Observational Protocol Template: UCLH/UCL Sponsored Studies
UCL/UCLH Research Office

Guidance

Intraoperative Hypotension in the Elderly: Observational Study of Intraoperative Hypotension in Elderly Patients in UK Hospitals
iHypE

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Supported by:
The Research and Audit Federation of Trainees (RAFT)

Sponsored by:
University College London (UCL)

Protocol version number and date:
Version 5.4 31/10/2016

R&D / Sponsor Reference Number(s):
15/0970
Study Registration Number: 15/0970

PROTOCOL VERSIONS

Version Stage	Versions No	Version Date	Protocol updated & finalised by;	Appendix No detail the reason(s) for the protocol update
Current	5.4	31/10/2016	A Wickham	Study date window amended (section 6.2 & 9.1)
Previous	5.3	9/6/2016	A Wickham	Submitted to IRAS
Previous	5.2	8/1/2016	A Wickham	Change in format
Previous	5.1	1/12/2015	A Wickham	Post HSRC review – Observational study
Previous	4	18/11/2015	A Wickham	Pitched to HSRC
Previous	3	9/9/2015	A Wickham	Outcomes included
Previous	2	25/8/2015	A Wickham	For review by RAFT members
Previous	1	25/6/2015	A Wickham	Initial pitch to RAFT

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.

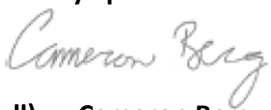
Chief Investigator:

Signature: **Date: 31/10/16**

Print Name(in full): **Dr Daniel Martin**

Position: **Consultant Anaesthetist**

On behalf of the Study Sponsor:

Signature:  **Date: 31/10/2016**

Print Name(in full): **Cameron Berg**

Position: **Portfolio Coordinator**

STUDY SUMMARY

Identifiers	
IRAS Number	186097
REC Reference No	
Sponsor Reference No	15/0970
Other research reference number(s) (if applicable)	Not applicable
Full (Scientific) title	Intraoperative Hypotension in the Elderly (IHypE): Observational Study of Intraoperative Hypotension in Elderly Patients in UK Hospitals
Health condition(s) or problem(s) studied	Intraoperative hypotension in surgical patients aged over 65 years
Study Type i.e. Cohort etc	Retrospective observational cohort study
Target sample size	Approximately 3000
STUDY TIMELINES	
Study Duration/length	30 days
Expected Start Date	21st November
End of Study definition and anticipated date	28th February 2017, after 30 day outcome data collected.
Key Study milestones	1st patient recruited:21st November 2016 Last patient recruited: 28th January2017 e.g. study submission, budget and contract to be finalised,
FUNDING & Other	
Funding	Not funded
Other support	Research and Audit Federation of Trainees (www.raftrainees.com)
STORAGE of SAMPLES (if applicable)	Not applicable
Human tissue samples	Not applicable
Data collected / Storage	Intraoperative hypotension data. Stored on NHS Scotland servers
KEY STUDY CONTACTS	
Chief Investigator	Dr Daniel Martin, Consultant in Anaesthesia and Critical Care, Royal Free Hospital, Senior Lecturer UCL Division of Surgery and Interventional Science. E-mail: daniel.martin@ucl.ac.uk
Trainee Lead	Dr Alex Wickham, Anaesthetic registrar, Imperial School of Anaesthesia Phone: 07734819931 E-mail: alex.wickham@nhs.net

KEY ROLES AND RESPONSIBILITIES

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

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

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

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

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

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

OTHER:

Dr Alex Wickham, Anaesthetic registrar, Imperial School of Anaesthesia. Trainee Lead
Dr Tom Clark, Consultant Anaesthetist, Torbay & South Devon Hospitals NHS Foundation Trust, RAFT Lead.
Dr David Highton, Anaesthetic registrar, UCL Hospitals NHS Foundation Trust
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Dr David Fallaha, Consultant Anaesthetist, Golden Jubilee National Hospital, NHS Scotland
Dr Sam Clark, Clinical Fellow in Intensive Care Medicine, Oxford University Hospitals NHS Trust

KEY WORDS

Intraoperative hypotension. Elderly. Anaesthesia. Vasopressor.

LIST OF ABBREVIATIONS

AAGBI	Association of Anaesthetists of Great Britain and Ireland
AE	Adverse Event
AKI	Acute Kidney Injury
AR	Adverse Reaction
ASAP	Anaesthetic Sprint Audit of Practice
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
DMC	Data Monitoring Committee
GAfREC	Governance Arrangement for NHS Research Ethics
HTA	Human Tissue Authority
IB	Investigator Brochure
ICF	Informed Consent Form
iHypE	Intraoperative Hypotension in the Elderly
IOH	Intraoperative Hypotension
MABP	Mean arterial blood pressure
MD	Medical Device
ISRCTN	International Standard Randomised Controlled Studies Number
PI	Principle Investigator
PIS	Participant Information Sheet
QA	Quality Assurance
QC	Quality Control
RAFT	Research and Audit Federation of Trainees
REC	Research Ethics committee
SAR	Serious Adverse Reaction
SAE	Serious Adverse Event
SDV	Source Data Verification
SOP	Standard Operating Procedure
SSI	Site Specific Information
TMF	Trial Master File
95% CI	95% confidence interval

CONTENTS

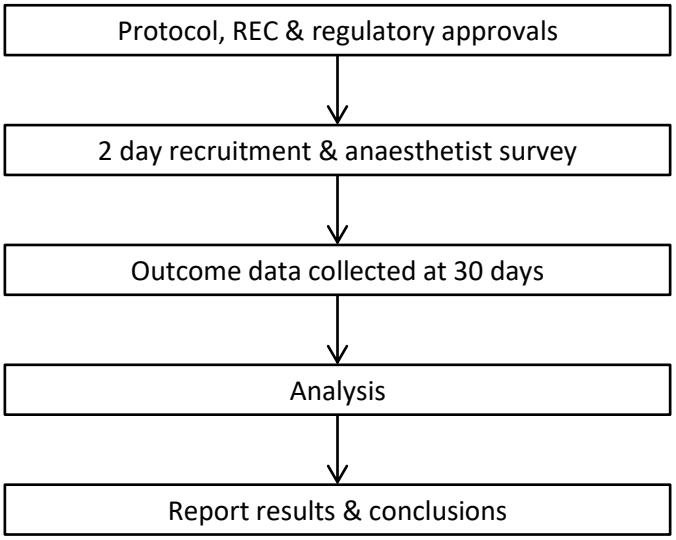
1 INTRODUCTION

Intraoperative hypotension (IOH) is a potentially avoidable complication of anaesthesia associated with stroke, acute kidney injury, myocardial infarction, and mortality in older patients. Better control of intraoperative blood pressure may have the potential to improve perioperative outcomes. Defining current UK practice is a crucial step towards future research into improving intraoperative blood pressure management.

We aim to determine the prevalence, magnitude, duration and treatment thresholds for IOH in patients aged >65 undergoing surgery in the UK. We hypothesize that IOH is widely prevalent and may be in part a disparity between the clinically applied treatment threshold and literature definitions for IOH.

A 30 day observational study will be delivered entirely by regional trainee led research groups affiliated to the Research and Audit Federation of Trainees (RAFT). Episodes of IOH will be determined from anaesthetic records and compared with a clinician survey on treatment thresholds.

The results from this large-scale project will generate a true representation of practice across the UK, highlighting the prevalence of IOH amongst older patients undergoing surgery and power a future interventional study.



2 LAY SUMMARY

Low blood pressure during surgery (also known as intraoperative hypotension or IOH) is thought to be a common occurrence. It happens as a side effect of the medicines used during an anaesthetic. In patients aged over 65 years this may lead to an increased risk heart attack, stroke, kidney failure and death following surgery. This risk increases as the degree and duration of low blood pressure increases. Patients aged over 65 years are at increased risk because their body is less able to cope with low blood pressure. Quantifying the prevalence of IOH has been problematic as it lacks a clear and universally accepted definition.

We aim to determine how often IOH occurs in patients aged 65 years and over throughout the UK. We also aim to discover what blood pressure anaesthetists consider to be too low, how they subsequently treat this low blood pressure and their perceptions of its overall importance. We can use this information to describe what practising UK anaesthetists think constitutes IOH. We will also identify any patients suffering a stroke, heart problem, kidney injury or death after surgery to identify the risk level of the older surgical population.

Using an already established national audit and research network, we will conduct this study across multiple hospitals simultaneously throughout the UK. We will review the paper or electronic anaesthetic charts of patients undergoing surgery and record instances of IOH, its magnitude and duration. Other key medical and demographic information will be recorded for each patient. Data will be collected for a total of 48 hours at each hospital. Patients included in the study will be followed up to assess their postoperative course up to 30 days after surgery. All information will be obtained from patient records rather than face-to-face encounters. As all data collected will be

anonymized and already documented as part of routine care we do not anticipate consent from participants will be necessary. All data will be entered into a common database in order for it to be analysed nationally.

The other component of the study involves giving a questionnaire to anaesthetists in participating hospitals. The questionnaire will ask about individual practice in relation to the treatment of low blood pressure during surgery. The anonymised responses will be collected and assessed to determine national consensus on this topic.

We hope to be able to quantify the prevalence of IOH across the UK. The coordinated efforts of the network should produce a comprehensive description of the extent of IOH today, its association with important clinical complications and the view of anaesthetists on when and how to treat it.

Defining and quantifying this important problem will provide anaesthetists with a clear picture of its extent in the UK. This will enable quality improvement programmes to reduce IOH and the harm associated with it. Furthermore, information from this study may help to unify the definition of IOH in order for anaesthetists to more easily identify and report it.

3 BACKGROUND AND RATIONALE

Intraoperative hypotension frequently occurs when patients are anaesthetised for surgery and is associated with adverse outcomes in the elderly [1]. This happens as a consequence of the drugs used to provide general or regional anaesthesia, but may be compounded by a patient's physiology, pathology and other pharmacotherapy. In non-cardiac surgical populations intraoperative hypotension has been associated with the following:

- Stroke: adjusted odds ratio of 1.013 (95% CI 1.000 – 1.025) per minute of MABP drop >30% from baseline [2].
- Impaired neurological performance: each 10mmHg increase in MABP in hip fracture patients with an intraoperative MABP of <80mmHg was associated with an odds ratio of 0.21 (95% CI 0.05–0.86) for post-operative delirium on day 2 [3].
- Myocardial injury: MABP <55mmHg for 20 minutes associated with an adjusted odds ratio of 1.82 (95% CI 1.31 – 2.555) [4].
- Acute kidney injury: MABP <55mmHg for 20 minutes associated with an adjusted odds ratio of 1.51 (95% CI 1.24–1.84) [4].
- Mortality: intraoperative systolic hypotension <80mmHg predicts 1 year mortality (odds ratio 1.036 (95% CI 1.006–1.066) per minute of hypotension) [5]. Intraoperative MABP of <70mmHg for 10 minutes associated with increased 30 day mortality (odds ratio 1.04 (95% CI 1.03–1.05)) [6].

If we suppose there is a causative link between intraoperative hypotension and these outcomes one would expect increased risk with prolonged duration and increased degree of hypotension. The longer patients spent with a MABP <55mmHg, the greater the likelihood of developing acute kidney injury (odds ratio 1.18 (95% CI 1.06–1.31) for 1-5 minutes vs 1.51 (95% CI 1.24–1.84) for >20 minutes) and myocardial injury (odds ratio 1.30 (95% CI 1.06–1.58) for 1-5 minutes vs 1.82 (95% CI 1.31–2.55) for >20 minutes) [4]. Additionally, the greater the degree of hypotension, the higher the risk of 30 day mortality (odds ratio 1.02 (95% CI 1.01–1.03) if MABP <80mmHg for 10 minutes vs 1.23 (95% CI 1.15–1.30) if MABP <50mmHg for 10 minutes) [6].

Best practice guidelines on perioperative care of the elderly from the Association of Anaesthetists of Great Britain and Ireland (AAGBI) recommend that intraoperative hypotension should be avoided in older patients [7], though acknowledge that there is continued debate over the thresholds that constitute best the definition. Despite the evidence and recommendations, there is recent evidence suggesting that intraoperative hypotension remains extremely common. A 25 centre investigation in London identified that up to 89% of 481 patients aged over 65 fulfil the AAGBI definition of hypotension and that it is often prolonged, persisting for over 20 minutes in 28% [8]. The

recent national AAGBI ASAP audit emphasised the large scale of this issue and potential burden of harm in the fractured neck of femur population [9].

Whilst optimal patient-specific blood pressure limits may exist, predicting these is not straightforward, and there is continued debate over appropriate population based definitions of intraoperative hypotension [10-12]. Thus intraoperative hypotension might range between an unanticipated inadvertent event, a recognised but undertreated event, to a different interpretation of what constitutes hypotension in a particular patient or cohort of patients. In addition to lack of a clear definition, the frequency of intraoperative hypotension in the elderly in the UK is not known, there are no studies assessing physician views on intraoperative hypotension or how vasopressors are used for its treatment routine clinical practice. Additionally, data on how often the above complications occur in elderly surgical patients in the UK is not available. We hypothesise that:

- Prolonged severe intraoperative hypotension is common in elderly surgical patients.
- Intraoperative hypotension is inadequately treated, in part due to lack of a clear definition.
- Intraoperative hypotension leads to increased risk of cardiovascular complications.

Our work will deliver a snapshot of UK anaesthetic practice, will allow characterisation of the nature of intraoperative hypotension, enable a clinician derived definition of intraoperative hypotension (based on values triggering vasopressor usage) and will elucidate any increased risk of cardiovascular events. This will complement other emerging research on intraoperative hypotension to inform future improvements in anaesthetic management of older patients.

By performing the study in all hospitals affiliated to the Research and Audit Federation of Trainees (RAFT), a network of trainee anaesthetists, we can comment on intraoperative hypotension across the UK with as much authority as possible. Approximately 150 hospitals will collect data and based on our pilot [8] we anticipate that by conducting the study over two 24 hour periods we will obtain data from several thousand operations. Asking trainees to collect data over this short period of time will ensure both that the project is feasible and that a useful quantity of data is obtained. Engaging trainee anaesthetists in perioperative research whilst in training may also lead to further engagement with and production of useful research in the future.

4 OBJECTIVES

4.1 Primary Objective

To determine the proportion of elderly patients developing intraoperative hypotension, the percentage drop from baseline blood pressure and the duration of hypotension.

4.2 Secondary Objectives

To document adverse outcomes associated with intraoperative hypotension.

To determine anaesthetists perceptions of and treatment thresholds for hypotension by:

- Identifying blood pressure thresholds triggering vasopressor use.
- Surveying anaesthetist attitudes towards intraoperative hypotension via a tick box questionnaire.
- This will enable us to derive a ‘clinician derived’ definition of hypotension

The findings will allow participating hospitals to review the care they provide for elderly patients having surgery, consider their current management strategies and compare themselves with others. Nationally, there is considerable established and emerging work on the clinical relevance of intraoperative hypotension in the elderly, and this work will assist in translating these findings into clinical practice by establishing the status of current practice, with the goal of reducing a potentially avoidable harm.

5 STUDY DESIGN

National, retrospective observational 30 day cohort study.

5.1 Study population and setting

Patients aged 65 years or older having a surgical procedure in an operating theatre under general or regional anaesthesia.

5.2 Study setting

NHS hospitals with trainee anaesthetists affiliated to the Research and Audit Federation of Trainees (RAFT). To increase coverage of the UK, the project is being advertised to trainees in hospitals not part of a formal research network.

5.3 Study organisation

iHypE will be led by the RAFT project management committee who will be responsible for study administration, data collation and management.

Regional trainee project co-ordinators will lead iHypE in their areas. Their responsibilities are to:

- Identify local trainee leads and consultant supervisors in participating hospitals.
- Distribute paperwork and other materials.
- Ensure regulatory approvals are completed prior to the start date.

Local iHypE co-ordinators in individual hospitals are required to:

- Provide leadership for the study in their institution.
- Ensure that there are sufficient data collectors to cover all recovery/ PACU's if the hospital has more than one.
- Enrol a consultant supervisor.
- Ensure all regulatory approvals are completed prior to the start date for their institution.
- Collect data.
- Guarantee data quality and integrity.
- Communicate with their regional co-ordinator.

6 STUDY SCHEDULE

6.1 Enrolment

Patients will be enrolled over two consecutive locally agreed 24 hour periods during weekdays between Monday 21/11/2016 and Friday 28/01/2017.

6.2 Follow-up

Outcomes will be followed up at 30 days after surgery.

6.3 Participant withdrawal

Patients are not being consented for data collection.

Anaesthetists may withhold consent from completing the questionnaire (appendix 2). If an anaesthetist completes a questionnaire but later wishes to withdraw their data they should notify their local data collectors who will destroy the information provided confidentially.

6.4 End of study

The end of the study is defined as the end of the 30-day follow-up for the last patient recruited. Data analysis will follow this.

7 CONSENT

We anticipate that patient consent will not be required for this study as the dataset will only include information already recorded as part of routine clinical care (see appendix 1 and 3), all data will be anonymised and no identifiable information (apart from gender) will be shared outside of the individual hospital where the patient is treated. We will apply for Section 251/ Confidentiality Advisory Group approval.

By taking consent for inclusion, we could bias the results by excluding sicker and frailer patients whose blood pressure and outcomes data is potentially the most interesting, and who, in future, would benefit most from this study's findings. Identifiable patient data will not leave the hospital where each individual patient is treated. The data being collected is not sensitive or embarrassing. No additional tests or interventions are being made and no changes will be made to patient care. The clinicians collecting the data will be part of the anaesthetic department in the NHS hospital in which the patient is being treated and can therefore be considered part of the normal care team. Additionally, asking for consent would be impractical in this number of patients and could reduce the size and therefore generalisability of the findings.

Study information will be displayed in patient areas within operating theatre departments of participating hospitals to ensure that patients can register dissent in relation to the research activity. Patients will be able to decline participation or withdraw at any time without providing a reason.

Similarly, the survey of anaesthetists (see appendix 2) asks no sensitive questions and collects no anaesthetist or patient identifiable data. Information will be provided about the study for the anaesthetists. Completion of the proforma will be considered as the anaesthetist providing their consent to be included in the study.

8 ELIGIBILITY CRITERIA

7.1 Inclusion Criteria

Aged >65 years

Underwent general anaesthesia or regional anaesthesia either alone or in combination for emergency or elective surgery.

7.2 Exclusion Criteria

Procedure requires cardiopulmonary bypass.

The patient has sedation alone (i.e. not in combination with regional anaesthesia).

9 RECRUITMENT

9.1 Participant identification

Patient participants will be identified by local data collectors (independent of delivery of anaesthesia but part of the anaesthetic department of the hospital) by screening daily operating department lists, whilst in recovery after surgery and from emergency operating lists (for overnight surgery) on the days of the study. Such information is published daily, either printed or electronically, in operating theatres (where public access is restricted).

Anaesthetists whose patients were included in the study will be asked to complete the survey (adapted from Burns SM et al [14]) about their attitudes towards intraoperative hypotension. If more than one anaesthetist was present in theatre (e.g. both a consultant and trainee), both will be asked to complete the survey. If a particular anaesthetist has more than one patient included in the study, they will only be asked for their opinions once.

9.2 Recruitment schedule

Data collection will begin at 0800 on the selected weekday between 21/11/2016 and 28/01/2017. It will end 48 hours later at 0800.

Data will be collected on all eligible patients who undergo elective or emergency surgery in theatre during the study period.

9.3 Documentation of ineligibility

Data collectors will record the number of surgical procedures occurring on the dates of the study to determine denominator numbers.

10 STATISTICAL METHODS

The key intended outputs delivered from this project are to:

1. Document the proportion of elderly patients developing intraoperative hypotension, the percentage drop from baseline and the duration of hypotension in elderly non-cardiac surgical populations.
2. Elucidate anaesthetists' threshold for treating hypotension and compare this to their stated clinical opinion on treatment thresholds.
3. Document adverse outcomes (mortality, renal and cardiovascular) associated with intraoperative hypotension.

This will allow us to differentiate between inadvertent intraoperative hypotensive events from intentioned disagreement with recognised definitions of intraoperative hypotension.

10.1 Sample size:

Our plan is to recruit as many NHS hospitals affiliated to RAFT as possible. Additionally, we intend to recruit hospitals not affiliated to RAFT, via the NIAA QUARC network to ensure as broad a coverage as possible. We have not performed a sample size calculation.

Approximately 2.9 million general anaesthetics are given annually in the UK. An unknown amount (but much smaller) of procedures are performed under regional anaesthesia.

Simple calculations suggest that approximately 8000 operations take place per day. Patients aged over 65 years old are estimated to make up 17% of the population (ONS, 2014). Therefore there is an event rate of ~2800, however this overlooks the fact that the elderly are over-represented amongst the surgical population. In a pilot study in London [10] each hospital recruited a mean of 15 patients. At a conservative capture rate of approximately 50% we hope to collect data on 1500 patients.

10.2 Data analysis:

10.2.1 Hypotension and vasopressor data

Descriptive statistics will be used to describe national rates of intraoperative hypotension, degree of hypotension and duration.

We will compare:

- Frequencies, degree and durations of intraoperative hypotension from paper anaesthetic charts and electronic data collection.
- Pre-operative blood pressure with pre-induction blood pressure
- Associations between different surgical specialities and anaesthetic techniques and IOH.

No comparisons will be made between hospitals as it is unlikely that individual centres will recruit enough patients to conduct meaningful evaluations.

Our results will be reported numerically and graphically.

10.2.2 Anaesthetist survey

The anaesthetist survey will be analysed using descriptive statistics, frequencies and one and two way tables. The intraoperative data will be compared to the survey data to identify any differences between practice and perceptions. Individual clinician responses will not be linked to their blood pressure data.

10.2.3 Outcome data

The proportion of patients having one of the described clinical outcomes will be reported.

- In hospital mortality up to 30 days.
- Acute kidney injury within 7 days of surgery: defined as a postoperative creatinine increase ≥1.5 times the baseline value or ≥26.5µmol/L (KDIGO definition [17]). If no creatinine test is performed, patients will be assumed to not have renal injury.
- Myocardial injury: Defined as a postoperative troponin enzyme concentration within 7 days of surgery that is above the 99th percentile of the upper reference limit [18]. The exact limit is dependent on the assay manufacturer. If no troponin test is performed, patients will be assumed to not have myocardial injury.
- Stroke: Defined as an ischaemic stroke reported from a computed tomography (CT) scan of the brain within 7 days of surgery. If no CT scan is performed, patients will be assumed to not have a stroke.

Based on existing datasets, we do not anticipate this study being powered to determine associations between intra-operative hypotension and outcomes, accordingly, no statistical power calculation has been performed.

11 PATIENT AND PUBLIC INVOLVEMENT (PPI)

The project aligns with 3 of the 10 'most important research topics' agreed by the James Lind Alliance and National Institute of Academic Anaesthesia Perioperative Care Priority Setting Partnership in 2015, namely:

1. “How can we improve recovery from surgery for elderly patients?”
2. "What long term harm can result from anaesthesia?"
3. “How can patient care around the time of emergency surgery be improved?”

The James Lind Alliance is a not for profit organisation that brings patients and clinicians together in Priority Setting Partnerships (PSPs) to identify and prioritise research into the top 10 'unanswered questions'. This ensures that research is directed at topics of importance to patients.

Additionally the King’s College Hospital Pathfinder Patient Panel reviewed the project when piloted in London across 25 hospitals as an audit). This collected a similar dataset using similar methodology, but instead against several defined national standards, but did not include outcomes.

12 FUNDING AND SUPPLY OF EQUIPMENT

The study funding has been reviewed by the UCL/UCLH JRO Research Office, and deemed sufficient to cover the requirements of the study.

No funding has been secured for the study. No significant costs are anticipated. Trainee anaesthetists will complete the work as part of their educational requirement to engage with audit, research and quality improvement.

13 DATA HANDLING AND MANAGEMENT

All data collected, analysed and stored for iHypE will remain strictly confidential. Data handling will comply with the National Institute for Health Research (NIHR) Clinical Research Network (CRN) Good Clinical Practice guidelines, the Data Protection Act 1998 (UK) and the NHS code of confidentiality.

Data (see appendices 1-3) will be collected from the paper or electronic anaesthetic record on paper data case report forms (CRFs). Only routine clinical data will be included and where this is unavailable the domain will be left blank. Identifiable patient data (hospital number) will be collected in order to allow follow-up of clinical outcomes. Anaesthetist surveys will be completed on the 2 recruitment dates. Completed CRFs will be taken to a secure location accessible by the local investigator. All information in paper format for the trial will be held securely and treated as strictly confidential according to NHS policies. Outcome data will be collected at 30 days after surgery.

The data will be entered electronically from NHS desktop computers via a secure encrypted connection into an online portal managed by RAFT and hosted by NHS Scotland. The software used for data capture will be REDCap (Research Electronic Data Capture – http://www.project-redcap.org). REDCap is a mature, secure web application for building and managing online surveys and databases. Access to the REDCap data entry system will be protected by username, password and 2 step verification created during the investigator registration process. Data collected will be anonymous and contain no person or patient identifying data (see appendix 1 and 3) apart from gender. Each patient dataset entered on REDCap will generate a unique identifier; local investigators will be asked to keep a log of their unique identifiers linked to local hospital identification numbers. No personal identifiable information (apart from gender) will be transferred outside the local hospital environment either electronically or on paper. The hospital number will remain within the respective trusts, meaning only the local NHS staff responsible for care have access to personal identifying information.

When data from the CRFs has been entered into REDCap, they will be shredded and disposed of confidentially as per local NHS Trust guidelines. All staff involved in the study share the same duty of care to prevent unauthorised disclosure of personal information.

The study database will be closed for data entry 2 weeks after the end of final follow-up. Only the iHypE trainee lead will have full access to the complete electronic dataset. All actions on the REDCap system are logged. The anonymised information from participating hospitals across the country will be analysed by a team of researchers.

14 PEER AND REGULATORY REVIEW

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

The project is being submitted for approval from an ethics committee (proportionate review), the Health Research Authority and the Confidentiality Advisory Group (formerly section 251 approval) via the Integrated Research Application System (IRAS). Each approval will be obtained before the study commences.

Centres will not be allowed to record data without confirming that the necessary ethics or governance approvals are in place and that they have an nhs.net e-mail for data transfer.

This study has been peer reviewed within UCL, by an independent and relevant peer reviewer on the 4th February 2016. The Sponsor has accepted these reviews as adequate evidence of peer review.

15 ASSESMENT AND MANAGEMENT OF RISK

There are no safety considerations relating to the iHypE study. There is no risk of physical, psychological, social, legal or other harms to patients, anaesthetists or investigators.

16 RECORDING AND REPORTING OF EVENTS AND INCIDENTS

The trial involves negligible risks to patients, anaesthetists and investigators. Adverse events will not be monitored or reported.

17 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.

18 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 UCL for 10 years 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 2 years and in line with all relevant legal and statutory requirements.

19 PUBLICATION AND DISSEMINATION POLICY

Participating anaesthetic departments will receive their results with national data for comparison to facilitate local quality improvement programmes.

A writing committee will write scientific reports in a timely manner. The results will be reported in peer reviewed scientific journals, at conferences as posters or oral presentations and after this, on the study website (www.i-hype.org). Authorship and contributorship opportunities will be based on contribution to the primary study and will follow the precedent set by SWARM [18]. The publication will complement other planned studies (from different research/ audit groups) looking at intraoperative hypotension in hip fracture patients and the effect of hypotension on post-operative delirium.

20 REFERENCES

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21 APPENDICES

21.1 Appendix 1 Patient Data Collection form

Hospital Number: ……

Inclusion: ≥65 yrs old, general &/or regional anaesthesia Exclusion: cardiopulmonary bypass, sedation only, X-ray

1	Patient	**Gender**	Female ☐ Male ☐
		Age	65-69 ☐ 70-74 ☐ 75-79 ☐ 80-84 ☐ 85-89 ☐ 90-94 ☐ 95-99 ☐ >100 ☐
		Comorbidities	Cerebrovascular Disease ☐ Chronic Kidney Disease ☐ Diabetes ☐ Heart Failure ☐ Hypertension ☐ Ischaemic Heart Disease ☐ Peripheral Vascular. Disease ☐ None ☐
		Anti-hypertensive Medications	ACE Inhibitor/ Angiotensin 2 Receptor Antagonist ☐ Beta Blocker ☐ Calcium Channel Blocker ☐ Diuretic ☐ Other ☐ Vasodilator infusion e.g. GTN ☐ Not taking these medicatons ☐
		ASA score	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ Not recorded ☐
2	Surgery	**NCEPOD Urgency**	Immediate ☐ Urgent ☐ Expedited ☐ Elective ☐
		Surgical speciality	Cardiac ☐ ENT/ Head & Neck ☐ General Surgery☐ Gynaecology ☐ Ophthalmology ☐ Orthopaedics ☐ Other ☐ (detail……) Neurosurgery Plastics ☐ Spinal ☐ Thoracic ☐ Trauma ☐ Urology ☐ Vascular ☐
		Operative severity	Minor ☐ Intermediate ☐ Major ☐ Major + ☐
		Cancer surgery	Yes ☐ No ☐
		Procedure	Surgeon might request hypotension? Yes ☐ No ☐ e.g. middle ear surgery etc
3	Anaesthesia	**Seniority**	Consultant ☐ SAS ☐ ST5-7 ☐ ST3-4 ☐ CT 1-2 ☐ PA(A) ☐
		Number	NB. This is not being collected to identify individuals, instead to identify how many anaesthetists practice the data represents.
		Induction	Intravenous ☐ Inhalational ☐
		Maintenance	Intravenous ☐ Inhalational ☐
		Regional block	Yes ☐ No ☐ Upper limb ☐ Lower limb ☐ Trunk ☐ Plexus ☐ Single nerve ☐ Field block ☐ Neuraxial: Spinal ☐ Epidural ☐ CSE ☐
4	Blood Pressure	**Data source**	Paper anaesthetic chart ☐ Electronic record print out/ monitor ☐
		Intra-operative monitoring	Non-invasive ☐ Invasive ☐
		Pre-operative BP Source	Systolic (mmHg) …… Diastolic (mmHg) …… Pre-op clinic ☐ Referral/ GP letter ☐ Patient notes/ obs chart ☐ Pt reported ☐
		Pre-induction BP	Systolic (mmHg) …… Diastolic (mmHg) …… Not recorded ☐
		Lowest intra-op BP & duration	Systolic (mmHg) …… Diastolic (mmHg) …… Duration ……mins
		Hypotension Timing	First 30mins after induction ☐ Middle ☐ Last 30mins of op ☐
		Duration of systolic hypotension	20.0 – 40.0% of pre-induction value …… mins >40.1% of pre-induction value …… mins
		Duration of surgery	…… mins (time in mins from first to last recording on anaesthetic chart)
5	Vasopressor use	**On vasopressor infusion pre-op?**	Yes ☐ No ☐ Number of agents: ……
		Vasopressor total dose used intraoperatively	Metaraminol …… Phenylephrine …… Ephedrine …… Adrenaline …… Noradrenaline …… Other ……
		Vasopressors given as infusion intra-op?	Drug: …… Min. rate ……mls/hr Max. rate ……mls/hr Duration of infusion: …… Continued in recovery? Yes ☐ No ☐
		BP value immediately preceding vasopressor use	Episode 1 2 3 4 5 SBP DBP
6		**How many surgical procedures took place on the day of data collection?** Total: …… >65 years old…….	

21.2 Appendix 2 – Anaesthetist Survey

You have been asked to complete this form because a patient you anaesthetised has been included in a national trainee led project called iHypE (for further information please see www.i-hype.org). Your answers to this survey will be anonymous. You will not (and cannot) be identified, nor can your answers be linked to the patients you anaesthetised or your institution. Completion of this form will be taken as consent for your answers to be included in a national survey of anaesthetic perceptions of intraoperative hypotension.

Anaesthetist seniority Consultant ☐ SAS ☐ ST5-7 ☐ ST3-4 ☐ CT 1-2 ☐ PA(A) ☐

Which do you think best represents baseline blood pressure in elderly patients? Please tick all that apply

Immediate pre-induction blood pressure	☐
Recording from pre-operative assessment clinic	☐
Recording from ward observations chart	☐
Blood pressure from GP notes/ referral letter	☐
Self reported 'normal' BP value	☐
Other ……	☐

Which blood pressure parameter do you use to titrate fluid and vasopressor therapy? Please tick all that apply

Systolic ☐ Mean ☐ Diastolic ☐ Other ☐

What degree of hypotension would trigger you to use a vasopressor in patients >65yrs old? Tick all that apply

Absolute systolic BP (mmHg)	Please specify value ……mmHg	
Relative drop in systolic BP	Please specify percentage ……%	
Combination of absolute & relative systolic BP	☐	
Absolute mean BP (mmHg)	Please specify value ……mmHg	
Relative drop in mean BP	Please specify value ……%	
Combination of absolute & relative mean BP	☐	
Absolute diastolic BP (mmHg)	Please specify value ……	
Relative drop in diastolic BP	Please specify value ……	
Combination of absolute systolic and mean BP	Systolic value ☐	Mean value ☐
Other combination (please detail)	……. ☐	……. ☐
BP not used as a trigger	☐	

How do you administer vasopressors? tick all that apply

Bolus doses given prophylactically	☐
Bolus doses given as required	☐
Bolus doses given prophylactically + bolus doses as required	☐
Added to bag of IV fluid; given prophylactically	☐
Added to bag of IV fluid; given as required	☐
Added to bag of IV fluid & given prophylactically + bolus doses as required	☐
Added to bag of IV fluid & fluid flow rate speeded up as required	☐
Given prophylactically by infusion	☐
Given as required by infusion	☐
Given prophylactically by infusion + bolus doses given as required	☐
Other (please detail)……..	☐

21.3 Appendix 3 – Outcome Data

Hospital Number: ……

Mortality	Alive ☐ Dead ☐ If died, number of days between surgery and death: …….. (day of surgery = day 0)	
Renal injury	Pre-operative creatinine value closest to surgery (µmol/L) Highest post-op creatinine value within 7 days of surgery (µmol/L)	
Myocardial injury	Rise in cardiac enzyme concentration within 7 days of surgery that is above the reference range for your trust?	Yes
		No
	No cardiac enzyme test performed (tick if applies).	
Stroke	CT reported ischaemic stroke within 7 days of surgery	Yes
		No
	No CT brain performed (tick if applies).	