Perioperative Quality Improvement Programme: Patient Study

Short title: PQIP Patient Study

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1.9
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R&D / Sponsor Reference Number(s):

Study Registration Number:

KEY WORDS

Perioperative

Quality Improvement

Health Services Research

PROTOCOL VERSIONS

Version Stage	Versions No	Version Date	Protocol updated & finalised by;	Appendix No detail the reason(s) for the protocol update
Current	1.9	03/03/2020	S Warnakulasuriya G Singleton SR Moonesinghe	1. Amendment to research questions to include a question about the impact of COVID-19 (p.9) 2. Amendment to recruitment/ sampling approach to include all institutions performing surgery under the NHS (p.9) 3. Amendment to study schedule to include option of completing preoperative questionnaire by telephone, by email by using the online questionnaire (p.11) 4. Amendment to consent process to allow verbal consent (p.11 and 12) 5. Amendment to recruitment strategy to allow distribution of PIS by email (p.12)
Previous	1.8	21/01/2019	Prof. S.R. Moonesinighe	6. Minor changes to CI's titles and contact details (p1, 4) 7. Minor clarification to text regarding sampling strategy (p 8) 8. Minor change to communications plan regarding patient sampling (p 8)
Previous	1.6	20/10/2017	Dr A. Sahni	1. Amendment to inclusion criteria to make explicit selected adult non-cardiac major, major+ and complex surgical procedures are eligible (p7,8 and 11). 2. Amendment to include option to send PIS by post with covering letter (p10) 3. Update study schedule to make it consistent with previous amendment to recruitment/sampling approach (p10)
Previous	1.5	28/11/2016	Dr S Ramani Moonesinghe	1. Amendment to recruitment/sampling approach (page 7) 2. Amendment to study end date – clarification that end will be at 4 years or when recruitment target has been reached, whichever occurs later (p3 study summary and p9)
Previous	1.4	21/09/2016	Dr Duncan Wagstaff	Consent /recruitment amended as per JRO suggestions
Previous	1.3	19/09/2016	Dr Duncan Wagstaff	Minor amendments (internal)
Previous	1.2	19/09/2016	Dr S Ramani Moonesinghe	Minor amendments (internal)
Previous	1.1	17/09/16	Dr Duncan Wagstaff	Minor amendments (internal)
Previous	1.0	16/09/16	Dr Duncan Wagstaff	First draft

DECLARATIONS

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

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

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

Chief Investigator:

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

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

Position:.....

On behalf of the Study Sponsor:

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

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

Position:.....

SIGNED ELECTRONICALLY VIA IRAS

STUDY SUMMARY

Identifiers	
IRAS Number	**215928**
REC Reference No	
Sponsor Reference No	16/0577
Other research reference number(s) (if applicable)	
Full (Scientific) title	Perioperative Quality Improvement Programme: Patient Study
Health condition(s) or problem(s) studied	Post-operative complications after major elective surgery
Study Type i.e. Cohort etc	Cohort
Target sample size	70,000 patients
STUDY TIMELINES	
Study Duration/length	4 years
Expected Start Date	November 2016
End of Study definition and anticipated date	November 2020 or after 70,000 patients recruited, whichever is later
Key Study milestones	Protocol submission, REC approval, HRA approval, patient level data gathering, annual reports, study completion.
FUNDING & Other	
Funding	The Health Foundation The Royal College of Anaesthetists
STORAGE of SAMPLES (if applicable)	
Human tissue samples	n/a
Data collected / Storage	n/a
KEY STUDY CONTACTS	Full contact details including phone, email and fax numbers
Chief Investigator	Professor SR Moonesinghe Centre for Perioperative Medicine Department for Targeted Intervention Division of Surgery and Interventional Science University College London Charles Bell House 43-47 Foley Street London W1W 7TS 07956 620717; ramani.moonesinghe@nhs.net

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1 INTRODUCTION

This proposal is to gather and analyse patient data for the newly established National Perioperative Quality Improvement Programme (PQIP), led by the National Institute for Academic Anaesthesia's Health Services Research Centre (NIAA-HSRC), based at the Royal College of Anaesthetists. PQIP will measure complications and outcome from the patient perspective after major surgery. Patients will be approached at random, in participating hospitals, to give consent to have their data collected and used for research. The data collected will include information about patients, the surgery that they undergo, and the care that they receive.

Over 70 hospitals have indicated that they would like to contribute take part in this project. The project is being funded by the Royal College of Anaesthetists and the Health Foundation. The programme is being managed by the NIAA-HSRC with support from a steering group comprising a comprehensive group of stakeholder representatives including surgeons, anaesthetists, physicians, nurses and patients.

The PQIP Database has already received a favourable REC opinion (Appendices 1,2 & 3). This protocol details the initial collection and analysis of PQIP patient data.

2 BACKGROUND AND RATIONALE

Over ten million operations take place in the UK NHS every year. [1] The number of patients which are at high risk of adverse postoperative outcomes has grown substantially in recent years: this is attributable to a combination of an ageing population, the increased numbers of surgical options available for previously untreatable conditions, and the increasing numbers of patient presenting for surgery with multiple comorbidities. Estimates of inpatient mortality after non-cardiac surgery range between 1.5 and 3.6% depending on the type of surgery and patient related risks. [2] [3]. Major or prolonged postoperative morbidity (for example, significant infections, respiratory or renal impairment) occur in up to 15% of patients, and is associated with reduced long-term survival and worse health-related quality of life; this signal has been consistently demonstrated across different types of surgery, patient and healthcare system. [2] [4, 5]

Data from the US [6] [7] demonstrate wide variation in risk-adjusted mortality & morbidity rates between healthcare providers, suggesting that at least some complications after surgery could be avoidable if standards of care were improved. It is likely that the same is true in the UK; however, there is currently no unified national system for measuring complications or

patient reported outcomes across different types of major surgery in the NHS. In order to address this gap, the National Institute for Academic Anaesthesia's Health Services Research Centre (NIAA-HSRC) is launching the Perioperative Quality Improvement Programme (PQIP) for the UK. PQIP will measure risk-adjusted morbidity and mortality, as well as process and patient-reported outcome data in adult patients undergoing major surgery (e.g. lower GI resection, upper GI resection, liver resection, cystectomy, major head and neck reconstructive surgery, thoracic resection). Our dataset has been informed by previous systematic [8] and structured reviews, [9] and over 60 UK NHS hospitals have volunteered to take part. Our clinical reference (steering) group has met and comprises representation from all key stakeholder groups: patient representatives, the Royal College of Surgeons (Eng), Royal College of Physicians, Royal College of Nursing, Faculty of Intensive Care Medicine, Faculty of Pain Medicine, and a wide range of national surgical specialist societies.

3 OBJECTIVES

3.1 Aim

To comprehensively measure, report and improve risk-adjusted outcome from major surgery in the United Kingdom.

3.2 Objectives

1. To measure and report risk-adjusted complication, patient reported outcome and mortality rates after major surgery
2. To analyse variations in structure, process and outcome after major surgery between NHS institutions
3. To support local quality improvement through feedback of data to clinicians and managers, using near-real time feedback

3.3 Research Questions

1. What is the failure to rescue rate in the NHS and how does it vary between hospitals?

2. What is the relationship between short-term complications and longer-term Health Related Quality of Life (HRQOL), and can longer-term HRQOL be improved through reducing postoperative complications?

3. Can the quality of care be improved through the feedback of data to clinicians and managers, leading to improvements in complications and failure to rescue?

4. What has the impact of COVID-19 been on the processes and outcomes after major surgery for NHS patients?

4 STUDY DESIGN

Data will be collected on either a sample of patients or all patients undergoing major surgery (defined prospectively) in participating hospitals.

Sampling strategy:
All NHS hospitals in the UK and all institutions from the independent sector that are performing surgery under the NHS will be invited to participate. Only adult patients undergoing selected major, major+ or complex non-cardiac surgery will be eligible for inclusion. Each hospital will be offered the opportunity to either approach all eligible patients for consent (in totality or within a specialty or specialties) or plan to recruit a maximum 5 patients per week. Where a sampling approach is taken, the patients to be approached for consent will be based on a

random sampling strategy which will involve an 8-day rolling sampling cycle (i.e. the first 5 patients starting from Monday morning in week one, followed by the first 5 patients starting from Tuesday in week two etc etc). If any of the first 5 patients approached refuse consent, then consecutive patients will be approached for consent until the target recruitment number has been achieved.

Data collection:

Each consenting patient will complete baseline questionnaires (Appendix 4) before their surgery, and 1 day, 3 days, 6 months and 12 months after their surgery. Objective risk, process and outcome data will be collected on patients during their inpatient stay. Hospital data will be linked with Hospital Episode Statistics (HES) and Office of National Statistics (ONS) mortality data at patient identifiable level. This is necessary to track adverse outcomes which occur after discharge from hospital (e.g. readmission within 30 days of surgery - from HES data; longer term mortality - from ONS)

Dataset:

All data collected are evidence based and where appropriate, formally validated.

These include:

- Patient risk factors for the purposes of risk adjustment (the components of risk adjustment systems identified in a published systematic review as being accurate)- Patient morbidity data - using the validated Post-Operative Morbidity Survey (POMS) on Day 7 post-op and the Clavien Dindo surgical complications grading system on discharge from hospital
- Patient reported outcome data - the EQ5D is a validated measure of health-related quality of life; the Quality of Recovery - 15 score is a validated measure of recovery from surgery; the Bauer patient satisfaction measure is a validated measure of postoperative discomfort and satisfaction with anaesthesia care; the WHO Disability Assessment Schedule 2.0 has been validated for use in patients undergoing major surgery

Analysis plan:

Our primary outcome is POMS-defined morbidity on day 7. Our primary analysis will measure risk-adjusted variation between providers (comparing observed: expected ratios) in morbidity, mortality and failure to rescue rates, following standard methodology for ascertaining FTR rates described by Dimick. Secondary outcomes will include mortality at 90 days, disability-free survival at one year; patient reported outcome (change in health-related quality of life; time to full recovery). Analyses will include hierarchical regression modelling to determine the relationship between structure, process and outcome. Regular reports will be provided to participating sites in order to assist local quality improvement efforts.

5 STUDY SCHEDULE

For hospitals approaching all patients for participation, screening and approach for consent will be conducted at the earliest opportunity after listing for surgery. For hospitals using the random sampling strategy, clinicians in participating hospitals will identify 5 patients each week to be recruited to the study. A random sampling technique for patient identification will be used, based on an 8-day rolling rota: e.g. the first 5 patients admitted on Monday for qualifying surgical procedures in week 1, followed by the first 5 patients on Tuesday in week 2, the first 5 patients on Wednesday in week 3, etc. The sampling strategy will be communicated by the central database team at the Royal College of Anaesthetists to local sites, and local principal investigators (PIs) will be responsible for ensuring that the patients recruited adhere to the strategy. If a patient refuses consent, the next sequential patient will be approached until 5 patients are recruited.

Patients will complete health related quality of life questionnaires (Appendix 4):
- at the time of consent (in person on paper, or by phone with a member of staff, or by online questionnaire, according to patient preference)
- on days 1 and 3 after surgery
- at 6 and 12 months after surgery patients will be contacted by telephone or email (patients will be able to choose their preferred means of communication at the time of consent).

Patients can choose to be withdrawn from the study at any time.

The study will end after 4 years or when 70,000 patients have been recruited, whichever is the later.

6 CONSENT

No data will be collected from patients before consent has been obtained. The consent process will be determined by local circumstances and will be either written or verbal. Wherever possible written consent will be obtained. Prior to obtaining written consent, there will be a minimum of one hour for patients to consider the information. Posters will be displayed in preoperative assessment clinics and surgical admission wards, giving patients brief details of the study (see Appendix 5). The patient will be provided with a Participant Information Sheet (PIS, Appendix 4) (in person, by post or by email). A member of the research team will explain the study to the patient either in person or by telephone or video call, providing all the relevant information and allowing the patient to ask questions. After allowing the patient a minimum of

one hour to consider whether to participate in the research or not the researcher will answer any additional questions and will obtain verbal consent (if by telephone or video call) or written consent (if face to face) from the patient to participate. Consent will be taken prior to surgery and preoperative questionnaires completed at the time of consent.

7 ELIGIBILITY CRITERIA

7.1 Inclusion Criteria

1. Adult patients aged 18 or older

2. Undergoing an elective major non- cardiac surgical procedure (as listed in Appendix 8 at the time), this will be updated by the study team.

3. Has capacity to give consent to participate in this study

7.2 Exclusion Criteria

1. Aged less than 18years

2. Does not have capacity, or refuses, to give consent to participate in this study

8 RECRUITMENT

Patients will be identified, according to the sampling strategy described above, by clinicians in the course of routine healthcare provision or by local research nurses who will be bound by the principles of GCP. No data will be collected from patients before consent has been given. Posters will be displayed in preoperative assessment clinics and surgical admission wards, giving patients brief details of the study (see Appendix 5). If patients attend preoperative assessment clinic, they will be offered a PIS (PIS, Appendix 4) at that time. Patients may receive a PIS either by post or email (this will be at the discretion of local research teams). Otherwise, they will be provided with a PIS on arrival in hospital for their surgery. Consent will be taken prior to surgery and preoperative questionnaires completed at the time of consent.

9 STATISTICAL METHODS

Sample size: 70,000 patients.

This is achievable based on a target recruitment rate of 5 patients per hospital per week for 4 years in 70 hospitals.

Our aim will be to expand the study to as many UK hospitals as want to participate - therefore the sample size may exceed our target; however, our end point will be dictated by the number of

years of the study (as we wish to study how patient outcomes change over time to assess the impact of the data collection and feedback on outcome) – the planned study (recruitment) duration is 4 years: year one to establish baseline rates of complication rates and develop bespoke risk-adjustment models, year two to compare risk-adjusted outcomes between institutions and years 3 & 4 to evaluate changes in processes and outcomes.

Descriptive statistics will be used to describe basic demographics of participants. Risk-adjustment will be based on based on backward stepwise logistic regression, including multiple patient-level and operation-level variables such as age, sex, operation type and known validated risk prediction scores and their constituent variables such as the Portsmouth Physiological and operative score for the enumeration of morbidity and mortality (P-POSSUM) and the Surgical Outcome Risk Tool (SORT). Risk-adjusted morbidity and mortality will be compared between hospitals using funnel plots. Variable life-adjusted displays will be used to feedback outcome data to clinicians in near-real time. Hierarchical regression modelling will be used to analyse the relative contributions of patient and hospital factors on patient outcomes.

10 PATIENT AND PUBLIC INVOLVEMENT (PPI)

We will address areas prioritised by 4 James Lind Alliance Priority Setting Partnerships (JLA-PSPs): anaesthesia/perioperative care, intensive care, dementia & pressure ulcers.

We received detailed structured feedback on our protocol from members of the PCPIE group at the National Institute for Academic Anaesthesia's Health Services Research Centre (NIAA-HSRC).

Our Clinical Reference Group has two lay members. Ms Elspeth Evans is a member of the RCoA lay committee and has provided feedback on this project proposal throughout development. Ms Siobhan Atherly volunteered to be a patient voice through the Royal College of Surgeons; she is currently in follow-up from surgery & is actively involved with her local Trust Board.

11 FUNDING AND SUPPLY OF EQUIPMENT

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

Research costs have been secured from three sources:

1. The Health Foundation. An Improvement Science Fellowship (£374,709) has been awarded to the Chief Investigator
2. Royal College of Anaesthetists.
    a. PQIP funding stream (£260,000).
    b. Health Services Research Centre project support (£72,000).
    c. Health Services Research Centre statistician (£71,892).

12 DATA HANDLING AND MANAGEMENT

All investigators and study site staff will comply with the requirements of the Data Protection Act 1998 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

Patient level data will be entered by local reporters directly into electronic CRFs on the web-based study database. The database will be hosted on servers managed by UK Fast on behalf of the Royal College of Anaesthetists (RCoA). Local investigators will have access to their own full datasets.

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

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

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

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

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

The following paragraphs describe the process of linkage, between the PQIP database and external national databases (ONS mortality data from the Health and Social Care Information Centre (HSCIC) and Hospital Episode Statistics (HES) data.

The minimum amount of patient identifiable data will be extracted from the study database by the central investigation team, onto a password protected Excel spreadsheet, and emailed securely to the HSCIC and to the RCS-CEU. These fields will be used to ensure individual patient

records within the PQIP system are managed correctly, keeping distinct treatment episodes linked to the correct patient.

Four patient identifiers will be used to facilitate data linkage: patient name, date of birth, NHS number and postcode. The NHS number is not completely populated in the other routine datasets and the other patient identifiers are used when the NHS number is absent. In addition, by using these four identifiers in combination, possible erroneous record linkages are flagged.
A file (P) containing these patient identifiers only will be extracted from the full dataset hosted in the study database, and will be sent securely to a trusted Data Linkage Service (TDLS). File (P) will contain the following identifiers:

- PQIP anonymised identifier
- NHS number
- Date of Birth
- Sex
- Postcode

For each patient in the file, the TDLS will identify the matching ONS or HES ID. The TDLS will then return to the Royal College of Anaesthetists a 'look-up' file (L) containing only the PQIP identifier and the HES or ONS ID identifiers, and a MATCH_RANK field which indicates the strength of the match.

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

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

The Data Custodian will be Ms Sharon Drake, Director of Quality and Research, Royal College of Anaesthetists. The full anonymised dataset will only be accessible to named members of the study team. Requests for access to the full dataset by external parties for secondary analyses will be considered by the Project team following a formal application which includes details of purpose, ethics, information governance and data management.

13 PEER AND REGULATORY REVIEW

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

- The Sponsor considers the procedure for obtaining funding from The Health Foundation and the Royal College of Anaesthetists to be of sufficient rigour and independence to be considered an adequate peer review.

14 ASSESMENT AND MANAGEMENT OF RISK

This is an observational study and we do not see major ethical or other issues.

The PQIP database protocol and linked IRAS application (Appendices 1 & 2) detail procedures for maintaining data security, confidentiality and information governance.

14.1 Protocol deviations and notification of protocol violations

A deviation is usually an unintended departure from the expected conduct of the study protocol/SOPs, which does not need to be reported to the sponsor. The CI will monitor protocol deviations.

A protocol violation is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the participants of the study; or

(b) the scientific value of the study.

The CI and sponsor will be notified immediately of any case where the above definition applies during the study conduct phase.

14.2 Monitoring and Auditing

The Chief Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality.

The Chief Investigator will inform the sponsor should he/she have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

15 TRAINING

The Chief Investigator will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files.

16 INDEMNITY ARRANGEMENTS

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

17 ARCHIVING

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

18 PUBLICATION AND DISSEMINATION POLICY

We will register the study on clinicaltrials.gov and publish our protocol after ethics approval received. All participants will be given a patient information leaflet prior to consent. This will include details of the study website; all reports / results will be published on there and therefore participants will be able to access if they wish. In addition, the research will be disseminated by:

- Publications in open access peer reviewed scientific journals
- Face to face presentations
- live-action & animated video content on our own open-access Youtube channel
- Social media
- Conference presentations
- Professional literature (e.g. Royal College literature)

19 REFERENCES

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20 APPENDICES

1. PQIP Database protocol
2. PQIP Database IRAS form
3. PQIP Database favourable REC opinion
4. Participant Information Sheet
5. Participant Information Poster
6. Participant Consent Form
7. Patient Questionnaire
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