16 17] Participants who have had other operation types will be sent the SF-12 V.2 health questionnaire.[18]

Analysis of data

Recruitment and retention rates will be described. The frequency of MACE (and the individual component events), the time to first MACE event, the time to death and quality of life at 3 and 12 months will also be described. The frequency of different outcome events for different patient populations will be described to inform sample size calculations of future randomised controlled trials. The populations analysed for this purpose will be dependent on the proposed trial inclusion criteria.

The analyses of the OMACS data pertaining to specific observational research questions will be described in the protocol for those studies.

We will develop algorithms to check for data quality and consistency between data sources (eg, events identified through the CROQ and HES). Event rates will also be compared against the published literature to check for validity against national databases.

Patient and public involvement

The Bristol BRC-CV has an engaged cardiovascular patient advisory group (PAG). At the beginning of the OMACS study, the BRC-CV PAG provided in depth feedback on the Participant Information Leaflet and consent form. Subsequent amendments to the protocol and study

documents were also reviewed by the group and the documents were updated in line with their comments.

Participants will be informed of studies which use samples and data collected in the OMACS study through annual newsletters, which they can opt into receiving for 5 years postoperatively. The study newsletters will also be available on the study website https://bristoltrialscentre.blogs.bristol.ac.uk/details-of-studies/omacs/. Our BRC-CV PAG have been involved in the generation of these newsletters to ensure the content is relevant and accessible for participants.

Ethics and dissemination

The study received Research Ethics Committee (REC) approval from the East Midlands—Nottingham 2 Research Ethics Committee in December 2014 (REC reference: 14/EM/1222). Participants have the right to withdraw their consent at any time. Patients who withdraw their consent will be treated according to usual hospital procedures. Participants who choose to withdraw will have the option of participating in the quality of life follow-up questionnaires.

Findings of this study will be disseminated via typical academic channels (eg, peer-reviewed publications, conferences) as well as through newsletters to participants.

The study is sponsored by University Hospitals Bristol and Weston NHS Foundation Trust and is coordinated by the Bristol Trials Centre, which is a UK Clinical Research Collaboration registered Clinical Trials Units (registration ref. 70).

DISCUSSION

The OMACS study proposes an efficient mechanism to collect large-scale data and tissue samples from a broad cohort of cardiac surgery patients from a large cardiac centre in the UK.

The high-quality data obtained in this study will be combined with samples collected immediately before, during and shortly after surgery. Secondary research will be able to analyse these to answer specific research questions. For example, to identify potential markers of postoperative complications using large-scale genomic and metabolomic techniques, or to assess the response to different surgical techniques through markers of systemic inflammation. This has the potential to advance understanding of specific surgical techniques and postoperative complications, which could improve treatment for patients.

Furthermore, the high-recruiting nature of the study means it is an ideal platform to embed SWATs for fast assessment of interventions aimed at increasing recruitment and retention to clinical studies. To date, three SWATs have been added to the protocol and it is intended that SWATs embedded into the OMACS study will be published separately. One has reported results on the most effective way to format patient information leaflets to maximise recruitment.[19]

OMACS study challenges

Recruitment to the OMACS study began in May 2016, and recruitment will continue until at least November 2022 with extension dependent on continued funding. So far, more than 4000 participants have consented to the study, with over 1100 providing samples, allowing us to collect a large bank of data relating to cardiac surgery outcomes.

Our experience so far has presented several challenges which we will briefly discuss.

Recruitment of participants

Approximately 100 patients are screened and approached for the OMACS study each month. During recruitment significant changes have been made to the clinical patient pathway (eg, timing of preadmission clinics) necessitating flexibility in how and when informed consent is sought so that potential participants are not missed. The protocol was designed to allow patients to be approached for consent preoperatively for collection of samples and data, or postoperatively for collection of data only. Consent may be obtained during a consultation, or remotely by post and telephone. This flexibility maximises the number of patients who can be approached for the study and allowed us to react quickly to recruitment challenges posed by COVID-19 by increasing the number of patients consenting remotely. In addition, hospitals that regularly refer inpatients to the BHI for surgery have been opened as consenting sites. This approach enables patients sufficient time to review study documents before being transferred for surgery, reducing the chance of patients being missed due to late transfers. This facilitates the recruitment of patients undergoing urgent transfer, who typically have higher rates of postoperative complications and mortality, thus making the dataset more representative of the entire cardiac surgery population.

Using multiple consent pathways requires multiple types of patient documents to cover each consent method (preoperative/postoperative and remote/face to face). This relatively straight forward study has seven patient-facing documents approved relating to consent. Having multiple patient document types adds an extra layer of complexity in document management and implementing study amendments.

Use of routine data and quality monitoring

Manual data entry onto specially designed CRFs ensures high-quality data collection but presents a significant burden on research nurse time considering the high recruiting rate on this study. To reduce this pressure, it is intended that routinely collected clinical data will be used as much as possible, reducing manual data collection and entry. Further, where participants are coenrolled on other studies managed by the Bristol Trials Centre (BTC), relevant baseline and complication data may be shared to prevent duplication of data collection and entry

across several studies. We plan to obtain bulk extracts of data, such as demographic information, operation data and details of comorbidities from centralised databanks used by the hospital Trust for financial or audit purposes. However, due to pressures on the hospital Trust informatics teams and lengthy data cleaning processes, we have found that these data can be difficult to obtain in a timely matter.

As well as the issue of timeliness of obtaining routine data, we have also found issues with data accuracy. For example, we intended to collect details about the operation via Office of Population Censuses and Surveys (OPCS) codes assigned to each procedure. OPCS codes are assigned by clinical coders following a national standard and are used for a wide variety of purposes, including financial reimbursement to the hospital Trust. When comparing these codes against the operation notes filed in participant's medical records, we found that up to 20% had been coded incorrectly. This is in line with findings from other centres.[20] Further, where OPCS codes are correct, they often do not provide enough granular detail about the operation type for use in research.

To overcome these challenges, we have developed a bespoke study database which tracks patient consent, clinical data entry, questionnaire follow-up and sample management. Our statisticians have developed algorithms to detect discrepancies between data extracted directly from patient notes and those data obtained from routine sources.

Large-scale sample collection and storage

The logistics of collecting, processing and storing samples from up to 50 participants per month has proved challenging. Our standard sample collection protocol requires 14 samples to be taken over 48 hours resulting in a total of 72 aliquots per participant. This has required significant investment in specialist laboratory solutions, and dedicated laboratory staff who are responsible for processing samples within strict time limits to ensure sample integrity.

Multiple staff groups are involved in the collection of biological samples. This requires extensive clinical and research staff time to ensure samples are collected within the defined time windows. The process involves cooperation between operation department practitioners, anaesthetists, surgeons, research nurses, ward nurses, research administrators and laboratory technicians. Involving these staff groups has improved the culture of research in the BHI.

CHANGES TO THE PROTOCOL SINCE REC APPROVAL

The study began recruiting in May 2016 with V.1 of the protocol. At this stage, all participants were sent a study invitation letter, consent form and questionnaire 3 months after their surgery. The protocol was amended in March 2017 to approach participants face to face and add the collection of blood and waste tissue samples. The latest version of the protocol was approved in December 2020, following an amendment to add the option of obtaining informed consent remotely. The current version of the protocol is V.6 dated 6 November 2020.

Study progress

The study opened on 1 May 2016 and 4064 participants have been recruited to date with 2021 opting to donate samples as well as data (correct as of 7 March 2022).

AVAILABILITY OF DATA AND MATERIALS

Data storage

Participant documentation will be stored in a secure location for 5 years after the end of the study. After the end of the study all patient identifiable paper records will be destroyed by using confidential methods. Any paper CRFs and participant questionnaires will be retained until the data is clean and then destroyed using confidential methods. Digital copies of the consent forms will be stored securely on an NHS server with password-controlled access.

In compliance with MRC policy on data preservation, the full dataset and 'meta-data' about the study will be held indefinitely on a secure University of Bristol server. These will not contain direct participant identifiers but will contain a unique participant identifier. A separate file containing a key to link the participant identifiers with key personal identifiers will be stored indefinitely on an NHS server. This will be retained in case of a need to use the raw data for secondary research.

Data sharing

Data will be available for sharing in an anonymised format conditional on compliance with MRC policy on data preservation and sharing. A protocol will be required describing the purpose, methods and analysis of the secondary research. Participant identifiers would be made available for record linkage subject to ethical approval of the secondary research by a UK REC or similar. Data may not be released unless all BTC and sponsor requirements are met (e.g. REC approval).

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Contributors TWS and KJ drafted the manuscript, coordinate the study and oversee study conduct, acquisition and monitoring of data. RM and HS reviewed the manuscript and are responsible for statistical monitoring of the data, drafting the statistical analysis plan and data reports. EH reviewed the study protocol, recruits participants to the study and collects inpatient data. RB drafted the study protocol. BCR, GDA and CAR developed the concept of the study and developed the initial protocol. LC was the chief investigator of the study, drafted the protocol and manuscript and has oversight of the study.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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REFERENCES

1 NICOR, T.N.I.f.C.O.R. National cardiac audit programme annual report; 2021.
2 Ball L, Costantino F, Pelosi P. Postoperative complications of patients undergoing cardiac surgery. *Curr Opin Crit Care* 2016;22:386–92.
3 Huen SC, Parikh CR. Predicting acute kidney injury after cardiac surgery: a systematic review. *Ann Thorac Surg* 2012;93:337–47.
4 Englberger L, Suri RM, Li Z, *et al*. Clinical accuracy of rifle and acute kidney injury network (akin) criteria for acute kidney injury in patients undergoing cardiac surgery. *Crit Care* 2011;15:R16.
5 Peretto G, Durante A, Limite LR, *et al*. Postoperative arrhythmias after cardiac surgery: incidence, risk factors, and therapeutic management. *Cardiol Res Pract* 2014;2014:1–15.
6 Arribas JM, Garcia E, Jara R, *et al*. Incidence and etiological mechanism of stroke in cardiac surgery. *Neurologia* 2020;35:458–63.
7 Liu Y, Li C-P, Wang Y-Y, *et al*. Prediction of major adverse cardiovascular events and slow/no-reflow by virtual histology imaging after percutaneous interventions on saphenous vein grafts. *Angiology* 2020;71:263–73.
8 Caliskan E, de Souza DR, Böning A, *et al*. Saphenous vein grafts in contemporary coronary artery bypass graft surgery. *Nat Rev Cardiol* 2020;17:155–69.
9 UK10K Consortium, Walter K, Min JL, *et al*. The UK10K project identifies rare variants in health and disease. *Nature* 2015;526:82–90.
10 Drenos F, Davey Smith G, Ala-Korpela M, *et al*. Metabolic characterization of a rare genetic variation within APOC3 and its lipoprotein lipase-independent effects. *Circ Cardiovasc Genet* 2016;9:231–9.
11 Timpson NJ, Walter K, Min JL, *et al*. A rare variant in APOC3 is associated with plasma triglyceride and VLDL levels in Europeans. *Nat Commun* 2014;5:4871.
12 Nordestgaard BG, Palmer TM, Benn M, *et al*. The effect of elevated body mass index on ischemic heart disease risk: causal estimates from a mendelian randomisation approach. *PLoS Med* 2012;9:e1001212.
13 Palmer TM, Nordestgaard BG, Benn M, *et al*. Association of plasma uric acid with ischaemic heart disease and blood pressure: mendelian randomisation analysis of two large cohorts. *BMJ* 2013;347:f4262.
14 Varbo A, Benn M, Smith GD, *et al*. Remnant cholesterol, low-density lipoprotein cholesterol, and blood pressure as mediators from obesity to ischemic heart disease. *Circ Res* 2015;116:665–73.
15 Interleukin-6 Receptor Mendelian Randomisation Analysis (IL6R MR) Consortium, Swerdlow DI, Holmes MV, *et al*. The interleukin-6 receptor as a target for prevention of coronary heart disease: a mendelian randomisation analysis. *Lancet* 2012;379:1214–24.
16 Schroter S, Miles R, Green S, *et al*. Psychometric validation of the coronary revascularisation outcome questionnaire (CROQv2) in the context of the NHS coronary revascularisation PROMs pilot. *BMJ Open* 2017;7:e015915.
17 Schroter S, Lamping DL. Coronary revascularisation outcome questionnaire (CROQ): development and validation of a new, patient based measure of outcome in coronary bypass surgery and angioplasty. *Heart* 2004;90:1460–6.
18 Gandek B, Ware JE, Aaronson NK, *et al*. Cross-validation of item selection and scoring for the SF-12 health survey in nine countries: results from the IQOLA project. international quality of life assessment. *J Clin Epidemiol* 1998;51:1171–8.
19 Culliford L, Brierley R, Clout M, *et al*. The OMACS-PIL study: a randomised controlled trial within the OMACS observational study. *Trials* 2019;20:772.
20 Bortolussi G, McNulty D, Waheed H, *et al*. Identifying cardiac surgery operations in hospital episode statistics administrative database, with an OPCS-based classification of procedures, validated against clinical data. *BMJ Open* 2019;9:e023316.